1-03-01 TRANSCRANIAL DOPPLER (TCD) PREDICTION OF STROKE IN SICKLE CELL DISEASE (Hb SS)

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Objective: Hb SS causes severe anemia and stroke. Children especially develop brain infarction due to stenosis of the internal carotid (ICA) and middle cerebral (MCA) arteries similar to early Moyamoya. We have developed TCD criteria to detect children at high risk.

Methods: Prospective study involving 284 Hb SS children (mean age 8.5 ± 4 years) studied with TCD prior to clinical symptoms of stroke and followed (36 ± 18 months) for clinical stroke. Highest mean velocity (VEL) was related to clinical outcome. Results: During follow-up nine children had infarction 1 - 35 months post TCD. In 8/9 VEL was ≥ 170 cm/sec and in 6/9 ≥ 200 cm/sec. Of 13 patients with VEL ≥ 210, 6 have had stroke. Relative risk was high at 170 cm/sec (44 ± 5-346); (p = .00001); higher cutoff VEL led to increasing positive predictive value, going from 25% at 190 to 56% at 230 cm/sec. Robust criteria for stroke risk which can be used for screening and primary stroke prevention in children with Hb SS.

1-03-02 PONTINE ATHEROMATOUS BRANCH DISEASE

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Caplan proposed the term intracranial branch atheromatous disease as a neglected, understudied, and underused concept to describe possible causes of pontine lacunar infarction.

Using a high-resolution MRI system and cerebral angiography, we studied 47 patients with pontine infarction. Among those patients, 11 showed atheromatous branch occlusion type (ABOI), 30 showed hypertensive small artery type (HSAI), 2 borderzone territory type between pontine arteries and 4 unclassified.

Angiogram revealed unilateral or bilateral VA occlusion in 30% of ABOI, in 23% of HSAI. Two patients with borderzone type infarcts showed bilateral distal VA occlusion or proxymal BA occlusion, respectively.

Supratentorial small high intensity areas or periventricular hyperintensity on T2-weighted images were seen in 79% of HSAI, but only 33% of ABOI.

Patients with pontine infarcts should be evaluated with MRI and routine or MR angiography to clarify underlying mechanisms of infarct and vascular pathology.

1-03-03 L-NAME REDUCES INFARCT VOLUME WITHOUT AFFECTING CBF IN THE RAT MCAO/REPERFUSION MODEL

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Ischemic injury of the nervous system has been associated with neuronal release of excitatory amino acids that may induce nitric oxide (NO) release that further mediates injury.

The present study examined the immediate effects of low dose NO inhibition using L-NAME (10ug/kg/min) on CBF and cerebral infarct volume administered during three hours of middle cerebral artery occlusion (MCAO) and two hours of reperfusion in the spontaneously hypertensive rat. Low dose L-NAME inhibited the systemic hypotensive effects of acetylcholine mediated by NO release. This dose of L-NAME did not decrease total or regional CBF measured by 14C-iodoantipyrine. In contrast, as demonstrated by TTC staining after 5 hours of MCAO/reperfusion, low dose L-NAME reduced the percent area of infarction by 55% from 29% in the control group to 13% in the experimental group (p<0.0001). These findings suggest an important neurotoxic role for NO during ischemic injury of the central nervous system. Of potential clinical importance is the observation that low dose NO inhibition may substantially lessen ischemic brain injury.

1-03-04 EVALUATION OF BASAL CEREBRAL ARTERIES WITH TRANSCRANIAL COLOR DOPPLER IMAGING

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This study assessed the ability of transcranial color coded duplex ultrasonography (TCDI) to visualize the basal cerebral arteries, and the practical potential of this new noninvasive method in comparison with the conventional transcranial Doppler ultrasonography (TCD).

Fifty patients were examined with color Doppler imaging system Acuson 128 XP 10 with a 2.0 MHz sector transducer. Under visual control, the angle between the ultrasonic beam and the anatomic course of the vessel could be adjusted.

The mean angle of incidence was in the MCA 33°±15°, in the ACA 35°±17°, in the PCA 45°±18° and in the basilar artery 15°±14°. In comparison with the conventional TCD method, the measurements of blood flow velocity under consideration of the angle of incidence resulted in increase in velocity values (15% in the MCA, 18% in the ACA, 30% in the PCA and 3% in the BA).

Examples of pathologic findings, diagnosed with TCDI, demonstrate the practical advantage of this noninvasive method.

1-03-05 SPACE-OCCUPYING SUPRATENTORIAL INFARCTIONS - CLINICS AND SHORT TERM PROGNOSIS

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Of 55 patients with space-occupying supratentorial infarctions, medical records, cerebral angiography, CT-scans and dopplersonographic findings were evaluated retrospectively. The mean age was 62 years. 39 of the patients died due to the stroke (71%). Age, sex, risk factors, etiology, angiographic and dopplersonographic findings had no significant prognostic influence comparing patients who survived the stroke with those with a fatal outcome. Computertomographic findings were not significantly different at the time the patients were admitted to hospital. CT-controls in patients with a fatal outcome showed significantly 1. more space-occupying effects in the contralateral hemisphere (p<0,05), 2. more hydrocephalic enlarged contralateral lateral ventricles (p<0,01). Patients who survived had more often previous ischemic events (p<0,05). Following signs and symptoms were statistically associated with a fatal outcome: 1. impaired orientation (p<0,01), 2. respiratory dysregulation (p<0,01), 3. dyscoria (p<0,0001), 4. oculomotoric palsy (p<0,01).

1-03-06 CAROTID ARTERY DISEASE IN PATIENTS WITH INFRATENTORIAL TIA OR STROKE

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Of 549 patients with infratentorial TIA or stroke, medical records, cerebral angiography, CT-scans and dopplersonographic findings were evaluated retrospectively. Angiography or dopplersonography revealed a concomitant carotid artery occlusive disease in 62 patients, 33 of them had a high grade stenosis (>75%) or even occlusion. These patients were significantly older (p<0,01); and more often had: 1. coronary heart disease (p<0,0001), 2. diabetes mellitus (p<0,0001), 3. previous TIA (p<0,0001) or stroke (p<0,05) in the carotid artery territory, 4. lacunar infarction in CT-scan (p<0,05), 5. occipital lobe infarction in CT (p<0,05), 6. subcortical infarction in CT (p<0,05). In particular, patients with high grade stenosis more often were hypertensive (p<0,05) or had a disturbance of consciousness due to the stroke (p<0,01). In a multiple logistic regression analysis patients with a poor outcome 1. were older than 70 years (p<0,01), 2. had infratentorial (p<0,0001) or supratentorial (p<0,01) lesions in CT-scan, 3. had vertebral (p<0,01) or basilar (p<0,01) artery occlusive disease. Concomitant carotid artery disease was an independant risk factor for a disabling or fatal outcome after vertebrobasilar ischemia (p=0,0130).

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-03-07 SYGEN IN INTRAPARENCHIMAL CEREBRAL HEMORRHAGE: A DOUBLE BLIND PLACEBO CONTROLLED TRIAL

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Ganglioside GM1 (Sygen®) has a potent neuroprotective action by counteracting the toxicity induced by the release of excitatory aminoacids. When administered within the first hours after ischemic stroke, it was shown to reduce neurological disability in large randomized placebo controlled trials. Preliminary data have suggested that Sygen® may also be beneficial in spinal trauma and subarachnoid hemorrhage.

The present randomized, double blind, placebo controlled trial was designed to assess the efficacity and tolerance of Sygen® in intraparenchymal cerebral hemorrhage (putamen and internal capsule).

21 patients were included within 30 hours from stroke (11 Sygen®, 10 placebo); they were aged 30-75 years, had a persistent motor deficit (≤ 55 at the Orgogozo neurological score), scored ≥ 8 at the Glasgow coma scale and had a primary cerebral hemorrhage of medium size (3-7 cm at the CT-scan). Sygen® was administered for 2 weeks: after a loading dose of 500 mg i.v. in bolus, the maintenance dose was 100 mg/iv/daily.

The main outcome measure was the Barthel index at day 90. Secondary measures included mortality, vigilance (Glasgow coma scale), the Orgogozo neurological score, the Clinical Global Impression (GCI) and the clinical and biological tolerance.

3 patients died (1 on Sygen® because of mesenteric infarction, 2 on placebo) ; two dropped out (both on placebo). Analysis of the Barthel index shows a better improvement over time in the Sygen® treated group.

The neuroprotective and antioedematous effect of Sygen® at the periphery of cerebral hemorrhage may explain the effects observed in this pilot trial.

1-03-08 NEGLIGIBLE RISK OF PERIOPERATIVE STROKE IN ASYMPTOMATIC CAROTID STENOSIS.

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A prospective study was undertaken of 358 consecutive non carotid major vascular (145) or coronary artery bypass (213) operations. All patients had pre-operative duplex carotid ultrasound and there was a moratorium on endarterectomy for asymptomatic carotid stenosis. Forty-nine patients had prior symptoms of cerebral ischaemia and three perioperative (within 72 hours) strokes occurred in this group, two mild and ipsilateral to carotid occlusion and one severe ipsilateral to an 80% stenosis.

In the 309 asymptomatic cases two mild perioperative strokes occurred ipsilateral to 30% stenosis. There were fifty-three cases with greater than 50% asymptomatic carotid stenosis or occlusion including twenty-eight with greater than 80% stenosis. None had ipsilateral perioperative stroke (90% CI 0-6.72%).

We conclude that the risk of perioperative stroke of asymptomatic carotid stenosis is negligible.

1-03-09 TRANSCRANIAL DOPPLER SONOGRAPHY IN ACUTE ISCHEMIC STROKE

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We assessed cerebral intracranial hemodynamic through transcranial Doppler sonography (TCD) in patients with acute ischemic score. Twenty subjects were submitted to neurological examination, cerebral computed tomography (TC), carotid bifurcation sonography and TCD in the first six hours after stroke onset. Forty-eight hours later another TC was performed in those patients with first normal TC. Seventeen patients showed no ischemic lesion at first TC, whereas this examination revealed an early ischemic lesion in the remainig four subjects. All patients had a middle cerebral artery occlusion (showed by TCD) or internal carotid artery occlusion. Our study demonstrates the importance of TCD in early diagnosis of medial cerebral artery occlusion. As supported by licterature data, TCD can be an alternative to angiography to select in shorter time patients with a cerebral artery occlusion without an ischemic lesion at early TC. These patients could benefit by early artery recanalization through thrombolysis in that useful time called "therapeutic window".

1-03-10 CHANGES IN NEUROPEPTIDE Y AND CALCITONIN GENE-RELATED PEPTIDE CONCENTRATIONS IN CEREBROSPINAL FLUID IN PATIENTS WITH CEREBRAL VASCULAR DISEASE

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Concentrations of Neuropeptide Y (NPY) and Calcitonin gene-related peptide (CGRP) in CSF in patients with cerebral vascular disease were measured by radioimmunoassay. Two groups were recognized: 1, hemorrhagic cerebral vascular disease (HCVD); 2, ischemic cerebral vascular disease (ICVD). NPY was found to be higher in 10 cases of HCVD (4148 ± 397.2 pg/ml), a very significantly higher than that in the 11 cases of control (1083.7 ± 245.8 pg/ml) with $P < 0.01$, while NPY in 14 cases of ICVD was (2214 ± 289.2 pg/ml), not much different from control. CGRP in HCVD in 7 cases (3965 ± 680 pg/ml) was very distinctly higher than 12 cases of control (49 ± 7 pg/ml) with $P < 0.001$, while CGRP in 10 cases of ICVD (152 ± 60 pg/ml) was not changed from control. Among the patients, simultaneous measurements were done in 6 cases of HCVD and 11 cases of ICVD. Thus both NPY and CGRP were markedly increased in HCVD but not in ICVD, and a significant positive correlation was found between NPY and CGRP. ($r = 0.86$).

1-03-11 STROKE IN YOUNG ADULTS: PRELIMINARY REPORT OF 45 CASES

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Although their clinical characteristics are not different, strokes occuring before the age of 45 lead to specific questions about their management. 45 consecutive patients (17-45 years, 24 women, 21 men) referred to the Neurology department entered this ongoing study since april 1992. All of them underwent neurological examination and conventional CTScan at their admission. An arteriography was performed in most of them(40/45). For ischemic strokes specific investigations were scheduled concerning: heart (transoesophagial echocardiography, 24 hours ECG recording, testing of atrial vulnerability), hemostasis, immunology and vascular risk factors. Detection of drugs was systematically performed .

An hemorragic stroke was diagnosed in 17 patients (38%). Intracranial aneurisms(10), angioma(2), cavernoma(1), and hematologic disease(1) were detected in 14 patients while no cause was found in 3 subjects.

Cerebral ischemia was recognised in 28 subjects (62%). Large vessels disease was found in 7 subjects. In 12 patients a cardiac morphological abnormality was diagnosed (foramen ovale, septal aneurism) associated(5) or not to dysrythmia(7). Atrium was found vulnerable in 9 subjects. Drug detection was positive in 4 patients. No cause was found in 5 patients.

This results suggest that functional cardiological investigations can help for the etiology of ischemic strokes in young adults.

1-03-12 EFFECTS OF SPINAL CORD STIMULATION ON CEREBRAL PERFUSION

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A Cerebral blood flow (CBF) increase was observed in experimental models as well as in human beings during spinal cord stimulation (SCS). The purpose of this study was to verify this effect in ten patients who received a thoracic (5 pat) or cervical (5 pat) epidural leads by percutaneous insertion. Regional CBF (rCBF; 133 Xe inhalation – 32 epicranial probes and transcranial Doppler (TCD) were performed in all and in seven patients respectively, at baseline and after 30 minutes of SCS. A symmetrical anterior rCBF increase was found in 3/5 patients with cervical lead (ranging from 3 to 21%); no rCBF change was seen in all the other patients. There was non correlation between the haemodinamyc changes and the induced paraesthesiae. We conclude that cervical, but not thoracic, SCS causes a CBF increase, mainly in anterior regions of the brain. Such an effect could be related to CBF autoregulation, although the mechanism is still unknown.

1-03-13 CALCIUM-DEPENDENT GLUTAMATE RELEASE IN AN IN-VITRO MODEL OF CEREBRAL ISCHEMIA

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Objective: To determine the mechanisms regulating presynaptic release of glutamate following sustained K+ - induced depolarization.

Methods: Gerbil cerebral cortical synaptosomes were depolarized with K+ and glutamate release measured every 2 sec. spectrofluorophotometrically.

Results: Depolarization produced an increased rate of glutamate release that was calcium dependent, glutamate release being blocked by use of Ca^{2+}-free incubation medium. This calcium dependent glutamate release was also blocked by cadmium, omega-conotoxin and flunarizine, but unaffected by nimodipine, nifedipine, nickel, tetrodotoxin, NBQX, AMPA, NMDA, Kainate or dihydrokainate. In addition glutamate release was increased by caffeine and blocked by dantrolene.

Conclusions: Using K+-induced depolarization as an in vitro model of cerebral ischemia, we have demonstrated that calcium dependent presynaptic glutamate release occurs by at least 2 methods: 1) Calcium influx-dependent release that is possibly mediated in part by N-type but not L or T type voltage operated channels, and is unaffected by presynaptic glutamate receptor agonists or antagonists. 2) Mobilization of the receptor mediated intracellular calcium pool from the endoplasmic retidulum.

1-03-14 CLINICAL VALUE OF TCD AND SPECT IN ACUTE STROKE

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Since Transcranial Doppler Sonography (TCD) allows non-invasive examination of the circle of Willis and Single Photon Emission Computed Tomography (SPECT) assesses perfusion of brain parenchyma, their combination may prove valuable in acute stroke.

We evaluated prospectively 300 consecutive patients with hemispheric stroke and found hyperperfusion on HMPAO-SPECT associated with cerebral embolism (cardiac or artery-to-artery), normal perfusion – with lacunar stroke, and focal absence of perfusion – with the poorest short-term outcome. In 100 cases serial TCD and SPECT were performed starting within the first 8 hours after onset. The following patterns were reported for SPECT: *normal, high, mixed, low,* and *severe perfusion deficit*; and *normal, collateral, stenotic,* and *occlusive* – for TCD. We derived a relative criteria – *cerebral perfusion Index* (CPI) – related to the short-term outcome: the highest grade – 12 - 20 – indicates reversible neurologic deficit, the grade 6 - 12 – medium recovery, and 1 - 5 – the poorest prognosis. CPI has the best predictive value at 10 - 24 hours while in the immediate phase it may change dramatically related to the underlying pathogenesis.

The combination of TCD and SPECT (CPI) may prove a non-invasive substitute for cerebral angiography.

1-03-15 A LINK BETWEEN URIC ACID AND STROKE.

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The evidence that uric acid has a deleterious effect on the arteries is many sided:

1. In a survey of serum uric acid in 66 males and 49 females with acute cerebral infarction hyperuricemia was found in 17 males and 24 females (36 per cent).

2. There is a bulk of evidence of a relationship between the metabolism of purines and that of lipids. In our series, 17 patients revealed hyperuricemia as well as hypercholesterolemia.

In another study hyperuricemia was found in 15 patients among 59 mainly cardiac patients with hypercholesterolemia.

3. The potent uricosuric effect of certain anticoagulants is of interest in connection with the significance of the level of uric acid in the pathogenesis of atherosclerosis. A single dose of 500 mg dicoumarol increases the urinary excretion of uric acid with about 30 per cent.

The presence of an elevated serum uric acid in stroke in the absence of any conventional cause poses an interesting question. Does uric acid act as an intimal conditioning agent, which is conducive to cholesterol deposition?

1-03-16 ISCHEMIC OR HEMORRHAGIC STROKE? THE VALUE OF BEDSIDE DIAGNOSIS VERSUS SIRIRAJ STROKE SCORE.

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In a consecutive series of 1000 patients from one hospital with stroke-like symptoms, the diagnosis of cerebral ischemia or intracerebral hematoma was made as an informal bedside diagnosis prior to computed tomography. The accuracy of this bedside diagnosis was also compared with the results of the Siriraj stroke score, in a sub-sample of 120 patients with cerebral ischemia and 157 patients with intracerebral supratentorial hemorrhage from two hospitals.

A bedside diagnosis of cerebral ischemia was made in 845 patients (correct in 780 patients) and of intracerebral hemorrhage in 155 patients (correct in 85). The diagnostic sensitivities and positive predictive values of the bedside diagnosis for cerebral ischemia were 93% and 92%, respectively, and for intracerebral hemorrhage 66% and 55%. The diagnostic sensitivities and positive pre-dictive values of the Siriraj stroke score for cerebral ischemia were 67% and 65%, respectively, and for intracerebral hemorrhage 41% and 83%.

We conclude that in Dutch patients the diagnosis of cerebral ischemia and intracerebral hemorrhage can be made at least as well with an educated guess as with the Siriraj stroke score.

1-03-17 TRANSCRANIAL DOPPLER (TCD) COLLATERAL PATHWAYS IN INTERNAL CAROTID ARTERY OCCLUSION

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METHOD: Clinical status, extracranial doppler estimation and angiography was carried out in 24 patients with at least 1 totally occluded carotid artery attending the Johannesburg Hospital TIA/Stroke clinic. Standard TCD of the anterior and posterior intracranial circulation was correlated with the clinical and extracranial vascular status.

RESULTS: There were 16 males and 8 females, mean age = 60 years (38 - 80 years). 14 presented with a stroke, 4 a reversible ischaemic neurological deficit, 5 had amaurosis fugax and 1 had global symptoms. Extracranial doppler and angiography revealed contralateral stenosis of 0 - 30% in 16 patients, 30 - 80% stenosis in 5 patients and complete bilateral occlusion in 3 patients. There was diminished or absent flow in the middle cerebral artery adjacent to the occlusion in all patients. TCD demonstrated no collateral flow in 7 patients (1 with bilateral occlusion, 3/5 with 30 - 80% contralateral stenosis and 3/16 with recent endarterectomy resulting in contralateral stenosis of < 30%). There was no correlation between the area of collateral flow and clinical patterns in the remaining 17 patients.

CONCLUSION: Lack of collateral support on TCD was found in 7 patients all with recent poor bilateral carotid artery flow. 4 patients with good collateral flow and bilateral disease were asymptomatic on follow-up. Future decisions may be re-evaluated in patients with poor collateral intracranial support and bilateral carotid artery disease.

1-03-18 BEDSIDE SCORING SYSTEM IN DIFFERENTIATION OF CEREBRAL INFARCTION (CI) AND HAEMORRHAGE (CH)

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In developing countries where CT scan of brain is not widely available, a modified system has been presented in accordance to similar systems evolved earlier.

Two hundred cases of acute strokes have been sequentially included; headache, level of consciousness, vomiting and diastolic blood pressure were clinical parameters for CH(plus points); the history of ischaemic heart disease,diabetes mellitus, intermittent claudication and atherosclerosis were included for CI(minus points). Accordingly, each was given a numerical score, the total points with plus and minus connotation for each of these two disorders were equated and was accounted against a constant obtained from a stastistical consideration. A numerical score more than 100 was CH and below -100 was CI. A value between -100 and +100 was uncertain; at 20 probability equal. The diagnosis arrived by score system was verified by CT scan of brain.

These results gave an overall accurate diagnosis of 85%. In the remaining a probability curve giving the chances of its being either CH or CI has been worked out.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-03-19 DETECTION OF CEREBRAL EMBOLI IN AN IN VIVO MODEL

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Theoretically one would expect to be able to detect circulating cerebral emboli as high intensity signals using Doppler ultrasound, and recently such signals have been noted in patients with potential embolic sources.

In a validation study pathological embolic materials (thrombus, atheroma, and platelet aggregates) were introduced into the sheep proximal carotid artery while the ipsilateral distal carotid artery was insonated using a transcranial Doppler ultrasound machine. 79 emboli, with sizes as small as 0.2 mm, were introduced. All were detected as short duration high intensity signals. Smaller emboli could not be made, but microspheres as small as 10 microns were detected. A logarithmic positive relationship was found between embolus size and amplitude of signal (thrombus Spearman's rho=0.87, platelet rho=0.97, atheroma rho=0.89); the signal associated with platelet emboli was significantly less intense than that with thrombus ($p<0.05$) or atheroma ($p<0.005$). A significant linear correlation was found between embolus size and duration of high intensity signal (thrombus Pearson's r=0.91, platelet r=0.82, atheroma r=0.82).

Emboli could be detected and discriminated from artefact with a sensitivity of 98.7% and specificity of 98.0%, using an off-line pattern recognition system (courtsey of Dr R Brucher) programmed to detect the typical frequency distribution associated with emboli.

This new technique allows detection of circulating cerebral emboli with a high sensitivity. It will give information on the size and possibly the type of detected emboli. It may allow selection of patients at high risk of subsequent embolic stroke. Automated detection systems will make prolonged patient monitoring possible.

1-03-20 RANDOMIZED TRIAL OF NIMODIPINE IN ACUTE ISCHEMIC HEMISPHERIC BRAIN INFARCTION

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The value of oral nimodipine 120 mg per day for 21 days in acute hemispheric stroke was assessed in a multicenter trial of 345 patients treated within 48 hours from the onset of symptoms. Randomization was stratified by severity of the stroke, age of the patient and the onset of therapy. 174 patient received placebo and 171 nimodipine. The primary end-points were neurological score, motility and Rankin grade at one year follow-up. Therapy did not affect case fatality rate. Explanatory analysis showed that major strokes fared worse during nimodipine with respect to neurological score, on the other hand, if medication was started < 12 hours mobility improved better during nimodipine. There were no differences in the primary end-points between the two groups or between stratified subgroups at one year follow up. Severity of stroke on admission was the only factor explaining the one year outcome in multiple stepwise logistic regression analysis. In conclusion nimodipine had no beneficial effects neither on the case fatality nor the functional outcome of patients with carotid territory ischemic brain infarction.

1-03-21 HOW TO TREAT ELDERLY STROKE PATIENTS?

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Patients aged 65 or over with acute cerebrovascular disorder (CVD) were randomized to Departments of Medicine (n=122) or Neurology (n =121) and followed up to one year. There were no differences in sex and age structures, severity or type of stroke, other diseases or social factors between the two groups. Patients treated at the Department of Neurology were discharged on an average 2 weeks earlier (24.1 vs. 40.4 days) and more often directly home (75% vs 62%). Their functional status was better according to Barthel index and Rankin grades up to one year follow up. The severity of stroke on admission, department, previous stroke, and sex, respectively were independent factors for the functional outcome in multiple stepwise logistic regression analysis. Independent factors for the length of hospital stay were the severity of stroke and department, respectively and for likelihood to go directly home on discharge severity of stroke, department, living in nursing home or need for help in everyday life before the stroke and intermittent claudication, respectively. Results suggest that organized management of elderly stroke patients not only increase the likelihood of a better outcome but also is an economic choice.

1-03-22 SERUM FERRITIN IS A STRONG PREDICTOR OF CAROTID ATHEROSCLEROSIS.

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The formation of foam-cells and fatty streaks requires a postsecretory oxidative modification of native LDL that targets it for a rapid uptake by macrophages via the scavenger receptor(s). Lipidperoxidation may depend on the concentration of tissue iron, one of the major oxidants in vivo. We tested for a potential relation between sonographically assessed carotid atherosclerosis and body iron stores in a randomized population of 909 men and women aged 40-79 years (The Bruneck Ischemic Heart Disease and Stroke Prevention Study '90).
Results: Serum ferritin emerged as a strong independent predictor of carotid artery disease, even at levels generally regarded as normal. The relative increment of risk associated with serum ferritin was slightly more pronounced in women and clearly elevated in the middle-aged (40-50 years). Our analyses yielded a strong synergism between hypercholesterolemia and high iron concentrations (exponentiated risk) which fits well in the theory of an iron catalysed lipidperoxidation. Sex-specific variations in body iron stores may in part account for the premenopausal sex differences in atherosclerotic diseases.
Conclusion: Our study provides further strong empirical evidence for a role of body iron stores in atherogenesis.

1-03-23 A STUDY ON EPILEPSY IN ACUTE STROKE

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Cerebrovascular disease (CVD) is one of the commonest cause of epilepsy is older patients. Seizures may occur any time during the temporal profile of an acute stroke - at onset, during the course or long after. The present study was undertaken to determine which of the patients are at a risk of developing seizure.

The clinical parameters, EEG, and Cranial CT Scan (CCT) of 90 acute stroke patients of age less than 70 yrs were studied during a period of 1 year excluding patients of Subarachnoid Haemorrhage, Vertebrobasilar stroke and pts. with other severe diseases from the study. The patients were followed-up for a period of 2 yrs.

2 patients (2.2%) developed epilepsy at the onset, 4 patients (4.4%) during treatment and 9 (10%) during 1 yr after the episode. Of the patients having evidence of Cortical lesions alone 37.5% developed epilepsy and same percentage of patients having both cortical and subcortical lesions developed epilepsy. Of patients having only subcortical lesions none developed epilepsy. Infarctions producing seizures were more common than haematomas.

1-03-24 LONG TERM OUTCOME AFTER THALAMIC INFARCTION

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The long term outcome of neurological and neuropsychological disturbances after thalamic infarction was studied in nine patients, who had memory disturbances severe enough to necessitate for neuropsychological consultation and rehabilitation. The mean age of the patients was 47±5 years and the mean follow-up time 19,6±14,4 months. Seven of the nine patients had a left tuberothalamic infarction, one a left paramedian and one a left posterior choroidal infarction. The acute neurological symptoms apart from a visual field defect (one patient) and memory disturbances (9 patients) improved well. Seven patients had, at the acute stage, psychic symptoms (psychosis, depression, anxiety) severe enough to demand psychiatric consultation and medication. Inactivity and mild depression were the most common residual symptoms. Memory disturbances remained the main disability of the patients. At the end of neuropsychological rehabilitation (the mean 13,2±10,6 months) clear residual disturbances in verbal memory and learning were still observed. None of the patients showed any signs of true dementia. Problems relating to memory disturbances prevented return to work in all but two cases. Our results suggest that unilateral infarct limited to the territory of the tuberothalamic artery should be differentiated from the other thalamic syndromes.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-03-25 PREDICTION OF OUTCOME WITH HMPAO SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) IN ACUTE ISCHEMIC STROKE

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We prospectively studied the predictive value of HMPAO SPECT performed within 7 days after an acute infarct in the middle cerebral artery territory (MCA) in 70 patients (47 men, 23 women) aged 41-88 (mean 71) years. The data were reconstructed in 8 consecutive parallel axial slices with 12 symetric cortical regions of interest (ROI). In each ROI, interhemispheric differences of at least 10% were considered as significant. Degree of focal hypoperfusion were calculated by two blinded investigators. On day 28 after onset, the clinical outcome was evaluated according to the modified Rankin Scale. A linear correlation was found between the degree of hypoperfusion and the clinical outcome ($p<0.001$;Spearman). Patients with <15% hypoperfusion compared with those with >15% hypoperfusion were independent in daily life in 89% (39/44) vs 61% (16/26) and dependent on others in only 11% (5/44) vs 39% (10/26) ($p<0.001$;Cochran). Mortality rate was 23% (6/26) in patients with >15% hypoperfusion and nil with <15% hypoperfusion. Our data show that HMPAO SPECT may be useful to predict outcome in patients with acute infarct in the MCA territory.

1-03-26 SPONTANEOUS DISSECTION OF THE VERTEBRAL ARTERY

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Spontaneous vertebral artery (VA) dissection is an infrequent cause of vertebrobasilar ischaemic stroke in children and middle-aged adults. The diagnosis of VA dissection is based on the accurate identification of clinical features and of angiografic signs dissection. We describe four cases of VA dissection: 1) a cerebellar infarction in a 9-year-old boy with fibromuscular dysplasia of VA complicated by a dissecting aneurysm at the C1 level; 2) a pontomedullary syndrome confirmed by magnetic resonance imaging (MRI) in a 34-year-old man with a AV hypoplasia and an irregular stenosis at $V4_2$, more severe at $V4_3$ and, 3) a medial medullary syndrome, confirmed by MRI, in a 37-year-old man with a VA hypoplasia and a small aneurysmal dilatation at the C_1 level followed by tapered occlusion. The angiography 3 months after the onset showed resolution of the signs of dissection; 4) a left posterior medullary syndrome in a 44-year old man whose angiography showed a left VA dissection and a right VA dysplasia.

We conclude that the spontaneous VA dissection should be considered in the differential diagnosis of the vertebrobasilar young patient strokes. Repetition of angiography is indicated not only to confirm the diagnosis of dissecting aneurysm, but also to asses the resolution of it. This cases support the theory that an underlying arteriopathy can be an important predisposing factor to arterial dissection in young patients.

1-03-27 STUDY OF EFFECT OF PICOTAMIDE, ASA, AND PICOTAMIDE PLUS ASA ON PLATELET AGGREGATION IN ISCHEMIC STROKE

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In a blind study, we compared the effect of Picotamide, a thromboxane synthetase inhibitor (at the dose of 900 mg/die), ASA (150 mg/die), ASA plus Picotamide (150 and 450 mg/die respectively) on platelet aggregation in PRP. The study sample consisted of 48 patients affected by ischemic stroke after 7 and 90 days of treatment and 17 controls. Platelet aggregation, obtained by collagen (1, 2 μ/ml) and ADP (1 and 0.1 μM), but not by PAF (1 μM) was significantly enhanced in the patients within the first 24 hours from the onset of symptoms. ASA reduced only the platelet aggregation induced by collagen (1 μg/ml). Picotamide and ASA plus Picotamide reduced the aggregation with all doses of the two platelet agonist at 7 and 90 days of therapy. Our results indicate that inhibition of thromboxane synthetase is more efficacious than inhibition of cycloxygenase in reducing platelet aggregation in acute stroke patients.

1-03-28 PLATELET STUDY IN ISCHEMIC STROKE: RELEVANCE OF DENSE BODY SECRETION

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We studied collagen (1.0 and 2.0 μg/ml), PAF (1.0 μM) and ADP (0.1 and 1.0 μM) induced platelet aggregation and the secretion of 5-HT, ATP and PF4 in PRP and the basal platelet 5-HT levels. The sample was 48 patients affected by cerebral ischemic stroke, studied within the first 24 hours from the onset of symptomatology, and 17 healthy controls. Both basal 5-HT levels and the 5-HT secretion induced by PAF was lower ($p > 0.04$ and $p > 0.05$) in the patients. In contrast, the ATP secretion induced by 1 and 2 μg/ml collagen was increased ($p > 0.02$ and $p > 0.002$). These data suggest that after ischemic stroke platelet present an abnormal dense body secretion. This may be of particular importance in the evolution of ischemic neuronal area since 5-HT is considered a toxic agent for the neuron. It is possible that pharmacological control of dense body secretion in combination with an antiserotonergic drug, may be the outcome of the ischemic stroke.

1-03-29 CLINICAL-ANATOMIC CONTRIBUTION ABOUT CEREBELLAR HEMORRHAGE

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The study (clinical-anatomic) included 19 cases of cerebellar hemorrhages from 759 patients with cerebral vascular processes admitted to the Clinic of Neurologie during the last ten years, a percentage of 2,5%.

We emphasize the severe prognosis of this disease. The cases were classified in five groups: 1. Hemorrhages of the cerebellar hemispheres (most cases 7); 2. Hemorrhage of nucleus dentatus and cerebellar hemispheres (3 cases); 3. Spread hemorrhages (cerebral, brainstem and vermis) – (4 cases); 4. Secondary cerbellar hemorrhage (4 cases); 5. Cerebellar infarction (1 case).

1-03-30 THE CASE OF SPONTANEOUS DISSECTING ANEURYSM OF THE BASILAR ARTERY WITH MANY YEARS SURVIVAL

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A case of spontaneous aneurysm of the basilar artery reported in diagnostic examination in the patient with right sided hemiparesis. Case report; male, 45, who had suffered from arterial hypertension, had been treated for the reason of periodically occurring pains in occipital region. Shortly after the check out from the hospital the patient suffered additionally from headache, from periodically occurring vertigo, diplopia, left ears buzzing and choking while eating and drinking, the right side hemiparesis which gradually developed following the formication. Neurological deficiency was realized by the presence of right side hemiparesis which included the paresis of facial nerve, increased musculov tension, more lively deep reflex with Babinski's sign on the right side. EEG showed slight changes in afterbrain with advance on the left side. Angiographic examination; a part of dissecting aneurysm was pictured at the level of bifurcation which could be associated with numerous thrombuses in its lumen, CT showed crystal creature located in the upper part of the ponscerebellum's left angle. MRI entricked the data concentrating the anuerysm by revealing the presence of tumor-like structure of diameter 3 centimetres. Patient was treated with vessear-antiagregation and sedative medicines, and treatment of arteriale hypertension was continued. Survival was to 3 years.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-06-01 VESTIBULAR CORTEX LESIONS AFFECT THE PERCEPTION OF VISUAL VERTICAL

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Bilateral vestibular input from otoliths and vertical semicircular canals stabilizes eye and head in normal upright position in the roll plane and dominates our perception of verticality. Ponto-medullary lesions of these pathways have been shown to induce ipsiversive deviations of subjective visual vertical (SVV), e.g. in Wallenberg's syndrome. Ponto-mesencephalic and meso-diencephalic lesions cause contraversive tilts. In patients with acute infarctions of the thalamus (n=35) eight of 14 patients with paramedian lesions exhibited a contraversive tilt of SVV while 11 of 16 patients with posterolateral lesions revealed moderate tilts of SVV either ipsiversive (n=7) or contraversive (n=4).

A systematic study is currently being performed in patients with acute infarctions within the territories of the anterior (ACA, n=4), middle (MCA, n=50) or posterior (PCA, n=10) cerebral artery in oder to determine the differential effects of vestibular cortex lesions on the perception of verticality. Twelve patients with cortical infarctions in the MCA-territory (involving the parieto-insular vestibular cortex, PIVC) displayed contraversive tilts of SVV. These infarcts centered on the posterior part of the insula and the parietal operculum including the long insular and the adjacent superior temporal gyrus as demonstrated by axial neuroimaging and the lesion extend projected onto the appropriate sections from the atlas of Duvernoy (1991). It is less probable in our patients that the vestibular areas 2v, 3a or 7 were involved. With respect to the roll plane lesions of the vestibular thalamus and the PIVC predominantly manifest as an apparent tilt of the internal representation of space.

1-06-02 CORTICAL MAGNETIC STIMULATION IN MULTIPLE SCLEROSIS PATIENTS WITHOUT PYRAMIDAL SIGNS

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Objective: To know the sensitivity of Cortical Magnetic Stimulation to detect subclinical lesions in Multiple Sclerosis (MS).

Background: Central motor conduction time (CMCT) measured by cortical magnetic stimulation (CMT) is increased in MS patients. Its usefulness for diagnosis, assessment, and detection of subclinical corticospinal lesions is controversial.

Methods: 51 patients (mean age 40 ± 10) with clinically definite MS, Poser's categoric 1a, and 50 aged matched controls were studied. Motor evoked potentials (MEP) in both Abductor Digiti Minimi after cortical and cervical magnetic stimulation were recorded. CMCT, normalized amplitude, and side asymmetries were calculated. Results from healthy volunteers were used to delimit normality (mean ± 2.7 standard deviation). 99 percent confidence limits were used for CMCT, while the lower normal limit of the amplitude was defined by the 2.5 percentile.

Results: Patients without pyramidal signs (group I, n=14) and patients without only pyramidal signs in the upper extremities (group II, n=26) had longer central conduction time than controls ($p<0.001$). At the group of patients without pyramidal signs in upper nor lower extremities sensitivity of magnetic stimulation was 28.57% (14.29% for CTT, 14.29% for MEPA, and 7.14% for asymmetries). At the group of patients without pyramidal signs in the upper extremities, 65% of patients had abnormal magnetic stimulation (44,4% asymmetries, 40,4% time central conduction, 7.41% amplitude).

Conclusion: Magnetic stimulation recognizes subclinical lesions of the pyramidal pathway in Multiple Sclerosis patients. Its sensitivity can be estimated as 52.5%.

1-06-03 IMPAIRED VISUAL EVOKED POTENTIAL IN DIABETIC PATIENTS

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[Purpose] A recent report has shown significantly longer P100 wave latency and an axonopathy of the optic nerve fiber in diabetic BB/W-rats. We investigated visual evoked potential (VEP) in diabetic patients, the presence or absence of the optic neuropathy and the relationship between VEPs and central neuronal disturbances. [Subjects] We evaluated 11 non-insulin-dependent diabetic patients (age 61±7 yr (mean±SD), fasting blood sugar (FBS) 158±58mg/dl, HbA1C 9.5±2.7%), who had different types of diabetic retinopathy (nothing, simple, pre-progressive, and progressive). [Methods] We used Neuropack4 (Nihon Kohden Co.) to mesure the VEP (P100 latency). The stimulus was a reversed checker board on television. [Results] The P100 wave latency in diabetic patients was 94.6±8.7(mean±SD)msec in the right eye and 97.4±10.8msec in the left eye. There were no significant differences regarding of P100 latency between diabetics and the controls. But in diabetics, the prolongation of P100 wave latency correlated with age, FBS, and HbA1C. [Conclusion] These results suggests that the deterioration of glycemic control affected the P100 latency. The hyperglycemia may have also caused metabolic changes in the brain and it provids the delay of P100 latency. There might be some kind of central neuropathy in bad glycemic controled patients and VEPs could serve as a tool to confirm it.

1-06-04 DEMYELINATIVE POLYNEUROPATHY IN DIABETICS

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In this communication we report our experience of demyelinative polyneuropathy due to Diabetes detected electrophysiologically.

37 patients with diabetes and clinical neuropathy evaluated electrophysiologically formed the material of this study. Motor and sensory nerve conduction studies, F waves, H reflex and Blink Reflex were evaluated using Medelec MS 6 and Neurostar machines.

5 patients were found to have predominant demyelinative polyneuropathy on electrophysiologic evaluation. 2 patients had clinical features of AIDP but were detected to be diabetics and one who had Insulin Dependent Diabetes Mellitus had features of chronic motor sensory neuropathy. All these patients had grossly lowered motor nerve conduction velocity, some with conduction block and abnormally prolonged or absent F response and H reflexes. Two of these patients had abnormal blink reflex as well. All the patients improved to a varying degree with control of hyperglycaemia.

Demyelinative polyneuropathies in Diabetics are not rare and responds to control of hyperglycaemia.

1-06-05 CORTICOSPINAL EXCITABILITY IN THE SILENT PERIOD PRODUCED BY MOTOR CORTEX STIMULATION IN PARKINSON'S DISEASE

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In normal active muscles, TCMS can produce a silent period lasting 150 ms. Responses to a second test TCMS in this period are larger if subjects are activated rather than relaxed throughout the experiment. Text H-reflexes are little changed by activation.

METHODS: Five patients with idiopathic Parkinson's disease were studied 12 hours after withdrawal of therapy. Conditioning TCMS at 1.5 times relaxed threshold were followed by H-reflex or TCMS test stimuli at interstimulus intervals of 25 - 150 ms. Patients were tested both active or relaxed and compared with 7 age-matched normals.

RESULTS: When relaxed, conditioning shocks produced similar suppression of TCMS test responses in both groups. When active, test TCMS responses were larger in normals. H-reflex test responses were the same in both groups active or relaxed.

CONCLUSION: The component of voluntary input to motor cortex which can maintain corticospinal excitability after a conditioning shock is reduced in Parkinson's disease.

1-06-06 EFFECT OF AGING ON PATTERN REVERSAL ELECTRORETINOGRAM AND VISUAL EVOKED POTENTIALS.

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Simultaneous recording of pattern ERG and midoccipital VEP was performed in 114 healthy subjects, during monocular fullfield pattern reversal stimulation. Their ages ranged from 15 to 85 years (mean 45). Each check size subtended an angle of 15, 30 and 60 min. The entire stimulating field subtended an angle of 32 degrees.

Pattern reversal of 0.8 Hz or 5.0 Hz produced either transient or steady state evoked responses.

Significant effect of aging was recognized in the following parameters; 1)transient ERG latency(check sizes; 15, 30,60 min), 2)transient VEP latency(checks, 15.30,60 min), 3)steady-state ERG latency(checks, 30,60 min), 4)steady-state VEP latency(checks, 30,60 min), 5)transient ERG amplitude(checks, 15,30,60 min), 6)steady-state ERG amplitude (checks, 15,30,60 min). Hypothetical causes of such aging effect are changes in neurons, loss of optic nerve axons and reduced retinal illuminance.

1-06-07 PHRENIC NERVE ELECTROPHYSIOLOGICAL STUDIES IN DUCHENNE MUSCULAR DYSTROPHY (DMD).

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In a former communication, we performed Phrenic Nerve (PN) conduction studies in 25 patients carrying different neurogenic conditions. Latencies and amplitude of the evoked potencials were mesured in PN and Common Peroneal Nerve in order to asses PN involvement in these diseases; we noticed that both parameters were reduced in almost the same proportion in both nerves (Munch. 1990).

In the present paper we performed PN conduction studies in 30 Duchenne Muscular Dystrophy (DMD) patients ranging from 7 to 19 years old; and 20 controls.

Conduction velocities and latencies were within normal values (6.2 ± 1.03).

We took amplitude as a posible mesure of ventilatory failure; this parameter showed an important reduction respecting normal values (76.66 ± 37 in DMD patients and 192 ± 21 in the controls).

We showed that reduction of PN amplitude seems to correlate with the general decline in DMD patients being this parameter an objective one, non dependant of volitional activity.-

1-06-08 NEUROPHYSIOLOGIC FINDINGS IN PATIENTS WITH SUBACUTE SCLEROSING PANENCEPHALITIS

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Subacute sclerosing panencephalitis (SSPE) is a progressive, chronic measles virus infection of the brain. We report the neurophysiologic findings in 7 patients with SSPE (5 males, 2 females; average age 9.5 years, range 5-24 years). Diagnosis was confirmed by progressive clinical deterioration and elevated measles antibody titers in serum and CSF. Periodic complexes were seen in the EEG in all patients during the course of their illness. One patient had a normal EEG in the early stage of the disease. Latency of P100 in visual evoked potentials was significantly increased bilaterally in three patients and unilaterally in two. One patient had abnormal brainstem auditory evoked potentials characterised by prolongation of the III-V interpeak interval. One patient had prolongation of the central conduction time with median nerve somatosensory evoked potential (SSEP). In one patient the posterior tibial SSEP showed a conduction block after the lumbar potential with a normal median SSEP indicating a spinal cord pathology (in spite of a normal MRI of the spine). Various neurophysiological disturbances occur in SSPE indicating a widespread involvement.

1-06-10 P3 AND INTELLECTUAL IMPAIRMENT IN HEMODIALYSIS PATIENTS TREATED WITH ERYTHROPOETIN (rHuEPO) AND WITHOUT rHuEPO

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To evaluate the effects of chronic hemodialysis on intellectual functions, and the effects of rHuEPO on their improvement, a group of 40 patients was studied by event-related P3. The group was divided into two subgroups of 20 patients each, the first one with average history of hemodialysis 2.2 years, while the average in the second group were 5.7 years. In the last six months the patients from the second group was treated with rHuEPO. The hematocrit was 0.24 ± 0.06 in the first group, and 0.32 ± 0.04 in the second group, and Hb 84.8 ± 19.2 vs. 108.5 ± 13.6. P3 peak latency was compared between those two group and with the group of 32 healthy subjects of the same age. The same procedure was conducted for the P3 amplitude. T-test was used for the statistical processing. P3 peak latency elicited by tone discrimination paradigm showed improvement in the group with rHuEPO (327 vs. 319ms; $p<0.1$), confirming beneficial effects on cerebral cognitive processing, and suggesting that severe anemia may contribute to uremic brain dysfunction. P3 amplitude over Fz (9.1 vs. 8uV) and Pz (7.9 vs 7uV) did not show any statistic significance. P3 amplitude over Cz (9.6 vs. 7.2uV; $p<0.1$) showed significant difference.

1-06-11 RECOVERY OF BRAINSTEM AUDITORY EVOKED POTENTIALS AFTER A SEVERE HYPOXIC ISCHEMIC INSULT.

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A 35 years old female patient in coma 4 days after cardio-pulmonary arrost showed bilateral absence of all brainstem auditory evoked potentials(BAEPs)contrasting with preserved brainstem reflexes and the absence of previous hearing dis order .Subsequently,spontaneous breathing recove red and the patient was in an apallic state.EEG was flat.MRI of the brain disclosed abnormal sig nal return from the whole of the white matter of both cerebral hemispheres with marked enlarge- ment of the ventricles and cerebral sulci asso- ciated with diffuse atrophy.BAEPs,performed 6 weeks later,reappeared and were particularly well defined on the right.

This case demonstrates that BAEPs can return after they have been lost for several days.Pro- longed survival is compatible with the temporary loss of BAEPs. Transient hypoxic-ischemic coch- lear damage (E.Brunko et Al Electroenceph.clin. neurophysiol.1985,62: 338-342) might interfere with the activation of auditory pathways after cardio-pulmonary resuscitation.

1-06-12 WITHDRAWN

1-06-13 CEREBRAL HEMISPHERIC ASYMMETRY IN THE CONTROL OF SMOOTH PURSUIT EYE MOVEMENTS.

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Pursuit of predictable sinusoidal target motion was studied at frequencies of 0.2, 0.4, 0.8, 1.2, and 1.6Hz in 35 patients with unilateral focal cerebral lesions. Nineteen of the patients had focal lesions in the right cerebral hemishere, and 16 had lesions in the left. Lesions involved the frontal, parietal, temporal, and occipital lobes of each hemisphere either alone or in various combinations of contiguous lobes. Among the right hemispheric group there were 5 patients whose deficit consisted of marked velocity oscillations at low target frequencies and no significant pursuit movements in both horizontal directions at target frequencies beyond 1.2Hz. The pathology common to this class of patients was a destructive lesion that affected the head of the right caudate nucleus and the putamen. Patients with similar lesions on the left did not show similar pursuit deficits.

The results show that whereas a lesion in each cerebral hemisphere can markedly impair pursuit to that side, certain lesions in the right hemisphere can, in addition, almost completely abolish smooth pursuit to both sides at higher frequencies of target motion.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-06-14 AUDITORY EVOKED POTENTIALS IN DEVELOPMENTAL DYSLEXIA

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Auditory brainstem responses (ABRs) and long latency auditory evoked potentials (LLAEPs) were recorded for 20 subjects with severe developmental dyslexia and 10 normal readers, latencies of ABRs components I, III and V had the same values in both groups. A significant right-left difference in inter-peak latency V - I was observed in control group but not in dyslexic group. The dyslexic group had prolonged latencies of the LLAEPs components N1 and P2. The prolongation was more marked when the right ear was stimulated. In 3 dyslexics LLAEPs could not be obtained, they were suggested to represent a distinct sybtype of developmental dyslexia. The results were consistent with a disturbance in the neural functions in the region of the temproparietal cortices (The generator of the LLAEPs). We conclude that LLAEPs could be useful in identifying high risk children for developmental dyslexia.

1-06-15 STIMULATION OF THE DESCENDING TRACTS AT SEVERAL LEVELS IN SPINAL CORD DISORDERS

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The descending tracts were activated at four levels by the electrical stimulation: the motor cortex, the brainstem (around the pyramidal decussation), and the first and sixth thoracic vertebral level (T1, T6). The motor roots were also stimulated at the conus medullaris and at their exit from the spinal canal, and F-waves were recorded. The subjects were eight normal volunteers and eleven patients with various spinal cord disordes. Response was recorded from the tibialis anterior (TA) or extensor digitorum brevis (EDB) muscle. The relation between the latencies of these responses and the length of the desceding tracts was analyzed.

In normals, the conduction velocity of the activated tract was estimated to be 61-66 m/s, and the estimated synaptic delay at the motoneurons was some 0.3 ms, which suggested a monosynaptic conection. Both the estimated conduction velocity and monosynaptic connection are consistent with the corticospinal tract.

In patients with diffusely affected descending tracts, such as Fridreich ataxia and leukodystrophy, the present technique showed slowed conduction along the descending tracts at all levels and prolonged synaptic delay at the motoneurons. In patients with a localized lesion, localized conduction delay was demonstrated at comparable segments. The present method revealed that there seemed to be two physiological types of idiopathic spastic paraparesis: demyelinating and axonal.

The descending tracts in the spinal cord, which are not activated by magnetic stimulation, can be activated using the electrical stimulation technique described here.

1-06-16 UNUSUAL NEUROPHYSIOLOGICAL FINDINGS IN SYRINGOMYELIA AND SYRINGOBULBIA

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We describe in the present study unusual neurophysiological and neuroradiological findings gathered during the evaluation of a consecutive series of 62 patients with syringomyelia and syringobulbia. The neurophysiological assessment included somatosensory and motor evoked potentials (n=30), polysomnography (n=20), and MRI (n=50). Our sample included 34 females and 28 males. MRI scans showed communicating syringomyelia (63%), idiopathic syrinx (13%), syrinx associated with spinal arachnoiditis (11%), syrinx associated with spinal cord tumors (8%), and post-traumatic syrinx (5%). During a 10-years follow-up period, 2 patients died during sleep and 1 was sucessfully resuscitated*- during a nap. All 3 patients had IXth and Xth cranial nerve involvement and a fixed heart rate. Polysomnographic abnormalities without a clinical manifestation were found in 50% of the 20 patients studied. Finally 5% also showed spinal myoclonus, and inverse masticatory muscle activity.In conclusion, the present study illustrates the heterogeneous landscape of imaging findings in syringomyelia and syringobulbia, and also demonstrates rare but important clinical abnormalities, ranging from movement disorders to a life-threatening periodic respiratory dysfunction.

1-06-17 CONDUCTION OF THE CENTRAL MOTOR PATHWAYS AFTER TRANSCRANEAL MAGNETIC STIMULATION IN DEGENERATIVE ATAXIAS AND HEREDITARY NEUROPATHIES.

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Central motor conduction time (CMCT) was perfor med by magnetic stimulation of the cortex in 20 patients with Friedreich's ataxia (FA), 20 cases with Late Onset Ataxic Disorders (LOAD) (often OPCA), as well as 13 other patients with Hereditary Motor and Sensory Neuropathy (HMSN), one of them with additional features suggesting upper motor neuron involvement.

CMCT was abnormal in all patients with FA. CMCT values and reduction in amplitude of CMAP were found significantly related to time of evolution of the disease and disability. Therefore, abnormalities of the CMCT may be the third electrophysiological diagnostic criterion in FA. CMCT was also slightly prolonged in the case with HMSN and possible piramidal tract involvement. CMCT was ab normal only in 6 patients with LOAD, suggesting heterogeneity in these disease.

CMCT may be a better index of the FA and LOAD worsening, since this is well correlated with reduction in amplitude of CMAP.

1-06-18 EVENT RELATED DESYNCHRONISATION (ERD) AS A MEASURE OF TONIC AND PHASIC ACTIVATION.

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ERD reflects the activation of brain regions due to the processing of incoming information. From studies by Pfurtscheller et al. it became clear that physical stimulus properties and task requirements relate to the onset and amplitude of ERD. They analyse changes of spectral power in specific frequency bands in successive time intervals.
We analysed the relevance of ERD of the a-band (7-13 Hz) for cognitive information processing in the temporal domain, hence with the same time resolution as the EEG. Through instruction (fast vs accurate task performance) we manipulated the tonic activation state of the subject and by task difficulty and stimulus probability we influenced phasic arousal. Instruction only influenced the prestimulus a-activity and may be used as a measure of tonic activation state. Difficult tasks led to a larger ERD amplitude with a maximum about 500 ms after stimulus onset. ERD amplitude therefore may reflect the more phasic activation of specific brain regions due to the (expected) stimulus. These measures can also be interpreted as the allocation of processing capacity to specific brain regions.
A review of the literature shows that ERD as a measure of functional activation of brain regions can be described as changes in specific frequency bands. A proposal is made for a strategy to extract functional frequency information from the EEG with the same time resolution as the EEG.

1-06-19 DIPHENYLHYDANTOIN HAS DIFFERENT EFFECTS ON THRESHOLDS OF PROXIMAL AND DISTAL MOTOR RESPONSES EVOKED WITH MAGNETIC STIMULATION.

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Magnetic stimulation was performed before and after a unique loading dose (16 mgr/kgr) of diphenylhydantoin (DPH) with recording electrodes placed over ADM, APB and Biceps. The 8 normal volunteers (mean age : 27 years, range 21 - 35) had a mean DPH serum level of 23.7 μgr/ml (range 14.2-32.4). The ADM and APB motor threshold increased from 50 to 60% (n=16, $p<0.0007$) while Biceps motor threshold increased from 55 to 75% (n=7, $p<0.01$). The median of the difference between proximal and distal threshold increased from 7.5 to 17.5% (n=14, $p<0.01$). Our preliminary data suggest that proximal muscle motor thresholds are more sensitive than distal muscle thresholds to DPH effect. This reflects probably the different synaptic organisation of distal and proximal fast conducting motor pathways.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-06-20 COMPARISION OF THREE DIFFERENT AUTOMATIC EPILEPTIC DISCHARGE RECOCGNITION SYSTEMS.

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Modern long-term EEG monitoring systems produce large amounts of data to be analysed. To make that task more manageable, several different systems for recocgintion of epileptic activity has been introduced. The most common system in use is the one introduced by Gotman in 1982. We compared two more recently developed systems to it.

The other two systems were developed in Tampere (IMAPS) and in Prague (Wavefinder). As a test material for the comparison twelve 30 minutes long segments of EEG recorded from six epileptics were used. Segments contained sharp-slow wave bursts, sharp waves and also technical and physiological artefacts, so that evaluation would correspond to the actual everyday use of the program.

It was found that all programs were reliable to use for recognition of clear epileptic bursts. Especially low amplitude sharp wave were difficult for all systems. As an average the Tampere system was more sensitive than the system of Gotman, but its' specifity was poorer. The Wavefinder performs as well as the other programs when recognizing epileptic bursts. It is somewhat better in the recocgnition of sharp waves. The detailed results of the comparisions will be presented.

Supported by the Academy of Finland.

1-06-21 LANGUAGE-RELATED POTENTIAL REPETITION EFFECTS DIFFER BETWEEN AMNESICS AND CONTROLS.

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Event-related potentials during a semantic categorization task were studied in 9 amnesic patients (6 with Korsakoff's syndrome) and 9 controls. Subjects decided if visually-presented target words were congruent with a preceeding category definition. Targets (50% congruous and 50% incongruous) were repeated after either short or long intervals. Unexpectedly, memory tasks (cued recall and recognition) followed the recordings.

In both groups, the N400 component was larger to incongruous than congruous targets and decreased in amplitude with repetition. Upon repetition, a late-positive component (LPC) following the N400 increased in amplitude for incongruous targets and decreased in amplitude for congruous targets; these effects were significant in controls only. For both groups, congruous targets were recalled and recognized better than incongruous targets. The controls outperformed the amnesics on all recognition measures and on recall of congruous targets.

The similarity of the N400 repetition effect in amnesics and controls suggests that it is related to semantic or perceptual priming processes. In contrast, the LPC repetition effect seems related to explicit memory, reflecting an updating of short-term memory with the contents of long-term memory. This updating would be necessary on initial presentation or if target-category associations have been lost from short-term memory.

1-06-22 EEG MAPPING AND COGNITIVE PERFORMANCES IN ELFERLY PEOPLE.

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Changes in neurophysiological parameters have been reported in elderly subjects with different degree of cognitive impairment. Studies with computerized EEG frequency analysis (CEEGFA) have shown conflicting results. We have evaluated in a preliminary study with EEG mapping and CEEGFA 8 old subjects (range: 65-84 years), normal or with mild cognitive impairment without dementia. All patients have been evaluated for cognitive and motor performances with the following battery of tests: 1) Mini Mental State Examination, 2) Activities of Daily Living, 3) Instrumental Activities of Daily Living, 4) Geriatric Depression Scale, 5) Motor Performances Scale. We found the following results: a) decrease in the peak power frequency b) reduction in the relative power of the alfa band c) increase in the relative power of the theta band d) anteriorization of the localization of the peak power. Possible relationship between changes in EEG parameters and cognitive and motor performances will be discussed.

C.N.R. grants P.F. 40.92.00314

1-06-23 NEW METHOD FOR TESTING SPATIAL CONTRAST SENSITIVITY IN PARKINSON'S DISEASE, WILSON'S DISEASE AND MULTIPLE SCLEROSIS.

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Aim of this study was to verify the feasibility and reproductibility of the results obtained by a new, simple and attractive test for measuring spatial contrast sensitivity in neurological patients.12 patients (6 Parkinson's, 3 Wilson's diseases, 3 multiple sclerosis) and 12 age and sex matched normal controls were studied. The easy and convenient test consists of presentation on a high resolution monitor screen, of vertical stationnary grattings with a sinusoidal luminance profile decreasing along the horizontal axis. By acting a joystick, the subject positions a cursor at the constrast threshold ; 6 spatial frequencies (SF) are tested from 1.6 to 19 cycles/degree ; 4 backgrounds (white, red , green and blue) are randomly used. The procedure was run 3 times. The data are stored and plotted in a microcomputer connected to this system A two-way variance analysis (ANOVA) with one factor replication (k=3) was used to analyse the reproductibility and showed no statistical differencies between the 3 sets of measurements for all of the 6 SF and 4 backgrounds in the 2 groups together and separately This test shows an excellent intraindividual reproductibility and appears to be a promising, pratical and sensitive method for routine neurological use.

1-06-24 ENMG STUDY IN PRIMARY HYPOTHYROIDISM

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Eleven patients with primary hypothyroidism were evaluated by thyroid hormonal level; TRH test; thyroid antibodies detection; cintilographic and USG methods. They were submitted to an extensive ENMG protocol and muscle enzymes determination before treatment. We found evidence of some myelin and axonal damage in all of them; carpal tunnel syndrome in 5 (45.5%); H reflex abnormalities in 5 (45.5%); myopathic changes in 3 (27.3%) and the presence of myotonia in 2 (18.2%). Muscle enzyme levels were elevated in 3 (27.3%). These findings could not be correlated to any group of patients according to their endocrinological profile.

1-06-25 MAGNETIC MOTOR EVOKED POTENTIALS (MEP) IN PATIENTS WITH SPONDYLOTIC CERVICAL DISC DISEASE

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Twenty-one patients with spondylotic cervical disk (SCD) disease were recruited for MEP and cervical spine MRI studies. Thirteen patients (group 1, G1) showed clinical signs of cervical radiculomyelopathy, and 8 (group 2, G2) with cervical radiculopathy only. MEPs were recorded simultaneously from abductor digiti minimi (ADM) and biceps (Bic) in 42 limbs following magnetic coil stimulations at Cz and Cv7 respectively. MEPs from 76 limbs of 38 normal subjects were obtained for comparison. F-responses were measured also.

Prolonged F-waves were found in 7(53.8%) G1 patients and in 12.5% of G2 patients. However, MEP abnormalities were observed in 12(92%) G1 patients, and in 5(62.5%) G2 patients respectively. The types of MEP abnormalities in G1 patients were: (1)reduced amplitude/dispersion of Cz-ADM, (2)delayed latency of Cz-ADM, (3)delayed latency of Cz-Bic, (4)absent/delayed latency of Cv7-ADM and/or Cv7-Bic, (5)delayed motor conduction time to ADM, and (6)abnormal R-L interside difference. In contrast, MEPs abnormalities in G2 patients were: absent/delayed latencies of Cv7-Bic and/or Cv7-ADM (3 cases), and delayed CMCT to ADM/Bic (2 cases). MEPs abnormalities in Bic/ADM may correctly predict the level of involvement at/above C5 or below C5. The author concludes that MEPs were more sensitive than F-wave and were useful as adjunctive test for localization of the level of lesion of SCD disease.

1-06-26 MEASURING 'PERIODIC LEG MOVEMENTS' (PLM) IN PATIENTS UNDER MADOPAR: A COMPARISON OF EMG AND ACTIGRAPH RECORDINGS.

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In a pharmacological study 30 restless-legs patients under MADOPAR vs. placebo medication are investigated for 'periodic leg movements' (PLM) by polysomnographic and actigraph recordings. The patients spend three nights in a sleep-laboratory with a month between each night. EEG, EMG (M. tibialis anterior) and actigraph recordings are taken of these sleep-lab nights. Additionally, PLM are measured by actigraph, only, in the following two consecutive nights spend at home. PMS/PLM are defined for all nights in both methods. The correspondence of EMG and actigraph is calculated for the sleep-lab data. Actigraph recordings allow a comparison of sleep-lab and the nights at home. Correlational techniques support the hypothesis that PML are reliably detectable by actigraph. Additionally, periodic movements in sleep (PMS) defined by EMG/EEG can be well predicted by PLM. Our study demonstrates the applicability of actigraph in PML/PMS detection. Furthermore, a preliminary analysis shows statistically significant differences between sleep-lab and nights at home. If these result will be supported by a further study the amount of PLM in sleep-lab settings might overestimate the 'real' individual level. Therefore longer and more stable measurements in the natural enviroment are a necessary requirement of estimating PLM-symptoms.

1-06-27 **LESIONS OF THE CENTRAL NERVOUS SYSTEM BEFORE AND AFTER HEART TRANSPLANTATION SURGERY.**

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In order to evaluate risk-factors of patients who expose lesions of the central nervous system (CNS) after heart transplantation (HTX), 28 patients [aged 54 (40-65) y.] were examined before [average 2.7] and also 1 [mean 1.2] and 12 months [mean 12.9] following HTX. Visually (VEP) and acoustically evoked potentials (AEP) were recorded, in addition to neurological examinations.

By the VEPs, 50% of the patients showed pathological latencies of P100 already before HTX. In 20% of all cases new pathological results or a deteriation occurred following HTX.

In one third of the patients, the AEP exposed prolonged latencies of components III and V, preoperatively. Following HTX, pathological AEP were recorded in 57% and 59% of the cases at 1 month and after the 1. year, respectively.

At risk for CNS lesions after HTX, detected by the AEP and/or the VEP are the older Patients with a pre-operative ischeamic cardiomyopathy, episodes of cardiac rejection and/or cytomegalovirus infections ($p<.05$), and higher serum levels of cyclosporine A ($p<.05$).

1-13-01 **mtDNA PLEIOPLASMY IN MITOCHONDRIAL DISEASE.**

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We screened muscle biopsies from 23 patients with established or suspected mitochondrial myopathy for mtDNA deletions using the polymerase chain reaction (PCR). Deletions were detected in 15 patients, both with and without ophthalmoplegia. Three elderly patients had multiple deletions, including the common deletion. The common deletion was also detected in biopsies with the mtDNA $tRNA^{Lys}$ $A \rightarrow G^{8344}$ mutation in three other unrelated patients.

In a young patient of a three generation family, with progressive ptosis and mitochondrial myopathy of successively earlier onset in each generation, no deletions were detected. This possibly represents anticipation in an autosomal dominant disorder and without nucleus-driven multiple deletions.

A low fraction of deletions does not cause mitochondrial myopathy on its own, but in the presence of a deleterious mtDNA point mutation may contribute to disease.

1-13-02 THE PHENOMENOLOGY AND THE DIFFERENTIAL DIAGNOSIS OF TORSION DYSTONIA AND ESSENTIAL TREMOR

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Torsion dystonia (TD) and essential tremor (ET) are hereditary extrapyramidal diseases and can be strictly separated in the classic forms. Differential diagnosis in the atypical variants of TD and ET is not so easy. Under our observation there are more than 500 families with TD and ET. We analysed 26 TD patients (aged from 7 to 41) and 14 ET patients (aged from 18 to 60), which had atypical clinical signs: TD patients besides dystonia had tremor, and ET patients had focal dystonic symptoms. The main criteria for differential diagnosis of TD and ET are: dynamics of clinical syndroms in all members of family; pharmacological tests with different medicines; clinical and EMG characteristics of tremor (ET patients were characterized by statokinetic tremor with frequency 6-8 a sec., TD patients had predominantly static tremor with frequency less than 6 a sec.). All these methods help to clarify the diagnosis of TD and ET and to carry out adequate treatment and medicogenetic councelling.

1-13-03 FAMILIAL SPINOCEREBELLAR ATAXIA IN SOUTHERN AFRICA.

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The spinocerebellar ataxias are an uncommon group of genetic disorders which have been well characterised in North America and Europe. Information concerning these conditions in Africa and other parts is scant. In order to address this problem a large scale survey has been undertaken in the Cape Province of South Africa. In this investigation more than 500 persons in 18 families have been analysed in detail.

Molecular linkage studies were done in 6 families with similar phenotypes in which the condition was transmitted as an autosomal dominant trait. A PCR primer based system was used to look for linkage bwtween the putative disease gene and the D6S89 locus. Tight linkage to the D6S89 locus on the short arm of chromosome 6 was documented in 2 large South African families. This provides a practical solution in the management of the disorder through prenatal and presymptomatic testing in these linked families. Problems relating to the implementation of a predictive testing service in a developing country will be indicated.

1-13-04 A NEW SYNDROME OF AUTOSOMAL RECESSIVE SPINOCEREBELLAR DEGENERATION ASSOCIATED WITH HYPOALBUMINEMIA.

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We have identified a new syndrome of autosomal recessive spinocerebellar degeneration associated with hypoalbuminemia. The clinical features of affected patients are characterized by early childhood onset, cerebellar ataxia, mental retardation, areflexia, weakness of the lower extremities, impairment of deep sensation, and absence of cardiac involvement. All the patients showed decreased serum albumin and elevated cholesterol levels. Complete co-segregation of hypoalbuminemia and spinocerebellar degeneration in these families raised the possibility that the new syndrome is a result of abnormality of a new single gene. Since the syndrome has a clinical features overlapping with those observed in Friedreich's ataxia(FRDA) mapped to chromosome 9q13-21.1, we performed genetic linkage analysis to the locus. Utilizing 29 members of 6 familics including 14 affected individuals, we have analyzed linkage between the locus of the disease and 5 microsatellite polymorphisms on the short arm of chromosome 9. Although 3 recombination events between the disease locus and GS4/D9S15/GS2 were observed, the maximum lod score of 3.04(θ=0.10) is obtained. As recombinations have rarely been observed between FRDA and GS4/D9S15/GS2, the new syndrome is likely to be caused by a new gene adjacent to FRDA gene.

1-13-05 MOLECULAR GENETIC STUDIES OF FRIEDREICH ATAXIA IN CYPRUS

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OBJECTIVE: The aim is to confirm linkage of the Friedreich ataxia (FRDA) locus to 9q13-21.1 in Cypriot families and identify the disease haplotype(s).

BACKGROUND: Friedreich ataxia is an autosomal recessive disease the gene for which has recently been localised to chromosome 9q13-21.1. A cluster of FRDA families has been identified in neighbouring villages of the Paphos district, Cyprus.

DESIGN/METHODS: Eight families with 60 individuals, 9 of whom are affected have been included in this study. Molecular genetic analysis was done by Southern analysis using probe 26P, and PCR analysis of the microsatellite polymorphisms GS2, MCT112 and GS4. The above polymorphisms map to 9q13-21.1.

RESULTS: The disease cosegregates with the 2-2-7-13 haplotype (26P-GS2-MCT112-GS4) in six of the families (K-A) and with the 3-2-3-6 haplotype in one family (P). In the eighth family the proband has inherited both the above haplotypes one from the father (K-A) and the other from the mother (P). Both haplotypes are in linkage disequilibrium with the disease locus. No recombinants have been identified.

CONCLUSION: We have identified the disease haplotypes in our families. Carriers among these families have also been identified and we are in a position to offer them prenatal diagnosis upon request.

1-13-06 LINKAGE ANALYSIS SHOWS EVIDENCE FOR THREE DIFFERENT SPINOCEREBELLAR ATAXIA LOCI.

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The spinocerebellar ataxias (SCAs) are a clinically heterogeneous group of neurodegenerative disease. To date two loci have been identified: one on chromosome (ch) 6p and one on ch 12q, SCA-1 locus and SCA-2 locus respectively. We have studied 4 large pedigrees, from different ethnic backgrounds, segregating an autosomal dominant form of SCA. A total of 266 individuals, including 64 affected, were ascertained. Family members were examined and bloods were collected. We performed linkage analysis using anonymous DNA markers which flank the two previous described loci. Our results have shown that 1 kindred is linked to SCA-1 (ch 6p), 2 kindreds are linked to SCA-2 (ch 12q) and the remaining kindred is significantly excluded from both, the SCA-1 and SCA-2 loci. The two SCA-2 kindreds were the largest pedigrees under study: the Gaspé kindred, one of the largest SCA pedigrees described and the Saskatchewan kindred which includes branches in Austria.

In conclusion we have shown that the SCA-2 locus is not a private gene. Furthermore, we have found evidence for a third locus, which is responsible for the disease in one of our pedigrees. Analysis using informative markers throughout the human genome will be required to map this third locus.

1-13-07 AUTOSOMAL DOMINANT SPASTIC PARAPLEGIA WITH ADDITIONAL UNIQUE FEATURES IN A LARGE KINDRED OF GERMAN ORIGIN.

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The hereditary spastic paraplegias (HSP) are generally divided into two groups: pure hereditary spastic paraplegia implying pyramidal signs in the lower limbs and increased tendon reflexes in the upper limbs but no other neurological features and the complicated forms which may show additional signs such as amyotrophy, extrapyramidal involvement or other features. The complicated forms are extremely rare.

We describe a large kindred of 13 affected individuals in 4 generations with an autosomal dominant syndrome of complicated spastic paraparesis. Features include spastic paraparesis, hypomimia, badykinesia, rigidity, dysarthria, a complex eye movement disorder and incontinence. The pattern of expression varies in different family members. Intensive investigations were carried out on 4 affected members but no biochemical defect or cytogenetic was found. Linkage analysis for mapping the disease gene is in progress.

1-13-08 LINKAGE STUDIES IN TIBIAL MUSCULAR DYSTROPHY (TMD)

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A large consangious Finnish TMD kindred was recently described by Udd et al. Two distinct phenotypes segregate in the same pedigree: a severe proximal form (resembling LGMD) and a mild distal tibial dystrophy. Seggregation analysis suggest heterogenous manifestations of one mutation.

Different models were constructed for linkage analyses to cover different modes of inheritance. Models include recessive and dominant inheritance patterns, where the affected individuals are considered either homozygous (rec.) or heterozygous (dom.) regardless of severity of the phenotype. In synthesis model individuals with distal phenotype are taken as heterozygous carriers whereas the proximal phenotype represents the homozygous form of the disease.

Using linkage analysis, several candidate loci were excluded including titin, desmin, DMDL, LGM1 and LGM2. DLMD locus in chromosome 13 is currently under study. For the random search of the TMD locus, the family material was tested with the simulation program SLINK. In 200 simulations, under single locus models described above, the obtained maximal LOD scores were 10.13, 2.40 and 7.77 at $\theta = 0.1$ for the dominant, recessive and synthesis models respectively. The results demonstrate, that this TMD pedigree can provide sufficient information for conclusive mapping of the TMD assuming a single causative locus.

1-13-09 BRAIN IMAGING IN ADULT ONSET GM_2 GANGLIOSIDOSIS.

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Adult onset GM_2 gangliosidosis is a rare disease occurring mainly in Ashkenazi Jews and manifested by the combination of cerebellar dysfunction, motor neuron disease, psychosis and intellectual decline. A detailed neuroradiological study has never been reported. We describe the brain CT scan and MRI characteristics of ten patients suffering from this disorder: The striking radiological findings included cerebellar atrophy, particularly of the vermis, in all patients in the presence of normal-appearing cerebral hemispheres. The severity of these finding did not correlate with the age of onset, disease duration, severity of neurological impairment or mode and distribution of the various clinical presentations. In particular, no cerebral pathology was found by neuroimaging in seven patients with intellectual decline or in five patients with recurrent psychosis, while prominent cerebellar atrophy was present even in the only patient who was free of cerebellar symptoms or signs. **Conclusion:** Cerebellar atrophy is a prominent neuroradiological feature of adult onset GM_2 gangliosidosis.

1-13-10 A NOVEL FORM OF AUTOSOMAL DOMINANT NON-PROGRESSIVE SPINAL MUSCULAR ATROPHY.

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A 34 year old man, was assessed for multiple contractures of shoulders, hips, knees and feet, and marked diffuse weakness of leg muscles. These problems were present at birth, and appeared to be minimally progressive.

On examination, he had marked hypoplasia and weakness of the trapezii, and marked weakness and wasting of all leg muscles. Absent reflexes and hypotonia were present in the legs. Sensory exam was normal.

Nerve conduction studies were normal, as was nerve biopsy. EMG revealed decreased recruitment, and scattered large potentials in affected muscles. Muscle biopsy was compatible with recurrent denervation and reinnervation, with a predominance of type I fibers.

His son, one year of age, had been born with identical findings and had identical test results. There was no other family history.

Review of literature revealed only one similar previously published case, which was reported as an "arthrogryposis".

The muscular atrophy and contractures in this family appear to be due to a rare form of an autosomal dominant spinal muscular atrophy, which is maximal in severity at birth.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-13-11 SPINOCEREBELLAR ATAXIA 1 (SCA1) AND MACHADO-JOSEPH DISEASE (MJD): A COMPARISON OF THEIR CLINICAL FEATURES.

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Some families with hereditary spinocerebellar degeneration (SCD) have recently been reported to have the gene locus which is tightly linked to a polymorphic DNA marker, D6S89, and this form of SCD is called SCA 1. MJD is another form of hereditary SCD which is defined by the neuropathological criteria. The purpose of the present study is to clarify if it is possible to distinguish them by clinical symptoms and signs.

[Methods] We used one pedigree (7cases) of SCA 1 which was diagnosed by the linkage analysis (D6S89), and two pedigrees (7 cases) of MJD which was diagnosed by neuropathological study. The linkage analysis (D6S89) was negative in the MJD families.

[Results] The clinical symptoms and signs which were more frequently observed in the patients with SCA1 were: (1) nystagmus only at the early stage of the disease, (2) slow eye movement, and (3) psychological symptoms and dementia at its end stage. Although akinesia and dystonia were frequently observed in the patients with MJD, these were rare in the SCA1 patients. Hyperactive deep tendon reflexes and spasticity were more severe in the MJD patients.

[Conclusion] The present study indicates the possibility that SCA1 and MJD can be distinguished by clinical symptoms and signs.

1-13-13 STUDY OF 4q DNA MARKERS IN BRAZILIAN FASCIOSCAPULOHUMERAL MUSCULAR DYSTROPHY (FSHD) FAMILIES

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The gene reponsible for FSHD, an autosomal dominant neuromuscular condition has been mapped to chromosome 4. Linkage analysis with the new marker p13E-11, which recognizes de novo rearrangements in isolated cases of FSHD characterized by shorter EcoRI fragments, usually shows that a smaller fragment segregates with the disease gene among the affected individuals from each genealogy. Results from linkage analysis with the marker loci D4S163 and D4S139 in 6 FSHD families and with p13E-11 in these and 6 other additional Brazilian families (n=12) do not suggest genetic heterogeneity for FSHD in our population. With exception of one family, in which the normal individuals had a smaller EcoRI fragment than the affected ones, in all others a shorter specific EcoRI band was found to segregate in all affected patients from each genealogy. Such fragment varied in size from 13.5 to 29 kb but was constant within each genealogy. These preliminary results suggest that the use of the marker p13E-11 for preclinical and prenatal diagnosis should be done with caution and that new mutations are aparently not rare in FSHD. Supported by FAPESP and CNPq .

1-13-14 INTRAFAMILIAL VARIABILITY IN DYSTROPHIN ABUNDANCE CORRELATED WITH DIFFERENCE IN THE SEVERITY OF THE PHENOTYPE IN XP21 MUSCULAR DYSTROPHY

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In Duchenne muscular dystrophy (DMD), the progression of the disease is always severe and predictable while in Becker (BMD) dystrophy there is a wide variability (intra and interfamilial) in the severity of the phenotype. Patients affected by DMD are confined to a wheelchair before age 12 while BMD patients are able to walk beyond age 16. Here we report a family in which the proband, currently aged 15, is showing a severe DMD progression (confined to wheelchair at age 10) while his affected uncle, aged 29, was able to walk until age 18 and is showing a more benign course, compatible with BMD. No DNA deletion was detected in the patients. Dystrophin analysis through immunofluorescence and western blotting showed a negative pattern in the youngest patient and a positive one in the oldest. Apparently, this is the first report on intrafamilial variability in dystrophin abundance correlated with a difference in the severity of the phenotype. Supported by FAPESP and CNPq.

1-13-15 CORRELATION BETWEEN CTG TRINUCLEOTIDE REPEAT LENGTH AND CLINICAL PICTURE IN BRAZILIAN PATIENTS AFFECTED WITH MYOTONIC DYSTROPHY

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Myotonic dystrophy (DM), an autosomal dominant disorder, is characterized by an extremely variable clinical picture (within and between families) which appears to be more severe from one generation to the next, a phenomenon called antecipation.The mutation responsible for DM has been identified as an expansion of a CTG repeat in the 3' untranslated region of a gene encoding protein kinase activity (DM-kinase). A correlation between the increase in the number of (CTG)n repeats and the severity of the disease in sucessive generations has been reported. We have studied the molecular abnormality in 120 individuals from 20 Brazilian unrelated families with DM patients whose clinical picture varied from mild to the severe congenital form. Our data confirmed the correlation between the mutation-expansion and the severity of the phenotype in patients from the same family. However, DNA fragments of comparable length were found in unrelated patients with different clinical pictures suggesting that in addition to the increase in the number of CTG repeats, other factors are responsible for the severity of the phenotype in DM. FAPESP, CNPq.

1-13-16 KNOBLOCH SYNDROME AND SEVERE CHILDHOOD AUTOSOMAL RECESSIVE MUSCULAR DYSTROPHY (SCARMD) IN A LARGE CONSANGUINEOUS BRAZILIAN FAMILY

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Knobloch syndrome is a rare genetic disorder characterized by high myopia, vitreoretinal degeneration with retinal detachment and occipital encephalocele. The inheritance is apparently autosomal recessive (AR) but in addition to the original report (McKusick 267750) with 5 affected patients only one other family with 2 affected sibs has been described (Czeizel et al., 1992). We have studied a large consanguineous genealogy in which 12 patients, all with a congenital occipital meningoencephalocele, have a clinical picture typical of Knobloch syndrome and two have high myopia confirming thus an AR pattern of inheritance. Diagnosis of Knobloch syndrome was established through detailed clinical and ocular examination , CT scan and MRI. Another 8 patients from this family are affected by SCARMD, which was confirmed through clinical data and deficiency of 50K associated glycoprotein (Zatz et al., 1993). Although the two diseases are very rare, the occurence of both in the same genealogy has apparently occured by chance (FAPESP, CNPq, ABDIM, PADCT, Hospital Alberst Einstein).

1-13-17 MOLECULAR GENETICS OF CTX IN MOROCCAN JEWS

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Cerebrotendinous Xanthomatosis (CTX), a rare autosomal recessive lipid storage disease is characterized by tendon xanthomas, cataracts, a multitude of neurological manifestations and is caused by mutations in the sterol 27-hydroxylase gene. A relatively high prevalence of the disease has been noted in Israeli Jews originating from Morocco. Skin fibroblasts were isolated from five CTX patients from four Jewish families from Morocco. RNA, DNA blotting analysis, single strand conformational polymorphism (SSCP) and DNA sequence analysis were used to determine the nature of the mutations. RNA blotting analysis revealed that the mutant alleles do not produce any detectable sterol 27-hydroxylase mRNA. The mutations do not cause major gene rearrangements. SSCP and sequence analysis identified the exact location of two underlying mutations: deletion of thymidine in exon 4 and a guanosine to adenosine substitution at the 3' splice acceptor site of intron 4 of the gene.

Conclusions: Two mutations in the sterol 27-hydroxylase gene cause CTX in Moroccan Jews.

1-13-18 FAMILIAL AMYLOIDOSIS, FINNISH TYPE (FAF): CLINICAL AND MOLECULAR BIOLOGICAL FINDINGS

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Familial amyloidosis, Finnish type (FAF) is a systemic, autosomal dominant disorder related to a variant gelsolin. Our study was designed to characterize its neurological manifestations, to study its molecular genetics and develop a diagnostic DNA test, and to develop a method for measuring gelsolin concentrations.

All clinically examined patients (n=30, 27-74 years) had cranial neuropathy affecting especially trigeminal and facial nerves. Mild peripheral polyneuropathy was common. Amyloid was found in all 11 sural nerve biopsies. Carpal tunnel syndrome was a typical, although often asymptomatic feature. ENMG with signs of axonal degeneration and eventual demyelination confirmed the clinical findings. MRI, neuropsychological testing, evoked potential examinations and ^{99m}TcHMPAO-SPECT suggested subclinical CNS affection and cardiovascular reflexes a minor autonomic nervous system dysfunction. A simple method, solid-phase minisequencing, for detection of known point mutations, revealed the previously reported G_{654}->A mutation of gelsolin changing ASP_{187} to ASN in all 94 affected individuals who represent one third of all estimated Finnish FAF families. A RIA for gelsolin quantitation was developed and used for serum and CSF analysis.

The homogeneous clinical picture and molecular genetic results suggest a single mutation as the cause of FAF in these patients.

1-13-19 MIGRAINE WITHOUT AURA AND MIGRAINE WITH AURA ARE MOST LIKELY GENETICALLY DETERMINED DISEASES.

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193 patients (probands) with a diagnosis of migraine without aura (MO) or migraine with aura (MA) according to the criteria of the International Headache Society were included in a family study of MO and MA. The probands were interviewed about the occurrence of MO and MA among their first-degree relatives and spouses. MO and MA were analysed separately. 121 probands had MO and 72 probands had MA. We found a 3- and 2-fold increase in familial aggregation of MO and MA in first-degree relatives of proband with MO and MA, respectively. Spouses of probands were not MO or MA prone. The combination of familial aggregation and no increased risk in spouses strongly suggests that both MO and MA have a genetic cause. The inheritance was analysed according to the family tree and with a segregation analysis. Preliminary results are that X-linked dominant or recessive, autosomal dominant or recessive or mitochondrial inheritance could not be accepted for neither MO or MA. Multifactorial inheritance seems most probable for both MO and MA, but it can not be excluded that both MO and MA are genetically heterogeneous diseases.

1-13-20 DYSMYELINATION IN GALACTOSEMIA: IMPLICATION OF GALACTOSE-1-PHOSPHATE URIDYLTRANSFERASE IN MYELINATION

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Galactosemia, an inborn error of galactose-1-phosphate uridyl transferase (GALT), leads in severe cases to mental retardation and dysmyelination. The enzymatic defect causes an accumulation of galactose-1-phosphate and a deficiency in UDP-galactose (UDP-Gal), which is the only donor for galactosylation of proteins and lipids. Galactosyl-ceramides are early markers for myelinogenesis and constitute major components of the myelin. The syntesis of these glycolipids depends on UDP-Gal and therefore, the whole myelination process might be greatly affected in galactosemic patients.

The quantitation of GALT mRNA and protein in the central and peripheral nervous system of rats showed that GALT is differentially expressed during late embryonic development and has a second peak of expression which correlates with postnatal myelinogenesis. In rat dorsal root ganglia culture, GALT was specifically expressed in myelinating Schwann cells as shown by immunolabelling with anti-human GALT monoclonal antibodies.

The chronic neurological complications observed in galactosemic patients could be related to the developmentally regulated expression of GALT in myelinating cells.

1-13-21 FACIO-SCAPULO-HUMERAL MUSCULAR DYSTROPHY (FSH): PATIENTS' INTEREST IN PRECLINICAL TESTING, EFFECTS OF GENETIC COUNSELLING (GC) AND FITNESS ESTIMATION.

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A questionnaire about the interest in preclinical testing, effects of GC and fitness was sent to 46 patients affected with FSH. Most (86%) are interested in preclinical testing for their children to seek for treatment (35%) or to avoid the progression of the disease (21%), although they had been told that FSH is still untreatable. In case of a positive result, 69% would transmit the information as soon as possible to their children. Although 76% favour prenatal diagnosis, only 8% would interrupt pregnancy of an affected fetus. As the risk of an asymptomatic young adult is only 5% it is expected that genetic testing will be requested to reassure at-risk persons that they do not carry the gene, to confirm or not the presence of the gene in cases of clinical uncertainty, for early diagnosis in at-risk children and more rarely for prenatal diagnosis. GC had no effect upon the number of children of FSH patients as compared to those of their healthy sibs because they were submitted to it late. Accordingly, there is no reduction of fitness in our population. Since 25% of the patients could not yet accept their disease emotional preparation is essential in the case the FSH gene is detected.

CNPq, FAPESP, ABDIM.

1-13-22 PHENYLKETONURIA WITH ADULT-ONSET NEUROLOGICAL MANIFESTATIONS:
A TRIAL OF VALINE, ISOLEUCINE AND LEUCINE

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We report a male patient with phenylketonuria (PKU) who developed neurological deficits during the adult life. His neuropsychological development was entirely normal and he was a good athlete until the age of 33, when his vision was blurred. In three months his gait progressively deteriolated to bind him to wheel chair. On examination he had red hair and gray eyes. IQ was 68. Visual field showed concentric narrowing. The limbs were spastic and weakened. He claimed pain in extremities. T2-weighted MRI revealed high-intensity areas in the white matter. Aminogram had elevated phenylalanine (Phe) as 1663 nmol/ml (normal range 50-90) and reduced tyrosine. Despite a strict dietary control (oral intake of Phe less than 0.5 g/day) serum Phe level remained high around 500 nmol/ml and his neurological deficits still worsened. Amino acid mixture with adequate valine, isoleucine and leucine (VIL) was added; serum Phe was decreased to 82-198 nmol/ml. His neurological condition ceased to progress and MRI abnormality remained unchanged for 6 months during VIL treatment. This is the first patient of PKU with normal development unless no Phe restriction in childhood. VIL treatment may be favorable to support a dietary teatment by competitively reducing the intestinal absorption of Phe.

1-13-23 A STUDY ON DIAGNOSIS AND PATHOGENESIS OF WILSON'S DISEASE

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We have studied copper (Cu) and metallothionein (MT) Metabolisms in cultured skin fibroblasts of patients and heterozygotes with Wilson's disease (WD) and controls (5 cases each) after incubation in medium containing Cu (C1: 15.74 μmol/L; C2: 78.70 μmol/L; C3: 157.38 μmol/L; C4; 314.76 μmol/L). The results show: copper/protein ratio (Cu/P) of patients in significantly higher than that of other 2 groups after incubated in C4 medium for 12 or 24h, and Cu/P, in cytosols of 3 groups are only raised in C4 medium with time (within 72h) and higher in patients than in other 2 groups. Cu in cytosols distributed similarly in 2 peaks of high molecular weight protein and MT fraction. Cu content found in MT of patients is much higher than that of heterozygotes and controls. After incubation in C4 (not C1, C2, C3), MT of 3 groups are elevated, patients group show higher than other 2 groups. The results suggest: Cu content measurement in C4 medium can be used in distinguishing WD patient from heterozygote and normal. MT may have an agnormal high Cu affinity and high inductivity by Cu, preventing Cu further transportation, resulting in deposition of Cu in WD cells.

1-13-24 Late onset Friedreich's disease. A clinical and genetic linkage study.

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The genetic locus of Friedreich's disease (FD) has been mapped to chromosome 9q13-q21. Onset age is usually before age 20, but a late onset is possible. We observed 19 patients from 14 families with onset between 21 and 36 years. Their clinical picture did not differ from that of 80 FD patients, but they lost independent walking later (12.6±4.0 vs 8.3±4.6 years from the onset). We also studied linkage between the disease locus and marker loci of the region 9q13-q21 in 8 families. No recombination event was found. Late onset and slower progression in our patients can be explained by environmental factors and/or a favourable genetic background or alternatively by at least one different allelic mutation.

1-14-01 PREVALENCE OF HEADACHE IN SAUDI NATIONALS: A COMMUNITY - BASED STUDY.

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Information on headache syndromes in Saudis are based on hospital populations, are result of a community-based survey on the prevalence of headache in Saudi Arabia (SA) is reported.
A total population survey of Thugbah was undertaken in two phases consisting of an initial screening using a questionnaire and evaluation of those with potential diseases by a neurologist to find cases using defined criteria.

Headache syndromes were more prevalent in females (145/10,000) than males (917/10,000) with an overall crude prevalence ratio of 1,207/10,000. Headache was uncommon in children, and its prevalence increased steadily with age although the peak for males was the 4th decade as against the 7th for females. tension - type headache (961/10,000) was more prevalent than migraine (504/10,000). Migraine headache showed a consistent female predilection at all age groups.

Headache syndromes are common in Saudi nationals. Environmental and sociocultural factors may be responsible for the high prevalence of headache in the community. The role of other factors needs tuther evaluation.

1-14-02 PAIN IN 1,250 CANCER PATIENTS IN CHINA: A STUDY OF TRANSCULTURAL AND ETHNIC DIFFERENCE OF PAIN

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Retrospective study of 500 deceased cancer patients was carried out by the criterion of pain on the patients' intake of narcotic analgesics during one month before death. The BPI (Brief Pain Inventory of Wisconsin-Madison University) was adopted prospectively to the study on 1,020 patients with cancer involved in different systems at various stages. The emotional reactions of some patients were investigated with depressive and anxious questionnaires.

Results: The pain incidence was about 30% of all patients. Only 4% of the patients in prospective group took narcotic analgesics. Patients at acute stage had more pain symptoms. More depressive reactions were seen in the patients with pain. Many biological factors, such as sex, age, systems involved by cancer, surgical operation and radiotherapy, etc. were not related to pain incidence.

Conclusions: The pain incidence of our patients is at a very lower level as compared with that in western world (about 50% at early stage and 70% in terminal patients). There is a transcultural and ethnic difference of pain between the Chinese and the western people. That many biological factors are not related to the pain indicates that sociopsychological influences might play an important role in these differences. Narcotic analgesics which is advocated strongly in western world are not necessary for the treatment of pain in China.

1-14-04 EDWARD FLATAU (1868-1932) AND PRESENT MIGRAINEOLOGY

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Dr Edward Flatau, prominent Polish neurologist, worked in Warsaw and was a head of Neurological Department at Jewish Hospital. In 1912 he published in Polish his famous book on migraine (Migrena, Warsaw 1912) translated shortly after into French and German. It belongs to the classic books concerning migraine and is cited in the handbooks and monographs worldwide. Flatau's work, based upon the observation of 500 patients and over 500 references, is still of actual value. Constructing the modern models of migraine pathomechanism we should not forget Flatau's opinions, expressed 80 years ago. Flatau was convinced that neither vascular, nor central, nor toxic theories can solely explain the pathogenesis of migraine. He claimed migraine is a kind of "neurotoxic trait" that results in central disturbances. However, he denied the theories favoured the precise organic localization of possible "migraine dysfunction". Flatau supported also the idea, that the interictal symptoms and signs are of special value for the understanding of migraine pathogenesis. Besides of the migraine problems Flatau was active in the different fields of neurology (e.g. meningeal sings, neuroanatomical studies). Prof. E.Herman, founder of our Department(1945), was Flatau's coworker and pupil, thus our Migraine Center is connected with Flatau's tradition.

1-14-05 SPINAL PUNCTION HEADACHE PREDISPOSING FACTORS.

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About 15-45% of patients receiving a spinal puncture (SP) may develop spinal puncture headache (SPH). Some predisposing factors (great needle diameter and/or early standing-up) have been accepted, but the physiopathology is yet elusive. Possible mechanisms such as cerebrospinal fluid (CSF) hypotension, CSF leakadge and/or cerebro-meningeal vasodilatation have been proposed to explain it.

In order to clarify this matter, we have studied 135 patients (62 males and 73 females) aged between 14 and 88 years, who received a diagnostic LP during 1991. 19 G sized puncture needle were used and a similar CSF volume (mean±SE=13.6±0.4 ml) was removed in each case. All patients were asked to drink > 2000 cc water and to have an horizontal bed rest during the next 24 hours. SPH appeared in 55 cases (40%) after 0.5 - 4 days and lasted 3 days (range=1-9). Statistical analysis did not show any difference in the final CSF pression, sex nor in traumatic SP; however, age was significatively lower in patients who developed a SPH (mean±SD=45±19 years) if compared with that of those who did not (mean±SD=53±19 years) ($p<0.05$).

These data suggest that a young age can be a determinant factor in the development of a SPH and that, opposite to expected, no traumatic SP nor final spinal CSF hypotension seem to be so. Future research should be done to evaluate a possible vasodilatation of cerebro-meningeal vessels leading to an increased cerebral blood flow.

1-14-06 SENSORY ABNORMALITIES ACCOMPANYING HERPES ZOSTER AND POST-HERPETIC NEURALGIA

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To elucidate the mechanisms of post-herpetic neuralgia (PHN) the sensory abnormalities were followed prospectively during the first three months after the onset of herpes zoster.

52 patients (21 men, 31 women; age 60-89 years, mean 73) with herpes zoster, recruited from an ongoing double blind study of the preventive effect of prednisone for PHN were examined with somatosensory tests during the acute phase (<1 week), at 3 weeks and 3 months after the onset. The clinical sensibility tests included touch (cotton wool), pinprick and cold. Quantitative tests for touch (von Frey filaments), temperature, and cold and heat pain (Thermotest) were done 3 months after the infection.

14 patients had developed PHN at 3 months (27%). All PHN patients had abnormal sensibility at 3 weeks and 3 months, whereas only about 40% of the others were abnormal then. In the quantitative tests at 3 months, for each modality, about 55% of the patients with PHN had sensory abnormalities, compared to about 30% of the patients without pain. The abnormalities included both increased thresholds (touch, temperature, pain) and hypersensitivity. Allodynia (23%) and dysesthesias (55%) were frequent in the PHN group. 9% of the patients without pain had dysesthesias.

PHN patients had more severe sensory abnormalities than the no-PHN patients. The results also indicate that both large and small diameter sensory fibers are affected in post-herpetic neuralgia.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-14-07 OCCIPITAL NEURECTOMY FOR OCCIPITAL NEURALGIA

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The term 'Occipital Neuralgia' (ON) is now used to describe headaches which are persistently unilateral and are associated with circumscribed tenderness of the greater occipital nerve (CON) as well as sensory changes in its area of distribution, such as hyper- or hypo-algesia or dysaesthesiae.

To assess the extent of the problem, 620 new patients with 'idiopathic headache' had the clinical features of their attacks analysed, and of those 101 (16%) were found to be suffering from 'Occipital Neuralgia'. To produce a significant period of headache freedom, 65 patients, 20 male and 45 female, were subjected to occipital neurectomy and collectively they had 82 operations. Of the 17 re-operations, 7 were done because the original operation failed to produce relief, whilst the remaining 10 were performed because of the success of that operation. The mean period of relief for those who responded to the initial operation was 8.4 months.

The above results suggest that occipital neurectomy is an appropriate treatment for patients with Occipital Neuralgia and should be used in severe cases, until alternative therapies have been devised.

1-14-08 EFFECTS OF SUMATRIPTAN IN NITROGLYCERIN-INDUCED HEADACHE IN MIGRAINE PATIENTS.

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The mechanism of action of sumatriptan in aborting migraine attacks is still under debate. Studies in rats show that the drug inhibits plasma protein leakage in dura mater due to trigeminal ganglion stimulation, suggesting an action on 5-HT1 autoreceptors on sensory fibers innervating vessels. Although sumatriptan constricts isolated blood vessels and reduces blood flow in A-V shunts, Doppler studies in humans do not show any significant effect in large caliber blood vessels. The effects of sumatriptan (6 mg s.l.) were studied in sumatriptan-responder migrainous following nitroglycerin (NTG) s.l., 5 mg. NTG induced headache in 4 out of 5 patients studied so far. Sumatriptan was given 10 min after pain onset. Headache disappeared in 10, 30, 90 and 95 min, respectively. Although in two patients spontaneous recovery might have occurred, sumatriptan seemingly aborted NTG-induced headache in the other ones. According to the animal data reported above, sumatriptan might abort NTG-induced headache by inhibiting sensory fibers activation induced by distended vessels. The limited number of patients studied to date and the variability of response do not allow so far to draw conclusions on sumatriptan mechanism of action in aborting NTG-induced headache.

1-14-09 HEADACHES IN CHRONIC HEMODIALYSIS PATIENTS

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Neurological complications in chronic hemodialysis (HD) patients are frequent and well known. Headache is one of the most frequent complaint and usually occurs as a symptom of the disequilibrium syndrome, or as a peculiar entity related to HD, with a specific diagnostic criteria (International Headache Society (IHS) Classification 10.5). However, the prevalence of metabolic and idiopathic headaches in HD is unknown. This study was performed to correleted the headache symptom/ syndrome with the renal disease type and HD modality prescribed. One hundred patients of two HD clinics were observed by 4 neurologists. Separately, the nephrologists caracterized the metabolic and HD parameters. The parameters studied was the following: 1- Headache type (IHS diagnostic criteria); 2- Time relation headache/ HD onset; 3- associated diseases (hypertension, diabetes, depression); 4- additional neurologic problems; 5- duration and frequency of HD sessions ; 6- mean arterial tension on HD; 7- hematocrit, and erithropoietin treatment; 8- acetate versus bicarbonate dialysates; 9- biocompatibility of HD membranes. The data obtaned was compared with a controle paired matched group without renal disease, and the differences detected are comented on.

1-14-10 SAFETY AND EFFICACY OF DIVALPROEX SODIUM IN THE PROPHYLAXIS OF MIGRAINE HEADACHE: A MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Based on previous reports of valproate efficacy in migraine prophylaxis, this study was conducted to evaluate the safety and efficacy of divalproex sodium (Depakote®, USA; Epival®, Canada) monotherapy in the prophylaxis of migraine headache.

A 4-week, single-blind baseline phase was followed by a 12-week, double-blind treatment phase (4-week dose adjustment period followed by an 8-week dose maintenance period) in this placebo-controlled, randomized, parallel-group, multicenter study.

Data from 107 randomized patients (70 Depakote, 37 placebo) indicated that Depakote-treated patients had a significantly lower mean 4-week migraine headache rate than placebo-treated patients during the treatment phase (3.5 vs 5.7, $p \leq 0.001$). The mean Depakote dosage was 1087 mg/day and mean trough concentration was 66 mcg/ml. Treatment-emergent adverse events for which the treatment difference was statistically significant included: nausea, asthenia, somnolence, abdominal pain, vomiting, tremor and alopecia. In general, nausea and vomiting were limited to the first four weeks of the treatment phase. Drug discontinuation due to intolerance occurred in 13% of Depakote-treated patients and 5% of placebo-treated patients.

The overall safety profile seen for Depakote in this population was similar to that seen in the epileptic population. In this trial, Depakote was well tolerated and Depakote-treated patients had significantly less-frequent migraine headaches than placebo-treated patients.

1-14-11 VASCULAR MALFORMATION OF THE CEREBELLOPONTINE ANGLE CAUSING ATYPICAL CLUSTER-TIC

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A 70 year old male patient has shown two types of unilateral headache for 15 years. When the disease began, pain was occasional and short-lasting. After three years, the crises appeared in bouts every year, and lasted weeks or months. For the last eight years, pain has been present daily.

Pain was located from the forehead, supraorbitally, to the temporal region, always at the right side. The patient complained of neuralgic paroxysms, lasting a few seconds, without evident trigger zone. He also complained of another long-lasting pain, with the same localization, but these attacks could last from 30 seconds to one hour, and were generally accompanied by tearing of the right eye, homolateral rhinorrhea and polyuria.

Neurological examination was normal. Both CT with intravenous contrast and MRI, as well as angiography, showed a vascularmalformation of the cerebellopontine angle.

1-14-12 CLUSTER-TIC SYNDROME

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Cluster-Tic syndrome (CTS) causes trigeminal neuralgia (TN) like pains and cluster headache (CH) like headaches. The disorder is considered to represent the coexistence of both diseases, TN and CH. This paper reports on 10 new CTS cases. Standard studies including questionaires, CT,MR,and blink-reflex studies were carried out. Clinical findings were compared to those found in 120 CH and 139 TN typical cases. In adition to TN and CH like pains, 9 CTS patients also had a third type of pain attack which should be considered pathognomonic for this condition. It started as a neuralgic pain inmediatedly followed by a homolateral headache accompanied by autonomic signs. All pains were provoked by similar manoeuvers. Clinical symptoms toghether with age at onset and sex of patients make CTS different from any other condition already described. The disorder is undoubtedly due to a trigeminal lesion of unknown level. The existence of different types of pain can be related to the involvement of both, myelinated and unmyelinated trigeminal sensory fibers in CTS.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-14-13 HEMOSTATIC VARIABLES, ANTIPHOSPHOLIPID ANTIBODIES AND MIGRAINE.

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Increased prevalence of atherosclerotic related diseases and ischemic stroke has been reported in migraineurs. To verify whether a hypercoagulable state exists in migraine, plasma levels of thrombin-antithrombin complex (TAT), prothrombin fragment 1+2 (F1+2), fibrinogen (FNG), D-dimer (DD), IgG and IgM anticardiolipin antibodies (aCL) and lupus anticoagulant (LA) were determined in 20 patients (13 females, 7 males; mean age 29±14 yrs, range 15-50) with recurrent headache and in 20 age and sex matched controls, TAT and F1+2 plasma levels were significantly higher in migraneurs ($p<0.01$), as well as IgG and IgM aCLs ($p<0.02$). LA was constantly absent. Increased levels of TAT and F1+2 suggest that the coagulation system is in a state of activation in migraineurs, at least in the initial phase. A prospective study is needed to verify whether markers of increased thrombin generation and aCL may help identify migraineurs at risk for stroke.

1-14-14 GAP IN MIGRAINE WITH AURA. IMPLICATIONS IN PHYSIOPATHOLOGY.

I Legarda (1), JN Blau (2), A Macgregor (2), W Laughey (2) and JM Martínez-Lage (1).

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Diagnostic criteria for migraine with aura in the International Headache Society Classification mention that headache can follow aura with a free interval of less than 60 minutes.

Blau reported recently a retrospective study of twenty five migraineurs who had noted a gap; twenty two of them reported some symptoms during this interval.

Now, we report a prospective study of twenty six migraineurs with aura who attended the City of London Migraine Clinic during September and October 1992. All of them were asked about the gap and the symptoms during it. 13 patients (50%) had noted a gap and 10 of them (76%) reported symptoms such as disturbances of speech or thought, alterations in mood, somatic sensations and other feelings and sensations which they found difficult to describe. In four patients these symptoms persisted during the headache phase.

These results support the retrospective study by Dr. Blau and they are in accordance with disfunction of the whole brain early in the attack. These findings permit new approaches to the understanding of the physiopathology of migraine.

1-14-15 VALPROATE AS MIGRAINE STABILIZATION THERAPY

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A prospective controlled study was conducted using Valproate in the treatment of migraines without and with aura as well as tension type headaches. 150 patients were included between the ages of 8&82 years for a period of 4 years. 16 patients dropped out either because of side effects or noncompliance. Of the 134 patients 102 (76%) patients experienced significant improvement in severity and frequency of headaches. 12 (9%) experienced only moderate improvement. 20 patients (15%) showed no improvement. Valproate was given in the doses of 500 mgs. to 2000 mgs. a day in divided doses for a period of at least six months. Weight gain, nausea and tremors were the most common side effects. A blood level of at least 60ug/ml but no greater than 100ug/ml was maintained. Appropriate blood tests to monitor side effects were done periodically. In conclusion Valproate is an important addition to the drugs that can be used in the prophylaxis of migraine and tension type of headaches. This study revealed a 76% improvement. Further double blind controlled studies will probably help confirm this observation.

1-14-16 BASILAR MIGRAINE: UTILITY OF THE DIAGNOSTIC CRITERIA

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Basilar migraine is a unique type of migraine and is difficult to differentiate from seizure or vertebrobasilar insufficiency because of its common symptoms of loss of consciousness, stereotyped aura, and frequent brainstem syndromes. So we investigated the clinical utility of the diagnostic criteria proposed by the International Headache Society (1988).

We investigated 14 patients with basilar migraine. Thirteen of them were female and mean age was 23.8 years (± 14.7 years). Mean duration of illness was 38 months (± 4.3 months), and mean follow-up duration was 12.3 months (± 9.8 months). Most common presenting symptoms were vertigo, visual symptoms, decreased level of consciousness, and ataxia in decreasing order. Among them, visual symptoms and vertigo frequently occurred during aura phase but decreased level of consciousness and ataxia were frequent symptoms during ictal period. Decreased level of consciousness not necessarily accompanied complete loss of consciousness (60%). Neuroimaging studies were fruitless in nine out of 10 patients but interictal EEG revealed abnormalties in half of patients and focal epileptiform discharges were detected in two patients. More detailed diagnostic criteria are needed.

1-14-17 VALIDITY OF A QUESTIONNAIRE IN THE DIAGNOSIS OF MIGRAINE

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The Headache Classification of the International Headache Society provides operational diagnostic criteria for migraine that could be used in a questionnaire for epidemiological studies. We have performed a national population-based study to know the prevalence of migraine and have designed a study to know the validity of the questionnaire versus a clinical interview.

320 people were interviewed at home by professional interviewers using a structured questionnaire based on the operational criteria of the IHS. The same patients were interviewed and examined by neurologist and the result of this clinical interview was used as an index of validity.

Sensitivity and specificity values, predictive value and kappa index were 19%, 94%, 62%, (PV positive), 71% (PV negative) 16% respectively for those patients with migraine complying strictly with IHS criteria. For patients with "borderline" migraine (at least, five attacks with three of the four characteristics defined by IHS) the results were 30%, 88%, 54% (VP positive), 72% (VP negative) and 19% respectively.

The values of the accuracy and concordance index show that interviews not performed by clinicians, even using the IHS criteria in the questionnaire, are not a satisfactory tool in diagnosing migraine.

1-14-18 SOLITARY EOSINOPHILIC GRANULOMA (EG) OF THE SKULL. CLINICAL PRESENTATION AND FOLLOW-UP.

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In this study we review the clinical presentation, treatment and follow-up of EG in a group of 13 patients.

5 women and 8 men, with ages ranging from 9 to 35 years (average: 21.7), were included in the study.

Headache was the cardinal manifestation in all patients. All reported a characteristic headache: constant, intense, dull, oppresive pain located in one spot of calvarium and intensified with minimal pressure or friction. On examination, a soft mass with a hypersensitive area, without evidence of inflammation on the scalp was observed. Time from the initial headache to diagnosis ranged from 12 to 60 days (mean: 26). The diagnosis was confirmed by radiographs, CT-scan and radionuclide bone scan. All patients were operated with apparent total extirpation of involved bone and then treated with radiotherapy (total dose: 8.0 Gy). Patients were followed up for 2-8 years (mean: 4.4). One patient had a local recurrence. Two had a distal recurrence (costal and pelvic).

We emphasize the importance of the clinical presentation for diagnosis: young man with recent, localized, dull headache with a soft very hypersensitive mass on examination. We haven't observed any local recurrence with surgical resention followed by local radiotherapy.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-14-19 CATECHOLAMINE RESPONSES TO EXERCISE IN MIGRAINE

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The influence of exercise on catecholamine (CA) excretion was studied in 23 migrainous patients and 20 control subjects. In migrainous patients exercise induced constantly a rise in epinephrine (E) excretion and a depression in norepinephrine (NE) excretion, while in control subjects opposite changes, i.e., a rise in NE and a depression in E excretion. The abnormal E release produced in migrainous patients by exercise was also noted in them after high luminosity exposure. As both conditions may precipitate a migraine attack the abnormal CA release of migrainous patients may play a part in the pathogeny of their affection.

1-14-20 GLIOSIS OF BRAIN IN THE MIDDLE CRANIAL FOSSA REGION AS A POSSIBLE CAUSE FOR TRIGEMINAL NEURALGIA

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Trigeminal neuralgia is characterised by the lancinating paroxysms of pain within the territory of innervation of trigeminal nerve, lasting for a few seconds to minutes and usually triggered by stimulation of the face. In this case study of 2 cases of atypical presentation of headache, diagnosis could be confirmed by therapeutic trial of carbamazepine. The presentation of headache did not conform to the classical picture of trigeminal neuralgia in the longer duration of pain and fixed periodicity. Both the cases were thoroughly investigated for the cause of headache. The findings in the CT head scan suggested that gliosis (degenerative phenomenon of excessive growth of neuroglial tissue) of the brain in the region of middle cranial fossa in both the cases could be the central pathology leading to the trigger of trigeminal neuralgia. This is possible as gliosis occurring in middle cranial fossa region leads to irritation of adjacent cortical neurons which by virtue of their connections with sensory trigeminal nuclei of contralateral side via the collateral branches and secondary affarent trigeminal neurons triggers trigeminal neuralgia.

1-14-23 FLUNARIZINE PREVENTS ICE-CREAM AND COOL PRESCIPITATED HEADACHES

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Calcium channel-blocking agents are a well known prophylactic treatment of migraine and other vascular headaches. Pathophysiology of cool-induced and ice-cream headaches is not well known, although a vascular mechanism has been proposed. We report two such patients in whom flunarizine prevented headache. A 21-year-old woman developed a severe throbbing left perocular headache with nausea and photophobia about 5 minutes after swimming in cold water. She had been doing this since she was sixteen and gave up this practice because of headache. She could practice other exercises without headache. Flunarizine 10 mg at bed time during summer months solved this problem. A 10-year-old boy presented a frontal headache about 1 minute after ice-cream eating. A trial of flunarizine 5 mg sublingual ten minutes before ice-cream eating had an excellent response.

1-14-24 ORAL SUMATRIPTAN 100 MG IN THE TREATMENT OF ACUTE MIGRAINE A MULTI CENTRE OPEN STUDY OF 70 PATIENTS

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70 patients satisfying the International Headache Society's diagnostic criteria for migraine with and without aura, were recruited to take 100 mg sumatriptan orally for acute migraine. There were 36 female and 34 male patients with a mean age of 30.8 ± 11.7 years. Fifty one of these patients were Chinese and 36 had migraine without aura. Each patient kept a headache diary and graded headache severity from grade 1(mild) to 3(severe). A satisfactory treatment response was taken to be reduction of headache severity from grades 2 or 3 to grade 1 or 0.

A total of 543 individual headache episodes were recorded and treated during the study period. 45 of these episodes required rescue medication despite sumatriptan. Of the 281 headache episodes graded as severe, 42.3% responded favourably by 2 hours and 72.9% at 4 hours after treatment. For grade 2(moderate) headaches, 71.1% and 89.1% of the headaches had responded at 2 and 4 hours respectively. Associated symptoms of nausea, photophobia and phonophobia also improved, albeit less markedly. 14 patients reported adverse events with the majority(9) having drowsiness and 2 curiously developing thirst.

We conclude that oral sumatriptan 100 mg is an effective treatment for acute migraine headaches. Adverse effects were generally mild and self limiting in nature.

1-14-25 THE BURDEN OF MIGRAINE

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The burden of migraine was assessed in terms of direct, indirect and human costs. Direct and indirect costs were measured in a survey of over 600 patients who met International Headache Society criteria for migraine. Nearly half of the respondents reported attending an emergency room or an urgent care center for treatment of their migraine and over 90% reported at least one clinic visit, during the previous 12 months. The mean direct cost for migraine-related healthcare resource use was $817 per patient per year. In the four weeks previous to the survey, just over half the working patients missed 2.2 days of work, and nearly 90% worked a mean of 5.6 days with 57% productivity because of migraine symptoms. The weighted average monthly cost of lost labor was estimated to be $438 - $572 for men and $264 - $300 for women ($5.6 - $17.2 billion extrapolated to the U.S. migraine population).

The burden of migraine in quality of life terms was assessed using the Medical Outcomes Study Short Form-36. The QOL profile for migraineurs was significantly lower on all measures than a healthy population sample. The pain and physical disability observed exceeded that for CHF; the emotional disability was second only to that reported for depressive disorder. Migraine appears to be a condition of physical morbidity with consequent social and role disability. The burden of this illness tends to fall not on the health care system, but on patients and employers.

1-14-26 CARDIOVASCULAR REFLEXES IN PATIENTS WITH CLUSTER HEADACHE.

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To investigate autonomic nervous system involvement in cluster headache (CH), we compared the cardiovascular reflex responses of CH subjects to a group of controls.

The Valsalva manoeuvre, deep breathing test, sustained handgrip test and orthostatic test were performed in a group of 7 patients of both sexes aged 29 to 62 years (average age 41.3 years) and in an age-matched control group of healthy volunteers. Data were acquired and processed by an IBM PC/AT-compatible computer.

Diastolic blood pressure increase and heart rate increase during orthostatic test were significantly reduced in the headache group when compared to the control group, while the results of the remaining tests were not significantly different.

Our data confirm an autonomic, predominantly sympathetic dysfunction.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-14-27 THE EPIDEMIOLOGY OF MIGRAINE: A UNIFIED IMAGE

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There has been heightened interest in migraine epidemiology research since the publication of the 1988 International Headache Society criteria. Much of the recent research has focused on determining population prevalence, but a large body of research is evolving concerning the impact of the disease in particular patient groups usually measured in terms of decreased productivity and cost. Studies have appeared examining the co-existence of migraine with other diseases. Similarly, further research has been conducted to explore the genetics of migraine.

This poster presentation attempts to assimilate the data from current epidemiology studies and place their findings into a unified, graphic representation of migraine epidemiology. Emphasis is placed on the descriptive epidemiologic data on prevalence, incidence and demographics as current research has afforded us a broader and more systematic view of the magnitude of the disease. Work describing the relationship of migraine to socioeconomic status (SES) is also presented as is data regarding the relationship of migraine to other headache syndromes, and psychiatric and clinical disease. The impact of migraine on populations is also incorporated as it provides compelling evidence of the population-level impact of this disease.

1-14-28 SUMATRIPTAN: EFFECT ON VASCULAR TONE AND SENSORY NEUROTRANSMISSION IN ISOLATED CEREBRAL ARTERIES

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The anti-migraine agent sumatriptan is a selective agonist for a subtype of receptor (at present called a vascular 5-HT_1 receptor) that mediates vasoconstriction predominantly within the cranial vasculature. Sumatriptan contracts dog, monkey and human isolated basilar artery via activation of 5-HT_1 receptors on the vascular smooth muscle. In guinea-pig isolated basilar artery, we have attempted to chemically activate perivascular sensory nerves to cause relaxation. Preparations were precontracted with PGF_{2a} and changes in isometric tension recorded. Experiments were performed in the presence of atropine (3mM) and guanethidine (3mM) to block cholinergic and sympathetic nerve mediated responses. Capsaicin (0.1-100nM) and nicotine (100mM) caused relaxations of guinea-pig basilar artery. These responses were significantly blocked by prior exposure to capsaicin indicating that sensory nerves were involved. Capsaicin-induced relaxations were blocked by the CGRP receptor antagonist, $CGRP_{8-37}$ (1mM), but not by the NK_1 antagonist, GR82334 (10mM) whilst the reverse was the case for nicotine, suggesting that relaxations were mediated via CGRP and substance P respectively. Sumatriptan (0.3-3mM) had no effect on capsaicin-induced relaxations of guinea-pig basilar artery. However sumatriptan (0.3mM) significantly inhibited nicotine-induced relaxations (-47 $\pm$ 7% and -20 $\pm$ 5% relaxation before and in the presence of sumatriptan respectively, $P<0.05$, $n=8$). These data may reflect an inhibitory effect of sumatriptan on trigeminal sensory neurotransmission.

1-14-29 CONCORDANCE OF HEADACHE IN MONOZYGOTIC AND DIZYGOTIC TWIN PAIRS RAISED TOGETHER AND APART

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To clarify the genetic component of headache syndromes, a standardized interview concerning providing details of headache history was administered to 257 pairs of twins, 192 raised together (TG), 65 raised apart (AP). Variables were grouped to diagnose migraine with aura (MA), without aura (MW), and non-migrainous headache (NM) according to criteria of the International Headache Society (IHS). Concordance for each diagnostic group was studied in monozygotic (MZ) vs dizygotic (DZ) pairs. Concordance of migraine with aura was not increased MZ vs DZ TG pair (5, 4.3% vs 8, 14.0%) nor in AP pair (0 vs 2, 6.5%). Concordance of MW, however, was significantly more concordant in MZ TG pair (16, 13.8% vs 1, 1.87%. p. = 0.012). AP twins also had suggestion of greater concordance for MW but numbers were small (3 vs 1). Concordance for any type recurrent headache was not significantly increased in MZ over DZ pairs (37.1% vs 28.1%).

Data suggests that MW (as defined by IHS criteria) has a strong genetic component, but that MA does not and further supports the concept of these being different syndromes. Data further does not support importance of a genetic component in the tendency to non-migrainous recurrent headache.

1-14-31 HEADACHE, TRANSIENT NEUROLOGICAL DEFICITS AND CSF PLEOCYTOSIS: AN UNDERDIAGNOSED BENIGN SYNDROME

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We have previously reported two patients with one or two attacks of transient neurological deficits and headache, accompanied by CSF pleocytosis (Headache 25:271,1985). Since then, we have encountered three further patients with a similar syndrome. All five (three females) were young (15-39y) with no history of headaches or migraine. Their illness began with transient hemispheral neurological deficit (hemiparesis in two, hemihypesthesia in two, dysphasia with dyslexia in one) accompanied or followed by non-pulsating, bilateral headache, sometimes also by nausea, without photo- or phonophobia, fever or meningeal signs. The neurological symptoms disappeared in a few hours, but in three a new episode with the same symptomatology recurred within the next two days. The headache persisted for less than 48h. Lumbar puncture, performed during the period of neurological deficit or headache in all patients, revealed a lymphocytic pleocytosis of 16-350 cells/mm^3.

Clinically, all patients were similar, thus they may constitute a rarely recognized entity. The headache did not have many of the usual migraine characteristics and there were no recurrencies during a long follow-up period (1-7y, mean 5y).

1-14-32 LONG-TERM TOLERABILITY AND SAFETY OF SUMATRIPTAN DURING A 2-YEAR PERIOD

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Two multinational, multicentre, open studies investigated the long-term tolerability and safety of multiple-dose subcutaneous and oral sumatriptan in the acute treatment of migraine.

Patients treated all migraine attacks at home during a 2-year period. Each attack was treated as soon as possible after symptom onset. In the subcutaneous study, patients self-injected 6mg sumatriptan and could take a second sumatriptan injection after one hour for inadequate symptom relief. Rescue medication was permitted after 2 hours if the headache had not resolved. In the oral study, patients treated each attack with up to 3 sumatriptan 100mg tablets during a 24-hour period, with at least 2 hours between each dose. The first 2 doses were used to treat the initial migraine symptoms and rescue medication was available after 4 hours if the headache had not resolved. A third dose was available to treat headache recurrence. The primary endpoint was the tolerability and safety of sumatriptan.

During the 2-year study period, some 14,000 attacks have been treated with subcutaneous sumatriptan and almost 12,000 with oral sumatriptan. Full tolerability and safety results will be presented.

1-14-33 A DIARY STUDY TO MONITOR SUMATRIPTAN IN CLINICAL PRACTICE

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This multinational diary study represented the first opportunity to investigate sumatriptan use by patients in clinical practice. It monitored the headache attacks experienced by patients over 5 months, investigating their nature, the treatment taken and its efficacy. All patients had been prescribed sumatriptan, but had other treatments freely available to them.

100 migraine patients were recruited in each country via their general practitioners. To ensure an objective assessment of their opinions, patients did not know that this was a study of sumatriptan.

Patients were initially interviewed and completed a questionnaire detailing their headache patterns. They were then given diaries to complete over the following 5 months every time they experienced a headache which interrupted their routine or required medication. The diary collected information about the nature and resolution of the attack, together with detailed information about all drugs taken. At the end of the diary period, patients were interviewed and completed a follow-up questionnaire detailing their experience with sumatriptan: efficacy, acceptability, side-effects and comparison with previous medications; and effect on quality of life.

Results are analysed to evaluate changes in headache patterns and treatment of attacks during the 5-month period, and how patients used sumatriptan in relation to other therapies.

1-14-34 THE EFFECT OF FOOD ON THE PHARMACOKINETIC PROFILE OF SUMATRIPTAN

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The rate of oral drug absorption is generally reduced in the presence of food, as a result of delayed gastric emptying, which may often be present in migraine. Patients may need to take sumatriptan at any time of the day for the acute treatment of migraine, and any sizeable reduction in its rate or extent of absorption may be undesirable.

This open, randomised, 2-way crossover study compared the bioavailability of sumatriptan under fed and fasted conditions. 12 healthy male subjects received oral 200mg sumatriptan following a standard breakfast and following an overnight fast, with at least 3 days between the treatments. Blood samples were taken before treatment and at intervals up to 13 hours after treatment. Mean sumatriptan pharmacokinetic parameter values were calculated for the two treatments. Safety and tolerability were assessed.

Sumatriptan pharmacokinetic parameters were similar in the fed and fasted states. There was a tendency for food to delay the time to maximum plasma concentration (t_{max}), but this did not reach statistical significance. Sumatriptan was well tolerated, with adverse events being similar to those reported previously.

The pharmacokinetic profile of sumatriptan is unchanged after food.

1-14-35 SUBCUTANEOUS SUMATRIPTAN IN THE ACUTE TREATMENT OF MIGRAINE

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Sumatriptan has been developed as an acute treatment for migraine when given by subcutaneous injection, in a series of large, international, placebo-controlled clinical trials.

A 6mg dose had the optimum efficacy to safety profile. Headache relief (improvement in headache from moderate or severe to none or mild) with the 6mg dose was rapid, commencing within 10 minutes. Significantly more patients ($p<0.001$) reported headache relief on sumatriptan than on placebo one hour (72% v 25%) and 2 hours (86% v 37%) after a single dose. Maximal improvement was seen at 2 hours. Administration of a second dose of sumatriptan did not increase the response seen after a single dose. However, a second dose effectively treated headache recurrence, which is reported by up to one third of patients.

Efficacy was similar when subcutaneous sumatriptan was administered by a physician in the clinic or by the patient at home using an autoinjector. Subcutaneous sumatriptan was generally well tolerated.

An initial dose of 6mg sumatriptan given by subcutaneous injection is an effective and well tolerated acute treatment for migraine. When needed, a further dose effectively treats headache recurrence, permitting a flexible and convenient regimen for clinical use.

1-14-36 ORAL SUMATRIPTAN IN THE ACUTE TREATMENT OF MIGRAINE

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Sumatriptan has been developed as an acute treatment for migraine, in a series of large, international, controlled clinical trials.

When oral doses of 25-300mg were evaluated, the 100mg dose had the optimum efficacy to safety profile. Headache relief (improvement in headache from moderate or severe to none or mild) with the 100mg dose was rapid, commencing within 30 minutes. Significantly more patients reported headache relief on sumatriptan than on placebo 2 hours after a single dose (51% v 31%, $p<0.01$) and 4 hours after one or two doses (71% v 35%, $p<0.001$). Maximal improvement was seen after 4 hours. Sumatriptan effectively treated the non-headache symptoms of migraine. Routine administration of a second dose did not offer additional benefit. However, in the event of headache recurrence, a second dose was significantly more effective than placebo (70% v 30% of patients, $p>0.001$). Oral sumatriptan was more effective than two other commonly used oral acute combination therapies for migraine; 2mg ergotamine plus 200mg caffeine and 900mg aspirin plus 10mg metoclopramide. Oral sumatriptan was generally well tolerated, adverse events were transient and self-limiting.

100mg oral sumatriptan is an effective and well tolerated acute treatment for migraine. A second 100mg dose is effective in the event of headache recurrence.

1-14-37 INTRANASAL SUMATRIPTAN IN THE ACUTE TREATMENT OF MIGRAINE

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Intranasal administration may offer useful benefits to some migraine patients, due to rapid absorption and ease of administration.

In an initial study, intranasal sumatriptan (20mg plus 20mg) was significantly more effective than placebo in the relief of migraine headache after 2 hours (75% v 32% of patients, $p<0.001$).

A multinational, multicentre, double-blind, placebo-controlled, parallel-group trial was set up to define the optimal intranasal dose of sumatriptan. Patients treated a single migraine attack with placebo or 1, 5, 10, 20 or 40mg sumatriptan, administered via one nostril. The primary end point was headache relief (improvement in headache from moderate or severe to none or mild) after 2 hours. 5, 10, 20 and 40mg sumatriptan were all significantly more effective than placebo in the relief of headache after 2 hours. The best response was reported after the 20mg dose (78% headache relief and 43% pain free, 35% and 13% for placebo, respectively). Significant relief was reported within 30 minutes after the 20mg and 40mg doses. Sumatriptan was generally well tolerated. Administering the dose via two nostrils (in a second trial) did not improve the response reported after single nostril administration.

Intranasal sumatriptan is a rapidly effective and well tolerated acute treatment for migraine. A further definitive single nostril, dose-ranging study will be undertaken.

1-14-38 LONG-TERM EFFICACY OF SUBCUTANEOUS SUMATRIPTAN USING A NOVEL SELF INJECTOR

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This multicentre, open study investigated the long-term efficacy, safety and acceptability of subcutaneous 6mg sumatriptan administered using a novel cartridge-system self injector in the acute treatment of migraine.

Patients treated all migraine attacks for 6 months at home with subcutaneous 6mg sumatriptan. A second identical injection was available after 1-24 hours for inadequate relief, or headache recurrence, and rescue medication could be taken from one hour after the second dose.

The primary endpoint was headache relief (improvement from moderate or severe to none or mild headache) reported one hour after the first injection. The acceptability of the device to patients and safety and tolerability were assessed.

80 patients treated 1566 attacks (median 18 per patient); of these, 69 patients completed the 6-month treatment period. Overall, headache relief one hour after the first injection was reported in 77% of attacks. The device was well accepted by patients; 84% found it easy to use and 92% wanted to take the medication again. Adverse events were similar to those seen previously with sumatriptan.

Sumatriptan is an effective and well tolerated long-term acute treatment for migraine when administered subcutaneously using a novel self injector.

1-14-39 INTENSIVE ECG SURVEILLANCE AFTER TREATMENT WITH SUMATRIPTAN

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Chest symptoms (including tightness, heaviness or pressure) are reported after 2-5% of migraine attacks treated with sumatriptan. It has been suggested that they may be symptoms of asthma or ischaemia, though extensive clinical data do not support this.

During clinical trials, ECG monitoring in over 6,000 migraine patients has shown no evidence of myocardial ischaemia following subcutaneous and oral sumatriptan. ECG changes following sumatriptan have been prospectively investigated in an open study. 67 patients treated a migraine attack with oral 100mg sumatriptan and ECGs were recorded at least hourly for a minimum of 3 hours after treatment. There were no ECG changes suggestive of ischaemia after treatment.

A multinational, multicentre, single-blind, controlled study rechallenged migraine patients who had previously noted chest symptoms after sumatriptan. 20 patients received subcutaneous injections of placebo followed after one hour by 6mg sumatriptan. After rechallenge, 3 patients (15%) reported chest symptoms after sumatriptan, and 2 of these 3 patients reported similar symptoms after placebo. Continuous ECG monitoring showed that the chest symptoms were not associated with ECG abnormalities.

Chest symptoms are reported inconsistently after treatment with sumatriptan and there is no evidence of associated ECG abnormalities. In a further ongoing study, healthy subjects are receiving subcutaneous 16mg sumatriptan, with continuous Holter ECG monitoring during any chest symptoms. Full results will be presented from this study.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-16-01 IN SITU PCR IN HTLV-I MYELOPATHY.

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The pathogenesis of HTLV-I associated myelopathy (HAM) is unknown but may be related to high viral load and auto-immune tissue damage. An accurate estimation of the number of HTLV-I infected cells and the proportion expressing viral RNA in vivo, is therefore important in understanding pathogenesis and also to monitor the efficacy of new anti-viral therapies. This has not been previously possible as latent proviral DNA could not be detected in intact cells. We used the new technique of in situ PCR to amplify a fragment from the tax gene of HTLV-I in peripheral blood mononuclear (PBMN) cells from 11 HAM/TSP patients, 4 HTLV-I carriers and 3 sero-negative individuals. PBMN cells from the same individuals were also analysed for HTLV-I tax RNA by in situ hybridisation. The percentage of infected PBMN cells ranged from 1.1% to 8.6% in carriers (mean 4.9%) and 5.9% to 13.4% (mean 9.4%) in HAM/TSP patients. HTLV-I RNA was detected infrequently in patients and carriers in 1 in 1100 to 1 in 10000 PBMN cells (thus 1 in 700 to 1 in 200 infected cells expressed viral RNA). HTLV-I is present in a latent state in most infected PBMN cells in vivo.Although HAM/TSP patients generally have more infected PBMN cells than carriers, there is no correlation between the number of cells expressing HTLV-I RNA in circulating PBMN cells with occurence or severity of HAM/TSP.

1-16-02 HIV COAT PROTEIN (gp120) NEUROTOXICITY IS PREVENTED BY THE ANTIGLUMATE RILUZOLE IN PRIMARY NEURONAL CULTURES

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Objectives Neuronal degeneration is observed in brains of AIDS patients. Gp120 the HIV coat protein possesses in neuronal cultures toxic properties, which are blocked by NMDA antagonists. We have tested another antiglutamate Riluzole against gp120 toxicity. Riluzole reduces glutamate release from nerve terminals.

Methods Primary cortical neurons taken from embryonic rat were used in this study. These cultures were exposed for 24 hours to gp120 (20 pM) alone, or associated with MK801 (20 µM) or Riluzole (10^{-7} M). Neuronal survival was assessed by cell counts in predetermined fields.

Results The neuronal survival observed after gp120 exposure is 52 ± 10.2 percent. The addition of MK801 blocks the gp120 neurotoxicity (neuronal survival 87.3 ± 2.3 percent compared to control cultures without gp120 : 84.5 ± 4.9 percent). Similarly Riluzole also prevents the gp120-induced neuronal degeneration (neuronal survival 83.7 ± 5.6 percent).

Conclusion The antiglutamate Riluzole reverses gp120-induced neuron death in cell cultures and could represent a useful pharmacological agent in AIDS-affected patients.

1-16-03 NEUROLOGICAL COMPLICATIONS OF INFECTIVE ENDOCARDITIS

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We reviewed the files of 77 successive patients with native and prosthetic valve endocarditis admitted to Riyadh Armed Forces Hospital. Neurological complications occurred in 25 (32%) patients. The valves involved were native mitral valve in 9 (36%), prosthetic aortic valve in 4 (16%), native aortic valve in 5 (20%), prosthetic aortic valve 3 (12%), combined mitral and aortic lesions in 2 (8%) and others in 2 (8%). Common organisms were streptococcus faecalis in 4 (16%), staphylococcus aureus in 4 (16%); staphylococcus epidermidis in 3 (12%); and streptococcus viridans in 2 (8%); other organisms were less common. Compared to the 52 infective endocarditis patients without neurological complications, the complications occurred more frequently in male patients, in those with mitral valve lesion, those with atrial fibrillations and when the infective organisms were streptoccocal faecalis, staph aureus and staph epidermidis. 8 patients died (32%), 10 (40%) recovered with motor sequelae, 8 (32%) of them also had seizure disorder, and 7 (28%) had full recovery. The incidence of neurological complications and mortality is higher than reported in the literature which can be explained by the fact that the hospital has an advanced cardiac centre with many referrals of complicated cases from other units in the Kingdom.

1-16-04 CEREBRAL PERFUSION DYNAMICS IN ACUTE AND POSTACUTE MENINGOENCEPHALITIS

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In a three year period 110 patients with CNS infections of various etiology were examined serially by means of transcranial Doppler sonography (TCD). The M1-Segment of the middle cerebral artery (MCA) was examined on a daily basis. In viral induced infections no changes of flow velocity were seen whereas in bacterial meningitis a significant increase of blood flow velocity in the MCA was recorded (Student's t-test $p < 0.05$). Its extent was mainly associated with the type of the infectious agent, most frequently observed in pneumococcus meningitis (77 %). The increase was up to 100 % of the baseline values and was reversible in all cases. In a second phase of our study eight more patients suffering from bacterial meningitis underwent HM-PAO SPECT examinations, both during the acute phase - associated with highest TCD velocity values - and the postacute phase when flow velocities had returned to normal values. Focal cerebral hypoperfusion (5 cases) and normoperfusion (3 cases) were detected during the acute phase and normal SPECT-scans in the follow-up examination in all cases. These data point to a pathophysiologic process leading to lumen narrowing of the basal cerebral arteries during the acute phase of bacterial meningitis.

1-16-05 SCRAPIE-INDUCED INCREASE IN ACIDIC FIBROBLAST GROWTH FACTOR IN THE HAMSTER BRAIN.

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In the current study, we investigated the relationship between acidic fibroblast growth factor (aFGF) and astrocytosis in scrapie-infected hamsters(SH). Female, weanling Syrian hamsters, strain LVG/LAK, were injected intracerebrally with either normal hamster brain homogenate or scrapie strain 263K or 139H. Sections from SH and control hamsters (CH) were examined with histological and immunocytochemical staining. By using antibodies for aFGF and glial fibrillary acidic protein, we observed a low level of aFGF immunoreactivity (ir-aFGF) in the ependymal cells and a few neurons in the hypothalamus of CH. In contrast, there was intense ir-aFGF in neurons, astrocytes, pericytes, and ependymal cells in SH. ir-aFGF was located primarily in the cortex, hippocampus, thalamus, hypothalamus, and fimbria and around the pia mater, ventricles, and blood vessels in SH. We also found extensive astrocytosis in these areas. Our results suggest that astrocytes can produce and/or absorb aFGF during scrapie infection. These findings indicate that aFGF might play an important role in astrocytosis in SH.

1-16-06 PRESENCE AND THE SEQUENCE OF HTLV-I PROVIRAL DNA IN THE CENTRAL NERVOUS SYSTEM OF PATIENTS WITH HTLV-I-ASSOCIATED MYELOPATHY

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The polymerase chain reaction (PCR) method was used to determine the presence of human T-lymphotropic virus type I (HTLV-I) proviral DNA in the central nervous system (CNS) tissues of 6 patients with HTLV-I-associated myelopathy (HAM), 1 adult T-cell leukemia (ATL) patient with CNS infiltration of leukemic cells, and 9 controls with other neurological diseases. The HTLV-I pX and env but not pol DNA were detected in the CNS tissues from 5 of 6 HAM patients. The ATL sample showed the positive signals on the pX, env and pol PCR. None of the control samples constantly showed positive signals on HTLV-I PCR. The quantitative PCR method combined with histological studies revealed that the amount of HTLV-I pX DNA were greater in the HAM samples than in the ATL sample, although the extent of mononuclear cell infiltration was far less in the HAM samples than in the ATL sample. The nucleotide sequence analysis of the pX PCR products (6549-8294) confirmed the HTLV-I sequence of the amplified DNA with several nucleotide substitutions. Therefore, HTLV-I may be present in the constituent cells of the CNS as well as in the infiltrating cells in HAM.

1-16-07 CT AND MRI IN JAPANESE ENCEPHALITIS.

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CT and MRI findings of Japanese Encephalitis(JE) have not been well documented, although histopathological changes are known to be localized largely to the gray matter with greatest involvement in the thalamus and brainstem. We reviewed the clinical, CT, and MRI findings in 10 patients with serologically diagnosed JE who had focal neurological symptoms and signs. CT scans demonstrated low density areas in the thalamus, basal ganglia, and midbrain in 4 patients. They were noted to have a mixture of pyramidal and extrapyramidal dysfunction. In 1 patient with quadriplegia and extrapyramidal signs, T2-weighted MRI showed multiple areas with high signal intensity in the thalamus, basal ganglia, substantia nigra, and pons. Also petechial hemorrhages were seen in the thalamus and cerebral cortex. The distribution of lesions on CT and MRI was compatible with the pathologic findings of JE. Therefore, CT and MRI may provide valuable informations in clinicopathologic correlation of JE.

1-16-08 SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE): EARLY DIAGNOSIS, PROGNOSTIC FACTORS AND NATURAL HISTORY

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We studied the value of long video-split electroencephalographic monitoring (VSEEG) in detecting myoclonus in early SSPE and evaluated the natural history and outcome-affecting factors. 32 newly diagnosed patients had 3 hours VSEEG to detect myoclonus and its correlations with EEG periodic complexes. Disease-progression was monitored by a special "outcome" score; the chi-square test and multi-variable statistics analysed the outcome score in relation to different variables such as age at onset, sex, duration of symptoms at presentation, CSF measles antibody titre, type of and interval between EEG discharges. Myoclonus (segmental) or subtle atonia occurred in all patients and was time-related to the EEG periodic complexes. In 32% of patients this was missed clinically. The EEG periodic complexes were of 3 types: Type I (16 patients) periodic giant delta waves; Type II (10 patients) periodic giant delta waves intermixed with rapid spikes or fast activity; and Type III (6 patients), long spike-wave discharges interrupted by giant delta waves. Outcome score was associated with symptoms duration ($p<0.01$) and EEG discharge type ($p<0.05$). Symptom duration was inversely related to final outcome (multivariable analysis). Long VSEEG monitoring greatly improves early diagnosis and detection of atonia or myoclonus. Prognostic factors were type of EEG discharges and duration of symptoms at presentation.

1-16-09 INVESTIGATIONS ON THE COURSE OF ACUTE BACTERIAL MENINGOENCEPHALITIS

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104 patients were investigated who had suffered from bacterial meningitis (n=34) or from bacterial meningoencephalitis (n=70). Letality was 23% in meningoencephalitis and 7% in patients who only showed signs of bacterial meningitis. The patients who survived were examined more than 6 months after the acute disease. 46 patients answered to a questionaire, 30 patients came to an out-patient examination including neurological examination, neuropsychological testing, EEG and HmPAO-SPECT-examination of the brain. 30 patients suffering from meningitis without signs of encephalitis also answered to a questionaire asking for remaining complaints.

Surprisingly many patients suffered from perfusion irregularities and defects. 8 of the patients examined did not show pathological results, except for pathological SPECT-findings.

More than six months after the acute disease, 43% of the patients still had mild neurological deficits, 7% still suffered from severe deficits, only half of the patients had a normal neurological and neuropsychological examination. The meaning of the pathological findings and the perfusion irregularities will be discussed.

Although all patients received a combination therapy of 3 antimicrobial agents, many patients still suffered from grave disorders. In spite of the improvement during therapy bacterial meningoencephalitis remains a severe disease with high mortality and frequently remaining' defects.

1-16-10 NON-VACUOLAR MYELOPATHIES IN HIV DISEASE

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Thirty-eight patients with myelopathy, seen over 18 months, were drawn from a population of 488 patients with AIDS, 1015 symptomatic non-AIDS/PGL, 407 well seropositives, 10 with seroconversion illness, and 21 of undetermined status.

Eighteen patients had clinical, radiological and/or pathological data incompatible with a diagnosis of vacuolar myelopathy (VM). All were male homosexuals; median age 34 years (range 21-61), median CD4 count 49 cells/ml, (2-520). Seven had acute myelopathies (H.zoster 2, probable CMV 2, extradural lymphomatous deposits 1, cord contusion 1, undetermined 1). Five had acute myeloradiculopathies (H.zoster 1, CMV 4). One had a subacute myeloradiculitis (CMV). Four had chronic myelopathies (cervical spondylosis 2, undetermined 2), one recovered spontaneously, having had chronic intellectual impairment and myelopathy mimicking VM. One had a hysterical paraparesis. The diagnosis was confirmed pathologically in 2 (H.zoster myelitis, CMV radiculomyelitis).

The annual incidence of non-vacuolar myelopathies in our population was 1.4% in AIDS, 0.5% in symptomatic non-AIDS/PGL and 0.2% in well seropositives. Potentially treatable causes included cervical spondylosis, CMV myelitis/myeloradiculitis and H.zoster myelitis. Subacute/chronic myelopathies should not be diagnosed as VM without adequate investigation. CMV infection was common in acute myelopathy/myeloradiculopathy; concomitant retinitis should be sought for.

1-16-11 SPECIFIC IGG SUBCLASS REACTIVITY IN LYME BORRELIOSIS

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Objective::Characterization of the Borrelia burgdorferi (B.b.) specific IgG subclass response as a potential diagnostic tool to differentiate symptomatic (SI) and asymptomatic infections (AI). Background: In parasitic and viral infections different predominant or restricted subclass patterns were detected in dependence on the disease activity. Methods: 20 untreated patients (neuroborreliosis, acrodermatitis chronica atrophicans (ACA), erythema chronicum migrans) and 20 blood donors with a positive serology were studied. The immunoblot technique and subclass-specific monoclonal antibodies were used. Results: A IgG3 predominant pattern was demonstrated in AI, in contrast to a IgG1 predominant pattern in SI, most significant in ACA patients. Qualitative analysis of the immune response revealed antigens which were patient independent (e.g.: 100 kd (IgG1), 15 kd (IgG3), 12 kd (IgG2)) detected. In contrast antigens (e.g. 61 kd, 30 kd, 18 kd) existed, that were recognized in AI (IgG3) and SI (IgG1) differently. Conclusion: Our findings demonstrate that B.b. posseses antigens that can trigger a patient dependent as well as an independent subclass specific immune response. Therefore, the disease activity dependent subclass patterns in viral, parasitic and B.b. infections might originate from different dominating antigens. With the use of IgG subclass specific ab. currently used assays might be easily improved.

1-16-12 JAPANESE ENCEPHALITIS AND STROKE – LIKE ATTACKS

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In Japan, the incidence of Japanese encephalilitis (JE) has decreased markedly since 1967, however 70 cases of JE per year still occur during the period from August to early September, mainly in Kyushu, southern Japan. In this study, stroke – like attacks in JE were evaluated by clinical charts, risk factors and CT • MRI.

Patients & Methods

Between 1985 and 1991, 20 patients of JE (mean age 63 years) were admitted in summer to our hospital. Serological diagnosis depended on the serological criteria of the research group for JE in Japan. Stroke – like attacks and the risk factors such as hypertension were analysed by clinical charts. CT and MRI were carried out from the acute stage to the convalescent stage.

Results

Six patients had stroke – like episodes, of whom five had acute hemipleqia preceded or followed by JE, and two had hemiplegia or seizure with thalamic hemorrhage during the convalescent stage. CT • MRI revealed main lesions in both thalami, internal capusuls and putamina, with white matter lesions, while these episodes were not correlated to the risk factors in stroke.

1-16-13 CENTRAL NERVOUS SYSTEM PARACOCCIDIOIDOMYCOSIS.

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The aim of this study is to show the experience of the Department of Neurology of São Paulo University Medical School with central nervous system (CNS) paracoccidioidomycosis. In a time period between 1961 and 1992, 34 cases with neuroparacoccidioidomycosis were studied, probably the greatest casuistics, ever published up to now. Clinical aspects, diagnosis and treatment are reported. All the 34 cases have the anatomo-pathological examination. Results allow to conclude: 1) CNS paracoccidioidomycosis, caused by Paracoccidioides brasiliensis, is a fungal disease frequently observed nowdays; 2) this pathology must receive more attention in Tropical Neurology studies; 3) CNS impairment is always secondary, the initial focus is located mainly in the lungs on in pharyngeal mucosa; the yeast reaches CNS by lymphatics or blood; 4) the clinical picture is quite variable and the lesions may be seen in the meninges or in the parenchyma; meningoencephalitic syndromes and mass lesion syndromes are more frequently observed; 5) diagnosis is difficult and biopsy is necessary; 6) treatment must begin early and the drugs of choice are amphotericin B and sulfas.

1-16-14 THE EIGHTH CRANIAL NERVE IN LEPROSY; AN EXPERIMENTAL STUDY.

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In previous studies, humming in the ear of leprotic patients was noticed and studied. Further evaluation of the vestibulocochlear system was recommended. In the present study the bacilary suspension was injected into the feet pads and the ears of fifteen Swiss white mice, five of them were weakened immunologically by total body irradiation. The histopathological findings proved that the eighth cranial nerve seems to be not susceptible to involvement in leprosy; at least on experimental level . Discussion and review of the literature reinforced the idea that leprotic bacilli tend to multiply in relatively cooler tissues and superficially exposed nerves.

1-16-15 CLINICAL NEUROPHYSIOLOGICAL AND RADIOLCGICAL CHANGES IN JAPANESE ENCEPHALITIS (JE)

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Recent advances in neurophysiology and imaging provide a unique opportunity of studying JE. Five patients of serologically confirmed JE whose age ranged between 9 and 47 Y, presented with the symptoms of fever, headache, vomiting and loss of consciousness. The neurological signs included pyramidal (5), cerebellar (1), focal wasting (3), and dysautonomia (2). One patient was unresponsive, one had diencephalic syndrome and 3 had extrapyramidal features which included tremor (2), hypophonia and hypokinesia (3 each). EEG changes in the first week revealed diffuse delta activity which changed to theta after 1 mo and was normal in 3 patients after a mean duration of 2 mo; one patient had alpha coma. Evoked potential studies done in 3 patients revealed normal ABR and SEP. CMCT in upper limbs was delayed in two patients. CT scan of 4 patients showed hypodensity in thalamus (3), Pons (1), haemorrhagic lesion in thalamus (1) and diffuse cerebral oedema (4). MRI of 5 patients revealed mixed intensity lesions in thalamus (5), Pons (2) caudate (1) and spinal cord (1), the latter correlated with MEP and clinical abnormalities. Midbrain including substatia nigra was normal. High frequency of extrapyramidal features may be due to involvement of thalamus and thalamocortical pathway, for motor initiation and programming.

1-16-16 PROGRESSIVE FOCAL LEUCOENCEPHALOPATHY BY JC VIRUS —— AN UNUSUAL TYPE

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A 59-year-old male patient presented in 1991 with left-sided hemiplegia and hemihypesthesia and left homonymous hemianopsia lasting for the preceding 12 months. MRI and XCT revealed a unilateral large well-demarcated lesion extending in the right cerebral hemispheric white matter, and several very small plaques in other areas of the brain. The JC virus hemagglutination-inhibition antibody titers were 1:32 in serum and 1:8 in CSF; the antibody titer ratio and index both suggested an intrathecal antibody production. There was no underlying illness and the patient was not immunocompromised. Pathological examination of a brain biopsy specimen from the large lesion demonstrated profound demyelination with preservation of axons, a large number of macrophages and spotted perivascular lymphocyte cuffings. The JC virus DNA was detected by PCR method in the brain tissue. After 18 months the patient is still alive with the large brain lesion which has spread across the splenium to the other hemisphere.

Based on this experience, we conceive a less progressive, less well developed type of progressive focal encephalopathy occurring in a less or not immuno-compromised subject.

1-16-17 CLINICAL EXPERIENCES OF FLUCONAZOLE MONOTHERAPY IN CRYPTOCOCCAL MENINGITIS: REPORT OF FOUR CASES

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Four patients with cryptococcal meningitis were treated with fluconazole in the past two years at the Department of Neurology, National Cheng Kung University Medical Center. There were three women and one man. Two patients had a history of anemia and one received splenectomy due to hypersplenism. Two patients were healthy before onset of meningitis.

After giving fluconazole 300mg per day, three patients were cured without clinical evidence of recurrence after follow-up lasting from two to seventeen months. One patient died from pneumothorax as a complication of the procedure subclavin vein cannulation. During the treatment course, there was no side effect except on patient had transient elevation of GOT, GPT value which was spontaneously reversible without changes of dosage.

In the three successfully-treated cases, the cryptococcal antigen titers began to decrease after the first week of treatment. Our preliminary experience showed that Fluconazole alone was an effective and safe drug for the treatment of cryptococcal meningitis.

1-16-18 AN EXPERIMENTAL STUDY OF THE ACYCLOVIR RESISTANT HERPES SIMPLEX VIRUS

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Object: We isolated ACV resistant herpes simplex virus (HSV) strains in vitro, and investigated pathogenicity.

Methods: We inoculated virus suspension into the peritoneal cavities of mice. We examined their brains, livers, and spinal cords with histological and virological methods.

Results: YH-L (HSV-1 wild strain) killed almost all mice inoculated with virus more than 10^3pfu. Positive results were aquired from the specimen of the brains. Of the two resistant strains, LA^{r-2} strain makes larger plaques, so it seems more virulent, but it didn't kill the mice. Only, subtle symptoms were observed. The plaque assay didn't detect viruses in the brains. $10^{4.1}$pfu of the viruses per 1g of the tissue were recovered from the liver on the 2nd day after the inoculation. Microscopic examination of HE stained brain tissues disclosed mild infectious changes in the lower parts of the temporal lobes. The brain on the 5th day was positively stained with the ABC method. There were neurons with intranuclear eosinophilic inclusion bodies in the posterior column of the spinal cords. The changes in the spinal ganglia were prominent. We will continue the histological study with in situ hybridization.

Conclusions: Infection of a resistant strain (LA^{r-2}) to the CNS occurs, but pathogenicity was considered evidently weaker than that of the wild strain (YH-L).

1-16-19 NEUROPARACOCCIDIOIDOMYCOSIS(NPCM): CLINICAL AND MORPHOLOGICAL ASPECTS

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We analysed the data of 12 patients with NPCM from HUCFF-UFRJ. They represent 5.76% of all patients with paracoccidioidomycosis(PCM) admitted at our Hospital. The neurological manifestation was the first symptom of the disease in 10(83.3%). Seizures were the most frequent symptom (58.3%). Hemiparesis and intracranial hypertension occured in 16.6%. Syncope and movement disorders were less common (8.3%). The CT scan showed unique lesion in 2 cases (16.6%) and multifocal lesions in 10(83.3%). All of them were a nodular lesion with ring enhancement. In 3 the diagnosis were made by pathological examination obtained from a brain biopsy. It showed meningoencephalitic lesion in 2 cases and pseudo-abcess form in one. We concluded that NPCM is a frequent disease and that all patients with PCM have to be submitted an accurate neurological examination and even a brain CT scan.

1-16-20 RAPID DIAGNOSIS OF TUBERCULOUS MENINGITIS BY POLYMERASE CHAIN REACTION

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Polymerase chain reaction (PCR) method is designed for in vitro enzymatic amplification of a specific segment of DNA. In the present work, PCR method was used to detect any M. tuberculosis DNA in the cerebrospinal fluid specimens from 14 patients clinically diagnosed as tuberculous meningitis. We synthesized two oligonucleotide primers derived from the sequence of a gene that codes for the 65-Kilodalton antigen of M. tuberculosis. The amplified 165bp genomic DNA of M. tuberculosis was detected in 3 patients (21.4%) with polyacrylamide gel electrophoresis. Subsequent southern blot analysis confirmed these mycobacterial DNAs and detected another amplified DNA (28.6%) that was not seen on the polyacrylamide gels.

Conventional detection methods including smear and culture for M. tuberculosis showed these specimens to be negative. It is recommended that PCR and combined southern blot analysis are most effective in early and rapid diagnosis of tuberculous meningitis.

1-16-21 HTLV-I AND MYELOPATHY IN SALVADOR (NORTHEASTERN BRAZIL): A CASE CONTROL STUDY

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From the same hospital, twenty-eight cases of myelopathy and twenty-eight cases showing no neurological disorder were studied using blind selection matched 1: 1 by age and sex. The twenty-eight pairs underwent HTLV-I serology tests. In those with a positive result anti-HTLV-I antibodies were investigated in the CSF the ELISA method was used, complimented by the Western-blot test. Myelopathy was considered associated with HTLV-I only when the CSF was positive indicating neurotropism of the virus. The mean age of the cases was 44.6 ± 15.6 years and the control group was 43.5 ± 16.0 $p > 0.05$. An OR of 9.0 was detected with a reability interval (95%) of 1.652 - 48.866 and X2 significant at the 0.02 level. Despite a strong degree of association and considering the low level of precision, there is a need for analytical studies with larger samples which besides improving the precision, will allow for greater control of the confounding variables.

1-16-22 LONGTERM MORBIDITY FOLLOWING BOTULINUM TYPE B

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26 survivors of an outbreak of foodborne botulism were followed for 30 months. 21 were seen personally by EMRC and all completed a questionnaire in Jan. 1992. 16 patients had prolonged symptoms.

The youngest patients tended to show the best improvement. Among the elderly it is possible that secondary factors may have delayed recovery. The middle group, including 4 sports fanatics, recognised the most symptoms. Changes in life style, stamina, sleep difficulties, breathing, speech, coordination, vision, swallowing and concentration were observed.

The relationship to the post-infective fatigue syndrome in five adult patients with prolonged symptoms 38 months after the onset of the acute phase was examined with psychological tests, laboratory screening, pulmonary function and electromyography.

1-16-23 CURRENT PREVALENCE OF RETROVIRUS IN AFRICAN TROPICAL SPASTIC PARAPLEGIA

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Introduction

Historically, Tropical Spastic Paraplegia (TSP) is one of the two major clinical forms of Tropical Myeloneuropathies (TMN). This concept has been progressively defined since the beginning of the century. In Africa, African Tropical Spastic Paraplagia (ATSP) has been reported in most countries of Sub-Saharan Africa. The onset is slow and insidious; the pyramidal syndrom is diffuse and of variable intensity. The etiology remains often unclear even if nutritional deficiency and toxic nutritional states seem to be main causes.

In some tropical countries, retrovirus HTLV-1 is the predominant etiology.

Objectives

The aim of this work is to identify the role of HTLV-1, HIV, and coinfestations in ATSP.

Patients and methods

A clinical and serological study was conducted from March 1987 to July 1991, among all the 1872 patients hospitalized in the Neurological Departments in the University Hospitals of five West African countries.

Results

The general HTLV-1 prevalence alone or associated with HIV-1, HIV-2, in neurological diseases is low (2.6 %). A statistically significant correlation (18.7 %) was found only in the 107 ATSP (<0.001). Half were also associated with HIV-1 or 2.

In 80 % of all ATSP cases, no retrovirus involvement was detected. Most of them have other etiologies.

1-16-24 A METHODOLOGICAL APPRAISAL OF RANDOMIZED CONTROLLED TRIALS OF DEXAMETHASONE IN ACUTE BACTERIAL MENINGITIS

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Objective. Analysis of existing randomized controlled trials on use of dexamethasone as an adjunct therapy in acute bacterial meningitis (ABM) was done to identify studies that adhere to basic methodological principles and to identify underinvestigated questions.

Methods. Studies were eligible for analysis if they were published in peer-reviewed journals after 1966, and were randomized controlled trials using dexamethasone as adjunct to antimicrobials in patients with ABM. All studies were extracted and their adherence to 15 methodological principles was graded as good, fair or poor.

Results. No study adhered to all the principles, but two adhered to the six most important ones (baseline comparability of groups, adequate sample size, relevant and masked outcome measurements, appropriate follow-up, analysis, and control treatment). Aspects of dexamethasone therapy in ABM that have not been completely investigated include its role in meningococcal and pneumococcal meningitis and in adults with ABM.

Conclusion. It is concluded that only a few published investigations on dexamethasone in ABM are methodologically sound. This finding helps explain why there is controversy on the topic. Further research should target underinvestigated topics.

1-16-25 **DISCORDANCE IN MRI AND CLINICAL COURSE IN FOCAL ENCEPHALITIS**

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Objective: The early diagnosis of herpes-simplex encephalitis (HSE) is essential for the outcome of the patients. MRI has been suggested to be more sensitive and earlier in detecting HSE than CT. We were able to follow five patients with focal temporal encephalitis with CT and MRI. Methods: Five patients (three with proven HSE) were followed by CT and MRI (T2-weighted, proton density-weighted, and T1-weighted transversal and coronal images before and after administration of Gadolinium-DTPA) from early stage up to one year.Results: At the onset with severe neurological deficit, MRI revealed lesions predominantly situated in the temporal lobe without significant-enhancement, whereas CT was normal. Later than expected, when clinical symptoms had already improved under therapy with aciclovir, the MRI deteriorated with the spreading of the lesions and intense contrast enhancement over a period of nearly two month. Typical defects could be detected only after one year of follow-up. Conclusion: MRI is very sensitive in detecting early focal lesions in HSE. However, the course of the disease cannot be monitored by MRI, as the imaging signs worsen while the patients improve. In these cases the contrast enhancement does not indicate an acute blood-brain barrier disruption but the longer lasting infiltration of immunological active cells.

1-16-26 INSIGHTS FROM ANIMAL LENTIVIRUS INFECTIONS

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HIV is one of the lentiviruses, a relatively recently recognised group of non-oncogenic retroviruses which also includes visna-maedi of sheep, CAEV of goats, EIAV of horses, SIV of non-human primates, and FIV of cats. Lentiviruses produce persistent, ultimately fatal, infections in their natural hosts following prolonged incubation periods. They infect cells of the immune system, and show restricted viral replication *in vivo* despite their ability to produce cytopathic effects *in vitro*.

Many of the biological characteristics of visna-maedi and CAEV are similar to those shown by HIV, and for this reason studies of the neuropathogenesis of these animal diseases are highly relevant to HIV involvement of the nervous system. For example, visna-maedi has an affinity for cells of the monocyte-macrophage lineage, produces a lymphoproliferative response with marked lymphadenopathy, induces an interferon, and probably produces neurological disease though indirect mechanisms - features which are also characteristic of HIV infection. Recent work has also demonstrated upregulation of MHC antigen expression in macrophages in both visna-maedi and HIV, indicating an indirect mechanism of immunopathogenesis. Recent studies of EIAV, SIV and FIV have also demonstrated interesting parallels with the human and ruminant lentiviral diseases, and may prove to be of value in evaluating both the pathogenesis and therapy of these diseases.

1-16-27 THE TREATMENT OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY WITH SYSTEMIC AND INTRATHECAL ALPHA INTERFERON.

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Therapeutic options for the treatment of progressive multifocal leukoencephalopathy (PML) are limited. A report of the efficacious treatment of a 37 year old man with sarcoid related PML, with systemic alpha interferon has recently been made.

A 65 year old woman presented for further evaluation of an eight month course of progressive neurologic decline, culminating in severe dementia and quadraparesis. Extensive workup, including brain biopsy, was consistent with PML. There was no clear identification of underlying disease state, despite exhaustive search. The patient was treated with subcutaneous alpha interferon 3 million units (MU) daily, along with weekly intrathecal alpha interferon of 6 MU. There was no significant adverse reaction noted, excepting fever related to intrathecal dosing. This was continued for 30 days with four total intrathecal infusions. In spite of this therapy the patient continued to decline neurologically, therapy was discontinued secondary to the continued decline and a septic episode.

There was no clear efficacy of the alpha interferon noted in this patient, but little adverse effect was apparent. Intrathecal infusion was utilized as systemic alpha interferon alone does not reach measurable levels in the cerebrospinal fluid. This case suggests the possibility that the effectiveness of alpha interferon in the previously described patient may have been related to treatment of the underlying sarcoid. Other differences including age, debilitated status, chronicity of PML, and relative brevity of treatment may have contributed to the ineffectiveness of this therapy in our patient. Continued trial of alpha interferon in PML is warranted. The lack of significant adverse effects of combined systemic and intrathecal dosing, suggests further consideration of this more aggressive approach.

1-26-01 DIAGNOSTIC IMPORTANCE AND CLINICAL COURSE OF ONE-AND-A-HALF SYNDROME

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The one-and-a-half syndrome is the disorder of extraocular movement characterized by a lateral gaze palsy in one direction associated with an internuclear ophthalmoplegia in the other direction. This syndrome is usually due to an unilateral lesion affecting ipsilateral PPRF and internuclear fibers of the MLF, however there are several theoretical combinations of lesions reported to be responsible for this syndrome. We studied 20 patients with acute cerebrovascular disease (12 infarctions and 8 hemorrhages: 9 men, 11 women: 14 to 81 (average 55.5) years old) presented with this syndrome. X-ray CT and MRI were performed in all the patients to determine the localization of the responsible lesions. The observation of clinical course of eye signs revealed that in the majority of patients this syndrome was transient (averaged duration was 25.4 days) and recovered into the other form such as bilateral or unilateral MLF syndrome, unilateral gaze palsy, and unilateral abducens palsy, depending on the presumable lesions. Neurootological examinations suggested clinically similar nonuniformity in lesions. However, all the diagnostic images failed to disclose the precise localization of the lesions. Only the careful observations of the clinical course of eye signs well suggested the combinations of the lesions. We would like to emphasize the importance of serial observations of clinical signs to understand pathophysiology of this syndrome.

1-26-02 FAILURE OF FIXATION SUPPRESSION ASSOCIATED WITH DECREASED GAINS OF PURSUIT AND OPTOKINETIC NYSTAGMUS IN THE DIZZY PATIENTS OF CENTRAL ORGIN

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Twelve patients of definite posterior fossa lesion proved by MRI or CT scan were selected as a central group, and fourteen patients of peripheral vestibulopathy as a peripheral group.

Percent change in slow-phase velocity with visual fixation during the period of maximum intensity of caloric nystagmus (fixation suppression) was 56.8 ± 9.0% in peripheral group, which was no significant difference compared with normal control group (59.4 ± 8.3%, $p > 0.01$). However, failure of fixation suppression was noted in all patients of central group and its mean value was 92.6 ± 7.3%, which was significant statistical difference compared with other two groups ($p < 0.01$, $p < 0.01$, respectively). And the defective fixation suppression were more remarkable when the direction of caloric nystagmus was induced toward the lesion site in six patients among the eight patients of unilateral cerebellar hemispheric lesion. Abnormal vestibular paresis pattern was found in 12 of peripheral group, but only 1 patient in central group ($p < 0.01$). Directional preponderance did not show significant difference between the peripheral and central groups ($p > 0.01$). In addition, the gains of pursuit and optokinetic nystagmus were significantly reduced in central group (0.64 ± 0.12, 0.24 ± 0.07) compared with peripheral group (0.87±0.17, 0.41±0.11) ($p < 0.01$, $p < 0.01$, respectively). Therefore, fixation suppression, vestibular paresis, and the gains of pursuit and optokinetic nystagmus would be useful diagnostic parameters in differentiating the dizziness of central origin from that of the peripheral.

1-26-03 EYE MOVEMENTS IN PURE AKINESIA AND PROGRESSIVE SUPRANUCLEAR PALSY.

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Pure akinesia (PA) is a rare extrapyramidal syndrome characterized by freezing when walking and poor response to L-dopa (Narabayashi et al, Adv Neurol, 1986, 45, 593-602). There are few clinico-pathological observations which suggest that PA could be a variant of progressive supranuclear palsy (PSP) (Matsuo, JNNP, 1991, 54, 397-400). Impairment of eye movements is typical in PSP while there is little available data in PA. We compared in a quantitative way eye movements in patients suffering from PA or PSP.

We prospectively studied horizontal random reflex saccades and sinuoïdal smooth pursuit (40°/sec) in 9 PA, 9 PSP and 11 age-matched controls (Electrooculography, Pathfinder, Nicolet Biomedical Intruments) (for method see Rascol et al, Brain, 1989, 112, 1193-1214).

The mean saccades latency was longer in PA (212 ± 50 msec) and PSP (218 ± 47 msec) than in controls (175 ± 17 msec) ($p = 0.04$). The mean index of saccades velocity was slower in PSP (0.75 ± 0.23) than in PA (0.96 ± 0.18) and controls (1.05 ± 0.12) ($p < 0.002$). Saccades amplitude was not significantly different among the 3 groups. The mean smooth pursuit's gain was smaller in PA (0.78 ± 0.08) and PSP (0.67±0.25) than in controls (0.94±0.08) ($p = 0.004$).

Horizontal saccades and pursuit are impaired in PA. Abnormalities in eye movements are not strictly similar in PA and PSP.

1-26-04 SKEW DEVIATION WITH OCULAR TORSION, A VESTIBULAR SIGN OF TOPOLOGICAL DIAGNOSTIC VALUE ?

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Sixty-five patients with unilateral brainstem infarctions presenting with skew deviation of the eyes were analyzed for vestibular function in the roll plane. Based on our prior observations of a frequent coincidence of skew and ocular torsion (OT), fundus photographs were taken in order to determine OT in all patients. Ischemic lesions were allocated to the level and side of the brainstem by the clinical syndrome and neuroimaging. CT and MRI scans, oriented to the fronto-occipital line as baseline, were taken to identify the infarcted areas and project them onto the appropriate transverse sections of the stereotaxic atlases of the brainstem (Olszewski and Baxter, 1982) and thalamus (Van Buren and Borke, 1972). Two new findings of clinical relevance were obtained: (1) All skew deviations were ipsiversive (ipsilateral eye undermost) with caudal pontomedullary lesions and contraversive (contralateral eye undermost) with rostral ponto-mesencephalic lesions; (2) all skew deviations were associated with concomitant ocular torsion and tilts of subjective visual vertical towards the undermost eye. Thus, skew deviation or, more correctly, ocular skew torsion is a sensitive brainstem sign of localizing and lateralizing value. Evidence is presented that the ocular skew torsion sign indicates a vestibular tone imbalance in the roll plane secondary to graviceptive pathway lesions.

1-26-05 ACUTE PAINFUL OPHTHALMOPLEGIA DUE TO THROMBOSIS OF SPONTANEOUS DURAL CAVERNOUS SINUS FISTULA.

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Spontaneous dural arteriovenous fistulas involving the cavernous sinus usually present insidiously. We report four patients in whom thrombosis of the cavernous sinus / ophthalmic veins was the cause of acute exacerbations of ocular symptoms. All were women aged from 40 to 72 years. Mild symptoms (ocular pain, transient diplopia, mild proptosis) were present 6 weeks to 6 month prior to the acute event. In two the thrombosis occurred spontaneously and in two it was precipitated by embolization/angiography. Thrombosis was demonstrated by angiography. Arterial supply was from the internal carotid artery branches in two and from both internal and external carotid arteries in two. All patients had acute ocular pain, complete ophthalmoplegia, proptosis (up to 6 mm), decreased visual acuity (20/80 to blindness), increased intraocular pressure (28-60 mmHg), severe chemosis and conjunctival edema. None had a bruit. The pupil was spared in all but one patient. Treatment consisted of acetazolamide, topic beta-blockade and low dose of heparin. The intraocular pressure decreased after a few hours in all.Three returned to the baseline in 48 hrs. In one patient in whom treatment was started several hours after the onset of thrombosis visual acuity did not improve. Acute ocular symptoms in our patients with cavernous sinus dural fistula were caused by sudden blockage of venous drainage of the orbit by thrombosis.

1-26-06 NONPARALYTIC PONTINE EXOTROPIA.

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A form of pontine exotropia without gaze palsy, nonparalytic pontine exotropia, was observed in the acute or chronic stage of brainstem infarction in 6 alert patients. Five patients had internuclear ophthalmoplegia (INO) in one eye and outward deviation of the other eye; 1 patient showed bilateral INO with alternating exotropia. In addition to the relevant lesion in the pontine tegmentum, MRI revealed resolution of the contralateral exotropia, and mild outward deviation of the eye ipsilateral to the INO during eye closure. The cause of exotropia has been held to be contralateral conjugate deviation of the eyes due to an acute involvement of the paramedian pontine reticular formation (PPRF) combined with the coexistent INO. An incomplete PPRF lesion is assumed to be responsible for the absence of gaze palsy. In our study, however, visual fixation at a distant target, covering the eye ipsilateral to the INO, the use of Frenzel lenses or eye closure resolved the exotropia opposite the lesion. These findings indicate that nonparalytic pontine exotropia results from the increased input to the contralateral PPRF which is required to bring the dominant eye ipsilateral to the INO to midposition.

1-26-07 EDROPHONIUM'S EFFECT ON SACCADIC VELOCITIES IN MYASTHENIC AND NON-MYASTHENIC OCULAR MOTOR PALSIES.

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We studied with magnetic search coil oculography 7 myasthenic patients with positive single-fibre EMG results, 3 normal subjects, and 9 patients with ocular motor palsies from proven central or peripheral causes. Subjects made saccades to a target stepping from primary to 20° left and right at 1 second intervals and received 10 mg edrophonium after 4 minutes. We analyzed saccades away from primary position at the start, just prior to and 1 minute after injection. We constructed amplitude/velocity curves and derived an asymptotic velocity (*Vmax*) for each interval.

The *Vmax* of myasthenic subjects increased with edrophonium in both clinically affected and unaffected eyes. *Vmax* decreased slightly in normal subjects. *Vmax* also decreased in subjects with non-myasthenic palsies, sometimes dramatically. Saccadic slowing could also occur in the yoke movement of the other eye.

We conclude that the edrophonium effect on saccade velocity can distinguish myasthenic from neurogenic ocular motor deficits. Furthermore, paradoxical slowing of saccades can occur in non-myasthenic palsies and should not be considered diagnostic of myasthenia.

1-26-08 GUAM RETINAL PIGMENT EPITHELIOPATHY (GRPE): SEEING LYTICO-BODIG, INDIRECTLY

J.C.STEELE, S.D.HANLON, R.T.Tablante, Tamuning

In the Western Pacific, on the small tropical island of Guam, a curvilinear (snail tracks) depigmentation of the retinal pigment epithelium (GRPE) ressembling ophthalmomyiasis interna posterior is present in 19% of native Guamanian Chamorros born before 1940, but it is absent in those born after 1952. It is asymptomatic, nonprogressive, and bilateral in 1/3. We have now identified it in 159 subjects.

GRPE also is present in 53% of patients with lytico-bodig, an endemic and idiopathic neurodegenerative disease of Chamorros. That disease has been intensively studied for 40 years, but because neurologists examine by direct ophthalmoscopy, GRPE was not identified in these patients until neuroophthalmologist Tery Cox (Ophthalmology 1989,96:1731) visualized their fundi by indirect binocular ophthalmoscopy.

Knowing the cause of GRPE will provide understanding of lytico-bodig, and thereby of related neurodegenerative diseases elsewhere including Alzheimer's and Parkinson's disease, amyotrophic lateral sclerosis, and progressive supranuclear palsy.

1-26-09 MICROANGIOPATHY IN LEBER'S HEREDITARY OPTIC ATROPHY WITH 13708 AND 3394 mDNA POINT MUTATIONS.

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Leber's hereditary optic atrophy (LHOA) is maternally inherited mitochondrial disease characterized by loss of vision. LHOA is associated with well-defined point mutations of mitochondrial DNA(mDNA), that in various degrees correlate with development of blindness and clinical prognosis.

We carried out morphological studies of muscle and skin biopsies as well as determinations of ten mDNA mutations, in nine families with LHOA. The patients included clinically affected males and females as well as female carriers. Electron microscopy revealed slight abnormalities of mitochondria (M) in biopsies as well as in cultured muscles, fibroblasts and Schwann cells; they were present in carriers and in the affected individuals. Only blind patients (including females) and those with optic disc microangiopathy showed marked thickening and reduplication of vascular basal lamina (BL), necrosis of pericytes and necrotic debris in walls of capillaries. These changes were not seen in the unaffected carriers. All families showed 13708+3394 mDNA mutations, usually not associated with blindness; they were all negative for the remaining known mDNA mutations.

Our studies indicate that both, the carriers as well as the affected LHOA patients show morphological abnormalities of M and contain mutant mDNA in many cell types. Since loss of vision correlates with the presence of microangiopathy in muscle biopsies, LHOA is probably related to development of similar changes in the optic nerve.

1-26-10 PARIETAL LOBE LESIONS ALLOW SMOOTH PURSUIT EYE MOVEMENTS TO BE DISRUPTED BY DISTRACTING BACKGROUND PATTERNS

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The oculomotor smooth pursuit system is driven by the slip of the target image upon the retina generated by errors in matching eye and target velocities. Pursuit of an object moving against a structured background will result in retinal flow in the direction opposite to target movement. Central mechanisms allow these distracting signals to be overridden effortlessly. To isolate the anatomical substrate of this capacity we studied the effect of the presence of a structured background upon smooth pursuit in 27 patients with focal cerebral lesions. Studies on normal subjects confirmed that a background has little effect upon pursuit.

Eye movements were recorded by the scleral search coil method or infrared oculography. The target was a bright spot moving horizontally in a triangular waveform of amplitude 22.5 deg visual angle, at either 10, 20, 30 or 36.5 degs/sec. Data was collected in darkness and with a structured background. Fourteen patients showed a significant reduction of gain with a structured background, while the remaining 13 showed little or no effect. Comparison of the location of the cerebral lesions in these two groups suggested that lesions in the inferior parietal cortex (area 40) results in disruption of pursuit in the presence of a background.

1-26-11 ONE- AND- A- HALF SYNDROME COMBINED WITH PERIPHERAL TYPE FACIAL PALSY. CLINICAL FEATURES AND MAGNETIC RESONANCE IMAGING IN FOUR CASES.

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Fisher described the one- and -a-half syndrome as a combination of horizontal gaze palsy and internuclear ophthalmoplegia (1967). Cranial nerve involvement or other neurological deficits may occur depending on the localisation and extend of the pontine lesion (Wall and Wray, 1983). Only a few cases of coincidence with facial palsy have been reported.
Within 2 years, 4 patients showed one- and- a- half syndrome in the presence of peripheral- type facial palsy in our clinic. There was no impairment of taste in any case. Etiology was multiple sclerosis in 3 cases and encephalitis of unknown cause in the other. In all cases, Magnetic Resonance Imaging showed a uniformely located, circumscript lesion of the ipsilateral paramedian tegmentum of the caudal pons. There was rapid and nearly complete restitution in all cases.
We conclude that the rare combination of one- and- a- half syndrome and peripheral- type facial palsy is a reliable clinical sign for a circumscript unilateral lesion of the caudal paramedian pontine tegmentum.

1-28-01 PERIPHERAL NERVE FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Peripheral neuropathy (PN) has been reported in many uncontrolled reports on patients with rheumatoid arthritis (RA). 31 females with RA and 42 female controls were examined with a clinical scoring system, instrumentally determination of vibration and temperature/pain thresholds, assessment of cardiovascular autonomic nervous system (ANS), nerve conduction velocity (NCV) and quantitative EMG studies. Also MRI of the wrist was performed to image the median nerve and its surroundings. Scores of "neuropathic" symptoms and clinical findings (sensory and reflex scores) were significantly higher in the patients while vibration, temperature/pain thresholds and ANS function were not consistently more abnormal in the patients. MRI did not reveal more structural changes in the median nerve of the patients. Motor and sensory nerve amplitudes and automatic EMG analysis showed small, but statistically significant differences in the direction of a minimal diffuse axonopathy in the patients. We could thus not demonstrate consistently general evidence of more clinical or subclinical PN in RA patients, but the neurophysiological data suggested a trend towards axonal dysfunction in the patients compared with controls. PN in patients with RA and caused by that disease may have been overestimated.

1-28-03 MEDIAN NERVE CONDUCTIVE STUDY IN ASYMPTOMATIC COMPUTER TYPISTS

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Repetitive or sustained wrist motions may be contributed to carpal tunnel syndrome. The objective of this study is to observe whether the movement of typing entraps distal median nerve.

We collect 16 computer typists. All are females and asymptomatic. The ages range 21 to 36 years and the mean is 27.6 years. The length of the employment is 2 to 3 years in 12 women, more than 3 years in 2, and less than 2 years in 2. The time of typing per day is 6 to 8 hours in 14 women and 4 hours in 2. As compared with control group who are 24 females and the mean of the age is 25.2 years, the statistics of distal motor and sensory latencies on stimulating the wrist are not significant ($P>0.05$), neither is nerve conductive velocity across the carpal tunnel. However, those of both onset and peak distal sensory latencies on stimulating the palm (antidromic method) are significant ($P<0.05$).

Conclusively, less than 3 years of the employment in computer typists is not so long as to impair the median nerve in the carpal tunnel. The possible explanations of slower median sensory nerve conduction distal to the palm will be discussed.

1-28-04 RETROGRADE NERVE CONDUCTION CHANGES FOLLOWING TRAUMATIC DIGIT AMPUTATION: A SOMATOSENSORY EVOKED POTENTIAL STUDY

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Following nerve transection, nerve conduction proximal to the lesion becomes slower. To determine the effect of small fiber injury on retrograde nerve conduction, somatosensory evoked potentials (SEPs) to median nerve stimulation at the wrist were carried out in 6 subjects who suffered from traumatic digit amputation 5 months to 15 years prior to the testing. SEPs were recorded from Erb's point, cervical region (C2) and contralateral scalp C2 or C4 location. The mean latencies of Erb's (N9), cervical (N13), and short-latency cortical (N19) SEP components were respectively 10.6 ± 1.1 ms, 14.0 ± 1.1 ms and 19.5 ± 1.2 ms from amputated side and 10.1 ± 0.6 ms, 13.2 ± 0.9 ms and 19.1 ± 1.1 ms from normal side. The mean amplitudes of N9, N13, N19 components were respectively $1.9 \pm 1.0^{**}$ uV, $1.0 \pm 0.5^{*}$ uV and $1.8 \pm 1.0^{*}$ uV from amputated side and 5.9 ± 1.7 uV, 1.7 ± 0.3 uV and 3.5 ± 1.7 uV from normal side ($^{**} = p < 0.005$ and $^{*} = p < 0.05$, paired t-test). The present data suggest that traumatic nerve transection of small fibers causes mainly retrograde axonopathy.

1-28-05 FEVER-RESPONSIVE NEUROPATHY (FRN) BENEFITTED BY LONG-TERM INTERFERON ALPHA-2A (Iα) TREATMENT

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FRN is a chronic dyschwannian motor neuropathy that has 1-2 weeks of transient improvement following intercurrent fevers. Repeated Poly-ICLC, an I-inducer producing transient fever, caused sustained improvement in chronic FRN (Lancet, i:503, 1978). We now record cumulatively dramatic long-term benefit from Iα used to produce repeated fevers in a non-monoclonal FRN patient who had had 12 1-2 week improvements following flu syndromes. Now 21, at age 11 (1983) he gradually developed distal lower-limb weakness that evolved into generalized arreflexic weakness; infrequent fasciculations; sensation normal. CSF: protein 56, wbcs 2, no bands. Motor nerve conductions: very slow, amplitudes nearly normal. EMG and muscle biopsy: reinnervation and recent denervation. Previously the patient had not responded to: prednisone, azathioprine, cyclosporin, plasmalymphopheresis or IVIG. By 10/89, he had been severely weak for 5 years: all limb muscles were 0/5; v.c. 1.5L; he wrote holding the pencil in his mouth. We began solo treatment 11-04-89 with Iα $3x10^6$ units (3MU) i.m. 1x/wk. Optimum dosage for 33 mos. has been 12 MU 2x/wk. Beginning 5d after the first injection, strength has been gradually improving. Now, 1/93: proximal muscles are 4+; biceps 4; quads 4+; distal flexors 3+, extensors 2. He has been walking for 8 months.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-28-06 NEUROPATHY ASSOCIATED WITH SPASTIC PARAPLEGIA; EVALUATION AND CLUSTER ANALYSIS OF CLINICOPATHOLOGICAL CHARACTERISTICS

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Classification of peripheral neuropathy associated with spastic paraplegia in degenerative neurological diseases remains obscure. Although hereditary motor and sensory neuropathy type V is thought to be one of those conditions, the disease entity is not necessarily distinct because of limited numbers of reports with pathological study of the nerve. We reported here clinicopathological study in 12 patients of neuropathy accompanying spastic paraplegia including those from two families. Weakness of lower extremities were observed in all patients. Eight patients had sensory impairment including deep sensory disturbance in 6 patients. Five patients revealed extrapyramidal signs and/or ataxia. Sural nerve biopsy was performed in 7 patients showing decreased density of large myelinated fiber in these patients. Onion-bulb formation was seen in 2 patients. Computed cluster analysis (modified single-linkage method) of these clinicopathological findings as parameters suggests that these patients were divided into two subgroups as follows. Type I: Pure form of spastic paraplegia plus neuropathy. Type II: Spastic paraplegia plus neuropathy with other signs of central nervous system.

1-28-07 A CONTROLLED STUDY OF PERIPHERAL NEUROPATHY IN SLE (SYSTEMIC LUPUS ERYTHEMATOSUS)

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The purpose was to study the occurrence of peripheral neuropathic features in SLE patients in comparison with age and sex matched controls. In 34 patients with systemic lupus erythematosus (SLE) and 34 age and sex matched healthy controls we performed standardized quantifiable neurological testing for neuropathic symptoms (Neuropathic Symptom Score) and deficits (Neurological Disability Score), as well as nerve conduction velocity studies (NCV) and determination of vibration thresholds (VT). SLE patients had more total neuropathic symptoms and deficits than controls (p=0.0001). Sensory and reflex (hyporeflexia) deficits, being most indicative of neuropathy were higher in patients than in controls (p=0.01 and p=0.03, respectively). The majority of quantitative and qualitative NCV attributes showed no difference in patients and controls, but if categorized as NCV abnormalities of 2 or more nerves in each individual, a frequency of polyneuropathy of 21% was seen in SLE patients compared to 6% in controls. The study confirms that peripheral neuropathy, including polyneuropathy, occurs in SLE, but the amount of electrophysiological abnormalities in particular is modest when compared to sex and age matched controls.

1-28-08 CLINICAL AND NEUROPHYSIOLOGICAL FINDINGS IN 24 PATIENTS WITH HIGH TITERS OF ANTI-GM1 ANTIBODIES

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High titers of serum anti-GM1 antibodies have been seen in most patients with Motor Multifocal Neuropathy (MMN) and more rarely in other neurological diseases. During April '91 to Dicember '92, 360 patients neurologic patients underwent to anti-GM1 antibodies assays. Very high titers, more than 1:10,000, were found in 24 patients. 12 had an asymmetric motor neuropathy, prevailing in the upper limbs in 10;4 had a Guillain Barré Syndrome (GBS); 5 had a chronic motor or sensory-motor polyneuropathy; 2 had an ALS and 1 a radial mononeuropathy. Neurophysiological study showed conduction blocks in 11 out of 24 patients: 8 with asymmetric motor neuropathy, 1 with radial mononeuropathy and 1 of the 2 patients with GBS. 70% of the patients with asymmetric motor neuropathy prevalent in the upper limbs had evidences of MMN at the neurophysiological studies. Our data confirm that high titers of anti-GM1 antibodies can be found in a wide spectrum of acute and chronic neuropathies and motor neuron syndromes, being preferentially associated to MMN.

1-28-09 DIAGNOSTIC PROBLEMS IN BRACHIAL PLEXOPATHY SECONDARY TO BREAST CANCER WITHOUT PRIOR RADIATION

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Progressive disease of brachial plexus (BP) in breast cancer patients, unexposed to radiation, was encountered seven times in six years in a tertiary EMG laboratory. Records were assessed for diagnostic difficulties. Malignant plexopathy was diagnosed in six. One patient had late-stabilizing disease contralateral to a tumor which presented a year later. Disseminated tumor was evident in three, with severe pain in five and Tinel's sign over brachial plexus in two patients. Local mass effect was never initially apparent. Motor and EMG signs most commonly involved distal upper trunk derivatives. Sensory nerve action potentials were depressed in seven. MR/CT BP scans were initially negative in all of five patients. Surgical BP exploration was positive in one patient and negative in two without actual nerve biopsy. Treatment was delayed because of misdiagnosis of bone, root or benign BP disease, inadequate nerve biopsy and patient opposition to radiotherapy. Treatments included steroids, azathioprine, tamoxifen, and radiotherapy. The latter was delayed for up to four years after plexopathy onset, providing symptomatic relief in two of four patients. Although one of our cases may be paraneoplastic, sheet-like BP infiltration with negative imaging remains a diagnostic challenge in breast cancer.

1-28-10 EFFECT OF AMINOGUANIDINE ON NERVE BLOOD FLOW, VASCULAR PERMEABILITY TO ALBUMIN, ELECTROPHYSIOLOGY, AND OXYGEN FREE RADICALS.

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Since advanced glycosylation endproducts (AGE) have been suggested to mediate hyperglycemia-induced microvascular atherogenesis, and since aminoguanidine (AG) prevents AGE generation, we examined if AG will prevent or ameliorate the physiologic and biochemical indices of streptozotocin (STZ) induced experimental diabetic neuropathy in the rat. Four groups (n=8 each) were studied. Gp I: STZ + 25mg/kg/d AG; Gp II: STZ + 50mg/kg/d AG: Gp III: STZ alone; Gp IV: Controls. We monitored nerve conduction studies (NCS) on sciatic-tibial and caudal nerves, nerve blood flow (NBF), oxygen free radical (OFR) activity (conjugated dienes and hydroperoxides), and blood-nerve barrier function using labeled albumin. STZ diabetes (Gp III) developed a reduction in NBF by 57%; abnormal NCS of caudal and sciatic-tibial nerves and an increase in conjugated dienes (by 60%). NBF was normalized by 8w in AG (Gps I, II) and NCS significantly improved in a dose-dependent manner by 16w in sciatic-tibial and 24w in caudal nerves. BNB to albumin was not impaired and OFR indices were not ameliorated by AG. We suggest that AG prevents nerve ischemia and more gradually improves NCS by an action potential on nerve microvessels. AG has potential in the treatment of diabetic neuropathy.

1-28-11 NEUROPATHY DUE TO LYMPHOMA

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During the past three years, we encountered four patients in whom neuropathy was directly attributable to lymphoma. Symptoms of neuropathy preceded the diagnosis of lymphoma in the three with polyneuropathy, and preceded systemic relapse in one with sciatic neuropathy. Lymphoma was detected by nerve biopsy in three and by CT of the thigh in the patient with sciatic neuropathy. In two patients, the neuropathy improved after chemotherapy. One was not treated due to advanced age and poor general health, and progression was arrested after radiation therapy to the sciatic nerve in the fourth. These patients represent 33 percent of the 12 lymphoma patients referred to us for evaluation of neuropathy during the same period. Lymphomatous infiltration was likely but not proven in three others. The remaining patients were thought to have vincristine neuropathy (2), diabetic plexopathy (1), peroneal pressure palsy (1), and spinal accessory palsy due to lymph node biopsy (1). Therefore, malignant infiltration was the most common cause of peripheral neuropathy in this group of patients. It is important to consider this diagnosis, since treatment can lead to considerable improvement in the quality of life.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

1-28-12 17p11.2 DUPLICATION IN HMSN I VARIANTS

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We looked for the duplication of chromosome 17p11.2 which characterizes Hereditary Motor and Sensory Neuropathy type Ia (HMSN Ia) in four families with variants of HMSN I. All the families had a complete clinical, electrophysiological and morphological evaluation. Southern blot analysis of DNA was performed employing probes pVAW409 and pVAW412. In Family A, five members had the Roussy-Levy Syndrome (RLS), which is considered a variant of HMSN I with essential tremor. In Family B, HMSN I was associated with hearing loss and mental retardation. In Family C, two siblings, born to unrelated, unaffected parents, had hypertrophic HMSN. In Family D, two sisters with a HMSN I phenotype were born to first cousin unaffected parents. The 17p11.2 duplication was found in Family A and constitutes the first molecular genetic evidence of the equivalence of RLS with HMSN I. The duplication was detected also in Family B, suggesting that its effects may not be limited to the peripheral nerve. On the contrary, our families with HMSN I of most likely autosomal recessive inheritance, did not carry the duplication and must be considered entities genetically separate from HMSN Ia.

1-28-13 THE EXPRESSION OF PMP-22/GAS-3 GENE IN CULTURED SCHWANN CELL LINE

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Gas genes were originally reported in fibroblast cell line. They are highly expressed on growth arrest and down-regulated in growing cells. PMP-22, one of peripheral myelin proteins, is identical to the product of Gas-3 gene. The duplication of PMP-22 gene and the point mutation in this gene have been reported in Charcot-Marie-Tooth disease type 1A. We investigated the expression of PMP-22 gene in cultured rat Schwann cell line by Northern blot analysis. High level of PMP-22 mRNA was observed in serum-free medium. After seeding in the medium containing 10 % serum Schwann cells proliferated while the expression of PMP-22 gene was down-regulated. In contrast to fibroblasts, PMP-22 mRNA was detectable in Schwann cell 48 h after seeding in 10 % serum.The addition of forskolin to 10 % serum medium resulted in the decrease of the expression of PMP-22 gene and the proliferation of Schwann cells. Phorbol ester did not change the gene expression and the rate of the cell proliferation. Similar results were obtained when the expression of Po gene was examined in this Schwann cell line. From these data it seems that the expression of PMP-22 and Po genes is regulated by the same mechanism. The results do not suggest that down-regulation of PMP-22 gene expression stimulates the proliferation of Schwann cells.

1-28-14 HYPERALGESIA IN THE DIABETIC PERIPHERAL NEUROPATHY

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I designed new device: Algesiometer, multi-roulet type, to estimate the hyperalgesia in the diabetic peripheral neuropathy. It has been suggested that hyperalgesia is due to hyperactivity in regeneration of A δ fibers, on the other hand, the painful diabetic neurophthy is due to spontaneous hyperactivity in C fiber. And I applied this device to estimate the function of A δ fiber.

Method: 1) 56 patients of non insulin dependent diabetes mellitus(43 ~ 81 y.o.) were examined with Algesiometer and conventional electrophysiological studies.
2) 9 patients with painful neuropathy were treated with Mexiletine (Na-channel blocker) and followed up with former examinations.

Results: 1) Hyperalgesia was related to diabetic control and period of desease. But no relation to nerve conduction velocities except for SCV in median nerve and vibratiory sensation on upper extremity.
2) Mexiletine treated patients showed improvement of pain (paresthesia) in all cases but temporarily increasing of hyperalgesia in 5, finally improvement of hyperalgesia in 6.

Conclusion: It was suggested that the function of A δ fiber could be estimated with Algesiometer better than with conventional studies, and Mexiletine improved C fiber function and then A δ fiber.

1-28-15 FAMILIAL GUILLAIN BARRÉ SYNDROME

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The Guillain Barré syndrome (GBS) is an acute, progressive, inflammatory polyneuropathy, usually of sporadic occurrence. We report an uncommon familial presentation of GBS in two brothers. A man aged 25 was admitted to hospital with acute weakness of the four limbs, general areflexia, transient hipoesthesia of the lower limbs and moderate but progressive dyspnea and dysphagia in March, 1990. His elder brother was admitted in April, 1992 at the age of 30 with acute tetraparesis and general areflexia. Both of them showed severe motor weakness and required mechanical ventilator support. Their CSF revealed a high increase of proteins with normal cell counts and the electrodiagnosis confirmed a neurogenic pattern in polyradicular distribution with severe nerve conduction block. Secondary axonal degeneration was detected in posterior evaluations. Four sessions of plasmapheresis were performed in both, with marked clinical improvement after therapy. The HLA typing showed noticeable similarity, having both A2, B35, Bw4 and Cw4. Although the pathogenesis of GBS is still unclear, an HLA-linked genetic susceptibility may play a role in some of the cases.

1-28-16 SINGLE FIBER ELECTROMYOGRAPHY IN DIABETIC POLYNEUROPATHY

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Single fiber electromyography (SFEMG) was studied in a group of fifty-six diabetic patients. The patients were divided into three groups : Group I, 16 cases of diabetic control subjects without clinical or electromyographic evidence of polyneuropathy (Male : Female = 7 : 9) ; Group II, 28 cases of diabetic subjects with clinical and electromyographic features of polyneuropathy (M:F=15:13) ; and; Group III, 12 cases of diabetic subjects with obvious muscular atrophy and prominent denervation pattern on EMG study (M:F=6:6). SFEMG was performed in the extensor digitorum communies and anterior tibialis muscles. Twenty healthy subjects were collected as a control group. The results revealed that jitter values were significantly prolonged in all three groups as compared with the control group (mean + 3SD). Fiber densities were high in group I and II, but lower than normal in group III.

In conclusion : (1) axonal degeneration is a main pathologic mechanism in diabetic polyneuropathy and does occur in asymptomatic diabetic subjects. (2) Reinnervation or regeneration processes were not observed in cases with prominent muscular atrophy.(3) SFEMG is a sensitive method for assessing axonal degeneration or reinnervation process in diabetic subjects.

1-28-17 HEREDITARY MOTOR AND SENSORY NEUROPATHY TYPE I: CLINICAL AND NEUROGRAPHICAL FEATURES OF THE 17P11.2 DUPLICATION SUBTYPE.

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Forty-four affected individuals, aged 8 - 68 years (mean 34 years), from six families with hereditary motor and sensory neuropathy type I (HMSN I, Charcot-Marie-Tooth disease type I) were investigated to determine the clinical and electroneurographical characteristics of the HMSN I subtype that is defined by the presence of a DNA duplication on chromosome 17p11.2. Clinical features did not differ essentially from what has been described in general HMSN I populations. Neither clinical severity, measured by means of the Neurological Disability Score (NDS), nor motor nerve conduction velocity (MNCV) in the median nerve were significantly related to age on regression analysis, although the small number of children seemed to be less severely affected than young adults and older individuals. NDS values were strongly inversely related to MNCV, and, to a lesser extent, to compound muscle action potential amplitude. These results suggest that the primary pathologic process is not, or only slightly active after childhood.

1-28-18 THERMOGRAPHIC ABNORMALITY IN PATIENTS WITH POLYNEUROPATHY

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The role of thermography in the evaluation of polyneuropathy is not established. We studied skin temperature changes of hands and feet in 53 patients with polyneuropathy using thermography. Sixteen patients with diabetic neuropathy,10 with chronic inflammatory demyelinating polyneuropathy,8 with toxic neuropathy,6 with Guillain-Barré syndrome and 13 others were examined. When compared to age-matched normal controls, 40 cases(75%) showed abnormal thermograms which consisted of either diffuse or localized decrease of skin temperature. The incidence of abnormal studies in hands was similar to that in feet, 62% and 68% respectively. These changes were not correlated with the conventional electrodiagnostic parameters. We found a significant relationship between the thermographic abnormalities and the findings of autonomic nervous system dysfunction, especially in younger subjects. In contrast, such a correlation was not so remarkable in older patients. Thermographic study may be useful in clinical evaluation of polyneuropathy. However further studies should be necessary to interprete these abnormalites.

1-28-19 ANTIBODIES TO GANGLIOSIDES GM1, GD1b AND TO CAMPYLOBACTER JEJUNI IN PATIENTS WITH AN ACUTE GUILLAIN-BARRÉ SYNDROME

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Infections by campylobacter jejuni (CJ) have repeatedly been observed in association with an acute Guillain-Barré-syndrome (GBS). In a variety of motor neuron diseases, neuropathies and also in patients with an acute GBS elevated titers of anti-ganglioside antibodies have been reported.

We investigated the prevalences and the correlations of elevated titers of serum antibodies to the gangliosides GM1,GD1b and to C.jejuni in 42 patients with recent onset of an acute GBS and in 52 healthy blood donors as controls by quantitative ELISAs.

In patients with GBS we found significant increases of anti-CJ-IgG ($p<0.001$), -IgA and -IgM (both $p<0.05$), of anti-GM1-IgA, -IgG and -IgM and of anti-GD1b-IgA and -IgG (all $p<0.001$) in comparison with the control group (rank sum test). Anti-CJ-IgG correlated with anti-GM1-IgG and anti-CJ-IgM with anti-GM1-IgA (both $p<0.05$) in the GBS group. No correlations were found in the blood donors.

The results suggest a relation between antibodies to C.jejuni and to GM1 in acute GBS which might be of pathogenic relevance.

1-28-20 ROLE OF PERIPHERAL AND SPINAL NOCICEPTIVE SYSTEMS IN MAINTENANCE AND SIGNALLING OF SPONTANEOUS AND TOUCH-EVOKED PAIN IN PERIPHERAL NEUROPATHIES.

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Recent studies indicate that certain neuropathic pain syndromes following partial peripheral nerve lesions (i.e. tactile allodynia) or following complete nerve transsections (i.e. phantom limb pain) can be explained by a central reorganisation of synaptic structures either in the spinal cord or in the brain. Is ongoing nociceptive C-fiber input from the periphery necessary to maintain the altered central process? 1. In ten patients with postherpetic neuralgia and allodynia (PHN) peripheral nociceptive C-fiber function was quantitatively assessed by axon reflex reactions. In the allodynic skin no ongoing C-fiber activity could be demonstrated. In contrast, C-fiber function was considerably impaired and the fibers degenerated. Intensity of neuropathic pain was positively correlated to C-fiber impairment. 2. A patient suffered multiple fractures of the right leg and a left brain stem infarction involving the anterolateral fasciculus of the central nociceptive system following a polytrauma. Later, the right leg was amputated resulting in spontaneous and touch-evoked phantom pain (PP). Quantitative sensory testing revealed analgesia and thermanesthesia of the right body side but nearly intact touch and vibration senses. Epidural and spinal anesthesia had no effect on spontaneous pain. Conclusion: In some cases of neuropathy activity in peripheral and spinal nociceptive systems is not necessary to maintain central processes that account for spontaneous and touch-evoked pain. In PHN, activity of mechanoreceptors travelling in Aß-fibers may be transferred to central pain signalling pathways in the spinal cord depending on C-fiber degeneration. In PP, activity in Aß-fibers, dorsal columns and medial lemniscus system may produce pain in higher brain centers.

1-28-21 CLINICAL COMPARISON OF CABRAL AND MUSKEL TRANCOPAL IN LOW BACK PAIN

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The clinical comparison of Cabral (Phenyramidol - Kali Chemie Pharma GmbH) and Muskel Trancopal (Chlormezanon - Winthrop) in the treatment of low back pain was carried out in a double-blind study at the Department. The treatment period was one week The diagnosis was based on the case history, clinical symptomes as well as X-ray examinations, and the clinical parameters were studied before and after the treatment. 13 patients were chronic cases and 7 had an acute process, 15 were male and 5 female.

All patients had paravertebral spasm before and 11 (5 in Cabral - 6 in Muskel Trancopal group) after treatment. No significant difference was found between the two groups in the subjective improvement. The average changes of the ground-fingertip distance were 8.6 cm and 6.5 cm respectively. The average change of the Schober distance in both group was the same (0.65 cm). The rotation, retro- and lateroflexion of the vertebral column showed similar angle changes in both groups. Somnolence was found in 2 cases in the Cabral and in 5 cases in the Muskel Trancopal group. In addition, 2 patients of the Muskel Trancopal group complained of dizziness. On the basis of these clinical observations it is concluded that Cabral and Muskel Trancopal are virtually equieffective, and administration of Cabral can be recommended for the treatment of low back pain.

1-28-22 HEPATITIS C AND MONOEURITIS MULTIPLEX: A NEW CAUSE OF VASCULITIC NEUROPATHY

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Hepatitis C virus is found with increasing frequency in patients with type II cryoglobulinemia, a disorder associated with vasculitis of the peripheral nerves and other organs. This is the first detailed report of the neuropathy sometimes seen in this syndrome.

A 40-year-old man developed a purpuric erupation on the legs and buttocks, diagnosed as leukocytoclastic vasculitis. Within weeks he became numb and weak in the right, then left foot. Later, on two separate occasions, he noted the sudden onset of numbness in the distribution of the left medial cutaneous nerve of the thigh and the right medial antebrachial cutaneous nerve. Electromyography demonstrated a multifocal sensory motor polyneuropathy. Vasculitis was found when we biopsied a sensory nerve. Serologic studies showed elevated cryoglobulins, rheumatoid factor (1:640), and mildly abnormal liver enzymes. Hepatitis C virus was found by RIBA and PCR. He had no risk factors for hepatitis or other causes of peripheral neuropathy. Plasmapheresis and prednisone 60 mg per day for several months were ineffective. Alpha interferon resolved the rash.

We conclude that patients with vasculitis and cryoglobulinemia should be evaluated for hepatitis C infection, which is potentially treatable with alpha interferon.

1-28-24 SUBACUTE PREDOMINANTLY MOTOR UREMIC POLYNEUROPATHY

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Polyneuropathy complicating renal failure typically presents as a slowly progressive predominantly sensory polyneuropathy. We report a 27-year-old man with end-stage renal failure secondary to Alport's syndrome, who developed a subacute predominantly motor neuropathy. This form of uremic neuropathy is rare, and detailed clinical, electrophysiologic, and pathologic descriptions are lacking.

The neuropathy initially manifested as toe paresthesias after which hemodialysis was begun. Despite dialysis, he developed weakness involving proximal and distal leg muscles, which progressed over the next two months such that he could not walk independently. Electrodiagnostic studies indicated an axonal polyneuropathy with absence of sural sensory, peroneal motor, and tibial motor responses. EMG revealed fibrillation potentials in distal leg muscles. Sural nerve biopsy showed severe axonal degeneration. CSF protein was 91 mg/dl.

Because of the unusual presentation for uremic neuropathy and the high CSF protein, an inflammatory demyelinative neuropathy was considered. However, the electrophysiologic and nerve biopsy evidence favored an axonal process. He was treated with more aggressive hemodialysis and the progression of weakness halted. Over the next several months, proximal lower extremity strength gradually improved.

Clinicians should be aware of this rare form of uremic neuropathy and differentiate it from acquired demyelinative polyneuropathy, which it mimics.

1-28-25 IMPROVEMENTS OF DISABILITY IN CHRONIC INFLAMMATORY DEMYELIINATING POLYNEUROPATHY: COMPARISON BETEWEEN PLASMAPHERESIS; CORTICOIDS AND HIGH-DOSE INTRAVENOUS IMMUNOGLOBULIN

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Controlled studies showed that corticoids and plasmapheresis (PP) are effective in chronic inflammatory demyelinating polyneuropathy (CIDP). In 8 of 9 CIDP patients disability improved associated with high-dose intravenous immunoglobulin (IVIg) and in a controlled study IVIg was efficient in selected patients. This high rate of improvement seemed discrepant to our experience with 58 acute therapeutical interventions in 28 consecutive CIDP patients. Therefore we retrospectively compared improvements of disability within 2 months after treatment with corticoids, PP, and IVIg. Patients improved after 15 of 30 PPs, after 3 of 11 IVIg treatments and after 7 of 17 corticoid treatments. Regardless of therapy improvements occured with a rate around 50 %. Mortality was 1 in 30 PPs. Corticoid induced cataracts in 2 patients and stress fracture in 1 patient. No morbidity was associated with IVIg. 4 patients were treated with PP and, later, IVIg. 1 patient improved with both treatments, 1 patient improved after PP but not after IVIg and 2 patients did not respond to either treatment. 1 patient was excluded because he improved only after PP combined with IVIg. IVIg enriches the therapeutical repertoire. Effective therapy has to be selected by trial and error in every single case. Low morbidity recommends IVIg for a first attempt.

1-28-26 MAGNETIC STIMULATION IN EVALUATION OF DIABETIC NEUROPATHY

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In the present study we evaluated whether magnetic stimulation is of value in studying diabetic neuropathy, and whether there are changes in the central motor tracts in diabetes. Cadwell MES-10 stimulator was used in magnetic stimulation of the motor cortex and the neck (at C7 level) of 23 patients with adult-type II diabetes. Induced motor evoked potentials (MEPs) were recorded from hypothenar. Peripheral nerve conduction velocities and vibration sense threshold were also measured. MEPs correlated significantly with peripheral conduction velocities of median nerve ($r=0.697$, $p=0.012$) and of ulnar nerve ($r=0.409$, $p=0.059$). MEPs were not related to duration of diabetes or clinical neuropathy. However, blood glucose level did correlate with MEP ($r=-0.817$, $p=0.006$) but not with peripheral nerve conduction velocities. Magnetic stimulation is a valuable tool for evaluation of diabetic neuropathy. It enables also the analysis of the changes in the CNS among diabetics.

1-28-27 LIGHT AND ELECTRON MICROSCOPIC STUDY OF ALCOHOLIC POLYNEUROPATHY

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Alcoholic polyneuropathy is a sensorimotor disorder due to malnutrition, a direct toxic effect of alcohol, or both. Pathologically, there is degeneration of both myelins and axons; it is not certain which occurs first. Although myelinated nerve fibers are easily damaged, unmyelinated fibers have been considered invulnerable. Four patients, aged 38-61 years, were diagnosed as alcoholic polyneuropathy from history and clinical symptoms. Sural nerve biopsy was performed in all patients; two at mild stage, one at very advanced stage and one at recovery stage. At mild stage, small-sized myelinated fibers were decreased in number more strikingly than large-sized ones. However, the number of unmyelinated fibers was similar to that of normal control. At very advanced stage, the number of both myelinated and unmyelinated nerve fibers was decreased. At recovery stage, both myelinated and unmyelinated fibers showed almost normal appearance, though with axonal sprouting formation of myelinated fibers suggestive of regeneration.

Alcoholic polyneuropathy can improve with adequate treatment. In our cases, myelinated fibers were damaged as in the previous reports. However, unmyelinated fibers could also be injured in very severe case, indicating an importance of early diagnosis and adequate treatment.

1-28-28 HEREDITARY LIABILITY TO PRESSURE PALSIES MEDIATED BY NEURAL ARTERY THROMBOSIS: A NEW DISEASE.

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We present five members of three generations of a family with a tendency to recurrent acute mononeuropathies, involving both sensory and motor peripheral nerves and usually precipitated by minor trauma. Episodes of mononeuropathy are usually painless and transient, with resoluton of the deficit over several hours, but are occasionally associated with severe pain for several weeks and permanent nerve deficit. The tendency to recurrent pressure palsies begins in the second decade, and some affected individuals develop widespread livedo reticularis at this time. All the affected individuals have reduced serum IgA; most have antibodies to reticulin/gliadin. Nerve biopsy suggests an ischaemic aetiology with patchy axonal degeneration and some axonal regeneration affecting large and small myelinated fibres and to a lesser extent non-myelinated fibres, and platelet thrombi in epineurial arteries. There is evidence of epineural artery occlusion and revascularisation. Tomaculous change is not seen. The tendency to recurrent mononeuropathy is prevented by aspirin therapy. The pattern of inheritance suggests an autosomal-dominant disorder with variable expression. We propose that this thrombotic form of hereditary neuropathy with liability to pressure palsies represents a new and treatable condition.

1-28-29 STUDIES OF FAMILIAL AMYLOIDOTIC POLYNEUROPATHY TYPE I HAPLOTYPES IN CYPRUS

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OBJECTIVE: The aim is to investigate the haplotypes of our Familial Amyloidotic Polyneuropathy (FAP) Type I patients in an attempt to identify the origin of the disease in our families.

BACKGROUND: The disease is dominantly transmitted and is associated with a mutation in the transthyretin (TTR) gene at 18q11.1-12.3, changing a ^{30}Val to Met which introduces an Nsi I site. Fourteen families with FAP Type I have been ascertained, clustered in two areas of the island of Cyprus.

DESIGN/METHODS: Seventy seven individuals from ten families have been included in this study. PCR and Nsi I digestions were performed to identify carriers. Haplotypes were established using four polymorphisms within the TTR gene (I, III, V and VII). These were detected by PCR, dot blotting of products and oligo specific hybridisation.

RESULTS: Most of our families were not informative for the above polymorphisms. The Portuguese haplotype was present in all our families but it is also very frequent in the Cypriot population (50%).

CONCLUSION: No direct conclusion could be drawn as to the relation of the Potruguese haplotype with the disease in the Cypriot population. More polymorphisms are being analysed in an attempt to distinguish the disease haplotype(s).

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-03-01 INHIBITION OF NITRIC OXIDE SYNTHETASE FAILS TO PREVENT ISCHEMIC CA1 INJURY.

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Glutamate released by ischemia via the NMDA receptor may activate the production of nitric oxide (NO), by stimulating NO synthetase (NOS), leading to delayed neuronal injury. We tested this hypothesis in rats exposed to severe forebrain ischemia. Male Wistar rats (n=31) were subjected to 10 min of severe 4-VO ischemia. N-Nitro-L-arginine was infused IV pre-ischemically. Saline-injected animals served as controls. The number of damaged hippocampal CA1 neurons were counted and expressed as a percentage. A Mann-Whitney U test was employed.

Group(n)	% CA1 Injury (mean ± SD)
Saline (8)	77 ± 10
Nitro-arginine	
2 mg/kg(7)	80 ± 7
10 mg/kg(8)	78 ± 11
20 mg/kg(3)	54 ± 13
40 mg/kg(5)	74 ± 19

These data fail to show that NOS inhibition prevents in vivo ischemic injury.

2-03-02 ATRIAL SEPTAL ANEURYSM AND CEREBRAL EMBOLISM.

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Atrial septal aneurysm is an uncommon cause of cerebral embolism generally undetectable by clinical and ECG examinations. Echocardiography and mainly transesophageal echocardiography are necesary to identify this cardiopathy.

We report a 32-year-old pregnancy woman without cerebral-vascular risk factors who suddenly developed a regressive right hemiparesis associated with persistent right homonimus hemianopsia. A MRI showed a T2 left occipital triangular hiperintensity suggestive of ischaemia of embolic origin. Cardiological and ECG examinations were normal. Laboratory data including immunology, cryoglobulins, C and S proteins, luetic serology, antitrombin-III, lupic and antiphospholipidic anticoagulants, complement fractions, and platelet aggregation study were normal. Transcraneal and supraaortic Echo-Doppler were also normal. Transthoracic echocardiography showed an atrial septal aneurysm without other associated abnormalities. The patient was anticoagulated and no other events were present.

This case illustrates the necessity to perform a complet screening, including echocardiography, in all young patients with stroke despite the absence of abnormalities in the cardiological and ECG examinations.

2-03-03 MAGNETIC SOURCE IMAGING OF SOMATOSENSORY EVOKED FIELDS IN ADULT AND NEONATAL STROKE.

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We used magnetic source imaging (MSI), a noninvasive method to integrate functional magnetoencephalographic findings with structural magnetic resonance images, to study 6 patients with strokes of varying duration involving the somatomotor system. Somatosensory evoked magnetic fields were recorded using a 7 or 37 channel BTi neuromagnetometer to estimate the location of cortical responses to median nerve stimulation. In adults with stroke, the location of the estimated dipole, when present, was always in non-infarcted tissue at or near the contralateral somatosensory cortex and has not yet been found in ipsilateral cortex. The estimated current dipole strengths correlated (r=0.95, p 0.02) with the patients graphesthesia ability. A 23 year old male suffered a left middle artery stroke that destroyed the primary and secondary somatosensory areas at 1 month of age. He had mild right hemiparesis, hemisensory loss and Broca's aphasia. Right median nerve stimulation evoked activity in an intact region of the left inferior temporal gyrus and ipsilateral right mesial parietal cortex. To date, sensory recovery following stroke in adults appears to involve regions at or near the original somatomotor cortex while recovery in neonates can involve bilateral neural reorganization.

2-03-04 MILD HYPOTHERMIA IN ACUTE CEREBRAL ISCHEMIA: A FEASIBILITY STUDY

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Mild hypothermia confers striking neuronal protection in experimental focal cerebral ischemia. We attempted to induce mild hypothermia (1-3°C) for 12 hours in patients with acute cerebral infarction, presenting within 24 hours of stroke onset, using a cooling blanket and intermittent 2.5 mg boluses of intravenous chlorpromazine. Sixteen of 110 patients with acute cerebral infarction participated in the study. The mean time of entry into the study was 13 hours 15 minutes (range 4-23 hours). Hypothermia was maintained for a mean of 9 hours 31 minutes (range 30 minutes to 12 hours). The patients tympanic and rectal temperatures fell by a mean [±SD] of 1.3 ± 0.8°C (range 0.0-2.4°C) and 1.4 ± 0.9°C (range 0.1-2.9°C) respectively. Five (31%) stopped participating prematurely due to side effects which consisted of agitation due to urinary retention (1), feeling cold (1), anxiety (1), unrelated low back pain (1) and significant, but none detrimental, hypotension (1). One patient died on day 17 due to massive cerebral infarction. Although transient side effects were common, this method was effective in producing minor (mean [±SD], 1.3 ± 0.8°C) hypothermia. It is unknown whether this reduction was sufficient to have a therapeutic effect.

2-03-05 EFFECTIVENESS OF EXCITATORY AMINO ACID ANTAGONISTS, LAMOTRIGINE AND BW619C89 IN EXPERIMENTAL EPILEPSY AND STROKE IN RATS

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We have established the minimum effective doses (P<0.05) of excitatory amino acid (EAA) antagonists acting at NMDA (MK801) and non-NMDA (NBQX and GYKI52466) receptors and of compounds which reduce amino acid release possibly by an interaction at Na^+ channels (lamotrigine and BW619C89) in models of reflex epilepsy and of stroke in rats.

Minimum effective doses (mg kg^{-1}, i.p.) to reduce clonic seizure in genetically epilepsy prone rats were: MK801 (0.003), NBQX (20), GYKI 52466 (10), lamotrigine (5), BW619C89 (10).

Minimum effective doses (mg kg^{-1}, i.v or i.p.) to reduce cortical infarct volume after permanent occlusion of the middle cerebral artery were: MK801 (1.5), NBQX (60), GYKI52466 (40), lamotrigine (8), BW619C89 (10).

Differences between anticonvulsant and cerebroprotective doses are smaller for lamotrigine and BW619C89 than for the EAA antagonists that we have studied.

2-03-06 PREVENTION OF CHRONIC CEREBRAL VASOSPASM (CCVS) BY DIAZOZIBEN IN EXPERIMENTAL SUBARACHNOID HEMORRHAGE (SAH)

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The flow velocity of middle cerebral artery (FVmca) determined by transcranial Doppler ultrasonography (TCD) and the middle cerebral artery (MCA) diameter measured by cerebral angiogram (CAG) were used to evaluate CCVS.

Thirty-four rabbits were randomly divided into 3 groups: Group A (Control, n = 10), Group B (SAH, n = 12), and Group C (SAH + dazoxiben, n = 12). Experimental SAH was induced by percutaneous administration of 2 mL/kg body weight of fresh autogenous arterial blood into the cisterna magna. For Group C, the rabbits were given 10 mg/kg body weight of dazoxiben intravenously every 8 hours.

Two cisternal autologous arterial blood injections successfully established the SAH model. The mortality was 13%. No differences in serum TXB2, 6-keto-PGF1a, FVmca and CVI were found among groups (P > 0.2) before SAH induction; The serum TXB2 level in Group B was tripled at the 7th day. The serum 6-keto-PGF1a was decreased. In Group C the serum 6-keto-PGF1Aa at 7th day was 4X higher than pre-SAH (P < 0.05).

Our data suggest that the imbalance of intracranial TXA2 and PGI2, the abnormal increase in TXA2 synthesis and the decrease of PGI2 production were the main pathogenesis of CCVS after SAH; Dazoxiben at a total dosage of 100 mg/kg body weight was able to prevent CCVS effectively through inhibiting TXA2 synthesis and facilitating PGI2 production.

2-03-07 THE TREATMENT OF 412 CASES OF CEREBRAL INFARCTION USING DEFIBRINOGENASE

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We have used defibrinogenase (DFA) from the Agkistrodon acutus venom *treating 412 cases of cerebral infarction. This drug was separated and purified by* Dr. Zhang Hong-ji et al. In 412 cases, 327 were males, 85 were females. Age 41 - 59 years group there were 210 cases, over 60 years 202 cases. Most cases had atherosclerosis, 327 cases had acute infarction. They were treated within 2 weeks of their stroke, 85 cases were in recovery and sequelae. They be treated from 3 months to 8 years. Dosage and method: The DFA was intravenously infused 10 μ for 4 hours once every 3 - 7 days. Results: Among the acute infarction 327 cases, 111 cases (33.9%) were cured, 100 cases (30.6%) markedly improved, 73 cases (22.3%) improved, 30 cases (9.1%) showed no improvement, 13 cases (5%) died. All together 86.9% cases of the treatment was effective. In 85 cases, recovery and *sequelae, 4 cases (4.7%) were cured, 12 cases (14.1%) showed marked* improvement, 16 cases (18.8%) showed improvement, but 53 cases (62.4%) showed no improvement. Only 37.6% cases showed effective. At the same time Fibrinogen in plasma, thrombinogen time and blood clotting time were markedly changed. Fibrinogen was in a mean of 312.9 mg/dl before the treatment but decreased to 57.4 mg/dl (or 20 mg/dl). Among 412 cases 359 cases (87.6%) decreased to less 60 mg/dl. The thrombinogen time was prolonged from mean 16.3 sec to 120 sec blook clotting time was prolonged from mean 11 min to over 30 min. The principle for the DFA treatment. The DFA can degrade fibrinogen into FDP pieces, so the blood cannot coagulate. The thrombin time and blood clotting *time were prolonged. The thrombosis was prevented. Meatime the DFA can* dissolve the formed fibrin clotting and help to force it into f d p pieces. In our experiments, we found the FDA was better than urokinase and the DFA was with few bleeding.

2-03-08 EUROPEAN STROKE PREVENTION STUDY 2

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During the past years, the secondary prevention of cerebral ischemic lesions has made considerable progress. Different antiaggregating substances like aspirin (risk reduction 18%), ticlopidine (risk reduction 21%), or the association aspirin/dipyridamole (risk reduction 33%) have been considered. The best results have been obtained in the ESPS 1 with the association aspirin/dipyridamole. However, all these preventions bring about secondary side effects. To try prevent these secondary side effects, a new European study has been started : ESPS 2. The latter compares a placebo, 50 mg aspirin, 400 mg dipyridamole and the association 50 mg aspirin with 400 mg dipyridamole a day, recruiting 7000 patients. The recruiting of patients will end in March 1993. The follow-up will end in March 1995. 16 countries and 55 centres collaborate in this study.
The dose of dipyridamole chosen is aimed at compensating the dose reduction of aspirin by increasing the dose of dipyridamole. The placebo has been considered to be necessary due to the great variability observed in the results gathered from the aspirin studies. Also the secondary side efects due to aspirin are not to be overlooked.
An interim analysis performed on 4000 patients has shown that the randomization of these patients is excellent.

2-03-09 BRAIN MRI,CT AND SPECT IN ATAXIC HEMIPARESIS.

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Ataxic hemiparesis is the syndrome presenting with both cerebellar and pyramidal components.We studied 8 patients of ataxic hemiparesis using brain MRI,CT and SPECT.

The lesions were in corona radiata(infarct;3),in thalamus/posterior limb of internal capsule(infarct;2,hemorrhage;1),and in ventral pons (infarct;2,hemorrhage;1).One patient had two lesions(infarcts in corona radiata and ventral pons).

Five of 8 patients were evaluated with SPECT.They had corona radiata infarct(n=2),thalamus/posterior limb of internal capsule infarct(n=1)and pons infarct(n=1)and hemorrhage(n=1).In 4 of 5 patients,SPECT showed decreased blood flow in the contralateral cerebellar hemisphere.

The lesions were located in three different sites and all lesions interrupted both cerebrocerebellar pathways and pyramidal tract.SPECT suggested neuronal depression secondary to damage of the corticopontocerebellar pathway or dentate-rubro-thalamic pathway.

2-03-10 MENINGOCEREBRAL SHUNTS: A MEANS OF AUGMENTING CEREBRAL PERFUSION.

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Anastomotic end to end emissary arteries permitting communication between the external and internal carotid systems were found adjacent a chronic subdural hematoma in a man in whom virtually asymptomatic contralateral internal carotid artery occlusion had been previously discovered. Descriptions of subdural hematoma occurring under similar circumstances and involving seven different individuals have been recorded in prior medical literature. Such anastomotic arteries connecting the dural and pial circulations have been shown to be extremely fragile. The propositus, a 67 year old apparently previously well man, sought relief from left sided headache of recent onset, transient left crural weakness, and nonspecifically impaired memory. Neurological examination was, however, unremarkable. Magnetic images of the brain and selective transfemoral cerebral arteriography revealed a large and diffuse chronic left subdural hematoma, minimal left subarachnoid hemorrhage, complete occlusion of the right cerebral internal carotid artery, marked narrowing of the cavernous portion of that on the left, and seemingly end to end arterial channels connecting several left dural and leptomeningeal arteries. It is suggested that among possible compensations for impaired cerebral blood flow is the utilization of potential shunts within the meninges connecting the internal and external carotid streams, included among which may be rarely identified natural emissaries between the dural and pial circulations. Should these channels dilate widely as do "moya-moya" vessels elsewhere they may of their own accord and without trauma bleed readily into one or more meningeal spaces resulting inter alia in subdural hematoma and subarachnoid hemorrhage.

2-03-11 DOPPLER FLOW IMAGING VALUE IN ISCHAEMIC STROKE PROGNOSIS

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The Doppler image was performed in 152 patients with ischaemic stroke in the first 24 hours of the illness with continuous wave in common carotid artery (CCA) where resistance index (Ir) was calculated. In 142 patients the flow volocity in medial cerebral artery (MCA) was also estimated with pulsative wave.

The increase of value Ir (Ir > 0,75) was confirmed in 129 patients. From among 54 cases with bad prognosis where stroke resulted in decease or serious disability Ir was increased in 92,6% while in patients with good prognosis the increase of Ir was observed in 80,6% (statistically significant difference, $p < 0,05$). The reduction of flow velocity in MCA was confirmed in 69 patients. From among 49 patients with unfavourable prognosis up to 92,6% had the flow reduction in MCA at the onset of the stroke as compared with only 29% of the patients with favourable prognosis (difference statistically strongly significant, $p < 0,001$).

The increase of Ir and the flow reduction in MCA suggest unfavorable prognosis and indicate close observation and more intensive treatment of these patients.

2-03-12 STROKE IN THE RIJEKA REGION, CROATIA: ENVIRONMENTAL ETIOLOGICAL APPROACH

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The Rijeka region, which is situated in the northwestern part of Croatia, is formed by three different geographic-climatic zones: islands, littoral and continental-mountainous. Stroke-mortality in the whole region, for the period from 1986 to 1990 amounts to 111.2 per 100,000 inhabitants. It is extremely high on the island of Rab, 223.6/100,000 and Pag, 278/100,000, which is respectively two and three times higher if compared to average rates recorded in the region. The analysis of possible causes of such high mortality rates on both islands showed a high rate of morbidity of hypertension, especially on the island of Pag where it is almost four times higher if compared to the region as a whole. The cause of the high hypertension rate is to be found in spring water used on the island. The chemical analysis of the water has disclosed a three to five times higher concentration of minerals than that found in the littoral and continental belt of the region.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-03-13 **APATHY FOLLOWING CEREBROVASCULAR LESIONS**

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Apathy is defined as the absence or lack of feeling, emotion, interest, or concern. In this study, we have systematically examined the presence and severity of apathy in a consecutive series of 80 patients with acute stroke lesions. Apathy was measured using a specially designed Apathy Scale. The AS showed a high inter-rater reliability, a high internal consistency, and validity. Apathy was present in 22% of the patients, half of whom were also depressed. Post-stroke apathy was significantly associated with older age ($p<.05$), major depression ($p<.02$), more cognitive impairments ($p<.001$), more deficits in activities of daily living ($p<.0001$), and a higher frequency of lesions involving the posterior limb of the internal capsule ($p<.01$). This structure contains the ansa lenticularis, which connects the internal pallidum with both the *mesencephalic locomotor region (related to goal-oriented locomotor* behavior) and the substancia nigra (related to the sequencing of motor and cognitive functions). Thus, damage to the ansa lenticularis may produce the clinical syndrome of apathy. In conclusion, apathy is a frequent finding among elderly stroke patients with or without depression. The finding that apathy and major depression are associated suggests that depression and apathy may be causative of one another, or may share a neural substrate which can be affected by a single lesion.

2-03-14 A PROSPECTIVE COMMUNITY-BASED STUDY OF STROKE IN WARSAW, POLAND: PRELIMINARY INCIDENCE RATES

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First year preliminary results are presented of a prospective stroke register being carried out on residents of the 2nd and 3rd Health Care Units of Warsaw, Poland (population: 182,285) a well-defined district in the Mokotów region. Case-finding involves surveying hospital admissions, outpatient visits and death certificates. During the first year of our study (1991) 306 cases were registered; 213 with first ever in a lifetime (FEL) strokes and 93 with recurrent strokes. Computerized tomography or necropsy was performed in 64% of FEL stroke cases. Our crude annual incidence rate for FEL strokes was 117/100,000 (95% confidence intervals [CI] 104-139); the rate standardized to the European population was 102 (95% CI 89-117).

The incidence rates for strokes rose steeply with age and were higher in men than women at all ages. Our FEL stroke rates were found to be comparable to those of other "ideal" studies in age groups below 65 years, but low above that age. This suggests the possibility that potential stroke patients are dying off prematurely with ischemic heart disease. As this is the first prospective stroke register performed in Poland, we anticipate that this information will provide insight into the study of stroke in our country and can be used to help guide allocation of future health care resources.

2-03-15 CORTICOMENINGEAL CEREBELLAR HEMORRHAGE

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Spontaneous subarachnoid hemorrhage in the posterior fossa is uncommon. We report upon the clinical and radiological characteristics of two nonhypertensive patients with corticomeningeal cerebellar hemorrhage (CCH). They presented with clear-cut meningeal symptoms, but with no cerebellar or other localizing signs. CT scans showed a very unusual pattern of bleeding into the surface of the superior vermis and cerebellar hemispheres. Vertebral angiography was normal. Detailed MRI studies were also performed in both patients. They took a distinctly benign course and were discharged without sequelae.

Although a small (cryptic) arteriovenous malformation or aneurysm of the distal superior cerebellar artery cannot be completely ruled out in CCH, a venous or capillary source of the hemorrhage seems more likely. Repeated angiography does not seem warranted in these patients.

2-03-16 TRANSCRANIAL DOPPLER: DIFFERENT PATHOGENETIC MECHANISMS OF STROKE.

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We studied 92 patients with hemispheric stroke by three dimensional transcranial doppler (TCD 3D: EME, 2Mhz probe), computed tomography (CT) and magnetic resonance angiography (MRA: FISP 3D). We recorded the following doppler parameters: interhemispheric asymetry index (AI), mean flow velocity (mv) and pulsatility index (PI). On the basis of pathogenetic mechanisms *patients were divided in 3 groups. The first group (32 pz.) presented a significative* decrease ($p<0.0001$) of mv on the middle cerebral artery (MCA) in the infarcted side and a significative increase of AI ($p<0.0001$). MRA showed signal loss in the presence of mv slowing. TC highlighted MCA territorial infarcts. These data suggest a tromboembolic mechanism as the MCA distal branches occlusions. In the second group (30 pz.), in comparison with controls, PI showed a significative increase on all intracranial vessels ($P<0.001$). CT imaged a lacunar infarcts (3 to 12) with or without leuko-araiosis. The PI increase is due to peripheral resistences increase denoting a suffering of penetrating arteries, cause of lacunar strokes. In the third group (carotid stroke) we observed 6 mv focal increase of internal carotid artery (stenosis) and 6 mv remarkable decrease (<15cm/s) (5 occlusions, 1 dissection), 1 bidirectional flow (kinking) and collateral blood supply. MRA visualized a signal loss. CT imaged 5 watershade infarcts suggesting low flow mechanism. In conclusion TCD is useful in the quantitative evaluation of hemodynamic changes and collateral blood supply in the stroke allowing a better definition of the different pathogenetic mechanisms.

2-03-18 CEREBRAL VASOREACTIVITY TO ACETAZOLAMIDE: A TRANSCRANIAL DOPPLER AND HMPAO SPECT SIMULTANEOUS INVESTIGATION.

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The assessment of vasomotor reactivity allows the evaluation of the cerebrovascular reserve capacity in subjects with carotid stenosis.
The aim of this study was to investigate the acetazolamide (ACZ) effect on intracranial hemodynamics by means of transcranial doppler (TD) and Tc-99m HMPAO SPECT, simultaneously applied during the same test.

We examined 20 normal subjects (average age 60.7 years) by two test protocols. In the first protocol the rest and the stress conditions were investigated during the same day, being the baseline examination (rest) followed by 1 g i.v. ACZ administration (stress); after 15 minutes a fresh solution of Tc-99m HMPAO was injected and 5 minutes later SPECT scanning was restarted. Flow velocities from middle cerebral arteries (MCA) of both side were measured immediately before the first and the second SPECT scanning. In the second protocol the rest and stress condition were obtained in different days after a 48-hours interval with the same parameters.

Our data showed that mean spatial velocities in MCA constantly increased after ACZ administration, according to its vasodilatory effect on the small resistance arteries. On the contrary, a global decrease of cortical Tc-99m HMPAO uptake was detected in comparing the rest/stress data. These results suggest that caution should be posed when using ACZ test applied to patients with cerebrovascular occlusive disease, as different instrumental approaches can provide conflicting results due to a not sufficient knowledge of their basic mechanisms.

2-03-19 CONTINUOUS CEREBRAL BLOOD FLOW MEASUREMENT IN A PIG MODEL OF INCREASED INTRACRANIAL PRESSURE

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We have developed a method for continuous measurement of brain blood flow by positioning single fiber laser Doppler probes on the brain surface, within the cortical gray matter and within the subcortical white matter and changes in brain circulation in response to increased cerebrospinal fluid pressure can be studied at several locations.

Eleven piglets anesthetized with pentobarbitone were used. Blood pressure and cerebrospinal fluid (CSF) pressure were continuously monitored. Continuous measurement of cerebral microcirculation with laser Doppler flowmetry (LDF) was performed with a Periflux PF 2B laser Doppler flowmeter.The response to high CSF pressure was tested by infusion of artificial CSF into the cisterna magna.

All four intracraniel probes showed parallel variations. High CSF pressures was followed by a sharp decrease of LDF signal. When the LDF signal approached zero the arterial pressure started to rise followed by a rise in LDF signal. After 10 minutes of high CSF pressure the LDF signal was 39 % of baseline signal. After reduction of CSF pressure to normal the LDF signal increased to 170 % of baseline.

LDF signals during high CSF pressure are consistent and reproducible at several intracerebral locations, and this technique is well suited to study rapid changes in cerebral perfusion during high intracranial pressure.

2-03-20 SNEDDON'S SYNDROME: VALUE OF ANTIPHOSPHOLIPID ANTIBODIES AND CUTANEUS BIOPSY. ANALYSIS OF A SERIES.

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Sneddon's Syndrome (S.S.) as defined by systemic *livedo reticularis* and cerebrovascular lesions is an occlusive, progressive, non-inflammatory arteriopathy affecting small and middle-sized vessels. Its most frequent neurological manifestations are ischaemic strokes, dementia and seizures. Family history is a well-documented fact and recently it has been related with Antiphospholipid Syndrome (APS) by some authors.

We have studied the neurological outcomes in 4 patients suffering from S.S. There was a family history of stroke in one and *livedo reticularis* in two cases. MRI and/or CT showed ischaemic brain infarcts in all the patients and one of them also presented a cerebral haemorrhage, which is an exceptional feature in S.S. Brain and hand angiographies in the four patients showed stenosis and occlusions of small and middle-sized arteries as well as intracranial avascular areas and transcerebral anastomotic networks. Systemic vasculitis was ruled out and antiphospholipid antibodies were negative in each case. Skin biopsy was normal in all patients; digital biopsy showed an intimal hyperplasia in one case and a corticomeningeal biopsy from another case presented hyalinized areas in arterioles, capillaries and venules.

Analysis of this series indicates that clinical, neuroradiological and digital artery histopathology data, but not cutaneous biopsy, support S.S. diagnosis. The negative result for antiphospholipid antibodies suggests that APS and S.S. are two different diseases.

2-03-21 ISCHEMIC STROKE AND THE PRIMARY ANTIPHOSPHOLIPID SYNDROME.

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Ischemic stroke is a well recognized occurrence in patients with antiphospholipid antibodies (aPL). From a cohort of patients with idiopathic anticardiolipin antibodies (aCL) and/or lupus anticoagulant (LA), 10 were identified with at least one cerebral ischemic event, meeting the criteria for primary antiphopsholipid antibody sindrome (PAPS). Male/female ratio was 1:1, mean age 44±14 (range 28-76). Ischemic stroke occurred twice in 1 patient and as an isolated event in 5 patients. In other 3 patients, ischemic stroke was accompanied by deep vein thrombosis (DVT), by DVT and pulmonary embolism, and by splenic infarction. Cavernous sinus occlusion with 3 DVT occurred in another patient. Patients with a history of multiple occlusive events were positive to more than one LA test, showed elevated levels of IgG aCL, fibrinogen and von Willebrand Factor. The serial determination of these hemostatic variables may prove useful to identify idiopathic aPL patients at higher risk for stroke.

2-03-22 STROKE IS BECOMING A DISEASE OF ELDERLY WOMEN IN FINLAND.

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A community-based stroke register has been operating in the city of Turku in southwestern Finland. Acute stroke events occurring at any age are registered using the methods of the WHO MONICA project. During 1982-1989 altogether 4197 acute stroke events were diagnosed, 73% of them were first stroke attacks. Of all stroke events 60% occurred in women. Half of the events (n=2112) occurred in subjects aged 75 years or more and of these elderly cases 73% (n=1152) were women. The overall annual age adjusted incidence of stroke was 2.7/1000. The incidence was higher in men (3.2) than in women (2.3). During the 8 years of the study, the proportion of population aged 75 years and more increased by 30% in Turku. The incidence of stroke fell significantly in men but not in women during the 8-year period. There was no variation in trends of stroke by age. SAH accounted for 5% and ICH for 10% of all events. Of the infarctions one-fourth were classified as cerebral embolism. After 28 days 28% of patients were deceased. Of the survivors, 43% (1430) were still hospitalized and of these 640 (45%) were elderly women aged 75 years or more.

2-03-23 SUPERIOR SAGITTAL SINUS THROMBOSIS DUE TO FREE PROTEIN S ANTIGEN DEFICIENCY MIMICKING THE ANTICARDIOLIPIN ANTIBODY SYNDROME.

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We report a patient with superior sagittal sinus thrombosis (SSST) due to free protein S antigen deficiency mimicking anticardiolopin antibody syndrome.

A 31 year-old woman, with a history of "toxemia" and premature delivery (33 wks), followed by inferior vena cava thrombosis (IVCT), and two spontaneous abortions (10 and 22 wks), developed headaches, seizures and tetraparesis. CT, angiography and MRI showed SSST with bilateral confluent hemorrhagic venous infarcts. Lupus anticoagulant and anticardiolipin antibody tests were negative; antithrombin III and protein C levels were normal; free protein S antigen level 10% (53-157%). Anticoagulation therapy (heparin) was initiated and continued (warfarin) without complications. Her twin sister, with a history of a spontaneous abortion (10 wks) and a premature delivery (33 wks), had a free protein S antigen level of 20%.

This patient is unique because of the multiple conditions (complicated pregnancies, IVCT and SSST), most likely due to free protein S antigen deficiency, mimicking the anticardiolipin antibody syndrome and an identical twin sister with free protein S antigen deficiency and complicated pregnancies.

2-03-24 SILENT CEREBROVASCULAR LESIONS IN PATIENTS WITH FIRST EVER STROKE

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Out of 201 patients admitted for first ever stroke and no prior history of transient ischemic attacks, 45 (22%) were found to have evidence of prior subclinical cerebral infarction on computed tomography (CT) or magnetic resonance imaging (MRI), so-called "silent strokes." Twenty one had only one additional lesion, 5 had two, and 19 had three or more. Compared with other patients without additional lesions on CT and/or MRI, atherosclerotic stroke subtype was significantly more prevalent (36 vs. 19%) ($p < 0.02$), and hemorrhagic stroke significantly less prevalent (2 vs. 20%) ($p < 0.01$) in patients with subclinical infarcts. Age (mean of 70 years in silent stroke patients vs. 67 years in the other group) and sex distribution (53% vs. 50% male) were similar in both groups. Patients with silent strokes tended to have hypertension more often (69 vs. 53%), but this and other risk factor levels between the two groups were not statistically significant. The average Mini-Mental State Examination (MMS) score was lower in patients with silent lesions (21.6 out of 30) than without (24.5 out of 30).

In conclusion: Patients with silent strokes had a higher frequency of atherosclerotic and a lower frequency of hemorrhagic stroke subtypes. Age, sex, risk factor and MMS comparisons revealed no significant differences.

2-03-25 DISCORDANCE OF LANGUAGE LATERALIZATION AND HANDEDNESS IN SITUS INVERSUS TOTALIS

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OBJECTIVE: To determine whether language dominance and handedness follow similar hemispheric lateralization in a patient with situs inversus totalis. BACKGROUND: Patients with situs inversus totalis have dextrocardia, visceral reversal but have normal organ structure and function. The language-dominant hemisphere has a strong correlation with handedness.

DESIGNS/METHODS: A 76-year-old, right-handed woman presented with acute right hemiparesis, right hemianopia, and right hemisensory deficit. Language function was excellent. Her parents, five siblings, seven children and 23 grandchildren were right-handed. Two left-handed grandchildren had a left-handed father, unrelated to our patient.

RESULTS: MRI of the brain revealed a large left middle cerebral artery infarction. The posterior Sylvian fissure was higher on the right, with a two-part division of the planum temporale.

CONCLUSION: Although handedness and language often link with hemispheric function, the two may have separate determinants. The gross anatomic structure of the Sylvian fissure and planum temporale appear to relate more closely to language function. As 40% of patients with situs inversus are left-handed, this patient with such a lesion without aphasia suggests an anomalous dominance of language.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-06-01 EEG/REACTION TIME CORRELATIONS IN SCHIZOPHRENICS AND NORMALS

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Reaction time (RT) to tones of intensities 40, 60, 80,100 dB (presented in randomized order) was measured in 9 unmedicated male schizophrenics (SCH) with marked negative symptoms and 14 healthy men. All subjects were right-handed, matched for age and apparently cooperative. Background monopolar EEG was recorded 10 min later. As it was found SCH had 1)marked slowing of RT,2)nonsignificant changes in delta-band except for spectral power amplitude (ASP) of 2.5 Hz increased in left centro-parietal regions, 3) decreased ASP for 7.5 -8.5 Hz in left hemisphere and increased for 10.5-12 Hz for both hemispheres. In SCH group RT for all intensities correlated positively with ASP frequencies in delta, theta, alpha and beta-bands, while in normals RT correlated negatively with ASP in delta, theta and alphal (7.5-10 Hz) frequencies and positively - with ASP in alpha2 (10.5-12.7 Hz).

EEG abnormalities in SCH as well as EEG/RT correlations (especially those for delta and alpha2 frequencies) are discussed.

2-06-02 EEG MAPPING IN CHILDREN WITH GILLES DE LA TOURETTE'S SYNDROME.

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EEG mapping was carried out in 21 children (age 8-13) with Gilles de la Tourette's syndrome (GTS). Background EEG was recorded before and during treatment with neuroleptics, cerucalum and anticonvulsants. EEG maps of this clinical group were compared to those of age matched 68 healthy children, and of 11 schizophrenics with Tourett-like disorders (GTL). Statistical analysis (Mann-Whitney rank sum test) of spectral powers in 6 EEG frequency bands was performed. Significant increase of delta and theta activity in GTS and GTL groups compared to normals was found. It was most pronounced in central regions of children with GTS, and in parietal-occipital regions of those with GTL. Alpha and beta activities were reduced in temporal regions of right hemisphere in GTS and in fronto-temporal regions of left hemisphere in GTL. Neuroleptic treatment was accompanied with decrease of alpha and beta activity in the GTS group and did not change EEG in GTL. Anticonvulsants caused reduction of delta-theta activity in all cortical regions of both clinical groups. Cerucalum did not influence on EEG spectral power.Thus, the differences between EEG children with GTS and GTL was found in topography of abnormalities and reaction to neuroleptic treatment.

2-06-03 HEMISPHERIC ASYMMETRY IN THE RECOGNITION OF EMOTIONAL FACIAL EXPRESSION IN HEALTHY AND DEPRESSED SUBJECTS.

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The recognition of emotional facial expression was studied in 25 unmedicated right-handed depressed patients, 10 of them with major depressive disorder (group I) and 11 - with schizotypal personality disorder (group II), and in 15 right-handed healthy subjects. The drawn sad, neutral and happy faces followed by masking stimulus were presented in a random sequence in right or left hemifields. The healthy Ss revealed the right hemisphere advantage in recognition of all types of facial stimuli. The most significant interhemispheric differences were observed for happy faces. Depressed patients demonstrated the worsening of emotion recognition, the most prominent for sad faces. The difference in the number of mistakes when recognizing happy and sad faces was much more marked in group I than in group II and healthy Ss. Compared to normals all depressed patients showed the reduction of interhemispheric differences of the recognition accuracy. In group I there was the inversion of the interhemispheric pattern in recognition of happy faces with left hemisphere preference.

2-06-04 POST-POLIOMYELITIC SYNDROME IN SENEGAL - CLINICAL AND NEUROPHYSIOLOGICAL STUDY

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Objective: To estimate PPS frequency in African patients with acute paralytic poliomyelitis antecedents, from a clinical examination and a neurophysiological investigation.

Patients and Methods: The study was carried out in the Department of Neurology in the Dakar University Hospital in July 1992. 17 patients (12 females, 5 males, mean age = 31.9 ± 7.8 years) who had suffered from an acute poliomyelitis in their childhood were included. In every case, the retroviral serology were negative. All patients underwent a complete neurological exam, a study of motor and sensory conduction velocities and needle electromyogram. The reference values were established among 17 healthy subjects matched with the patients on sex and age.

Results: 2 groups of patients could be made on the clinical plane:

- 11 patients (7 females, 4 males, mean age = 32.4 ± 7.7 years) were suffering from sequelae of a musculosquelletic syndrome, severe amyotrophy, vertebral or limb deformations.
- 6 patients (5 females, 1 male, mean age = 31.2 ± 8.6 years) presented a neuromuscular and progressive PPS fulfilling the Dalakas et al. criteria (1). In 2 cases, the relapse occurred in a territory different from that of the original disease. The period of time before the reappearance of symptoms could be assessed with accuracy only in 3 cases: 24, 28 and 42 years.

The neurophysiological explorations showed no significant difference between the two groups of patients. Motor and sensory conduction velocities were similar. Six patiens (4 in the first group and 2 in the second) suffered from a sensitive axonal neuropathy, with reduction of amplitude of sensory potentials. In 2 cases, there was a troncular palsy of the ulnar nerve in the elbow. The electromyographic study showed neurogenous activity with polyphasic potentials and sometimes denervation, in the two groups.

Conclusion: PPS seems comparatively frequent in Africa (37.3% in this series).

2-06-05 CORTICAL MYOCLONUS AS PRIMARY MANIFESTATION OF MALIGNANT LYMPHOMA.

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We report a 65 year old white male, who presented with spontaneously occurring, irregular, jerky movements of fingers and hands, left more than right, identified by EMG as myoclonic bursts. Simultaneous recordings during an episode of repetitive jerking of the left upper extremity showed a regular sequence of myoclonic bursts, proximal muscles being activated before distal ones. A cortical origin of the myoclonus was suggested by the presence of exaggerated long-loop responses, mainly in left hand muscles, giant somatosensory evoked potentials and a spike over the right central-parietal cortex, preceding myoclonic bursts, as shown by jerk-locked back-averaging of the EEG. Initial work-up revealed IgM lambda paraproteinemia (1860 mg%), a bone marrow biopsy suggestive of malignant lymphoma, bilateral posterior uveitis, essential tremor in the upper extremities, and a chronic, predominantly axonal, motor peripheral neuropathy. HIV serology, CSF, and imaging of brain and viscera were unremarkable. 18 months later, the patient developed left facial-brachial weakness and a right temporal-parietal mass lesion was discovered, surgically removed, and identified as a malignant lymphoma, type B, lambda chain immunopositive. Cranial radiotherapy was performed and IgM lambda paraprotein levels fell to 477 mg%.

We suggest that the myoclonus is caused by direct invasion of the motor cortex by metastatic spread of systemic malignant lymphoma.

2-06-06 PHARMACO-EEG MAPPING PROFILE OF GINKGO BILOBA EXTRACT (EGb 761)

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Electroencephalography is one of the most convenient method for functional explorations of the brain. The recent introduction of the EEG and ERPs (i.e. P300 and C.N.V) mapping methods allows nowadays to investigate accurately the effects of psychoactive substances. The aim of this study was to evaluate, in a group of 15 young healthy volunteers, the pharmaco-EEG profile of EGb 761 (Tanakan ®), using mapping methods. The study included two major parts, with a first part investigating the effects of 80 and 160 mg in single dose administration, versus placebo and the second part investigating the subacute effects of daily doses of 160 mg. During each session EEG and ERPs mapping data were collected over a 6 hours kinetic. The SDT (Statistical Decision Tree) method was used for statistical evaluation purposes. EGb 761 induced a marked increase in the alpha and beta bands with a concomitant decrease of the theta band. P 300 mean latencies were also decreased with an amplitude decrease at the peak of CNS effects of EGb 761. This EEG and ERPs mapping profile confers to this extract nootropic capacities (enhancement of vigilance and improvement of some cognitive functions). EGb 761 extract has shown nootropic effects, but also other possible therapeutic indications when administered subacutelly. These latter indications are possible effects like CNS regulations: anxyolitic capacities? (beta effect) which have to be confirmed in future studies carried out in patients.In conclusion, EGb 761 may be indicated in elderly individuals who suffer from beginning senile cognitive impairment.

2-06-07 TOPOGRAPHICAL EEG CHANGES DURING ORTHOSTATIC MANEUVERS

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Scalp EEG topographic analysis was performed in order to verify whether or not the EEGs change during orthostatic maneuvers. 23 healthy volunteers (15 M and 8 F, mean 24.8 ± 1.7 years) were examined. Subjects were reclined on the tilt table and EEGs were recorded through 16 monopolar electrodes (10-20 system) with eyes closed for 50 seconds of each session during supine and standings position. They were computed with a signal processor by FFT and displayed topographically. The equivalent potentials for each spectral band during standing position were compared with those during supine position using significance probability mapping(SPM). Systemic blood pressure and pulse rate were also measured after each EEG sampling epoch. The potentials of alpha-2, beta-1 and beta-2 band during standing tended to increase significantly as compared to those during supine position. The potentials of alpha-2 increased in 17 of the 23 subjects, those of beta-2 in 12 and beta-1 in 10. EEG changes in theta and alpha-1 were not consistent. As to the cardiovascular parameters, percent change equivalent potentials of alpha-2 and beta-1 were correlated significantly with change ratio of mean blood pressure or pulse rates. These results indicate that the EEG changes during orthostatic maneuvers might be related to cardiovascular functions.

2-06-08 MOTOR EVOKED POTENTIALS OF THE DIAPHRAGM IN HUMANS ELICITED THROUGH MAGNETIC BRAIN STIMULATION.

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The function and integrity of the corticospinal tracts can be studied through magnetic transcranial stimulation (TCS) of the motor cortex. In this study magnetic TCS of the diaphragm muscle was carried out in 10 healthy volunteers (5 women, 5 men, age between 20 and 40). The motor cortex was transcranially stimulated at 2 cm anterior to C3/C4, and then the cervical roots in order to calculate the central motor conduction time (CMCT). Motor evoked potentials (MEP's) were detected through cup-electrodes with the active electrode at the xiphoid processus and the reference electrode at the inferior border of the rib cage at the midclavicular line, and the ground electrode at the manubrium sterni. The MEP latency time was found to be 16.21±0.33 msec, the MEP amplitude 3.52±2.40 mV, and the CMCT 8.39±0.41 msec. No significant differences were been between left and right side.
In conclusion, this technique can be applied to offer useful additional information about the function and integrity of the central motor conduction properties of respiratory muscles in healthy subjects as well as in patients with various neurological and respiratory disorders.

2-06-09 HYPOTHALAMUS-PITUITARY MODULATE HEARING THROUGH NEUROTENSIN IN GUINEA PIGS.

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The determination of Neurotensin (NT) in the cochlea, brain blocks and plasma in guinea pigs were performed with radioimmunoassay (RIA). The brain stem auditory evoked potential(BAEP) was used as an index to assess hearing.

We found the level of NT in the cochlea was very high in normal. But it was quickly and significantly decreased ($p<0.001$) after radiation of microwave (RM). It is interesting that the latency of wave I of BAEP was simultaneously shortened after radiation($p<0.025$), i.e. the hearing of animals was improved. The NT in the pituitary and the hypothalamus after RM was gradually increased up to 3 and 2 times ($p<0.001$ and $p<0.005$); there is no significant change in NT in other parts of brain. The NT in plasma after RM also rose up to 5 times paralleled to the change in the pituitary and hypothalamus.

On the basis of findings, we advance the HYPOTHESIS OF INHIBITORY MODULATION of the neurotensin and the pituitary-hypothalamus on hearing: (1) The NT plays a role of modulating hearing, an inhibitory modulation; (2) The point of modulating of NT is at the cochlea and/or from it to auditory nerve; (3) The hypothalamus-pituitary take part in the modulation of hearing in cochlea through neruotensin.

2-06-10 THE LACRIMATION IN THE PARKINSONIAN PATIENTS: EVALUATED BY SHIRMER TEST

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We have observed that the parkinsonian patients with marked expression difficulty show less amount of tearing even in conditions of crying or laughing. The Shirmer test is carried out to objectify lacrimation with 44 clinically diagnosed parkinsonian patients (M: F = 2.13: 1, mean age = 65.5) and 50 age-matched controls (M: F = 1.75: 1, mean age = 62.0).

The Whatman No. 2 papers prepared in precut strips 5 mm by 35 mm, were placed in the cul-de-sac for 5 minutes, after then the wetted lengths were measured.

We noted that lacrimation amounts were decreased in parkinsonian patients compared with controls: the averages were 3.09/3.18 (right/left) in the former and 7.17/8.42 in the latter (lt = 4.26/4.07). We suggest that decrease of lacrimation is associated with mask like face and autonomic dysfunction. Lacrimation may be under control of the basal ganglia.

2-06-11 TEMPORAL FREQUENCY DEFICIT IN PATIENTS WITH SENILE DEMENTIA OF ALZHEIMER TYPE: A VISUAL EVOKED POTENTIAL STUDY.

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In order to study the visual processing of senile dementia of Alzheimer type (SDAT), we recorded steady-state visual evoked potentials (VEPs) to LED goggle stimulation at 5 different temporal frequencies in 14 patients with SDAT and 14 control observers. In comparison to SDAT, 14 patients with vascular dementia (VD) were also studied. All subjects were female and their ages were closely matched. Temporal frequencies were 5, 10, 15, 20 and 30 Hz. Steady-state VEPs were Fourier analyzed and the amplitude and phase of the first harmonic response were obtained. A significant difference in amplitude was found across 3 groups for 15, 20 and 30 Hz stimulation, while there was no difference for 5 and 10 Hz stimulation. Multiple comparison tests revealed that SDAT had significantly smaller amplitude than normal controls. VD showed lower amplitude when compared with normal subjects, however, there was no statistically significant difference. In phase data, there was no statistically significant difference across 3 groups for all temporal frequencies. These results indicate that there exists a temporal frequency deficit in SDAT. It could be explained by the pathology of SDAT which affects an early stage of visual signal processing.

2-06-12 SPREADING DEPRESSION OF LEÃO IN HUMAN CORTEX. R.S. McLachlan and J.P. Girvin. University Hospital, London, Canada

Spreading depression (SD) is a reaction to local stimulation of grey matter characterized by attenuation of spontaneous and evoked electrical activity, a DC potential shift and dilation of arterioles which slowly spreads at a rate of 2-6 mm/min. It has been implicated in the pathogenesis of several neurological conditions, particularly migraine. We explored the nature and extent of SD in human cerebral cortex exposed during surgery for intractable epilepsy. Patients were awake under neuroleptanalgesia. A linear array of four platinum ball electrodes (0.5 mm with 1.5 mm centres) was applied to the surface of the cortex and connected via a Ag-AgCl half cell to DC and AC amplifiers. Chemical (15% KCl), electrical (monopolar 0.8 mA, 2 ms, 50 Hz), mechanical or thermal stimuli were applied 2 mm from the first electrode. Recordings were made in 22 patients, age 20-49 years, from temporal (19), frontal (2), and occipital (1) cortex. In none was evidence of SD obtained. A stationery DC shift occurred particularly following KCl application. Spontaneous interictal spike activity was increased and in 2 patients seizures occurred after KCl. No differences were observed in 4 patients with common migraine. These results support previous observations that SD is more difficult to obtain from animals high in the phylogenic scale and raise doubts about the role of SD in the pathogenesis of human disease.

2-06-13 EEG MAPPING STUDY OF ALPHA GENERATORS.

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Recent advances in topographic EEG mapping permit precise and quantitative analysis of electrical activity of the brain. Topographical EEG analysis was performed using R-EEG16 computer system to study the correlation between anatomical localisation of hemispheric cerebrovascular lesions and the concomittant field power asymmetries in the alpha frequency range. Peak power frequency, asymmetries of dominant alpha fields and alpha/theta ratios and time sequences during photic drive were evaluated. Cortical, cortico-subcortical and thalamic lesions were selected based on CT scan findings. According to the topographic character of cerebral infarcts the following types of alpha power asymmetries could be recognized: 1. In the cases of infarcts in the territory of posterior cerebral artery circulation significant power field reduction was observed on the ipsilateral hemisphere. 2. Subcortical lesions (thalamic infarcts and circumscribed bleedings) did not influenced the amplitude of resting alpha activity, and the photic drive, but reduced the peak power frequency.

2-06-14 MOVEMENT RELATED CORTICAL POTENTIALS PRECEDING SELF-PACED RANDOM OR SINGLE DIRECTION MOVEMENTS IN PATIENTS WITH PARKINSON'S DISEASE AND NORMAL CONTROLS.

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The movement related cortical potential was recorded from scalp leads during self-paced movements of a joystick on the right hand side of 8 patients with idiopathic Parkinson's disease and eight normal age-matched control subjects. Two different tasks were compared: repeated movements in the same (forward) direction, or movements made in one of four different directions chosen randomly by the subject prior to each movement. In normals, the amplitude of the early (BP) peak premovement negativity was significantly larger at the vertex, the bilateral motor areas and frontal leads during, the random task than during the repetitive task. The late (NS') component was larger only at the vertex - left motor area. In parkinsonian patients, the only significant increase in the random task was for the BP in the left frontal lead. These results suggest an impairment of motor preparation prior to randomly chosen movements which may reflect dysfunction of the supplementary motor area.

2-06-15 DIAGNOSTIC VALUE OF BEAM IN PATIENTS WITH INTRACRANIAL SPACE-OCCUPYING LESIONS

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To see BEAM of patients with intracranial space-occupying lesions, 45 cases verified by CT scan and/or cerebral angiography entered into the study. The types of BEAM were divided into coincidence, approximate coincidence, and non-coincidence compared with operative results. The accurate ratio of localization diagnosis of BEAM is 51.1%, which is significantly higher than that of EEG (15.5%), $p < 0.01$. The research also found that the examination results are relative to the locations of lesions. Positive ratio of BEAM is 96.5% to supertentorial lesions, while positive ratio of EEG is 82.7%, to hypotentorial lesions, the positive ratioes of both BEAM and EEG are less than 50%. In addition, the article discuss the principle and advantage of BEAM.

2-06-16 MULTI-MODALITY EVOKED POTENTIALS AND AUDITORY AND VISUAL COGNITIVE POTENTIALS IN PATIENTS WITH SEQUELAE OF SUBACUTE MYELO-OPTICO-NEUROPATHY(SMON).

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In order to investigate the lesions of central nervous system in patients with sequelae of SMON, we examined 21 cases, using multi-modality evoked potentials. Central conduction time derived from somatosensory evoked potential was delayed in 3 cases (14%). Non-invasive measurement of spinal cord conduction velocity was decreased in 6 cases(29%). In 3 cases(14%), I-V interpeak latency of brainstem auditory evoked potentials was prolonged or the 5th wave was not evoked. Pattern reversal evoked potential was delayed or not evoked in 3 cases(14%). Although definite dementia was not observed, abnormality of cognitive potentials was found in 1/11 cases(9%) in red /green visual test, 2/12 cases(17%) in tone/clic auditory test, and 4/11 cases(36%) in tone/tone auditory test. In conclusion, the present electrophysiological study suggested that the lesions of patients with sequelae of SMON were distributed widely but with lower frequency in the spinal cord, brainstem and optic pathway, and that their cognitive dysfunctions were subclinical.

2-06-17 OBSESSIVE-COMPULSIVE DISORDER: AN ELECTROPHYSIOLOGICAL APPROACH TO PATHOGENESIS

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Studies performed in last decades on obsessional compulsive disorders (OCD) seem to contrast the current psychiatric opinion which considers this behavior as a syndrome without any demonstrable brain dysfunction. In particular, some recent anatomoclinical and neuroimaging studies as well as surgical observations suggest possible relations between OCD and brain damages like frontolenticular lesions, basal ganglia cavitations, dysfunction of the local glucose metabolism and excessive release of norepinephrine by locus coeruleus. Bioelectrical abnormalities have also been found in frontomedial and posttemporal regions.

To assess the electrophysiological changes in brainstem structures in OCD patients, recordings to BAEP were carried out in 60 consensient neurotic patients of whom 30 were affected by OCD and 30 were suffering from anxiety neurosis (ANX); 25 age-matched volunteers were used as controls.

Results:

- An increase in absolute latency of both I and V waves and of I-III and I-V interpeak latencies was found in the global neurotic group as compared with controls.
- The latency of wave I was significantly higher in ANX patients whereas the latency of waves III and V was observed increased in both the subgroups of neurotic patients.
- The III-V and I-V interpeak latencies were increased in OCD subjects as compared with ANX patients and controls.
- The I-III interval was increased in both patients groups.

The above BAEP changes could be accounted for a brain-stem dysfunction with a probable involvement of serotoninergic central pathways.

2-06-18 **Vibrometry, a new tool of screening procedure in patients suspected for a peripheral neuropathy, especially sensitive at entrapments.**

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In our laboratories we have evaluated the diagnostic universe for Vibrometry (Brüel & Kjær, type 9627) in relation to sensory nerve conduction studies.

Patients clinically suspected for an ulnar nerve entrapment at the elbow (UNE) or an idiopatic polyneuropathy (IPN) were included. Vibrometry was performed at the second and fifth finger in seven frequencies (8 - 500Hz) and considered abnormal with age adjusted negative sumscores > 49 and/or a diphasic curve with only normal values in the area of 125 Hz. Sensory nerve conduction velocities (NCV) and amplitudes were determined in either the ulnar nerve or three nerves including the median nerve.

Fiftynine persons participated in the study with 39 in the group of UNE and 20 in the IPN group. A clinical suspicion was confirmed with vibrometry in 81% of the investigated versus 58% with the conduction study. Especially at the UNE 89% respectively 49% were found. In relation to NCV the nosographic sensitivity of vibrometry is 85%, at SUE it was found to be 89%.

In conclusion vibrometry is a very sensitive screening method with a better correlation to the symptoms than the conduction studies.

2-06-19 PHONATION-DEPENDENT CHANGES IN THE HUMAN AUDITORY CORTICAL RESPONSIVENESS

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The activity of the human auditory system was investigated during vocalization in order to study the neural mechanism of the audiovocal control system. The experiment was carried out on normal adults. Vocalization-related potential(VRP) was obtained by our own method(Kikuchi & Kita 1992;Kita & Kikuchi 1992). The recorded vocalizations were played back to the subjects through a headphone in order to record the auditory cortical response. As a result, the auditory response was highly attenuated only during phonation. The remarkable suppression was observed in all the subjects. The results of the present study provided evidence of phonation-dependent changes in the human auditory cortical responsiveness.

2-06-20 VOCALIZATION RELATED POTENTIAL AND ITS CONSTITUENT COMPONENTS

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The purposes of the present study were to record and to examine the scalp-potentials related to vocalization. The vocalization-related potential(VRP) could be recorded from normal adults, under a simple vocalization condition. VRP was mainly composed of N1v,P1v and N2v("v" shows vocalization). The topographical study showed that N1v and P1v corresponded respectively to the sink and the source of an identical dipole located in the oro-facial area of the central fissure. N2v was highly attenuated by auditory masking. Therefore,this component was related to the auditory activity. The present results showed that VRP consisted mainly of the moto-sensory components and the auditory component.

2-06-21 PAIN-RELATED AND ELECTRICALLY STIMULATED SOMATOSENSORY EVOKED POTENTIALS IN CEREBROVASCULAR ACCIDENT

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Pain-related somatosensory evoked potentials (pain SEPs) and electrically stimulated SEPs (electric SEPs) were examined in 13 patients with cerebrovascular accident to investigate correlation between sensory disturbance, cerebral lesions and SEPs. Pain SEPs after CO_2 laser stimulation to the dorsum of the hand were recorded at Cz. Electric SEPs after median nerve stimulation at the wrist were recorded at C3' and C4' (2cm behind C3 and C4). P340 in the pain SEPs and N19 in the electric SEPs were under consideration in this study. In 5 patients with a putaminal lesion, P340 was absent or its latency was delayed, and N19 was absent or reduced in amplitude. In 3 patients with a thalamic lesion, P340 and N19 showed various patterns according to involved sites. In 4 patients with a lesion in the corona radiata, P340 and N19 were normal. In one patient with a brainstem lesion representing Wallenberg syndrome, P340 was absent and N19 was normal. Abnormal P340 and N19 were related to impairment of pain and vibration sense, respectively. Thus, it could be possible to study sensory function of each structure in the central nervous system.

2-06-22 INCREASING DOSES OF L-SULPIRIDE REVEAL A DOSE- AND SPATIAL FREQUENCY-DEPENDENT EFFECT OF D2 SELECTIVE BLOCKADE IN THE HUMAN ELECTRORETINOGRAM.

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In order to study the electrophysiological role of retinal D2 receptor subtype in the human retina, we recorded the pattern ERG produced by a square grating steady state stimulation, before and after the acute im. administration of increasing doses of L- sulpiride, a selective D2 blocker. Three spatial frequencies (.25, 1 and 4 c/d) were sequentially modulated in counterphase at 7.5 Hz to produce the visual stimulus. The amplitude and the phase of the second harmonic (15 Hz) of the electroretinographic responses to each spatial frequency were studied before and 30 minutes after the systemic administration of the drug. 5 mg were administered to 20 subjects, 25 mg to 18 different subjects and 100 mg to other 17 subjects. The results show that L-sulpiride does not modify PERG responses to .25 at any doses in a statistically significant way. The response to 1 c/d stimulation was significantly ($p = .02$) decreased of 14.1 % only by the administration of 100 mg. Moreover the effect of the drug was clearly dose-dependent on the pattern ERG responses to 4 c/d. The second harmonic mean decrease was 7.4 % after 5 mg of L-sulpiride, of 20.4% after 25 mg, and of 26.4 % after 100 mg. The two last variations were significant respectively at the level of $p = .01$ and $p = .002$. These data suggest that a dose-dependent effect on the retinal response to 4 c/d stimuli exists. This suggest that the effect is mediated by a coupling between l-sulpiride and D2 receptor in the human retina. Moreover, since mainly the responses produced by 4 c/d stimulation are affected, our data suggest that D2 receptors are mainly located on medium spatial frequency retinal pathway, and therefore probably involved in the origin of visual defect in Parkinson's disease.

2-06-23 CORRELATION BETWEEN EPILEPSY AND MIGRAINE -QUANTITATIVE EEG ANALYSIS.

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A total of 60 patients with common migraine were classified into three subgroups from clinical and electroencephalographic aspect: migraine associated with autonomic syndrome (Gr.-1), migraine with seizure pattern (Gr.-2), and that with normal EEG(Gr.-3). Background EEGs were quantitatively analysed according to power spectral density estimation based on Fourier transformation using FFT (qEEGs). 30 epileptic cases showing mainly autonomic manifestations were correlated with each one of migraine groups concerning the analysis results of qEEGs. Parameters demonstrated statisticaly significant difference were most frequent between Gr.-3 and epileptic group being followed by Gr.-2 and Gr.-1 in descending degree. Only slight difference was observed between Gr.-2 and Gr.-3. Epileptic group was most closely related to migraine group associated with autonomic symptoms, whereas migraine group without EEG abnormalities was most loosely related to epileptic group. Positive correlation of epilepsy with migraine as well as existence of transitional type were suggested.

2-06-24 MOTOR AND SOMATOSENSORY EVOKED POTENTIAL (MEP AND SEP) RECOVERY PATTERNS FOLLOWING TREATMENT OF SUBACUTE COMBINED DEGENERATION

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Motor and somatosensory pathway function was studied in a patient with subacute combined degeneration (SCD). Electrophysiological studies consisted of magnetically induced MEPs, SEPs to median and tibial nerve stimulation, and F-wave responses. Initial evaluation revealed (1) prolongation of central and peripheral motor conductions to lower limbs; (2) absence of cortical and lumbar SEPs to tibial nerve stimulation; and (3) prolongation of F-wave responses to tibial and peroneal nerve stimulation. After 6 months' treatment, there was a marked improvement in gait. Follow-up studies disclosed (1) normalization of peripheral motor conduction and improvement of central motor conduction to lower limbs; (2) reappearance of lumbar SEP but absence of cortical SEPs to tibial nerve stimulation; and (3) normalization of F-wave responses.

The present data indicate that both central and peripheral functions of motor and somatosensory pathways are impaired in SCD. The data further indicate that peripheral motor and sensory systems are more responsive to long-term treatment.

2-06-25 **PREVALENCE OF SUBCLINICAL NEUROPATHY IN A COHORT OF NEUROLOGICALLY ASYMPTOMATIC HIV INFECTED SUBJECTS**

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To determine the prevalence of peripheral nerve abnormalities by Nerve conduction studies at different stages of HIV infection, we performed Nerve Conduction studies (NCS) on the right upper and lower extremities of 102 HIV negative controls, 332 asymptomatics (CDC stages II, III, IVc2) and 79 symptomatic "other" CDC stage IV subjects. Those receiving ddI/ddC, or with a significant history of ETOH use and those with clinical neuropathy were excluded. The means of nerve conduction velocities and late responses of each group were compared to controls using ANOVA with a post-hoc analysis to determine which group contributed to the overall difference. Prevalence of abnormalities was compared across groups using Chi-square test. Abnormal NCS's were found in 2/102 (2%) controls, 15/332 (5%) of asymptomatic subjects and 22/79 (28%) of the "other IV" group. No significant differences were found between group means of controls and asymptomatics. In contrast, group means of symptomatic (other IV) subjects were significantly slower than controls and asymptomatics (II,III,IVc2). We conclude that subclinical HIV-related peripheral neuropathy as detected by NCS, even by the most conservative estimates, is common in the more advanced CDC stages, occurring in 28% of those with ARC/AIDS (other IV), but uncommon in the asymptomatic (II,III,IVc2) subjects.

2-06-26 ELECTROPHYSIOLOGICAL STUDY OF A POSSIBLE LINKAGE BETWEEN VISUAL CORTEX AND MIGRAINE SUBGROUPS.

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To determine whether migraine with or without aura is characterized by abnormal reactivity of the occipital cortex, 10 migraineurs without aura, 10 with aura in < 50% of attacks, 10 with aura in > 50% of attacks, and 30 headache-free age-matched controls were studied with EEG at baseline, photic stimulation at 10 and 20 f/s, and full/half field pattern visual evoked potentials (FFVEP, HFVEP) recorded with linked cheeks reference. Recordings from the occipital areas were studied, and the asymmetry index between sides were calculated. Comparison between migraineurs and controls by t-test and between groups of migraineurs by ANOVA were done.

The results showed no significant difference in VEP (P100 latency, N75-P100 amplitude) and baseline EEG (mean alpha band power, peak frequency, alpha rhythm amplitude) between migraineurs and controls, or between groups of migraineurs. With photic stimulation, however, alpha band power at 02 at 20 f/s was significantly lower (p=0.02) and asymmetry index of alpha band power at 10 f/s was significantly higher (p=0.05) in migraineurs.

It is concluded that quantitative EEG analysis, FFVEP, and HFVEP in occipital areas revealed significant difference between migraineurs and controls or between groups of migraineurs with or without visual aura, only in photic stimulation response.

2-06-27 SCALP POTENTIALS PRECEDING IMAGINARY FINGER MOVEMENTS OF NORMAL SUBJECTS.

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To characterize the nature of slowly developing negative potentials(readiness potential RP) preceding motor acts, we investigate scalp potentials preceding imaginary finger movements of normal subjects. Subjects performed two to four tasks of the followings; self-paced voluntary finger movements(VM), auditory triggered finger movements(ATM), auditory triggered imaginary finger movements(ATI) and auditory stimulation without tasks(AEP). Scalppotentials were averaged from 2.4 seconds before to 0.6 seconds after a trigger point. The trigger point was either anonset of EMG or tone click. When scalp potentials were averaged by the trigger point at the onset of EMG, a steeper negativity(NS') was observed with predominance on the hand motorarea of the hemisphere contralateral to fingers. The distribution, onset and amplitudeof the RP were almost identical with VM and ATM when triggered at the onset of EMG, and with ATM and ATI when triggered at the onset of a tone click. The NS' was not identified when triggered at the onset of a tone click. There was little RP with AEP.

It was suggested that slowly developing negative potentials is not associated with motor act itself and that it reflects the levelof intention, thinking or attention.

2-06-28 FACTOR ANALYSIS OF THE IBIS MULTI-USER COMPUTERIZED PSYCHOMETRICAL TEST SYSTEM AND CORRELATION WITH QUANTITATIVE EEG PARAMETERS.

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During the validation of the IBIS multi-user computerized psychometrical test system dependency of test performance upon external factors as well as interdependencies of different test parameters were investigated. Over 200 healthy male or female volunteers aged 20 - 45 years performed tests of abstract language-free logics, free memory recall (word pairs or figures), calculation, vigilance, complex and simple reaction time. In about half of these volunteers 3-minutes EEG recordings were made and quantitatively analyzed by Fourier transformation. Multivariate analysis revealed significant influences of education on logics performance. Factor analysis showed logics performance to be correlated with memory, calculation and complex reaction performance. Poor performers on this factor of central information processing had higher EEG alpha power of a slower frequency. Vigilance performance was correlated with shorter reaction times and with higher EEG delta and theta power. These findings suggest that psychometrical test performance is influenced by at least two independent factors which can be differentiated by quantitative EEG analysis.

2-06-29 EVALUATION OF CONSCIOUSNESS LEVEL BY "AUTOMATED FLUCTUATION ANALYSIS" OF HUMAN HIGH FREQUENCY EEG FITTED BY DOUBLE LORENTZIANS

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This study is done to clarify the clinical meaning of "Automated Fluctuation Analysis" of high frequency EEG in man expecially focused on the fine alteration of consciousness level of the subjects.

Seventy-four scalp recording EEGs in twenty normal subjects were studied. They were divided into three groups: A-wakeful state with subject denying sleepiness; B-sleepy state with subject acknowledging sleepiness; and C-sleep state 1. "Automated Fluctuation Analysis" of high frequency EEG is made of three steps, amplification of EEG signal, A/D conversion and Fast Fourier Transform by signal processor. Power spectral density (PSD) was displayed on log-log graph. Then the third step, extraction of Lorentzian parameters is performed by the best curve fitting program to the following Lorentzian equation, $S(f) = S1/[1 + (f/fc1)^2] + S2/[1 + (f/fc2)^2]$.

As results, 1. PSD of human high frequency EEG was composed of double Lorentzians and vanished into white level at around 700 Hz. 2. A topographical display of S1 value of initial Lorentz revealed hyperfrontal in group A. This pattern disappeared in group B and C.

2-13-01 *HUNTINGTON DISEASE: ANALYSIS AND COMPARISON OF SPORADIC CASES IN CANADA AND ITALY*

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The diagnosis of Huntington disease (HD) is based on a family history, clinical signs and symptoms. However, there are many instances where only one affected individual exists in the family. Reasons include incomplete pedigrees, mild, late onset, a phenocopy, nonpaternity, and adoption. We have investigated the frequency of isolated cases of HD in Canada and Italy. Where possible, records of HD families have been investigated. Data from this study are shown.

	Canada	Italy
No. of living patients	837	150
Isolated cases	116 (13.9%)	15 (10%)
Negative family history	60	9
• History incomplete	29	0
• Adoption	3	6
• Non paternity	6	0
• Possible new mutation	22	3
Suspicious family history	56	6

A total of 22 (2.6%) individuals from Canada and 3 (2%) from Italy who represent potential new mutations were identified. Their parents were over 70 years of age and paternity was confirmed, where possible.

These data suggest that at least 50% (56/116 in Canada and 6/15 in Italy) of all isolated cases, on close examination, may have a family history of HD. It is likely that new mutations account for a very small but recognizable number of persons with HD. The diagnosis of HD should be seriously considered even in the absence of a family history in persons with a classical clinical phenotype.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-13-02 THE MOLECULAR-GENETIC AND CLINICO-GENEALOGICAL ANALYSIS IN SOME HEREDITARY DISEASES OF THE NERVOUS SYSTEM

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Huntington's chorea (HC), Friedreich's disease (FD) and Wilson's disease (WD) are severe progressive hereditary diseases of the nervous system. Preclinical and prenatal diagnosis is of great importance both for employment of effective presymptomatic treatment in WD patients and for prophylaxis in HC, FD and WD families. Moscow Institute of Neurology has an extensive data base of the families with HC (150), FD (100), WD (500) from various ethnic groups. We carryed out the prognosis testing in 30 informative families by means of genealogical analysis and DNA-diagnostic procedure (PCR method and comparative analysis of the family member haplotypes). We have received the definite and actual data concerning clinically healthy relatives. These results allow to start specific treatment in presymptomatic WD patients and carry out some prophylactic measures in HC, FD families.

2-13-03 LATE ONSET ADRENOLEUKODYSTROPHY IN TWO UNRELATED FRENCH CANADIAN FAMILIES: CLINICAL FEATURES IN AFFECTED MALES AND ASYMPTOMATIC CARRIER FEMALES

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Adrenoleukodystrophy is a rare sex-linked familial disease and has been described in people of different ethnic backgrounds. The vast majority of patients present in childhood, early adult life but rarely middle age. Two unrelated families of French Canadian origin have been studied in which features of both adrenoleukodystrophy and adrenomyeloneuropathy have their onset in middle or late adult life. Non neurological features include early balding, peculiar hair changes and in one family the onset of cataracts. The hair changes were seen both in affected males and asymptomatic carrier females, and appear long before neurological involvement and thus may serve as clinical markers of the disease.

2-13-04 MOST SPORADIC CASES OF HEREDITARY MOTOR AND SENSORY NEUROPATHY TYPE I ARE NEW MUTATIONS.

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Hereditary motor and sensory neurophaty type I (HMSN I) is transmitted with autosomal dominant pattern in most families. However, sporadic cases are observed that may be subjets of recessive inheritance, or represents either phenocopies or new mutations. The presence of a duplication of D17S122 locus in patients with HMSN I can be useful in the diagnostic of isolated cases. Analysis of the duplication of the region D17S122 was carried out in 8 sporadic patients with HMSN I. DNA was digested by MspI and hybridised with single copy fragments of the chromosome 17p probes pWA409R3a and pEW401HE. The duplication was demostrated either by differences in hybridation densities between two bands of a restriction fragment length polymorphism or by the presence of all three alleles. We have found that the duplication was present in 6 of the 8 sporadic patients and absent in all parents. This finding indicates that a de-novo mutation is by far the most frequent cause of sporadic cases with typical HMSN I and has important implications for genetic counselling.

2-13-05 FAMILIAL PROGRESSIVE EXTERNAL OPHTHALMOPLEGIA WITH MULTIPLE DELETIONS OF MITOCHONRIAL DNA: CLINICAL, BIOCHEMICAL AND MOLECULAR GENETIC FINDINGS

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We have previously reported a patient suffering from progressive external ophthalmoplegia (PEO), inherited autosomal dominantly, and severe retarded depression (J Clin Invest 1992;90:61-66). Because of wide-spread distribution of multiple deletions of mitochondrial DNA (mtDNA) in this patient, especially occuring in the brain, we examined the entire family of the patient to determine the clinical presentation of the syndrome, previously regarded as a muscle disease.

We examined 17 members from two generations of the family. Muscle biopsy was taken from 15 subjects, and RRFs and deletions were found in all 7 clinically affected patients as well as in 3 asymptomatic subjects. In the clinical examination, all the older patients (54-70 yrs of age) had prominent PEO, while it was only marginal in the younger patients (32-39 yrs of age). Muscle cramps, weakness and atrophy were occasionally present. Serum CK activity and EMG were abnormal in 8 subjects. Psychiatric interview revealed mild depressive tendency in several family members, but the depression did not clearly cosegregate with mtDNA deletions. The analysis of the respiratory chain enzyme activities in the muscle (10 subjects examined) showed partial complex I deficiency in 3 out of 5 patients, and one patient had low cytochrome c oxidase activity.

Although deleted mtDNA is present in various organs of the patients, the clinical symptoms are in most cases mild and confined to ocular muscles. Partial reduction of complex I activity is frequent, but not a constant, abnormality.

2-13-06 LINKAGE ANALYSIS IN BRAZILIAN FAMILIES WITH THE NON-15q MILD FORM OF LIMB-GIRDLE MUSCULAR DYSTROPHY (LGMD)

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The autosomal recessive (AR) form of LGMD seems to be heterogeneous with at least two genes responsible for this phenotype. One gene has been located to chromosome 15q (1). Only 2 among 9 large Brazilian families showed so far to be linked to chromosome 15q (less than 25%). Therefore, it will be extremely important to find the gene(s) responsible for the other AR LGMD phenotypes. Until the present moment 70 primers were tested in two large genealogies (each with 7 affected individuals) with high consanguinity, not linked to 15q. No evidence of linkage has been found. In addition, markers close to Dystroglycan (2), a potential gene for LGMD mapped on 3p21, were tested and excluded as candidate gene for this form of muscular dystrophy. (Fapesp, CNPq, PADCT, N.W.O.).

2-13-07 DETERMINATION OF THE 50KDa DYSTROPHIN-ASSOCIATED GLYCOPROTEIN IN BRAZILIAN PATIENTS WITH SEVERE CHILDHOOD AUTOSOMAL RECESSIVE MUSCULAR DYSTROPHY (SCARMD) SUGGESTS GENETIC HETEROGENEITY FOR SCARMD

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Dystrophin, the protein product of the human Duchenne muscular dystrophy (DMD) gene, exists in skeletal muscle as a large oligomeric complex which contains four glycoproteins of 156 kD, 50 kD, 43 kD and 35 kD and a protein of 59 kD. Recently, we have demonstrated the specific deficiency of the 50kDa dystrophin-associated glycoprotein (50DAG) in patients from North Africa affected with severe childhood autosomal recessive muscular dystrophy with DMD-like phenotype (SCARMD) . Dysfunction of the dystrophin-glycoprotein complex is presumed to lead to muscle necrosis in SCARMD. Here we demonstrate the deficiency of the 50DAG in Brazilian patients with severe muscular dystrophy indicating that SCARMD is not confined to North Africa. On the other hand, our finding of normal expression of the 50DAG in patients with a phenotype indistinguishable from that of SCARMD suggests genetic heterogeneity for the phenotype of SCARMD. Supported by FAPESP, CNPq, PADCT, ABDIM and MDA.

2-13-08 PROGRESS IN THE LINKAGE ANALYSIS OF OCULOPHARYNGEAL MUSCULAR DYSTROPHY.

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Oculopharyngeal muscular dystrophy is a rare late onset autosomal dominant disease world wide except for a much higher prevalence in French Canada. 530 individuals from nine large Quebec families were recruited to partake in a genetic linkage study. The largest family, which includes 41 affected patients, was used for preliminary linkage analysis using dinucleotide repeat polymorphisms as markers. Our present results exclude 35 percent of the human genome as possible loci for the gene responsible for this muscular dystrophy. Further progress will undoubtedly establish the chromosomal localization of this prototypic French Canadian neurogenetic disease.

2-13-09 MITOCHONDRIAL DYSFUNCTION IN CTX: BIOCHEMICAL, HISTOLOGICAL, P31 MR SPECTROSCOPY STUDY

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Cerebrotendinous Xantomathosis (CTX) is a recessive inherited disease characterized by cataract, tendon xanthomas, mental deteroration and cerebello-pyramidal signs. The discussion about either microsomal or mitochondrial localization of a defective hydroxylation enzyme activity is still open. Here we report a case of CTX in whom the classical biochemical abnormalities (increased serum cholestanol) were associated with increased serum levels of pyruvic and lactic acidosis and ultrastructural evidence of mitochondrial abnormalities in the muscle. Brain P31 MR spectroscopy, never previously performed in this disorder, showed a sharp decreased energy reserve with decreased PCR/Pi ratio and increase of lactate. Muscle respiratory enzyme activities in isolated mitochondria were all decreased. Recently we described in muscle biopsies of several cases of CTX ultrastructural abnormalities suggesting the presence of a mitochondrial dysfunction (Federico et al., Ann. Neurol., 30: 731, 1991). The improvement of the P31 MR changes and the normalization of blood lactate and pyruvate levels following the decrease of the amount of plasma cholestanol, obtained after chenodeoxycholic acid therapy, confirms the hypothesis that mitochondrial changes are related to cholestanol levels.

Supported by Telethon and CNR (Rome) to AF.

2-13-10 GENETIC ANALYSIS IN A LARGE NEUROFIBROMATOSIS TYPE 2 KINDRED

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Neurofibromatosis type 2(NF2) presents with bilateral vestibular schwannomas in the second and third decades of life. The NF2 gene has been located in the long arm of chromosome 22(22q). Our study was designed to test if the NF2 in a very large Finnish pedigree cosegregates with chr 22 markers, to further analyze the linkage to a limited region of 22q and to improve presymtomatic molecular diagnostics. Adults at risk to have NF2 were examined by magnetic resonance imaging (MRI) to detect early lesions.

Examination of the brain and spinal cord by MRI revealed three new NF2 cases presenting with bilateral schwannomas. In the two-point linkage analyses (MLINK) the maximal lod score of 3.32 (theta=0) was obtained with a polymorphic marker at the D22S268 locus. Markers at the D22S280, the heavy neurofilament subunit (NF-H) gene and the CRYB2 gene locus also demonstrated a tight linkage to NF2 in this family. On the basis of the multipoint-likelihood (LINKMAP) calculations the risk for an individual to be healthy or affected could be predicted with over 92% certainty.

The results in this family support genetic homogeneity of NF2 and markers closely linked to the NF2 locus could be used for presymptomatic diagnostics.

Note: New number 2-13-11 see 8-17-08 for Abstract.
New number 2-13-12 see 8-17-10 for Abstract.

2-14-01 DOUBLE-BLIND CONTROLLED TRIAL OF DOTARIZINA IN MIGRAINE

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Dotarizina is a novel selective 5-hydroxitryptamine ($5\text{-}HT_2$) receptor antagonist which may be effective in the prophylactic treatment of migraine. We tested the efficacy of two doses of Dotarizina in a double-blind, cross-over study versus placebo in the prohylaxis of migraine without aura and with aura. The study was carried out on fifty patients affected by either migraine without aura and migraine with typical aura according to the criteria proposed by the Headache Classification Committee of the International Headache Society. Thirteen (26%) were males and thirty-three (74%) females. Their ages ranged from 19 to 64 (mean ± SD= 38.0±11.2). We evaluated reduction in migraine attacks frequency and in the corrected headache unit index (CHUI).There was a statistically significant reduction in attack frequency from basal values for both doses of Dotarizina and placebo. Reduction in attack frecuency and in the CHUI (180% of benefit in CHUI values) produced by dotarizina (100 mg) were significantly bigger than placebo and dotarizina (50 mg). Dotarizina was well tolerated and no marked side effects were reported during the trial, except for an appetite stimulation which seemed to depend on the dosage.

We conclude that dotarizina 100 mg/day may be an effective drug in migraine prophylaxis and it should be studied in following studies.

2-14-02 VISUAL EVOKED POTENTIALS IN PATIENTS WITH MIGRAINE

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We studied pattern reversal Visual Evoked Potentials to different stimulus frequency in migraine patients, divided in two groups – 8 with aura and 8 without aura during the pain free interval.

In the group of patients without aura we observed augmentation of the amplitude of the waveform produced by stimulus with 12 Hz frequency compared with the age-matched controls.

Normal values were obtained in the group of patients with aura.

In both groups there was no alteration of latency of the wavecomplex.

2-14-03 THE EFFICIENCY OF TRANSCUTANEOUS NERVE STIMULATION AND CONNECTIVE TISSUE MASSAGE IN PROPHYLACTIC THERAPY IN MIGRANEOUS PATIENTS

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It has been suggested that migraine is a result of dysfunction of endogenous opioid pathways involving ß-endorphine. Transcutaneous Nerve stimulation (TNS) and Connective Tissue Message (CTM) are therapeutic modalities which are used for prophylactic therapy in migraine patients. But there is no sufficient data about their effect on prophylaxis in the patients with migraine.

Aim of this study is to assess the efficiency of TNS and CTM in migraine and look for the correlation of this efficiency with blood ß-Endorphin levels. 38 patients (mean age 34.8) with migraine volunteered in this study. 19 of the patients treated with TNS 5 days in a week for 3 weeks and the other 19 patients treated with CTM for the same period.

All patients were asked for the duration, frequency and intensity of their migraine crisis, and blood was collected for plasma ß-endorphine levels before and after the treatment sessions. Paired-t test and t-test were used to seek for the efficiency of these modalities, and relation to ß-endorphine levels. We found that in both TNS and CTM groups, differences in clinical parameters of pre- and post-treatment periods were statistically significant ($p < 0.001$ for TNS and CTM groups). Pre- and post-treatment plasma ß-endorphine levels were not significantly different ($p > 0.005$). In our series the relation between clinical parameters and plasma ß-endorphine levels did not reach statistical significance.

We conclude that TNS and CTM can be used but their effectiveness cannot be explained by plasma endorphine levels.

2-14-04 TREATMENT OF ACUTE MIGRAINE ATTACK WITH SUMATRIPTAN: CLINICAL AND TRANSCRANIAL DOPPLER DATA IN EARLY POSTHEADACHE PERIOD

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A group of 8 patients with migraine without aura, 4 - with migraine with aura and 3 patients with Cluster Headache, (following the criteria of International Headache Society) were studied.

Sumatriptan was given subcutaneously in a single dose of 6 mg to each patient in the beginning of the headache attack, using standard Glaxo autoinjectors. Transcranial Doppler (TCD) was made in the first 24 hours post injection.

In 10/12 patients with migraine, headache dis appeared completely 30 min post injection. In 2/12 - a second dose was needed 2 hours later. In 2/3 Cluster patients a single dose was suffi cient, while in 1/3 a second dose was given. TCD revealed increased vascular resistance in 8/12 migraine patients and in 1/3 Cluster patients.

Sumatriptan is an effective drug in the treat ment of acute migraine and Cluster Headache attacks. TCD data suggest arterial vasoconstric tion in the early period after treatment.

2-14-05 IMPROVED DESCRIPTION OF THE MIGRAINE AURA BY A DIAGNOSTIC AURA DIARY.

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A diagnostic aura diary for prospective recordings of migraine with aura is presented. Three questionnaires are supplemented with sheets for drawings and plottings of visual and sensory disturbances. Twenty patients with migraine with aura recorded 56 attacks. Forty attacks had visual aura including 2 attacks of migraine aura without headache, 1 had only sensory aura, and 15 had both visual and sensory aura. The visual aura were usually a flickering semicircular zig-zag line (fortification) gradually progressing from the center of the visual field towards the periphery, but about 1/3 of the attacks started in the periphery. The sensory symptoms were usually gradually progressing. Both the visual and sensory auras usually lasted 20 minutes. The visual and sensory aura preceeded and were contralateral to the headache. The headache started about 35-45 minutes after the first aura symptom and was found to be milder than in attacks of migraine without aura. The prospective recordings gave a very precise descriptions of the aura and headache symptoms. This is importatant in nosographic studies, but also in clinical practice in order to distinguish between transient ischemic attacks, partiel epileptic phenomenona, psychogenic illusions and the migraine aura.

2-14-06 SENSITIVITY TO NITROGLYCERIN IN MIGRAINE.

Thomsen LL, Iversen HK, Brinck TA, Olesen J.

The sensitivity to nitroglycerin (NTG) in relation to headache and intracranial arterial responses was studied at 4 different doses in 17 patients with migraine without aura (MO) and compared to 17 healthy subjects (HS) and to 9 patients with episodic tension-type headache (ETH). Headache was scored on a 10 point verbal scale every 2 min during NTG infusion and during a 60 min period after NTG infusion. The mean blood velocity (V_{mca}) of the middle cerebral artery (MCA) were measured with transcranial doppler at the end of every infusion period, and 30 and 60 minutes after NTG termination. Median peak headache intensity and the area under the pain curve were higher in the MO group ($p<0.001, p<0.01$, respectively). One hour after termination of the NTG infusion 13 MO patients, 7 ETH patients and 7 HS still had headache. At this time the headache fulfilled the operational diagnostic criteria for migraine without aura in 11 MO patients, 1 ETH patient and 0 HS. The decrease in V_{mca} was more pronounced in migraine patients at all doses, but only to a significant level at the higher doses ($p < 0.05$). Since NTG acts as an exogenous source of nitric oxide (NO) these data suggest that nitric oxide mechanisms may be involved in migraine pathophysiology.

2-14-08 INTEROBSERVER RELIABILITY OF SYMPTOMS NECESSARY FOR THE DIAGNOSIS OF PRIMARY HEADACHES ACCORDING TO INTERNATIONAL HEADACHE SOCIETY CLASSIFICATION.

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We have recently shown (Granella et al., 1992) that inter-observer reliability for primary headaches of International Headache Society (IHS) classification is substantial at the one digit level, but only moderate at the two digit level. The aim of this study was to investigate the sources of interrater variability.

We studied 103 consecutive headache centre patients. Each patient was interviewed using a questionnaire containing all the information needed for the diagnosis of primary headaches according to the IHS criteria. The interviews were recorded on videotape and reviewed separately by four clinicians. The agreement between observers was measured using Kappa statistics (K).

We found the following results: duration of attacks: K = 0.69; pain location: K = 0.78; pain quality: K = 0.84; pain intensity: K = 0.80; aggravation by physical activity: K = 0.73; nausea: K = 0.89; vomiting: K = 0.81; photophobia: K = 0.87; phonophobia: K = 0.84. No single item accounted for a major part of variability. Some minor changes will be suggested to improve IHS diagnostic criteria reliability.

2-14-09 INABILITY TO CLASSIFY ALL THE CHRONIC DAILY HEADACHE SUBTYPES BY INTERNATIONAL HEADACHE SOCIETY CRITERIA

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The aim of this study was to determine whether and where it is possible to place chronic daily headaches (CDH) within the International Headache Society (IHS) classification. We defined CDH as idiopathic headaches occurring daily or almost daily for at least 6 months. One hundred and forty two consecutive patients with CDH were included. Applying the diagnostic criteria of IHS to the current CDH, we found that: a) 53 patients fulfilled the criteria for chronic tension-type headache (CTTH); b) 60 patients showed both migraine (M) and CTTH; c) 16 patients had the coexistence of M and a headache which did not fulfill any diagnostic criteria; d) 13 patients had an unclassifiable headache. Within this last group, 9 patients fulfilled diagnostic criteria for M, except for the duration of attacks. Considering the outcome of patients with previous M, we found that M had evolved to a) in 12 cases, to b) in 49 cases, to c) in 16 cases and to d) in 13 cases. Therefore, headaches could not be classified according to IHS criteria in 29 patients (20.4%), all of them with previous M. Some changes to IHS classification seem to be needed to classify all the subtypes of CDH. Proposed ad-hoc diagnostic criteria will be discussed.

2-14-10 SUMATRIPTAN vs USUAL ACUTE TREATMENT OF MIGRAINE

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246 migraine patients suffering 1 to 6 severe attacks per month diagnosed according to the IHS criteria were randomised into a multicentre, cross-over study comparing s.c. sumatriptan 6 mg (SUM) with usual acute treatment (UT). They received either SUM by auto-injector, or an UT prescribed by their physician, for 2 months or up to 12 attacks. UTs were: ergotamine: 23%; various combinations: 23%; dipyrone: 17%; acetaminophen: 10%; NSAIDs: 10%; aspirin: 9%; DHE: 8%. Results of the first treatment period are presented here.

Headache severity was assessed on a 4-point self-rating scale (0: none, 1: mild, 2: moderate, 3: severe). The main end-point was headache relief (from 3 or 2 to 0 or 1) 2 hours after the first dose. Quality of Life (QoL) was assessed before and after each period using a validated migraine-specific questionnaire. SUM was significantly superior to UT for all efficacy end-points ($p < 0.001$):

	SUM	UT
Headache relief at 2 h (% attacks)	75	26
Pain-free at 2 h (% attacks)	55	11
Relief of nausea at 2 h (% attacks)	77	39
% patients assessing treatment as very effective or effective	76	14

Improvement in QoL was 3 times greater in the SUM group ($p<0.0001$). Minor adverse events were more frequent in the SUM group but similar to those previously reported. In patients with severe migraine attacks, subcutaneous sumatriptan is superior to usual acute treatment for both the relief of all migraine symptoms and the improvement of quality of life.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-14-11 USE OF MEDICAL SERVICES OF MIGRAINE SUFFERERS IN FRANCE

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The use of medical services of 340 migraine sufferers from a representative nationwide sample in France was retrospectively analyzed over a six months period. Data on demographic and clinical features, use of medical services and satisfaction and confidence were collected at home by lay interviewers. Among the 340 migraineurs, 189 (56%) had ever consulted a physician. Of 189, 59 (31%) consulted at least once a general practitioner during the six months period, 68 (36%) at least one specialist. Five of them (3%) were hospitalized and 51 (27%) had complementary exams. This diagnostic and therapeutic management, which was in part inadequate and concerned a small proportion of migraineurs, was observed along with a large dissatisfaction and a poor confidence. Using multivariable logistic regression, we compared the migraineurs who never consulted with the one who consulted at least once a phycisian in their lifetime. The poor confidence, the length of the disease, the frequence and the intensity of the attacks and the individual social insurance were predictive of the use of medical services.

Key words: migraine, medical consumption, satisfaction

2-14-12 REDUCTION OF POST-LUMBAR PUNCTURE HEADACHE WITH A NEW "ATRAUMATIC" NEEDLE TYPE

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Approximately one-third of the patients develop headache after a lumbar puncture (LPHA). In order to reduce this figure different efforts including the use of a smaller needle size, a delayed recumbent position or the deposition of an epidural bloodpatch have been made without convincing succes. During the last year we investigated the usefulness of a new, "atraumatic" needle type in LPHA reduction. This "atraumatic" needle is a 22 Gauge one and has a relatively blunt tip, the opening is located at the side of the tip. We performed a study with 104 pts. who where unaware of the needle type used. They where randomly assigned to the group with the common or the "atraumatic" needle type, and each completed a questionaire at the third day following the procedure. There was a marked decrease of LPHA ($p<0.005$) in the pts.group punctured with the "atraumatic" needle. Particularly no patient of this group suffered severe LPHA. Therefore, we conclude, that the use of the "atraumatic" needle is an easy to perform and efficient possibility to avoid or to at least reduce the incidence and the severity of LPHA.

2-14-13 SUBCUTANEOUS SUMATRIPTAN IN THE ACUTE TREATMENT OF CLUSTER HEADACHE ATTACKS

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Sumatriptan has been investigated as an acute treatment for cluster headache attacks when given as a single 6mg subcutaneous injection.

In a randomised, double-blind, placebo-controlled, 2-period crossover trial in 39 patients, significantly more patients on sumatriptan than on placebo reported headache relief (improvement from moderate, severe or very severe to none or mild) 15 minutes after treatment (74% v 26%, $p<0.001$). These results were confirmed in a similar larger trial in 134 patients; 49% and 75% of patients, respectively, reporting headache relief 10 and 15 minutes after 6mg sumatriptan. Headache relief was very rapid, commencing within 5 minutes of treatment. Increasing the sumatriptan dose to 12mg gave no added benefit.

A multinational, multicentre open trial is investigating the long-term safety and efficacy of 6mg sumatriptan during a 2-year period. In an interim analysis of 3-month data, 138 patients had treated 6353 cluster headache attacks. Sumatriptan was generally well tolerated; adverse events were similar to those seen in long-term migraine studies and their incidence did not increase in patients who used sumatriptan frequently. Sumatriptan effectively treated cluster headache attacks over the 3 months, with no evidence of tachyphylaxis.

Subcutaneous 6mg sumatriptan is a rapidly effective and well tolerated long-term acute treatment for multiple cluster headache attacks.

2-14-14 MUSCLE CONTRACTION HEADACHE AND POSTURE. WITH SPECIAL REFERENCE TO ISCHEMIC CONTRACTION OF THE POSTERIOR NECK MUSCLES.

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Cause of muscle contraction headache results from sustained contraction of scalp and neck muscles. The purpose of our report is to examine the effect of posture on the circulation of posterior neck muscles.

Laser doppler flowmetry was performed in 40 patients with chronic muscle contraction headache using needle shaped probe which was inserted into the posterior neck muscle. At the same time, electromyography of this muscle and the angle of orbitomeatal line against horizontal plane was monitored with the patient sitting on a chair.

Mean blood flow (ml/min/100g) of the posterior neck muscle decreased from 11.7(20 degrees upward) to 4.1 (30 degrees down). Contrary to the blood flow, amplitude of EMG increased from 42.4 micro V (20 degrees up) to 94.2 micro V (30 degrees down). Mental calculation did not change the degree of muscle contraction . However, it decreased the blood flow and induced a ischemic contraction. In the case of voluntary contraction, blood flow gradually increased preventing ischemic contraction.

2-14-15 A CORRELATION OF CEREBRAL VASOREACTIVITY (CVR) AND 5-HT LEVEL IN PATIENTS WITH MIGRAINE

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In order to assess CVR changes in migraine, 23 patients with common and 25 with classic migraine were analyzed by Transcranial Doppler (TCD). The aims were: 1. to assess TCD and plasma 5-HT level during attack and headache-free period, and 2. to compare this findings.

The results have shown that during headache-free period in 70% of all patients the mean blood flow velocities (MBFV) were increased. During attack MBFV had been reduced, especially in MCA and PCA on the headache side ($p<0.05$). The level of plasma 5-HT in the headache-free period was normal, but during attack was significantly reduced in patients with aura ($p<0.001$).

The reduction of MBFV during migraine attack indicates vascular dilatation that might be a consequence of lower 5-HT level.

2-14-16 CLINICAL ANALYSIS OF MIGRAINE AURA WITHOUT HEADACHE SHOWING MIDDLE AGE ONSET

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In the IHS classification of headaches, migraine aura without headache is mentioned as one type of migraine, but there have been of few report of such cases.

In the present study, 6 patients who complained of scintillation scotoma but never showed any headache were studied clinically. The patients were from 56 to 69 years old with the mean of 64.0. All cases were female. The onset of scintillation scotoma was from 47 to 65 years old. The frequency of visual disturbance ranged from3 to 48 times per year. Duration of the symptoms continued from 3 to 20 minuites. No cases had migraine in the families, whether in parents, siblings or children. One case revealed small brain infarction by MRI, but the occipital lobe was intact. Another case showed hyperglycemia. EEGs were normal in all cases. Somethimes patients suffering from migraine with aura experienced only aura as they grew older. Such cases are diagnosed as migraine aura without headache. But apart from those cases, the present cases had experienced not any headache. These cases were diagnosed as migraine aura without headache only symptomatologically. The detailed etiology is still unknown, but the possibility orf TIA or epilepsy can not be neglected. Or there might be a clinical entity. More detailed investigation is necessary to resolve these questions.

2-14-17 CLINICAL EVALUATION OF CAPSAICIN CREAM ON PAIN OR DYSESTHESIA IN PATIENTS WITH HAND ARM VIBRATION SYNDROME

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Capsaicin is one of alkaloids causing release of substance P from primary sensory neurons. Systemic treatment with capsaicin results in decrease of substance P in the spinal cord and reduction in nociceptive responses in the rat and application of capsaicin is expected to relieve intractable chronic pain or dysesthesia. Twenty three patients with Hand Arm Vibration Syndrome (HAVS) was treated with dermal application of capsaicin cream containing 0.025% capsaicin on their left hand. Both individual skin temperature and periflux blood flow in the finger tip was measured with a thermograph and a periflux laser doppler flowmeter before and after application of capsaicin cream. All patients recognized warmness in their both hands in varying degrees. In 16 patients (70%) increase of their skin temperature and in 20 patients (87%) increase of their finger skin blood flow were observed not only in ipsilateral but in contralateral hand. These results suggest that capsaicin cream is useful for the treatment of HAVS which often induces coldness of extremities resulting in pain and dysesthesia.

2-14-18 DURING ACUTE CLUSTER HEADACHE THE TRIGEMINOVASCULAR SYSTEM IS ACTIVE IN MAN

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Cluster headache is a rare form of vascular head pain the pathophysiology of which is not understood. The syndrome is characterised in its episodic form by attacks of short lasting unilateral excruciating head pain often localised behind the orbit and associated autonomic features. Although the pain is certainly located in the distribution of the trigeminal nerve, its activation has never been measured. Patients (10 males and 3 females) aged 38±9 years were seen during acute attacks of Cluster headache having had the diagnosis made on clinical grounds by one of us (PJG) and fulfilling the operational diagnostic criteria of the International Headache Society. At the time of review the patients were requested to participate in the study and gave informed consent to the protocol approved by an Institutional Review Panel (PJG). The patients had blood sampled from the external jugular vein while they were headache free and then again during headache. Samples were always taken ipsilateral to headache and the time from the onset of the individual attack to the sampling was 41±7mins. At the time of sampling none of the patients were either on prophylaxis for the attacks nor had they been treated for the sampled attack. To assess the activation of the trigeminal system we measured the calcitonin gene-related peptide (CGRP). Inter-ictally the level of CGRP (39±5pmol/l) was unaltered from a control population (40±6pmol/l). During headache there was a remarkable, up to three-fold, increase in CGRP levels (110±7pmol/l). This patient study for the first time confirms the clinical view that there is increased trigeminal nerve activity during Cluster headache.

2-14-19 DOES SUMATRIPTAN HAVE ACTIONS ON CENTRAL TRIGEMINAL NEURONS?

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It has been proposed that the site of action of sumatriptan, a highly effective treatment of the acute attack of migraine, is either on cranial blood vessels as a vasoconstrictor or in the periphery at the trigeminal innervation of the vessels. In this study single unit activity and trigeminal somatosensory evoked potentials in central trigeminal neurons were monitored during electrical stimulation of the superior sagittal sinus and mannitol was used to disrupt the blood-brain barrier. The studies were conducted in the α-chloralose (60mg/kg, ip) anaesthetised cat. A circular craniotomy was carried out and the superior sagittal sinus isolated from the cortex for electrical stimulation (0.3/sec, 250μsec duration, 100V). Cell firing and trigeminal evoked potentials were monitored at the level of the C_2 spinal cord in the dorsolateral region of the cord using tungsten-in-glass microelectrodes. Animals were randomly allocated to receive either sumatriptan (100μg/kg, ivi) followed by mannitol or mannitol alone. Stimulation of the superior sagittal sinus produced reproducible field potentials and cell firing in the C_2 spinal cord. Intravenous administration of sumatriptan did not alter trigeminal evoked activity or cell firing in the intact animals. After disruption of the blood-brain barrier in the presence of sumatriptan both trigeminal evoked potentials and cell firing were reduced. The peak-to-peak amplitude of evoked potentials were reduced by 40±6% and the probability of firing of single units by 30±9%. These data suggest that under normal circumstances sumatriptan does not have access to central trigeminal neurons since intravenous administration of the drug did not effect them.

2-14-20 TENSION HEADACHE IN CHILDHOOD AND ADOLESCENCE.

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In contrary to the frequent occurrence of tension type headache (TH) in childhood and adolescence there is little information on its clinical feature in these age groups. This may be explained by the observation that many authors continue to use own diagnostic criteria, although the International Headache Society (IHS) published a classification of headaches which should be generally used in all age groups. The aim of our study was to elucidate the clinical feature of tension headache in children and adolescents based on the diagnostic criteria of the IHS.

Out of a total number of 242 consecutive children and adolescents suffering from headache 84 fulfilled the diagnostic criteria of tension headache according to the IHS. The patients (44 girls and 40 boys) were 11.3 ± 3.0 years of age and suffered from headache since 36.8 ± 29.8 months. One headache episode lasted for a mean of 8.6 hours and headache occurred on 10.0 ± 8.9 days per month. Accordingly, 42 patients were classified as episodic (IHS 2.1.) and 21 as chronic tension headache (IHS 2.2.), another 21 patients suffered from "possible" tension headache (IHS 2.3.). The quality of headache was predominantly dull and its localization bifrontal in the majority of patients. Psychological and psychosocial factors were significantly more important then disorders of the pericranial muscles.

We believe that non-migrainous headache in childhood and adolescence should be diagnosed according to the classification of the IHS - without any exceptions or modifications, since this is the only way to guarantee comparability of studies on this field.

2-14-21 NALOXONE TEST AS A TOOL IN THE NEUROENDOCRINE ASSESSMENT OF MIGRAINE WITHOUT AURA

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The opiate antagonist naloxone (Nlx) is known to stimulate the secretion of gonadotrophin-releasing hormone (GnRH) and corticotrophin-releasing hormone (CRH), via blockade of μ- and δ binding sites, respectively. Determination of plasma levels of luteotrophic hormone (LH) and cortisol (C) in response to Nlx is thus viewed as a simple method to investigate central opioid activity. A deranged LH response to this test has been reported in episodic and chronic migraine without aura (MWA), as well as in menstrual migraine. In this study, we measured LH and C plasma levels (every 15 mins) over a 75-min naloxone test (0.2 mg/Kg i.v.) in 35 patients with episodic MWA aged 34.3±9 yrs (M±SD), during a pain-free phase. Eleven healthy, age-matched subjects served as control group. While in the MWA group the M±SD basal values of C, but not LH, were found higher than those of controls (136±85.7 and 78.5±28 ng/ml, respectively, $p<0.05$), the secretory area of both hormones was markedly reduced compared to controls ($p<0.001$ in either case). In addition, 33/35 patients with regard to LH, but only 13/35 with regard to C, proved to be "responders" to the test. The severity of headache, assessed by the Headache Index (n. of attacks/month x intensity of pain) was found to correlate inversely with the area of secretion of either LH ($p<0.02$) or C ($p<0.05$).

While showing impaired hypothalamo-pituitary-gonadal, and especially -adrenal responses to Nlx challenge in MWA, these data further suggest changes in central opioid function which parallel the severity of pain in this type of headache.

2-14-22 ELECTROPHYSIOLOGICAL INVESTIGATION OF CORNEAL REFLEX IN MIGRAINE

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Neurophysiological studies play an important role in the advances of the knowledge of migraine pathogenesis. The electrically elicited corneal reflex represents a useful tool for exploring trigeminal sensorimotor mechanisms, and antinociceptive system in particular. Fortytwo migraine without aura patients (aged 22-61 years, mean age: 33.8 ± 10.4 yrs.) were investigated. Diagnosis was made according to the Classification criteria set forth by the IHS. When considering patients according to pain side 28 suffered from strictly unilateral headache, while in 14 the pain shifted side or it was bilateral. Patients were examined in headache free-period. Sixteen healthy subjects were studied as controls (mean: 25.8 ± 2.4 yrs.). Electrical stimulation was delivered with thin cotton thread emerging from a glass pipette filled with gauze soakes in saline solution and connected with the cathode of a constant current stimulator. The muscular response was recorded from the orbicularis oculi. During the examination the minimal intensity nedeed to obtain corneal reflex (Tr), the subjective tactile perception (Ttp) and subjective pain perception (Tp) were evaluated. Migraine patients significantly showed reduced Ttp, Tr and Tp values in comparison with controls both on symptomatic ($p<.001$; Anova one-way) and non-symptomatic side (respectively: $p<.001$, $p<.025$, $p<.0015$; Anova one-way). Moreover, unilateral migraineurs had lower threshold when compared with bilateral migraine patients both on symptomatic and non-symptomatic side. In conclusion, our data suggest that sensorimotor mechanism and/or pain control system are impaired in migraine. The bilateral location of these abnormalities also in unilateral form may suggest a centrally located dysfunction.

2-14-23 SLEEP MICROSTRUCTURE ANALYSIS IN PATIENTS COMPLAINING OF CHRONIC PAIN

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Pain related sleep disturbance is often characterized by alpha intrusions and microarousals (MA's). The aim of this study was to develop a MA analysis to quantify the duration of alterations of the sleep microstructure. The MA analysis was proofed in 10 healthy volunteers and the resulting MA pattern was compared with the sleep data obtained before and after a special rehabilitative training from 23 outpatients with chronic back pain. In addition the v. Zerssen depression score and a fitness power score was taken into account. The results showed after the training a significant reduction of MA disturbed sleep time, whereas the classical sleep parameters remained unchanged. To our opion the microarousal analysis provides a useful tool, that could be used in addition to the standard sleep criteria.

2-14-24 ABNORMAL BRAIN PERFUSION IN CHRONIC DAILY HEADACHE(MIGRAINE-TENSION-TYPE HEADACHE COMPLEX).

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SPECT provides useful information about the cerebral perfusion in neurological disease such as epilepsy, cerebrovascular disease, abnormal movements, dementia and depression. In migraine with and without aura SPECT has been reported to be abnormal during ictal and interictal periods.

99mTC-HMPAO SPECT was done in 15 patients with episodic migraine (12 with aura, 3 without) and in 44 patients with chronic daily headache. Both visual and quantitative analysis was done. SPECT scan showed reduced perfusion in 38.6% and irregular perfusion pattern in 34.1% with chronic daily headache compared to reduced perfusion in 40% and irregular perfusion in 13.4% in the episodic migraine group. Reduction was more marked in patients with associated neurological symptoms. Two patients showed cerebellar hypoperfusion with associated ataxia and dizziness during headache. One patient had focal hyperperfusion correlating with the location of the headache.

CONCLUSION: Migraine and chronic daily headache show similar pathophysiological abnormalities supporting the continuum theory of primary headache disorders.

2-14-25 SERIAL MEASUREMENT OF MUSCLE HARDNESS IN PATIENTS WITH TENSION-TYPE HEADACHE

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To investigate the relation between subjective symptom and changes in muscle stiffness, we serially measured muscle hardness of trapezius muscle in patients with chronic tension type headache. Thirty patients (7 male, 23 female, age from 41 to 78) were studied. Muscle hardness is measured by a newly developed pressure-displacement transducer. After the initial assessment muscle relaxant (Eperizone) administration was started in 27 patients. Muscle hardness was examined serially for more than 6 months. There was no significant correlation between the duration of illness and the initial values for hardness. At the second visit muscle relaxant showed a reduction in hardness and an improvement of symptoms which was more marked in patients with higher values for hardness. Longterm observation disclosed considerable fluctuations of the hardness in some patients which occasionally did not correspond to the severity of symptoms. Conclusion: In tension-type headache muscle hardness is the major but not the only factor contributing to the development of symptoms.

2-14-26 THE CLINICAL PHARMACOLOGY OF SUMATRIPTAN

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Clinical pharmacology studies have been conducted with sumatriptan in both young and elderly healthy subjects, and in migraine patients. Absorption was rapid after subcutaneous and oral administration, where the mean absolute bioavailability was 96% and 14%, respectively. The mean plasma half-life was approximately 2 hours and sumatriptan was eliminated primarily by metabolism to an inactive indoleacetic acid analogue.

Mean pharmacokinetic parameters were similar in all subject groups studied, were linear with respect to dose of sumatriptan and were not altered by the presence of food, alcohol, dihydroergotamine or a selection of prophylactic migraine medications. The 100mg sumatriptan film-coated tablet (the marketed formulation) is bioequivalent to the dispersible tablet (used in early clinical trials).

Sumatriptan use is associated with a characteristic pattern of adverse events. Transient, modest rises in blood pressure are reported in young subjects; slightly higher rises are noted in elderly subjects. These are not of clinical consequence.

Patients with hepatic impairment tolerated sumatriptan well. Compared with healthy subjects, they exhibited similar sumatriptan pharmacokinetics and pharmacodynamics after oral and subcutaneous dosing, except for higher plasma sumatriptan concentrations with oral dosing.

2-16-01 **MOLECULAR DIAGNOSIS OF TUBERCULOUS MENINGITIS (TBM) USING THE POLYMERASE CHAIN REACTION (PCR) - AN EVALUATION OF THREE PRIMERS**

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Since the standard diagnosis of TBM by culture of *M. Tuberculosis* takes up to 8 weeks, DNA amplification by PCR provides an alternate method for the rapid diagnosis of TBM. In this study, we evaluated 3 different primers pairs, specific for the MBP64 protein, ISS6110 insertion element, and the 65 kD heat shock protein(HSP), for the diagnosis of TBM. DNA from 6 TBM positive CSF specimens, and 18 TBM negative CSF controls from other forms of meningitis were obtained by phenol chloroform extraction. Under optimal PCR conditions, all 6 positive specimens were positive for 3 primer pairs. Oligoprobing following PCR was required in 2/6 specimens for the MPB64 protein primers. Despite requiring this additional step, the MPB64 protein primers was the most useful, as it did not give any false positive results. In contrast, the ISS6110 insertion element gave 3/18 false positive tests on the CSF specimens, while the 65kD HSP was positive with non-TB bacteria (Klebsiella sp, Pseudomonas sp). We conclude that careful evaluation is necessary before PCR can be widely used a diagnostic test for TBM.

2-16-02 POLYMERASE-CHAIN REACTION (PCR), TUBERCULO-STEARIC ACID (TBSA) AND STANDARD METHODS IN TUBERCULOUS MENINGITIS, A COMPARATIVE IN-VITRO-STUDY

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In a collaborative study of four laboratories 43 specimens of artificial cerebrospinal fluid spiked with different mycobacteria in various concentrations were examined using conventional methods (Löwenstein-Jensen medium, Middlebrook 7H9 medium, guinea pig test) and 2 rapid assays (PCR, TBSA) in order to compare the performances of these techniques. Löwenstein-Jensen medium yielded a greater number of positive results than Middlebrook medium. The animal test did not improve the detection rate. The combined use of the conventional methods identified M.tuberculosis in 5 specimens. The PCR protocol correctly identified the M.tuberculosis genome in 5 specimens. TBSA detection was highly sensitive (no false negative result), but was hampered by one false positive result and could not differentiate between various M.species.

Our results show the potential of PCR for diagnosing tuberculosis but also show that presently PCR methods are less sensitive than conventional culture techniques.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-16-03 SEROEPIDEMIOLOGICAL STUDY OF HTLV-I/II INFECTION AMONG PATIENTS WITH MYELOPATHY OF UNKNOWN ORIGIN AND THEIR RELATIVES IN RIO DE JANEIRO, BRAZIL.

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To determine the frequence of HTLV-I/II infection among patients with myelopathy of unknown origin and their relatives, we studied 112 neurological patients and 125 relatives of 31 patients found seropositive. The sera sample were screened by indirect immunofluorescence and the ones found positive were confirmed by western blot p21e (DuPont). 54 out of 112 patients (48.2%) were positive for HTLV-I/II antibodies and therefore suffer from Tropical spastic paraparesis/HTLV-I associated myelopathy (TSP/HAM). 17 out of 125 relatives (13.6%) of 31 TSP/HAM patients were infected by HTLV-I/II. The seropositivity among relatives was distributed as follows: 7 out of 18 female spouse (38.8%); 2 out of 8 male spouses (25%) 3 out of 53 offspring (5.6%); 4 out of 12 parents (33.3%); 1 out of 29 sibblings (3.4%) and finally none of 5 other relationships. These results show a high prevalence of TSP/HAM in Rio de Janeiro as well as a high prevalence of HTLV-I infection among relatives of patients. In the last group the acquisition of infection was both horizontal and vertical transmission.

2-16-04 SPONDYLITIS: SYMPTOMATOLOGY, DIAGNOSIS AND DIFFERENTIAL OPERATIVE PROCEDURE IN DEPENDENCE OF NEUROLOGICAL STATUS AND EXTENT OF INFLAMMATION

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The spondylitis is the most frequent adult manifestation of an osteitis. Due to polymorphous symptoms the disease is often not diagnosed at an early stage, when the treatment is simple and efficacious.

Therefore, we present of 14 patients treated in our clinic the neurological status, the neuroradiological findings, the analysis of the cerebrospinal fluid and the neurosurgical intervention. In 12 of 14 patients we succeeded to detect the microorganisms by CT guided puncture, by blood culture or intraoperative smear. On hospital admittance, 7 patients revealed signs of transverse syndrome, 3 developed signs of a radiculitis and in four cases a meningitis or meningoencephalitis was assumed up to final diagnosis of a spondylitis. According to the benign neurological state four patients were treated conservatively either in a plaster bed or by a halofixateur. We performed in 4 cases a laminectomy, in 3 patients a costotransversectomy and in 4 cases a spondylectomy with spondylodesis. The neurological state improved in 10 cases, 3 remained unchanged and one patient died.

In summary, early diagnosis is mandatory to treat spondylitis successfully.

2-16-05 PROSPECTIVE RADIOIMMUNODETECTION OF INTRACRANIAL ABSCESS BY Tc-99m ANTIGRANULOCYTE ANTIBODY

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The brain tumour is a serious postinfectious, post traumatic and iatrogenic complication. The usually performed neuroradiological diagnosis (CT, MRI) do not permit a clear differentiation of brain abscess, - tumour and metastasis. In a prospective study, 27 patients were enrolled under the assumption of a brain abscess. Approximately 4-7 hours after injection of Tc-99m antigranulocyte antibody planar scans of the whole body and SPECT scans of the head were performed. The immunoscan was true positive (abscess) in 7 patients, true negative (brain tumour) in 19 and false positive in 4 cases, whilst 3 patients were examined twice. In conclusion, in spite of 4 false positive results, the Tc-99m antigranulocyte antibody is a useful tool in the differentiation between brain abscess and tumours as well as in the decision to not to perform neurosurgical revision.

2-16-06 MORPHOMETRIC STUDY OF THE FRONTAL CORTEX IN SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE)

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The neuropathological features of SSPE have been largely described, although reliable quantitative studies have not been performed. We estimated in biopsic material the number and size of neurons from the frontal cortex (layers II and III) of 6 patients with SSPE, 5 to 16 years-old and the results were compared with those obtained in 4 patients with posterior fossa tumors, 7 to 17 years-old. The material for control purposes was collected during neurosurgical procedures. Neuronal numerical densities were obtained in serial semithin sections using the disector method. The mean diameter of neuronal nuclear profiles and the layer's thickness were determined in the same sections. No significant differences were found between the numerical densities and the nuclear diameters of SSPE and controls. The layer's thickness show that the shrinkage from SSPE and controls did not differ. Our results indicate that neuronal death does not occur in the frontal cortex of patients with SSPE and thus reinforce the view that neuritic degeneration underpin the marked functional and behavioral changes. Although neuronal degeneration might occur in other brain regions, the role displayed by neuronal circuitry cannot be disregarded. Finally, we demonstrate how important is the choice of unbiased estimators to get reliable results.

2-16-07 EVOLUTION OF BRAIN TUBERCULOMAS UNDER STANDARD MEDICAL TREATMENT.

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Eighteen cases (ages 13-80y) of brain tuberculomas treated medically and followed up for>18 months were evaluated. All patients had serial brain computerized tomograms(CT) (mean 4.2/patient). The number of tuberculomas per patient varied from 1 to 5. Patients who had additional surgery were excluded. All patients were treated with 3 antituberculous drugs for 3 months and 2 drugs for another 9 to 15 months. Regression of CT images started after 6 to 8 weeks. In most patients, the lesions disappeared between 9 and 12 months. In 2 cases, an initial worsening was noted and the CT image continued to regress after stopping the medications in one case. Residual stable images were observed in 2 patients. No clear relationship between the rapidity of response to treatment and the size, number or CT characteristics of the lesions was noted suggesting that the immunological reaction of the host may play a role.

2-16-08 TUBERCULOSIS OF SPINAL CORD IN SAUDI ARABIA

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Medical records of 21 patients (aged 22 to 70 years) with cervical or thoracic spinal cord tuberculosis (TB) observed between 1984 and 1990 at King Khalid University Hospital were reviewed. Out of 21 patients,15 had spinal epidural abscess with cord compression, 3 were with transverse myelitis, and the remaining 3 had syringomyelia secondary to tuberculous meningitis. Treatment associated surgical decompression and antituberculous therapy. A follow-up of 1 to 2 years showed an excellent recovery in 81% of cases (17/21). The outcome and the clinical manifestations of spinal cord TB will be presented.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-16-09 HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION IN CHILDREN IN RIO DE JANEIRO. NEUROLOGICAL ASPECTS.

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A transversal descriptive study was designed, in order to check the prevalence of neurological manifestations, and their clinical spectrum, in the group of HIV infected children attending the specific out-patient clinic in the University Hospital.

Central nervous system (CNS) involvement was observed in 35.6 % of the 63 infected children. Neurological manifestations were detected only in patients classified as P-2 according to the Centers for Disease Control.

The clinical features, including investigations and postmortem findings were, as a whole, similar to those described previously by other authors.

Because only a few of these children have been examined by the child neurologist and because CNS involvement is reasonably common, this specialist should probably be sought more often.

2-16-10 DUAL HTLV-I AND HIV-1 INFECTIONS IN NATAL, SOUTH AFRICA

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Six patients with dual HTLV-I and HIV-1 infections were identified during an ongoing study of a HTLV-I associated myelopathy (HAM/TSP) study. Their clinical and laboratory profiles were studied and compared to the isolated HAM/TSP cases.

There were 3 men (aged 26,34 & 40 years) and 3 women (two aged 19 years and one 25 years). Myelopathy was the sole clinical manifestation in 4 patients. Patient 5 had myelopathy and generalised lymphadenopathy whilst patient 6 had myelopathy, conjunctivitis and seborrhoeic dermatitis. No patient had dementia. Antibodies to HTLV-I and HIV-1 were detected in the serum and CSF. Significant CSF lymphocytosis was present in 4 patients. Oligoclonal bands were present in all 4 CSF samples tested. The CD4 counts, measured in the peripheral blood of 4 patients, were greater than 500/mm^3. Two had elevated CD8 counts as well. The CD4 and CD8 counts did not differ significantly from those in patients with isolated HAM/TSP.

Our findings suggest that in the dually infected patients seen at Wentworth Hospital the myelopathy is more often HAM/TSP than the vacuolar myelopathy of advanced HIV infection.

2-16-11 NEUROTRANSMITTER AND AMINO-ACID LEVELS IN THE CSF OF HIV PATIENTS

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Methods: Simultaneous determination of MHPG, 5-HIAA and HVA in CSF samples of n. 51 HIV pts. (M:33, F:18, mean age 26.5±6.3 yrs) by direct injection on a liquid chromatograph (HPLC) with coulometric detection; evaluation of Aspartate and Glutamate CSF levels by reverse-phase HPLC (Analyzer: System 6300, Beckman U.S.A.) in a subgroup of n.10 pts. Results: The HIV group (n.26:CDC stages II-III-IVA; n.15:IVB, n.10:IVC) showed reduced CSF levels for 5-HIAA and HVA vs n.30 controls age and sex-matched ($p<0.001$ Anova 1W). Reduced levels of MHPG vs controls ($p<0.05$) were found only within the subgroup (n.18/51) with altered BBB. Four to ten-fold increase of Glutamate was seen in 4/10 cases with primary CNS diseases, while asymptomatics (n.4) and neurotoxo pts.(n.2) showed levels within the control range (mean:7.9±4.6 uM/L). Conclusion: A progressive neurotransmitter alteration is observable in HIV, with a derangement paralleling the evolution of the disease. Elevate Glutamate level in IVB cases with primary CNS involvement confirms the role of excitotoxic mechanisms in the production of the brain damage in primary HIV disease. Study supported by ISS Grant AIDS Project '92.

2-16-12 KINETICS OF INTRAVENOUS VANCOMYCIN IN PATIENTS WITH SUBARACHNOID HEMORRHAGE

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Meningitis of methicillin resistant *S.aureus*(MRSA) has become a serious problem. Though intraventricular vancomycin (VCM) is shown to be effective in treating central nervous system infection, little has been reported on its kinetics in CSF when administered intravenously. We investigated the kinetics of intravenous VCM in 4 patients with subarachnoid hemorrhage whose blood-CSF-barriers were disrupted. One g of VCM in 100mL saline was administered intravenously for 60-min. CSF and blood samples were taken at predetermined time points. VCM concentration were measured by bioassay and its kinetic parameters were established by non-linear least square method. In plasma, the average maximum concentration(Cmax) of VCM was 44.5±6.8 μg/mL, the area under the concentration curve(AUC) for 0~12 hours was 132.1±25.9 μg · h/mL and half-life(T1/2) was 4.4±1.0h. In CSF, Cmax was 2.1±0.3 μg/mL, AUC was 16.6±3.3 μg · h/mL and T1/2 was 4.4±1.0h. Cmax and AUC in CSF were 4.7% and 12.6% of those in plasma, respectively. These results suggest CSF concentration of VCM, when administered intravenously, is high enough in the treatment of MRSA meningitis.

2-16-13 HERPES SIMPLEX VIRUS TYPE2 MYELITIS.
– DETECTION OF HSV2 DNA IN CEREBROSPINAL FLUID.–

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Polymerase chain reaction(PCR) technique has been successfully used to detect herpes simplex virus(HSV) from patients with HSV encephalitis. By PCR assey possible to type of HSV1 and 2, we detected HSV DNA in cerebrospinal fluid(CSF) from patients with HSV myelitis and discussed the clinical findings of them.

Three cases of HSV myelitis (a 49-year-old female,a 38-year-old male and 44-year-old male) were studied.All cases were characterized by transverse myelopathy of thoracic cord, and two patients had recurrence.In all cases of them HSV1 antibodies were elevated in serum and CSF. But HSV2 DNA in CSF was amplified by PCR,and HSV2 DNA was detected at both first and second episode in two relapsing myelitis.

No case of relapsimg myelitis by HSV2 was reported.The PCR technique is useful for diagnosis of HSV1 and 2 myelitis,and it would suggest that relapsing HSV myelitis may not be rare.

2-16-14 DETECTION OF EPSTEIN-BARR VIRUS IN THE CEREBROSPINAL FLUID FROM PATIENTS WITH NEUROLOGICAL DISEASES BY POLYMERASE CHAIN REACTION

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Epstein-Barr virus (EBV) was detected in the cerebrospinal fluid (CSF) from patients with variety of central nervous system disorders. Using nested polymerase chain reaction, we evaluated CSF from 98 patients with neurological disorders for presence of EBV genomes. EBV DNA was found in CSF from 7 patients: Three patients had acute or subacute meningo-encephalitis with focal symptoms such as convulsion; the 4th patient had clinical diagnosis of multiple sclerosis; the 5th had chronic inflammatory demyelinating polyneuropathy with central nervous system involvements; the 6th had leukoencephalopathy with hypertension; the 7th had akinetic rigid syndrome with lacunar infarction.

Those 7 patients were not immunodeficient hosts. The findings indicate that the role of EBV in diverse neurological diseases must be evaluated further not only with immunodeficiency but without severe immunological disorder.

2-16-15 NEUROPSYCHIATRIC MANIFESTATIONS IN WHIPPLE'S DISEASE

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Whipple's disease is a rare disorder, usually presenting with systemic symptoms like lymphadenopathy, diarrhea, arthralgia. Nervous system involvement has been reported in more than 10 percent. Etiological factors shall be immunological disturbances together with infections. We present a case of a 69 y old man, who developed an amnesic syndrome and polyneuropathy together with typical systemic onset. About 3 years following systemic remission under antibiotic treatment, he developed typical temporal lobe seizures. In addition, the patient showed schizophrenia-like symptoms for 22 years before systemic onset. We present data of CSF investigations, neuropsychological and neurophysiological results, MRI (periventricular white matter lesions) and repeated cerebral blood flow investigations using 99mTc-HMPAO and single photon emission tomography (SPECT) (left temporal hypoperfusion with amelioration tendency) and present the course under different treatment strategies. We also discuss similarities to other neuroimmunological disorders like systemic lupus erythematosus.

2-16-16 KLEBSIELLA OZAENAE MENINGITIS: REPORT OF TWO CASES AND REVIEW.

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Meningitis is rarely caused by Klebsiella ozaenae, a colonizer of the oral and nasopharyngeal mucosa. We herein describe two patients with Klebsiella ozaenae meningitis. Both patients suffered from a primary disease of nasopharyngeal pathway; one had nasopharyngeal carcinoma and the other, ozena. Review of the English-language literature from 1966 to the present revealed only two cases of Klebsiella ozaenae meningitis; pneumonia and hyperglycemia were noted in one patient and otitis media, sinusitis and diabetes mellitus, in the other. All these four patients were over 50 years old. Of the four patients, two treated with third-generation cephalosporins recovered whereas one of the two treated with chloramphenicol died. The patient who died had a positive blood culture for Klebsiella ozaenae. Blood culture was positive only in one of the three survivors. Whether chloramphenicol should be replaced by third-generation cephalosporin and whether blood culture indicates a poor prognosis in Klebsiella ozaenae meningitis remain to be determined.

2-16-17 *BENIGN BRAINSTEM ENCEPHALOPATHY: A NEW CLINICAL SYNDROME (?)*

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In a previous study performed at this hospital, we reported 3 cases of benign brainstem encephalopathy with truncal ataxia (Brain and nerve 44: 893-898, 1992). Since that time, we have had 3 additional cases. This report concerns 6 cases of benign brainstem encephalopathy including 3 cases previously reported, and we propose a new clinical syndrome. Our patients ranged from 30 to 49 years of age. Three patients were males, and 3 patients were females. Four patients had prodromal symptoms. Neurological examination revealed truncal ataxia in all cases. Additional neurological signs such as ophthalmoplegia, ptosis, nystagmus, anisocoria, mydriasis, transient opsoclonus, and facial palsy were seen. Neither drowsiness nor myoclonus nor areflexia occurred in any of the 6 cases. Examination of cerebrospinal fluid showed a moderate rise of protein in 2 cases, but did not reveal pleocytosis in any of the 6 cases. Magnetic resonance imaging of a patient revealed an area of high intensity in the left pontine tegmentum by T_2-weighed imaging. Motor nerve conduction velocity of the 6 cases were within normal limits. The prognosis for all 6 cases was good, and the reappearance of neurological signs was not present until now.

2-16-18 ELEMENTARY STUDY OF TREATING INFECTIOUS POLYRADICULITIS BY INFUSING SOME DRUGS INTO EPIDURAL CAVERN

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Infectious polyradiculitis was traditionally treated through the general modality, but, the results are that the disease recover slowly and the sequels are more than that of the new method. 22 Patients with infectious polyradiculitis (14 acute, 8 chronic convalescents) entered into this study. After the interspaces of a cervical and a lumbar vertabrae were punctured into epidural cavern, the drugs (Vitamin B1, B6, B12, Calanthanmium and dexamethasone) were infused into epidural cavern through peridural catheters. The doses of drugs were different according to age of patients and severity of the disease. Because the drugs directly affect the phlogistic nerves and nerve roots, the results are very satisfaction. In the acute group, 61% of them were improved after 48 hours following treatment. 70% were able to walk around freely after the first course of treatment, 86% were recovered after the second course. 14% of acute and the majority of chronic convalescents required to be treated continually. The average time of hospitalization in the acute patients is 28 days. The new method has been proved to be able to shorten the time of recovery and reduce the sequels distinctly.

2-16-19 ^{99m}Tc-HMPAO LEUCOCYTE SCINTIGRAPHY IN DIFFERENTIAL DIAGNOSIS OF BRAIN ABSCESS

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Aim: Brain abscess is a serious clinical condition demanding rapid diagnostic and therapeutic decisions. However, CT scan and MRI may be unable to differentiate an abscess from other types of lesions, tumoral or vascular. We assessed the sensitivity and the specificity of ^{99m}Tc-*hexamethylpropylenamine oxime (HMPAO) leucocyte scintigraphy*, a non invasive method for the detection of soft tissue infection that may be useful in the differential diagnosis of intracerebral mass lesions.
Methods: We have studied till now 18 patients with focal neurological signs and cystic masses, contrast enhanced, at the CT scan.
WBC were extracted from 60 ml of venous blood sample and incubated with ^{99m}Tc-HMPAO. Doses of185-222 mBq were injected and planar images were obtained 1,3,24 hs later by means of a maxi camera.
Results: Seven leucocyte scintigraphy were positive and the final diagnosis turned out cerebral abscess in all these cases. Eleven patients obtained a negative results; their final diagnosis was glial or metastatic tumors, old hematoma or cysticercosis. No false positive or false negative cases were present at this phase of enrollement and therefore the sensibility and sensitivity are 100%.
Conclusions: ^{99m}Tc-HMPAO leucocyte scintigraphy may add an useful dimension to the diagnosis of a brain abscess.

2-16-20 APOLIPOPROTEIN A II INTRATHECAL SYNTHESIS (ITS) IN NEURO-AIDS

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Apo A II was determined by EID and EIA in serum and CSF of 109 (41 definite MS + 30 HIV1 infected + 38 other neurological) patients compared to 9 controls. In the HIV-1 group (9 AIDS dementia complex, 9 opportunistic infections of the CNS, 6 other neurological diseases, and 6 without neurologic or psychiatric symptoms) serum Apo A II was under the lower normal limit in 20/30 patients, with a significant ($p < 0.001$) decrease comparatively to the mean of the 79 other neurological patients. In the CSF the frequency of Apo A II ITS, which is rare (14/109 patients) was significant (9/30 vs. 5/79: $p < 0.001$). These 9 ITS were observed in 5 AIDS dementia complex, 2 CMV (1 meningo-encephalitis, 1 meningo-radiculitis) infections, 1 progressive multifocal leucoencephalopathy and 1 patient without neurological symptoms. Thus Apo A II may be a marker of CNS involvement in HIV-1 patients.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-16-21 HIVp17-LIKE-IMMUNOREACTIVE 23 kDa PROTEIN (HIP 23) IN NON-AIDS HUMAN REACTIVE ASTROCYTES AND NEURONS.

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HIVp17 is a core protein of HIV (human immunodeficiency virus) with a molecular weight of~17kDa. This protein has been reported only in HIV and AIDS research. We report a novel protein, HIP 23, in reactive astrocytes and neurons in non-AIDS brains. [Materials & Methods] Formalin-fixed, paraffin-embedded sections of the brains and /or spinal cords from 2 cases of non-neurological diseases and 15 cases of various neurological diseases including Alzheimer's disease (3), motor neuron disease (4), spinocerebellar degeneration (3) and cerebrovascular disease (5) were immunostained with anti-HIVp17 (Chemicon) and anti-glial fibrillary acidic protein (GFAP; BioMakor) by the ABC method. Tris-buffered saline extract of unfixed brain tissue from another case of Alzheimer's disease was processed for Western blot study with anti-HIVp17. [Results] The anti-HIVp17 intensely labelled the cytoplasm and cell processes of virtually all, GFAP-positive, reactive astrocytes in affected areas of the brains and spinal cords. In non-affected areas, although several neurons were positive, normal-looking astrocytes were only rarely stained with anti-HIVp17. In Western blot study, the antibody recognized~23 kDa band. [Conclusions] 23 kDa protein with an epitope similar to HIVp17 was markedly increased in astrocytes in their reaction and transformation.

2-16-22 QUALITATIVE AND SEMIQUANTITATIVE ANALYSIS OF THE ANTIBODY RESPONSE IN ASYMPTOMATIC AND SYMPTOMATIC BORRELIA BURGDORFERI INFECTIONS

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Objective: Identification of specific Borrelia burgdorferi (Bb) antigens might be useful for selective antibody tests to increase sensitivity and specifity of currently used assays. Background: Symptomatic (SI) or asymptomatic infections (AI) which might be of recent or past origin can't be differentiated by conventional ultra sonicate ELISA's. Methods: 100 patients with a neuroborreliosis, Stage II, 204 healthy blood donors with a positive B.b.-ELISA and 50 control patients with a negative Bb serology were studied. The immunoblot technique with the B31 strain was used. Results: Antibodies against the 100-, 21-, 18- and 10 kd antigen correlated signif. with high ELISA-titres and were rarely detected in the control group. SI compared to AI were characterized by a signif. pronounced IgM-response against several outer surface proteins (21-, 30-, 35 kd) independent from the age of the infection. This specific IgM immune response revealed to be most sensitive to antibiotic therapy. Cross reactive IgM (e.g.60-,41 kd) or single IgG antibodies were decreasing in intensity but haven't dissapeared over the follow up period of 4 1/2 years. Conclusions: The most reliable and predictive serological results should be obtained by a IgM assay using the 100-,35-,30-,21 kd proteins as antigen.

2-16-23 NEURORADIOLOGIC CHANGES IN PATIENTS WITH SUBACUTE SCLEROSING PANENCEPHALITIS

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Subacute sclerosing panencephalitis (SSPE) is a slow virus disease caused by the measles virus. Following the introduction of measles vaccine it has been nearly eradicated from many developing countries. Very little data on the neuroradiologic changes of the disease are reported. We describe CT and MRI findings from 12 patients (age 3½-24 years, 7 males and 5 females). Clinical diagnosis was confirmed by characteristic EEG changes and elevated measles antibody titres in the CSF in all. Brain CT was performed in 8 patients, 2-30 months after the onset of the disease. Four CTs were normal while the other 4 showed low density areas of various sizes in the periventricular distribution. Twelve MRIs were performed in 10 patients, 2 weeks to 2½ years after the onset of the disease. Two MRIs were entirely normal. T2-weighted sequences revealed increased signal intensity lesions in the periventricular white matter in 6, and in the basal ganglia bilaterally in 2 patients. Multiple small areas with similar signal characteristics were seen scattered in the white and grey matter in one study. Moderate degree of ventricular dilatation was seen in two patients. SSPE should be suspected in patients with radiologic findings described above.

2-16-24 INTRATHECAL HYALURONIDASE IN THE MANAGEMENT OF SPINAL BLOCK DUE TO TUBERCULOUS SPINAL ARACHNOIDITIS

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Despite the appropriate chemotherapy and steroids, spinal arachnoiditis, as a complication of tuberculous meningitis, is not uncommon in developing countries. The various treatment methods previously tried for it are unsatisfactory due to serious side effects and/or doubtful therapeutic value. The proteolytic enzyme, hyaluronidase, by virtue of its action of its action of hydrolyzing the glucosaminidic bonds of hyaluronic acid and other mucopolysaccharide of the ground substance, offers a promising mode of treatment. The present report describes the effectiveness of intrathecal injection of hyaluronidase in spinal block due to spinal tuberculous arachnoiditis. Paraparesis and sensory changes were developed in a 25-year-old female patient diagnosed as tuberculous meningitis in spite of the antituberculous regimen combined with steroid therapy. At that time, the CSF protein level were 6500 mg%, and the myelogram and MRI showed definite block of CSF flow in subarachnoid space from the second to the ninth thoracic level. After the fifth intrathecal hyaluronidase injection with the interval of two weeks (total 7500 unit), the neurological deficits were markedly improved to nearly normal state and the CSF protein level converted to 128 mg%. Repeated thoracic myelogram showed the improvement of passage of contrast media. Thus this case may provide the therapeutic role of hyaluronidase as an adjuvant management of spinal arachnoiditis complicating tuberculous meningitis for which no satisfactory treatment exists.

2-16-25 A NEUROLOGICAL AND NEUROPATHOLOGICAL STUDY OF HTLV-1 INFECTED RATS.

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Human T lymphotropic virus type 1(HTLV-1) is considered a causative agent of HTLV-1 associated myelopathy (HAM)/ tropical spastic paraparesis (TSP). Five out of 10 WKA rats infected by HTLV-1 developed spastic paraparesis 80 to 116 weeks after intravenous injection of HTLV-1 producing T cells. HTLV-1 infection was confirmed by the presence of anti-HTLV-1 antibody and detection of the proviral DNA in peripheral blood. The spinal cord showed largely symmetrical degeneration with macrophage infiltration in the peripheral area of the anterior, lateral and/or posterior funiculi. The peripheral nerve showed similar changes. In conclusion, HTLV-1 infected rats could develop myelopathy and peripheral neuropathy, and would be useful in studying pathogeneses of HTLV-1 associated human diseases.

2-16-26 MONOCLONAL ANTIBODY ANALYSIS OF BLOOD AND CEREBROSPINAL FLUID IN ADULT ASPETIC MENINGITIS

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To comprehend Immune Response of Aseptic Meningitis in Adult, we, presuming the last headache as the onset of it first of all, analyzed the change of element of cells and surface maker of lymphocyte in peripheral blood and cerebrospinal fluid (CSF) using monoclonal antibody in 157 cases (15 to 76, ave. 33.8 yrs). As the result, on the 5th to 6th day after the last headache pleocytosis in CSF was at its maximum and afterwards it was tend to decrease in almost cases. Regardless of the change of the cell count and its element in CSF, the percentage of matured T-cell was continuously high and pan B-cell was low in CSF compared with peripheral blood from first to last. And after one week from last headache, activated T-cell began to increase, and the inflammation went to an end. It suggested that there was different immune response between peripheral blood and CSF and its feature was characteristic to other inflammatory diseases in Central Nervous System.

2-16-27 ANALYSIS OF THE BRONCHOALVEOLAR LAVAGE FLUID IN HAM/TSP PATIENTS

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Previous studies have demonstrated the association of HTLV-I associated myelopathy (HAM) and systemic non-neurologic manifestations as vasculites, uveites arthropathy, cryoglobulinemia, polymiosites and adult T-cell leukemia-lymphoma. We studied the bronchoalveolar lavage fluid (BLV) of 19 HAM patients and compared with 10 controls that had sera and CSF HTLV-I negative myelopathies. Three of the HAM patients were smokers; 21% presented respiratory complains as dry cough and mild dyspnea. No patients or controls had respiratory diseases for four weeks or were using drugs as corticosteroids for six months before examination. None of the controls had respiratory symptoms or were using medications.

We found 79% of our patients with more than 20% of lymphocites in the BLV. We conclude that HAM is associated with alveolites.

2-27-01 THE NOVEL DOPAMINERGIC AGENT ROPINIROLE SELECTIVELY BINDS TO CLONED DOPAMINE D_3 RECEPTORS

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Ropinirole is a well-tolerated non-ergoline, selective dopamine agonist in advanced development for Parkinson's Disease. Previous studies in vitro, using rat and human tissue, have shown that ropinirole is a potent agonist at D_2 receptors with no affinity for D_1 receptors.

We have now studied the binding of ropinirole to cloned human receptors (stably expressed in Chinese Hamster Ovary cells or mouse fibroblasts). Ropinirole did not inhibit binding of [^{3}H]-SCH 23390 to D_1 receptors (Ki >10,000nM). 2 binding sites were identified in D_2 and D_3 clones using [^{125}I]-iodosulpiride. Ki for ropinirole for inhibition of binding to the high affinity site was 1400nM for D_2(L) and 70nM for D_3. This 20-fold selectivity for D_3 binding is of the same order as found for dopamine itself, quinpirole and quinelorane (17,11 and 24-fold) but greater than pergolide (5-fold). Apomorphine, lisuride and bromocriptine showed little selectivity (0.7,0.9 and 1.6-fold).

The cellular and functional significance of the D_3 affinity of ropinirole is being explored. Binding to the D_3 autoreceptor decreases dopamine turnover with the potential for decreased free radical generation. Selective binding to D_3-rich limbic areas might also explain the anxiolytic and antidepressant activities noted in other experimental studies.

2-27-02 NEUROCHEMICAL SELECTIVITY OF ROPINIROLE, A NOVEL DOPAMINE AGONIST

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The non-ergoline dopaminergic agent, ropinirole is in advanced clinical trials to study both early and late stage usage in Parkinson's Disease.

In order to help interpret the clinical response, we have explored the pharmacological activity in vitro and in vivo. Studies on binding in vitro, using human, rat and bovine tissues, showed selective dopamine (DA) receptor binding (Ki, $3x10^{-8}$M for human caudate D_2-like receptors). No binding (10^{-4}M) was detected at serotonin, 5-HT_1, benzodiazepine, gamma-aminobutyric acid, α_1 and β-adrenoceptors and only very weak affinities (approximately 10^{-5}M) were detected at β_2-adrenoceptors and 5-HT_2 receptors. Comparator DA agonists were less selective: for example, pergolide and bromocriptine bound at 5-HT_1 receptors. Ropinirole also showed no affinity for rat monoamine transporters: there was no inhibition of DA, 5-HT or norepinephrine (NE) uptake in vitro.

In acute dose-response (0.03-10mg/kg i.p.) studies in mice, ropinirole was selective for DA turnover - no significant effects on 5-HT,NE or their metabolites were observed. The dose-dependent decrease in DA metabolites is consistent with autoreceptor activation: this effect of ropinirole was more potent and prolonged than bromocriptine.

The present results confirm the neurochemical selectivity of ropinirole and accord with the favourable safety profile observed in clinical trials.

2-27-03 RELATIONSHIP BETWEEN PROPRANOLOL METABOLISM AND GENOTYPING IN CHINESE

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RFLP analysis was performed through cleavage of DNA by restriction enzyme endonuclease Xba I and then agarose electrophoresis. Southern blotting was performed using nitrocellulose filter paper and hybridization with ^{32}P labelled Caucasian P450 IID6 cDNA. Exon sequencing with PCR for CYPIID6 for 4 extensive metabolizer was performed with specific primer. A PCR-based test for C/T_{188} polymorphism was developed. When the C_{188} in the CCACC sequence was substituted with T_{188} TCACC becomes an endonuclease site for Hph I. Samples with C_{118} gave 59 and 213 bp bands and samples with T_{188} gave 59, 101, and 112 bp bands after the DNA fragment (following PCR) subjected to digestion with Hph I prior to electrophoresis (2% agarose). The T/T, C/T, and C/C distributions in the three major genotype were 29/29 kb: 35%, 27% and 38% (n = 37); 44/29 kb: 51%, 46% and 3% (n = 65); 44/44 kb: 84%, 11% and 5% (n = 19). Seventeen subjects with T/T, nine subjects with C/T and seven subjects with C/C were performed with pharmacokinetic evaluation for P after informed consent obtained. The volunteers should receive no drugs, restrained from alcohol for 24 hours and have normal physical examination and also hepatic and renal function by laboratory screen. Each subject received 40 mg of P orally. Ten milliliter blood samples were obtained before and 38 minutes and 1, 1.5, 2, 3, 4, 6, 8, 10 and 12 hours afterward. All urine excreted by each subject in 48 hours after administration of the dose were collected. The concentration of P and its metabolite 4-OH-P were measured by HPLC. The total clearance of P was obtained through the dose of P (40 mg) divided by area under curve of P. The renal clearance was obtained through the total amount of unhydrolized P in the urine divided by the dose of P (40 mg) and then multiply with the total clearance. The formation clearance of 4-OH-P was obtained through the toal amount (in nmole) of 4-OH-P in urine, divided by the dose (in nmole) and then multiply with the total clearance. The total clearance and the amount of 4-OH-P production were significantly larger in the C/C than those in the T/T volunteers (8.58 ± 5.77 vs. 4.47 ± 2.06 in total clearance, $p < 0.05$ and 8.04 ± 9.41 vs. 2.62 ± 2.31 in 4-OH-P, $p < 0.05$) with the values in between (6.75 ± 5.37 in total clearance and 3.69 ± 3.10 in 4-OH-P) among C/T subjects. The values of renal clearance also revealed similar tendency without reaching statistical difference.

2-27-04 THE EFFLUX MECHANISM OF METHYLMERCURY FROM CULTURED ASTROGLIAS.

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Methylmercury(MHg) is a pathogen of Minamata disease, but the cytotoxic effect and intracellular kinetics remains unsolved. The study was undertaken to investigate the efflux mechanism of MHg from central nervous cells. Primary cultured astroglias pbtained from neonatal rats were incubated with MHg-cysteine (10 μ M) for 30 minutes, and washed with the mercury-free medium, and then the concentration of mercury was determined in the medium. The efflux was gradually increased and reached to the maximum plateau at 2 hours. A cysteine precursor, 2-oxothiazolidine-4-carboxylate, increased cellular amounts of cysteine and glutathione, and also significantly increased the efflux of mercury (1.7-folds). MHg found in the medium was exclusively the glutathione-conjugated form, which was determined by an ion-exchanged column-chromatography. These results sugest that the conjugation with glutathione is a major pathway of efflux of MHg, and the intracellular concentration of glutathione promote the efflux in rat astroglias.

2-27-05 EFFECTS OF LIPOIC ACID ON REDOX STATES OF CO-ENZYME Q IN THE MPTP-MODEL

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MPTP-toxicity is suggested to be due to interaction of MPP^+ with complex I of the respiratory chain (RC). In this case cellular energy supplies, like ATP, rapidly are depleted and calcium homeostasis is disturbed. Coenzyme Q (CoQ) interferes with various pathways including the RC. DDC plus MPTP treatment (6 x 400 mg/kg DDC ip. plus 12 mg/kg MPTP ip.) of C57BL/6 mice 96 hrs. after intoxication resulted in a significant decrease of CoQg and CoQ_{10} in the frontal cortex (FC) and hippocampus (HIP) at otherwise unchanged concentrations of total CoQ's. Lipoic acid (LA) (one hour prior to DDC + MPTP) counteracted these changes in FC, HIP and striatum. This finding may indicate a neuroprotective effect of LA.

2-27-06 ESTIMATION OF BLOOD-TO-CEREBROSPINAL FLUID PASSAGE OF DRUGS BY THEIR LIPOPHILICITY AT pH 7.4, MOLECULAR WEIGHT AND BINDING TO SERUM PROTEINS

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In humans with cerebrovascular diseases who had undergone external ventriculostomy for occlusive hydrocephalus the passage of glycerol, sorbitol, cefotaxime, ceftriaxone, ciprofloxacin, ofloxacin, rifampicin and netilmicin into the cerebrospinal fluid was studied after intravenous administration. Serum and CSF was drawn repeatedly after the first drug infusion, and drug concentrations were measured by HPLC, enzymatic or immunologic methods.
Due to the slow elimination from the CSF compartment the ratio of drug concentrations in CSF and serum drawn simultaneously increased with the time interval from the infusion. For this reason the ratio of the areas under the concentration-time curves in CSF and serum (AUC_{CSF}/AUC_S) and the ratio of AUC_{CSF} and the fraction of AUC_S not bound to serum proteins (AUC_{CSF}/AUC_{Sf}) were taken as measures of CSF passage.
The quotients of the octanol/water partition coefficient at pH 7.4 (PC) as a measure of lipophilicity and the square roots of the molecular weight ($\sqrt{MW}$) of the drugs investigated were related to AUC_{CSF}/AUC_{Sf} by the equation

$$AUC_{CSF}/AUC_{Sf} = 0.95 + 0.21 lg(PC/\sqrt{MW})$$

For $0.000093 \leq PC/\sqrt{MW} \leq 1.7$ this function may be of value for the estimation of CSF penetration in humans when only the physicochemical properties of a drug are known and when active transport or metabolism are negligible.

2-27-07 THE EFFECT OF SUBSTANCE P ON DENDRITIC DEVELOPMENT AND ARBORIZATION OF PURKINJE CELLS OF RAT'S CEREBELLUM CULTURED IN VITRO

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In previous studies we have found that intraventricular administration of Substance P induces unattached Purkinje cell dendritic spines in the rat's cerebellum. Proceeding to in vitro studies, in this work, we found that Purkinje cells of new born rat's cerebellum cultured in vitro in a nutrient enriched with Substance P developed a thick three dimensional dendritic tree, which in correlation with the dendritic arborization of Purkinje cells of control explants of the same animal, demonstrated a 30% increase in the number of the secondary and tertiary dendritic branches. All of the dendritic branches were covered with spines of various shape and size, some of them been unattached. In the second week of the in vitro culture of the cerebellar cortex, the explants cultured in a feeding medium enriched with substance P demonstrated a marked increase in the number of synaptic vesicles in the presynaptic terminals of the parallel fibres, a fact suggesting that Substance P serves as a neuromodulator, facilitating the neurotransmitter accumulation in the presynaptic terminals in the axodendritic synapses.

2-27-08 DOPAMINE D-1 MEDIATED RESPONSES IN AN EXPERIMENTAL MODEL OF PARKINSON'S DISEASE: THE PRIMING PHENOMENON INVOLVES TRANSDUCTIONAL PATHWAYS.

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'Priming' is a phenomenon of behavioural sensitization observed in 6 OH-DA lesioned rats following the administration of a dopamine agonist: a single dose of the D-1 agonist SKF38393 (3mg/kg; sc) induces controlateral turning only in rats previously challanged with L-DOPA while the same dose is inactive in drug-naive, lesioned animals. We report the results of investigations on both the activity of adenylate cyclase and the "in vivo" phosphorylation (back-phosphorylation) of DARPP-32 and ARPP-21, two phosphoproteins functionally linked to D-1 receptors in striatum. All assays were performed in striata of both lesioned and unlesioned sides. A significant increase (25%) of affinity of adenylate cyclase stimulated by SKF38393 was observed in primed rats. A significant decrease of the dephospho forms of DARPP-32 (26%) and ARPP-21 (24%) was observed in the lesioned side striata of primed rats, indicating an increased phosphorilation "in vivo" of both phosphoproteins as a consequence of 'priming'. This study indicates that the 'priming' phenomenon involves an alteration of trasductional pathways.

2-27-10 THREE DIMENTIONAL TOPOGRAPHIC SIMULATION OF CHEMICAL WAVES CONCERNED THE DYNAMIC MODELS OF NEUROTRANSMITTER RECEPTOR INTERACTION.

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Chemical waves of dose-response of drugs are the interesting phenomena of unlinear reaction of system which is far from the ststes of the equilibrium. The methods of system's parameter regulation and three dimentional topographic of the dynamic models of neurotransmitter receptor interaction's results show that these models have the properties of local chemical waves, which the pharmacological values are the feedback vibration regulation of the system leading the selfoganization of the chaos waves. Analysis of chemical waves could help the understanding of complex phenomena ofdrugs.

2-27-11 EFFECT OF GLUCOCORTICOID ON IN VIVO RELEASE OF NEUROTRANSMITTERS FROM THE RAT HIPPOCAMPUS.

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we confirmed that glucocorticoid potentiated kainate-induced cytotoxicity on cultured hippocampal neurons. In relation with these results, we performed microdialysis experiments on rat hippocampus to observe glucocorticoid's effect on neurotransmitter release. Wistar strain male rats were anesthetized and a guide canula was stereotaxically inserted into the hippocampus. Amino acids were assayed following Laura's method with use of a fluorescence detector. Acetylcholine (ACh) and catecholamine were assayed by means of HPLC-ECD. Glucocorticoid was injected intraperitoneally. Dexamethasone injection caused decrease of amino acids. The decrease was more prominent in GABA than the excitatory amino acids. Dexamethasone caused biphasic changes of ACh release, i.e. decrease then increase. Norepinephrine and dopamine did not show much change after medication.

2-27-12 BRAIN EDEMA AND CELL CHANGES INDUCED BY HEAT STRESS IN RATS ARE REDUCED BY PRETREATMENT WITH INHIBITORS OF PROSTAGLANDIN SYNTHESIS.

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The possibility that prostaglandins (PGs) play an important role in the pathophysiology of heat stress (HS) was examined in a rat model. Exposure of young rats (80-90 g, 7-8 weeks old) to heat at 38°C in a biological oxygen demand (BOD) incubator (relative humidity 45-57 %, wind velocity 20-25 cm/sec) for 4 h resulted in hyperthermia (41.56±0.34°C) and behavioural symptoms such as salivation and prostration. These symptoms are very similar to the clinical conditions of HS in children. About 30 % hyperthrmic animals (42.24±0.12°C) died immediately after HS. A visual inspection of brain showed many micro-haemorrhages, profound swelling and softening of various cerebral components. Ultrastructural studies showed neuronal, glial and vascular damage. Treatment with PG synthesis inhibitor indomethacin (10 mg/kg) or paracetamol (50 mg/kg) (i.p., 30 min before HS) resulted in less hyperthermia (39.36±0.32°C) and symptoms. The visual swelling and the cell changes in drug treated animals were minimal. These observations indicate that inhibition of PG synthesis prior to HS has beneficial effects. However, further studies are needed to evaluate the potential efficacy of these compounds for a therapeutic value in HS.

2-27-13 MODIFICATION OF LEVODOPA PHARMACOKINETICS AFTER CONCOMITANT LISURIDE ADMINISTRATION IN PARKINSON'S DISEASE (PD).

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We recently found that bromocriptine modifies plasma LD levels (Clin. Neuropharmacol. 14:514-522, 1991). Here we measured plasma levodopa (LD) in PD patients (pts) receiving LD orally together with lisuride (LIS) (Dopergin, Schering, Berlin). Eighteen PD pts (mean age 68y) chronically treated with LD and LIS, given at 0 time, 125mg LD ± 12.5mg carbidopa alone and on another day together with 0.2mg LIS (12h off medication). Plasma LD levels (HPLC) and the motor performance (Webster) were monitored over 4h: a) in 7 pts (6 with frequent dyskinesias) LD values were significantly higher ($p<0.01$) (paired T-test) when both drugs were given together; b) in 3 pts (all with severe akinesia) LD levels were lower when LIS was added; c) in 8 pts (2 with motor fluctuations) LD levels were similar. Webster scoring was similar, while severe dyskinesias correlated with higher plasma LD values. Dyskinesias and motor fluctuation observed when LIS is added to LD, may stem not only from striatal interaction but also from changes in LD pharmacokinetics.

2-27-14 GABAA AND GABAB RECEPTORS ARE REDUCED IN THE CEREBELLAR CORTEX FROM 3-ACETYLPYRIDINE-INDUCED ATAXIC RATS.

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3-Acetylpyridine (3-AP) induces cerebellar ataxia in rats by destroying inferior olive. As GABA is the major transmitter in the cerebellum, we measured GABAA and GABAB receptor densities in the cerebellar cortex from 3-AP-treated rats using film autoradiography. Rats were sacrificed 14 days after 3-AP injection (80mg/kg i.p.). Cerebellar sections were incubated with 50nM [^{3}H]GABA. For GABAA binding, incubation was performed in the presence of 100μM (±)baclofen, and for GABAB binding, in the presence of 40μM isoguvacine and 2.5mM $CaCl_2$. Receptor densities were expressed as mean±SE (fmol/mg tissue equivalent). In the cerebellar cortex from 3-AP-treated rats, GABAA receptor density in the granular layer was 692.2±14.5 (88.7% of control, $p<0.05$) and that in the molecular layer was 152.1±5.0 (80.2% of control, $p<0.05$). GABAB receptor density in the granular layer was 44.7±4.1 (53.2% of control, $p<0.005$) and that in the molecular layer was 106.8±21.0 (39.3% of control, $p<0.005$). GABAB receptors were more prominently reduced by 3-AP treatment than GABAA receptors. These results suggest that GABAB receptors in the molecular layer are located mainly on the climbing fibers originating from the inferior olive.

2-27-15 THE ANTIOXIDANT PROPERTIES OF A DOPAMINE AGONIST, BROMOCRIPTINE.

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Accumulating informations support the hypothesis that an oxidative stress involving lipid peroxidation may contribute to the pathogenesis of Parkinson's disease. Bromocriptine is now widely used for the treatment of Parkinson's disease. To examine the antioxidant properties of this agent, electron spin resonance (ESR) spin trapping technique was used.

Bromocriptine decreases the ESR signal intensity of 5,5-dimethyl-1-1-pyrroline-N-oxide (DPMO)-OOH spin adduct produced by the reaction between the superoxide radical and DMPO. This finding reveals the superoxide scavenging activity of the agent. Furthermore, bromocriptine inhibited the ESR signal of DMPO-OH in the Fenton system which was used as a hydroxyl radical generating system, without the iron chelation. The result shows that the agent can scavenge hydroxyl radical. The ESR signal of the stable free radical, diphenyl-p-picrylhydrazyl (DPPH) was reduced by the treatment of bromocriptine. Moreover, the drug inhibits the autoxidation of rat brain homogenates in vitro; 100 μM of it almost completely inhibits lipid peroxidation. These findings reveal the antioxidative or free radical scavenging effect of bromocriptine, and the effects may be beneficial to the treatment of Parkinson's disease.

2-27-17 DEPOLARIZATION OF HUMAN NEOCORTICAL NEURONS BY HISTAMINE: H_1 RECEPTOR ACTIVATION REDUCES A LEAKAGE POTASSIUM CURRENT

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Antihistamines exert sedative effects in humans, yet their locus of action in the brain is unknown. In order to better understand this phenomenon, the effects of histamine upon human cortical neurones were studied using intracellular recordings in brain slices maintained in vitro. Bath application of 50 μM histamine induced a depolarization which could be attributed to reduction of a background voltage-independent "leakage" potassium current. Depolarizing responses were blocked by the H_1 antagonist mepyramine, but not by the H_2 antagonist cimetidine nor the H_3 antagonist thioperamide. Depolarization of human cortical neurones by neuronal histamine acting at H_1 receptors will increase the likelihood that excitatory synaptic potentials will evoke an action potential. Moreover, by increasing whole-cell input resistance, H_1 receptor activation will make the cell more electrotonically compact, thereby altering its integrative properties. We hypothesize that this mechanism would allow histamine, acting at cortical H_1 receptors, to enhance behavioral arousal. During waking when histamine release is highest, blockade of H_1 receptors by systematically administered H_1 receptor antagonists would be sedating.

2-27-18 BOURNEVILLE'S DISEASE: FAMILY STUDY OF THE METABOLISM OF DEBRISOQUINE

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Bourneville's disease is a neurological disease that has a familial incidence and it is known that it is inherited in a dominant trait but the majority of cases appear to arise as fresh mutations.

We study a family from the southwestern of Spain with a sporadic case of Bourneville's disease. She is the last daughter of a no relative parents. She has mental retardation and seizures with a diagnostic cranial CT.

We have done a physical exam and a cranial CT to all family members, two parents and two daughters. A complete three generations pedigree was performed and disclosed normality in the mother's family and an uncle's father with mental retardation and seizures.

We have studied with Polimerase Chain Reaction and Reaction Fragment Length Polimerase techniques, the metabolism of debrisoquine in twelve members of the family. We found differences between the two parents families, although no conclusive results.

2-27-19 THE EFFECTS OF THIAMIN AND ITS PHOSPHATE ESTERS ON DOPAMINE RELEASE AND METABOLISM IN THE RAT STRIATUM

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The effects of thiamin and its phosphate esters on dopamine (DA) release and metabolism were examined in the rat striatum using in vivo microdialysis method. Intrastriatal administration of thiamin triphosphate (TTP) and thiamin pyrophosphate (TPP) induced a dose-dependent prolonged DA release (10^{-6}M-10^{-3}M), but thiamin monophosphate (TMP) and thiamin (T) did not show any change. TTP and TPP reduced the concentration of striatal dihydroxyphenylacetic acid and homovanillic acid. TTP-induced DA release was Ca^{2+}-dependent and abolished by the addition of TTX. ω-conotoxin, voltage-dependent calcium channel (VDCC) blocker, did not decreased the TTP-dependent DA release. Similar procedure revealed the DA release by ATP administration, which was also TTX-sensitive, Ca^{2+}-dependent and VDCC-independent. The results suggest that in contrast to TMP and T, TTP and TPP may play a specific role in nervous tissue, TTP inducing DA release by stimulation of ATP receptor.

2-27-20 SPINAL CORD EVOKED POTENTIALS IN ASSESSING CORD DYSFUNCTION FOLLOWING TRAUMA. EXPERIMENTAL OBSERVATIONS IN THE RAT.

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The possibility that spinal cord evoked potentials (SCEP) may have a prognostic value in assessing cord dysfunction following trauma was examined in a rat model. We used ibuprofen (a non-steroid anti-inflammatory drug) and dexamethasone (a synthetic gluco-corticoid); which are often used clinically to reduce the outcome of spinal cord injury (SCI) in clinical conditions, to examine whether they have a beneficial effect on SCEP and edema. The SCEP was recorded from epidural electrodes placed over right dorsal horn of T9 and T12 segments after stimulation of right tibial and sural nerves at ankle (n=10) in urethane anaesthetised rats (Wistar male 300-350 g). In 5 rats each either ibuprofen (10 mg/kg, i.p.) or dexamethasone (4 mg/kg, s.c.) was administered and an incision (2 mm deep and 5 mm long) was made in the right dorsal horn 30 min after the drug treatments. In untreated animals (n=5), SCI induced a long-lasting depression (mean 60 %) of the negative SCEP amplitude immediately at T9 recordings. This SCEP depression was markedly attenuated by ibuprofen whereas, dexamethasone had no effect. Five h after SCI, in untreated animals the traumatised segment showed a marked accumulation of water which was reduced by ibuprofen but not with dexamethasone. The results indicate that SCEP may have a prognostic value in assessing edema formation following SCI.

2-27-21 GRADED DOSE PHARMACOKINETICS AND COMPARATIVE BIOAVAILABILITY OF CARBAMAZEPINE

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As definitive guidelines are not available for initiation of carbamazepine(CBZ), the present study was aimed to evaluate the pharmacokinetics of CBZ during graded dose therapy. The present study was conducted in 34 epileptic patients in a double blind non-crossover design. Two formulations of CBZ were used in graded doses with weekly interval increments. Blood samples were collected at different time intervals for CBZ levels estimation by high performance liquid chromatography. At the end of first week, CBZ levels were 4.17 ± 2.08 and 4.47 ± 1.58 with formulations A and B respectively. The plasma levels estimated during and at the end of fourth week showed no significant variation between the two formulations. Area under the curve with formulation A was 60.88 ± 20.12 and with formulation B was 67.71 ± 26.67. Bioavailability of CBZ from both the formulations was found to be similar. The graded dose followed in the study was found to be suitable clinically and pharmacokinetically.

2-27-22 DIHYDROERGOKRYPTINE (DEK) IN THE DE NOVO PARKINSON'S DISEASE A DOUBLE-BLIND CROSS-OVER STUDY VERSUS BROMOCRIPTINE

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The aim of this study was to evaluate the efficacy and safety of DEK in the treatment of Parkinson's disease (PD) in a double-blind cross-over trial versus bromocriptine (BCR) in "de novo " patients. The subjects admitted to the study were 14 PD patients, (6M and 8F mean age 59.1 ± 11.1), belonging to the clinical stages II and III of Hoehn and Yahr. The patients were randomly assigned to two sequences of treatment for a total of 6 months. The patients treated with the DEK-BCR sequence first received DEK for 3 months (1st period) and then after a one week wash-out, BCR for further 3 months (2nd period). Patients of the BCR-DEK sequence received BCR for 3 months and then after a one week wash-out, DEK for further 3 months. DEK or BCR were given in a 4:1 ratio, according to a scheme of gradual increase providing a total daily dosage of 60 mg of DEK (15 mg of BCR) after 30 days until the end of the trial. The clinical assessment was made by the UPDRS (subitem II and III) at baseline and after every months. The antiparkinsonian effect of DEK overlapped that obtained with BCR with a maximum improvement in UPDRS score of 27%, observed during the DEK-BCR sequence. Side effects were observed in one patient during the DEK treatment (gastric pyrosis) and in 2 patients during the BCR treatment (nausea and sleepiness and nausea and vertigo, respectively).

2-27-23 INTRANASAL VERSUS INTRAVENOUS NEOSTIGMINE IN MYASTHENIA GRAVIS: ASSESSMENT BY COMPUTER ANALYSIS OF SACCADIC EYE MOVEMENTS.

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Intranasal (i.n.) neostigmine has been developed to obtain a quicker onset of action and a more adaptable dosage regimen than with oral neostigmine. The effect of this new neostigmine formulation in myasthenia gravis (MG) was studied by means of computer analysis of saccadic eye movements (SEM). Six MG patients were selected on the basis of a positive effect of Tensilon on hypometria of the first SEM. The effect of intravenous (i.v.) formulation (0.5 mg) was compared to 1,2,3,4 puffs of i.n. neostigmine (1 puff = 4.6 mg). The drug effect on SEM was monitored at intervals up to 2 hours. Administration of i.v. neostigmine produced a marked effect immediately after the injection and the benefit lasted over 1 hour. Following administration of i.n. neostigmine a marked effect was found for 2,3,4 puffs; the drug effect was evident within 3 min., peaked at 18-33 min. and lasted over 2 hours. Our data indicate the efficacy of the i.n. neostigmine formulation in MG as measured by means of quantitative analysis of SEM.

2-27-24 THE EXPRESSION OF NEUROTROPHINS IN HUMAN FETAL ASTROCYTES IN CULTURE.

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In the central nervous system, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and other neurotrophins are expressed in some neuronal cell populations. The present study was undertaken to investigate the capacity of glial cells to produce neurotrophic factors. Enriched populations of neurons and astrocytes were prepared from human fetal brain tissues. The purity of neurons and astrocytes was > 95% as assessed by immunostaining with MAP2 and glial fibrillary acidic protein. Total mRNA was extracted from cultures, reverse transcribed into cDNA, and neurotrophin-specific fragments were amplified using the polymerase chain reaction. Results showed that human fetal astrocytes constitutively express NGF and BDNF mRNA and release NGF into the medium (as shown by Western blot analysis of medium). These observations provide evidence that astrocytes actively support neuronal survival and differentiation. The impairment of astrocyte secretory activity may be relevant in the pathogenesis of neurodegenerative diseases associated with loss of neurotrophin-responsive neurons.

2-27-25 MIDKINE, A NEUROTROPHIC FACTOR, IS PRODUCED BY FETAL HUMAN ASTROCYTES IN CULTURE.

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Midkine (MK) is a member of a new family of heparin-binding growth factors, structurally unrelated to the FGF family. Previous studies have demonstrated that MK is expressed transiently in various tissues, including the CNS, during the mid-gestation period of mouse embryogenesis. To identify the precise cell types producing MK in the human CNS during development, astrocyte- and neuron-enriched culture preparations were prepared from human fetal brain tissues of 12-15 weeks gestation. Production of MK was identified by immunoblotting in the conditioned medium of astrocyte-enriched cultures but not in the medium of neuron-enriched cultures. The addition of recombinant human MK (10-100 ng/ml) in the serum-free culture medium resulted in a 3-fold increase in the number of surviving neurons. These results indicate that in the developing human CNS, MK is secreted by astrocytes and has potent trophic activity specific for CNS neurons.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-28-01 THE ROLE OF VIBRATORY AND SENSITIVE TESTS IN DIABETIC PERIPHERAL NEUROPATHY: A MULTICENTER STUDY ON 467 DIABETIC PATIENTS

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Specificity (SP), sensibility (SE) and diagnostic accuracy (AD) of biotesiometer (VPT), Diapson (IP) and Thermocross (TPT) were evaluated as regards clinico-elettrophysiological diagnosis (clinical evaluation of neuropathy's symptoms and inferior limbs orteo-tendon reflexes, measurement of motor conduction (VCM) and sensitive (VCS) speeds respectively to the external popliteal sciatic and the sural nerves). We studied 467 diabetic patients (coming from 6 national centres (PD, PG, MI, RM, FI, BO) aged between 51.3 ± 15 (M ± DS), 197 type 1 (D1) and 267 type 2 (D2), with a diabete duration of 14.6 ± 10 years and HaA1c of 8.20 ± 1.8%, not suffering from hepatosis, nefrosis, obliterative artheriopathy or other known causes of peripheral neuropathy and that were not following a specific therapy for the neuropathy. For the gold standard (presence of neuropathy) we considered the simoultaneous alteration of motor and sensitive conduction velocities in the two nerves. We obtained the following results:

Site	TPT (SE,	SP,	AD)	VPT (SE,	SP,	AD)	DP (SE,	SP,	AD)
		%			%			%	
Allux+	54	69	65	37	83	69	33	73	62
Malleolus	52	72	66	82	45	56	20	80	64

The VPT is connected with VOM, VCS, TF and TPT ($p < 0.001$). The TPT at the internal and esternal malleolus is connected with VPT, VCS and TF $p < 0.001$, with VOM $p < 0.02$. VPT-TPT, TF-related are connected with age and duration of the disease $p < 0.0001$; VOM is connected with age $p < 0.007$ but not with disease's duration, VCS is connected both with disease and duration's age $p < 0.007$.

2-28-02 ELECTROPHYSIOLOGICAL ASSESSMENT OF LOWER URINARY TRACT IN CAUDA/CONUS SYNDROME.

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To investigate the visceral and somatic nerves 15 patients with cauda-conus syndrome were studied by recording the bulbocavernosus reflex (BCR) and cerebral potentials (CEP) evoked by stimulation of visceral and somatic nerves of lower urinary tract. Cystometry was also recorded.

The CEPs by stimulation of pelvic nerves at vesico-urethral junction and cystometry were abnormal in all patients. Out of 15 patients, CEP following the stimulation of pudendal nerve at glans level were abnormal in 14. BCR to pelvic and pudendal nerve stimulation was either absent or prolonged in latency in 11 cases. CEP by posterior tibial stimulation were abnormal in only 10 cases, uni-or bilaterally.

These three parameters (BCR, CEP and cystometry) are also strongly correlated with the clinical severity of the syndrome. The most predictive ones are the CEPs and BCR to visceral nerve stimulation and cystometry.

2-28-03 SEASONAL GUILLAIN-BARRÉ SYNDROME IN NORTH CHINA: A STUDY OF CLINICO-ELECTROPHYSIOLOGY IN 44 CASES

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The clinical and magnetic stimulation motor evoked potenials (MEP) study was made in 44 patients in Shijiazhuang city from July to September, 1991. Age from 5 to 63 (mean 19.5) including 18 cases below 14 (mean 5.4) years old. Male 24 and female 20. MEP were tested on the 2nd to the 54th day after onset and were sequentially done 3 to 12 (mean 8) times. The latencies and amplitudes from C7, Erb's point and elbow to hypothenar muscle and L4 and popliteal fossa to anterior tibial muscle. Age matched 70 subjects for control. We found 35 cases (79.5%) with 50 to 396% prolonged latency more than 2 times or 2 sites in which 23 pts. with recovery of low amplitude within 6 weeks. Three (6.8%) with one time prolonged latency (56 - 404%) and one with mild prolonged latency and very low amplitude which recovered to normal in 4 weeks, two with 30 - 49% prolonged latency and ongoing reduced amplitude in the 14th and 21st day after onset. Two with normal latency very much reduced amplitude, one with no response at all in 6 times measurement.

Three (6.8%) cases in our group, showed neurophysiological evidence of possibly predominant axonal changes.

2-28-04 THE ROLE OF SENSORY COMPLAINTS IN DIAGNOSING DIABETIC POLYNEUROPATHY.

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Sensory disturbances can be the first signs of diabetic polyneuropathy. These complaints may vary from sensory loss to spontaneous pain in the extremities. To determine the role of different sensory complaints in the diagnosis of diabetic polyneuropathy, 68 diabetic patients (37 insulin dependent and 31 non-insulin dependent) being consecutively referred because of suspected neuropathy were investigated. Their mean age ± SD was 51.7 ± 8.5 years and mean duration of diabetes 21.3 ± 11.2 years. Sensory complaints were quantified using a detailed questionnaire. The results were compared with the results of the clinical and neurophysiological examinations that were quantified with a previously described scoring system. In all patients both clinical and neurophysiological examination confirmed the diagnosis polyneuropathy. Only the scores of the clinical examination were significantly correlated with the scores of the sensory complaints ($r=0.31$, $p<0.01$). Using a factor analysis a cluster of complaints about sensory alteration (numbness and paraesthesias) could be divided from a cluster of complaints about pain (alpha coefficients 0.88 and 0.86 respectively). The scores of clinical and neurophysiological examinations were only significantly correlated with the cluster sensory alteration ($r=0.38$, $p<0.002$; $r=0.37$, $p<0.02$ respectively). These results implicate that compared with complaints of pain,complaints of numbness and paraesthesias in hands and feet are more important in diagnosing diabetic polyneuropathy and in assessing the severity of the disease.

2-28-05 INTRAVENOUS IMMUNOGLOBULIN INFUSION IN MULTIFOCAL DEMYELINATING MOTOR NEUROPATHY

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We reported a case with multifocal demyelinating motor neuropathy (MMN) presentating as gradual development of asymmetric weakness without sensory involvement. Electrophysiological studies showed mainly conduction block with normal or slightly slow nerve conduction velocity (NCV). CSF protein and serum protein electrophresis were normal but serum IgM anti-GM1 ganglioside antibody were elevated. The patient had poor responses to steroid, plasmaphresis and chemotherapy with cyclophosphamide, but significant improvements were noted after intravenous immunoglobulin infusion (IVIG). MMN is a potential treatable condition clinically mimicing a motor neuron disease and IVIG may be effective where treatment with steroid, plasmaphresis and cyclophosphamide has failed.

2-28-06 **THE EFFECT OF BEDREST FOR ACUTE, SUBACUTE AND CHRONIC LUMBAR RADICULAR SYNDROME**

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We started the study December 1992 to investigate the effect of bedrest in patients with a radicularsyndrome caused by a proven disc rupture L4/L5 or L5/S1 by MRI-scan of the lumbar region. We compare 3 groups depending on the duration of complaints: acute(less than 1 month), subacute(between 1 and 3 months) and chronic(longer than 3 months). The bedrest is strictly and takes 10 days. Patients are admitted in hospital. Each group contains 20 patients. After the bedrest (10 days) the MRI scan will be repeated and compared with the first MRI-scan. The effect of the bedrest will be measured by comparing the neurological physical examination and a questionnaire filled in by the patient before and after the bedrest. Possibel changes of the MRI-scan abnormalities will be correlated with the findings of the physical examination and the patient questionnaire. We assume that patients with chronic complaints will have less benefit of bedrest therapy. The study will be completed before next September.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-28-07 GUILLAIN-BARRÉ SYNDROME: A STUDY OF CLINICO-PATHOLOGY OF SURAL NERVE BIOPSY IN 30 CASES

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The pathological observations of sural nerve biopsy in 30 cases based on the recent 8 years' clinical research of 90 cases studied. Male 21, female 9. Ages of onset 7 - 68 (average 34). They were sporadic cases. The induction factors including: flu in 18 cases (60%), diarrhea 2, pulling tooth, delivery, vaccination 1 each, there was 1 case associated with lymphoma and uncertain 6. Onset acute 12 cases, subacute 6, chronic 12. Clinical features: limb weakness 25 cases, variant forms 5 (multiple cranial paralytic type 2, pan dysautonomia 1, Fisher syndrome, 1). Sensory disturbance 17 cases. The tendon reflex depressed or lost in all cases. Lab data: Electrophysiologic showed neurogenic lesions in all cases; elevation of CSF protein (> 50 mg%) 24. Oligoclonal bands positive in 13 (52%); elevation of IgG synthesis in 16 cases (88.9%). Neuropathological observation: mild to moderate reduction in the number of myelinated fibers, primary segmental demyelination in all cases, 1/3 of them had distal axonal degeneration; charonic onion bulb formation 10 cases. Electronmicroscopy showed variant small vessels permeability changes and sporadic monocytes in all cases. Treatment and prognosis: essentially cured 5 cases, much improved 18, a little improved 5, unclear 2.

2-28-08 CONDUCTION BLOCK FOLLOWING IN VITRO EXPOSURE TO ANTIGANGLIOSIDE ANTIBODIES OBTAINED FROM PATIENTS WITH INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY.

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We studied the effects of serum containing antiganglioside antibodies upon nerve conduction. The antibody-positive sera from 13 patients with inflammatory demyelinating polyradiculoneuropathy (IDP) were tested. The control consisted of the antibody-negative sera from 12 patients with IDP. The serum of each patient was applied in vitro to a restricted segment of a rat sciatic nerve, and the monophasic compound nerve action potentials of myelinated and unmyelinated fibers were recorded. Application of antibody-positive sera from 4 patients with IDP partially blocked myelinated fiber conduction at the segment; unmyelinated fiber conduction remained unchanged. The antibody-negative sera exerted no effects upon either myelinated or unmyelinated nerve conduction. Some antiganglioside antibodies may block conduction in myelinated nerve fibers and thereby play a role in the pathogenesis of IDP.

2-28-09 CLINICAL, ELECTROMYOGRAPHICAL AND ELECTRONEUROGRAPHICAL CORRELATIONS IN POLYNEUROPATHIES

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The author has carried out clinical, electromyographical and electroneurographical studies over 3000 patients with polyneuropathies. By correlating the clinical data with the EMG tracings and with the values of neuromuscular excitability and conductibility he noted that the concordance of these factors is not higher than 35 - 40%. In the rest, the correlation of data has evidenced 3 types of discordances: 1) electroclinical discordances (poor or no clinical symptoms while the EMG and the ENG disturbances are more or less evident); 2) discordance between discrete EMG disturbances or even interferential tracings, while the ENG parameters show signigicant alterations; 3) discordance between the data of excitability and of conductibility, when the alterations of the two functional parameters do not display a parallel evolution; in this category of discordances the excitability disturbances are higher, especially of sensitive fibers, in the lower limbs and at the distal points of stimulation.

2-28-10 SUBCLINICAL BERIBERI POLYNEUROPATHY IN SURABAYA, INDONESIA.

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Of the apparently healthy subjects in our study, 38.5% appeared to have subclinical beriberi polyneuropathy (PNP). Subjects in the low income group had a greater risk of developing beriberi PNP than those from the middle and high income groups. They had all low blood thiamine levels and a low thiamine intake.

Tingling sensations in the distal portion of the extremities, easy fatigability with slightly paretic dorsiflexion of the feet or great toes, slight disturbances of touch, pain, and temperature senses, especially in the distal portions of the legs and depression of the ankle jerks were the most prevalent neurological symptoms and signs of subclinical beriberi PNP.

Out of all the neurophysiological evaluations assessed, reduced distal amplitudes of peroneal nerve and H-reflex, as well as denervation activity in electromyography were the most frequently found abnormalities, followed by reduced amplitude of the proximal latency of the peroneal motor nerve and, much less frequently, of the sural nerve action potentials.

2-28-11 ESTABLISHMENT, EXPANSION AND IMMUNOCYTOCHEMICAL STUDIES OF HUMAN SCHWANN CELLS CULTURES TREATED WITH CHOLERA TOXIN.

Bianchini D, Anfosso S, Schenone A, Cingolani A, Zicca A, Cadoni A, Mancardi GL (Genova)

We established human Schwann cell (SC) cultures from patients with various PNS diseases using a new technique recently described (Rutkowski et al 1992). Sural nerve fascicles were incubated at least for one week with medium containing choler toxin, and then enzimatically dissociated and cultured with different mitogens. The amount of cell growth and the expression of myelin and non-myelin forming SC antigens, were analyzed and compared with the results obtained with the ordinary culture techniques. The following antibodies were utilized: anti S-100, anti vimentin, anti DR, anti GFAP, anti N-CAM, anti NGF-receptor, anti MBP, anti PO, Leu 7, Ki 67. SC proliferation resulted markedly increased in cultures treated with cholera toxin, allowing their expansion and repeated passaging. HAM F-10 medium was demonstrated to be effective in preventing fibroblast overgrowth, also in later phases of culture. Our preliminary data concerning SC antigenic pattern failed to show relevant modifications induced by the use of cholera toxin.

2-28-12 AMELIORATION OF EXPERIMENTAL DIABETIC NEUROPATHY BY 3-ISOBUTYRYL-2-ISOPROPYLPYRAZOLO [1,5-A] PYRIDINE.

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It has been considered that metabolic abnormalities and deranged vascular factors such as atherosclerosis and ischemia cause neuropathy in diabetes mellitus. Since 3-isobutyryl-2-isopropylpyrazolo [1,5-a] pyridine (ibudilast) has potential effects to ameliorate atherosclerosis and to dilate vascular smooth muscle, we tested the therapeutic effects of ibudilast on motor and sensory nerve conduction velocities (MNCV and SNCV) and endoneurial nerve blood flow (NBF) in sciatic nerves of experimental diabetic rats induced by streptozotocin (STZ).

Control rats (group 1), ibudilast-treated rats (group 2) and STZ-induced diabetic rats (group 3) were studied for 8 weeks (n=7 each). Ibudilast was given orally (10mg/b.w.kg/day). NBF was measured by hydrogen clearance method. In group 3 MNCV, SNCV and NBF were significantly reduced from those of group 1 at the end of experiments. But group 2 demonstrated normalized MNCV, SNCV and NBF. Ibudilast may modulate vascular factors in diabetic neuropathy.

2-28-13 A NEW CLINICAL SCALE OF PATIENTS WITH FAMILIAL AMILOIDOTIC POLYNEWLOPATHY (FAP) AND PROSPECTIVE STUDY

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In addition to polyneuropathy, patients with FAP type I show various clinical symptoms, such as autonomic disturbance, muscle weakness, and damage to several specific organs. The age of onset and the starting time of clinical symptoms are variable in each FAP patient. To know clearly the clinacal features of FAP patients, we classified characteristic symptoms of 20 FAP patients (male; 13, female; 7) into four types: sensory disturbance, motor disturbance, autonomic disorder, and visceral organ damage. Nine showed sensory type, 2, autonomic-sensory type, 4, autonomic type, 1, organ type, 1, sensori-organ type, 1, motor type, and 1, all disturbed type, respectively. To compare the severity of clinical symptoms and evaluate the prognosis of each FAP patient, we scored the characteristic clinical signs of the 4 outstanding symptoms and calculated the total points. By using this scale, the stages and the prognosis of FAP patients could be evaluated objectively and quantitatively. Since the highest score among the 4 symptoms tends to be the life-threatning factor in each FAP patient, this method may be helpful in treating FAP patients.

2-28-14 BINDING OF MUTANT TRANSTHYRETIN (VAL30-MET) WITH LOW DENSITY LIPOPROTEIN (LDL) AND HIGH DENSITY LIPOPROTEIN (HDL): A NOVEL FUNCTION OF VARIANT TRANSTHYRETIN

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Transthyretin (TTR) was identified in high density lipoprotein (HDL) as well as low density lipoprotein (LDL) of patients with familial amyloidotic polyneuropathy (FAP). Analysis by enzyme linked immunoreactive assay (ELISA) for these lipoproteins revealed that 0.01-0.02% of plasma TTR level was recognized in the LDL from FAP patients' plasma extracted by vertical-rotor centrifugation. On the contrary, trace amount of TTR was detected in this fraction from that of control subjects. 0.2-0.4% and 0.1-0.2% of plasma TTR level was confirmed in the HDL from FAP patients and control subjects, respectively, extracted by apolipoprotein AI and AII affinity chromatography. A immunochemical staining of electrofocusing of the HDL revealed that TTR was confirmed in both LDL and HDL from FAP patients. These results suggest that the binding of TTR to the lipoproteins may play an important role in the amyloid formation of FAP. Precise lipid metabolism should be studied further in FAP patients.

2-28-15 CHANGED AFFINITY OF APOLIPOPROTEIN AII TO HIGH DENSITY LIPOPROTEIN IN PATIENTS WITH FAMILIAL AMYLOIDOTIC POLYNEUROPATHY (FAP)

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Patients with familial amyloidotic polyneuropathy (FAP) showed extremely low serum apolipoprotein (Apo) AII levels while serum levels of AI, B, CII, CIII, and E were all within normal ranges. To know the reason of this phenomenon, we investigated the ratio of this protein contained in the high density lipoprotein (HDL) extracted from the serum of FAP patients by ultracentrifugation. The Apo AII/AI ratio in extracted HDL was much lower in asymptomatic carriers of FAP as well as FAP patients than that in control subjects. Electrophoresis of HDL extracted by agarose gel revealed that HDL from asymptomatic carriers of FAP as well as FAP patients increased negative charge.

Although urinary secretion of Apo AII was increased in FAP patients, there was little correlation between serum and urinary levels. Moreover, in patients with chronic renal failure who had more protein uria than FAP patients examined in this study did not decreased their plasma Apo AII/AI ratio. These results suggest that changed affinity of Apo AII to HDL may cause the decreased Apo AII level in the plasma and as the result of this phenomemon, increased urinary secretion of this protein occur in FAP patients.

2-28-16 PREDICTING FACTORS FOR RESPIRATORY FAILURE AND OUTCOME IN GUILLAIN-BARRE SYNDROME (GBS) - AN ANALYSIS OF 80 PATIENTS

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We studied eighty patients with GBS who were admitted at Chang Gung Memorial Hospital between May 1977 and Nov. 1989. Age ranged 1 to 73 years and male to female ratio of 3:1. Eighteen patients (22.5%), of whom one patient expired, had respiratory failure requiring assisted ventilator. Seventeen patients (21.3%) had motor sequelae.

We correlated respiratory failure and outcome with the following parameters: 1). History: age, antecedent events, and evolving period from onset to nadir; 2). Clinical features: bulbar muscle involvement and autonomic dysfunction; 3). CSF profile: WBC count and protein amount; 4). Electrophysiological studies: motor nerve conduction, sensory nerve conduction, F wave and EMG; and 5). Steroid therapy. Patient with bulbar muscle involvement and/or autonomic dysfunction are prone to develop respiratory failure. Severe compound motor action potential decrement, diffuse active denervation in EMG and respiratory failure are significant predictors to motor sequelae.

This study suggests that cardiorespiratory monitoring and aggressive therapy such as plasmapheresis are mandatory to the risk patient subgroup.

2-28-17 MARFAN SYNDROME AND TOMACULOUS NEUROPATHY

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Marfan syndrome is a connective tissue disease affecting multiple body systems. Complications secondary to arterial disease are the only common neurological sequels. We report a patient with Marfan syndrome and brachial plexopathy in whom investigations revealed tomaculous neuropathy.

A 19 year old student developed brief pain followed by weakness affecting right shoulder muscles after turning in bed. Two years previously he had sustained an ulnar neuropathy resolving over a week. Examination revealed stigmata of Marfan syndrome with high arched palate, joint hyperextensibility, pectus excavatum and span greater than height. Motor and sensory nerve conduction velocities were slowed, particularly over potential entrapment sites. Reduced interference pattern without spontaneous activity was demonstrated on electromyography. Sural nerve biopsy revealed numerous tomacula, loss of large myelinated axons and remyelination. Gradual improvement of strength occurred over 4 months.

Several reports describe plexopathy in another connective tissue disease, Ehlers-Danlos syndrome, purported to represent stretch injury caused by ligamentous laxity. The demonstration of underlying tomaculous neuropathy, implying dysmyelination in the present case and in a reported case with Ehlers-Danlos syndrome, suggests a more fundamental abnormality and further studies of the peripheral nervous system in connective tissue disease are indicated.

2-28-18 PROXIMAL CONDUCTION BLOCK STUDIES IN DIFFERENT INFLAMMATORY NEUROPATHIES

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Proximal conduction block (CB) studies were performed in 25 patients with different inflammatory neuropathies. A high-voltage stimulator was used for stimulation of the ulnar nerve at wrist, elbow, axilla, Erb`s point and C7. Proximal CB or temporal dispersion (TD) between Erb´s and axilla or C7 and Erb`s was the earliest sign of demyelination in 5 of 9 patients with Guillain-Barré syndrome, in 3 patients with tick-bite induced radiculopathies and in 2 patients with multifocal motor neuropathy. 8 of 9 patients with chronic inflammatory demyelinating neuropathy and 2 patients with vasculitis showed CB or TD, predominantly affecting the segments between wrist and elbow or C7 and Erb`s. Follow-up investigations revealed rapid disappearing of CB in responders to immunoglobulin therapy. Proximal conduction block studies improve the diagnosis of focal demyelination. They are of special importance in patients with normal results in routine tests of distal nerve segments.

2-28-19 PREVENTION AND SUPPRESSION OF EXPERIMENTAL ALLERGIC NEURITIS WITH ANTI-INTERLEUKIN-2 RECEPTOR ANTIBODIES

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Prevention and suppression of experimental allergic neuritis (EAN) by intraperitoneal administration of anti-interleukin-2 receptor antibodies were investigated in 32 Lewis rats. The mean clinical score at day 14, the height of the disease, in the prevention and suppression groups were significantly lower than that in untreated EAN rats. When changes in lymphocyte subsets in peripheral blood were compared with those in adjuvant controls, CD4+interleukin-2 receptor (IL-2R)+ and CD8+IL-2R+ cells in untreated EAN rats decreased significantly on day 7 and increased significantly on day 14 and 21. However, in the prevention group, CD4+IL-2R+ cells decreased significantly on day 14 and increased significantly on day 21. In the suppression group, CD4+IL-2R+ cells decreased significantly on day 14 and 21.

It was suggested that the prevention and the suppression of EAN might be accomplished by the manipulation of effector phase of the immune-mediated disease process.

2-28-20 GROWTH FACTORS FOR ADULT MOUSE SCHWANN CELLS IN CULTURE.

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Growth factors responsible for Schwann cell proliferation have a crucial role for the development and regeneration of the peripheral nervous system. In neonatal rat Schwann cell cultures, platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF) and tranforming growth factors-β (TGFs-β) are known to stimulate DNA synthesis. In these, mitogenic stimulations by PDGF and bFGF require the presence of forskolin to elevate intracellular cAMP. However, their reactivities to Schwann cells of different ages and species are largely unknown. In this paper, we studied mitogenic effects of the growth factors to adult mouse Schwann cells. Short- and long-term cultures of Schwann cells prepared from adult mouse dorsal root ganglia and peripheral nerves were incubated with the factors and bromodeoxyuridine (BrdU). Immunofluorescence for S-100 and BrdU was performed and % double-positive Schwann cells were counted. In serum-containing media, PDGF-BB, bFGF, TGF-β1 and β2 were all mitogenic for adult mouse Schwann cells. In serum-free media, PDGF-BB and bFGF were weakly mitogenic, whereas TGF-β1 and β2 were not. The presence of forskolin suppressed the mitogenic activity of these factors. These results show that adult mouse Schwann cells respond to the mitogenic stimulations by the growth factors in a different manner.

2-28-21 SARCOID POLYNEUROPATHY WITH GRANULOMA IN PERIPHERAL NERVE : HISTOLOGICAL STUDY OF TWO CASES.

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There have been few reports showing evidence of granuloma in peripheral nerve of patients with sarcoid polyneuropathy. We report two cases of sarcoid polyneuropathy with granuloma in peripheral nerve. The first case was a 53-year-old female and the second, a 78-year-old female. Both cases were diagnosed by histological examination of muscle and nerve biopsies. Transverse sections of sural nerve showed granulomatous tissue in the epineurium invading the wall of arterioles in both cases. Marked basal lamina layering in capillaries of sural nerve and peroneal muscle was observed in the first case by ultrastructural study. Pathogenesis of basal lamina layering will be discussed.

2-28-22 NATURAL KILLER CELL ACTIVITY AND SERUM INTERLEUKIN-2 LEVELS IN PATIENTS WITH GUILLAIN-BARRÉ SYNDROME

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To clarify the immunological mechanism of Guillain-Barré syndrome (GBS), natural killer (NK) cell activity, as defined by the lysis of ^{51}Cr-labelled K-562 cells, was measured in 16 patients within 14 days after the onset. Serum interleukin-2 (IL-2) levels, IL-2 production by T-lymphocytes and DNA synthesis of IL-2 stimulated T-lymphocytes were also serially measured in two patients. Steroids were not given at the time of measurements in all patients.

Results: NK cell activity in GBS was 33.9 ±13.6%, which was significantly reduced compared to 16 age-matched normal controls (56.9 ±12.2%). NK cell activity tended to become lower as the clinical disability score became higher. In 6 patients, NK cell activity remeasured one month afer the onset was 47.2±4.6%, which was significantly higher than the value in the acute stage (28.2±14.8%). Serum IL-2 levels measured by RIA did not increase (less than 0.8 U/ml) during the illness in these patients. IL-2 production and DNA synthesis were decreased immediately after the onset. However, these functions returned to normal soon after plasma exchange and remained within the normal range thereafter.

Conclusion: Our results suggest a defect in the specific immune mechanism (NK cells) in patients with GBS. In contrast to previous reports, T-lymphocytes were not activated, but rather were depressed in the acute stage.

2-28-23 GUILLAIN-BARRÉ SYNDROME AND CAMPYLOBACTER JEJUNI INFECTION: A STUDY ON THE ETIOLOGICAL CHARACTER OF GUILLAIN-BARRÉ SYNDROME IN CHINA

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The previous study of some aspects of 7056 Guillain-Barré syndrome (GBS) in China found some things different from the aspects of GBS in western countries. Those were younger, seasonal and cluster incidents. It lead us to consider different preceding infection occurred. Also, the campylobacter jejuni (CJ) infection had the same epidemiology in China. The relation with the GBS and CJ infection was studied. Stool culture for CJ with the method of Skirrow and serum specific antibodies (IgM IgA IgG) to CJ using a solid phase enzyme linked immunosorbent assay were performed in 17 cases of GBS, 17 other neurological disease and 33 normal controls matched with age and season. The results revealed as that: the incidence of CJ infection in GBS was much frequent than in the other two controls.

Younger cases and those onset in the phase between summer and autumn were more frequent than those onset in the elder and other seasons. These results indicate that CJ infection may be the most important preceding pathogen.

2-28-24 ATYPICAL FINDINGS IN TWO CASES OF MULTIFOCAL MOTOR NEUROPATHY

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The multifocal motor neuropathy (MMN) is a rare peripheral disorders characterized by persistent conduction blocks confined to motor axons at sites not prone to compression. Anti-GM1 ganglioside IgM antibodies at high titres are found in patients with MMN; in some of this patients the therapeutic reduction by immunosoppression of anti-GM1 antibody levels is associated with clinical improvement. This fact suggests a possible pathogenetic role of these antibodies in the MMN.

We describe two atypical cases of MMN simulating a motor neuron disease. In the first patient the symptoms were slowly progressive with bulbar muscle impairment, generalized weakness, muscular atrophy with cramps and fasciculations. Marked apraxia of the superior facial district with an inability to perform voluntary saccades and eye closure and speech impairment with reduction of verbal fluency were also evident. Multifocal conduction blocks resulted from EMG examination and high titres of anti-GM1 antibody were present in serum. In the second patient the clinical symptoms started with a progressive paresis of the left brachial plexus followed by controlateral plexus involvement and successive weakness of neck muscles. Multiple conduction motor blocks were evident in the arms; the legs were relatively spared, with only one block in the left peroneal nerve. Anti-GM1 antibodies were absent.

The spectrum of the clinical and laboratoristic characteristics of the MMN is quite wide. A precise definition of different subgroups in this syndrome is needed to clarify the pathogenetic mechanism and to develop specific therapeutic approaches.

2-28-25 IS THERE A SPORADIC FORM OF TOMACULOUS NEUROPATHY?

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A patient with recurrent peripheral nerve palsies is reported. Histopathologically, extensive irregularities of the myelin sheats with numerous tomaculous swellings were found. Electrodiagnostically, a clear decrease of nerve conduction velocity was seen in affected and unaffected nerves.
All of patient's relatives were investigated and showed entirely normal clinical and electrodiagnostical findings. Laboratory data excluded an aquired form of neuropathy; therefore, we rather believe in a new mutation.

2-28-26 CORNEAL SENSITIVITY AS A QUANTITATIVE INDICATOR OF PERIPHERAL SENSORY NEUROPATHY OF DIABETES.

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Cornea has a 30-600 times thicker innervation of sensory nerve than skin. Nerve fibers are A-delta fibers. We assessed the usefulness of corneal sensitivity (CS) as a quantitative indicator of sensory neuropathy of diabetes. CS was measured as follows by using a Cochet and Bonnet aesthesiometer: the length of the filament of the aesthesiometer was decreased from 60 mm by each 10 mm until a subject could perceive the exact number of attachment of the filament to the cornea. Determination was conducted at 6 portions of both eyes in total and the values were averaged to obtain CS. CS was measured on 167 patients with non-insulin dependent diabetes (mean age 50.1 yr.). The decrease in CS correlated significantly with the degree of diabetic complications evaluated by sensory symptoms, heart rate variability (CVR-R), motor and sensory nerve conduction velocities in four extremities, and diabetic retinopathy. CS was also decreased significantly in patients with insulin therapy compared with patients with diet or sulfonylurea therapy.

These data suggest that CS is useful as a quantitative indicator of peripheral sensory neuropathy of diabetes.

2-28-27 IMMUNOCYTOCHEMICAL ANALYSIS OF THE INTERCELLULAR ADHESION *MOLECULES IN THE VASCULITIC NEUROPATHY.*

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An important role of cell adhesion molecules (CAM) in mediating interactions between circulating leukocytes and non-haemopoetic cells at inflammatory sites has been suggested in vitro. We studied by immunocytochemistry the expression of intercellular adhesion molecule (ICAM-1),endothelial leukocyte adhesion molecule (ELAM-1), and vascular cell adhesion molecule (VCAM-1) in sural nerve biopsies from patients with *axonal neuropathy (AN) associated or not with vasa nervorum* vasculitis (VNV). Lymphocyte subsets and expression of CAM ligands (LFA-1,MAC-1,CD15,VLA-4) on inflammatory cells were evaluated in parallel. In all the cases with VNV examined, ICAM-1 was intensely expressed on the endothelial cells and on vascular smooth muscle cells. One case showed a regional induction of ELAM-1 and VCAM-1 expression on endothelial cells. In AN with no evidence of VNV, ICAM-1 expression was restricted to the endothelium but was stronger than in the controls. Our findings suggest that these CAM may be involved in *the pathogenesis of vasculitic neuropathy.* The detection of increased ICAM-1 expression in AN without VNV might contribute to reveal an early inflammatory process.

2-28-28 SCHWANN CELL PROLIFERATION IS PROGRESSIVELY IMPAIRED IN VITRO IN MURINE GLOBOID CELL LEUKODYSTROPHY (TWITCHER).

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Death or necrosis of Schwann cells has been infrequently demonstrated in neuropathies. We investigated Schwann cell function in the twitcher (twi/twi), a murine model of globoid cell leukodystrophy, using cellular proliferative activity as an indicator. Cellular proliferation was evaluated by thymidine autoradiography both in vivo and in vitro. In in vivo studies, Schwann cell proliferation persisted in the twi/twi, whereas it decreased rapidly in carrier (twi/+) or normal (+/+) nerves between postnatal days (P) 10 and 20. In contrast, proliferative capacity in vitro of twi/twi Schwann cells was progressively impaired. Reflecting in vivo activation of Schwann cells secondary to demyelination, labeling indices for the first 24-h cultures were transiently higher in Schwann cells from the twi/twi nerves, but were decelerated thereafter and failed to attain the values of twi/+ or +/+ Schwann cells during an 8 day period in culture. We conclude that in vitro kinetic studies would provide us the methodology to evaluate the Schwann cell dysfunction, which may contribute to the understanding of pathogenesis of various neuropathies.

2-28-29 ANIMAL MODEL OF ISCHEMIC NEUROPATHY WITH PROLIFERATIVE CHANGES OF NERVE MICROVESSEL WALL.

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In order to produce a model of ischemic neuropathy with neural microvascular alterations, sodium laurate (SL) (0.3 mg/0.1 ml saline) was injected into one femoral artery at the midthigh level and saline into the contralateral artery in Sprague-Dawley rats aged 11 weeks. The laurate-injected (LI) leg showed paresis during the experimental period. On day 1-7, various stages of Wallerian degeneration and acute microvascular changes were found and at month 1, regenerating myelinated nerve fibers (MNFs) were found at the central or total fascicular area mainly in the distal tibial nerve. Morphometric analyses suggested that MNFs other than regenerating fibers are atrophic ones. The number of nuclei of endothelial cells and the percent of closed epineurial microvessels were significantly larger on LI sides and inversely associated with the diameter of MNFs. At month 7, the attenuation of MNFs was more prominent and microvascular alterations were persistently observed. These findings resemble those of chronic ischemic neuropathy, suggesting that this model might provide useful clues for clarifying the pathogenesis and evolution of chronic ischemic neuropathy including diabetic neuropathy.

2-28-30 HLA ANTIGENS IN NEUROPATHY ASSOCIATED WITH ANTI-MAG IgM MONOCLONAL GAMMOPATHIES OF UNDETERMINED SIGNIFICANCE (MGUS)

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In order to investigate the role of genetic factors, we performed HLA typing in 25 patients suffering from neuropathy associated with anti-MAG IgM MGUS. Typing for the HLA-A and B was performed with the standard NIH lymphocytotoxicity test and typing HLA-DR and DQ (class II antigens) with the two-color fluorescence test using sets of allo-antisera and monoclonal antibodies. Controls consisted of 4023 healthy bone marrow donors. Differences between groups were tested with a chi-square test, and relative risks were calculated using Haldane's formula.

When the 25 anti-MAG IgM MGUS patients were compared to controls, significantly different frequencies were found for the HLA antigens B15 ($p = 0.003$), B21 ($p = 0.008$), and DR2 ($p = 0.019$). Relative risks were 3.39 (B15), 3.46 (B21) and 2.54 (DR2). However, further studies on larger series are needed to confirm an association between anti-MAG IgM neuropathy and genetic factors, since when the p values are corrected for the number of antigens tested, the results are no longer significant.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-28-31 TREATMENT OF RESTLESS LEGS SYNDROME WITH SMALL DOSES OF OPIATES.

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Fifty patients with clinical diagnosis of restless legs syndrome have been studied over a mean period of 2.3 years. One patient is lost to follow up. In the remaining forty-nine, thirty-nine have been treated with Codeine Phosphate (8-90 mg. per day). Of twenty-nine who initially responded nineteen continue to benefit from Codeine Phosphate. In the ten non-responders three require Methadone for severe symptoms, two are on a Benzodiazepine, one on Levo-Dopa and four do not require therapy.

Two of the ten patients who initially responded to Codeine Phosphate but who are now not taking the drug are on Methadone (7.5-15 mg. per day) for severe symptoms, three are on a Benzodiazepine, two have symptoms too mild to require treatment, one has died, one is reluctant to take Codeine and one is on Warfarin contraindicating its use.

This uncontrolled study of a large number of patients with restless legs syndrome suggests that Codeine Phosphate is a useful therapy for patients with mild to moderate symptoms and in patients with severe disabling symptoms Methadone is of benefit.

2-31-05 FOLLOW UP STUDY OF MINAMATA DISEASE

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Discharge of methylmercury, the cause of Minamata Disease (MD), ended in 1966. The purpose of this study is to reveal whether the clinical features of MD are still the same or not after the stoppage of the pollution. Series of 122 patients, who had had the neurological examination three times or more, and whose observation period was longer than three years, were studied. These patients were subdivided to four groups; 30 patients of officially diagnosed as definite, possible or probable MD, 62 patients of officially diagnosed as non-MD, and 30 patients whose diagnosis were postponed. Of 62 non-MD patients, 30 patients were diagnosed as the category non-MD with sensory disturbances of unknown etiology.

Factor analysis of MD was applied in the results of neurological examinations. The changes of factor scores between the neurological examinations, taken at the different times, were varied from constant to progressive or improved in each patient. The specific pattern of the change of the factor score was not found through the observation period, and also delayed onset or delayed worsening of the clinical features was not found. There were no significant differences in the chronological courses of the clinical features between these four groups.

2-31-08 PANIC ATTACKS LEADING TO FATAL ACCIDENTS IN SCUBA DIVERS

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According to the Diagnostic and Statistical Manual for Mental Disorders (DSM III) panic attacks (P.A.) are one aspect of free floating general anxiety. They are characterized by sudden onset, course and typical vegetative symptoms. Recurrent P.A. are defined as panic disorder. Fatal accidents of scuba divers are caused in most cases by pulmonary baro traumata, which at least are initiated in most cases by P.A. Since panic attacks can be provoked by application of 10 mg/kg coffein, 20 mg Yohimbin or parenteral dosage of Lactat or Flumazinil, etc. We investigated divers, who survived P.A. occurring under water. Most scuba divers are well educated, need certificates and underwent medical investigations before achieving the qualifying examination. One part of these medical investigations has to be P.A. provocation tests.

2-31-09 IN VITRO NEURONAL AND GLIAL PRODUCTION BY PRECURSOR CELLS DERIVED FROM ADULT HUMAN FOREBRAIN

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Neurogenesis has been demonstrated in forebrain cultures derived from a variety of adult infraprimates. This suggests the existence of residual neuronal and glial precursor cells in the adult vertebrate brain. We sought to determine whether the adult human brain might harbor such progenitors, by culturing temporal lobe dissociates under conditions permissive for neurogenesis.. Human temporal lobe samples were obtained during anterior temporal resection, and dissected into cortical, subcortical, and periventricular samples. These were dissociated and plated as single cell suspensions, to which ^{3}H-thymidine was added. The cultures were immunostained after 8-25 days for one of several neuronal (MAP-2, NF), glial (GFA), or neuroectodermal (A2B5, MAP-5) antigens, prior to autoradiography. Neuron-like cells were obtained from both subcortical and ventricular zone samples. Most were glia ($GFA^+/MAP\text{-}5^+/A2B5^-/MAP\text{-}2^-$); many of these were ^{3}H-thymidine$^+$, and likely type 2 astrocytes generated *in vitro*. GFA^- neuron-like cells were also found, including both antigenically undefined cells ($MAP\text{-}5^+/A2B5^-/MAP\text{-}2^-$) and presumptive neurons ($MAP\text{-}2^+$ or NF^+). Among these GFA^- neuron-like cells, a small number incorporated ^{3}H-thymidine, indicating their origin *in vitro*. Most, however, were unlabeled by ^{3}H-thymidine, and may have arisen from surviving parenchymal neurons, or from precursors induced to differentiate by the culture conditions. Selected cultures were also loaded with the calcium-sensitive dye Fluo-3, and exposed to 60 mM K^+ during confocal microscopy, in order to seek evidence of neuronal function. Neuron-like cells responded to K^+ with rapid and reversible, >10-fold increases in cytosolic calcium, which were accentuated by tetrodotoxin. These results suggest that the adult human forebrain may harbor precursor cells which retain the potential for neuronal and glial production *in vitro*, upon removal from their tissue environment.

2-31-11 ISOLATED POSTERIOR COLUMN DYSFUNCTION IN SPINAL CORD COMPRESSION

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We report two patients who presented with isolated posterior column dysfunction secondary to herniated intervertebral discs producing spinal cord compression. Neither had motor deficit, hyperreflexia, or pathological reflexes.

The first patient complained of paresthesias involving the legs and fingers. Examination revealed impaired vibratory and position sensations in the legs to the T7 level, with sparing of pain and temperature modalities. Thoracic spine MRI was normal. Tibial somatosensory evoked potential (SSEP) showed prolonged central conduction time. Median SSEP demonstrated prolonged P14 peak suggesting cervical cord pathology. A cervical spine MRI study revealed a herniated C5-6 disc producing cord compression.

The second patient presented with leg paresthesias and gait ataxia. Examination showed absent vibratory and position sensations below the L2 vertebral level, with normal pain and temperature sensations, ataxic gait, and a Romberg sign. Median SSEPs were normal. Tibial SSEPs showed normal N24 and absent responses proximally, localizing the lesion between the conus and the cervical cord. Thoracic spine MRI showed a herniated T11-12 disc producing cord compressions.

To our knowledge, spinal cord compression manifesting as isolated posterior column dysfunction has not been previously reported. Study of posterior column function with SSEPs may help localize the lesion.

2-31-12 NEUROLOGIC INVOLVEMENT IN ASYMPTOMATIC PATIENTS WITH BEHÇET DISEASE

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Background: The identification of asymptomatic neurological involvement could be important for prognosis and early treatment in BD. To our knowledge, there has been no reports concerning evoked potentials, nerve conduction studies, EEG and MRI in neurological asymptomatic patients with BD.

Design/Methods: 17 consecutive, neurological asymptomatic patients with BD were studied. Clinical history and neurological examination was done by the same neurologist. We performed evoked potentials, EEG, nerve conduction studies and MRI (1.5T) in these patients.

Results: Physical examination and EEG were normal in all patients. SEPs were abnormal in 2 out of 14 (14,3%), VEPs in 5 out of 14 (35,7%) and BAEPs in 5 out of 14 (35,7%). Nerve conduction studies showed abnormalities in 2 out of 13 (15,3%). MRI was abnormal in 5 out of 13 patients (38,44%). The common pattern was small lesions in the white matter that gave a high MRI signal intensity.

Conclusions: Asymptomatic neurologic involvement in patients with BD is quite frequent (76,4%). Abnormalities are more frequently found in BAEPs and MRI studies. VEPs alterations are not specific and are not necessarily related to CNS involvement. Peripheral nervous system involvement is infrequent and a causal relationship with BD is doubtful.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

2-31-13 A NEUROLOGICAL OUT-PATIENT CLINIC IN OPORTO - ANALYSIS OF REFERRALS

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The purpose of this study was to define neurologic outpatient referrals in Oporto, Portugal. We analysed 201 referral letters and clinical records at our Hospital, a 700-bed university hospital. The mean age of patients was 45 (2-85) years, 60% females and 70% urbans. 30% of patients were referred by general practitioners, 26% by emergency department, and 23% by ophthalmologists, internists, neurosurgeons and psychiatrists. Half of the patients observed had suffered for more than 1 year, and the average waiting time was 71 days. 28% of patients were given a prior CT scan. The neurologic examination was normal in 60%. The most common diagnosis was headaches (20%), epilepsy (20%), stroke (14%) Parkinsonism (10%) and psychiatric disorders (10%). Neurologists requested tests in 72% of all patients: CT scan (34%), EEG (19.5%), duplex (11%), EMG (6.5%), echocardiography (6%) and MRI (2.5%). Nearly 80% of all patients were scheduled to return, and only 2 cases were admitted to the Inpatient Department. Our study allows us to construct a picture of a typical outpatient referral in Oporto, and analyse it in relation to the health care organisation and medical education. Our results are compared with other studies.

2-31-16 THE CHANGE OF ENKEPHALIN OF OPIUM SMOKERS AND RECOVERY CURE

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This observational study compares plasma concentration of enkephalin (lek) in 30 healthy men vs. 224 opium smokers. The purpose of the paper is to discuss the pathological foundation of spiritual obstacles and to find the cure methods.

Our results show a higher lek level in the opium smokers both before and after cure, and after cure lek is higher than before. The result is statistically significant.

Results: 1, Extrinsic opium enters the body and causes abnormal metabolism of lek, causing an increased free lek in plasma. This is the pathological foundation upon which the opium smokers' spirit and body rely. 2, Abnormal lek has an obvious effect on men's affect and behaviour. They display agitation, anxiety, melencholy, and reliance(?). The author believes that the danger to opium smokers is not physiological, but the personality metamorphosis caused by pleasant sensation after smoking opium. 3, Cessation of opium smoking must rely on psychology and behaviour together with Chinese and Western medicine for recovery.

2-31-18 HOME INITIATION OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) THERAPY FOR SLEEP APNEA.

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Nasal CPAP is a safe and effective treatment for sleep apnea syndrome (SAS). The standard method of initiating CPAP is in the sleep lab under polysomnographic monitoring. However, CPAP can be safely started at home in most patients. A prospective randomized single blinded study was undertaken to attempt to demonstrate that CPAP therapy is as effective and is tolerated as well when initiated at home as when initiated conventionally under polysomnographic monitoring.

Patients with SAS without serious heart or lung disease requiring CPAP were randomized to conventional treatment with initiation of CPAP under polysomnographic monitoring, or CPAP started at home. Tolerance and efficacy were analyzed at 1, 3, and 6 mo after initiation of treatment with clinical evaluations and home oxygen saturation studies (3 mo). A one-tailed test was performed in order to compare tolerance and compliance between groups. Eighty patients were studied, and no significant differences were noted in apnea index, minimum oxygen saturation, compliance, tolerance or effectiveness of treatment.

We conclude that CPAP therapy can be initiated at home safely and effectively in SAS patients without serious cardiac or pulmonary disease. This method offers significant potential savings of resources in this common disorder.

2-31-19 EFFECT OF ETHANOL ON TRACE ELEMENTS IN THE BRAIN

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[Purpose] We performed this study to elucidate the effect of ethanol intake on trace elements concentration in the brain.

[Materials and Methods] 10 pairs of 8-year-old male Sprague-Dawley rats were fed on ethanol-containing liquid diet. One month after, trace elements level (Ca, Cu, Fe, K, Mg, Na, P, Sr, Zn, Mn) were determined by ICP luminescence analyzer (Hitachi luminescence analyzing system 360).

[Results] Natrium concentration was higher in ethanol group than controls in the cortex, white matter, cerebellum and liver. Potassium level of ethanol group was significantly lower in the cortex, white matter and cerebellum, whereas magnesium and zinc concentrations were significantly lower in the cortex.
No significant changes in concentration were found in other trace elements.

[Conclusions] By one month observation, ethanol intake makes an increase of natrium and a decrease of potassium in concentration in the many brain regions. Magnesium and zinc level decreases in the cortex. Any other elements were not influenced by ethanol intake.

2-31-20 WERNICKE'S ENCEPHALOPATHY DURING PREGNANCY

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Wernicke's encephalopathy is characterized by mental disturbance, disorders of eye movement and ataxia and is usually suspected in chronic alcoholic patients.

We describe a 21 year-old female who developed Wernicke's encephalopathy as a complication of her first pregnancy. She suffered from severe nausea and vomiting during the first trimester which required hospital admission. One month later she developed nystagmus and became disorientated. Clinical neurological examination showed that she was disorientated, had a vertical nystagmus, bilateral papilloedema, peripapillar hemorrhages and ataxia.

Serum thiamine monophosphate concentration was less than 1nmol/l (i.e. not measurable). MRI demonstrated increased signal in the periaqueductal region on T2 and proton weighted images and increased signal in the left nucleus caudatus. Serum thiamine increased slowly during intravenous thiamine treatment and the MRI findings gradually disappeared. The patient improved gradually and she gave birth to a healthy son.

This report stresses the importance of considering Wernicke's encephalopathy when neurological symptoms present in a patient with hyperemesis gravidarum.

2-31-22 THE HEALTHY BRAIN PROJECT OF FINLAND: EFFECTS OF HEALTH EDUCATION ON THE GENERAL POPULATION

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The Healthy Brain Project of Finland is a nation-wide health education campaign aimed at familiarizing the Finnish public in a positive way with the importance of healthy brains. Two cross-sectional surveys were carried out in order to study the effects of the project on general brain knowledge, attitudes and health behavior of the population. The first survey was carried out during the spring in 1991 and the second one, a year later, right after the active phase of the project. Studies were based on a representative sample of the Finnish adult population (N = 5000, the response rates were 76% and 74%, respectively). The evaluation survey was part of "The Survey on Health Behaviors among Finnish Adult Population", carried out annually since 1978 by the Institute of Public Health. The results showed a significant change in attitudes towards, for example, alcohol consumption and disuse of the brain as a risk factor for brain health. Those were the most emphasized aspects of the project. Respondents also reported that they had received more information on factors influencing the health and capability of the brain. However, the assessment of one's own possibilities to influence the health of the brain did not change notably during the campaign.

2-31-24 A HIGH INCIDENCE OF BREAST IMPLANT FAILURE IN WOMEN WITH NEUROLOGIC AND RHEUMATOLOGIC SYMPTOMS.

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We evaluated 100 consecutively presenting women between 1985 and 1992 who had developed neurologic and rheumatologic symptoms at an average latency period of 6 years (range 0-24 years) after receiving silicone-gel breast implants (n=95, 21 were covered with polyurethane), saline breast implants (n=5) or silicone fluid injections into breast (n=3). Commonest symptoms were weakness (95%), fatigue (95%), myalgia (90%), morning stiffness (89%), arthralgia (81%), memory loss (81%), sensory loss (77%), headache (73%) and dry eyes and dry mouth (72%). Laboratory results revealed abnormal levels of immunoglobulins or complement (57%) or autoantibodies (78%). Sural nerve biopsy showed demyelination (79%) and biceps muscle biopsy showed neurogenic atrophy (27%). At time of removal, a pectoralis major muscle biopsy was taken which showed neurogenic atrophy (55%). Ninety-three underwent implant removal and 60% were found to have ruptured implants. Biopsy of the implant capsule showed foreign body giant cells (69%) containing silicone. Silicone breast implants and silicone injections might cause an autoimmune disease with neurologic and rheumatologic symptoms. The presents of objective findings along with an increased rate of implant failure indicate the need for further attention.

2-31-25 POSTURAL CONTROL AND COURSE OF CHRONIC ALCOHOLISM.

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Impairment of postural control in chronic alcoholism is a well known phenomenon. Until now, however, there is little information about factors predicting the risk of postural instability in this disorder. Therefore, the aim of our study was to investigate whether the course of chronic alcoholism may correlate with postural instability.

We examined 103 patients (94 men and 9 women) aged 20 - 67 years (mean: 41.8 ± 9.6) admitted for alcohol withdrawal therapy 2 - 4 weeks after acute detoxification. The patients were attached to one of four groups characterizing the course of chronic alcoholism (abstinent course, controlled drinking, problematic course and bad course) and were examined by the means of a posturographic platform which provides quantification and analysis of body sway. In addition, they underwent a detailed neurological investigation. We performed a total of 20 posturographic measurements in each patient, 10 with eyes open and 10 with eyes closed and compared four parameters (sway path, sway area, anteroposterior and lateral sway) in patients with age matched healthy controls.

The posturographic examination revealed impaired postural control in 62 % of patients, whereas clinical investigation showed disturbance of stance or gait in only 24 %. Bad couse was associated with a significantly higher percentage of patients with postural instability compared to patients with abstinent course.

In conclusion, our study suggests that the occurrence of postural instability may be correlated to the course of chronic alcoholism.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-01-01 SPHEROIDS IN THE CSF OF NEURODEGENERATIVE DISEASE PATIENTS: HEAVY METALS IN ALS.

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A new research avenue was opened by the finding of spheroids in the CSF of ALS patients (Neurol. 38 (suppl.), 740; 1988), following our observations on how these microbodies are formed within the axoplasm of nerve fibers, grow in size and are released into the extracellular space to apparently migrate toward the CSF-bathed surface of the spinal cord and brain stem. Therefore, microanalysis of heavy metals within such nerve tissue particles was carried out on CSF samples from patients afflicted with neurodegenerative diseases, including ALS. Spheroids were stained by various methods and studied under the light microscope, or were collected unstained onto E.M. copper grids, identified by scanning electron microscopy and studied with energy-dispersive X-rays microanalysis. Spheroids were found in every CSF sample from ALS patients (N=12). They frequently showed a significant content of metals (including Al, As, Ca, Fe, Hg, Si and Ti). Studies on other neurodegenerative diseases are in progress.

3-01-02 PHARMACOKINETIC (PK) STUDY OF INSULIN-LIKE GROWTH FACTOR I (IGF-I) IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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IGFs are bound to proteins in serum known as IGFBPs. Six IGFBPs, sequenced and cloned, have both potentiating and inhibiting effects on IGF-I action. Growth hormone induces IGFBP-3, the most abundant IGFBP. However, I.V. recombinant hIGF-I does not induce this BP in normals. Since rhIGF-I (0.05-1.0 mg/Kg/day), subcutaneous, is given in a multi-center Phase II study of rhIGF-I in ALS patients, we studied rhIGF-I bioavailability, baseline levels and response of the four most abundant BPs, IGFBPs 1-4. Using inclusion/exclusion criteria (WFN, El Escorial, Spain Working Group June, 1990) ambulatory patients with probable and definite ALS within 18 months of diagnosis were studied. PK fasting blood glucose, insulin and glucagon levels with endogenous total, free and bound (to IGFBPs) IGF-I were measured. No qualitative differences were found since ALS and control plasma reacted with polyclonal antisera and bound ligand. In a single dose PK Study rhIGF-I did not induce IGFBPs. Changes in IGFBPs will be monitored in ALS patients over a 9 month treatment trial with rhIGF-I that is in progress.

Support by Cephalon, Inc. and VA Medical Research

3-01-03 ROLE OF GLUTAMATE AMPA/KAINATE RECEPTORS IN ALS NEURONAL DEGENERATION : A CELL CULTURE STUDY

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Objective : Glutamate toxicity has been proposed as a possible factor in amyotrophic lateral sclerosis (ALS) motoneuronal degeneration. We have analysed the cerebrospinal fluid (CSF) toxicity from patients with ALS in neuronal culture. We have studied if any cytotoxic effect would be blocked by antagonists acting on post-synaptic glutamate receptors.

Methods : Mature cortical neuronal culture (fetal rats) were used. CSF were obtained from 15 ALS patients, 15 neurological controls and 15 other controls. ALS CSF was added at dilutions of 50 %, 20 % or 10 %. Neuron survival was assessed after 24 H. The neuroprotective effects of two N-methyl-D-aspartate (NMDA) receptor antagonists (MK801 and AP7) and one AMPA/Kainate receptor antagonist (CNQX) were also assessed.

Results : ALS CSF was significantly neurotoxic with a neuronal survival rate of only 44 % compared with 80 % for control CSF. The neurotoxicity was blocked by CNQX but not by NMDA receptor antagonists.

Conclusion : ALS CSF contain a neurotoxic factor which is responsible for neuronal degeneration in primary cultures and activates glutamate AMPA/Kainate receptors. Supported by AFM.

3-01-04 COMPARATIVE STUDY ON SPINAL ANTERIOR HORN CELLS AND MUSCLE DEGENERATION IN AMYOTROPHIC LATERAL SCLEROSIS

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There are many reports concerned both of the number of spinal anterior horn cells (AHCs) and muscular degeneration in amyotrophic lateral sclerosis (ALS). However, the relation between the severity of AHCs deciduation and the degree of their innervated muscular atrophy is still obscure. The aim of this study is to clarify this relation. We examined in several spinal segments in 7 autopsied cases of ALS and one case of cerebral infarction (as the control). Each paraffin embedded spinal segments were sliced in 5 serial sections in 20 μm thickness, and each sections were stained with cresyl violet. Then, the numbers of AHCs with nucleole in both laminae VIII and IX (Rexed, 1952) were counted. Skeletal muscles in both cervical and lumbar spinal sections were sliced in 4 μm thickness and stained with hematoxylin and eosin. After the evaluation of their grade of muscular degeneration, we compared the loss of AHCs with the grade of muscular degeneration. Conclusions were followed:

1. The mean numbers of AHCs within 100 μm thickness both cervical and lumbar segments in ALS were 7.7 in lamina VIII and 23.0 in lamina IX (middle cervical segments) and 19.3 and 35.3 in third lumbar segment respectively. On the other hand, the mean numbers of them in control were 11.0 and 26.0 in 6th cervical segment and 27.0 and 93.0 in 3rd lumbar segment. 2. The grade of skeletal muscle degeneration was mild to moderate in all cases of ALS, and the examined muscles were estimated almost normal in control. 3. Apparent relation between the loss of AHCs and the degree of muscular degeneration was not found in this study. 4. The neuronal cell loss preceded the muscular degeneration in our impression.

3-01-05 PEOPLE IN WHOM AMYOTROPHIC LATERAL SCLEROSIS IS LESS COMMON

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Amyotrophic lateral sclerosis (ALS-MND) occurs ten times more frequently in Guam and in the Kii peninsula than other parts of the world, where it was considered to be evenly distributed. We have studied the mortality from ALS-MND in immigrants to England and Wales from the Indian subcontinent and West Indies. The ALS mortality among Caribbeans was somewhat lower than expected. The mortality among Asian immigrant males was half, and among Asian immigrant females one fifth the expected at English rates. As ALS among the Asians and Blacks paralleled the distribution of Multiple Sclerosis, we have studied another group where MS is less common: the white South Africans. MND-ALS was found to be half of the expected compared to England and Wales rates; with considerably lower mortality among the Afrikaans-speaking than among the English- speaking populations, as is the case with MS. The importance of identifying the cause of increased ALS prevalence among the peoples of the Marianna Islands is well appreciated. Clarifying the reasons why certain populations die less commonly from ALS may be an equally important clue in finding the cause of the disease.

3-01-06 MEASUREMENTS OF IGG SUBCLASSES IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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In order to get clues about T-cell independent versus T-cell dependent immune mechanism in ALS, we measured immunoglobulin G subclasses 1 - 4 in 25 patients with ALS : Sixteen patients had deficiency of T-cell dependent expressed IgG 1 or IgG 3 or both with essentially normal levels of T-cell independent expressed IgG 2 and IgG 4. Ten of these patients had no prior treatment and five out of these 10 had normal total IgG. Six patients had some immunosuppressive treatment before measurements of subclasses were done and all of them had deficiency of total IgG. Eight out of 14 patients who underwent a d-xylose breath test, had evidence of small bowel overgrowth, which was confirmed by cultures of duodenal aspirate. IgG 1 and IgG 3 are T-cell dependent antibodies against protein antigens with close linkage on chromosome 14. The findings suggest a defect in the IgG subclass expression in ALS.

3-01-07 SUICIDE IN MOTOR NEURON DISEASE

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A recent review of the literature on suicide in neurological diseases has shown that no proper studies concerning the suicide risk in motor neuron disease exist.

The aim of the present study has been, through an epidemiological study to assess whether patients with motor neuron diseases are at an increased suicide risk. The study involved 116 patients who in the period 1.4. 1973 to 31.10. 1991 were treated at Odense University Hospital with the diagnose motor neuron disease. In the study period 92 patients died, 45 females and 47 males. No patients committed suicide. The number of expected suicides was 0.27 for males and 0.12 for females, a total of 0.38. Neither for males nor for females the difference between observed and expected suicides was statistically significant. The results will be discussed in relation to mortality in other neurological diseases.

3-01-09 LONGITUDINAL ASSESSMENTS IN MOTOR NEURONE DISEASE (MND)- IMPLICATIONS FOR THERAPEUTIC TRIALS

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Many possible therapeutic agents need to be tested in MND. Definitive survival studies require large numbers of patients, are expensive and protracted. One strategy is to screen potential agents by assessing deterioration rates (over a reasonable time period) of bulbar and respiratory function, which relate to survival in MND.

We investigate the use of previously validated quantitative measurements of bulbar and respiratory function in monthly assessments of 30 subjects with MND (M/F= 2:1; mean age 54.5 yrs, SD 10.2). 18 had classical ALS and 12 bulbar palsy. Mean follow-up was 7.7 months, 8 completed 12 months of the study. Control values were obtained from 21 healthy volunteers (M/F= 9:11; mean age 56.2 yrs, SD 14.4). The data was used to calculate sample sizes required in a therapeutic trial. The effects of using different power, p-values and magnitudes of difference to be detected between treatment groups on sample sizes are investigated, as are the effects of stratification by MND-type and different dropout rates during follow-up. We demonstrate that differences of 50% in deterioration rates can be detected with sufficient power in small numbers of patients (ie. less than 10 per treatment group). A similar investigation is performed on longitudinal assessments of muscle force.

3-01-10 HEREDITARY MADRAS SYNDROME

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Madras pattern of motor neuron disease is a syndrome of spinal muscular atrophy (SMA) and sensorineural deafness which has been described in approximately 12 patients with young age at onset, sporadic occurrence and progressive but benign course. We now report a family with two male siblings and a maternal male cousin with SMA and sensorineural deafness. The older sibling presented at the age of 6 months with motor delay, progressive muscular atrophy and type grouping by muscle biopsy. Course was progressive and he died of respiratory complications at 16 years of age. His younger brother was also found to have a similar disease but milder in severity. To the best of our knowledge, previous reports of Madras pattern have been sporadic. Inasmuch as the genetic locus for SMA maps to chromosome 5q, further studies might elucidate a possible linkage between SMA and sensorineural deafness.

3-01-11 AUTOMATIZED ROBOTIC SYSTEM FOR ISOMETRIC MUSCLE STRENGTH MEASUREMENT IN HUMANS.

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Isometric muscle strength (IMS) is measured by subjective scales, handhold dynamometers or cable tensiometers, that in inexperienced hands have a high probability of technical error. We built a computerized automatized electromechanic System for IMS measurement of the major muscle groups. The System consists of a motorized chair; a cartesian robot with three servocontrolled movements that handles a gyratory head with a strength sensor; and hardware and software, based on a programmable logic controller and a microcomputer, that control all mobile components and security systems and acquire and manage all data. The idea is to position the examined person in the chair. The examiner selects from the computer the muscle to be examined and chair, sensor head and cartesian robot do the necessary movements to position the sensor at the exact place where measurement has to be taken. These movements have been previously recorded and stored and may be corrected by a hand programming module. After the examined person pushes against the sensor a strength curve shows at the computer's monitor, and different strength parameters are calculated. Once measurement finishes the robot executes the opposite movements to the ones carried on for positioning. Reliability studies demonstrate very high correlation coefficients and very low measurement errors. The System is original and unique

3-01-12 WITHDRAWN

3-01-13 LEUKEMIA INHIBITORY FACTOR (LIF) MEDIATED INCREASE OF CHOLINE ACETYLTRANSFERASE ACTIVITY IN MOUSE SPINAL CORD NEURONS IN CULTURE.

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The effects of leukemia inhibitory factor (LIF) on choline acetyltransferase (ChAT) enzyme activity in cultured mouse spinal cord neurons were examined. The administration of LIF to cultures at concentrations of 10 U/ml and higher enhanced ChAT activity approximately 3- to 4-fold. Among trophic factors tested, basic fibloblast growth factor (bFGF) and insulin-like growth factor I (IGF-I) stimulated the development of ChAT activity but to a smaller extent than LIF, while interleukin 3 (IL-3), interleukin 6 (IL-6) and nerve growth factor (NGF) showed no apparent effect on ChAT development. Our results indicate that LIF, which has not been known to have any trophic effect on central nervous system neurons to date, acts as a potent trophic factor for cholinergic neurons of mouse spinal cord in culture.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-01-14 **THE NEUROTOXICITY OF GLUTAMATE AGONISTS ON VENTRAL HORN NEURONS IN ORGANOTYPIC EXPLANT CULTURES OF SPINAL CORD.**

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We examined the neurotoxicity of various glutamate agonists on ventral horn acetylcholinesterase (AChE)-positive neurons (VHANs) in organotypic explant cultures of spinal cord (OTC-SCs).

The OTC-SCs were prepared as previously described (Delfs et al., Brain Res., 1989). After 17 days *in vitro*, OTC-SCs were incubated in control media, and media containing N-methyl-D-aspartate (NMDA), kainate, or quisqualate. After 72 hours, cultures were stained for AChE.

Treatment with NMDA caused a marked loss of staining and an obvious loss of smaller sized neurons. Cultures treated with kainate and quisqualate showed a dramatic absence of the larger VHANs. Morphometric analysis of cultures treated with either NMDA, kainate, or quisqualate revealed significant decreases in total numbers of VHANs as compared with control. Whereas the decrease of VHANs in NMDA treated cultures was observed in less than 500 μm^2 sized neurons, kainate and quisqualate reduced the number of VHANs in both less than 500 μm^2 and more than 500 μm^2 in areal size. They showed a preferential neurotoxicity for larger VHANs.

This study demonstrates that there are differences between the susceptibility of VHANs to NMDA and that of VHANs to non-NMDA agonists. Non-NMDA agonists appear to preferentially affect larger VHANs, a pattern which might be more likely to be seen in the spinal neuronal loss in ALS.

3-01-16 INTRATHECAL (i.th.) ADMINISTRATION OF RECOMBINANT HUMAN CILIARY NEUROTROPHIC FACTOR (rHCNTF) IN AMYOTROPHIC LATERAL SCLEROSIS (ALS) ? - PRECLINICAL STUDIES IN SHEEP

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rHCNTF is highly effective in preventing motoneuron degeneration *in vitro* and *in vivo*. Its action in animal models of degenerative motoneuron disease suggests a potential for clinical use in patients with ALS. The extremely short halflife of rHCNTF in the circulation after systemic injection and its side effects in the liver render it suitable for i.th. administration.

Programmable infusion pumps were implanted for chronic i.th. application in sheep. Stability was tested in the pump reservoir, rHCNTF content in CSF samples was determined and spinal cord was analysed histologically for potential actions of rHCNTF in cells other than motoneurons.

Bioactivity of rHCNTF in pump reservoir dropped within a few days and CSF and cell numbers increased, suggesting that rHCNTF induces enhanced permeability of blood-brain barrier. The results indicate that stability and tissue compatibility of rHCNTF should be established before initiation of chronic i.th. administation in humans.

3-01-17 A RATING SCALE FOR EMOTIONAL LABILITY

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Emotional lability is a common behavioral manifestation of diseases which affect both cerebral hemispheres. It is manifested by inappropriate tearfulness or laughter. To our knowledge no measure of this behavior has been reported in the literature. Construction and validation of such a measure will be described. Based on personal interview with patients, family members and physicians a 100 item questionnaire was developed. This was administerd to 25 patients with amyotrophic lateral sclerosis (ALS). Using correlation analysis the items were reduced to 65 questions. Subsequently, potential items will be administered to 150 ALS patients, with responses being analyzed to determine factor structure. reliability, stability, construct validity and criterion based validity will also be assessed. In its final version, this questionnaire will consist of approximately 20 to 40 items, and will assess the presence of cognitive, affective, behavioral, and situational factors associated with emotional lability. It is also anticipated that this measure will provide both a total score for emotional lability as well as separate subscores for each factor (i.e., subscales) retained.

3-01-18 **KONZO: A DISTINCT DISEASE ENTITY WITH SELECTIVE UPPER MOTONEURON DAMAGE**

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Two Tanzanian patients with konzo were invited to Sweden for examination with magnetic resonance imaging (MRI), peripheral nerve conduction, EMG, EEG, multimodal evoked potentials and ophthalmological investigations. Both patients were severely disabled by a non-progressive spastic paraparesis, since the sudden onset during an epidemic 6 years earlier. At onset they had a high dietary intake of cyanide from exclusive consumption of insufficiently processed bitter cassava roots.

MRI of brain and spinal cord were normal but motor evoked potentials on magnetic brain stimulation were absent in both patients, even in the only slightly affected upper limbs. Other neurophysiological investigations were largely normal, but the more affected patient had central visual field defects.

The results support the clinical impression from field surveys in Africa that konzo constitute a distinct disease entity with a very selective type of upper motoneuron damage.

3-01-20 SELEGILINE AND ITS METABOLITES PROTECT AGAINST DSP-4 TOXICITY

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Selegiline (SEL), an irreversible inhibitor of MAO-B, has been reported to protect against the depletion of noradrenaline (NA) caused by DSP-4. In order to confirm this finding and to investigate whether the metabolites of SEL contribute to this mode of action we administered the toxin 50 mg/kg i.p. to mice that had been given orally SEL 5 or 10 mg/kg or its metabolites (5 mg/kg) desmethylselegiline, levoamphetamine or levomethamphetamine 1 or 24 h before the administration of the toxin. The NA levels in the frontal cortex were significantly decreased by DSP-4 (16% left of the control values). The NA levels were substantially protected against DSP-4 (70-85% of the control values) when DSP-4 was given 1 h after SEL or any of its metabolites. After 24 h the protection was slight or nil (18-25%). Thus the protection by SEL against DSP-4 toxicity does not seem to be related to MAO-inhibition, which lasts well over 24 h, but rather to some other mechanism that most probably is associated with its metabolites.

3-01-21 **ON THE INCREASE OF MONAMINE OXIDASE-B (MAO-B) WITHIN THE SPINAL CORD IN AMYOTROPHIC LATERAL SCLEROSIS (ALS).**

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Using tritiated L-deprenyl, an irreversible monoamine oxidase-B (MAO-B) inhibitor, as a ligand for *in vitro* autoradiography, we observed a substantial increase in spinal MAO-B. The ^{3}H-L-deprenyl binding was preferentially increased in regions of neurodegeneration e.g. motor neuron laminae and corticospinal tracts in ALS. Correlations with cell counts and high resolution studies points to an enhancement of MAO-B protein in reactive astrocytes.

The activities of MAO-B and to a less extent catechol-O-methyltransferase (COMT) were elevated in spinal cord homogenates from ALS cases. In controls there was a significant positive correlation between the activities of spinal MAO-B and COMT, a relationship which was not seen in ALS. This might suggest different regulatory mechanisms of these enzymes in the process of neurodegeneration.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-01-22 A DOUBLE BLIND PLACEBO CONTROLLED TRIAL OF SELEGILINE IN ALS WITH SERIAL STUDIES OF FREE RADICAL ACTIVITY-TOWARDS LABORATORY CORRELATES OF DISEASE PROGRESSION?

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Monthly measurements of serum tocopherol & caeruloplasmin blood glutathione peroxidase (GSHPX) & superoxide dismutase (SOD), serum & leucocyte ascorbic acid were made during a double blind, placebo controlled crossover trial of selegiline in ALS. 58 patients were recruited, 32 completed the protocol. An interim analysis suggested that selegiline did not alter any of these parameters or modify disease progression. SOD activities were not altered in ALS. There was a progressive decline in serum caeruloplasmin (p=0.003) & blood GSHPX (p 0.001) as the disease continued based on 377 measurements from the first 45 patients. Blood GSHPX is a general index of body GSHPX status and this apparent trend was of clear interest in relation to our earlier work suggesting low spinal cord GSHPX activities in patients dying of ALS.

This trial has now been completed. The results from the full data set will be presented, as well as further studies aimed at elucidating the possible significance of these initial findings.

3-01-23 NEURONAL DAMAGE INDUCED BY β-*N*-OXALYLAMINO-L-ALANINE (BOAA), IN RAT HIPPOCAMPUS, CAN BE PREVENTED BY A NON-NMDA ANTAGONIST, 2,3-DIHYDROXY-6-NITRO-7-SULFAMOYL-BENZO(F)QUINOXALINE (NBQX).

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The neurotoxin β-*N*-oxalylamino-L-alanine (BOAA), found in *Lathyrus sativus* seeds, is thought to be the causative agent of neurolathyrism. We investigated the *in vivo* mechanism of action of BOAA, by focal injection in the rat hippocampus, and comparing the pathological outcome with the effects of injections of α-amino-3-hydroxy-5-methyl-isoxazole-4-propionate (AMPA), kainate (KA) or *N*-methyl-D-aspartate (NMDA). Cellular damage in the pyramidal (CA1-CA4) and dentate granule neurones (DG), induced by the excitatory amino acids, was assessed histologically 24 h after the injection. BOAA (50 nmol) induced hippocampal toxicity with a highly selective pattern of regional cellular damage. The CA1, CA4, and DG subfields showed between 70-90% neuronal injury, whereas in CA2 and CA3 there was only minimal damage. This pattern of cellular damage was similar to that induced by AMPA (1 nmol) and NMDA (25 nmol) but not KA (0.5 nmol). BOAA-induced neurotoxicity was prevented in a dose-dependent manner by focal co-injection of the non-NMDA receptor antagonist 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline (NBQX) (1-25 nmol) but not by MK-801 (3 mg/kg ip). These results indicate that the *in vivo* hippocampal toxicity of BOAA is mediated by the AMPA receptor site, rather than by the KA or NMDA receptors. Excitotoxic processes acting via AMPA receptors may play a role in the chronic loss of motor neurones seen in amyotrophic lateral sclerosis.

3-01-24 CORTICAL FUNCTION IN PROGRESSIVE MUSCULAR ATROPHY AND AMYOTROPHIC LATERAL SCLEROSIS.

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Using positron emission tomography (PET), we have previously demonstrated reduced regional cerebral blood flow (rCBF) at rest, and reorganisation during performance of a motor task, in the cortical motor system of patients with amyotrophic lateral sclerosis (ALS). We have recently used PET to image rCBF in 5 patients with progressive lower motor neurone degeneration (LMND). These patients had normal central motor conduction. Six patients with ALS and 6 normal volunteers were studied for comparison. rCBF measurements were performed on subjects at rest and during performance of paced, freely-selected movements of a joystick with the right hand. rCBF at rest was significantly ($p<0.01$) reduced in the motor cortex and motor association areas of ALS but not in LMND patients when compared to normal control subjects. Similarly, during performance of the motor task, the motor cortex was found to have undergone significant reorganisation in ALS patients, but not in LMND patients.

These results suggest that whereas ALS leads to degeneration of pyramidal cells in all cortical areas projecting through the corticospinal tract, cortical involvement in LMND is absent or minimal. Functional reorganisation of the motor cortex in ALS is likely to be directly related to loss of corticospinal motor neurones.

Supported by the Medical Research Council of Great Britain.

3-01-25 STUDY OF THE MOLECULAR PATHOLOGY OF CORTICAL DEGENERATION IN NON-MOTOR AREAS IN ALS, TO CLARIFY THE RELATIONSHIPS BETWEEN TYPICAL ALS, AND ALS WITH DEMENTIA.

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We examined the brain and spinal cord of 33 patients with ALS, including 8 cases with dementia of frontal lobe type (DFLT), 2 cases with severe non-specified (NS) dementia, and 4 cases with minor cognitive or behavioural impairment, in comparison with Pick's disease (PD), Alzheimer's disease (AD), and neurologically normal controls. Sections were probed with antibodies against ubiquitin, tau, and phosphorylated neurofilament (NF) proteins. All ALS cases showed typical pathological abnormalities of the motor system. Eight cases with ALS and DFLT, 2 with non-specified dementia, and 2 with minor cognitive and behavioural changes developing late in the course of the disease, had ubiquitin-immunoreactive (IR) inclusions in hippocampal dentate granule cells. Degeneration of frontal and temporal neocortex with degeneration of small neurones in layers 2 and 3 was also associated with ubiquitin-IR inclusions in patients with ALS and with dementia. Pick bodies, but not hippocampal or neocortical ubiquitin-IR inclusions in ALS, were labelled by silver stains and by antibodies to tau or NF proteins. We conclude that the molecular pathology of ALS with dementia is distinct from that of Pick's disease, and that small (granule) neurones of the dentate gyrus and frontotemporal cortex degenerate in ALS, indicating that some neurones in non-motor cortex share with motor neurones features determining susceptibility to the disease process.

Supported by the Wellcome Trust and the MNDA of Great Britain.

3-01-26 **RECOMBINANT HUMAN CILIARY NEUROTROPHIC FACTOR [rhCNTF] IN AMYOTROPHIC LATERAL SCLEROSIS [ALS] PATIENTS: DOSE SELECTION STRATEGY IN PHASE I-II SAFETY, TOLERABILITY AND PHARMACOKINETIC STUDIES** ***ALS CNTF TREATMENT STUDY [ACTS] Phase I-II Study Group:***

BR Brooks, M Sanjak, Univ Wisconsin, Madison, WI; H Mitsumoto, K Szirony, Cleveland Clinic, Cleveland, OH; H Neville, S Ringel, J Brinkmann, Univ Colorado, Denver, CO; A Pestronk, J Florence, Washington Univ, St Louis, MO; JM Cedarbaum, M Charatan, N Stambler, Regeneron Pharmaceuticals, Tarrytown, NY; J Wittes, E Brittain, Statistical Collaborative, Washington, DC

OBJECTIVE: Chronic systemic delivery of rhCNTF by subcutaneous administration was validated by pharmacokinetic determination of plasma rhCNTF concentrations with delineation of clinical and laboratory limits of safety and tolerability.

BACKGROUND: ALS is a progressive neurodegenerative disease with no known treatment. CNTF is a neurotrophic factor that, administered systemically, delays progression of weakness in murine motor neuron degeneration caused by motor neuron disease [mnd], wobbler bulbar spinal muscular atrophy [wb] and progressive motor neuropathy [pmn].

DESIGN/METHODS: rhCNTF dosage rates were determined from animal toxicology and treatment studies. Eight patients per dose level were admitted to four Clinical Research Units to receive subcutaneously rhCNTF or placebo. Serial plasma concentrations were obtained following the first and second dose of rhCNTF. Trough concentrations were determined on the subsequent doses. Clinical, electrocardiographic and laboratory monitoring was performed regularly during chronic administration of rhCNTF at each dose level. Home administration for upto 20 weeks was accomplished with no serious side effects.

RESULTS: rhCNTF administration is well tolerated with repeated administration at all dose levels currently studied. Plasma rhCNTF concentrations achieved were easily measurable and followed standard clearance kinetics. Clinical and laboratory effects of rCNTF administration will be described.

CONCLUSIONS: Subcutaneous administration of rhCNTF is safe, well tolerated and achieves biologically active concentrations.

3-01-27 **NATURAL HISTORY OF AMYOTROPHIC LATERAL SCLEROSIS [ALS]: EFFECT OF SITE OF ONSET AND TIME OF ONSET ON SAMPLE SIZE CALCULATIONS FOR CLINICAL THERAPEUTIC TRIALS EMPLOYING SLOPE OF STRENGTH LOSS**

BR Brooks, D Lewis, J Rawling, M Sanjak, D Belden, H Hakim, YD Tan, RL Sufit, J Gaffney, R DePaul, ALS Clinical Research Center, Neurology Dept, Medical School, University of Wisconsin, Madison, WI, USA

OBJECTIVE: In the therapeutic trials of new drugs, it is preferable to analyze measures that decline the most rapidly in order to obtain the highest sensitivity in testing therapeutic agents in clinical trials.

BACKGROUND: ALS is a neurodegenerative disease in which isometric strength loss is a direct measure of the disease progression.

DESIGN/METHODS: Presymptomatic and symptomatic changes in strength in 117 ALS patients have been studied over periods of 12 ± 10 months [range - 6 to 36 months]. All raw values were converted to Z-scores. Megascores were obtained by averaging composite Z-scores of anatomically related measurements [Arm, Leg, proximal and distal upper and lower extremities]. Megaslopes were calculated for each patient by least squares linear regression of megascore values over time. Megaslopes were analyzed according to site of onset and whether the initial test had begun within 12 months of onset of ALS.

RESULTS: Arm strength loss in ALS patients is identical regardless of site of onset but the standard deviation of the rate of arm strength loss is smaller in arm onset patients permitting smaller sample sizes in therapeutic trials. Arm strength loss in ALS patients studied within 12 months of disease onset [- 0.099 ± 0.089 (standard deviation) Z units/ month] is nearly twice that of patients [- 0.047 ± 0.052] studied initially after the first year of disease [$p < 0.0001$]. Similar results occur for leg strength loss.

CONCLUSIONS: Arm onset patients as a group have a smaller standard deviation for the determined megaslope and require a smaller sample size for showing clinically significant effects. ALS patients studied within 12 months of onset have an accelerated rate of strength loss in both arms and legs which permits efficiency in sample size calculations.

3-01-28 AMYOTROPHIC LATERAL SCLEROSIS: CORRELATION BETWEEN CLINICAL PICTURE AND NEUROPHYSIOLOGICAL TESTING

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In this study 21 patients affected by ALS have been examined at different stages of the illness. Clinical and neurophysiological parameters were matched against 20 controls comparable for age and height. Increased threshold with amplitude reduction of MEPs was found in 13 out of 21 (62%) upper limbs (57 ± 19%) and in 15 out of 20 (75%) lower limbs (84 ± 15%). A lowering of hand MEP threshold (mean: 35%) was found in 6 patients, which presented the shortest clinical history. Muscle contraction induced MEP desynchronization in 44% of upper limbs and in 57% of lower ones. The silent period duration shorter compared with that of control subjects (80.7 msec vs. 166 msec, P < .001). CCT prolongation was found only in 28% of examined limbs. Peripheral involvement was present in 42% of the examined limbs (24% for upper and 62% for lower limbs).

The comparison of neurophysiological data with the clinical picture indicates that at the early stages the disease is significantly correlated with the presence of the fibrillation potentials and with lowering of the excitability threshold by magnetic stimulation. In the subsequent middle and late stages the lack of inhibition dominates the features of both neurophysiological and clinical signs: severe reduction of the silent period, inversion of the MEP/F-H ratio and abundance of fasciculations.

Inversion of the MEP/F amplitude ratio was present in 40% of the examined limbs, indicating a major central involvement.

3-03-01 THE FREQUENCY OF CEREBRAL EMBOLI IN PATIENTS WITH RECENTLY IMPLANTED MECHANICAL PROSTHETIC CARDIAC VALVES.

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Objective. The aim of this study is to assess the frequency of cerebral emboli in a group of patients with recently implanted prosthetic cardiac valves.

Methods. Transcranial Doppler monitoring of the right middle cerebral artery (MCA) was carried out in twenty patients without cerebral symptoms before and five days after implantation of a mechanical prosthetic heart valve. All patients were treated with warfarin postoperatively. Doppler monitoring lasted 30 mins and the frequency of emboli was assessed by an automatic cerebral embolus detection system (EME) which automatically records and counts the number of emboli entering the MCA. In addition the Doppler findings were continuously recorded on a video tape for off-line analysis (audio and visual content).

Results. 1. Seventeen (85%) of the 20 patients had from 1-78 (mean 12) asymptomatic MCA emboli during the 30 min. observation period. 2. None of the patients had MCA emboli prior to valve implantation.

Conclusions. These findings suggest that transcranial Doppler monitoring may be used to detect asymptomatic cerebral emboli in patients with prosthetic heart valves. Furthermore that clinical studies should now be carried out to determine if the frequency of asymptomatic cerebral emboli may be useful in predicting the risk of stroke in this group of patients.

3-03-02 ANTICARDIOLIPIN ANTIBODIES IN CEREBRAL ISCHEMIA

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Anticardiolipin antibodies (ACA) and lupus anticoagulants (LA) are acquired antiphospholipid antibodies often found in patients with systemic lupus erythematosus (SLE) or related autoimmune diseases. There may also be an association between ACA and various neurological diseases as ischemic stroke and transient ischemic attacks (TIA).

The prevalence of ACA in a common stroke population has been prospectively studied in more than 500 patients since 1991. About 10% have slightly increased ACA levels (>3 units). In 8 patients, 4 males and 4 females with ages between 22-71 yr the ACA titers were highly increased (>15 units). All these patients, except one with amaurosis fugax, had cerebral infarctions and TIAs with ischemic changes on CT scan. Three patients had SLE and one sarcoidosis.

All patients got antithrombotic treatment, four with ASA and four with Warfarin. In two patients the initial ASA treatment was changed to Warfarin due to recurrent TIAs and infarctions and in one patient Warfarin was combined with Persantine. Immunosuppressive therapy with steroids was added into four patients.

We recommend screening for ACA and/or LA antibodies especially in younger stroke patients. When present, long-term antithrombotic therapy should be considered, sometimes combined with immunosuppressive therapy.

3-03-03 CORRELATION BETWEEN LOCALIZATION AND CLINICAL PICTURE IN PROGNOSIS OF INTRACEREBRAL AND SUBARACHNOIDAL HEMORRHAGES

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Having analysed the 25–th retrograde analysis of the appearance of the intracerebral and subarachnoidal hemorrhages, a correlative ratio of localization and clinical picture in their prognosis has been reported. Males dominated in 52.8 %, the age between 30 – 60 years in 62.9 %, with presented risk factors from hypertension in 61.8 %, smoking in 53.6 % and the psychophysiological exercises in 47.3 %. Hemorrhage was hemispheral in 67.7 %, while in 30.3 % it was subarachnoidal. According to the clinical picture and hemorrhage localization, the outcome of the patient has been divided into the following groups:

1. Patients with unaltered consciousness (7.8%) or slightly semiconscious (17.5%) in whom the hemorrhage was small and without compressive behaviour toward its surroundings..

2. Patients being somnolently soporose (22.6%), with a slight displacement of the medial structures while hematoma is in the deep brain structures.

3. Comatose patients (51.7%), with compression of the upper part of the brain stem (dilatated pupils, Babinsky sign positive, initial signs for decerebration, vital functions preserved). In this group are placed the patients in deep coma, with stiff pupils and more marked signs for decerebration having a bad prognosis.

A special problem are the hemorrhages in the cranial fossa posterior and cerebellum. Prognostically, they are with a high mortality rate.

It was stated that 58.8% of the comatose and 15.0 % of the soporose patients died.

3-03-04 VASCULAR REACTIVITY IN PATIENT WITH INTERNAL CAROTID LESION

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We studied reactivity of cerebral vessels to acetazolamide on 58 patients (24 women, 34 men; mean age 71.1 years) with unilateral carotid lesion. Radionuclide angiography using the bolus injection method of 99m-Tc pertechnetate was performed to evaluate cerebral circulation and vascular reactivity. In 27 of patients (12 women, 15 men; 74.4 years), vascular reactivity was well on both non-affected and affected hemispheres (group A) but in other 31 patients (12 women, 19 men, 68.1 years), it was low on affected side (group B). CT findings, clinical symptoms and patient outcomes were compared between group A and B. 6 of 27 cases (22.2%) in A and 23 of 31 (74.2%) in B had remarkable hemiparesis. 5 cases of TIAs, 10 of dizziness, 5 of gait disturbances and 2 of dementias were seen in A and 5 of TIAs, 2 of gait disturbances and one of dizziness in B. On all 31 of B, any size of low density areas were seen in CT but 15 cases (55.6%) in A had LDAs. 6 cases of B died in short period from ictus and 2 of A died in follow up period. We conclude that an internal carotid lesion may not be an important role in patients who have colateral circulation.

3-03-05 SPECT: IS IT USEFUL FOR SELECTING PATIENTS FOR REPERFUSION THERAPY AFTER HYPERACUTE STROKE?

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We prospectively studied 15 patients with acute ischemic stroke with single-photon emission computed tomography (SPECT) within six hours of symptom onset and again after 24 hours. All patients were candidates for a therapeutic trial of thrombolytic therapy. The SPECT blood flow defect was assessed in a semiquantitative manner using computer generated regions-of-interest. The severity of SPECT defect correlated with severity of neurologic deficit (evaluated with the NIH Stroke Scale) using a method of SPECT analysis including weighing both volume of tissue affected and the degree of ischemia (r=0.059, p=.02). A severe blood flow defect on the initial scan was positively associated with poor long term outcome measured with the Barthel Index (p=0.002), and the complications of cerebral hemorrhage and massive cerebral edema (p=0.004). In fact, there was a blood flow threshold effect below which all patients suffered poor long term outcome and cerebral hemorrhage and edema. Early SPECT yields valuable information for the decision making process in acute ischemic stroke, and may be particularly useful in excluding from reperfusion therapy those patients destined for cerebral edema/hemorrhage.

3-03-06 CLINICAL EXPERIENCE WITH CEREBRAL EMBOLUS MONITORING

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We have shown in an experimental animal model that Doppler ultrasound may be used to detect arterial emboli composed of materials that are often involved in cerebral emboli (Stroke 1991; 22: 253). Furthermore, that the intensity of the Doppler signal caused by arterial emboli depends on embolus type and size (Recent Advances in Neurosonology 1992: 57).

A transcranial Doppler monitoring system has now been developed which automatically detects and counts emboli entering the middle cerebral artery (EME). This method may differentiate emboli from artefacts and emboli composed of solid elements from gaseous emboli.

We have applied this method in the clinical situation and our experience suggests that transcranial Doppler may now be used to detect cerebral emboli in the following situations: 1. During invasive cardiovascular surgery such as cardiopulmonary bypass and carotid endarterectomy, 2. In patients with frequent cerebral TIAs to determine if they are due to hemodynamic or thromboembolic events and 3. In patients with a potential embolic source in the heart or carotid artery.

3-03-07 CEREBRAL VASOREACTIVITY AFTER ACETAZOLAMIDE: DOSE AND TEMPORAL PROFILE OF THE RESPONSE.

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Blood flow velocities (BV) in both middle cerebral arteries were continuously measured in 32 healthy subjects before and following the i.v. injection of 1 g acetazolamide (Acz) using permanently fixed probes and transcranial Doppler ultrasound (TCD). In 20 subjects rCBF was also measured before and 20 mins after Acz administration using SPECT and 133-Xenon inhalation. The dose in mg/kg was calculated and the serum concentration of Acz was measured in 15 subjects 5 mins after administration.

BV increased by 43.3 ± 2.7% (SEM) reaching a plateau phase after 8 mins which then lasted for 20 mins. After 45 mins (11 subjects) BV decreased to 67% of the maximal response. The relationship between dose and serum concentration was good ($r=0.84$; $p<0.001$). The % increase in BV was related to the dose and serum concentration of Acz and the dose response curve demonstrated no further velocity increase in subjects receiving doses greater than 15 mg/kg. No relationship was observed between the rCBF increase and Acz dose or serum concentration.

In conclusion this study strongly suggest that the assessment of vasoreactivity using Acz should be carried out 10 to 30 minutes following the injection of a 15 mg/kg dose.

3-03-08 SPONTANEOUS CAROTID DISSECTIONS - UNDERRATED FREQUENCY OF VESSEL WALL ABNORMALITIES

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Abnormalities of the cerebral vasculature, such as fibromuscular dysplasia and berry aneurysms, are reported infrequently in those with spontaneous carotid dissection. We identified 24 patients (10 men and 14 women) with spontaneous carotid dissection by reviewing all angiographic records at University and Victoria Hospitals, London, Ontario, from 1985-1992. Angiographic films and medical records were subsequently reviewed. The mean age of the 24 patients was 50 years (range 17-81 years). Twelve of the 24 patients (50%) had 14 abnormalities of the cerebral vasculature, consisting of 6 with probable fibromuscular dysplasia, 4 with berry aneurysms and 4 with dissection into an atherosclerotic plaque. Two patients had both fibromuscular dysplasia and berry aneurysms. Another 2 patients, one with fibromuscular dysplasia and one with a berry aneurysm, had a family history of berry aneurysms. These findings suggest that a disorder of the vessel wall may play a more important role in the pathogenesis of spontaneous carotid dissection than previously reported.

3-03-09 MOTOR RECOVERY AFTER STROKE: A SPECT ACTIVATION STUDY

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Aim of our study was to investigate the patterns of functional brain activation during a motor task, in patients who recovered from a previous ischemic stroke.

We studied 11 male and 3 female patients mean age 61 ± 10.4 years, presenting with a previous motor disfunction due to a single ischemic infarction. All the patients underwent a MR scan to exclude the possible occurrence of clinically silent lesion. Quantitative regional CBF was measured using SPECT and Xe-133 inhalation technique. In a single experimental session, each subject underwent three SPECT CBF scans: one at rest, and two during motor activation (finger opposition) of the normal and the previous paretic hand.

The movements of the normal hand showed the activation of the contralateral motor regions, while the performance of the same motor task by the previously paretic hand suggested the occurrence of more complex mechanisms, involving the motor areas of the affected as well as the unaffected cerebral hemisphere.

These results suggest that motor recovery is associated with a different pattern of activation of the brain motor areas.

3-03-10 PSYCHOORGANIC SYNDROME IN ANEURISMAL SUBARACHNOIDAL HEMORRHAGE

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Forty six patients with subarachnoidal hemorrhage with an average hospitalization of 3 days since the disease onset, age 51,4 years, referred to a neurosurgeron after 19 days, were subjected to brain computed tomography, angiography, CSF examination. The patients had: aneurysms 80,4% (anterior communicative artery 32,6%), vasospasm 54,3%, rebleeding 15,2%, delayed infarct 13%, hydrocephalus 8,6%; 15,2% died. 25 patients had psychoorganic syndrome (POS) - 54,3%. Clinical grade according to Hunt-Hess: I-II: 73,9%, III: 19,5%, IV-V: 6,5%. Disturbed behavior dominated. 80% of the patients were confusedly-agitated, anxious, uncritical, two were delirious (previous alcoholism). Rarely the patients were torpid, abulic, with or without altered consciousness. Amnesia was frequent, Korsakoff's amnestic syndrome was rare, 8% (aneurysms to ACoA). Slight depression or emotional lability was present. Hypomania and hallucination were rare. POS was influenced by unconsciousness, rebleeding, vasospasm, hydrocephalus, possible previous psychopathy and drunkenness. Rebleeding was more frequent in agitated patients. Agitated POS was treated by sedatives, barbiturates, neuroleptics, intensive care. POS was frequently transitory, but the sequels in memory and emotions are important.

3-03-11 MAGNETIC RESONANCE ANGIOGRAPHY APPLIED IN CEREBRO-VASCULAR DISEASE. PRESENT STATE.

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Magnetic resonance angiography (MRA) has been recently introduced into clinical setting. It has the capability to demonstrate the cerebrovascular system and the changes of the blood flow under pathological conditions. MRA is non-invasive procedure. Two techniques were used for MRA: time-of-flight and phase contrast imaging. Data were acquired using two- or three dimensional Fourier transformation methods. To increase the blood flow signal in selected cases contrast enhancers were used.

This analysis includes three groups of cerebrovascular disorders: occlusive vascular diseases, aneurysms and arterio-venous shunts. In our experience MRA of neck arteries can disclose plaques, ulcerations, stenosis and occlusions with great accuracy, as well as stenosis or thrombosis of intracranial arterial network and resulting infarcts (91%). It is more precise than other angiographic modalities in determining the size and rupture of an aneurysm (89%). MRA is a reliable technique for the evaluation of different arterio-venous shunts as shown in our previous studies.

Further improvements of MRA techniques will broaden its clinical usefulness, so that it may replace some invasive angiographic procedures used at present.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-03-12 TREATMENT OF ACUTE THROMBOTIC STROKE WITH SELECTIVE INTRA-ARTERIAL INFUSION OF UROKINASE

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Cerebral anglography and endovascular therapeutic procedures may result in thrombotic complications. We report our experience with treatment of such complications by intra-arterial infusion of urokinase.

In the period 1990-1992, four patients (three men, one woman) developed acute arterial occlusion/s following angiography or endovascular treatment. In three patients, thrombosis occurred during endovascular treatment of an aneurysm. Right middle cerebral artery (MCA) was involved in two patients, and basilar artery in the third patient. Urokinase (total dose 50,000-100,000 units) was administered, within thirty minutes of occurrence of symptoms, at the site of thrombosis using a pulse-spray technique. All symptoms and signs resolved within one hour and restoration of vessel patency was documented angiographically. The fourth patient developed intermittent, and then fixed aphasia and right hemiparesis following diagnostic angiography. Repeat angiography done seven hours later showed occlusion of the left MCA. Local infusion of 250,000 units of urokinase restored patency but did not alter the neurological deficit. Death from pulmonary embolism occurred 26 days later. Autopsy revealed multiple hemispheric infarcts without significant hemorrhage and a patent left MCA.

This limited experience suggests that the prompt intra-arterial infusion of urokinase following thromboembolic complications of angiography or endovascular intervention allows restoration of vessel patency and reversal of neurological deficit.

3-03-13 DECREASED CEREBRAL FLOW IN FABRY'S DISEASE.

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Fabry's disease(FD) is a lysosomal glycolipid storage disorder affecting mostly vessels of all caliber. Painful crises are common in children; young adults may seldom have strokes. Cerebral blood flow studies with Xe-133 and SPECT scans with HMPAO were obtained in 3 hemizygous males and one carrier female, aged 29 to 66 years. All subjects had focal hypoperfusion in both parietal lobes, 3 in one and 1 in both temporal lobes. A 40 yr-old male who had difficulty concentrating and staying alert had become unable to remain employed. He had a low tolerance for carbamazepine which however alleviated his chronic dyesthesia. He responded well to Diltiazem and the improvement in alertness has been sustained for a full year.

Impaired cerebral flow may result from vessel storage as well as autonomic impairment. Our data do not suggest age-dependent deterioration or obvious correlation with clinical problems in FD. SPECT scanning is a useful technique providing objective data on defects of cerebral blood flow which may be more common than suspected.

3-03-14 NEUROLOGICAL MANIFESTATIONS IN TAKAYASU'S ARTERITIS

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Takayasu's arteritis is a rare disorder which affects the aortic arch predominantly and produces occlusive changes in the major branches at their origins. Cerebrovascular attacks appear to be important clinical manifestations of this disorder. However, detailed pictures of the neurological manifestations have rarely been reported. We studied clinical figures, angiographic findings, computed tomography (CT) findings and results of flow imaging studies in 10 patients with Takayasu's arteritis. The patients consisted of one man and nine women. Their ages ranged from 36 to 71 years. All the patients were admitted in our department for neurological evaluations. The majority of them received the diagnosis of Takayasu's disease or radial pulse abnormality more than 10 years prior to the admission. All the patients had occlusion or severe stenosis of the subclavian, brachiocephalic, common carotid and/or vertebral arteries on angiograms. Small collaterals at the neck often supplied flow to the internal carotid artery. Eight patients had a history of cerebral ischemia, whereas the other two had no history of ischemia despite of severe occlusive changes in the common carotid and/or subclavian arteries. The major neurological symptoms were hemiparesis, sensory impairments, hemianopsia, dysarthria, syncope, visual disturbances or seizures. CT revealed cortical and subcortical ischemic lesions in four patients and no ischemic or hemorrhagic lesion in the remaining patients. Flow imaging studies indicated no focal flow reduction in the brain except for regions of infarction. Cerebral ischemic manifestations in Takayasu's arteritis appear to be generally mild probably because of development of collaterals at the neck area.

3-03-15 EFFECTS OF ISCHEMIC AND NON-ISCHEMIC CORTICAL LESIONS ON DELAYED NEURONAL DEATH OF THE ADJACENT HIPPOCAMPAL CA1 CELLS

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In our recent study, small infarction induced in the gerbil cerebral cortex protected the adjacent hippocampal CA1 neurons from the subsequent ischemic injury. The present study was performed to clarify whether other types of cortical injuries also exert similar protective effects. Sixty gerbils were divided into two groups. In Group A, small infarction was produced at the right parietal cortex employing the magnet attached to the skull plus intravenous injection of minute magnetite particles. In Group B, the similar size of cold injury was induced at the right parietal cortex. In both groups, 5-min forebrain ischemia was induced at 1, 3 or 7 days after the infarction or cold injury. In the histological examinations, Group A showed remarkable asymmetry in the extent of CA1 neuronal death. In the left hippocampus, more than 90% of CA1 cells were necrotic, whereas in the right hippocampus, only 30-40% of CA1 cells showed necrosis, provided 5-min ischemia was induced at 1 or 3 days after the infarction. In contrast, Group B showed no such asymmetry. More than 90% of CA1 cells always showed necrosis in both hippocampus. Thus, the small infarction in the parietal cortex protected the adjacent CA1 cells from the delayed neuronal death, whereas the cold injury in the same area did not exert such protective effects. The protective effects may be rather specific to the infarction, which is accompanied by more remarkable cellular and vascular responses in the surrounding tissue than the cold injury.

3-03-16 MR ANGIOGRAPHIC OBSERVATION IN PATIENTS WITH ISCHEMIC EPISODE OF VERTEBRO-BASILAR ARTERIAL PERFUSION AREA

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Object; Our aim of this study is differentiation of thrombosis and embolism by non-invasive MR angiography (MRA), which can be applied even for risky cases or outpatients.

Patients and Methods; Patients listed up were 85 cases (57.0±13.9 y/o), examined by MR angiography in our hospital from May to Dec.1992. Methods used for MRA were 2D,3D-TOF or 2D,3D-PC by 1.5T MR system (GE). Categorization of ischemic episodes in the vertebro-basilar artery (VBA) perfusion area, was made by neurological symptoms and MRI findings excluding cases tentatively diagnosed as "vertebro-basilar insufficiency" without objective signs.

Results; 7 cases (62.8±15.5 y/o) had MRI lesions including lacunar stroke in the VBA perfusion area, and MRA demonstrated evident stenotic lesions in 5 patients (71.4%), and 4 cases were confirmed by direct angiography. Cases with stenosis or occulusion at the major atherosclerotic lesions were mainly diagnosed as having thrombotic infarction.

Conclusion; MR angiography were suitable for screening on vertebro-basilar arterial stenosis, especially in risky cases for invasive angiography. Sequential MRA analysis could be applied for differentiation of thrombosis and embolism, and estimation of therapeutic effectiveness.

3-03-17 TRANSORBITAL DOPPLER AND CEREBRAL BLOOD FLOW MEASUREMENTS IN UNILATERAL CAROTID OCCLUSIVE DISEASE

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We compared the direction and velocity in OA flow with regional cerebral blood flow (rCBF) in 38 patients with strictly unilateral high grade internal carotid artery occlusive disease. Examination was performed before and 20 min after the i.v. administration of 1 g acetazolamide as a vasodilatory stimulus. rCBF was measured by SPECT using xenon-133 inhalation in the perfusion territories of anterior, middle and posterior cerebral arteries. The OA flow was evaluated by transorbital Doppler. The findings were compared with results from 15 healthy volunteers.

In a group of patients with anterograde OA flow both before and after acetazolamide, the baseline rCBF values did not differ significantly from the normal controls in any of the perfusion territories. They were, however, significantly lower on the stenotic side ($p > 0.01$) in a group where the OA flow was retrograde both at rest and after the vasodilatory stimulus, and in the third group, where OA flow was anterograde or "O flow" before and became retrograde after acetazolamide administration. The best vasoreactivity rCBF was found in the latter group.

This finding indicates that the OA is an important collateral pathway.

3-03-18 CLINICAL EVALUATION OF THE NEUROLOGICAL SYMPTOMS ASSOCIATED WITH ANTIPHOSPHOLIPID ANTIBODIES

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Since a clinical association between specific neurological syndromes and the presense of antiphospholipid antibodies(APLAb) has been reported, we have been aware of this association.

Fifteen patients (4 males and 11 females, mean age 40.2 ±10.6 y.o) with positive APLAb and neurological symptoms have been found in our department for 3 years. Seven patients (4 males and 3 females, age 37.4 ±7.2 y.o) complain of either amourosis fugax or scintilation scotoma, seven patients (1 male and 6 females, age 35.4 ±4.7 y.o) of migraine, one of repetitive episodes of cerebral infarction, one of choreoballistic movements with aneurysma and one of optic nerve atrophy with microphthalmia . Five patients have saticified the criteria of systemic lupus erythematodes.

Visual complaints have started at mean age 33.6 ±9.2 y.o and the frequencies of the attacks are various. All patients have no risk factors like hypertension, hyperlipemia diabetes melitus etc. CAT or MRI of CNS were normal except one male who had a small high signal spot at the centrum semiovale in T_2 weighed image. DSA has shown no obvious abnormalities. Four patients have been treated either anticoagulant or antiplatelet therapy. Attacks have been completely controlled by small dose of aspirin in two patients over 40 y.o.

Migraine have started at mean age 29.2 ±2.6 y.o. which is distinctly later than the average onset age of migraine. Though the continuous and tidy treatment has been done, one patient have suffered from several attacks of cerebral infarction and resulted in vegetative state. The further course of TIA and migraine would be followed up and clarified the serological difference between the groups with TIA, migraine, infarction etc.

3-03-19 THE USEFULNESS OF TRNSESOPHAGAL ECHOCARDIOGRAPHY (TEE) FOR DETECTION OF CARDIAC ABNORMALITIES IN EMBOLIC STROKE.

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To detect cardiac source of cerebral embolism we performed both transthoracic echocardiography (TTE) and TEE on 40 patients (men 27, women 13, age range 31-71 years and mean age 50.2 years) with cerebral emolism, and compared efficacy of TTE with TEE to detect intracardiac abnormalities.

Intracardiac abnormalities;	TTE	TEE
Thrombi in Lt. atrium and Lt. atrial appendage	10(25%)	26(65%)
Spontaneous echo contrast	0	6(15%)
Mitral valve calcification	3(7.5%)	4(10%)
Mitral vegetation	2(5%)	3(7.5%)
Intra-atrial septal anenrym	10(2.5%)	3(7.5%)
Patent foramen ovale	0(2.5%)	3(7.5%)

Our data indicate that TEE is very efficient and superior method to detect intracardiac source of cerebral embolism than TTE.

3-03-20 HEMORRHAGIC STROKES IN THE ELDERLY

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Strokes can occur at any age but the incidence rises rapidly in the elderly. An increasingly aging population will mean more stroke victims rather than less.

We retrospectively analyzed the hospital records of 104 patients aged 65 or older admitted to Mackay Memorial Hospital with the diagnosis of intracerebral hemorrhage between October 1991 and April 1992. We found out that hypertension is the most important risk factor. Putaminal hematomas were the most common (42.5%). Thalamic hematomas followed with 27% and lobar hematomas with 14.5%. Nine percent had cerebellar hematomas, 5% had pontine hematomas and 2% had primary intraventricular hemorrhage. The mortality rate was 42.3%. Intraventricular spread of the hemorrhage was found to be a major predictor of mortality. However, herniation of the brain substance and sepsis were also important contributing factors of mortality. Using the Rankin Disability Scale, 18.3% of the survivors had no significant disability, 13.3% were slightly disabled, 18.3% were moderately disabled, 21.6% were moderately severe disabled and 28.5% were severely disabled.

Our data indicate that age is by far the most important determinant of both functional and fatal outcome in patients with hemorrhagic stroke.

3-03-21 RIGHT HEMISPHERE CONTRIBUTION TO RECOVERY FROM APHASIA – PET IN WERNICKE-TYPE APHASIA.

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A verb generation task, which in normal subjects leads to activation of a frontal and a posterior area in the left hemisphere (Broca and prefrontal cortex respectively Wernicke), was used to study reorganizational changes in the language processing system after stroke.

We studied six male right handed patients who had recovered from Wernicke type aphasia due to a posterior middle cerebral artery territory infarction on the left side. The regional cerebral blood flow was measured with PET using an integral O-15 CO2 inhalation technique during rest, during repetition of legal neologisms and during a verb generation task. After transformation into the standard stereotactic space of Talairach & Tournoux and removal of global flow differences, a planned comparison on a pixel by pixel basis between conditions was performed.

In both tasks a frontal (50,24,12) and a posterior (50,34,16) area in the right hemisphere, homologous to Broca's/ lateral prefrontal cortex and Wernicke's in the left hemisphere, were activated. During the verb generation task there was additional activation in the left dorsolateral prefrontal cortex.

There is considerable scope for functional plasticity in the cortical network related to language. In recovery from Wernicke aphasia, activation of right sided cortical fields homologous to those in the left hemisphere in normals may represent language transfer to the right hemisphere.

3-03-22 A STUDY ON CHANGES IN CEREBRAL BLOOD FLOW DURING TILT TEST USING TRANSCRANIAL DOPPLER METHOD

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Cerebral blood flow was measured in patients during tilt test using transcranial doppler method. Subjects consisted of 8 healthy young adults, 9 patients with cerebral infarct and 13 patients with Parkinson's disease, totaling 30. Using Trans-scan (EME Inc.) to detect the left middle cerebral artery(MCA) of each patient in supine position on a tilt table, and to determine the waveforms of flow verocity(FV) at the site about 5~20mm from origin of MCA. The table was then raised to the standing position of 70 degrees. Waveforms were recorded at intervals between one and 10 min, and the subject was again brought down to the supine position to continue the measurements up to 10 min. Blood pressure(BP) and pulse rate(PR) of radial artery were also measured. In healthy volunteers BP and PR increased after standing but returned to the baseline values on reversion to the supine position. The FV of MCA and Pulsatility Index(PI) decreased after standing and returned after reverting to the supine position. In patients with cerebral infarct, BP,PR and FV of MCA were similar to those of healthy volunteers, however, PI increased after standing, and it returned on assumption of the supine position. In patients with Parkinson's disease, the values of nine patients were the same as the normal volunteers, while in the remaining four patients, BP and FV of MCA decreased and PI increased on standing and returned. There seemed to be differences in cerebrovascular reactivity on standing in patients with various diseases.

3-03-23 THE FOLLOW-UP STUDY OF BLOOD VISCOSITY IN THE PATIENTS WITH ACUTE ISCHEMIC STROKE.

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Hyperviscosity may be termed the physicochemical risk factors of stroke. The purpose of this study is to clarify whether elevated blood viscosity is causally related to the ischemic event or is associated with the epidemiological risk factors of stroke.

A total of 127 patients with acute ischemic stroke were included in the study. There were 25 females and 102 males with a mean age of 65±10 years. The same number of control cases matched with age and sex were selected from healthy volunteers. The fasting blood was taken for the meassurement of blood viscosity parameters.

The results showed impairement of whole blood viscosity ($P<0.001$), plasma viscosity($P<0.01$) and erythrocyte aggregability($P<0.001$) in the patients studied, but no significant difference in hematocrit and RBC deformability was found between study cases and controls. Longitudinal follow up study conducted 3 weeks(96 cases) and 3 months(64 cases) later showed that hyperviscosity phenomenon was persisted.

This study provides the evidence that impaired blood viscosities are present not only in patients with acute cerebral infarction, but also in those with chronic stage of stroke which may be associate with the risk factors of stroke such as hypertension, diabetes and heart diseases.

3-03-24 DO METEOROLOGICAL AND SEASONAL VARIATIONS EXIST IN STROKE?

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The aim of this study was to find out the possible relationships between climate and occurrence of CI. Materials consists of 826 pts with CI/cerebral infarction, hemorrhage § SAH. BI score and Glasgow coma scale were used for quantification of neurological deficit. Local climatological data during day and month, their actual values atmospheric temperature-At, equivalent temp-Eqt, atmospheric pressure-Ap, and humidity-Asp, and inter- and intradiurnal changes in relationship to occurrence of CI were analysed. Results showed significantly highest occurrence of CI in April. The occurrence of ICH was variable and lowest of SAH was in July. It was found significant correlation between CI and interdiurnal decrease of At and Asp and actual At below 0°C and actual Ap at 99.32 kPa.

3-03-25 THE IMPACT OF RACIAL ORIGIN ON ISCHEMIC STROKE ETIOLOGY: THE UCSD STROKE DATA BANK

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Although some evidence exists to suggest that stroke mechanisms and risk factors may vary according to an individual's racial origin, little is known regarding the relative incidences of ischemic stroke etiologies amongst different racial groups. We acutely evaluated 500 consecutive patients presenting with ischemic stroke and in each case assigned an etiology for the stroke according to predetermined diagnostic criteria. The following results were found:

Stroke Etiology%

Race(n;%)	LVA	CE	Lacunar	Other	Unknown
White(332;66)	12	15	33	15	25
Black(56;11)	20	5	36	10	28
Hispanic(77;15)	11	9	26	8	47
Other(35;7)	6	27	35	12	23
Total(500;100)	12	14	32	13	28

These data suggest that the specific etiologies of ischemic stroke do not vary significantly according to race in our urban Southern California population.
LVA = large vessel atherothrombotic/embolic
CE = cardioembolic

3-03-26 STROKE OUTCOME IN A POPULATION BASED REHABILITATION PROGRAMME

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A stroke register was started in August 1989 in two districts with an active rehabilitation programme (AD) and two control districts (CD) with a total study population of 135000. 585 patients in all were included during the two years. The total annual incidence was 217/100000/y. The mean age was 74±11 years for women and 68±13 years for men. The type of stroke was very similar in both districts: 79% were brain infarctions, 13% intracerebral hemorrhages, 5% subarachnoid hemorrhages and 3% unspecified strokes. The case fatality was 29% (90 of 307) in the AD and 38% (105 of 278) in the CD at one year ($p<0,05$). In the AD 48% (103 of 213) and in the CD 49% (80 of 163) were in Rankin grades I-II at one year. Of all patients 57% in the AD (175 of 307) and 43% in the CD (119 of 278) were living at home at one year ($p<0.05$). The total time of hospital care for stroke during the first year was 55 days in the AD and 54 days in the CD. In conclusion the case fatality was lower and more patients were at home in the AD without increase in hospital care days.

3-05-02 COMBINED MAGNETIC RESONANCE IMAGING (MRI) AND MAGNETIC RESONANCE SPECTROSCOPY (MRS) STUDIES IN SIX CASES OF LEIGH DISEASE

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We examined six children (3 males, 3 females, 1-12 years of age) with proven Leigh disease by means of MRI and localized proton MRS. Two children underwent serial studies.
The MRI protocol consisted of T1 and T2 weighted images. For MRS we used a stimulated echo sequence (STE) with a TR = 1500 ms and TE = 270 ms. Spectra were targeted to the basal ganglia in all and additionally to the deep white matter in four children.
MRI revealed typical lesions of the basal ganglia in all and abnormalities of the brain stem in four patients and cerebellum in three patients. In one patient lesions within the cortical gray matter were detected. The periventricular white matter appeared normal on MRI in all children.
Proton spectra yielded abnormally increased lactate of the basal ganglia in all and increase in cerebral lactate within the white matter in four occasions. Serial observations did not reveal significant changes.
These results suggest that proton MRS will become a powerful tool in the in vivo diagnosis of Leigh disease, as it does not only show metabolic changes within the MRI detected lesions, but is also able to demonstrate alterations on a subcellular level where images appear normal.

3-05-03 FAMILIAL OCCURRENCE OF ATTENTION DEFICIT, READING, MOOD & SLEEP DISORDER IN ADHD WITH AND WITHOUT READING DISORDER

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42 DSM IIIR ADHD patients, 13 of whom also met DSM IIR criteria for RD were compared by structured interview of parents and patients with 49 neurologic controls as to familial occurrence in first degree relatives of ADHD, RD, mood disorder and sleep disorder in a referral outpatient adult/developmental neurologic service. N = 29 ADHD without RD (25 M; mean age 12), 13 ADHD with RD (9 M; mean age 12) ad 49 neurologic controls with no ADHD or RD seen for non-behavioral symptoms (36 M, mean age 27). Dysthymic, major effective and bipolar disorders were combined. Analysis was by Cochran-Mantel-Haenszel statistic. Family history-ADHD: control 1 (2%); ADHD only 7 (24%) P = .002; ADHD + RD 4 (31%) P = .001. RD: controls 3 (6%); ADHD 9 (31%) P = .003; ADHD + RD 9 69%) P = < .001 and .02 vs. ADHD only. Mood Disorder: controls 7 (14%); ADHD only 13 (45%) P = .003; ADHD + RD 5 (38%) P = .013. Sleep Disorder: controls 0; ADHD only 0; ADHD + RD 4 (31%) P = .001. Concurrent family diagnosis: RD and ADHD - control 0, ADHD only 2, ADHD + RD 2; ADHD or RD with mood disorder - controls 0, ADHD only 5, ADHD + RD 4. Two of the 4 families with RD and sleep disorder included 2 with depression. Childhood ADHD with or without RD is associated with increased risk of familial occurring ADHD. Concurrent RD is associated with an increased risk of RD in family members. The RD in ADHD therefore may be familial and similar to other forms of familial RD. ADHD with or without RD increases the risk for familial mood disorder. Thus when mood disorder is co-morbid with ADHD it may be familial in origin. The presence of RD increases the probability of familial sleep disorder. Future investigation should correlate family history in ADHD with biobehavioral measures.

3-05-04 HEREDO FAMILIAL HORIZONTAL GAZE PALSY AND IDIOPATHIC SCOLIOSIS: A REPORT OF THREE CASES AND REVIEW OF THE LITERATURE.

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A report of three siblings of two families with paralysis of horizontal gaze associated with scoliosis of the same pattern and coexistence of B-Thalassemia Trait.

In one family, Two siblings have additional bilateral facial dyskinesias with fine, low amplitude, intermittent pendular nystagmus.

Normal vertical gaze and near triad with absence of oculocephalic and horizontal vestibulo-ocular reflexes are compatible with nuclear or paranuclear pontine structural lesion.
(MRI), Electrophysiological procedures, (HLA) tissue typing and chromosomal analysis are complementary investigations to Evaluate the Abnormalities detected.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-05-05 ORNITHINE TRANSCARBAMYLASE DEFICIENCY: CLINICAL FINDINGS AND OUTCOME IN FIVE SYMPTOMATIC FEMALES.

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Ornithine transcarbamylase deficiency (OTCD) is an X-linked recessive disorder of urea biosynthesis. We describe the clinical and laboratory findings in five heterozygous female children with OTCD. Onset of symptoms referable to the disease was in the first year of life, but diagnosis was delayed by up to 15 years. Symptoms included recurrent vomiting with lethargy (5 patients), protein avoidance or intolerance (5), irritability (4), severe encephalopathy (3), ataxia (3) and acute hemiparesis (2). All eventually had evidence of at least mild developmental delay or learning difficulties. Severe hyperammonemic encephalopathy was not invariably associated with serious neurologic sequelae (2/3). The diagnosis was confirmed by a finding of decreased hepatic OTC activity (3) or the presence of orotic aciduria in association with hyperammonemia (2); one had a positive allopurinol loading test. Computed tomography (CT) scans showed frontal hypodensities (3/4) and magnetic resonance (MR) scans demonstrated high signal intensity lesions in the same area (1/2), both consistent with cerebral infarction. OTCD should be considered in the differential diagnosis of acute or chronic encephalopathy in females at any age, because early treatment may improve the neurological outcome.

3-05-06 CARBAMAZEPINE MONOTHERAPY IN INFANTS

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Very little data on the use of carbamazepine in infants is available. We report our experience on the use of carbamazepine monotherapy in infants between the ages of one month and two year. Twenty infants with more than one seizure were enrolled. Ethical Committee approval and parental consent were obtained. All patients had a detailed neurological examination, EEG, CT/MRI and additional relevant studies. Seizures were classified according to the International Classification of Seizures. Loading dose of 10 mg/kg was followed by blood level measurements at 2, 4, 8, 12 and 36 hours. Maintenance dose of 20 mg/kg/day divided into three equal doses was started after 36 hours. Maintenance carbamazepine and 10-11-epoxide levels were done at 4, 8, 15, 30, 60 and 90 days and at monthly intervals thereafter. Liver function tests and full blood counts were checked on each visit. No other anticonvulsants were required. The patients were followed from 6-18 months.

Complete seizure control was obtained in almost all patients. No side effects were observed. Therapeutic levels were achieved in all. Details of the pharmacokinetic data will be presented.

3-05-07 INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM IN PEDIATRIC LUPUS ERYTHEMATOSUS

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Central nervous system involvement in systemic lupus erythematosus (CNS-SLE), is well known in adults, but rarely described in children. We retrospectively reviewed the charts of 91 patients with pediatric SLE and documented 39 cases of CNS-SLE. The mean age of onset of SLE was 13,5 years ranging from 7-17,5 years.

Of the 39 cases of CNS-SLE 16 (41%) had one or more neurological symptom. Seizures were present in 8 (21%), 5 had cerebral ischemic events (13%), 1 had chorea(2,5%), 1 had sinuous venous thrombosis (2,5%), 2 had papilloedema (5%) and 2 had peripheral neuropathy (5%). Neuropsychiatric SLE (NPS-SLE) was present in 19 children (48%) and this included depression, concentration or memory problem and frank psychosis in 11 cases. 6 patients had both neurological and NPS-SLE, 9 (23%) had merely lupus headache. In 19 cases the CNS manifestation was a primary symptom of SLE. In 12 patients CNS-SLE was present within the first year after diagnosis of SLE. Most patients (90%) had either complete resolution or significant improvement of their CNS-SLE, while 1 child died of cerebral haemorrhagic infarction and 3 others had significant persistent CNS deficits. In our retrospective study of 91 cases of pediatric SLE, we had a 42 % frequency of CNS-SLE and 79% presented within 1 year of diagnosis. The majority had excellent recovery from CNS-SLE including psychosis.

3-05-08 PREVALENCE OF EPILEPSY IN ELEMENTARY SCHOOL CHILDREN IN MEXICO.

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The objective was to know the prevalence of epilepsy in 23,000 elementary school children in México. The study was undertaken in the facilities of the Secretariat of Public Education. The INNN trained 46 center directors to undertake the study, and they in turn trained the teachers who administered a questionnaire to 500 children from each center in the country's 32 federal entities. The questions about epilepsy had a total sensitivity of 96% and 89% specificity. The results from 21,264 children are presented, equivalent to 92.5% of the population proposed for the study. The rates per 1 000 elementary school students studied are: global, 42.2. By state, the maximum value was for Sonora with 114.0 and the minimum was for Hidalgo with 8.0. In 4,000 students who also received a clinical diagnosis the prevalence rate of epilepsy was 11.4 per 1 000 students studied. By sex, a rate of 10.5 was found for male and 12.3 for female.

3-05-09 DOES SODIUM VALPROATE MONOTHERAPY CAUSE HEPATOCELLULAR DYSFUNCTION?

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Sodium Valproate (VPA) is the most effective anticonvulsant in childhood. However liver dysfunction including hepatocellular failure has been reported in children on VPA leading to the restriction of its use in young children.

In an ongoing study we assessed hepatic function in children prior to and after commencing monotherapy with VPA and also compared this to established values. As well as conventional hepatic function tests (aminotransferases, ammonia, coagulation) we radioimmunoassayed Glutathione-S transferase (GST) B1. This cytosolic detoxification enzyme has been shown to be the most sensitive index of intact liver function. 39 children (mean 4.7 yr, range 6m-10y) had baseline investigations prior to VPA and these were repeated once established on VPA therapy (20-50mg/kg/day). VPA levels were also assessed for compliance and toxicity. There was no clinical toxicity noted (one child was withdrawn from VPA due to alopecia). There was no significant difference in hepatic function including GST B1 after Valproate and also compared to age matched controls ($P = 0.57$). We noted abnormal GST B1 values in young children on combinations of anticonvulsants (Phenytoin, Carbamazepine) in the absence of clinical hepatic dysfunction.

This study shows that in these children, VPA monotherapy did not significantly alter hepatocellular function and suggests that in this group the risk/benefit ratio for VPA monotherapy is favourable.

3-05-10 OPERANT NEUROFEEDBACK TRAINING WITH ADD and ADHD CHILDREN.

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The development of computer-based power-spectral analysis and display of EEG is expanding the possibilities for the study of physiological correlates of cognitive tasks. This new technology now permits us to observe, record, and display the EEG patterns produced while doing a series of cognitive, school-type tasks.

Preliminary research has shown that the attention-disordered child produces a significantly different EEG pattern while on-task--typically producing large quantities of theta (4-8Hz) and relatively less beta (12-20Hz) when compared to age peers of average school performance.

We have been employing an operant neurofeedback training model to develop and strengthen a physiologic response that more closely approximates the on-task pattern of successfully attending children.

We report post-training follow-up data on several children. Parents and schools report improved academic and behavioral functioning.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-05-11 EFFECTIVENESS OF BACLOFEN IN UNVERRICHT-LUNDBORG DISEASE (ULD)

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AB, a 15 year old Polish girl, was well until 3 years of age when she developed progressive ataxia and myoclonus with slowly progressive intellectual deterioration. By 11 years she was wheelchair bound. She emigrated to the USA and was seen at Bellevue Hospital in December 1992. At that time she was noted to have severe poly-myoclonus and ataxia. She was unable to walk, sit unsupported, write, draw or feed herself. Speech was slurred. She was on therapeutic levels of Valproic Acid and Clonazepam. CT scan, BAER, VER, skin biopsy for La fora bodies, sialic acid, GM1, GM2, chromosomal analysis, organic and amino acids were all normal. An EEG showed diffuse slowing with occasional parasagittal bursts. A diagnosis of Unverricht-Lundborg Disease was made and the patient was placed on Lioresal (Baclofen) 120mg/day. With this therapy, AB can now stand alone, walk with support, write legibly, draw pictures and feed herself. As far as we know, this is the first report where Lioresal given to a patient with ULD resulted in sustained improvement of symptoms. Writing samples, drawings and a video will be demonstrated.

3-05-12 CLINICO-GENETICAL STUDY OF CEREBRAL PALSY(CP)

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To delineate the clinical types and study its relative incidence, including that of mental retardation present singly or in combination (Fay's classification - 1950). Genetic karyotype study was done to investigate the probability of any specific karyotype abnormality.

Fifty cases of CP have been studied. A thorough psychiatric and neurologic examinations done including a CT scan (MRI where indicated) and biochemical parameters to exclude recognised causes of mental retardation. Studies of chromosomal constitution of the patient and their parents by leucocyte culture, fetomaternal ABO and Rh combinations and pedigree patterns were done.

Mental retardation (45), motor weakness and/or spasticity (35), basal ganglia and mixed - (28), convulsive disorder (24): Fay's classification critically assessed. Greater amount of familial aggregation, chromosomal abnormality in the form of deep constriction in centromeric region of one of the A group chromosome and feto-maternal ABO incompatibility compared to those of the control population were observed.

This finding calls for attention for further genetic study of CP patinents for helping genetic counselling.

3-05-13 ISOLATION OF ADENOVIRUS TYPE 11 FROM THE BRAIN OF A NEONATE WITH PNEUMONIA AND ENCEPHALITIS.

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We report a fatal case of adenovirus pneumonia accompanied by encephalitis in a neonate. The patient was a 2,768g Japanese male infant vaginally delivered after 38 weeks' gastation without asphyxia. The mother had no illness during the pregnancy or labor. He became lethargic on the 6th day. On admission (the 9th day), his chest radiograph showed interstitial markings in both lung fields. After right hemiconvulsion on the 11th day, he went into coma and died on the 12th day. At autopsy, adenoviral particles as well as intranuclear inclusions were noted in pulmonary alveolar epithelium cells. The histology of the brain disclosed perivascular cuffing, which is one of the pathognomonic findings for acute viral encephalitis. Adenouirus type 11 was isolated from lung, hilar lymph node, and brain tissue. To our knowledge, only 15 cases of neonatal adenovirus pneumonia have been reported previously, but virus has not been isolated from the brain or cerebrospinal fluid despite the presence of neurological symptoms. This is the first instance of adenovirus isolation from brain tissue in a newborn infant. The virologic and neuropathologic findings suggest the invasion by adnovirus of neural tissue and substantiate the significance of neurological symptoms observed in neonatal adnovirus infection.

3-05-14 EFFECTS OF IN UTERO FETAL MEDICAL IONIZING RADIATION ON HEAD CIRCUMFERENCE AT BIRTH

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There are few studies that have investigated the effects of single or incidental medical ionizing radiation in utero on head circumference at birth. The nature of medical practice in Rochester, Minnesota, and the Mayo Clinic medical records-linkage system enabled unusually accurate retrospective determination of radiation absorbed dose of x-ray procedures in 9,790 pregnancies of 2,980 women pregnant in Rochester and the unincorporated surrounding area between 1918 and 1973. For each type of x-ray procedure, dosimetry was calculated for ovary and fetal exposure depending on the duration of the pregnancy and type and historical time of the procedure. Data were analyzed by multiple regression analysis for exposure for each trimester of the pregnancy. Only pregnancies with more than 80% available prenatal records were included in the study; neonates with gross anatomical abnormalities, such as hydrocephalus or meningomyelocele, were excluded from the study. Results indicate that medical ionizing radiation in the second ($p<0.001$) and third ($p<0.01$) trimesters of more than 300 mrad were related to significantly decreased head circumference ($N=7,479$). In contrast, there was no significant effect of radiation exposure in the first trimester. Although the magnitude of effect size was relatively small (0.4% range), it should be noted that the majority of exposures were single procedures during pregnancy.

3-05-15 A NEW SYNDROME OF PRIMARY SENSORY NEURON DEGENERATION.

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We describe a progressive disease consisting of visual loss, deafness and sensory ataxia of apparent autosomal recessive inheritance. Its pattern differs from that previously described in kindreds with these cardinal features. These deficits also occur in several metabolic disorders. After identifying the index case, we prospectively found two more children with the same clinical course. They had MRI scans, EMG and biochemical studies. All three children (two boys, one girl and two sibs) presented with sensorineural deafness or ataxia, and suffered progressive ataxia plus loss of hearing and vision. All had atypical pigmentary retinopathy, areflexia, distal sensory loss and dysarthria. Language was unaffected. MRI scans and metabolic studies were negative. EMG showed predominantly sensory neuropathy; audiograms confirmed sensorineural hearing loss. Sural nerve biopsy showed slight axonal loss and demyelination. Mild neurogenic atrophy was present in muscle. We have designated this syndrome Primary Sensory Neuron Degeneration to emphasize its earliest, most debilitating manifestations. We infer that the defective gene product in this disorder is critical to the metabolism of sensory neurons.

3-05-16 DIRECT MEASUREMENT OF FREE RADICALS IN NEONATAL MOUSE BRAIN SUBJECTED TO HYPOXIA : AN ELECTRON SPIN RESONANCE SPECTROSCOPIC STUDY

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Free radical generation in the neonatal mouse brain subjected to acute hypoxia was measured directly by using electron spin resonance spectroscopy. Free radical(FR) density was investigated during exposure to N_2 gas (N_2 group) or CO_2 gas (CO_2 group) and its subsequent recovery in air. FR density in the N_2 group declined during hypoxia and returned to the prehypoxic level during recovery. In the CO_2 group, it increased during hypoxia and returned to the control level during recovery. The main origin of the spectrum of control brain was considered as being the coenzyme Q_{10}(CoQ_{10}) radical in the mitochondria. The change of FR density during hypoxia and recovery in the N_2 group was thought to be correlated with changes in CoQ_{10} radicals. The increase of FR density in the CO_2 group during hypoxia suggested the generation of some FRs other than CoQ_{10} radical. We conclude that the FRs which appeared during CO_2 hypoxia may play some role in producing the difference in brain injury between the two kinds of hypoxia.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-05-17 DIURNAL VARIATIONS OF PLASMA VALPROIC ACID AND CARBAMAZEPINE CONCENTRATIONS IN CHILDHOOD AND ADOLESCENCE EPILEPSY. COMPARISONS BETWEEN SLOW RELEASE AND CONVENTIONAL FORMULATIONS.

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Serial measurements of valproic acid /VPA/ and carbamazepine /CBZ/ concentrations in plasma were performed within 24 hours in patients with epilepsy aged 3 to 18 years, receiving slow release or conventional forms of these antiepileptic drugs.

The plasma VPA and CBZ levels were estimated in the TDX Analyzer /Abbott/.

The diurnal oscillations in the VPA plasma concentrations were approximately half as large with Depakine Chrono /Sanofi/ than with the conventional from of this drug. The clinical efficacy of both drugs as well as the occurence of the side effects were comparable.

The diurnal CBZ plasma concentration curves during treatment with the slow release formulation /Neurotop Retard - Gerot/ showed significantly less variations over 24 hours than during treatment with ordinary preparations as measured by the fluctuation index. There were no differences in efficacy between the two forms of CBZ but there was a clear - cut reduction of reported side effects during the treatment with the slow release CBZ formulation, which is of particular importance for children and adolescents with chronic epilepsy.

3-05-18 THE EFFECTS OF LOW DOSE RADIATION ON NEURONAL MIGRATION IN THE RAT CEREBRAL CORTEX.

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In order to study the effects of low dose radiation on neuronal migration and cell adhesion molecules of cerebral cortex, pregnant Wistar rats on the 16 th day of gestation were intraperitoneally labeled with ^{3}H-thymidine, and irradiated with 5, 10, 15 or 20 cGy one hour after the labeling. After 24, 48, 72, 96 hours of radiation, the fetal brains were removed and paraffin sections of cerebral cortex were prepared. Neuronal migration was autoradiographically evaluated, and staining patterns of neural cell adhesion molecule (N-CAM), L1, neurofilament, tau protein and microtubule associated protein 2 (MAP2) were immunohistochemically studied. In 15 and 20 cGy radiation groups, neuronal migration was delayed, and staining pattern of N-CAM changed : N-CAM was not detected on matrix cell layer after 24-48 hours of radiation, but recovered after 72-96 hours. Staining patterns of L1, neurofilament, tau protein and MAP2 were not affected.

This study suggests that radiation as low dose as 15 cGy suppresses neuronal migration and that N-CAM may have an important role in neuronal migration.

3-05-19 MRI OF ULEGYRIA

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The term "ulegyria" (gyral scarring) refers to the scarring of the cerebral cortex following hypoxic-ischemic insult in perinatal stage or early life. Here we report 18 cases of ulegyria diagnosed by MRI. Five cases were caused by perinatal & neonatal asphyxia, 8 cases by infantile head injury (when 3 days to 7 months old), 5 cases by infantile meningitis (when 3 days to 7 months old). The locations of ulegyria caused by infantile asphyxia were in the parasagittal watershed areas. The infantile head injury caused strangulation of ICA leading to infarction, and finally developed ulegyria in the territory of ICA. The ulegyria in cases of infantile meningitis also in the territory of major arteries, possible is the result of occlusion due to arteritis.

So, despite the different etiology, the true mechanism of cause of ulegyria is hypoxic-ischemic insult in the infantile brain before the seventh month of life. The MRI can depict the ulegyria as early as 2 months after the brain tissue received hypoxic-ischemic insult.

3-05-20 LAMOTRIGINE AS ADD-ON THERAPY IN PAEDIATRIC PATIENTS WITH TREATMENT-RESISTANT EPILEPSY - AN OVERVIEW.

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Lamotrigine (Lamictal®, LTG) is being studied as add-on therapy in five open trials in paediatric patients (age 2-16 years) with refractory seizures of any type. LTG has been administered to 323 children at 37 centres at an initial dose based on the patients's body weight and concomitant antiepileptic drugs (AEDs). The dose was escalated over one month and could be increased to a maximum of 15 mg/kg (or 400 mg/d) in patients taking liver enzyme inducing AEDs and 5 mg/kg (or 200 mg/d) in those receiving valproate alone or in combination with other AEDs.

Analysis of 79 patients aged less than 6 years and 206 aged 6-12 years showed that the most commonly reported adverse experiences up to 48 weeks are somnolence, vomiting, increased seizures and rash. Laboratory parameters, vital signs and measures of growth did not show any consistent findings of clinical significance. The safety of LTG treatment up to 12 months has been demonstrated in these patients.

In the first 69 patients analysed, 37% showed at least a 50% reduction in total seizures in the first 12 weeks. Lamotrigine appears to be effective over a broad range of different seizure types and seizure syndromes.

3-05-21 FERRITIN, CREATINE KINASE, AND NEOPTERIN IN SUBACUTE SCLEROSING PANENCEPHALITIS.

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To study the disease process in the brain in subacute sclerosing panencephalitis (SSPE), sequential changes in ferritin, creatine kinase (CK), and neopterin in the cerebrospinal fluid (CSF) of two patients with SSPE were compared with the changes in the clinical signs and symptoms and the findings by magnetic resonance imaging (MRI). On the basis of changes in various substances in the CSF, especially ferritin, CK, and neopterin, we concluded that the high-intensity areas in MRI might be evidence of local inflammation and the resultant cell damage. Ferritin, CK, and neopterin seemed to be biochemical markers in patients with SSPE for evaluation of the extent of lesions, and their measurement may provide information useful for evaluation of the therapeutic response.

3-05-22 PAEDIATRIC NEUROCYSTICERCOSIS IN NORTH-WEST INDIA: A CLINICAL PROFILE

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Twenty-one patients (12 male, 9 female) in the age group of 3 1/2 - 15 years with cerebral cysticercosis were studied between 1986 - 1991 and followed up for a period of 6 - 12 months at Postgraduate Institute of Medical Education and Research, Chandigarh. There was a preponderance of male patients (12 males, 9 females). The duration of symptoms varied between 1 month - 3 years (median duration - 8 months). Seizures (partial 9.5%, and generalized 47.6%) were the presenting features in 11 (52.3%) patients. Twelve patients (57.14%), however, presented with symptoms of raised intracranial pressure. Seizures were not the predominant symptoms in these patients. Six patients had decreased vision (28.5%) while one had optic atropy (4.7%). One of these 21 patients showed evidence of chronic meningitis. The CT scan revealed diffuse parenchymal lesions in 7 (30%), hydrocephalus in 2 (9.5%) and was falsely negative in 4 patients. Cystic lesions were clearly demonstrable on MRI. Four patients had a positive blood serology while CSF serology was negative. EEG done in all these 21 cases showed abnormalities in the form of slowing in ten, siezure activity in eleven and polymorphic delta activity suggestive of mass lesion in two patients. Cysticidal therapy was given to eight patients (38%) having evidence of raised intracranial tension and/or epilepsy. Out of these, seven received albendazole while the eighth patient received praziquantel therapy. Steroids were given to 5 patients along with cysticidal therapy. It was seen that there was a decrease in cyst load after cysticidal therapy. However seizure control was poor or minimal. Five patients underwent surgery (23.8%). Four had frontal lobectomy while the fifth patient underwent shunt surgery.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-05-23 HIPERBILIRUBINAEMIA AS A RISK FACTOR FOR DEVELOPMENTAL DISTURBANCES

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Early diagnosis, as well as an early application of appropriate prophilactic measures and therapy can prevent one of the most difficult consequences: hyperbilirubinaemic encephalopathy, a damage of the basal nuclei and also of the cortex of the central nervous system. This damage may result in mental retardation and sometimes in impairment of perceptive hearing. In this paper the results of the assessment of psychomotoric and speech development in 24 three-year-old children have been presented. The results have shown a delayed onset of speech and walking in comparison with the children of the same age born without the risk. In addition, the level of psyhomotoric organization in these children was delayed, i.e., 66.7 of the children had disharmonic development, while difficulties in articulation were present in 22.8. A delayed development of certain factors and functions indicate the necessity of an early stimulation during the first months of life, which can prevent possible troubles in cognitive functioning.

3-05-24 A SYNDROME OF OLIVOPONTOCEREBELLAR ATROPHY WITH ONSET IN INFANCY.

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Olivopontocerebellar atrophy(OPCA) is rare in childhood and onset in infancy is uncommon.We describe the clinical and radiological features in 14 Omani children with OPCA of onset in infancy.There were 6 males and 8 females with ages ranging 2 to 8 years.The onset was in the first year and manifested as imbalance in sitting,standing and walking. Speech delay was present in 11 and seizures in 4 children. Consanguinity in the parents was seen in 8 and a family history in 5 cases.

On examination,height,weight and head circumference were below the 3rd centile in 8;impaired hearing and speech were seen in 11 children.Ocular abnormalities seen included convergent squint,reverse ocular bobbing,loss of saccades and retinitis pigmentosa.Cerebellar axial and appendicular ataxia was seen in all patients.

Complete blood counts,urine aminoacidogram and blood biochemistry were negative for metabolic disorders.The CT scan showed the characteristic fetures of cerebellar and pontine atrophy.Brainstem auditory evoked response abnormalities were seen in 7 patients.

The profile of OPCA of infantile onset is characterised by progressive cerebellar ataxia,high occurence of hearing and speech impairment and the typical CT scan features.

3-05-25 MIGRAINE IN STROKE AND STROKE IN MIGRAINE: TWO NEUROPEDIATRIC CASE REPORTS.

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Migraine may be associated with cerebrovascular disorders either by increasing the risk of stroke in general, or by causing a neurological deficit classifiable as migrainous stroke. In rare cases even children and adolescents with migraine may be afflicted by a cerebrovascular disorder. Out of 138 consecutive young patients with migraine we report two cases in which migraine was associated with stroke.

Case 1 is a 15 years old boy with a history of migraine with aura who suffered persistent left sided hemianopsia associated with a right occipital ischemic lesion in CT and MRI. In contrary to the initial diagnosis of migrainous stroke, further investigations revealed an open foramen ovale and an atrial septal aneurysm suggesting cardiogenic embolism mimicing migraine. Accordingly, the patient has received warfarin and has had no more headache or neurological symptoms since then.

Case 2 is an 8 years old girl with a history of minimal cerebral dysfunction and elementary partial seizures who presented with a dramatic condition including an initial generalized tonic-clonic seizure, headache, vomiting, drowsiness, short-lasting tetraparesis and prolonged blindness for 8 hours. The clinical course was consistent with basilar migraine. CT showed an ischemic lesion in the left occipital lobe, however, without clinical evidence of hemianopsia.

Our cases illustrate the spectrum of possible associations between migraine and stroke in young patients.

3-05-26 AN ASYMPTOMATIC CASE OF ADRENOLEUKODYSTROPHY(ALD) TREATED WITH BONE MARROW TRANSPLANTATION(BMT) AND DIETARY THERAPY WITH AN 8 YEAR FOLLOW-UP.

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BMT has been tried for the treatment of ALD without satisfactory results, and an attempt to reduce high plasma levels of very long-chain fatty acids(VLFA) was experimentally tried. We present an asymptomatic case, a sibling of a previously recognized case as ALD, treated with BMT and dietary therapy.

The present case, 7 year-old boy(M.F.) is a younger brother of a previously diagnosed case of ALD(T.F.). The proband(T.F.) began to manifest auditory and visual disturbance at 4 years of age and in spite of strict fat restriction and oleic acid therapy, he expired at 6 years of age. Demyclinating process revealed by MRI and increased serum VLFA levels confirmed the diagnosis. Blood examination revealed an increase in serum VLFA in the presented case, his mother, and grand mother. Because of the miserable outcome of T.F., informed consent was obtained from parents, and at 1 year and 10 months of age, M.F. underwent BMT from his elder sister, matched doner. Her VLFA was not increased. Adrenal dysfunction was confirmed by ACTH rapid test, and cortisol was administered form 4 years of age. Together with former treatment, dietary fat restriction and administration of GTO-GTE(Lorenzo oil)was started. At 7 years of age, the patient did not manifest any neurological deficits clinically, radiologically, and electrophysiologically. Serum VLFA was decreased to the normal level.

A long term follow up was considered necessary to determine the efficacy of BMT and dietary treatment in this disorder.

3-05-27 TIMING CEREBRAL PROCESSES FOR CONTROL OF SPEECH IN CHILDREN

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A poligraphic methodology for the measurement of latency times of oromandibular EMG, EGG, PNG and ACG (acousticograms) responses to couple of words and non-words with immediate execution of different delays (0.1, 1.5 sec) has been applied in our laboratory in the last 2 years in normal subjects and patients affected by neurological diseases (Pinelli and Ceriani, Speaking, Ed.Ambrosiana; Current Opinion in Neurology and Neurosurgery, 1992, 5).

In Italian speaking, 5 to 15 years old children the target couples of words presented in PC were: mamma/papà and mare/muro in 12 successive trials. Mean latency times, mean ACG duration and standard deviation have been measured. The methodology allows to analyze the development of the neural substrates for combinatorial hierarchical phonetic organization.

3-05-28 CLINICOPATHOLOGIC ANALYSIS OF 5 CASES OF INFANTILE PROGRESSIVE SPINAL MUSCULAR ATROPHY (WERDNIG-HOFFMANN DISEASE)

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Five cases of infantile progressive spinal muscular atrophy (IPSMA) having confirmed by clinicopathology were reported. 3 are males, 2 are females. Ages: 4 are 2 months old, one is 3 years old.

The disease onset just after birth in 4 cases, and all died within 3 months. 1 case began 2 months after birth and died at 3 years old. Clinical manifestations are progressive hypotonia and reduction of muscle power and spontaneous movement. Intercostal muscles actually fail, the chest collapses. All complicated with respiratory tract infection, and died from respiratory failure.

Pathologic change shows conspicuous loss of anterior horn cells. Motoneurons in the brainstem are also affected. Some of the residual cells are in the process of degenerating or are being phagocytized by satellite cells. The number of the cerebellum nerve cells are greatly reduced. Skeletal muscles showed atrophy of denervation.

3-05-29 INTRACELLULAR ALKALOSIS DURING HYPOXIA IN NEWBORN MOUSE BRAIN IN THE PRESENCE OF SYSTEMIC ACIDOSIS: A PHOSPHORUS MAGNETIC RESONANCE SPECTROSCOPIC STUDY

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We investigated changes in cerebral energy metabolism in newborn mice during hypoxia and resuscitation using ^{31}P-MRS. Eleven of twenty mice (55%) survived 8 hours of hypoxia produced by exposure to a 5% oxygen, 95% nitrogen gas mixture and were included in this study. The phosphocreatine/inorganic phosphate ratio decreased during hypoxia; the ATP concentration changed slightly. Intracellular brain pH (pH_i) increased from 7.20 ± 0.03 to 7.36 ± 0.03 ($p < 0.05$) within the first hour of hypoxia and remained elevated during hypoxia. Control mixed arterial and venous blood pH (pH_b) was 7.39 ! 0.01. pH_b decreased immediately following the induction of hypoxia and had fallen to 7.16 ± 0.01 ($p < 0.01$) at the end of hypoxia. The P_{co_2} did not change significantly during the first hour of hypoxia. The glucose concentration increased after 1 hour of hypoxia. Thus the alkaline shift in pH_i during hypoxia cannot have been caused either by systemic alkalosis due to hypocapnia or by hypoglycemia. These results suggest that there may be a protective system in the neonatal brain against systemic acidosis.

3-05-30 L-2-HYDROXYGLUTARIC ACIDURIA IN A BOY WITH MACROCEPHALY AND LEUKODYSTROPHY

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A 4-year-old Japanese boy was investigated for macrocephaly, psychomotor retardation, ataxic gait and recurrent afebrile convulsions. Cranial computed tomography and magnetic resonance imaging scans were suggestive of diffuse leukodystrophy especially in right frontal lobe and cerebellum. Electroencephalogram showed diffuse irregular slow basic activity with sporadic spikes on left central region. Nerve conduction velocity and auditory brainstem response were normal. The study of short latency somatosensory evoked potentials from each median nerve showed delayed central conduction time (L:10.7msec,+2.5SD, R:12.8msec,+5.6SD). Laboratory investigation revealed a marked excretion of L-2-hydroxyglutaric acid(L-2-HG), and slightly increased plasma lysine(358.8nmol/ml). Oral loading test with lysine(100mg/kg) or citrate(1g/kg) resulted in no increase in L-2-HG excretion. Oral administration of kanamycin(1g/day, for 2 days) caused reduction of L-2-HG excretion(about 50%). Although the metabolic defect of this patient remains unclear, intestinal bacterial flora seems to contribute to formation of L-2-HG.

3-05-31 P31 MR SPECTROSCOPY OF BRAIN AND MUSCLE AND MOLECULAR GENETIC ANALYSIS IN A CASE OF PDH E1 DEFICIENCY

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We report results of *in vivo* nMR spectroscopy in muscle and brain and molecular genetic and biochemical analyses on fibroblast and lymphoblastoid cell lines.

P31 MR spectroscopy of muscle and brain showed a decreased energy reserve with decreased PCR/Pi ratio and increase of lactate. Molecular genetic analysis showed a C to G change at 787, with a substitution of an arginine to a glycine in the coding sequence and translation of the cDNA in both cell lines, but the expression of PDH activity was decreased only in fibroblasts and normal in lymphoblasts. A similar mutation has been found only in two other cases with a similar clinical phenotype (FEBS Letters 282: 209, 1991) and it is different from the more common previously reported mutation of the PDH E1 gene, confirming that the heterogeneity of PDH deficiencies is reflected also on the clinical features, enzyme activity, protein levels in the different tissues and gene expression.

3-05-32 ADRENOLEUKODYSTROPHY: THE CASE REPORT OF A 13-YEAR-OLD BOY WITH THE CLINICAL PICTURE OF PSYCHOSIS

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At the age of 10, Addison's disease was diagnosed. Introducing the substitutional therapy his condition was improved in a satisfactory manner, and normal psychomotor development was progressing until he was 12 years old. From that time onward, the behavioural changes and gradual general psychological disturbances have been occurring. Progressive oblivion, decrease of learning potentials of the school boy, avoidance of social contacts and raised sexual instinct contributed to establishing a psychiatric diagnosis. A lack of spontaneous, verbalization with pronounced perseveration, echolalia, coprolalia as well as psychomotor restlessness accompanied with a profusion of stereotypic motor activities and general disorientation were found. The pronounced disinhibitive phenomena presented a matter of special interest since the predomination of signs of frontal lobe lesion used to be found in atypic forms of the disease. CT brain scanning and numerous additional investigations (including the characteristic fatty acids in plasma C 25:0 and C 26:0) pointed to the diagnosis of ALD. Especially significant was the phenomenon of similar cases in the family.

3-09-01 SPINOCEREBELLAR ATAXIA IN AN AUSTRIAN-AMERICAN-FAMILY

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The pedigree of a family with spinocerebellar ataxia dating back to the year 1811 will be presented. Main features of the disease include gait ataxia, dysarthria, dysmetria, pathological reflexes and oculomotor abnormalities. Historical and present information and clinical data of living family members reveal considerable variability within the family. Facultative symptoms are rubral tremor, myocloni, dystonia and dementia. Age at onset ranged from 5 to 60 years with a tendency to earlier onset in present generation combined with an increase in severity of symptoms. Analysis of pedigree confirmed autosomal dominant inheritance of the disease. Linkage studies in American family members strongly suggest that the disease is caused by mutation at the SCA 2 locus on chromosome 12. We will report detailed clinical, neuroradiological and neuropsychological data in 8 patients.

3-09-02 IMAGE ANALYSIS OF CALCIFYING PROGRESS IN IDIOPATHIC SYMMETRICAL CEREBRAL CALCIFICATION (FAHR'S DISEASE) BY X-RAY, CT AND MRI

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In this study, three cases were investigated by X-ray, CT and MRI. Firstly, CT roentgenograms were compared by changing window setting (level and window width). The level and window width for brain was named A-CT and those for bone B-CT. Images by both A-CT and B-CT were mutually compared and also with the images by MRI (T_1-, T_2-weighted and proton density). Images in the calcified area by A-CT showed homogenous high density, while those by B-CT were heterogenous, namely, largely high and partly low in density. It seems that high density area shows advanced calcification, while low density area indicates pseudocalcification, that is, early state of calcification. This distinction in B-CT appeared more evident in T_1-weighted images, and is much more clearly expressed in proton density images by MRI.

In conclusion, we suggest that heterogenity in images by B-CT (T_1-weighted and proton density images by MRI) reflects the different (early/advanced) stages of cerebral calcification.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-09-03 THE DISTRIBUTION OF DELETED MITOCHONDRIAL DNA IN THE SUBSTANTIA NIGRA OF PARKINSON'S DISEASE

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Recently, energy crisis due to mitochondrial respiratory failure has been proposed as one of the most important mechanisms for nigral cell death in Parkinson's disease. We have demonstrated accumulation of deleted mitochondrial DNA (mtDNA) in the striatum of patients with Parkinson's disease (PD) [*Biochem. Biophys. Res. Commun.* 170: 1044, 1990; *ibid.* 172: 483, 1991]. In order to elucidate the distribution of mtDNA deletion in each neuron in substantia nigra(SN), we analyzed histochemically five parkinsonian patients and four control patients by using the in situ hybridization method with non-radioactive probes.

In the control patients, the ratio of non-stained neurons using the probe of undeleted part of mtDNA is approximately as same as that using the deleted part of mtDNA. In contrast, in parkinsonian patients, the percentage of neurons with diminished staining using the probe of deleted part was larger than that using the probe of undeleted part.

By using the quantitative PCR approach, the deleted mtDNA were accumulated with the age. We postulate that the dysfunction of oxidative phosphorylation due to mutations of mtDNA one of the most important contributors of aging. In our histochemical study, age-related accumulation of deleted mtDNA is accelerated in the parkinsonian SN suggesting that the deletion contributes to pathophysiological processes underlying Parkinson's disease.

3-09-04 RELATIONSHIP BETWEEN IMPAIRED BLOOD PRESSURE AND MULTIPLE SYSTEM INVOLVEMENT IN ALCOHOLICS

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Impaired blood pressure control such as hypertension or orthostatic hypotension is known as an autonomic dysfunction in alcoholics. We speculated that abnormal blood pressure might affect the outcome of alcohol-related neurological symptoms. Thus, we examined the relationship between a history of alcohol abuse and the clinical characteristics of the patients with olivo-ponto-cerebellar atrophy, late cortical cerebellar atrophy and Shy-Drager syndrome. Twenty four patients (mean age:56.1 years old) with a daily alcohol intake exceeding 75g of ethanol/day for 25 or more years were studied. Twenty two of 24 patients had ataxia and/or peripheral neuropathy. Abnormal blood pressure was detected in 18 patients: hypertension in the supine position, 14; orthostatic hypotension, 13. Abstinence improved blood pressure and neurological symptoms in 14 patients. Ten patients with no improvement on abstinence had a long history of alcohol abuse and severe orthostatic hypotension. Five of them showed cerebrovascular lesions on MRI. On the test of event-related potential, the amplitude and latency of P300 were influenced by a change in blood pressure.
We considered that abnormal blood pressure affected the pathophysiology of diseases induced by alcohol.

3-09-05 CERVICAL MYELOPATHY IN IDIOPATHIC PARKINSON'S DISEASE

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Symptomes of pyramidal tract dysfunction, bladder dysfunction and sometimes radicular motor and sensory deficits in the arms are often observed in patients suffering from idiopathic Parkinson's disease (IDP) .
33 patients with idiopathic parkinson's disease were examined. After a neurological evaluation , a specific neuro-orthopedic examination, a X- ray of the cervical spine, a cerebral computertomography and in suspection of cervical myelopathy (CMP) a MR-tomography of the cervical spine were performed.
In 15 of 33 patients with IPD a CMP was diagnosed. 3 patients had marked symptoms of a CMP, 12 patients had moderate or mild symptomes of a CMP. In 9 patients a narrowing of the spinal canal with a consecutive vertebrostenoses of the cervical spine was dedected by MR-tomography. In the X-ray also severe or marked degeneration of the cervical spine were found. By the neuro-orthopedic examination marked joint dysfunction and posture disturbances of the cervical and thoracic spine were dedected.
Summary we suggest, that a relevant number of patients with parkinson's disease and spinal symptoms are suffering from degenerative disorders of the cervical spine, maybe related to the typical postural disturbance of patients with IDP.

3-09-06 MRI AND SPECT OF HEREDITARY SPINOCEREBELLAR DEGENERATION WITH DEMENTIA.

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We reported a Japanese family of hereditary spinocerebellar degeneration with dementia. The four patients of this family included one woman and three men. They mainly had slowly progressive spastic gait, cerebellar ataxia, bowel and bladder dysfunction and mild dementia. T-2 weighted MRIs revealed bilateral low intensity lesions in caudate nuclei, putamina and thalami and diffuse high intensity lesions in white matter in all cases. Only in one case T-2 weighted MRI revealed high intensity lesions in pons. ^{123}I-IMP SPECT revealed hypoperfusion in bilateral white matter in two cases, and hypoperfusion in frontal and parietal lobes in one of them. These findings were more obvious in an advanced case. There were no abnormality in nerve conduction velocity, serum very long chain fatty acids,and lysozomal enzymes of white blood cells. This family have a difference from typical hereditary spinocerebellar degeneration in their unique MRI and SPECT findings.

3-09-07 ENCEPHALOPATHY ASSOSIATED WITH L-2HYDROXY GLUTARIC ACIDURIA

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L-2 Hydroxy Glutaric Aciduria(HGA) was first reported in 1980 in a patient with a neurodegenerative disorder and only 8 cases have been published so far.In this paper, we present the clinical picture, the biochemical data and the MRI findings of a Greek 20 year old patient with HGA.
He presented seizures, mental retardation and ataxia progressively deteriorating. On examination pyramidal, extrapyramidal and cerebellar signs were revealed.The MRI showed cortical atrophy and subcortical white matter lesions. Lysosomal enzymes and urinary N-acetyl aspartate levels were normal.The GC/MS analysis showed increased of L-2 hydroxy glutaric acid in urine(1.249mmol/mol creatinine,normal$\bar{X}$:6) plasma (58 μmol/lt,normal $\bar{X}$:0,6) and CSF (43 μmol/lt,normal $\bar{X}$: 0,7).Lysine levels in plasma and CSF were elevated.
The function of HGA is not yet elucidated in vertebrates, but high levels of this acid in clinically similar cases, suggests a pathogenetic role.

3-09-08 ANTISULFATIDE ANTIBODIES IN NEURODEGENERATIVE DISORDERS

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Antibodies against glycolipids have been found in several neurodegenerative conditions, where they may play a role in the disease process.

The presence of antibodies against sulfatide, a major component of CNS myelin, was analyzed by TLC-immunostaining in the sera of healthy HIV+ individuals,of AIDS patients, and of patients with multiple sclerosis (MS) and systemic lupus erythematosus (SLE).

Antisulfatide IgG (>1:100 dilution) was found in the sera of all the 40 healthy HIV+ individuals and AIDS patients examined, of all the 11 MS patients, and in 8/10 SLE patients.
Specificity studies showed that the sera from the above patients reacted with sulfatide and with lactosylceramide sulfate. Under the conditions used, weak reactivity against sulfogalactosyl diglyceride was also detected, while no detectable reactivity against lysosulfatide and the parental glycolipid galactosylceramide was observed. Affinity purified antisulfatide IgG isolated from two HIV+ individuals showed the same pattern of reactivity as the sera from the above patients.

Although the role of antisulfatide antibodies in AIDS, MS and SLE is still not clear, they may represent a common pathogenetic factor of CNS disease in these disorders.

3-09-09 CORRELATION BETWEEN FUNCTIONAL DISORDERS AND NEURONAL DEGENERATION IN THE ATAXIC RAT CEREBELLUM TREATED WITH Ara C.

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To investigate the mechanism of worsening ataxia, we performed experiments of calcium imaging, immunohistochemical staining and protooncogene expressions in various developing stages of the rat cerebellums treated with cytosine arabinoside(Ara C).

Suckling rats were injected with Ara C(40 mg/kg) subcutaneously 2 and 3 days after birth. Ataxia was apparently worsened after postnatal day(P) 14. In immunohistochemical staining with anti-IP_3 Receptor antibody, it was shown that many undifferentiated cells in the external layer were disappeared in P 7, and degeneration of Purkinje cells and malformation of cortex were advanced between P14 and P 21. Quisqualate-and NMDA-induced calcium mobilization was unchanged in Ara C-treated cerebellum at P 7 and P14, but decreased between P14 and P 21. The expression patterns of three protooncogenes, c-myc, Ha-ras and c-fos, were different between Ara C-treated and untreated cerebellum. Especially the expression of c-fos, which seemed to be related to cell death, was increased transiently around P18 in the treated cerebellum but not in the untreated. Our studies suggest that the direct cytotoxicity of Ara C is most apparent around P 7 and functional disorders in the treated cerebellum is well correlated to the progress of neuronal degeneration.

3-09-10 PARKINSON' S DISEASE : A CLINICAL ANALYSIS OF 92 THAI PATIENTS

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A clinical analysis of Parkinson' s disease at Ramathibodi Parkinson clinic had been carried out. There were 92 patients, 58 males and 34 females. The average age of disease onset was 55.4 years, range 19-79 years and that mean duration of the disease was 7.4 years, with 1-24 years range. Most of them were idiopathic with the following distribution of clinical severity on the Hoehn & Yahr rating scale: stage I-23, II-46, III-19, IV-2, and V-2.

Tremor was the most common presentation. All other cardinal signs of Parkinson's disesae were also noted, no outstanding physical signs had emerged in the analysis.

There was no unique clinical feature among Thai patients with Parkinson' s disease. Most of the patients had been treated with levodopa for 1-20 years, average 5.4 years. Mean dosage of levodopa was 547.1 mg/day, definitely lower than those reported in western countries. After 3-4 years of levodopa therapy all forms of therapeutic problems had emerged but the incidence of freezing or on-off phenomenon was significantly lower.

3-09-11 ELECTROPHYSIOLOGICAL FINDINGS, MRI AND SPECT IN CORTICOBASAL DEGENERATION.

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Corticobasal degeneration (CBD) presents with focal dystonia of one upper extremity, myoclonus, "alien hand sign" and akinetic-rigid syndrome on middle adult life. It also accompanies parkinsonism, constructional apraxia, limb-kinetic apraxia, cortical sensory disorders and dementia in its clinical course. Three patients aged 64-82 years, diagnosed on clinical criteria, have been studied with NCV, Short latency somatosensory evoked potential (SSEP), Brainstem auditory evoked potential (BAEP), EEG, topography, P300, MRI and SPECT. MCV and SCV were reduced, however, compound muscle action potential and sensory nerve action potential were normal in median, posterior tibial and sural nerve in one case. SSEP showed unclear N20, which was originated by postcentral gyrus, and prolonged P45 latency. BAEP was normal. EEG and topography showed asymmetric theta predominance on the contralateral side of clinical features in parietal and frontal lobe. MRI also demonstrated contralateral slight cortical atrophy with reduced blood flow in SPECT. P300 latency was prolonged.

Peripheral nerve disturbance was difficult to explain, however, dysfunction of cortex and basal ganglia seemed primary in CBD. We thought electrophysiological study, MRI and SPECT would be useful to estimate the degree of CBD.

3-09-13 THE DISTRIBUTION OF THE STRIATAL DOPAMINERGIC LESION IN MPTP-EXPOSED HUMANS AND IN PARKINSON'S DISEASE DIFFER.

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Objective: To study the striatal distribution of the dopaminergic deficit in MPTP-exposed human subjects. Background: The striatal dopaminergic deficit in Parkinson's disease affects the putamen more than the caudate. This contrasts with the diffuse deficit in PSP. MPTP-induced lesions of the dopaminergic nigrostriatal neurons have been used as a model of parkinsonism but the striatal distribution of the dopaminergic deficit in human subjects is unknown. Methods: Six MPTP-exposed subjects, six patients with Parkinson's disease and six normal controls were studied with PET and [18F]-fluorodopa (FD) on an ECAT 953B/31 tomograph in 3-D mode. The ratio of the caudate to putamen FD accumulation was calculated. Results: In the MPTP-exposed subjects the ratio was 0.96 ± 0.041 (mean $\pm$ 1 standard deviation) which did not significantly differ from the normals (0.98 ± 0.052; $p = 0.49$). Both were significantly lower than the Parkinson's disease ratio of 1.16 ± 0.073 with respectively $p = 0.0008$ and $p = 0.0002$. Conclusions: In contrast to the pattern seen in Parkinson's disease, the striatal dopaminergic lesion in MPTP-exposed patients is uniform throughout the striatum. The animal experiments suggest that the relative involvement of caudate and putamen depends upon the dose of MPTP. The uniform involvement in these patients may derive from the relatively large and acute initial insult

3-09-14 CLINICAL STUDY OF FRIEDREICH ATAXIA IN VALENCIA (SPAIN)

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Friedreich Ataxia (FA) is the most frequent type of early-onset hereditary ataxias. It is defined by clinical criteria (Geoffrey 1976; Harding 1981) of which the onset of ataxia before age 20 and arreflexia are considered cardinal. We present a clinical study of a series of 44 cases of FA seen in a reference Hospital of Valencia in the period 1970-91.

Four cases showed atypical FA features : two because they had preserved tendon reflexes, although both had a brother with the full FA picture; and two with onset after 21 years. In the rest, mean age of onset was 9.2 years old. Apart from ataxia and arreflexia, loss of amplitude of sural nerve evoked potential was the universal finding. Dysarthria, loss of vibratory sensation, Babinski sign, orthopedic and ECG abnormalities appeared in more than 50% of cases.

Our findings are similar to other large series reported from Canada, England and Italy. We stress on the loss of sural nerve evoked potential and EEG abnormalities as the most useful tests in the diagnoses of FA.

3-09-15 BRAIN ATROPHY CAUSING BY VIBRATION

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115 patients – railway drivers – aged 23 - 56 (men) are examined. The duration length of service approximately 15 + 3 years.

On the CT in 78% of cases was seen marked regional simmetric external cerebral atrophy with sulcal dilatation. Progression of cortical atrophy changes as shown by CT was not correlated with progression of neurological disfunctions. Atrophical changes were discovered in temphoral (42%), fronto-parietal (14%), cerebellar (35%) lobes. Subarachnoid spaces on the brain convex expressed more dilatation, than ventricular size (69 - 31%). Less of gray-white matter discriminability was rated at the levels of basal ganglia, centrum semiovale and high convexity was significant (P = ,05) in 98% of cases. EEG was noted depression a activity and domination of B.

Exposed morphologic changes in central part of auditory and vestibular system analizator in patient with functional overload of receptors. CT proved promising in the evaluation of neuronal loss in vibration pathology.

3-09-16 HIGH-DOSE INTRAVENOUS CEFTRIAXONE IS NOT INFLUENCING THE NATURAL COURSE OF AMYOTROPHIC LATERAL SCLEROSIS

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Eight patients suffering from amyotrophic Lateral Sclerosis were treated with 2 grams of i.v. ceftriaxone for 3 weeks. Individual muscles strength and trophism for bulbar, axial and limb musculature as well as the number of fasciculations and the walking sped were scored by the same neurologist before treatment, at the trial and 1 mouth later.
Four patients referred subjective amelioration. In two of them both strength and trophism in the most affected hand improved in the clinical scores. Clinical scores were slightly improved also at the 1 mouth follow-up in 1 or 2 patients.
One patient referred subjective deterioration not substantiated by the clinical scores. No statistically valid differences were noticed in walking sped. None of the patients required to repeat the therapeutic trial.
In conclusion, this study does not support the conclusions provided by a recent report in which ceftriaxone was found to significantly improved patients with SLA. Unfortunately, did not observe such a dramatic changes neither during, nor immediately following and 1 mouth later the therapeutic trial.

1. *Smith L.G. Improvement of patient with amyotrophic lateral sclerosis given* ceftriaxone. Lancet 1992,339:1417.

3-20-01 MYASTHENIA GRAVIS IN SAUDI ARABIA.

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We reviewed the records of 69 patients with myasthenia gravis for whom follow up was available from one to ten years. The mean age was 29.1 years while thymomas as a group had a higher mean age of 40.5 for males and 35.6 for females. The majority of patients presented with ocular signs 76%, followed by generalized weakness 57%, and bulbar weakness 54%. Respiratory difficulty occurred in quarter of the patients and the disease remained purely ocular in 26% of the patients. The majority of patients underwent thymectomy, only 10 thymomas and one thymolipoma were found. All patients received immunosuppression with either corticosteroids, azathioprine, plasma exchange or a combination thereof. Ten thymoma cases received post operative mediastinal radiation therapy while one patient required total body irradiation. 38% went into remission, 5% expired and 13% were lost for follow-up. The rest had chronic or recurrent disease from mild to severe. HLA type A and B were done on 37 patients and HLA-D on 21 patients. A positive association with HLA-B35 and negative association with HLA-B5(51) was suggested.

We conclude that the disease follows a pattern similar to what is reported from other countries yet its HLA association is different.

3-20-02 EARLY THYMECTOMY IN THE MANAGEMENT OF MYASTHENIA GRAVIS IN CHINESE PATIENTS.

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Previous reports suggest a high incidence of thymoma among Chinese with myasthenia gravis (MG). The efficacy of thymectomy in this population is not clearly defined.

MG was diagnosed in 49 patients during 1985-91. Thymectomy was performed in 36 patients, 29 (81%) of whom were operated on within six months. The mean follow-up period was 47 months.

Thymoma was found in 11 (31%) of the thymectomized patients, of whom 10 had generalized and one ocular MG. All showed significant improvement. In the remaining 25 patients, the thymus was hyperplastic in 14 and normal or atropied in 11. Nine patients went into remission and 10 showed significant improvement; four did not improve and two died of uncontrolled disease within three months of operation.

There is a high incidence of thymoma among Chinese with generalized myasthenia. Early thymectomy is beneficial both to patients with thymoma and to those without.

3-20-03 MYASTHENIA GRAVIS IN CYPRUS

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Recent epidemiological studies on the prevalence of Myasthenia gravis (MG) have reported higher rates than before in a number of countries worldwide. We have identified 95 patients with MG in Cyprus. Our study based on the Cyprus population (680,000 people) confirms this and reports the highest prevalence rate yet. Though diagnostic techniques and survival rates have clearly contributed to the higher prevalence rates, our study shows that the incidence of MG is also significantly on the increase. Furthermore, the number of seronegative cases appears to be significantly higher than in previous reports. Other parameters including age, sex ratio and number of thymomas cases are similar with previous studies.

3-20-04 SOME CHARACTERISTICS OF THE PATIENTS WITH MYASTHENIA GRAVIS OVER THE AGE OF 51 YEARS

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Seventy-eight patients having Myasthenia gravis/MG/ were analysed,19 of them/24.5%/consisted a group of patients over the age of 51years.Corticosteroids were applied in 85% of the total number of patients,i.e. in 90% of the patients aged up to 50 years,and in 69% older than 51.Imuran was used in 24% of the total number of patients,and in 63% of the patients over the age of 51.Plasmapheresis was used in 23% of the total number of patients and in 26.4% of the patients over the age of 51.Thymectomy was done in 64% of the total number of patients and in 31% of the patients over 51.Histopathologically,thymoma was found in 8/16% of the total patients/,3 of which were over 51.Heart diseases were found in 15% of the total number and in 52% of the patients over 51.Pulmonal diseases were present in 10% of all patients,and in 42% of the patients over 51.Diabetes mellitus was found in 5% of all patients and in 21% of the patients over 51.In the patients over 51 it was suggested greater caution in the treatment with corticosteroids and thymectomy.

3-20-05 MYASTHENIA GRAVIS: INCREASED NUMBERS OF AChR REACTIVE T CELLS EXPRESSING mRNA FOR THE CYTOKINES IFN-γ, IL-4 AND TGF-ß

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In myasthenia gravis (MG), elevated numbers of T cells recognizing AChR have been reported, but the involvement of cytokines is less well defined. IFN-γ and IL-4, produced by the TH1 and TH2 subpopulation of $CD4^+$ T cells, respectively, could upregulate antigen-induced inflammation, while TGF-ß has immunosuppressive effects. We used in situ hybridization to detect mRNA for IFN-γ, IL-4 and TGF-ß in blood mononuclear cells (MNC) from 21 patients with MG and 21 controls after culture in presence of aChR and the multiple sclerosis-related control antigen MBP. Patients with MG had strongly elevated numbers of cells that responded to AChR by the production of IFN-γ, IL-4 and TGF-ß. Median numbers were 1 per 4,200, 1 per 5,000 and 1 per 5,000 MNC, respectively. In contrast, MG and control patients had low numbers of IFN-γ, IL-4 and TGF-ß mRNA positive cells after culture in presence of MBP; these numbers did not differ from those obtained after culture in absence of antigen. Our data indicate that MG is accompanied by AChR specific T cell responses that are reflected by abnormal production of IFN-γ, IL-4 and TGF-ß.

3-20-06 MECHANISMS OF ACTION OF HIGH DOSE INTRAVENOUS IMMUNOGLOBULIN (IVIg) IN THE TREATMENT OF MYASTHENIA GRAVIS (MG)

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We treated 20 MG patients with IVIg (7S IgG, 0.4 g/kg/day, for 5 days). Anti-AChR Ab (binding to bungarotoxin-labeled fetal calf muscle AChR) titer and binding avidity (time to one-half of maximal binding to AChR), clinical status and decremental responses to repetitive nerve stimulation were studied. In addition Ab titer and binding avidity were determined *in vitro* for each pretreatment serum tested with increasing amounts of commercially available IgG preparation or of F(ab)2 fragments (prepared by pepsin digestion and chromatography on protein-A sepharose) or of anti-anti-AChR anti-idiotypic Abs (isolated by an affinity chromatography column with anti-AChR Abs). The rapid clinical effect was associated with decreased anti-AChR Ab binding avidity 2 - 10 days after starting IVIg. Binding avidity was also decreased *in vitro* by IgG F(ab)2 fragments or anti-anti-AChR Abs. The reduction of anti-AChR Ab binding avidity for the post-synaptic receptor probably mediated by anti-idiotypic Abs may contribute to the clinical effect of IVIg in MG.

3-20-07 DYSTROPHIN RELATED PROTEIN AT THE MOTOR END-PLATE IN MYASTHENIA GRAVIS

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The dystrophin related protein(DRP) was been reported at the neuromuscular junctions of skeletal mature muscle fibers. However, the action of DRP at the motor end-plates has not been clarified. Myasthenia gravis (MG) is the most representative disease in which the motor end-plates are involved. We, therefore, studied the DRP at the motor end-plate in MG and compared with that in the other neuromuscular diseases.

We used anti-DRP (LDP), NCL DYS1, NCL DYS2, NCL DYS3, and peroxidase labeled α-bungarotoxin for the immunohistochemical staining of the end-plates. The intensities of the staining was quantitatively analyzed using interactive bioimage analyzer (IBAS Carl Zciss co.).Each sample was scored from 0 to 275 dependent on the intensities of staining.

Anti-dystrophin antibodies showed no significant difference between MG and controls or other neuromuscular diseases. But anti-DRP was decreased at the motor end-plates of MG patients in which α-BGT biding sites were also decreased.

Further studies are necessary to clarify that the reduction of DRP at the end-plates in MG patients is a primary or secondary phenomenon.

3-20-08 LONG TERM FOLLOW UP OF PATIENTS WITH MYASTHENIA GRAVIS AND THYROTOXICOSIS

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Fifty-one out of 291 patients with myasthenia gravis (MG) seen during 1969 - 1990 were found to have thyrotoxicosis (T) (17.5%). The female (F) to male (M) ratio was 2.6 to 1 and the mean ($\bar{X}$) age of onset of mayasthenia were 30.9 ± 10.2 years (M) and 25.9 ± 10.5 years (F). Thyrotoxicosis showed later age of onset (M = 31.7 ± 10.7 years, F = 28.3 ± 8.4 years). Thyrotoxicosis preceded MG in 40% of patients, occurred later in 18% and both were simultaneously present in 42%. Two-thirds had generalized myathenia. Anti-AchR Ab was present in all patient studied (n = 5). Antithyroid Ab was present in nearly 60% of patients (n = 18). Patients were followed up for a mean of 7.4 ± 4.6 years. The activity of both diseases showed evolutive paralellism in 59.5% and antagonism in 40.5%. Thirteen patients received high dosage prednisolone alone for 2.1 ± 1.7 years, 17 received prednisolone or methotrexate with antithyroid drugs for 3.3 ± 3.1 years and 1.2 ± 0.7 years respectively. Six patients who relapsed on antithyroid drugs alone were given additional prednisolone or methotrexate. High dosage prednisolone alone could induce remission of both diseases in over 90% of cases but relapsed after stopping treatment was high (MG 46.2%, $\bar{X}$ time 1.5 ± 1,8 years, T38.5, $\bar{X}$ time 1.0 ± 1.2 years). Relapses were fewer when antithyroid drugs were also given (MG 11.2%, $\bar{X}$ time 1.1 ± 0.6 years, T 29.4%, $\bar{X}$ time 0.7 ± 3.1 years). Thymectomy was effective in inducing remission of myasthenia but had no effect on the thyrotoxicosis.

3-20-09 OPTIMIZING ANTI-ACETYLCHOLINE RECEPTOR ANTIBODIES DETERMINATION USING RECEIVER OPERATING CHARACTERISTIC ANALYSIS AND INFORMATION THEORY.

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The discrimination power of a diagnostic test is determined by three parameters: the sensitivity and specificity of the diagnostic test itself, and the prevalence of the target disorder. The choice of a cut-off determines a sensitivity and specificity, and prior probability (prevalence) is essential to select a correct cut-off. Anti-acetylcholine receptor (AChR) antibodies determination is a sensitive and the most specific diagnostic test in myasthenia gravis (MG). Because of the non-Gaussian distribution of the titers, cut-off selection is arbitrary in all reports. Moreover, prevalence is not taken into account in this selection. So the test is not being used as appropriately as it would be desirable. In order to choose the appropriate cut-off, we have measured anti-AChR titers of 400 serum samples consecutively received to assay and 57 controls. Resulting titers have been mathematically transformed, in order to achieve their normal distribution. Transformed results have been submitted to receiver operating characteristic analysis and information theory. Cut-off was set at the value that provided maximal information at the MG prevalence of the population tested, that is the value where sensitivity and specificity are optimal. This is a feasible and rational approach to optimize anti-AChR determination.

3-20-12 MYASTHENIA GRAVIS;IN VITRO SECRETION OF ANTIBODY TO ACETYLCHOLINE RECEPTOR CORRELATES WITH THYMUS HISTOLOGY

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To better understand the relation between acetylcholine receptor antibody (AchRAb) secretion by immunocytes and myasthenia gravis (M.G.) we have isolated thymocytes in 24 consecutive generalized M.G. who underwent thymectomy. If number of cells $>10^7$ they were put in culture at 10^6/ml with and without mitogen . After 7 to 10 days in culture, supernatants were collected and assayed for AchRAb using human antigen (Neurology 1988;38:818-821)

Thymocytes isolated from each of the 16 patients with Lymphoid Follicular Hhyperplasia (LFH n=12) or thymoma (n=4) secreted antibodies. They produced 2.21 to $89.9X10^{-15}$ mol of alpha BT binding site per 10^6 cells/10 days. One patient with LFH had no Ab in serum but secreted 3.4 fm. Only 1/6 patients with atrophy or normal thymus secreted in vitro; 2 more had too few cells.

We conclude that secretion of AchRAb by thymocytes from M.G. patients with LFH or thymoma may contribute to disease pathogenesis and thus supports the use of thymectomy in these patients. The absence of such findings in those with normal or atrophic thymus may reduce need for thymectomy in this subgroup.

3-20-13 SISHEN PILL CAN RELIEVE OBSTINATE DIARRHEA CAUSED BY PYRIDOSTIGMINE IN PATIENTS WITH MYASTHENIA GRAVIS

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The pathogenesis of diarrhea caused by pyridostigmine, cholinesterase inhibitor, is its muscarinic effect. Therefore, most of the diarrhea can theoretically be relieved by atropine, muscarine antagonist. Eighty patients with myasthenia gravis treated by pyridostigmine were suffering from diarrhea. Of these in 75 patients diarrhea was not influenced by atropine. It is well known that Sishen Pill is one of the most effective traditional Chinese pills in treating morning diarrhea. While these 5 patients were treated by SSP, the diarrhea was discontinued immediately. Diarrhea in one of the 5 patients treated by SSP was reappeared while SSP was discontinued due to thymectomy. His diarrhea was relieved again due to reinstituting SSP. The mechanism of SSP in relieving diarrhea caused by pyridostigmine, could not be relieved by atropine, is still under investigation.

3-20-14 PYRAMIDAL SIGN (PS) IN SOME PATIENTS WITH MYASTHENIA GRAVIS (MG) MAY BE CAUSED BY INTRATHECAL SYNTHESIS OF AChR Ab (AChR Absyn)

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12 myasthenic patients with PS (MGPS) were treated by thymeotomy and other immunotherapy. Their PS disappeared while their MG improved. Their VEP, BAEP, SSEP and brain MRI were normal. IgG in CSF (IgGcsf) in MGPS (.0701 ± .038) was significantly (P < .05) higher than that in myasthenic patients without PS (MGoPS) (.025 ± .03) and normal controls (NC) (.0245 ± .014). Intrathecal de novo synthesis of IgG (IgGsyn) is significantly (P < .01) higher in MGPS (6.003 ± 4.25) than that in MGoPS (5.65 ± 5.84) and NC (5.6 ± 5.9). There is no significant (P > .05) difference of IgG in serum (IgGs) among MGPS (10.03 ± 2.48), MGoPS (11.05 ± 2.52) and NC (11.31 ± 2.52); and Albosf/Albs among MGPS (.004465 ± .009366), MGoPS (.0031 ± .0.0025) and NC (.0029 ± .00185). It suggests that increased IgGcsf in MGPS is due neither to increased IgGs nor to increased permeability of BBB, but to increased IgGsyn. In MGPS, AChR Abcsf/AchR Abs (.02156 ± .00656) is extremely significantly (P < .01) higher than IgGcsf/IgGs (.001688 ± .004). It suggests that there is increased AChR Absyn in MGPS. Our data are a circumstantial evidence of that PS in patients with MG may in turn be caused by increased AChR Absyn and dysfunction of cholinergic neurons within pyramidal tract.

3-20-17 DEGRADATION OF ACETYLCHOLINE RECEPTOR ON CULTURED RAT SKELETAL MUSCLE: VARIATION OF ACETYLCHOLINE RECEPTOR DAGRATION PATTERN AMONG EXTRA-OCULAR, GASTROCUNEMIUS AND DIAPHRAGM MUSCLES

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Myasthenia gravis (MG) is well known to be an autoimmune disease in which chemical transmission is disturbed in neuromuscular junction. Extraocular muscle (EOM) is easier to be involved than diaphragm muscle (DM) in MG patients. Using muscle tissue culture, degradation of acetylcholine receptor (AChR) was promoted by addition of anti-AChR Ab (Kao: 1977). Besids avidity of Ab to AChR on the involved muscle, there may be an important reason for the difference of susceptibility among muscles in MG patients such as AChR degradation. To make it sure, we studied AChR degradation rate using EOM, gastrocunemius muscle (GaM) and DM, by counting radioactivity of ^{125}I-BTX detached from muscle, based on Kao's method which was partially modified. AChR degradation rates were 4.43.3.87 and 6.19%/hr for EOM, GaM and DM, respectively. DM showed best degradation rate among muscle, meaning best turn-over rate in DM. This indicates the difference of turn-over may be an important factor for the susceptibility of muscles in MG.

3-20-18 IgG SUBCLASSES OF MYASTHENIA GRAVIS ANTI-TITIN ANTIBODIES.

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Introduction: Patients with myasthenia gravis (MG) have serum antibodies against acetylcholinc receptor as well as against non-receptor components of striated muscle. Titin has recently been identified as one non-receptor muscle autoantigen in MG, especially in patients with thymoma.

Methods: In the present study 72 MG sera from patients with defined thymus pathology were examined for muscle antibodies of subclasses IgG1, 2, 3 and 4 by 1) ELISA employing a recombinant titin fragment (MW 30 kD) as antigen; 2) indirect immunofluorescence employing sections of bovine striated muscle as antigen.

Results: By ELISA, most thymoma sera and about half of the thymic atrophy sera contained anti-titin antibodies, generally of all 4 IgG subclasses. Only 2 sera from thymus hyperplasia patients were positive. By immunofluorescence, sera from most patients with thymoma and about one half of sera from patients with thymic atrophy contained muscle antibodies of IgG1 and IgG4 subclasses, whereas only 2/34 sera from patients with thymic hyperplasia did. IgG3 antibodies were detected in about 15% of the sera, irrespective of thymus pathology, and IgG2 antibodies in none.

Comments: The rather differing results between the two assays indicate that the antigens operative also are different. Thus, titin seems not to be the only or most important muscle antigen binding MG muscle antibodies in immunofluorescence assay.

3-20-19 FAMILIAL MYASTHENIA: INVESTIGATIONS OF PATIENTS AND THEIR HEALTHY RELATIVES.

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Material comprises 8 families with at least 2 or 3 members suffering from myasthenia (17 myasthenic patients, altogether). Healthy members of those families were also studied.

In every subject clinical and electrophysiological investigations were performed: repetitive stimulation and SFEMG with estimation of jitter and blocking.

The HLA antigens, class I and II were studied. In myasthenic patients anti-AChR antibodies were detected in serum. In most of the patients HLA-B8 and DR3 were found. The occurrence of those antigens in patients with familial myasthenia was higher than in the healthy population and in the patients with not-familial myasthenia.

In 1/3 of healthy members of those families jitter abnormalities were found. In the majority of them HLA-B8 and DR3 were detected, as in the probands of the corresponding families.

The authors call attention to a frequent occurrence of subclinical n-m transmission abnormalities in the healthy relatives of patients with familial myastbenia with simultaneous presence of HLA B8 and DR3.

3-20-20 THE THYMUS IN EXPERIMENTAL AUTOIMMUNE MYASTHENIA GRAVIS INDUCED BY THYMIC ACETYLCHOLINE RECEPTOR-LIKE PROTEIN: COMPARISON WITH HUMAN THYMUS IN MYASTHENIA GRAVIS

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Thymus is supposed to have a trigger zone of autoimmune process against nicotinic acetylcholine receptor (AChR) in myasthenia gravis (MG). This study tried to detect the changes of the thymus in the EAMG in comparison with it in human MG. Lewis rats were immunized with AChR-LP (FCT) and the thymuses were examined weekly by immunohistochemical staining with avidin-biotin alkaline phophatase (ABC-ALP) method. Policlonal anti-AChR-LP (FCT), keratin, S-100, monoclonal anti-desmine, basement membrane, antibodies were used. Seven human thymuses obtained from patients with MG, three normal controls were examined. In immunized rats, generalized hypotonia was transiently observed by ten days after immunization. After booster immunizations, a part of them developed flaccid paresis. Thymus from chronic stage of the EAMG showed moderate architectural changes in thymic epithelium when it was stained with anti-AChR-LP antibody, distention of perivascular spaces, but no germinal centres. These results suggest the presence of chronic thymitis in EAMG induced by AChR-LP (FCT).

3-20-21 ACETYLCHOLINE RECEPTOR-LIKE PROTEIN IN HUMAN THYMUS FROM PATIENTS WITH MYASTHENIA GRAVIS : AN IMMUNOHISTOCHEMICAL AND IMMUNOELECTRON MICROSCOPIC STUDY

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We studied localization of nicotinic acetylcholine receptor-like protein (AChR-LP) in human thymus obtained from eleven patients with myasthenia gravis(MG) and five control thymuses obtained at cardiosurgery, by immunohistochemistry and immunoelectron microscopy (IEM). Tissue sections were stained by avidin biotin complex (ABC) method using Vectastein kit. The polyclonal antibodies against AChR-LP (fetal calf thymus), myoglobin, S-100 protein and monoclonal antibody against HLA-DR (OKIa-1, Ortho) were used. The part of the tissue section reacted the antibody was embedded in EPOK 812. The ultrathin section of them were observed by IEM without staining. The AChR-LP antibody reacted with epithelial cells in marginal zone of Hassall's corpuscle(HC) and some nonlymphoid cells in the medulla. By IEM AChR-LP were found in epithelial cells both in secretary type cell of HC and keratinized ones, more in the former. AChR-LP positive cells did not show myosin filaments by IEM. HLA-DR was positive on the cell membrane of HC. It is suggested that these positive cells to both AChR-LP and HLA-DR are antigen presenting cells in the MG thymus.

3-20-22 THE DIAGNOSIS AND TREATMENT OF MYASTHENIA GRAVIS WITH THYMOMA. A LONG TERM FOLLOW-UP OF 100 CASES.

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One hundred cases were observed of myasthenia gravis with thymoma, all of them were treated surgically. In 64 patients encapsulated and in 36 patients infiltrating thymomas were found.

Own long term results of surgical and immunosuppressive treatment are presented. Special attention is paid to early diagnosis using electrophysiological examination (repetitive stimulation and SFEMG with estimation of jitter and blocking).

Diagnostic value and sensitivity of pneumomediastinography and CT is also discussed on the ground of the material presented.

Thymectomy and immunosuppression were more effective in the early stage of the disease when the tumour was still encapsulated and did not infiltrate even its own capsule. Early diagnosis is of utmost importance.

3-20-23 **HLA ASSOCIATION IN CHINESE PATIENTS WITH MYASTHENIA GRAVIS (MG)**

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The Major Histocompatibility complex (HLA) was studied in 36 adult Chinese MG patients, and analysed in relation to their anti-acetylcholine receptor (AchR) titres, thymic histology, age of disease onset and presence of ocular or generalised disease. Eighty healthy Chinese acted as controls. HLA class 1 and class 2 alleles were typed by standard micro-cytotoxicity and PCR-SSO methods. As a group, the MG patients had higher frequencies of B46, and DRB3*0301 ($p<0.16$, RR=2.5; and $p<0.05$; RR=2.6; respectively), and lower frequency of DR4 ($p<0.01$; RR=0.3) compared to controls. B46 was particularly associated in those with younger disease onset (<35yrs), low anti-AchR titres (<5units), ocular MG and normal thymuses. In contrast, DRB1*14 was associated with thymic hyperplasia, younger disease onset, high anti-AchR titres (>10units) and generalised MG; and DRB1*1202 with thymoma, older onset patients, ocular disease, and mid to high anti-AchR titres (>5units). MG is therefore a heterogenous disease, with the various subgroups of the disease associated with different HLA alleles.

3-20-24 HTLV-I ASSOCIATED MYELOPATHY(HAM) AND MYASTHENIA GRAVIS(MG).

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We report the first known patient with HAM and MG. A 50-year-old woman with a previous blood transfusion noticed fluctuating weakness, ptosis, double vision, then leg stiffness. Neurological examination revealed moderate weakness and easy fatigability of the proximal upper limbs, which were restored by edrophonium, spasticity in the lower limbs, hyperreflexia and bilateral extensor plantar responses. She had no sensory or sphincter disturbance. Anti-HTLV-I antibody(HTLV-Ab) titer by PA method in serum was 1:40,960 and in cerebrospinal fluid(CSF) was 1:64. These were also positive on ELISA and Western blot analysis. Serum anti-AchR antibody(AchR-Ab) was 802 nmol/l. Electric evoked responses from the hand muscles waned with lower frequencies. Extended thymectomy revealed an involutional thymus with lymphoid follicular hyperplasia. Postoperatively, MG has improved, HAM remained unchanged and HTLV-Ab and AchR-Ab have decreased. Conclusion: autoimmune derangements by the retrovirus infection may be involved in the pathogenesis.

3-20-25 NEUROMUSCULAR DISEASES WITH OCULAR SYNDROME

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Thirteen patients with related clinical picture consisting of extra-ocular muscle involvement associated with a chronic skeletal muscle weakness of different clinical severity and predominantly proximal limb distribution,are reported.In these patients EMG,CPK serum concentration and muscle biopsy recognize a various nosological form of neuromuscular disease,out of Myotonic dystrophy and Myasthenia gravis.Mitochondrial myopathy has been diagnosed in five patients presenting a variable percent of "ragged red" fibres on muscle biopsy.Congenital myopathy/Nemaline myopathy/Centronuclear myopathy/Multiminicore myopathy/Congenital fibre type 1 predominance/has been proved in four cases.With positive clinical and electrophysiological and negative pathomorphological criteria,a diagnosis of Congenital myasthenia is made in three patients.One patient has a classical ocular myopathy only.Neuromuscular diseases with ocular syndrome present an important nosological heterogenity.Muscle biopsy is of significant value in their nosological distinction.In Mitochondrial myopathy extra-ocular involvement is remarkably frequent.

3-20-26 EVALUATION OF THE LARYNX MUSCLE DYSFUNCTION IN MYASTHENIA GRAVIS (MG): AN AID FOR DIAGNOSIS OF MG USING THE RESPIRATORY FUNCTION ANALYSIS

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The otorhynolaryngologic involvement in MG seldom occurs in moderate and ocular clinical form (OCF). 332 MG patients without respiratory symptoms were submitted to respiratory evaluation with vitalograph spyrometer and HP Vertek spyrometer. The FVC, VF = 1, FEV1, FEF, MFEF, FMFT, FTT, TLC, RV and shape of flow-volume curve the variables evaluated were 62 were OCF and 270 had generalized clinical form (GCF). The age of patients was 33 ± 18 years, 103 were male and 229 female. The female patients with OFC showed FVC, VF = 1, and RV statistically significant changed FMFT, VF = 1 and RV in those patients with GCF showed alteration in both male, and female patients, FMFT and MTT were also alteigeted in males with GCF. All patients with MG showed the "myasthenic pattern". The changes of respiratory function suggest "stenosis of the higher airways" but laryngoscopy and bronchoscopy were always normal.

In conclusion, all patients showed a myasthenic pattern and dysfunction of vocal chord muscles the same occurs in polysynaptic NMJ like stapedius muscle and one type of ocular muscle fiber.

3-20-27 THE CLINICAL AND ELECTROPHYSIOLOGICAL CORRELATION OF THE BLOCKING EFFECT OF ANTIACETYLCHOLINE RECEPTOR ANTIBODY IN A *IN VIVO* NEUROMUSCULAR PREPARATION OF RATS

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To evaluate the correlation between clinical symptoms, AAChR and eletrophysiological findings an experimental (MG) by immuneglobulin (IgG-AAChR) of MG patients to rats (Wistar, Louw M) and mice (Balb/C), was developed. In a neuromuscular preparation (NMP) (Kyoto rat) the *in vivo* mechanical contraction of the muscle was evaluated. Several levels of serum AAChR, saline solution 9/1000, normal IgG and gallamine were used. A decremental of contraction of muscle occurred with normal IgG, saline solutions administration, but none of animals developed respiratory failure (RF) or death. All the animals submitted to both IgG-AAChR developed RF and death. The lag of time to the development of RF or death in animals depended on the seric levels of AAChR.

The clinical (RF and deaths) and electrophysiological findings in NMP were proportional to levels of AAChR.

3-20-28 SEVERITY OF THYMOMA-ASSOCIATED MYASTHENIA GRAVIS IS RELATED TO THE PRESENCE OF RYANODINE RECEPTOR AUTOANTIBODIES.

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Some patients with myasthenia gravis(MG) and thymoma have autoantibodies to the ryanodine receptor(RyR)of skeletal muscle. We compared severity of myasthenic symptoms as assessed by a five point disability score in 16 MG thymoma patients with RyR antibodies and 17 MG thymoma patients without RyR antibodies. MG symptoms were significantly more severe in RyR antibody positive patients. Disability scores were 4.3±0.9 versus 3.2±1.0 (p=0.004)at peak of illness, and were 3.8±1.4 versus 1.9±0.9 (p=0.0002) at the end of the observation period. 8/16 RyR antibody positive patients died of MG as compared to 0/17 RyR antibody negative patients (p=0.0009).. RyR antibody level positively correlated to severity of myasthenic weakness (tau=0.59, p=0.0001). We conclude that high levels of RyR antibodies in in MG thymoma patients are associated with a severe form of MG with a high mortality.

3-20-25 TITIN IS A MAJOR AUTOANTIGEN IN MYASTHENIA GRAVIS

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Almost all patients with myasthenia gravis and thymoma (MGT) have antibodies that react with protein(s) in skeletal and heart muscle in a cross-striational pattern. We have shown by Western blot technique that this antigen shares electrophoretic mobility and antigenic determinants with titin. Titin is with a molecular weight of 3000 kDa the largest known protein, constituting 10% of the proteins of muscle. We showed by immunelectronmicroscopy that the localization of the binding of these antibodies to skeletal muscle corresponds to the described localization of one of the epitopes of titin. Isolated cDNA clones that reacts strongly with sera from MG patients with thymoma encode a 30 kDa region within the titin gene. The present data therefore indicate that the muscle antibodies found in the sera from some MGT patients are directed against one particular immunogenic region of the titin molecule.

3-23-01 ANERGY INDUCED IN VITRO BY TCR Vß8.2 (39-59) PEPTIDE SPECIFIC T CELLS IN EAE.

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T cell receptor peptide immunization in Lewis rats prevents induction of EAE. To address the mechanism of this immunoregulation CD_4+ TCR Vß8.2 (39-59) specific T cells were co-cultured with GPBP specific T cell lines in vitro and responses measured by proliferation and passive transfer of EAE. Co-stimulation of mixed TCR and BP reactive lines resulted in significant reduction of the response to GPBP and loss of proliferation to the major encephalitogenic epitope 72-89, but had little effect on response to TCR peptide or on expression of Vß8.2. Passive transfer of equivalent numbers of Vß8.2 (as detected by staining with antibody to Vß8.2) dramatically reduced EAE induction with co-cultured cells as compared to a BP line. These data demonstrate that TCR peptide specific T cells or their lymphokines directly inhibit but do not delete Vß8.2+ BP specific T cells and thus provide a plausible mechanism for their regulation of EAE in vitro. Supported by NIH grants NS23444, NS23221, Dept of Veterans Affairs and Xoma Corp.

3-23-02 FACILITATION OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS BY VIRUS INFECTION: LEAKAGE OF BLOOD-BRAIN BARRIER

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Experimental allergic encephalomyelitis (EAE) is a T cell mediated autoimmune disease of the central nervous system (CNS). In the Balb/c model of EAE development of both clinical and pathological signs are facilitated by infection with an avirulent mutant of Semliki Forest virus (SFV-A7). We have accomplished a time course study of the changes in permeability of blood-brain barrier (BBB) during an infection with (SFV-A7) and during the induction and development of the Balb/c EAE.

In the A7SFV infection viral antigen is found 2-3 days after an intraperitoneal injection in cerebral and spinal blood vessel endothelia and in the perivascular area. Blood-brain barrier leakage becomes evident 3-4 days postinjection adjacent to areas where viral antigen is detected. The animals remain neurologically healthy. In EAE, appearance of viral antigen is followed by a remarkable leakage of BBB in brain and spinal cord preceding the appearance of clinical signs.

We suggest that A7SFV infection facilitates the onset of EAE in Balb/c mice by altering the physiological functions of cerebral and spinal vasculature and disturbing the permeability of blood-brain barrier preceding an influx of immune cells and further immunological reactions in CNS.

3-23-03 CONDUCTION BLOCK AFTER INTRANEURAL INJECTION OF ACTIVATED T CELLS

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Experiments were conducted to investigate the role of activated T cells and their products in opening the blood nerve barrier (BNB) in Experimental Allergic Neuritis (EAN).

T cells reactive to the P_2 component of myelin cause EAN when injected intraperitoneally (IP) or intravenously (IV) but have no significant effect when injected intraneurally (IN). Conversely, EAN serum causes demyelination and conduction block when injected IN but has no effect when given IP or IV.

We injected P_2 reactive T cells or control medium into the sciatic nerves of Lewis rats. The animals also received daily IP injections of rabbit EAN serum or control serum. Marked conduction block was seen in T cell injected nerves of animals receiving EAN serum. No significant block was seen in control medium injected nerves or in the T cell injected nerve of animals given control serum. Pathological studies confirmed the presence of demyelination in nerves showing conduction block. Conduction block occurred, to a lesser extent, in nerves injected with T cells reactive to non neural antigens, again only in animals given EAN serum.

It is concluded that the cytokines of activated T cells open the BNB allowing circulating antimyelin antibody to enter the endoneurium with subsequent demyelination.

3-23-04 NEURON-SPECIFIC ENOLASE (NSE) AS A BIOLOGICAL MARKER IN FRIEDREICH'SATAXIA ?

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Friedreich's ataxia (FA) is a neuro-degenerative disease whose biochemical defect is still unknown. In order to determine a biological marker we measured the activity of NSE in plasma by radioimmunoassay and performed the phenotypic profiles of cell line derived from peripheral blood by indirect immunofluorescence in six patients with FA belonging to three differents families. Control was obtained from the parents of these patients. The NSE levels increase in patients with FA in comparison with their healthy parents and exceed 20 ng/ml. Comparison of phenotypic profiles of cell line in both control and patient with FA shown an increase of monocytes cell in FA. This finding let us think on the role of phosphatidyl inositol in the etiology of FA.

3-23-05 TCR VACCINATION IN EAE: INDUCTION OF DOWN-REGULATORY T CELLS SPECIFIC FOR Vβ17a CDR2 PEPTIDE.

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Protective effect of T cell receptor (TCR) peptides in experimental allergic encephalomyelitis (EAE) has been demonstrated. The aim of present study was to analyze the immune response to a synthetic peptide corresponding to the complementarity determining region 2 (CDR2) of Vβ17a, which is preferentially utilized by encephalitogenic T cells in SJL/J mice. We were unable to detect the CDR2 specific response by the conventional way in CDR2 primed lymphoid cells. However, when irradiated, activated T clone cells were put into culture, the primed spleen cells proliferated in response to CDR2 peptide. Peptide specific T cell line was established. The line cells were weakly CD8 positive and their activation was significantly blocked by anti-CD8 mAb. Finally, the line cells were shown to inhibit the antigen driven proliferation of encepalitogenic T cells. These results raise the possibility that such CD8 positive T cells might be involved in the immunoregulation of EAE.

3-23-07 IMMUNOHISTOCHEMICAL STUDIES OF A SURAL NERVE BIOPSY IN SARCOID POLYNEUROPATHY

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The pathogenesis of sarcoid neuropathy is poorly understood, since there have been only few bioptic or autoptic studies. We describe a 62-year-old women with typical sarcoidosis presenting with symmetric sensorimotor polyneuropathy. A sural nerve biopsy revealed a marked reduction of myelinated fibers (1560 /sq.mm) with affection of single fascicles in a differing degree. A small noncaseous granuloma and widespread infiltration of vessel walls were found in the epineurium. The perineurium was thickened and infiltrated with mononuclear cells. Immunohistochemical analysis (APAAP method) revealed a predominance of CD4 positive cells in all vasculitic infiltrates. CD8 positive cells were found more diffusely distributed in the endoneurial area. A surprisingly large number of cells in epineurial infiltrates were CD22 positive, which have only seldom been seen in other cases of vasculitic neuropathies. A large proportion of infiltrating cells were MHC II positive. CD68 positive cells (macrophages) were observed predominantly in the endoneurium. Immunoglobulins (IgM), complement (C3, C5, C9) and fibrinogen were positive in the endoneurium and the inner perineurial layers indicating a more unspecific disturbance of the blood-nerve-barrier. In conclusion, the most important mechanism of nerve damage in this case of sarcoid neuropathy seems to be a T-cell mediated vasculitis, probably followed by a reactio- against myelinated fibers.

3-23-08 ANTIBODY ACTIVITIES TO P0 PROTEIN AND OLIGOSACCHARIDE CHAINS OF P0 PROTEIN IN CHRONIC POLYNEUROPATHIES

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We have evaluated anti-P0 protein IgM antibody activity in sera from one case of chronic polyneuropathy with IgM paraproteinemia (IgM-CP), 6 cases of chronic inflammatory demyelinating polyneuropathy (CIDP), 7 cases of acute inflammatory demyelinating polyneuropathy (AIDP) and 10 cases of healthy controls. ELISA analysis for anti-P0 protein IgM antibody revealed extremely high titer in IgM-CP and significantly higher in CIDP than in AIDP and healthy controls ($p<0.01$, $p<0.01$).

Furthermore, we could determine the structure of oligosaccharide chains of P0 protein, GP 4 and GP 5. The differences between GP 4 and GP 5 is only non-reducing terminal sugar of these chains. GP 5 which HNK-1 antibody reacts with, has a sulfated glucuronic acid and GP 4 has a sialic acid at the terminal. From these reasons, we examined the reactivities of sera from one case of IgM-CP and 2 cases of CIDP with GP 4 and GP 5. The serum of IgM-CP reacted with GP 5, but not with GP 4. And the sera of CIDP reacted with both GP 4 and GP 5.

These data suggested the presence of anti-P0 protein antibody in the sera of IgM-CP and CIDP, and the epitope of the serum of IgM-CP might be the sulfated glucuronic acid in GP 5.

3-23-09 ACUTE , FULMINANT SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE) DURING PREGNANCY.

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We report the case of a 17 years old woman who presented during the second trimester of her first pregnancy abnormal movements starting initially on the right side.Rapidly,over the next few weeks,she developed more generalized,repetitive,involuntary movements suggestive of myoclonus.Rapidly,her comprehension deteriorated as well as her level of consciousness.The EEG showed periodic slow wave bursts of high amplitude at 5 to 6 seconds intervals,serum and CSF measles antibody titers were high at 1:640 and 1:256 respectively.A healthy male infant,premature , was delivered by cesarian section.During the next week,her condition worsened,the distressing spasms increased,she was urinary incontinent,ran a high fever and expired suddenly few days later. Autopsy was not permitted.

The immunosuppressed state of pregnancy might have triggered the delayed onset and fulminant course of SSPE in this patient as suggested by Wirguin et Al(Arch.Neurol.vol.45,Dec. 1988,1324-1325)

3-23-10 ANTICARDIOLIPIN ANTIBODIES IN LEPROSY

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In leprosy, antibodies play a role in the regulation of immune responses and are an integral part of effector mechanisms. They may not only reflect the previous experience of the immune system but also its ability to react to future challanges. We studied anticardiolipin antibodies, anti-nuclear factor, partial thromboplastin time (as indicative of Lupus Anticoagulant) in 40 leprotic patients (34 with lepromatous leprosy and 6 with tuberculoid leprosy) in additon to 6 cases as control. The laboratory findings have been correlated with the clinical data, previous treatment, and previous vaccinations. The results will be interpreted and discussed.

3-23-11 ADHESION MOLECULES IN CENTRAL NERVOUS SYSTEM DISEASES.

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To evaluate the role of various adhesion molecules in central nervous system (CNS) diseases, frozen brain and spinal cord sections from cases with primary inflammatroy diseases (multiple sclerosis-MS; subacute sclerosing panencephalitis-SSPE; tropical spastic paraparesis-TSP) and non-infalmmatory conditions (adrenoleukodystrophy-ALD; polyglycosan inclusion body disease; amyotrophic lateral sclerosis-ALD) were stained by immunocytochemical techniques for the localization of intercellular adhesion molecule (ICAM)-1, leukocyte function associated antigen (LFA)-1, CD2 and LFA-3. In the presence of CNS infiltrates, all markers were enhanced or abnormally expressed on endothelium, inflammatory cells and glial elements, respectively. White and grey matter parenchyma were reactive for ICAM-1 and LFA-3. Presence and distribution of parenchymal labeling correlated well to areas involved in the disease process even in the absence of inflammatory cells. These observations indicate that enhanced expression of adhesion molecules not only facilitates migration if inflammatory cells through endothelial cells into the CNS parenchyma but that they also can mediate binding of immune cells to the appropriate target structures of the disease process.

Supported in part by Grants from the NMSS (RG-1664-C3, and by NS 26368.

3-23-12 **THE ROLES OF ADHESION MOLECULES IN THE BINDING OF SJL MURINE T CELL CLONE SPECIFIC FOR MYELIN BASIC PROTEIN TO SJL ENDOTHELIAL CELLS FROM BRAIN MICROVESSELS.**

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Adhesion molecules are probably required for the migration of T lymphocytes to inflamed tissues, but the roles of these molecules have yet to be understood in the pathogenesis of inflammatory diseases such as multiple sclerosis. The adhesion of the SJL murine T cell clone specific for myelin basic protein (MBP) to endothelial cells (ECs) from SJL newborn brain microvessels was examined. Fifty percent of the 2 x 10^4 T cell clones stimulated once every two weeks with MBP were bound to ECs; whereas, less than 5 % of the same number of lymphocytes from peripheral lymph nodes were bound. This suggests that memory T cells have a greater ability to bind to brain ECs than do naive T cells. Monoclonal antibody to VLA-4 or VCAM-1 partially inhibited the binding of the T cell clone to ECs, and anti-LFA-1 did not; whereas, anti-ICAM-1 did so slightly. Binding of the T cell clone to ECs increased when the latter were incubated with ECs with IL-1 or TNF, but was partially inhibited by incubation with anti-VLA-4 or VCAM-1. We suggest that the VLA-4/VCAM-1 pathway functions in the binding of the T cell clone specific for MBP to brain ECs but that adhesion molecules other than VLA-4/VCAM-1 or LFA-1/ICAM-1 are involved because anti-VLA-4 and anti-VCAM-1 did not produce complete inhibition.

3-23-1 **CELLS EXPRESSING mRNA FOR INTERFERON-γ (IFN-γ), TRANSFORMING GROWTH FACTOR ß (TGFß) AND INTERLEUKIN-4 (IL-4) IN SPINAL CORD AND SYSTEMICALLY DURING THE COURSE OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS (EAE) IN LEWIS RATS**

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The functional differentiation of T cells, in form of cytokines produced in response to antigen, may be genetically regulated and also decisive for the outcome of an autoimmune response. In EAE, the production in the CNS of IFN-γ roughly correlates to the clinico-pathological course. IL-4 regulate B cells and have in many respects contrary effects compared to IFN-γ. TGFß is an immunosuppressive cytokine.

In situ hybridization detecting mRNA for IFN-γ, IL-4 and TGFß was performed on sections of spinal cords during EAE. Cell suspensions from lymphoid organs were cultured in absence or presence of myelin basic protein 63-88 and number of cells producing cytokines in response to this encephalitogenic peptide was enumerated.

In the spinal cords, IFN-γ mRNA expressing cells occurred during EAE. Their numbers correlated to the clinico-pathological course. TGFß producing cells appeared shortly before onset of clinical recovery. IL-4 expressing cells were present in low numbers throughout clinical EAE. Cells producing TGFß in respone to antigen appeared among lymphoid cells in the recovery phase of EAE. These data suggest that IFN-γ is an important disease upregulating cytokine in EAE, while production of TGFß in target tissue and systemically is associated with recovery.

3-23-14 DNA FRAGMENTATION IN CULTURED LYMPHOCYTES FROM NEUROIMMUNOLOGICAL DISORDERS.

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DNA fragmentation(FR) caused by the glucocorticoid(GC) seems to have a role in immunosuppression. To estimate its significance in patients treated with GC, we attempted to induce DNA FR in peripheral blood mononuclear cells and T-cells obtained from neuroimmunological patients. DNA FR was determined by electrophoresis of extracted DNA from cultured cells on 2 % agarose gel. In the cells obtained from subjects receiving prednisolone treatment, DNA FR was observed 24 hours after culture with phytohemagglutinin(PHA) and dexamethasone(DEX). On the other hand in the cells obtained from subjects not receiving GC treatment, induction of DNA FR required additional culture in PHA-free medium. However, DNA FR was not induced without PHA throughout the culture. In all these cases, DNA FR was not blocked by the addition of cycloheximide in the culture medium. Cyclosporine A and FK-506 also did not block the induction of DNA FR accompanied by the inhibited expression of IL-2 receptor. These results suggest that GC affects the cell at an early stage of the activated cell cycle, and induces DNA FR.

3-23-15 ANTI-GANGLIOSIDE ANTIBODIES FOUND IN PATIENTS WITH POSTINFECTIOUS POLYRADICULONEUROPATHY

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To detect serum anti-ganglioside antibodies, we studied fifteen patients with postinfectious polyradiculoneuropathy (seven patients, typical Guillain-Barre syndrome (GBS); six, Fisher syndrome; one, ataxic form of GBS; one, pharyngeal-cervical-brachial variant (Ph-C-B) of GBS). Anti-ganglioside antibodies were analyzed using TLC/immunostaining and ELISA methods. The absorption study was performed using Polystyrene beads (M.W. 50,000) coated with ganglioside. Eight patients had serum anti-ganglioside antibodies. Six patients with Fisher syndrome had anti-GQ1b and -GT1a antibodies (IgG), which recognized the common terminal residues to GQ1b and GT1a from the absorption study. The patient with Ph-C-B of GBS had anti-GD1a and -GT1a antibodies (IgG), which reacted independently with each ganglioside from the results of the absorption study. One of seven patients with typical GBS had anti-GM1 antibody (IgG). In patients with postinfectious polyradiculoneuropathy, anti-ganglioside antibodies were frequently found in the sera, and the possible correlationship might be exist between the species of anti-ganglioside antibodies and thier clinical manifestations.

3-23-16 LIPID PEROXIDATION AND ANTIOXIDANT ENZYMATIC SYSTEMS IN MULTIPLE SCLEROSIS

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Recently, it has been suggested a role for the oxygen free radicals (O_2^-, H_2O_2, $HO^\cdot$) in myelin injury. Although both O_2^- and H_2O_2 are potentially cytotoxic, most of the oxidative damage is caused by the $HO^\cdot$ radical, which is generated by the reaction of O_2^- and H_2O_2 with transition metal ions such as FE^{++}. As it is well known, cells possess antioxidant enzymatic and non-enzymatic systems. In some pathological conditions, intracellular concentration of oxy radicals at cytotoxic levels can give rise to an unbalance of these defense systems. One of the main consequences of this new state might be the peroxidation of the myelin sheet and its subsequent degradation. Stemming from these considerations in the present study we have assayed the antioxidant enzymatic activities of Cu, Zn-SOD, Mn-SOD, Cat, GSH-Px, GSH-Red and G6PD in lymphocytes obtained from patients with MS, evaluated by Poser's classification with defined MS. In parallel, the presence of conjugated diene levels in the CSF of the same subjects was also determined as a marker of lipid peroxidation damage. The preliminary results presented here indicate that the conjugated diene levels significantly increase during clinical exacerbations of MS, while the enzymatic activities are generally reduced. In particular we observe a drastic reduction of GSH-Px (practically it disappears in the acute phase). Differently, no change was observed for the Mn-SOD activity. We believe that these parameters could be envisage as useful markers to follow the evolution of MS. The research was partially supported by Regione Emilia-Romagna, 2° programma di ricerca sanitaria finalizzata (A.S.) and MURST 60% (A.S.).

3-23-17 LYMPHOCITE SUBSET FOLLOW-UP IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS DURING INTERFERON-BETA TREATMENT

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We present a study of longitudinal observations of lymphocite subset of a group of patients (n=10) with Multiple Sclerosis to evaluate modifications occurring in the course of the disease and different action on lymphocite subset during the treatment with IFN-beta.

Patients were grouped related to length of the course, number of attacks and disability degree established with Kurztke scale.

We compare results from these treated M.S. patients with them from a group of patients presenting similar aspects of the disease but not receiving IFN-beta.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-23-18 NEUROPSYCHIATRY MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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The incidence of neuropsychiatric manifestations in 370 patients with SLE was studied. Seventy-nine patients (21.35%) presented 117 episodes of neurological symptoms before or during the course of SLE. The manifestations that could be attributed to the underlying disease were: seizures (27 episodes); psychic (26); cerebrovascular disease (24); cranial neuropathy (9); peripheral neuropathy (5); Guillain-Barré syndrome (3); choreic movements (3); aseptic meningitis (2) and myopathy (1). Seven patients (8 episodes) presented infectious disease of the central nervous system (CNS). One patient developed a primary lymphoma of the CNS and another one had myasthenia gravis. The prognosis of the neuropsychiatric episodes was better in the diffuse symptoms (seizure) than in the focal ones (stroke) despite the treatment.

3-23-19 THE INVOLVEMENT OF ADHESION MOLECULES (LFA-1 / ICAM-1) IN EXPERIMENTAL ALLERGIC ENCEPHALO-MYELITIS

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To determine whether adhesion molecules (LFA-1/ ICAM-1) were involved in development of experimental allergic encephalomyelitis (EAE), we examined the effect of in vivo administration mAbs to LFA-1 / ICAM-1 on induction of EAE in rats. Male Lewis rats (6 to 10 wk-old) were injected intraperitoneally with anti - LFA-1 and/or ICAM-1 mAbs (both of mAbs 250 mg/ day each combined, 500 mg/day each) from day 0 to 9 post-immunization with guinea pig MBP(12.5µg /animal) and CFA. Rats were observed daily for clinical signs of disease until day 28 post-immunization. The incidence of EAE was 100% in all groups of anti - LFA-1 and/or ICAM-1 mAbs- treated rats and control rats. Anti - LFA -1 and/or ICAM-1 mAbs- treatment delayed the onset of disease significantly, compared with control rats ($p<0.01$). In respect of MBP specific T cell proliferation assay, all groups of anti - LFA-1 or / and ICAM-1 mAbs-treated rats exhibited lower response than control rats. As for peak disease score, there was no difference between all groups of anti - LFA-1 and/or ICAM-1 mAbs- treated rats and control rats. This study suggested that LFA-1 / ICAM-1 played an important role in the induction of EAE.

3-23-20 SEVERE FORMS OF GUILLAIN-BARRE SYNDROME AND HLA-SYSTEM

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This study is the first one to investigate antigens of class I (A,B) and II (DR) of HLA system in the Guillain-Barre syndrome (GBS) persons of Slavic origin. 26 patients (12 males and 14 females) aged 17-62 were examined. The diagnosis of GBS was established on the basis of Asbury-criteria. The typing of HLA antigens was made by using a standard two-stage lymphocytotoxic test. The set of antiHLA-sera consisted of the kits of sera of the firms Behring, Eurotransplant and St.Petersburg Institute of Hematology. The GBS frequency of antigen occurrence was compared with the control group (150 healthy donors). The significance of the data obtained was determined by using Yates criterion and the correction coefficient (Pcor).

There were no significant differences in HLA antigen frequencies between GBS patients and controls. Our results do not support the hypothesis that susceptibility to GBS in Russia and Ukraine is influenced by the HLA.

3-23-21 ANTIBODIES AGAINST GANGLIOSIDES IN PATIENTS WITH SYSTHEMIC LUPUS ERYTHEMATOSUS AND NEUROLOGICAL INVOLVEMENT

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Pathogenesis of neuropsychiatric manifestations of SLE has not been clearly defined and search for pathogenic mechanisms has focused on the importance of several autoantibodies. A strong relationship between antibodies against gangliosides and CNS-SLE has been reported.

Design/Methods: Serum from 100 patients was studied. Included in this study were 60 patients with SLE, (17 patients had experienced neuropsychiatric manifestations and 43 had no evidence of neurological involvement) and 43 had no evidence of neurological involvement) and 40 normal subjects. All serum samples were tested by ELISA for IgG and IgM reactivity with type II ganglioside extrated from bovine brain (Sigma), and asialoGM1 (Sigma).

Results: 10 out of 60 patients with SLE (16,6%) were positive for anti-type II gangliosides (5 IgM, 3 IgG, 2 both isotypes) and 13 out of 60 (21,6%) were positive for asialo-GM1 (8 IgM, 4 IgG, 1 both isotypes). 5 out of 17 (29,4%) CNS-SLE had anti-type II ganglioside antibodies and 4 out of 17 (23,5%) had asialo-GM1 antibodies.

Conclusions: The incidence of anti type 2-ganglioside antibodies was not significantly higher in patients with symptoms related to the nervous system than in SLE patients without neurological involvement. No correlation was found between antibodies against gangliosides and cardiolipin.

3-23-22 EXPRESSION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN (CALLA, CD 10) BY MYELINATED FIBERS OF THE PERIPHERAL NERVOUS SYSTEM.

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The common acute lymphoblastic leukemia associated antigen (cALLA, CD 10) was originally detected on lymphoblasts from patients with acute lymphoblastic leukemia, but subsequent studies demonstrated that this antigen was also present in a small population of other cells. In this report immunohistochemical and western blot techniques, making use of different anti cALLA (CD 10) monoclonal antibodies (mabs), were utilized to demonstrate that cALLA (CD 10) is also expressed by myelin sheaths of the human peripheral nervous system, but not of the central nervous system. Cryostatic sections of sural nerve biopsies of 8 normal control cases, 10 axonal neuropathies and 19 demyelinating neuropathies were utilized. Proper absorption tests were carried out incubating the anti cALLA (CD 10) mabs with lymphoblasts cALLA (CD 10) positive or with MAG. The cALLA positive immunoreactivity appeared to be localized in the outer and inner borders of myelinated fibers, in nodes of Ranvier and in the Schmidt-Lantermann clefts. cALLA (CD 10) is therefore another surface antigen shared by myelin and lymphoid tissue. Further studies are needed to investigate whether cALLA (CD 10) may be a target antigen in some immune-mediated peripheral nervous system disorders.

3-23-23 T CELL ACTIVATION MARKERS AND DISEASE SEVERITY IN GUILLAIN BARRE SYNDROME (GBS)

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GBS is believed to be an immunologically-mediated disease. We studied markers of T cell activation in 27 patients with GBS, and compared them with healthy controls. All patients were studied during the acute phase, and in 11 paired convalescent samples were obtained. Clinical severity of GBS was scored according to functional disability. T cell subsets (CD3, CD4, CD8), and activation markers (CD3+CD25[Tac], CD3+HLADR) were analysed by immunofluorescent staining and flow cytometry. Plasma soluble interleukin-2 receptor(sIL-2R) was measured by sandwich enzyme-linked immunoassay. Percent CD3+CD25 and CD3+HLADR cells were higher in the acute phase of GBS compared to controls, although this did not reach statistical significance. However, plasma sIL2R was significantly increased in the acute phase compared to controls ($p<0.007$), and remained increased although to a lesser extent in convalescence ($p<0.03$). There was also an absence of correlation of the immunological parameters with clinical severity of GBS. Elevated plasma sIL2R appears to be the only evidence of T cell activation in GBS, it however, does not predict disease severity.

3-23-25 CLINICAL, IMAGING AND TREATMENT CORRELATIONS OF URINARY MYELIN BASIC PROTEIN-LIKE MATERIAL IN PATIENTS WITH MULTIPLE SCLEROSIS.

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Immunoreactive material that appears to be a peptide of myelin basic protein (MBP) is present in normal urine and is increased in certain patients with multiple sclerosis (MS). Compared to normal controls, with urines collected randomly or in a clinical research unit, urine from 158 patients with MS had higher mean values of urinary MBP-like (uMBPL) material. In the other neurological disease (OND) control group (25 patients), those with other inflammatory diseases but not stroke or early phase Guillain-Barré syndrome also showed elevations. Among the subtypes of MS, those with secondary chronic progressive disease had the highest values. uMBPL material showed no definite correlation with treatment with glucocorticoids and cyclosporin A except that a lower uMBPL material level correlated with improvement following treatment with methylprednisolone/ prednisone and a higher level of uMBPL material correlated with a higher Kurtzke disability score. In a serial study of seven patients with unenhanced cranial MRI and 20 patients with gadolinium-enhanced cranial MRI, uMBPL material did not show a direct correlation with changes on serial cranial MRI. uMBPL material appears to reflect an ongoing process, possibly linked to attempted efforts at remyelination.

3-23-26 EFFECTS OF INTERFERON-γ AND ß ON THE ADHESION AND MIGRATION OF LYMPHOCYTES ACROSS HUMAN BRAIN ENDOTHELIAL CELLS IN VITRO

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Interactions between cerebral endothelial cells (EC) and lymphocytes are critical in the initial steps of CNS inflammation. In this study, the adhesion and migration of lymphocytes across cerebral EC was investigated in an in vitro model of the BBB. Human brain microvessel EC (HBMEC) were cultivated to confluency in a double chamber chemotaxis system (J. Neuropath. Exp. Neurol. 51: 104, 1992). Human peripheral blood T cells (TC) were used unstimulated or following 72 hrs stimulation with anti-CD3 (OKT3). Resting or stimulated TC ($1 - 2 \times 10^6$ cells/ml) were placed over intact HBMEC or EC previously treated with interferon-γ (IFN-γ, 150 U/ml) or IGN-ß (2,000 U/ml) for 3 days and incubated for 1 - 3 hrs at 37°C. The monolayers with the adherent or migrated TC were then processed for LM and EM. Adhesion and migration were quantitated by counting the number of adherent TC/mm^2 of monolayers and the number of migrated TC in 1 µm thick sections. A small number of resting TC adhered to intact HBMEC. Adhesion was increased after stimulation with OKT3. Adhesion of both resting and stimulated TC was greatly increased after pretreatment with IFN-γ, but not wih IFN-ß or combination of IFN-γ and ß. Migration of resting TC across intact HBMEC was minimal. Treatment with IFN-γ upregulated the migration of both resting and stimulated TC. Our results indicate that IFN-γ enhances the adhesion and migration of resting and non-specifically stimulated TC, most likely through a direct action on EC.

3-23-27 EXPRESSION OF VCAM-1 AND E-SELECTIN BY HUMAN BRAIN MICROVESSEL ENDOTHELIAL CELLS *IN VIVO* AND *IN VITRO*

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Leukocyte accumulation at sites of inflammation is a least in part dependent upon the expression of intercellular adhesion molecules by endothelial cells. The expression of vascular cell adhesion molecule-1 (VCAM-1) and E-selectin, surface glycoproteins implicated in the adhesion of lymphocytes/monocytes and neutrophils/CD4+ lymphocytes respectively, on cerebral endothelium was investigated *in vitro* and *in vivo*. Primary cultures of human brain microvessel endothelial cells were incubated with endotoxin, TNF-α or IL-1ß for 4 - 48h. VCAM-1 and E-selectin expression was detected by LM and EM immunocytochemistry, and by ELISA. All three cytokines induced upregulation of both adhesion molecules, maximal after 4h of treatment for E-selectin and 12 - 24h for VCAM-1, then declined to unstimulated levels by 48h. Ultrastructurally, localization of both adhesion molecules was greater on the apical than the basal cell surface. Cytokine treatment increased the apical expression several folds greater than the basal. *In vivo* expression of these molecules was investigated by the indirect immunoperoxidase technique in formalin fixed, paraffin embedded sections of brain. E-selectin was unregulated in the cerebral endothelium in meningoencephalitis with acute inflammatory infiltrates, while VCAM-1 was expressed in CNS diseases with predominantly lymphocytic/mononuclear cell infiltrates. Our results show that expression of these adhesion molecules may play an important role in the recruitment of leukocytes in CNS inflammation.

3-31-02 EFFECTS ON THE CENTRAL NERVOUS SYSTEM AFTER LONG TERM OCCUPATIONAL EXPOSURE TO ORGANIC SOLVENTS.

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The aim of the investigation was to study whether long term occupational exposure to organic solvents may result in demonstrable functional and structural alterations in the central nervous system. 36 men with more than ten years (mean 25 ± 1.3 (S.E.M.) years) occupational exposure to solvents and pair-matched controls were investigated.

Clinical neurological examination did not differ significantly in the two groups. At a battery of neuropsychological and cognitive tests, the exposed subjects performed significantly poorer than the controls at WAIS Digit Span, Digit Symbol Substitution, paired associate learning and continous word recognition. MRI, performed with an 1.5 Tesla scanner, revealed no preponderance of atrophy or white matter changes in the exposed group, conversely frontal and temporal sulcus width and left septum-caudatus distance were significantly larger in the control group. In conclusion, our findings support the hypothesis that long term low level exposure to organic solvents may induce cognitive dysfunction without concomitant signs of brain atrophy.

3-31-04 BIOCHEMICAL MUSCLE STRUCTURE CHANGES BY DRY WATER IMMERSION

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We present the biochemical findings of muscle enzymes evaluated in 6 volunteers who were exposed to simulated microgravity by dry water immersion for 3 and 5 days respectively. The right quadriceps femoris muscle a typical antigravitational muscle was loaded by 40 isometric contractions with maximum strenght. Each contraction lasted for 5 seconds followed by a 10 second recovery time. The examination took place 14 days befor and 2 hours after a 5 days exposure to water immersion. The muscle enzymes CK, CK mass, MHC increased dramatically. Both muscle growth factor and Troponin T did not change strikingly. Immobilisation secondary to immersion leads to diffuse lesioning of muscle cells. Since MHC is a typical enzyme of slow twitch fibers, the latter chatacterizing anti gravitational muscle, this muscle type seems to react primarily to decreased G-loads.

3-31-05 NEUROLOGICAL CHANGES SECONDARY TO 3 DAYS EXPOSURE TO DRY WATER IMMERSION

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Four main neurological alterations occur secondary to decreased G-loads, namely symptoms resembling motion sickness, disturbed motor functions, a shift in the sensory system and neuropsychological disorders. The neurological investigations in 15 volunteers took place immediately before exposure to water immersion and bed rest respectively as well as 24, 48 and 72 hours thereafter.In nearly all volunteers cerebellar signs occured after 24 hours of water immersion and increased within the following 48 hours. Probably this may be the consequence of decreased afferences to the cerebellar nuclei. The other symptoms mentioned above occured differently pronounced and in different percentage of volunteers.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

3-31-06 BENIGN PAROXSMAL POSITIONAL VERTIGO – FENESTRATION AND OCCLUSION OF THE POSTERIOR SEMICIRCULAR CANAL IN 15 CASES

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In benign paroxsymal vertigo (BPPV), the commonest peripheral vertigo, spontaneous remission usually occur within 1 year. A minority suffer frequently repeated attacks (intractable BPPV). 15 patients with intractable BPPV (5 male/10 female) aged 30 - 66 years (mean 47.6), duration of symptoms 1.1 - 10 years (mean 4.7), having received optimum medical therapy underwent fenestration and occlusion of the posterior semicircular canal (FOP) on the symptomatic side. Assessment included pre- and post-operative audiometry and electronystagmography (ENG). All patients remain free of BPPV to date (follow up 0.75 - 2.5 years). Abolition of nystagmus was documented by examination and ENG. Symptomatic hearing loss occurred up to 6 weeks post-operatively (mean 14.6 dB at 8 Hz) but thereafter returned to pre-operative level subjectively (observed hearing loss mean 6.4 dB at 250 Hz and 1.3 dB at 8 Hz). One patient developed acute unexplained sensorineural deafness at 22 months. All patients experienced non-disabling post-operative tinnitus. 4 patients who had no pre-operative tinnitus were still symptomatic at 6 months. 5 patients were free from tinnitus at 6 months post-operatively. The FOP procedure is effective treatment for selected patients. Transient sensorineural hearing impairment and non-disabling tinnitus are the main problems.

3-31-07 MONOCLONAL ANTIBODIES (MA) TO BRAIN ACETYLCHOLINESTERASE (AchE)

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Human AchE from the caudate and thalamus was purified by ConA Sepharose affinity chromatography. A single 66KD band was found on SDS-PAGE. Balb/c mice were immunized and 3 clones of hybridoma cells were established that produced Igm MAb that reacted with Torpedo AchE but did not cross react with RBC membrane AchE. The MAb did not inhibit AchE activity showing that the antibodies did not bind to the active center of the enzyme.

3-31-08 HEMORHEOLOGICAL STUDY IN PATIENTS WITH PROGRESSIVE SYSTEMIC SCLEROSIS

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In this study, we have tried to investigate disorders of some other hematological factors in PSS. The subjects were 8 patients with PSS and 10 healthy controls. Blood samples were taken from cubital vein and anticoagulated with heparin (50 unit/ml of blood). Routine hemorheological parameters and blood passage times (whole blood passage time, 40% RBC passage time; it reveals the disability of the deformability of erythrocyte, and plasma passage time) were evaluated. The negative pressure filtration technique using Nuclepore filter with 5 μm and/or 3 μm in diameter developed by Reid-Kikuchi was applied for measurement of the blood passage times, and measured three times for each sample. The results are summarized as follows:

1) In patients, hematocrit was slightly lower in females, and FDP was higher than the normal range.
2) Blood viscosity at all shear rates (18.8, 37.5, 75.0, 150.0, 375.0/sec) was elevated in patients.
3) Mean whole blood passage time and mean 40% RBC passage time were delayed more than controls signigicantly ($p < 0.01$).
4) Mean plasma time was not delayed more than controls.
5) There was significant positive correlation between whole blood passage time and blood viscosity at shear rates (37.5, 75.0, 150/sec).

These results suggest the disability of the deformability of erythrocyte as the other hematological factor in patients of PSS, and are very interested in relation to effects of prostaglandin therapy of insufficiency in microcirculations in the patients.

3-31-14 ACUTE INTERMITTENT PORPHYRIA , A 40 YEAR FOLLOWUP ON 150 PATIENTS - TREATMENT WITH CHELATING AGENTS

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Forty-seven patients with acute hepatic porphyria (AIP) not responding to withdrawal of precipitating agents, electrolyte balance, carbohydrate load and supportive therapy have been treated successfully with chelating agents in the form of ethylenediaminetetraacetic acid (EDTA) intravenously and/or dimercaptopropanol (BAL) intramuscularly. In more than 100 acute attacks we noted consistent response, including recovery from severe neurological and psychiatric symptoms and minimal recurrence during 40 years followup. Attacks and treatment response may be explained by porphyrin deficit in the nervous system caused by withdrawal and/or failure of replacement of normal zinc complexed porphyrinporphyrins. An enzymatic block (uroporphyrinogen synthetase URO-S) in porphyrin synthesis (due to excess zinc?) and relieved by chelating agents is defended. EDTA relieves this block and enhances porphyrin production. A toxic porphyrin theory is not valid. Hematin acts to shut down porphyrin precursor production and does not work favorably in AIP when neurological and psychiatric involvement are present.

The natural history of 150 AIP patients is described including precipitation by paints, solvents and starvation. A benign course is possible in AIP even after the most severe neurologic and psychiatric involvement.

3-31-23 SLEEP EXPERT - A COMPUTER BASED MEDICAL DECISION SYSTEM

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A new type of associative knowledge based decision support system for the diagnosis and classification of sleep disorders is described. Sleep Expert is based on the International Classification of Sleep Disorders (1990).
A high level language, which integrates object-oriented programming, hypertext and expert system technologies (Knowledge Pro)(Windows) was used.
Sleep expert is an interactive program composed of 288 separate integrated submodules and 264 textfiles. The user obtains a list of possible diagnoses on the screen. Reasoning questions help to select the right alternatives. The program has been written in such a form, that the user can freely associate and move forwards or backwards. Detailed information is included in hypertext.

Grant: Academy of Finland

3-31-24 EFFECT OF NIMODIPINE ON VASOSPASM AFTER EXPERIMENTAL SUBARACHNOID HEMORRHAGE IN RATS.

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In this study the effectiveness of Nimodipine (ND) was investigated by morphometric and ultrastructural studies of basilar artery in rats. This experimental vasospasm model was made by giving the autologous blood into the cisterna magna. Later ND was administrated by intracisternal or subcutaneous way, and by the light microscopic examination, the wall thickness, lumen, and diameter of basilar artery were measured and diameter/wall thickness (D/W), diameter/lumen (D/L) ratios were studied and compared with control group.

In the Group I, intracisternal ND was administrated immediately after SAH, ND doses were 10 μg/kg (n:5), 20 μg/kg (n:4) and 50 μg/kg (n:5). No significant difference was found between measurements of study and control groups (n:9). In Group II, which received s.c. 100 μg/kg t.i.d. for 72 hours. The wall thickness was found significantly thinner than control group ($P < 0.01$) but the other parameters have not changed.

The double-hemorrhage group (Group III) which received the same dose (100 μg/kg) of ND showed significant increase in the D/W ratio when compared to matching control group ($P < 0.01$). But there was no change in other parameters.

Electron microscopy was made only in Group II. Ultrastructural changes were endothelial changes, subendothelial blebs, corrugation of lamina elastica interna, endothelial demulation and intracytoplasmic vacuoles in both control and ND groups. Intracytoplasmic smooth-muscle vacuoles were less prominent in the rats receiving ND.

3-31-26 ALCOHOL-RELATED NEUROLOGICAL DISEASES
—HOSPITAL-BASED STUDY WITH POPULATION-BASED SPECULATION

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The frequency of chronic heavy drinkers(CHD) among 2,000 consecutive OPD patients and the frequency of alcohol-related neurological diseases among CHD were evaluated at three different hospitals in Tokyo; they were ca 10 and 30%, respectively. These data and the reported figures of the frequency of CHD in community-based studies in Japan combined together, population-based prevalence of those diseases were obtained:

Alcoholic polyneuropathies	472
Alcoholic spasticity	142
alcoholic cerebellar diseases	121
alcohol withdrawal syndrome	53
alcoholic dementia	37

per 10^5.

3-31-27 CLINICAL AND ANO-RECTAL PHYSIOLOGY FINDINGS IN PATIENTS WITH CONUS MEDULLARIS AND CAUDA EQUINA LESIONS

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The clinical features of conus medullaris and cauda equina lesions often overlap. Therefore, localisation is often difficult in clinical practice. This Study evaluates clinical and electro-physiological tests that help localise the site of the lesion.
Twenty-two patients (fourteen men and eight women) presenting with sphincter disturbances were included. All patients had detailed neurological examination and spinal imaging. The following clinical features were useful in identifying a conus medullaris lesion (7 patients): abnormality of proprioception, superficial sensory loss extending to the trunk and weakness of hip flexion; whilst the following signs localised the pathology to the cauda equina (8 patients): sensory abnormalities limited to the lower limbs, normal proprioception and clinically severe sensory and motor deficit combined. The symmetry of saddle anaesthesia was not a useful differential sign. Three patients had mixed conus and cauda equina lesions and in four the lesion was outside the spinal column.
Physiological studies of the pelvic and sphincter musculature showed increased motor latencies to the external anal sphincter muscles after translumbar stimulation at the L1 and L4 levels in cauda equina lesions. EMG studies were also often abnormal. A normal L4 spinal latency in a patient with suspected conus medullaris lesion was useful in excluding additional cauda equina pathology.

3-31-28 CODING OF VISUALLY GUIDED AND INTERNALLY INSTRUCTED MOTOR SEQUENCES IN THE PRIMATE SUPPLEMENTARY, PRESUPPLEMENTARY AND PREMOTOR CORTEX

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The aim of the present study was to compare neuronal activity in the (i) supplementary motor area (SMA), (ii) pre-SMA (the motor area immediately rostral to the SMA), and (iii) premotor cortex (PMC) in association with a sequential motor task. Three different movements (turn-push-pull) were performed to a manipulandum in two different conditions: 1) *internally determined* (I): the monkey had to generate the pre-determined sequence from memory and without visual guidance; 2) *externally triggered* (E): the movements were performed by following lights illuminated individually. Single cell activity of 425 task-related neurons was analyzed. Pre-SMA neurons were preferentially active during E in the pre-movement period but more related to I in the movement period. In contrast, more than one-half of the SMA neurons were preferentially or exclusively active in I, and more that 50% of the PMC neurons were more active in E during both the pre-movement and movement periods. Findings point to striking differences among neurons in each cortical area as to the manner in which they were involved.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-01-01 A SYNDROME OF MONOMELIC AMYOTROPHY WITH SPINAL HEMIATROPHY, ANTI-GM1 ANTIBODIES AND ABNORMAL F-WAVES: AN AUTOIMMUNE MOTOR NEURON DISEASE?

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We report eight Japanese patients with unilateral atrophy of the distal upper limb and the cervical cord. Symptoms typically began insideously in young adulthood, progressed for a few years and then stabilized. Distribution of the muscle weakness often conforms to the territories of a few peripheral nerves, but without any sensory deficits. Serum anti-GM1 IgG antibodies were frequently elevated. Electrophysiological evaluation disclosed chronic partial denervation in atrophied muscles, and absent or delayed F-waves in the nerve involved. One patient showed overt conduction block across the brachial plexus. Two showed partial clinical improvement after cyclophosphamide therapy or intravenous immunoglobulin. These findings suggest that this clinical condition is immune-mediated as in multifocal motor neuropathy, with its blunt of immune attack directed not only to peripheral motor nerves but also to spinal motor neurons.

4-01-02 TEMPORAL LOBE LESIONS IN AMYOTROPHIC LATERAL SCLEROSIS (ALS) WITH OR WITHOUT DEMENTIA.

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Pathological examination was conducted of the temporal lobes of five autopsied cases of ALS with dementia (ALSD+) [sections of the temporal tip (four cases), pes hippocampi (three), and gyrus ambiens (two) being available] and 44 cases of ALS without dementia (ALSD-). The ALSD+ cases showed previously unnoticed lesions: 1) in four cases, definite loss of cortical neurons in the apical temporal lobes, most prominent in the dorsomedial region; 2) in three cases, focal depletion of pyramidal neurons in the CA1-to-subiculum transitional area, with preserved ischemia-labile neurons in Sommer's sector; and 3) definite neuronal loss of the gyrus ambiens in both cases examined. Only a few ALSD- cases showed similar lesions. This study indicates that temporal lobe lesions are common in ALSD+. Regarding the relation of ALSD- with temporal lobe lesions to ALSD+, detailed clinicopathological study are required, because dementia in ALS can be difficult to assess.

4-01-03 FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS AND CNTF

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Familial ALS (FALS) can be classified into three groups; Group (A) linked to chromosome 21q22.1, (B) excluded from this region and (C) unclassified. Since CNTF promotes the survival of motor neurons and prevents the death of axotomized motoneurons, it might be a candidate gene for FALS. In collaboration with Drs. M. Litt and C. Jones, CNTF was assigned to chromosome 11q13.1-q13.4 by use of human/rodent somatic cell hybrid panels. Linkage analysis of FALS families from Groups (B) and (C) with DNA markers which map to chromosome 11q13 was also carried out. The combined LOD score = -5.82 at $\Theta = 0.00$ was obtained with INT2 which maps to chromosome 11q13 and linkage was excluded up to approximately 5 cM ($z < -2$ at 5 cM). Since CNTF is not located on chromosome 21, it is not a candidate gene for Group (A). Furthermore, it is unlikely to be a candidate gene for the other groups since linkage for chromosome 11q13 with those families was excluded.

4-01-04 SPECIFICITY OF UBIQUITIN-POSITIVE INCLUSIONS (Ubi) IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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[Purpose] Ubi in motor neurons have been considered to represent abnormalities specific for ALS. However, Ubi have not yet fully been investigated in other neurological diseases (non-ALS) and non-neurological controls. The purpose of this paper is to evaluate the specificity of Ubi in ALS by studying the motor neurons of various kinds of non-ALS patients (pts) and controls.

[Materials and Methods] We studied the lumbar cords of 22 pts with ALS, 22 non-ALS with 15 different neurological diseases and 36 controls. We stained paraffin-embedded sections of the lumbar cords by avidin-biotin complex method (Vectastain, Vector, USA) using polyclonal anti-ubiquitin antibodies (1:50) (Sigma), and examined the anterior horn motor neurons.

[Results] We observed Ubi in 19 out of 22 pts with ALS and 1 out of 22 non-ALS pts, but non in 36 controls. Ubi were more frequently observed in ALS than in non-ALS and controls ($p<0.01$). Ubi found in the one non-ALS pt were observed in the motor neurons with central chromatolysis due to the infiltration of the anterior roots by lymphoma cells.

[Conclusion] Our data further indicate the specificity of Ubi in ALS, although similar inclusions may rarely be seen in non-ALS.

4-01-05 VIALETTO-VAN LAERE SYNDROME [PONTOBULBAR PALSY WITH DEAFNESS] (VVLS) WITH DIFFERENT PHENOTYPIC PRESENTATION AND VARIABLE AGE OF ONSET

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VVLS is an autosomal recessive disorder caused by neuronal loss and gliosis in lower cranial motor and ventral cochlear nuclei.

A Saudi family had two out of eight siblings affected. Parents were first degree cousins. Case A: Deafness and bulbar weakness started at age 11. By age 15, he had severe weakness in cranial nerve V through XII innervated muscles (sparing VI) and a moderate distal wasting. Case B: Onset was age 20 with less severe facial and bulbar weakness, affecting the pyramidal more than the lower motor neuronal system.

Extensive metabolic work-up including lysosomal enzymes and mitochondrial studies was normal. Transcranial magnetic stimulation disclosed increased central conduction time. Blink reflex had prolonged late components (R2). Brainstem auditory evoked potentials initially showed small amplitude wave I with absent later components. Wave I was absent 2 years later.

This is the first documentation of delayed motor conduction time in VVLS. We confirmed the previously reported delayed later component of the blink reflex. This family demonstrate the phenotypic variability and different age of penetrance. This observation had not been reported previously in VVLS.

4-01-06 THE EXISTENCE OF ANDROGEN RECEPTOR IN THE RAT CENTRAL NERVOUS SYSTEM.

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Recently androgen receptor (AR) gene mutations with X-linked spinal and bulbar muscular atrophy(SBMA) have been reported. We proved AR abnormality in scrotal skin with SBMA (Neurology 9/92). Androgens play an important role in motor neuron growth, development and regeneration, but the distribution and identification of AR are unclear in central nervous system (CNS). To clarify the distribution of AR and detect AR protein in the rat CNS, we studied the immunohistochemical localization of AR (ABC method) with anti-AR monoclonal antibody and its immunoblotting analysis. Anterior horn cells in spinal cord were stained most intensely, while Purkinje cells and some other neurons were stained moderately. Western blotting revealed that AR protein in CNS is 41kD, different from two bands (95kD, 41kD) detected in prostate. This study confirms AR existence in CNS by immunohistochemistry and Western blotting, predominantly in anterior horn cells. AR abnormality might lead to the degeneration of lower motor neurons. There is some possibility that AR protein in CNS is expressed as tissue-specific form, different from other target organs.

4-01-07 INCREASING INCIDENCE OF MOTOR NEURON DISEASE (MND) IN NORTH-EAST ITALY

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The objective of our study is to determine if the incidence of MND is changing and its association with other diseases and trauma. All MND cases that occurred in Padua district (821,545 inhabitants) over 1980 - 1991 period were collected. Incidence rate was calculated every three years. Age at diagnosis, diagnostic interval, first symptom, associated diseases and previous trauma were reviewed. A case-control study was performed in 56 MND patients and 56 neurological controls to evaluate if prior trauma could be considered a risk factor for MND. 94 MND cases, were found. The mean age at diagnosis was 60 years. The first symptom was bulbar in 17% and spinal in 83% of cases. The onset was mostly asymmetric, with a preponderance of right side involvement in upper, but not in lower extremities. Among the associated conditions, only previous trauma resulted significantly related to MND. The MND incidence rate rose from 1.34 to 2.66 per 100,000 inhabitants in agreement with the world-wide rising trend.

4-01-08 MOTOR NEURON DISEASE/AMYOTROPHIC LATERAL SCLEROSIS (MND/ALS) : CONJUGAL CASES IN TWO FAMILIES OF SOUTH FRANCE.

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The pathogenesis of MND/ALS remains unknown but epidemiological studies have pointed to the putative role of environmental factors. Thus, geographical clustering, endemic areas of particular forms have been described. In the past only two conjugal cases of MND/ALS have been published, possibly accounting for a chance association. We now describe two other cases from south France. In the first family both the husband and the wife were affected by the age of 60, with a disease duration of 2 and 7 years, respectively. They both had limb onset of a typical ALS. In the second family the husband had respiratory type of ALS by the age of 83 with a 1 year course. The wife had typical ALS with bulbar onset occuring at 74 years old, she died 2 years after. Usual differential diagnoses were ruled out, and EMGs were typical for these four subjects. This may well be a chance association but a number of cases may be lost due to the late onset of the disease. These points are discussed and our cases are compared to those already published.

4-01-09 MOTOR NEURON DISEASE/AMYOTROPHIC LATERAL SCLEROSIS (MND/ALS) ASSOCIATED WITH KORSAKOFF'S PSYCHOSIS.

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MND/ALS may sometimes be associated with other neurological signs such as dementia or parkinsonism. In such cases the neuronal degeneration is frequently more diffuse in the brain and the authors tend to consider such syndroms as a distinct disease. We describe the case of a 70 years old man who presented with memory impairment, amyotrophy and fasciculations. The initial diagnosis was that of Korsakoff's psychosis with lower motor neuron signs. During the course of the disease pyramidal signs appeared both with weakness in the shoulders. MRI of the brain and cervical spinal cord showed a severe atrophy of the temporal lobes. Left temporal blood flow was markedly reduced on SPECT study. Inquiry did not found any antecedent of alcoholism, trauma or seizure. Diffuse denervation was seen in EMG without reduction of nerve velocities or conduction blocks. Anti-GM1 antibodies were absent. Comprehensive biological exams and lumbar puncture were normal. The pathogenesis of such an association is discussed.

4-01-10 JUVENILE DISTAL SPINAL MUSCULAR ATROPHY (JDSMA) OF UPPER LIMBS WITH MINIPOLYMYOCLONUS AND TREMORS: CLINICAL, RADIOLOGICAL AND SURFACE EMG STUDIES

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From 1985 to 1992, thirty cases of JDSMA were studied. All the patients were men. Muscle wasting and weakness of upper limbs were unilateral in 20 (66.7%) (90% in the right), billateral with asymmetry in 6 (20%) and symmetrical involvement of both arms in 4 (13.3%). The onset was insidious and the symptoms began between 16 and 19 years of age. The muscle wasting was confined to one hand for 1 to 3 years before progressing proximally to forearm and the other hand. Afterward, the disorder represented stational or very slowly progressive course. Other symptoms such as cold paresis, cramp were also noted. Clinical observation and surface EMG recordings evaluating the associated movements of the fingers revealed the following patterns: 1) typical minipolymyoclonus with irregular "piano-like" movement. EEG showed incomplete, poor and irregular interference pattern without burst formation. 2) enhanced physiological tremor-like pattern with 9 - 13 Hz, short duration burst formation. 3) combination of (1) and (2). 4) essential tremor-like pattern. Radiological studies of the cervical cord revealed focal cord atrophy.

4-01-11 ACCUMULATION OF IRON IN THE PRIMARY MOTOR CORTEX OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS.

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In amyotrophic lateral sclerosis (ALS), pathomechanisms of degeneration in the primary motor cortex is still unknown. Recently, marked hypointensity on T2-weighted magnetic resonance imaging (MRI) in the motor cortex have been reported in patients with ALS, which suggests a possibility of iron accumulation in this area. In order to verify this hypothesis, histological evaluation of inorganic iron (Perls' Prussian blue reaction) and ferritin immunohistochemistry were performed on paraffin sections of formalin-fixed motor cortices of patients with ALS (n=8), and of 8 controls. Perls' reaction was seen in microglia, macrophages, and more faintly in oligodendroglia in 6 ALS brains, while almost no reaction was observed in controls. Microglia and macrophages also had strong immunoreactivity which was associated with the severity of degeneration in the motor cortex but not with the degree of Perls' reaction. In conclusion, iron tends to accumulate in the primary motor cortex of patients with ALS, and the increase of iron may be responsible for the MRI finding characteristic of ALS.

4-01-12 THERMOGRAPHICAL STUDY ON PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Skin temperature is controlled mainly by the sympathetic (vasomotor) nervous system. This study was conducted to measure skin temperature in patients with amyotrophic lateral sclerosis (ALS) and investigate possible changes in the autonomic nervous system.

[METHOD] The skin temperature was recorded for 3 patients with ALS and 122 normal control subjects at the back of the hands and feet using a JTG3310 thermoviewer under the following conditions : 1) At rest, 2) Cold dip test; After soaking the bilateral surface of the hands or feet for 1 min in cold water at 10°C, the rate of recovery of skin temperature was determined at 1, 5 and 15 min.

[RESULTS] Skin temperature at rest of the feet of 2 patients with ALS was more than 2 SD below the mean value of normal subjects. Recovery rate also decreased. No significant decrease resting temperature or recovery rate could be detected for the hands. In one of the patients, skin temperature at rest of the hands and feet was slightly less than that in the control subjects. However, skin response following cold dip was essentially the same as that of the control subjects.

[CONCLUSION] Based on the present results, abnormality of sympathetic nervous function possibly occur in patients with ALS.

4-01-13 CLINICOPATHOLOGICAL STUDY OF AMYOTROPHIC LATERAL SCLEROSIS WITH DEMENTIA IN JAPAN

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To analyze the clinicopathological spectrum of amyotrophic lateral sclerosis (ALS) with dementia, we examined 13 patients including 11 sporadic cases and the first familial case in Japan consisting of 2 siblings.

The clinical picture in 11 sporadic cases represented bulbar-type of ALS. The type of dementia with uninhibited behavior and personality change closely mimicked that of Pick's disease. Language disorder was characterized by progressive reduction of speech output. Perseveration was observed in 10 cases.

Pathological examination was performed in 7 cases including one familial case, revealing frontal atrophy in 3 cases, frontotemporal atrophy in 2 cases and temporal atrophy in 2 cases. On microscopic examination there were mild neuronal loss, gliosis, mild spongy state of the cortical superficial layers and mild fibrous gliosis in the frontotemporal white matter. Neither circumscribed atrophy nor Pick body was found in any case. The substantia nigra showed a mild to severe loss of nerve cells without Lewy bodies in all cases. The pathological changes in motor neuron system were consistent with those of ALS.

The combination of ALS and dementia is a new clinicopathological entity.

4-01-14 ALUMINUM AND ITS ROLE IN THE FORMATION OF BUNINA BODIES IN AMYOTROPHIC LATERAL SCLEROSIS

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The purpose of the present study is twofold: firstly, to clarify the relationships between fifteen trace-elemental and clinico-pathological variables and the appearance of neurons containing BBs by multivariate analyses of data obtained from the spinal cord tissues of ALS patients; secondly, to determine the chemical composition of BBs at the ultrastructural level, using EELS. In the former study using both particle-induced X-ray emission (PIXE) spectrometry and morphometric analysis, multivariate analysis for the frequency of Bunina bodies (BB%) indicated that an increased amount of aluminum (Al) may stimulate the BB formation within motor neurons in concert with the magnesium (Mg) depletion, leading to the nucleolar dysfunction of rRNA synthesis (NF), and BBs may finally disappear with the duration of illness (DOI); (BB%) = 7.6646 x (Al) - 30.599 x (Mg) - 2.8899 x (NF) - 0.69331 x (DOI) + 63.11 ($F = 29.239$, $df = 4$, $p = 0.0011$; AIC = 64.931). In the latter EELS study, Al were detected within the BBs, showing amorphous whorls of various sizes including filamentous structures. Together with these results, it is indicated that Al may condense the DNA- and rRNA-containing chromatins and rRNA clusters by crosslinking with their phosphate groups and cause a progressive inhibition of protein and nucleic acid metabolism, consequently leading to the formation of intracytoplasmic inclusions such as Bunina bodies.

4-01-15 CHANGES IN FREE AMINO ACIDS IN NERVOUS TISSUE OF RATS ADMINISTERED WITH β,β'-IMINODIPROPIONITRILE.

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Swelling of the proximal axon is a morphological similarity between patients with amyotrophic lateral sclerosis(ALS) and animals administered with β,β'-imino-dipropionitrile(IDPN). The present study was undertaken to investigate whether these two states have something in common biochemically with each other. Thirty male Wistar rats were injected intraperitoneally with IDPN(2g/kg), and were sacrificed under anesthesia at a decided time after injection. Various changes in free amino acids(FAAs) were detected, suggesting diverse action of IDPN. The number of FAAs changed was 8 in the cerebrum, 10 in the spinal cord, 5 in the peripheral nerve, 10 in the skeletal muscle and 11 in the liver. Among these changes, elevation of taurine content in the cerebrum and the spinal cord seems to be important, because the same alteration has been reported in ALS patients. In relation to the increase in taurine, slowing-down of the metabolism in the folate cycle, which has also been reported in ALS, was suggested from reduced activity of 5,10-methylenetetrahydrofolate reductase, a key enzyme of this metabolic cycle. These results indicate that IDPN can provide a partial biochemical model of ALS, and suggest that the elevation of taurine content may have some bearing on the pathogenesis of ALS.

4-01-16 PATHOLOGICAL FINDINGS IN A CASE OF MULTIFOCAL MOTOR-NEUROPATHY.

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A 54-year-old female patient presented with rapidly progressive weakness of the left arm, which gradually spread to the other limbs over a 9 month period. Atrophy and hyporeflexia were noted in the left arm. No sensory or bulbar abnormalities were present.

Electrophysiological studies revealed denervation in the 4 limbs and motor conduction blocks in the right ulnar, median and peroneal nerves and in both tibial nerves. The patient was therefore considered to have multifocal motor neuropathy (MMN). The titer of anti-GM1 IgM's was marginally elevated, while IgG's were absent. Despite cyclophosphamide treatment the patient expired due to respiratory insufficiency.

Postmortem examination of the brachial plexus revealed patches of demyelinisation over the area of conduction block. However, in the spinal cord, atrophy with chromatolysis, spongiosis and gliosis of the ventral horns were seen, together with pallor of the pyramidal tracts.

These findings suggest that demyelinisation of peripheral nerve may underly conduction block in this patient with MMN. However, as degeneration of motor neurons was a predominant finding, the significance of such MMN as a clinical entity remains uncertain.

4-01-17 PET SCANNING FINDS EVIDENCE FOR A DOPAMINERGIC DEFICIT IN SPORADIC AMYOTROPHIC LATERAL SCLEROSIS (ALS).

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We have studied the integrity of the nigrostriatal pathway in sporadic ALS. Although unusual, ALS and Parkinson's disease (PD) may overlap in a single patient. The previous high prevalence of ALS-parkinsonism is also well noted in Guam. This background raises the possibility that ALS patients may have subclinical lesions of the nigrostriatal pathway. Fluorodopa (PD) PET provides in vivo information on nigrostriatal dopaminergic integrity. We have investigated 16 patients with sporadic ALS and performed FD PET with a graphical method for calculating the FD uptake rate constant. Three out of the 16 patients had FD uptake rate constants below the normal range. There was a significant negative correlation between FD uptake and duration of the disease ($R = 0.678$, $P = 0.004$). We found evidence for dysfunction of the nigrostriatal dopaminergic pathway in sporadic ALS. This supports the hypothesis that ALS and PD may share certain aspects of their pathogenesis and/or etiology.

4-01-18 CAUSATIVE MECHANISM OF JUVENILE ASYMMETRIC MUSCULAR ATROPHY IN THE HAND AND FOREARM (JAMAHF).

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JAMAHF characterized by juvenile onset in males, localized muscular atrophy in the hand and forearm, and non progressive course has been reported since 1959, mainly in Japan. The etiology has been unknown. We studied 8 patients with JAMAHF to clarify the causative mechanism. The initial symptom was distal muscle atrophy in most cases but sensory subjective radiculo-stimulating sign preceded muscle atropy in some cases. Body growth curves evaluating the arm growth revealed close relationship between the rapid growth period and the period from onset to arrest of symptom progression. Radiological findings revealed that slackness of the dorsal roots disappeared even in neck extension and that the lower cervical cord was shifted forward and to the affected side in neck flexion. These findings indicate the following pathogenesis of JAMAHF: nerve roots cannot grow as rapidly as the arm during a rapid growth period, and this makes the dorsal roots relatively shorter. In neck flexion the lower cervical cord is pulled forward by the shortened dorsal roots, which then causes chronic and latent compressive lesions on the anterior horn cells, and finally results in atrophy of the muscles innervated by motoneurons with longer axons.

4-01-19 HIGH-AFFINITY NERVE GROWTH FACTOR BINDING SITES DID NOT CHANGE IN THE WOBBLER MOUSE

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Re-expression of nerve growth factor (NGF) receptor in adult motor neurons is increased by axonal injury. This study was designed to examine whether high-affinity NGF receptor was re-expressed in the motor neurons undergoing chronic degeneration. The distribution of high-affinity NGF receptor was investigated, by *in vitro* autoradiography, in the cervical cord of the hereditary motor neuron disease mouse (wobbler). In normal mice, the highest specific [^{125}I]NGF binding was in the apical region of the dorsal horn, while the binding was much less dense in other regions of the gray matter. There were no significant differences in NGF binding in the cervical cord between wobbler and normal mice. This result suggests that the mechanism of motor neuron degeneration in the wobbler mouse is not associated with re-expression of high-affinity NGF receptor.

4-01-20 TIMED SWALLOWING IN NEUROLOGICAL PATIENTS.

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A previously validated test of swallowing speed was performed on 308 patients with a wide range of diagnoses. As in normal subjects swallowing was slower in female patients. The mean (sd) speeds of patients who did (n=118) or did not (n=186) complain of a swallowing problem were 5.9 (5.9) and 16.2 (10.1) ml/s respectively ($p<0.001$). Swallowing speed was reduced in those with abnormal speech ($p<0.001$) and was correlated with forced vital capacity ($r=0.55$, $p<0.001$). In patients swallowing speed was a linear function of average volume per swallow ($r^2=0.7$, $p<0.001$) and average log time per swallow ($r^2=0.4$, $p<0.001$).

The timed test of swallowing is a useful adjunct to the traditional lower cranial nerve examination which can be applied at the bedside or in the clinic and provides a ratio measure of swallowing capacity.

4-01-21 NEUROVEGETATIVE DYSFUNCTION IN AMYOTROPHIC LATERAL SCLEROSIS (ALS)

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Twenty-nine ALS pts aged 55±12. (18 males,11 females),13 with bulbar involvement, and thirty-three age-matched controls were studied to find out a possible autonomic impairment. We analyzed heart rate variability (HRV) on successive 600 beat time series, both in time domain: mean R-R interval standard deviation (SD), beat-to-beat mean square difference (MSD) and in frequency domain: low frequency (LF), high frequency (HF) component of HRV power spectrum, at rest, during passive orthostatism and controlled breathing (CB). The results show that ALS patients adequately respond to these stressors, but with significant differences compared to the control: a lower SD ($p<0.001$), a lower MSD ($p<0.01$) at each step, and a higher LF/HF ($p<0.01$) during CB. Pts with and without bulbar signs had not different HRV. In conclusion our investigation suggests a subclinical involvement of the autonomic nervous system in ALS particularly affecting vagal cardiovascular control. The clinical importance of an early detection may identify patients with augmented risk of sudden death.

4-01-22 A MOTOR NEURON DISEASE SYNDROME OCCURRING IN WOMEN WITH SILICONE BREAST IMPLANT FAILURE.

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Six (n=6) women developed a motor neuron disease syndrome (MNDS) on average 11 years (range 2 - 23 years) after receiving silicone-gel filled breast implants (n=5) and saline filled silicone covered breast implants (n=1). At explantation in five, all had ruptured implants with silicone spilled into tissue. In addition to the MNDS, patients had myalgia, fatigue, arthralgia, joint swelling and stiffness, rash, headache, Sjoegren's syndrome or Raynaud's phenomena. Some had autoantibodies such as anti-GM1, ANA or antimyelin antibodies or abnormal serum levels of immunoglobulins. Biceps muscle biopsy was done in five patients and showed neurogenic atrophy in all. Foreign material such as silicone breast implants might cause a MNDS probably indirectly through autoimmune mechanism. This report of six women can not answer any questions about the epidemiological occurrence of such a syndrome in the overall implanted population of women. However, the findings in our patients associated with implant failure raise the need of further investigations of the syndromic nature of MND associated with silicone breast implants.

4-01-23 A STUDY OF MOTOR NEURON DISEASE USING MAGNETIC RESONANCE IMAGING

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The degeneration of the pyramidal tracts in the brains of patients with motor neuron disease (MND) was studied using cranial magnetic resonance imaging (MRI) and neuro-pathological analysis. Nineteen patients with MND and 51 normal subjects were examined. The twelve of patients with MND had only lower motor neuron sign (SPMA type) and seven had both upper and lower motor neuron sign (ALS type).

Of the normal subjects, 24(47%) had the T2 prolonged small areas (high signal intensity areas) localized to the posterior internal capsule. High signal intensity areas with various extension were revealed in 12 patients(63%). In eight of 19 patients (42%), these areas extended from crus cerebri to corona radiata.This degree of extension was found in six of 7 patients with ALS type and in two patients with SPMA type. Morever,three patients were autopsied and studied for pathomorphology. In patients with extended areas of high signal intensity, the number of myelinated fibers in the posterior internal capsule was decreased.

These results warrant the conclusion that cranial MRI is useful for detection of degeneration of the pyramidal tracts in patients with MND.

4-01-24 INSULIN-LIKE GROWTH FACTOR BINDING PROTEINS (IGFBPs) AT MOUSE NEUROMUSCULAR JUNCTIONS (NMJ)

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IGF I and II effect many cells. In the nervous system IGF-I may be the endogenous nerve sprouting factor. In serum IGFs are specifically-bound with high affinity to IGFBPs. Six IGFBPs, sequenced and cloned, have both potentiating and inhibiting effects on IGF-I action. In experiments by others, sprouting induced by botulinum toxin was inhibited by IGFBP-4. We studied IGFBPs 1-4 in mouse muscle using specific polyclonal antibodies. NMJs were visualized with rhodamine-conjugated α-bungarotoxin (TRITC-α-BTX). NMJ, nerve neurofilaments (NF) and basement membrane (BM) proteins were stained with 1°Ab and FITC-2° Ab. Differential localization of IGFBPs was found. BP -1>-3>-4 stained pre-synaptic NMJ and intramuscular nerves but not the BM. IGFBP-2 intensely stained the BM, within and outside the NMJ, but not nerve. These results suggest differential neuromuscular function for these IGFBPs, in particular, IGFBP-1 and -2. They may help our understanding the IGF signaling system in the nervous system and may guide investigators interested in treatment of ALS patients with rhIGF-I. Local induction of one or more BPs might influence IGF-I effects on nerve and/or muscle.

Supported by Cephalon, Inc. and the VA Medical Research Service

4-01-25 RESTRICTION ENZYME ANALYSIS OF AMYLOID PRECURSOR PROTEIN GENE IN GUAMANIAN AMYOTROPHIC LATERAL SCLEROSIS AND PARKINSONISM-DEMENTIA.

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Neurofibrillary tangle is a prominent neuropathological finding in patients with Guamanian amyotrophic lateral sclerosis (ALS) and parkinsonism-dementia (PD). Codon altering point mutations in the amyloid precursor protein (APP) gene, leading to altered tertiary configurations, may explain the prominent intracellular amyloid deposition in these disorders. To determine if point mutations are present in the APP gene, high molecular weight DNA extracted from brain and lymphocytes of 4 cases each from patients with Guamanian ALS and PD were studied by polymerase chain reaction using primers 5'CCTCATCCAAATGTCCCCGTCATT3'and 5'GCCTAATTCTCTCATAGTCTTAATTCCCAC3' from exon 15 (APP695). Restriction enzyme analysis of the 319 bp enzymatically amplified product using MboII revealed digested products that may correspond to a point mutation Glu>Gln (amino acid 618) in Guamanian ALS and PD. Direct sequencing of exon 15 of the APP gene is underway to confirm this finding.

4-01-26 MUSCLE FIBER TYPE GROUPING IS NOT A USEFUL PREDICTOR FOR SLOWER COURSE IN AMYOTROPHIC LATERAL SCLEROSIS

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OBJECTIVE: There is no laboratory finding to predict outcome and the rate of progression in an individual patient with amyotrophic lateral sclerosis (ALS) at the time of diagnosis. Fiber type grouping in muscle biopsy, suggesting collateral reinnervation, has been suggested to be an indicator for a better prognosis. We examined the correlation between rate of clinical progression based on the disability scales (Appel et al. Ann Neurol 22:328-333, 1987) obtained during the course of illness and the degree of fiber type grouping.

METHODS: Muscle biopsies of 30 male and 30 female ALS patients, matched for age and duration of the disease, were studied. Total ALS scores at the time of biopsy and one year later were recorded and the difference of scores calculated. Biopsy histochemistry were reviewed by a blinded observer to the ALS scores. Fiber type grouping was classified according to the number of groups of both fiber types and correlation between the rate of progression in ALS score and the degree of fiber type grouping were calculated with ANOVA test.

RESULTS: The presence of fiber type grouping of any degree did not correlate with the rate of clinical progression(p>0.05).

CONCLUSION: Fiber type grouping is not a useful predictor for slower course in ALS.

4-01-27 ACTION OF CNTF, IGF AND NEUROTROPHINS ON DEGENERATING MOTONEURONS: CLINICAL IMPLICATIONS

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CNTF, FGF, IGF and BDNF are known to support survival of isolated embryonic motoneurons in cell culture. At least CNTF and BDNF are also capable of preventing motoneuron cell death during development and after peripheral nerve lesion in vivo. We have studied the physiological interactions of these neurotrophic factors on motoneurons in cell culture, in mouse mutants (pmn) and in transgenic mice where the gene for CNTF has been disrupted. Pharmacokinetic studies with CNTF in adult rats have shown that CNTF is rapidly eliminated from the circulation by the liver after systemic injection. Hepatocytes react by acute phase protein induction, making systemic bolus injection of CNTF unfavourable for clinical applications. Our results indicate that the potential therapeutic use of these factors in motoneuron disease depends on the identification of optimal ways of administration and a better understanding how these factors interact physiologically in regulating motoneuron function and survival.

4-01-28 INTRATHECAL CALCITONIN IN ALS: ENCOURAGING RESULTS?

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Calcitonin-like immunoreactive (C-IR) nerve fibers appear markedly decreased at most segmental levels in ALS spinal cords (V. DiCarlo, Neurol. 39, 322;1989). Considering that C-IR fibers often appear closely associated with or identical to serotoninergic fibers (V. Di Carlo, Neurosci. Lett. 51,295; 1986), and that TRH was also found to be present in serotoninergic neurons, we performed an open trial of calcitonin administration to ALS patients, by intramuscular and intrathecal routes. We summarized the main aspects of this work in J. of Neurol. 237,519; 1990. We wish here to add that the intrathecal treatment has consistently produced cessation of fasciculations and symptomatic improvement. In two cases, we observed survival since 1986, when the treatment was started. Actually, in one of these there was an apparent block of the disease progression, generalized increase of muscle bulk and strength, healthy aspect and feeling of well being. Moreover, when the patient decided to discontinue his treatment for three months, in the summer of 1992, his condition deteriorated, to improve again after the treatment was resumed.

4-01-29 EXTRAPYRAMIDAL SYSTEM INVOLVEMENT IN AMYOTROPHIC LATERAL SCLEROSIS

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The neuropathological characteristics of Amyotrophic lateral sclerosis (ALS) are known that the pathologic changes are almost limited in both upper and lower motor neuron system. However, we had reported that some ALS patients showed the apparent pathologic changes in extrapyramidal system, such as substantia nigra, globes pallidus and corpus Luysi (*J Neurological Sci. 108*:137, 1992.). The aim of this study was to clarify the frequency of the ALS patients whose extrapyramidal system were involved neuropathologically and to clarify what kind of transmitter systems were damaged in these cases from the histopathological view point. We examined sixteen cases with ALS who showed usual neurological symptoms without extrapyramidal symptoms nor dementia by both conventional neuropathological methods and immnohistochemical staining using the histophain SAB cuits, and anti-met-encephalin antibody (Ab), anti-substance P Ab and glial fibrillary acidic protein Ab (GFAP) as the first Ab.

Six out of 16 ALS patients showed both the neuronal cell loss and glial infiltration in substantia nigra (37.5 %), and nigro-pallido-luysian degeneration were shown in three patients (18.8 %). Neurotransmitter systems both encephlin neuron and substance P were rather concentrated in nigro-pallido-luysian system involved ALS patients from the immunohistochemical examination. Moreover, slight glial infiltration were also shown in that place. However immunoreactivities in met-enchephalin and in substance P were variable in only nigral involved ALS patients. Conclusively, extrapyramidal system were involved in subgroup of ALS. Further immunohistochemical examinations were desirable.

4-03-01 THE PREVALENCE OF DEPRESSION IN A POPULATION BASED STROKE REHABILITATION PROGRAMME

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A stroke register was started in August 1989 in two districts with an active rehabilitation programme (AD) and two control districts (CD) with a total study population of 135000. 585 patients in all were included with the mean age of 71,9 years. Depression was evaluated by using Beck Depression Inventory (BDI). Both the patient and the closest relative were investigated at three months and at one year after stroke. At three months the mean of BDI was 9,9±7,6 for patients in the AD and 11,8±6,8 in CD, at one year 10,0±7,2 and 11,1±7,5, respectively. 8,6% (14 of 163) of patients in the AD and 12,0% (14 of 117) in the CD had the sum of BDI greater than 20 points (a cut point value indexing depression) at three months. The respective figures were 8,6% and 9,4% at one year. Of the relatives 3,8% (4 of 104) in the AD and 8,5% (5 of 59) in CD had the sum greater than 20 points at three months. At one year the respective figures were 4,8% and 10,2%. Depression was less common in our population based stroke register than reported earlier. It was more common in the CD without rehabilitation programme than in the AD.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-03-02 STUDY ON CLINICAL VALUATION OF THE SHH FOR SAH

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The clinical valuation of SHH for the SAH was discussed by analysing 62 patients with SHH (in both eyes in 35 cases and in only one eye in 27) who were numbers of the 609 cases with SAH. The results which had made a comparison between the SHH group and no SHH group show that the clinical symptoms were more severe, the intracranial pressure was higher and the mortality in the SHH group was more than the no SHH group. It was demonstrated the SHH of 6 cases in only one eye located on the same side with ruptured intracranial aneurysm by autopsy.

4-03-03 CERVICAL (C2) HERPES ZOSTER INFECTION FOLLOWED BY PONTINE INFARCTION.

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A 56 year-old right handed man with a history of rheumatoid arthritis and hypertension developed a left retroauricular (C2) vesicular rash diagnosed as herpes zoster which resolved over a four week period. Five weeks following the initial cutaneous manifestation, the patient experienced facial paresis, upper extremity paresis and lower extremity plegia on the left. Serum and CSF studies revealed elevated varicella zoster antibody titers. Brain MRI (long TR, long TE) showed focal areas of increased signal intensity in the midpons (right tegmentum and basis, and left tegmentum). Cerebral angiogram showed segmental narrowing and dilatation of the left superior cerebellar artery and decreased filling of the distal branches of the left posterior cerebral artery. The patient was treated with prednisone and acyclovir, and regained some strength of his extremities.

There are only four reported cases of cutaneous (C2) herpes zoster with subsequent stroke in the distribution of the posterior circulation. The likely mechanism is viral invasion of the arterial wall via cervical nerve innervation of the posterior circulation.

4-03-04 CIRCADIAN RHYTHMICITY OF BLOOD PRESSURE AND OCCURRENCE OF ISCHEMIC STROKE IN THE NIGHTTIME

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Although ischemic stroke often occurs in the nighttime, the reason for such nocturnal occurrence of stroke has yet remained unclear. We studied the relationship between circadian rhythmicity of blood pressure and time for stroke occurrence in 110 patients with chronic cerebral infarction. According to the history of stroke onset, the patients were divided into three groups; Group A with attacks in the daytime, Group B1 with stroke during the sleep and Group B2 with attacks in the nighttime at the bathroom. The blood pressure was monitored every 30 min employing an ambulatory blood pressure monitoring system for 24 hours. Average blood pressure values for 24 hours showed no significant difference among the three groups. Averages for the daytime blood pressure values and the nighttime blood pressure values were also not significantly different among the three groups. The majority patients exhibited a noticeable blood pressure reduction for a short period in the nighttime in association with bradycardia. The minimum systolic blood pressure in the nighttime was significantly lower in Groups B1 (83±7 mmHg) and B2 (88±8 mmHg) as compared with Group A (110±21 mmHg). The minimum diastolic blood pressure in the nighttime was also significantly lower in Groups B1 (54±8 mmHg) and B2 (59±10 mmHg) than in Group A (70±13 mmHg). The present results suggest that patients with stroke in the nighttime may undergo a deep blood pressure drop in the nighttime. Such a deep blood pressure drop may play a role in the nocturnal occurrence of stroke.

4-03-05 CEREBROPROTECTIVE EFFECTS OF BW619C89 & BW1003C87 AFTER FOCAL AND GLOBAL ISCHAEMIA IN RATS

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We report the cerebroprotective effects of compounds which inhibit glutamate release after focal or global cerebral ischaemia in rats.

Cortical infarct volume after permanent occlusion of the middle cerebral artery is reduced with BW619C89 (20 mg kg^{-1}, i.v.) by 43% (immediate treatment), 61% (1-hour delay) and is unaffected after a 2-hour delay.

Hippocampal CA_1 neuronal cell loss after transient global cerebral ischaemia (20 min bilateral common carotid artery occlusion in vertebral artery-occluded rats) is reduced by 70% by BW1003C87 (10 or 20 mg kg^{-1}, i.p. -20 min to and +4h after ischaemia). Increases in extracellular glutamate, aspartate, taurine and GABA concentration were also reduced. BW1003C87 (10 or 20 mg kg^{-1}, i.p., 0 and +4h or +2h and +6h) and BW619C89 (20 mg kg^{-1}, i.p., 0 and +4h) reduced hippocampal CA_1 neuronal cell loss by 70-80%.

BW619C89 and BW1003C87 reduce ischaemic brain damage in rats.

4-03-06 SPECT FINDINGS IN TRANSIENT GLOBAL AMNESIA: REPORT OF 9 CASES

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The etiology of transient global amnesia is still unknown. In order to obtain further information on the pathophysiology we performed TC99HMPAO SPECT in 9 patients referred for TGA. They were 3 men and 6 women of mean age: 60.2 (range 41 - 72).

They were part of a group of 42 with symptoms fulfilling the criteria for TGA, observed between January 1989 and December 1992. Three patients underwent SPECT within the 6th hour from the onset of symptoms (early), while the others within the first week (late). Early SPECTS showed bilateral hypoperfusion (HP) in one patient, a right temporo-occipital HP in one and normal perfusion in one. Late SPECTS showed bilateral HP in one patient, temporal HP (2 right and 1 left) in three patients and a normal pattern of perfusion in two. Electroencephalogram and CT scan were normal. Our data suggest a presence of flow impairment either in early or later hours from the onset.

4-03-07 BILATERAL THALAMIC LESIONS DUE TO DEEP CEREBRAL VENOUS THROMBOSIS.

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Thrombosis of the Galenic venous system occurs rarely and is difficult to diagnose because of its non-specific clinical manifestations. We report on five cases with occlusion of the deep cerebral veins. In all cases (3 female,2 male; 36 to 59 years) focal neurological deficits and impaired consciousness appeared after a short period of non-specific clinical features. Computed tomography revealed bilateral hemorrhagic infarctions of thalamus and basal ganglia. In one case the first CT showed a unilateral thalamic hemorrhage which was classified as primary hypertensive hemorrhage. Extension of the hemorrhage to the contralateral thalamic region suggested its venous etiology. CSF analysis, which was done in two cases, showed a disturbance of blood brain barrier and signs of necrosis and hemorrhage. In four cases the diagnosis was confirmed by transfemoral carotid angiography. MRI was performed in three cases and could also demonstrate the thrombosis. All patients were treated with high-dose heparin in spite of hemorrhage. Good recovery was seen in all patients. No complications were observed during treatment. Among 31 published cases with deep cerebral vein thrombosis 10 patients had received high-dose heparin. Only 1 of them had died. Of those 21 patients without anticoagulation, 10 had a fatal course. Deep cerebral venous thrombosis should be considered in cases with bilateral lesions of thalamus and basal ganglia. As in dural sinus occlusion, early anticoagulation should be started even in cases with preexisting hemorrhage.

4-03-08 RISKS AND BENEFITS OF PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY FOR SYMPTOMATIC INTERNAL CAROTID ARTERY STENOSIS

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Percutaneous transluminal angioplasty (PTA) has been carried out in 20 patients (22 arteries) with symptomatic internal carotid artery (ICA) stenosis as an alternative to carotid endarterectomy (mean age 58 years, range 46-69). Successful dilation of the ICA was achieved in 15 arteries (68%). Difficulty canulating the ICA or crossing the stenosis prevented PTA in 7 arteries (32%). Complications included transient haemodynamic symptoms lasting up to 2 hours in 6 patients (30%), a minor stroke with full recovery within 7 days (5%) and a major stroke in one patient (5%). Asymptomatic complications included carotid dissection, spasm and pscudoancurysm formation. Follow up studies using transcranial Doppler measurements of middle cerebral artery flow have shown that successful PTA is accompanied by an improvement in cerebral vasodilatory reserve. The results support the need for further studies of this procedure.

4-03-09 PROTON MAGNETIC RESONANCE SPECTROSCOPY IN PATIENTS WITH BRAIN ISCHEMIA

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Combined Magnetic Resonance Imaging (MRI) and 1-H Spectroscopy (MRS) investigations were performed to evaluate the metabolic alterations in acute and subacute stage of brain ischemia. The investigation was carried out with a 1.5 T iron-shielded system (Magnetom-Siemens), using a Spin Echo (TE=135ms) sequence to acquire localized spectra from image-guided volumes of interest (16ml-27ml). Serial MRI-MRS examinations (on 1-2-3 weeks after stroke) were obtained in 5 patients. Lactate (LAC) intensity, N-acetylaspartate/Choline (NAA/Ch), NAA/Creatine (NAA/Cr) and Cr/Ch ratios were evaluated in infarcted area and compared with controlateral MRI-normal area and with healthy subjects brain. Preliminary data showed a decrease of NAA/Ch ratio and an increase of LAC in 6-day-old infarcted area. After three weeks, the LAC resonance was still detected, and NAA/Ch and Cr/Ch ratios were significantly decreased. MRI and MRS data comparison suggested an association between a decrease of NAA and highest levels of LAC in large ischemic lesions. The correlation between the MRS-profiles, MRI-size lesions and clinical status of a larger number of patients will be evaluate in order to verify the prognostic value and/or the marker role in therapeutical management of the MRS biochemical changes.

4-03-10 SECONDARY PREVENTION OF CEREBRAL ISCHEMIC EVENTS WITH MESOGLYCAN: THE RESULTS OF AN ASA-CONTROLLED, MULTICENTRIC STUDY (SIAM)

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The aim of the Studio Italiano ASA-Mesoglicano (SIAM) was to evaluate in patients with recent episodes of TIA or ictus of atherothrombotic origin the effect of a long-term treatment with mesoglycan, a natural glycosaminoglycan preparation, (100 mb/day) or aspirin (300 mg/day) in reducing the risk of new cerebral ischemic events and of vascular mortality.

A total of 1398 patients, 701 in the mesoglycan group and 697 in the ASA group, entered the study. At the end of the follow-up period (median duration: 18 months) no statistically significant differences were observed between the two treatments regarding fatal or not fatal vascular events. Deaths for vascular causes were 32 in the mesoglycan group and 37 in the ASA group. A comparable number of non fatal cerebro- and cardiovascular events was observed in the two treatment groups.

A signigicant ($p < 0.05$) higher number of patients with adverse drug reactions were reported in the ASA-treated than in the mesoglycan-treated group (146 vs. 50).

4-03-11 MODERATE POST-ISCHEMIC HYPOTHERMIA PROTECTS AGAINST NEOCORTICAL INFARCTION.

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Hypothermia has a dramatic protective effect when instituted intra-ischemically. This study was conducted to test the hypothesis that prolonged post-ischemic hypothermia can benefit cortical infarction in a transient focal ischemic model. Male spontaneously hypertensive rats (n=18) underwent 2hr transient right middle cerebral artery occlusion and permanent right common carotid artery occlusion. Upon reperfusion (RP), rats were either maintained normothermically, or were subjected to 6hr of whole-body mild hypothermia(32-34°C) or moderate hypothermia (28-30°C). After 46hr RP, rats were sacrificed and fixed for frozen brain sectioning. The volume of cortical infarction was measured and expressed as mm^3. One-way ANOVA was used. * $p < 0.05$

Group (n)	Cortical Infarction (mm^3) (mean±SD)
Normothermia (6)	175.4 ± 22.7
Mild hypothermia (6)	149.4 ± 38.7
Moderate hypothermia (6)	121.8 ± 56.5*

Post-ischemic but prolonged moderate hypothermia reduces infarct size.

4-03-12 SUCCESFUL CA1 PROTECTION WITH AN AMPA ANTAGONIST EIGHT HOURS FOLLOWING REPERFUSION.

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NBQX, a competitive antagonist of the AMPA class of glutamate receptor, was used to examine the effects of post-ischemic blockade of AMPA receptors, in the 2-vessel occlusion (plus hypotension) model of transient global ischemia, which reliably induces hippocampal CA1 neuronal injury. Male Sprague-Dawley rats (n=39) were subjected to 10 min. of cerebral ischemia (under general anesthesia, mechanical ventilatory support, meticulous control of temperature, arterial blood gas composition and fluid balance) and 7 days of reperfusion. Animals were randomly assigned to treatment with 3 doses of NBQX (30 mg/kg ip) 15 min. apart, beginning either immediately on reperfusion or after 8 hours; control animals received equivalent injections of sterile water. After 7 days, animals were sacrificed and histologic sections prepared. CA1 neurons of the dorsal hippocampus were counted and the ratio of damaged to total neurons calculated. The percentage of damaged CA1 neurons in the pooled control treatment group (n=20) was 69 ± 17% (mean ±sd). CA1 damage in NBQX treated animals was 12 ± 13.% for those given NBQX immediately on reperfusion (n=10) and in animals treated after 8 hours of reperfusion CA1 damage was still reduced to 49 ±25%. Thus NBQX treatment resulted in dramatic neuronal protection when administered at reperfusion ($p<0.0001$; ANOVA, Neumann-Keuls intergroup comparison test), and, when administration was delayed for 8 hours, significant protection was still achieved ($p<0.05$) in comparison with control treatment.

4-03-13 DELAYED TREATMENT WITH AN AMPA RECEPTOR ANTAGONIST CAN PREVENT ISCHEMIC NEURONAL INJURY

H. Li and A.M. Buchan. Neuroscience, Loeb Research Institute, Ottawa Civic Hospital, Ottawa, Ontario, Canada.

Delayed treatment with NBQX which is an AMPA glutamate receptor antagonist, was tested in a 4-vessel occlusion model of severe forebrain ischemia which reliably induces hippocampal CA1 injury. Adult male Wistar rats (n=25) were subjected to 10 min of forebrain ischemia and seven days of reperfusion. NBQX (30 mg/kg) was injected IP at the time of reperfusion, or following a delay of 6 hr or 24 hr post-ischemia. Damaged CA1 neurons of the hippocampus were counted and expressed as a percentage. *P<0.001 Mann-Whitney U test

Group (n)	% CA1 Injury (mean ± SD)
Saline (8)	81 ± 28
NBQX	
immediate(6)	17 ± 17*
delayed 6 hr(5)	21 ± 32*
delayed 12 hr(6)	25 ± 17*

AMPA receptor blockade delayed by 12 hr prevents CA1 injury, suggesting a causal relationship between selective injury and Ca++ entry through this glutamate-regulated but ischemia-modified ionophore.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-03-14 REMACEMIDE HYDROCHLORIDE, A MILD NMDA ANTAGONIST, REDUCES FOCAL CORTICAL INFARCTION.

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Glutamate receptor antagonists have effects in the treatment of focal ischemia, despite the controversy that still remains on their mechanisms of action. In this study, a "weak" non-competitive NMDA receptor antagonist, remacemide hydrochloride, was tested in a transient focal ischemia model in male Wistar and hypertensive rats (SHR). All animals sustained 2 hr of transient focal cerebral ischemia by common carotid and right middle cerebral artery occlusion, followed by reperfusion for 22 hr. Regional cerebral blood flow and physiological conditions were monitored during the experiment. The volume of cortical infarction was measured. Student's t tests were performed.

Group(n)		Cortical Infarction(mm3 ± SE)	Reduction(%)
Wistar	Saline (20)	153 ± 20	
	Remacemide (20)	115 ± 20	25
SHR	Saline (20)	206 ± 8	
	Remacemide (20)	155 ± 14	25**

**, p < 0.01

The anticonvulsant, remacemide, achieved a 25 percent reduction in the volume of cortical infarction in both Wistar and SHR.

4-03-15 CEREBRAL EMBOLI ONE YEAR AFTER MECHANICAL PROSTHETIC CARDIAC VALVE IMPLANTATION.

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Objective. The aim of this study is to assess the frequency of asymptomatic cerebral emboli in patients with mechanical prosthetic heart valves one year after surgery.

Methods. Sixteen patients have to date been included in the study, fourteen had a prosthetic aortic valve and two a prosthetic mitral valve. All patients were on warfarin treatment. Transcranial Doppler monitoring of the right middle cerebral artery (MCA) was carried out for 60 mins in each patient. Findings were assessed using an automatic cerebral embolus detection system (EME). This system automatically records and counts the number of emboli entering the MCA and differentiates embolic signals from those due to artefacts. The Doppler findings were also continuously recorded on a video tape for off-line analysis (visual and audio content).

Results. Asymptomatic MCA emboli were detected in 12 (75%) of the 16 patients. The frequency of emboli ranged from 1-68 per 60 mins (mean 25).

Conclusions. These findings suggest that asymptomatic cerebral emboli are frequent in warfarin treated prosthetic valve patients as long as one year after valve implantation. The clinical significance of these findings should now be evaluated.

4-03-16 ISCHEMIC STROKE IN PARKINSON'S DISEASE

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Various publications shows the lower incidence of ischemic strcke, in patients with P.D. as compared to controls attributed to various factors as dopamine deficiency, tobbaco chewing etc.

In our study of 30 newly diagnosed P.D. and 30 age & sex matched controls platelet aggregation was done. Diabetics, hypertension, smokers or patients on any treatment & low platelet counts were excluded.

Platelet aggregation was measured by the method (Bor GVR') using 4 channel aggrerecorder (Kyoto Daitchi-PA 3220) & Adenosine diphosphate, collagen & Epinephrin were used as inducers.

It has been observed that P.D. has significant decreased platelet aggregation as compared to controls which may contribute to the lower incidence of Ischemic stroke in these patients.

4-03-17 COMPUTED TOMOGRAPHY VERSUS CEREBRAL ANGIOGRAPHY IN INDIAN PATIENTS OF SUBARACHNOID HAEMORRHAGE.

Dr. Rohtas K.Yadav, Dr. D.S.Mishra, Dr.S.Dua, Dr. Rajnish. Medical College, Rohtak,Haryana,India

To assess and compare the relative diagnostic efficacy of computed tomography(CT)and cerebral angiography and to know the spectrum of various types of lesions in Indian patients of subarachnoid haemorrhage (SAH), this study was conducted in 50 clinically suspected and lumbar puncture proved cases of nontraumatic subarchnoid haemorrhage who were subjected to plain and contrast CT examination. CT examination was done within 24 to 48 hours of admission of the patient.

CT examination could detect the blood in subarachnoid space in all the 50 cases(100%). Correct etiological diagnosis of SAH could be made in 45 cases(90%). It included aneurysm of ACA-20, MCA-9,PCA-6,ICA-3,AVM-7 & angioma-2.There were 3 false negative diagnosis.

Computed tomography (CT) can help to avoid a risky lumbar puncture and can become the screening procedure of choice for a patient suspected to be suffering from SAH. CT examination should be done preferably within 24-48 hours of admission of patient. Since angiographic studies were based on CT examination findings, we had only three negative angiograms.

4-03-18 HEMODYNAMIC MONITORING OF THERAPEUTIC CAROTID OCCLUSION: A TRANSCRANIAL DOPPLER STUDY

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Therapeutic occlusion of the internal carotid artery (ICA) bears the risk of cerebral ischemia. We assessed the value of hemodynamic monitoring with transcranial Doppler (TCD) in 14 patients who underwent transarterial ICA occlusion for therapy of vascular malformations or tumors. Mean blood flow velocity (MBFV) and pulsatility index (PI) were continuously measured in the ipsilateral middle cerebral artery with a fixed probe. In 10 patients, changes of MBFV to motor stimulation were recorded before and after ICA occlusion.

Two patients suffered transient symptoms after ICA occlusion. MBFV were reduced by more than 50% in these patients compared to 20% (range, 0-31%) in the asymptomatic patients. The decrease of PI was higher in symptomatic (mean, 38%) than in asymptomatic patients (mean, 21%), but varied from 0 to 49%. Motor vasoreactivity after occlusion showed major variation, but was markedly reduced in symptomatic patients. We conclude that TCD monitoring is useful during this intervention, and that a drop of MBFV by >50% may herald risk of hemodynamic compromise.

4-03-19 LOCALISATION OF CEREBRAL LESION IN GLOBAL APHASIA.

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The localisation of cerebral lesions which were confirmed with CT are investigated in right-handed 25 patients with cerebrovascular disease. Modified aphasia test for Turkish citizen were given to the patients. It is demonstrated that 10 cases showed large hemispheric lesion affecting both anterior and posterior cortical areas of language. There were deep (subcortical) lesions in 10 patients, and anterior lesions (only in Broca's area) in 5 cases. We could not observe pure posterior (post-rolandic) lesion.

Our data suggest that, some certain limited areas of the left hemisphere are not responsible for global aphasia. It can be seen due to lesions in various localisations on the left hemisphere, except post-rolandic region. This fact related to the lesion localisation in global aphasia must be kept in mind during clinical evaluations.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-03-20 FACTORS DETERMINING THE OUTCOME OF INTRACEREBRAL HEMORRHAGE.

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The prognostic factors of intracerebral hemorrhage (ICH) are investigated in 316 cases under conservative treatment.

The mortality rate is 36.7 per cent. The most important determinant of mortality is the level of consciousness both at the beginning of the stroke and during admittance to our department ($p<0.001$). The prognosis is worsened when hemorrhage places in deep layers ($p<0.001$). Shift-sign on CT ($p<0.001$), the size of hematoma ($p<0.001$) and the presence of ECG abnormalities ($p<0.05$) are other determinants of bad prognosis. The sex and age are not found to be significant.

The mortality rate of our cases is not higher than those of the reports on conventional surgical therapy. Therefore, conventional surgical therapy should not be considered in most of the patients with ICH, unless the cases progressively worsen or in danger of herniation.

4-03-21 CAPSULOSTRIATAL APHASIAS.

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Twenty-nine, right-handed patients with left capsulostriatal lesions shown by CT-scan are investigated by a modified aphasia test.

Out of 11 patients with anterior putaminal lesions, 4 had global aphasia, 4 had atypical non-fluent and 3 had atypical fluent aphasia. In 4 of 8 patients with posterior putaminal lesion fluent aphasia was found. Two other cases had dysarthria, one had global and another one had non-fluent aphasia. Out of ten cases with a lesion involving anterior and posterior putamen, non-fluent aphasia was seen in 6, global aphasia in 3 and fluent aphasia in one patient.

Atypical aphasia patterns are seen in cases with capsulostriatal lesions. Periventricular extensions of cerebral lesion has a partial importance on the genesis of aphasia. Therefore, alike for the cortical areas, hemispheric dominance for subcortical regions should also be considered.

4-03-23 POST-STROKE DEPRESSION TREATED WITH CITALOPRAM - A SELECTIVE SEROTONIN REUPTAKE INHIBITOR.

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In a double-blind placebo controlled trial we investigated the efficacy and safty of citalopram in post-stroke depression.

In an unselected stroke population ≤ 80 years, 203 (71%) patients survived at least one month and could communicate reliably. Depression was diagnosed and assessed by the Newcastle Diagnostic Scale and the Hamilton Depression Scale (HDS). Baseline score ≥ 12 on the HDS. The unwanted effects were measured by the UKU side effect scale. Doses were 10 - 40 mg daily.

Eighti-five (42%) patients had HDS ≥ 13 and 66 patients (78%) entered the trial. Mean baseline HDS scores were 19.4 in the Citalopram group 18.9 in the placebo group. Demografic variables were comparable. Eighteen (27%) patients had an endogenous depression.

All statistical analyses showed a significantly greater improvement in patients treated with citalopram after 3 and 6 weeks of treatment.

No serious side effects related to the treatment could be detected. Side effects were mild and usually transient. We conclude, that citalopram is a safe and effective drug in post-stroke depression.

4-03-24 PATHOLOGICAL CRYING AND EMOTIONAL LABILITY - A CONTROLLED STUDY OF CITALOPRAM - A SSRI.

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In a double-blind placebo controlled crossover study we investigated the effect of citalopram in stroke patients with persistent emotional lability.

Sexteen consecutive patients (median age: 62.5, range 40-83) were included in the study, and 5 patients fulfilled the criteria for pathological crying. History of crying spells was based on a semi-structured interview and patients completed a diary. Video recordings were done. Six patients had right sided, 5 patients left sided and 5 patients brainstem lesions. One patient was withdrawn from the study after the first treatment periode (placebo), as he had a generalized seizure.

All patients responded to the treatment. The effect was immediate (1-3 days) and dramatic in 11 (73 %), and appeared somewhat slowlier (1-2 weeks) in the remaining patients.

The drug was well tolerated with few and transient side effects or mild side effects that disappeared completely after dose reduction.

We conclude that serotonergic neurotransmission plays an important role in emotional lability, and that citalopram, a selective serotonin reuptake inhibitor, is an effective drug.

4-03-25 CEREBROVASCULAR ISCHEMIC DISEASES IN YOUNG ADULTS

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61 young patients (under 50 years) with cerebrovascular diseases were treated in our ward between 1985-1990. The diagnostic possibilities were similar in this period. There were 23 women and 38 men with a mean age of 39.5 years (range 18-50). 30 patients had TIA, 18 PRIND and 13 CS. 35 patients recovered without symptoms, 16 with symptoms but without functional disturbance, 3 with severe symptoms but being able to live without support and 7 with severe symptoms but requiring help. TIA occurred previously in history of 19 patients. Localisation of ischemia was as follows: supplying area of carotid artery 26 cases, MCA 20, ACA 1, PCA 2, vertebrobasilar system 10, spinal artery 10. 29 patients had one or more risk factors, e.g. contraceptive pill. In this group only PRIND and CS were found. Cerebrovascular disorder occurred in the family of 9 patients. Stroke of cardiac origin was assumed in 10 patients. CT examination was carried out in 42 patients, out of them 15 were negative and in 27 cases infarct was detected. Angiography was performed in 26 cases: 16 were negative.

4-04-01 FLUORIDE IS A NORMAL COMPONENT OF THE CENTRAL NERVOUS SYSTEM

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A series of studies of determination of fluoride in CSF and brain tissue of mice were carried out with an ion selective electrode method.

1. Fluoride in CSF of 40 endemic fluorosis and in 32 surgical patients undergoing spinal anaesthesia was determined. The average value of CSF fluoride in Fluorosis (0.2 ppm) was higher than that of the control group (0.17 ppm). However, there is no significant difference ($t = 1.08$, $p > 0.05$).
2. The average fluoride level of 121 neurological patients with normal routine CSF examinations was 0.155 ppm. In 62 patients who were regarded as breakdown of their blood-brain barrier from the increase of CSF protein and cells, the average fluoride level of CSF was 0.162 ppm. There is no statistical differences between them ($t = 1.28$, $p = 0.2$).
3. The fluoride in the brain tissue of mice was measured after feeding with water containing NaF of 5 ppm, 10 ppm, 20 ppm, 40 ppm and 80 ppm and with the feeding time of 2, 4, 6 and 8 months. The normal controls were fed with water containing 0.5 ppm of NaF. The average tissue fluoride is increased after two months from 0.193 ppm (normal control) to 0.3, 0.36, 0.3, 0.27 and 0.3 ppm according to the sequence of NaF concentration in the drinking water. However, it was not in direct proportion to the time. After four months, the tissue fluoride was decreased and tended to maintain a stable state.

There is an active transport function to maintain the CNS fluorine in a dynamic steady level.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-04-02 SIGNIFICANCE OF CSF BIOPTERIN AND NEOPTERIN IN NEUROLOGICAL DISEASES

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Biopterin (BP) is the natural cofactor for tyrosine hydroxylase and neopterin (NP) is a degradation product of the first intermediate in the biosynthesis of BP. However, the distribution of NP in the human brain shows no correlation with that of BP, and NP has received much attention as an indicator of activation in the cellular immune system. We measured BP and NP levels in ventricular and/or lumbar CSF of patients with Parkinson's disease (PD) and various inflammatory neurological diseases (IND), and obtained the following results. 1) There was a rostrocaudal gradient for BP content and a reverse gradient for NP content. 2) In the PD patients, the BP levels significantly decreased, although the NP levels remained normal. L-Dopa administration had no direct effect on CSF BP content. 3) In the IND patients, the NP levels were markedly elevated in the exacerbation stage of their symptoms and remarkably decreased in the remission stage. However, the BP levels showed no substantial change. These results indicate that the significance of BP is quite different from NP. Analysis of BP appears to be a useful method for making an assessment of the dopaminergic function in PD patients, while NP a biochemical marker for evaluating the activity of inflammation within the CNS.

4-04-03 WHICH PARAMETERS INDICATE CNS INVOLVEMENT IN SYPHILITICS

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Increasing numbers of newly infected syphilitics raise the question as to how CNS involvement is recognized best. Since syphilitics often belong to risk groups, concomitant infectious diseases such as HIV can be present. Inflammatory CSF reactions may be induced either by the one or the other infection. Because of the differing treatment, identification of the causative agent responsible for the CNS symptomatology is necessary. In more than 500 consecutive patients with positive TPHA and FTA- Abs test, we assessed the reliability of various serologic test and indices, respectively, for establishing a neurosyphilis. Test results were compared with clinical symptomatology and CSF findings. Our study revealed that the index formed of the ration of treponemal specific IgG referred to total IgG in CSF divided through the identical ratio in serum (antibody index) is most reliable for proving syphilitic CNS involvement but not for estimating process activity.

4-04-04 IMMUNONEPHELOMETRIC RATE MEASUREMENT OF IgA IN THE CEREBRO SPINAL FLUID.

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IgA in human CSF is about 0.2 mg/dL; its assay is difficult by standard Immunonephelometry. We use a Reaction Rate Measurement method on a Beckman APS Immunonephelometer adding polyethylene glycol 6000 (34 g/L) to the buffer to enhance the speed and rate of the reaction. Blank value is pre-determined reading separately the reagents. To increase sensitivity we select opportune gain enhancement and raise the concentration of IgA using 100 µL of CSF. Diluted standard serum is used to draw reference curves, where Lectures -in Rate Units- are converted into mg/dL. Sensitivity is 0.07 mg/dL; variation coefficients are 2% to 8% in intra and interassay. We assayed CSF and Serum IgA in 18 Multiple Scleroses (MS) and 16 Normal controls (NC) calculating the IgA Index (CSF/Serum IgA : CSF/Serum Albumin). In NC mean (± s.d) IgA index is 0.21 ± 0.09, in fit with the literature (Takeoka et al,1990). In MS IgA Index is 0.30 ± 0.10, higher than in NC (Mann-Withney test: $p<0.05$); IgA and IgG Indices correlate ($r=0.54$; $p<0.01$) indicating parallel intrathecal production of both IgG and IgA and supporting the reliability of our method.

4-04-05 INTRATHECAL IGA, IGM, C3 AND C4 IN HTLV-1 INFECTED PATIENTS.

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IgM (by EIA), IgA, C3 and C4 (by EID) were determinated in serum and CSF of 139 patients (31 HTLV-1, 30 HIV1 and 78 other neurologic diseases, inclunding 41 MS). In the HTLV-1 group, an intrathecal decrease of C3 (22/31:70%) was the main abnormality with a significant higher frequency ($p<0,001$) than in the other two groups. The frequency of C4 intrathecal synthesis was also high (14/31 45%), close to that of HIV1 patients (18/30:60%) but significantly different from OND group (18/78:23%). IgA intrathecal synthesis was significantly less frequent (6/31:22%) than in HIV1 (18/30:60%) and not significantly different from OND. IgM intrathecal synthesis (6/31:22%) was also rarer than in HIV1 (12/30:40%) and very close to the MS group (6/41:15%). These differences of intrathecal immunity are discussed.

4-04-06 DIFFERENTIATION OF HERPES SIMPLEX VIRUS TYPES 1 AND 2 BY STRINGENT HYBRIDIZATION OF PCR – AMPLIFIED DNA FROM CSF OF PATIENTS WITH HSV ENCEPHALITIS AND MENINGITIS

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Herpes simplex virus (HSV) types 1 and 2 differentiation by microplate – hybridization of amplified DNA segments was carried out for cerebrospinal fluid (CSF) from 13 patients with HSV encephalitis and meningitis, which were diagnosed by the clinical features and serological tests. The common sequences between HSV types 1 and 2 were amplified by PCR from CSF of 9 patients, then the amplified DNA segments were diffentiated into types 1 and 2 by stringent microplate – hybridization using specific biotin – labeled probes for each type.

Ten patients were positive, of which 6 HSV types 1 and 4 HSV types 2 were identified, repectively. In 1 case of brain stem encephalitis and 2 cases of meningities, HSV type 1 was detected, although the type of brain stem encephalitis is uncertain and the miningitis is usually produced by type 1. In 1 case of adult acute encephalitis which is regarded as type 1 infection, HSV type 2 was found. Our report indicates that this method is useful for typing of herpes simplex viruses in CNS infection.

4-04-07 2'-5'OLIGOADENYLATE SYNTHETASE ACTIVITY IN SERUM AND CEREBROSPINAL FLUID FROM PATIENTS WITH ASEPTIC MENINGOENCEPHALITIDES.

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[Purpose] 2'-5'oligoadenylate synthetase (2'-5'AS) is one of the enzymes induced by interferon (INF), and 2'-5'oligoadenylate has been known as an anti-viral effector of INF. Increase of 2'-5'AS activity in cerebrospinal fluid (CSF) has been recently reported in patients with mumps meningitis on acute stage. We attempted the estimation of 2'-5'AS activity in serum and CSF from patients with aseptic meningoencephalitides.

[Methods] The materials consisted of serums and CSFs from one patient with herpes simplex virus meningoencephalitis (HSVE), four with clinically suspected but non-specified viral meningoencephalitides (VE), and three with post- or para-infectious acute disseminated encephalomyelitides (ADEM). We measured 2'-5'AS activity in serum and CSF from these patients on acute stage.

[Results] 2'-5'AS activity in serum showed high values in all patients. 2'-5'AS activity in CSF showed a markedly high value in the patient with HSVE, and a mildly high value in one of the four patients with VE. However, the activity in CSF did not present any high value in three of the four patients with VE and in any patients with ADEM.

[Conclusion] The estimation of 2'-5'AS activities in serum and CSF on acute stage of aseptic meningoencephalitides might be useful to indicate that these diseases are due to viral infection.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-04-10 MIGRAINE WITH PLEOCYTOSIS IN THE CEREBROSPINAL FLUID

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In a woman of 39 and in a man of 21 we observed, over a period of several weeks, recurrent migrainous-like attacks with nausea, lasting hours, heralded by brief episodes of sensory-motor defects, visual symptoms and aphasia. Patients were afebrile and had no history of migraine. Nuchal rigidity was never preminent; headache improved only after lumbar punctures; overall, 7 taps were performed in the 2 patients over a period of 2 months. CSFs were clear and mildly hypertensive. Cells (lymphocytes) ranged from 15 to 500/cumm and protein from 67 to 130 mg/dl.. The CSF/Serum Ratio for Albumin always exceeded 0.008, indicating a damage of the Blood-Brain Barrier. No CSF IgG Oligoclonal Bands were detected. Bacteriology and serologic studies for syphilis, borreliosis, brucellosis and viruses were negative in CSF and blood. EEG, CT and MRI scans of the brain were normal. No recidives occured in a follow-up of 2 years. Migraine-like attacks with CSF pleocytosys have been reported (R.Fishman,1992) as a be nign self-limiting inflammatory syndrome. This should be kept in mind to avoid invasive procedures such as cerebral angiography.

4-04-11 PROTON MAGNETIC RESONANCE SPECTROSCOPY IN CSF OF MULTIPLE SCLEROSIS PATIENTS.

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Proton Magnetic Resonance Spectroscopy (^{1}H-MRS) was performed in CSF of 14 patients with Multiple Sclerosis (MS) and 18 neurological controls by spectrometer Brucker 300, 7.05 T. Peak intensity of α–β Glucose, Lactate (LAC), N-acetylaspartate (NAA), Citrate, Creatine (Cr) and Creatinine was evaluated. The LAC/Cr ($p=0.03$) and NAA/Cr ($p=0.03$) ratios were significantly higher in MS patients than in neurological controls. Dynamic changes of CSF metabolites seem to be related to MS clinical events. An increase of CSF LAC was found in two relapsing-remitting (RR) patients during exacerbation phase, characterized in MR-Imaging (MRI) by Gd-DTPA enhanced plaques. Both LAC and NAA were increased during inactivity phase in two RR patients. High levels of NAA were detected in one chronic progressive patient. Changes in CSF LAC may depend on infiltrating leukocytes in hyperacute plaques. The CSF NAA increase could reflect the enhanced release and/or the lower uptake occuring in chronic plaques. MRI and ^{1}H-MRS in vivo on localized demyelinating areas during different stages of plaques evolution is in progress in order to obtain correlations with CSF MRS data.

4-04-12 **SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE): TWO CASES WITH REMARKABLE RECOVERY.**

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Unusual clinical course with improvement has seldom been reported. A 12 year-old boy had learning difficulties for a year, then frequent falls in 10/79. SSPE was diagnosed in 1/80. AED were started and Inosiplex added in 6/80. In 12/80 seizures and myoclonus ceased. Medications were discontinued a while later. In 3/85 he appeared completely recovered. IGG synthesis was up to 82mg/day in '87, Inosiplex was resumed. From 3/90 he had progressive dystonia, loss of speech and ambulation. Case #2 had measles at 18 months of age, a single seizure at 2 yrs. At age 7 seizures recurred but were controlled with AED for 20 months. At age 10 he had a typical onset of SSPE. He was given AED and Inosiplex for about a year. For the last 5 years he has been doing quite well except minor learning difficulties. Protracted apparent cure for 5-10 years has not been previously reported. The clinical spectrum of SSPE may be wider than recognized. CSF study is essential for diagnosis and monitoring as it may provide the only clue to the diagnosis.

4-04-14 **ALPHA-N-ACETYL-ß-ENDORPHIN IN HUMAN CEREBROSPINAL FLUID THROUGHOUT LIFE**

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Alpha-N-Acetyl-ß-endorphin (Ac-ß-EP) is a post-translational product of ß-endorphin (ß-EP) which does not bind to opiate receptors. The importance of Ac-ß-EP derives from its lack of analgesic properties, and hence its possible role as a physiological opiate antagonist. The presence of Ac-ß-EP in human CSF may represent a confounding factor when ß-EP immunoreactivity is assessed using conventional methods. The aim of this study was to evaluate CSF Ac-ß-EP values in normal subjects, with particular regard to the influence of gender and age.
We therefore measured CSF levels of AcßEP (by HPLC fractionation, and immunoreactive Ac-ß-EP peak detection) in 49 healthy subjects aged 15 to 87 years. Subjects underwent lumbar puncture just before spinal anesthesia for orthopedic surgery; they did not complain of chronic pain. The mean ($\pm$SD) CSF Ac-ß-EP values were 6.49 ± 6.16 fmol/ml (range 0.8-31.5); in 5 subjects Ac-ß-EP was below the limit of assay sensitivity (0.8 fmol/ml). No sex and age-related differences were observed for both ß-EP and Ac-ß-EP. However, when individual values were considered, the ß-EP/Ac-ß-EP ratio was lower ($p<0.05$) in older subjects (>60 yrs: 1.71 ± 1.15) than in other age groups (15-30 yrs: 4.51 ± 8.4; 31-65 yrs: 9.2 ± 11.5). These data indicate the occurrence of a relative excess of central Ac-ß-EP over ß-EP in physiological aging.

4-04-15 NEW NON-INVASIVE RAPID DIAGNOSTIC METHOD FOR HERPES SIMPLEX VIRUS ENCEPHALITIS (HSVE) BY QUANTITATIVE DETECTION OF INTRATHECAL ANTIGEN USING CHEMILUMINESCENCE ASSAY.

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[**Purpose**]To see if HSV antigen detection in cerebrospinal fluid (CSF) by antigen-antibody complex-activated complement-stimulated chemiluminescence in normal granulocytes could be a diagnostic method for HSVE.

[**Methods**]The materials consisted of 10 CSFs from 6 patients with HSVE and 11 with other CNS infections (non-HSVE). The chemiluminescence of normal granulocytes was measured in two assays: one including CSF (assay A) and the other including CSF and anti-HSV antibody (assay B). The alteration in chemiluminescence with these assays was evaluated as the ratio of values (B/A ratio) for each sample. Detection of the HSV antigen by this assay required 5 hours. Cultured HSV was diluted with a control CSF to a concentration of 10^6 to 10^1 infectious units. The values of the diluted samples were measured in assay B.

[**Results**]The B/A ratios of all CSF samples taken from the 5th to 38th day of HSVE were higher than 1.3, while that of all non-HSVE samples were lower than 1.0. The difference in frequency of B/A ratios above 1.3 between the two groups was significant($p<0.01$). The increase of chemiluminescence values in samples including HSV correlated well with the infectious units. The relationship between the common logarithm of the infectious units and chemiluminescence values was statistically linear($p<0.01$).

[**Conclusion**]The present method represents a valuable, quantitative and rapid diagnostic tool for intrathecal HSV antigen in HSVE.

4-04-16 ANALYSIS OF THE ACTION OF HUMAN ATRIAL NATRIURETIC PEPTIDE IN CEREBROSPINAL FLUID

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The human atrial natriuretic peptide (hANP) has been known to be concerned with the regulation of water–Na balance. Recently hANP was also found broadly in central nerve system, but the action of hANP in human brain is still unknown.

To clarify the function of hANP in cerebrospinal fluid(CSF), we examined the ANP in CSF about various neurological diseases. Subjects were 37 patients;12 were the cases with intracranial hypertension(IH), and 25 were cases without IH. HANP both in CSF(l-hANP) and in serum(s-hANP) were measured by RIA, and the patients with IH were followed. We analyzed the relationship between l-hANP and the other findings in CSF.

Results were as follows.

1) The increase in consentration of l-hANP statistically correlated with the increase of the intracranial pressure($r=0.72$), but was no relationship with the other CSF findings and s-hANP.

2) In follow-up study of the patients with IH, the concentration of l-hANP was observed to be parallel to the change of intracranial pressure in each case.

It is concluded that l-hANP is closely related to the regulation of the intracranial pressure in human.

4-04-17 CSF-PARAMETERS IN PATIENTS WITH VIRAL OR BACTERIAL MENINGITIS AND ENCEPHALITIS.

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Aim of Investigation: We investigated the ability of CSF-parameters to differentiate between patients with meningitis and encephalitis of bacterial or viral cause.

Methods: CSF-parameters of 635 patients with an ensured diagnosis of bacterial (N=75) or viral meningitis (N=245), bacterial (N=36) or viral encephalitis (N=279) were analysed with regard to cytology and profile of proteins. The proteins were evaluated by the blood-CSF-barrier-model of Reiber and Felgenhauer (Clin Chim Acta, 1987, 163:319).

Results: In patients with bacterial infections, the number of cells, the amount of total proteins, the intrathecal IgG production were significantly higher, and the disturbance of the blood-CSF-barrier was more pronounced than in patients with viral infections (rank sum test: $p < 0.01$). Differences between patients with meningitis and encephalitis were only significant in case of a viral infection: in patients with encephalitis, the amount of total proteins, the number of cells were lower, and the intrathecal production of IgG and IgM was higher.

Conclusion: The CSF-parameters had a high sensitivity to separate between bacterial and viral infections and a lower one to differentiate between meningitis and encephalitis.

4-04-18 POLYCLONAL AND OLIGOCLONAL IgA SYNTHESIS IN THE CSF OF NEUROLOGICAL PATIENTS

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IgA is present in normal CSF at about one-tenth of the IgG concentration and is mostly (>95%) monomeric. The occurrence of oligoclonal IgA bands in MS and other neurological disorders have been disputed. We describe a very sensitive immuno-affinity mediated capillary blot technique for the detection of polyclonal and oligoclonal IgA.
Patients : we studied 115 patients including 16 controls, 33 with MS, 37 with CNS infections, 8 with GBS, 7 with other inflammatory and 14 with non-inflammatory disorders of the CNS.
Methods : isoelectric focusing was performed in agarose gel plates containing a mixture of ampholines; after focusing, IgA was blotted onto an PVDF sheet coated overnight by an anti-IgA antiserum or by viral antigens. The immunoblots were stained by alkaline phosphatase conjugated anti-human IgA antiserum.
Results : only 5 samples displayed oligoclonal IgA bands, including 2 (out 33) with MS. In herpetic encephalitis (N = 5) and varicella-zoster meningitis, a strong intrathecal production of virus-specific IgA antibodies was detectable. In such cases, faint oligoclonal IgA antibodies were superimposed on a polyclonal background.

4-04-19 OLIGOCLONAL IgM SYNTHESIS IN THE CSF OF NEUROLOGICAL PATIENTS

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IgM is present in minute amounts in normal CSF (mean : 180 ng/ml; upper reference limit : 380). As for IgG, an *intrathecal synthesis of IgM could be oligoclonal and* superimposed on a polyclonal background derived from the blood through the blood-CSF barrier. We describe a very sensitive immuno-affinity mediated blot technique for the detection of such oligoclonal IgM bands.
Patients : we studied 141 patients including 10 controls, 55 with MS, 40 with CNS infections, 8 with GBS and 22 with other neurological disorders.
Methods : samples were pre-treated with dithiothreitol in order to obtain a migration of the IgM molecule into the agarose gel. The latter contained a mixture of ampholines, pH 3.5 to 9.5 and 4 to 6. After focusing, IgM was blotted onto a PVDF sheet coated overnight by a rabbit anti-IgM antiserum (μ specific). The immunoblot was stained with a second peroxidase-conjugated anti-IgM antiserum.
Results : the detection limit was 7 ng in 15 μl CSF; IgM was therefore not detected in CSF samples with an IgM concentration below 450 ng/ml. Oligoclonal IgM bands restricted to the CSF were observed in 24% of patients with MS, but also in 30% of patients with CNS infections.

4-04-20 AIDS: A CSF LABORATORY EXPERIENCE ON 610 CASES IN A 8 YEAR TIME PERIOD.

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In a eight-year time period (July 1984 to June 1992) were studied CSF samples of 40718 new patients, 610 of them with AIDS. Number of AIDS patients represents 1,50% of total cases examined in the laboratory during this time period, and in 1992 this number went up to 3,4%. Normal CSF was observed in only 18 (3%). Associated pathologies occurred in 395 cases (65%). Hemorrhage in 14, primary lymphoma in 14, aseptic meningitis in 63 and opportunistic infections in 304 cases (49,8%). Among these infections as seen world wide, toxoplasmosis (15,7%), cryptococcosis (10,3%) and syphilis (5,1%) prevailed. Chagas disease was detected in two patients: acute meningoencephalitis occurred in both and presence of Trypanosoma cruzi in the CSF has been shown in them. Association of infections occurred in 57 cases and the most frequent was toxoplasmosis with cryptococcosis. HTLV-1 antibodies were detected in 4 cases. Some remarks must be emphasized in report to AIDS and CSF: 1) CSF must be analysed in every AIDS patient independently of phase of the disease; 2) systematic examination, as complete as possible, must be carried out in every CSF sample; 3) CSF changes are frequently detected; in this series changes were observed in 97% of the cases.

4-04-21 INTRATHECAL SYNTHESIS OF BETA-2 MICROGLOBULIN (B2-M) AND NEOPTERIN (N) IN NEUROLOGIC HIV-1 SEROPOSITIVE PATIENTS.

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We assayed by R.I.A. B2-M and N in CSF and Serum (S) of 45 HIV-1 seropositives (HIV+) and 20 HIV-1 seronegative non-inflammatory neurologic diseases (NIND). In HIV+ mean B2-M & N are significantly higher (unpaired "t" test) both in CSF & S (data not shown), in accord to literature. CSF/S Ratios are raised in HIV+ (Mann-Whitney test: for B2-M: mean $\pm$ s.d. = 1.36 $\pm$ 1.2 vs. 0.55 $\pm$ 0.28 : $p<0.005$. For N: 0.91 $\pm$ 1.01 vs. 0.27 $\pm$ 0.20 : $p<0.0001$). In analogy with the IgG Index we empirically elaborated CSF/S Indices for B2-M & N that are higher in HIV+ (Mann-Whitney test: for B2-M; mean $\pm$ s.d. = 152.43 $\pm$ 110.34 vs. 56.68 $\pm$ 37.28 : $p<0.0001$. For N: 91.42 $\pm$ 62.09 vs. 27 $\pm$ 22.38: $p<0.0001$). These results suggest local synthesis of B2-M & N. Separating, on the basis of CSF/S Ratio for Albumin, the HIV+ with damaged (BBBD;n = 29) and intact (BBBI; n = 16) Blood-Brain Barrier, each parameter remains significantly higher vs. NIND in both sub-grounds (data not shown) thus confirming that raised CSF B2-M & N in neurologic HIV+ patients might really indicate local synthesis, expression of autochtonous cellular immune activation in the CNS.

4-04-23 NEUROSTEROIDS IN CEREBROSPINAL FLUID

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Significant amount of 3 β-hydroxy-Δ_5-steroids including dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) have been found in brains of several mammalian species. Since they might be synthesized and accumulated through mechanisms at least partly independent of peripheral sources, they have been termed 'neurosteroids'. Measurement of DHEA and DHEAS in human cerebrospinal fluid (CSF) has not yet been carried out. CSF levels of DHEA and DHEAS were determined by radioimmunoassay in 57 patients with various neurologic disorders and 26 patients with non-neurologic disorders. The content of CSF DHEA as well as DHEAS was significantly higher in the Guillain Barré syndrome (GBS) as compared to non-neurological patients. This change may be explained by the breakdown of blood-nerve barrier in GBS. A significant positive correlation was observed between DHEAS but not DHEA and total protein in CSF. The level of CSF DHEAS, but not DHEA, was significantly higher in males than in females. In males but not females, a negative correlation was observed between CSF DHEAS and aging. As far as sex and age are concerned, DHEAS in CSF was similar to that in plasma. DHEA in CSF may have more close relationship with DHEA in brain as compared to that of DHEAS.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-04-24 NORMAL CEREBROSPINAL FLUID(CSF) VALUES IN TERM (TN) AND PREMATURE(PTN) GESTATION NEWBORN INFANTS

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Reference values for normal CSF are important to clinicians making management decisions. The purpose of this study is to compare and delineate the composition of noninfected and nonhemorrhagic CSF obtained in PTN and TN infants due to Central Nervous System(CNS) alteration or infection suspicion. We studied all newborn CSF exams carried out from 1988 to 1992.The criteria for inclusion were: absence of hemorrhage,no evidence of bacterial CNS or congenital infection, newborn age up to 28 days and accessible clinical data.We analysed 63 exams,25 of TN and 38 of PTN.By using Student t test and chi square test ($\alpha \leq 5\%$), we observed that the protein means and standard deviations(M±SD) were 78±32mg% and 101±45mg% respectively($0,02 \leq p \leq 0,04$).The difference between both groups considering white blood cell count (WBC),glucose(G),chloride(C)neutrophils,and Pandy test was not statistically significant.The M±SD of WBC/mm^3,G,C were 4,5±3,6 and 5,1±5,8;67±26 and 67 ±33mg%;688±28 and 689±53mg% respectively in TN and PTN.

4-04-25 CORRELATION BETWEEN SPINAL CORD INFLAMMATION AND CEREBROSPINAL FLUID(CSF) RESPONSE DURING TROPICAL SPASTIC PARAPARESIS(TSP) EVOLUTION

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An association between TSP and HTLV-1 has been described since 1985 in many parts of the world. Histopathological data from autopsy have shown that the inflammatory alterations of the spinal cord tend to become scarce or even absent in long term cases.In order to verify whether there would be a correlation between the intensity of cord tissue inflammation and CSF findings, we have retrospectively studied from 1990 to 1992 78 TSP cases focusing the period of evolution and CSF profile. The patients were divided into 4 groups according to the period of evolution: 2months⊣ 2 years(ys), 2ys⊣ 5ys, 5ys⊣ 10ys, ≥10ys. CSF parameters studied were: white blood cell count, presence of plasma cells, protein content, and gammaglobulin increase. The means and the proportions were analysed by using Student t test and Fisher exact test ($\alpha \leq 5\%$). According to the results, there must be an association between tissue inflammation and CSF response. So, CSF can be a reliable marker of tissue inflammation grade

4-09-01 MULTIPLE DELETIONS OF MUSCLE mt DNA IN A PATIENT WITH PARKINSON'S DISEASE (P.D) AND SENSORY NEUROPATHY

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In this paper we present a patient with P.D,sensory neuropathy and asymptomatic mitochondrial myopathy where,for the first time as far as we know, multiple deletions of muscle mt DNA was revealed.The patient has no family history of P.D or neuromuscular disease.At the age of 54 he presented bradykinesia with difficulty in walking which steadily progressed.On neurological examination (at the age of 57)bradykinesia and extrapyramidal rigidity of all four limbs was prominent, while tremor was absent.L-Dopa therapy was not effective.Mild hypoaesthesia of the distal parts of the limbs was present and a great reduction of SCV's were found while MCV's were normal. Brain C/T scan was normal. Muscle biopsy showed ragged red fibers and biochemical analysis of the muscle homogenate showed complex I and IV defects. Southern blot and PCR analysis revealed multiple deletions of the mt DNA.
CONCLUSION:Multiple deletions in muscle mt DNAwere revealed in a patient with P.D,sencory neuropathy and asymptomatic mitochondrial myopathy and the question which arises is if this case represents a new type of mitochondrial encephalomyopathy.

4-09-02 THE DNA-ADDUCT 8-HYDROXY-2'-DEOXYGUANOSINE IN PARKINSON'S DISEASE

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Increasing evidence suggests that free radicals play an important role in the pathogenesis of Parkinson's disease (PD). Among other molecules, DNA is one of the targets of free radicals. Deoxyguanosine (dG), one of the DNA-nucleotides, can be oxidized to the dNA-adduct 8-hydroxy-2'-deoxyguanosine (8OHdG). Accumulation of 8OHdG in the double helix has been shown to lead to misreading of the template, which may lead to a failing cell-homeostasis, and evantually cell-death.

To explore the role of free radicals in PD, we determined 8OHdG in DNA of peripheral tissue (mononuclear blood cells) using HPLC-EC (high-performance-liquid-chromatography with electrochemical-detection).

The results from 13 PD-patients and 5 healthy control individuals showed no significant differences in the $8OHdG/10^5dG$ ratio, between PD-patients (mean 3.6 ± SD 1.3) and controls (mean 3.5 ± 1.0). Our findings indicate that there is no increased oxidative stress reflected by 8OHdG levels in mononuclear blood cells in PD. However, this does not exclude accumulation of 8OHdG in the CNS, expecially in the pars compacta of the substantia nigra, and its role in the pathogenesis of PD.

4-09-03 SYMPTOMATIC LATERALITY AND MAGNETIC RESONANCE IMAGING (MRI) OF THE PUTAMEN IN STRIATONIGRAL DEGENERATION (SND).

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Asymmetrical onset of parkinsonism, especially of rigidity,appears to be not uncommon in SND. This study investigated anatomical asymmetry in the putamen in relation to symptomatic laterality using MRI.

We studied 6 of clinically-diagnosed SND patients with asymmetrical onset of parkinsonism, ranging in age from 49 to 73 years. All of them subsequently had variable cerebellar or autonomic signs. The Yahr grade was IV in 3 patients and I, III, or V in the others. Five patients were studied with a 1.5-T MRI system and one with a 0.5-T system, using T1-weighted inversion recovery (IR) and T2-weighted spin-echo sequences.

With IR sequences, putaminal atrophy was demonstrated in all cases, and was more intense on the contralateral side to the more symptomatic limbs. The anatomical asymmetry and the symptomatic laterality were less pronounced in an advanced case. A low signal intensity on T2-weighted images was also demonstrated in the posterolateral putamen, but its relationship to symptomatic laterality was less clear.

We conclude that putaminal MRI using IR sequences is quite useful for the diagnosis of SND, especially in patients with asymmetrical parkinsonism.

4-09-04 EVALUATION OF GASTRIC EMPTYING IN PARKINSON'S DISEASE -AFFECT OF L-DOPA TREATMENT-

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In Parkinson's disease (PD), constipation is the most common symptom among digestive disturbances. However, the complaints in the upper digestive tract are often overlooked or insidious. To evaluate the function of the upper digestive tract, we studied gastric emptying using an acetaminophen (AAP) method in 22 patients with PD. The AAP is not absorbed through the gastric mucosa at all, but is very soon absorbed through the intestine into the blood after oral administration. Therefore, the plasma AAP content is related to the gastric emptying time. The plasma AAP content in patients with PD was significantly lower than that in controls, indicating that a delay of gastric emptying existed in PD. The plasma AAP content was correlated with the coefficient of variation of R-R interval in PD. The decreased plasma AAP content was related to the severity of PD. Also, the plasma AAP content was significantly decreased by L-dopa treatment. We considered that the abnormality of gastric emptying indicated the impairment of autonomic nervous system in PD and that the gastric emptying was affected by the treatment of L-dopa.

4-09-05 Gait Pattern Disturbances in Patients With Subcortical Arteriosclerotic Encephalopathy (SAE): Results of a prospective study

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Neither the clinical criteria of SAE nor its natural history - in particular during silent initial stages - are well established. Neuropsychological features of the disease are often uncharacteristic and may hence impede an early diagnosis. Investigations of gait disturbances and MRI in 20 patients at risk (age >45, hypertension, diabetes) and with manifest SAE (N=20) were performed to assess objective criteria of manifestation in a prospective follow-up study. Using a quantitative computerized gait analysis system several factors with high predictive value for the disease could be established. Multifactorial analysis with the incidence and degree of white matter lesions revealed a significant association with gait modalities both in terms of extent and topography. In the absence of neuropsychological and psychiatric abnormalities these findings may be useful for an early treatment to prevent further deterioration.

4-09-06 CLINICAL FEATURES OF SYRINGOMYELIA

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We have studied the clinical semiology of 100 patients with syringomyelia. Spinal cord cavitations were evident on MRI studies in all cases. There were 48 women and 52 men with ages ranging from 11 to 71 years and a mean age of 38.4 years. Mean time of evolution since the onset of neurological manifestations was 7.5 years. Loss of pain and thermal sense was the most frequent finding on physical examination (92%), followed in decreasing order of frequency by upper limbs weakness (85%), areflexia (85%), pyramidal signs (65%), amyotrophy (59%), scoliosis (45%), paraparesis (41%) and vibratory and position sense impairment (40%). Forty-eight percent of patients presented arm and neck pain, 42% paresthesias, 28% burns and 10% ulcers. Symptomatology was unilateral or more marked on one side of the body in 72% of subjects. Upper level of sensory dysfunction involved trigeminal inervation territory in 30% of cases and cervical dermatomes in 54 % of cases. Back level commonly reached dorsal (62 %) and lumbosacral dermatomes (37%). Chiari I malformation (76 % of cases), short-neck (11 %), spinal arachnoiditis (3%), spinal cord tumor (3%) and traumatic myelopathy (2%) were the commonest associated abnormalities. Two major clinical pictures can be easily distinguished in syringomyelic patients, so a differentiation between cases with prominent motor manifestations (69% of patients) and other cases in which pain and sensory impairment were the outstanding features (31% of patients) is proposed. An analysis of the clinical symptomatology and their relationships are reported.

4-09-07 JUVENILE ONSET OLIVOPONTOCEREBELLAR ATROPHY

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Olivopontocerebellar atrophy, a progressive degenerative disorder of the cerebellar cortex, pons and inferior olives is rare in children. We present the clinical and radiological features of OPCA of juvenile onset in 7 Omani children - 3 males and 4 females with ages ranging 9 to 15 years. A family history was seen in 3; consanguinity amongst parents was seen in 4 and all came from Northern Oman. The presenting symptoms were progressive ataxia (all patients), visual impairment in 4, seizures in 2, urgency of micturition in 1.

Examination revealed axial and appendicular cerebellar ataxia and exaggerated tendon reflexes in all, dysarthria in 2, spasticity in 2 and sinus tachycardia in 2. Ocular abnormalities were retinitis pigmentosa in 4, loss of saccades in 2, nystagmus in 1 and ptosis in 1.

Complete blood counts, urine aminoacidograms and blood biochemistry were negative for metabolic disorders. CT scan showed the characteristic features of cerebellar and pontine atrophy. Brainstem auditory evoked response abnormalities were seen in 3 patients. The clinical profile of OPCA in these children with a juvenile onset is characterized by progressive cerebellar ataxia, higher occurrence of retinitis pigmentosa and typical CT scan features.

4-09-08 HEREDITARY MOTOR AND SENSORY NEUROPATHY ASSOCIATED WITH CEREBELLAR ATROPHY (HMSNCA).

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The authors present 6 patients in 4 families with HMSNCA, of whom 4 are males and 2 are females. All of their parents are first cousins. This disease may be inherited as an autosomal recessive trait. The onsets of symptoms were various, in early childhood to age 54. Their clinical features were very similar to each other. The initial symptom was a slowly progressive disturbance of gait. Postural or intentonal tremor in hands and heads became obvious in addition to cerebellar ataxia. Nystagmus and dysarthria were observed in all. Marked distal wasting and weakness producing a "stork-leg" appearance were noted. Superficial and deep sensations were impaired or absent in the extremities, more marked in the diatal parts. Deep reflexes and Babinski's sign were absent. Cardiomyopathy was never revealed. Brain CT showed marked cerebellar atrophies in all and cerebral atrophies in 3 patients older than age 50. Motor and sensory nerve conduction velocities were markedly delayed. Sural nerve biopsy showed a severe loss of myelinated fibers. Hypoalbuminemia (1.6 to 4.0g/dl) was noted. Half-life periods os serum albumin were normal (11.03 and 11.14 days) . Clinical features and laboratory data showed HMSNCA as a distinct nosological entity.

4-09-09 CEREBRAL BLOOD FLOW AND EVENT RELATED POTENTIAL IN PATIENTS WITH PARKINSON'S DESEASE

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Some authors have suggested congnitive impairments in parkinson's disease(PD), but the data are still insufficient to clear. Then in order to evaluate the congnitive function in PD , we studied the relationship between P300 topography and cerebral blood flow(CBF).

Eighteen patients with PD were divided in two groups according to neuropsychological test(WAIS-R);HIQ(IQ of over 80):8 cases(mean age 67.1 ±6.2 y.o), LIQ(IQ of under 79):10 cases(mean age 57.3 ± 14.2).

Considering the Yahr scale;7cases were Stage II(HIQ:5 cases. LIQ:2cases.) , 10cases were StageIII(HIQ:3cases. LIQ:7cases.), and 1case was StageIV (LIQ:1case).

ERP sclap topography was determined from the amplitudes of each component, recorded from 16 scalp electrodes place according to the international 10-20 system by a auditory odd-ball stimulus paradigrm. We also made an overall mean peak voltage of each component. CBF were meseared using ^{123}I-IMP as the tracer by single photon emiission computed tomography. The RI count index was expressed as a ratio of activity in each regions of interest(ROI) to mean counting rate over cerebellar regions. We have considered the RI count index as stand for the index of CBF in each ROI.

The maxium voltage area in P300 topograpy has moved more right wards from Pz in LIQ groups than in the HIQ groups. This difference in the pattern of P300 topography might reflect congnitive differences. However there was no significant correlation between the amplitude of P300 and the mean CBF in the two groups. These results suggest that congnitive function assessed by ERP may not cause by the change of CBF.

4-09-10 LOCALIZED PROTON MAGNETIC RESONANCE SPECTROSCOPY OF THE CEREBELLUM IN PATIENTS WITH SPINOCEREBELLAR DEGENERATION.

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Localized Proton MR spectroscopy of the cerebellum has been undertaken in 14 healthy volunteers and in 19 patients with spinocerebellar degeneration(SCD). Siemens Asahimeditic Magnetom 2.0T combined imaging and spectroscopy system was used for this study. Localized proton spectra were obtained using the stimulated echo method (STEAM) with selective water presaturation. The ratios N-acetylaspartate(NAA)/Choline(Cho) and NAA/(Phospho Creatine(PCr)+Creatine(Cr)) were calculated. For the SCD patients, the following values were found (means±1SD): NAA/Cho=1.06±0.19 and NAA/(PCr+Cr)=0.76±0.19. In the normals, these values were NAA/Cho=1.36±0.26 and NAA/(PCr+Cr)=1.14±0.11. It is concluded that these ratios are significantly lower in the SCD patients($p<0.001$). Because NAA is thought to be a metabolic marker for normally functioning neurons, these findings suggest the presence of neuronal loss or injury in SCD.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-09-11 ADULT CHÉDIAK-HIGASHI SYNDROME PRESENTING AS PARKINSONISM, DEMENTIA, AND PERIPHERAL NEUROPATHY

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Chédiak-Higashi syndrome (CHS), rare autosomal recessive disorder, is often a fatal disease of childhood. A 39-year-old female developed hands tremor at age 22. Mental deterioration (IQ 60), nystagmus, oculogyric crisis, resting tremor at tongue, rigidity, and unsteady gait were found. Although juvenile parkinsonism was suspected, there was no favorable reponse by levodopa. On admission at age 39, partial ocular albinism, limbs muscle atrophy, paraplegia, and decreased DTR were observed. MRI showed marked brain atrophy mimicking Pick's disease. EMG disclosed neurogenic pattern and NCV were slowed. Sural nerve biopsy showed a loss of myelinated fibers and giant granules in Schwann cells. HVA in CSF was markedly decreased to 10% of controls as well as 5-HIAA. Peroxidase-positive panleukocytic granules and profoundly decreased NK-cells activity were compatible to CHS, but the neutrophil function studies revealed normal chemotaxis and bactericidal activity, resulting in her long survival.

In conclusion, adult CHS may appear primarily with systemic neurological dysfunction and should be considered in a differential diagnosis of parkinsonism, dementia, and peripheral neuropathy.

4-09-12 A PROSPECTIVE STUDY OF DEPRESSION IN FRENCH PATIENTS WITH PARKINSON'S DISEASE. THE DEPAR STUDY.

Collège National de Neurologie des Hôpitaux Généraux. France.
(presented by P.Davous).

To evaluate the prevalence and aetiology of depression in Parkinson's disease (PD) in France, a consecutive series of 500 patients with PD were prospectively studied. Patients attending neurology services in French General Hospitals were included during a period of 4 months, from october 1992 to january 1993 at a unique follow-up visit or during their hospital stay. The accuracy of clinical diagnosis of idiopathic PD was based on the U.K. Parkinson's disease Society Brain Bank criteria and results of CT scan or MRI. All the patients were interviewed for duration of illness, duration of L.Dopa treatment, use and side effects of anti-parkinsonian drugs. Cognitive decline was screened by the Katzman's short orientation memory concentration test. Psychiatric examination included a semi-structured interview on family and personal history of depressive disorders and, if any, their temporal relationship with PD. The severity of depression was scored by the MADRS scale. According to clinical assessment and cut-off scores of the scales, the patients were diagnosed as depressed or not and cognitively impaired or not. Results will focus on the prevalence of depression in PD, its relationship to motor and cognitive dysfunction, to duration and type of antiparkinsonian treatment.

4-09-13 MR IMAGES OF THE CEREBELLAR VERMIS IN THE SPINOCEREBELLAR DEGENERATION(SCD).

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Objective We evaluated the extent of atrophy of cerebellar vermis with sagittal MR images of cerebellum in 24 patients with SCD.

Methods 24 patients were classed into 13 cases with the cerebellar form and 11 cases with OPCA. Controls were 30 normal persons. With 1.5 Tesla MRI(Toshiba;MRT-200),T1-weighted sagittal images(TR;500msec,TE;20msec)of cerebellar vermis were analyzed concerning the anterior lobe(A) and a part of the posterior lobe(part from primary fissure to prepyramidal fissure)(B). The extent of atrophy was graded as follows;Grade 0:no atrophy,1:partial atrophy, 2:every folia is separated,3:width of sulcus is equal to that of folia,4:width of sulcus is larger than that of folia.

Results A mild atrophy of part A was observed in 98% controls;the grade was 1.2±0.5(mean±S.D.) in controls. The grade was 0.4±0.5 in the part B of controls. In all cases of SCD,part A and B were both atrophic.In OPCA,the part A(2.5±0.5)was more atrophic than B(2.0±0.6).However,in the cerebellar form the atrophy of B(3.1±0.9)was greater than that of A(2.2±0.7).69% cases of cerebellar form showed the dominant atrophy of B.The grade of atrophy was correlated with the length of clinical course. Present results might be useful for the clinical classification of SCD.

4-09-14 AUDITORY EVOKED POTENTIALS IN SPINOCEREBELLAR DEGENERATION
-CORRELATIONS WITH CLINICAL SUBTYPE TO ATAXIA-

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Objective/Background. Auditory evoked potential(ABR) abnormalities in Spinocerebellar degeneration(SCD) were previously reported, but there were few reports analyzed on clinical subtypes. To determine the difference of ABR in SCD subtypes, correlations with clinical subtypes to degree of ataxia.

Methods. Thirty SCD patients(14 males and 16 females) were examined. ABR recordings were followed by Guidelines for Clinical Evoked Potential Studies in American EEG Society. Subtypes of SCD and degree of ataxia were followed by criteria of research committee of ataxic diseases, the ministry of health and welfare of Japan. We evaluated the latency and IPL in ABR, abnormality ratio in subtypes, correlation to degree of ataxia.

Results/Conclusion. There were no correlations with ABR abnormalities to deep sense and ataxia. Spinal form showed no ABR abnormalities but others showed abnormal findings. Dentatoruburopallidoluysian atrophy showed extreme abnormal ABR. ABR abnormalities were different from SCD subtypes.

4-09-15 ANIMAL MODEL OF NEURODEGENERATIVE DISEASES. NEUROTOXICOLOGIC APPROACH USING ALUMINUM COMPOUNDS.

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Using aluminum compounds we produced progressive encephalopathy partially resembling human neurodegenerative diseases in cats. Holt's adjuvant of 50-200 μl was injected in the left forebrain of about 20 rabbits and cats, respectively. Following lucid intervals(1-40 days according to the doses) rabbits and cats developed subacute panencephalopathy consisting of apathy, dystonia, myoclonus and usually terminal generalized convulsions. Mean survival period was about twice longer in cats than in rabbits (with 50 μl injection mean survival was 18 days in rabbits and 34 days in cats) with longer lucid time in the latter. Neurofibrillary changes(NFC), argentophilic and neurofilament (200 kD)-antibody positive, were observed in the neurons of neocortex, hippocampus and brainstem in both rabbits and cats, more marked in cats probably reflecting longer survival. In contrast to the rabbits that showed fatal deterioration in all, a few cats showed various courses: (1)asymptomatic, (2)survival with neurologic deficits and (3)later onset after long lucid time(40 days in mean) with fatal outcome. The amount of NFC in the cat brains was greatest in the ordinary fatal progressive type, followed by later onset one, survival with neurologic deficits and asymptomatic type in this order. Although the cause of different courses in the cats was unclear, progressive encephalopathy with longer course may help to elucidate human neurodegenerative diseases.

4-09-16 STUDY OF SOMATOSENSORY EVOKED POTENTIALS IN SPINOCEREBELLAR DEGENERATIONS

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Spinocerebellar degeneration (SCD) is a variable disease entity and the degree of the pathological changes of the spinal dorsal column is different among its subtypes. By the way, the examination of the somatosensoryevoked potentials (SEP) is known to be quite useful to evaluate the dorsal columnal function. So, in the present report, we studied the SEP of thirty-two SCD cases of various subtypes to reveal the correlation between the related clinical symptoms and the SEP findings. SEP recordings were performed according to the Guidline for Clinical Evoked Potential Studies by American EEG Society. The obtained SEP findings were different among the each cases, but generally the detected frequency of SEP abnormality was highest in olivo-ponto-cerebellar atropy (OPCA) group, and the degree of the abnormality seemed to be correlated to the distarbance of vibratory sensation rather than ataxia. The SEP abnormality has not always gotten much attention until today, but it may be strongly suggested that SEP examination is very useful to research the pathophysiology of SCD, particularly not only of the spinal ataxic form but also of OPCA.

4-09-17 THE MECHANISM OF AMANTADINE-INDUCED DOPAMINE RELEASE IN THE RAT STRIATUM

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The effect of amantadine on extracellular dopamine (DA) level in the rat striatum was studied using both in vivo microdialysis and in vitro uptake of [^{3}H]DA. In vivo microdialysis experiments revealed that, either intrastriatal (i. s., 0.01-0.1 mM, 20 min) or intraperitoneal (i. p., 100 mg/kg) administration of amantadine induced a prolonged DA release (maximum; 203% of control), but the release was completely attenuated by pretreatment of MK-801, a non-competitive NMDA antagonist (0.00039-0.00156 mg/kg, i. p. or 0.01-0.1 mM, i. s.). When given alone, MK-801 did not show a significant effect on the concentration of extracellular striatal DA. Administration of amantadine (0.01-0.1mM, i. s.) also increased the extracellular glutamate (maximum; 349% of control) by a Ca^{2+}-dependent manner. Amantadine did not inhibit the [^{3}H]DA uptake in the preparation of synaptosomes or slices in vitro. The results indicate that a part of amantadine-induced DA release "chain" might be coupled with an enhanced release of glutamate from corticostriatal terminals, perhaps through the strio-thalamo-cortical feedback circuit.

4-09-18 BRAINSTEM MEASUREMENTS IN PATIENTS WITH HEREDITARY ATAXIAS A USEFUL AID IN RADIOLOGICAL EVALUATION.

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By mean of ratios measures with Ct-Scan, different brain areas of 36 patients with Friedreich's ataxia (FA) and 33 with olivopontocerebellar atrophies (OPCA) were evaluated and compared with age-matched controls. A cut off point between mild and severe atrophies was established for the different OPCA subgroups. The correlation between age,lenght and severity of disease with severity of atrophie was evaluated.
FA patients show some difference with the controls in the midbrain and a tendency of dilatation in fourth ventricle. OPCA patients show all infratentorial parameters with statistical significant atrophy ($p<0.001$). The dominant forms of OPCA specially the slow saccades group exhibit the more severe atrophy. We found some interelation in the atrophie in different structures:
We don't found a correlation between the length and severity of atrophy in the OPCA subgroup.
The Ct-scan and the resonance magnetique studies should help the neurologist identified the different hereditary ataxic subgroups.

4-09-19 ORTHOSTATIC CIRCULATORY RESPONSE IN PROGRESSIVE AUTONOMIC FAILURE (PAF) EVALUATED BY NONINVASIVE CONTINUOUS BLOOD PRESSURE (BP) MEASUREMENT.

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We quantitatively assessed the orthostatic response of BP during active standing in 18 patients with PAF, including 10 with multiple system atrophy (MSA) and 8 with Parkinson's disease (PD). Thirteen age-matched healthy subjects, 26 PD patients without PAF, and 9 patients with spinocerebellar degeneration (SCD) without PAF were also studied. BP was recorded continuously using a Finapres. During standing, the normal individuals showed a transient reduction of BP followed by recovery within 30 seconds. In contrast, both PAF groups had a significant BP reduction and a poor recovery (more pronounced in the MSA group) that was significantly delayed. The PD without PAF group, despite absence of orthostatic hypotension, also had a large transient reduction of BP and long delay of recovery , while no significant abnormalities were observed in the SCD group.

This method appears useful for quantitatively assessing orthostatic BP responses, even in patients with early dysautonomia.

4-09-20 STRIATAL DYSFUNCTION OF ROLLING MOUSE NAGOYA.

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Rolling mouse Nagoya(rolling) is a neurological mutant mouse that shows frequent falling over on walking.We have found in rolling pathologically increased local cerebral glucose utilization(LCGU) in target structures of the striatum(ST),such as the globus pallidus(GP),entopeduncular nucleus,substantia nigra pars reticulata and compacta,and subthalamic nucleus.We studied whether the primary site of the basal ganglia dysfunction of rolling was in ST or in the target structures of ST.

Electrical stimulation of ST revealed in rolling a diminished inhibitory influence of ST on the GP neurons,and an increased spontaneous firing rate of the GP neuons, indicating dysfunction of the striatal projection neurons. Administration of apomorphine,2 mg/kg i.p.,caused decreases in LCGU in the target structures of rolling,a similar modification observed in rats with a striatal lesion,in contrast with LCGU increases in normal mice. Locomotor activities were also differently modified by apomorphine in rolling.Immunocytochemical staining of parvalbumin,a marker of the GABAergic interneurons of ST,revealed a decreased number of stained neurons in rolling.

These results suggest that ST is the primary site of the basal ganglia dysfunction in rolling.

4-09-21 TYROSINE HYDROXYLASE (TH) ACTIVITY IN SPINOCEREBELLAR DEGENERATION (OPCA VARIANT)

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Decrease in the number of neurons in the substantia nigra pars compacta (SNC) is regarded to be a cause of parkinsonism. Three autopsy cases of hereditary spinocerebellar degeneration of SCA1, wherein two cases were classified by genetic analysis and one case was diagnosed by pathological features, were analyzed in terms of TH activity in the substantia nigra (SN) and the striatum. On neurologic examination, all cases showed, no rigidity, but dystonia in the neck and/or extremities as an extrapyramidal sign. Histological examination demonstrated a moderate decrease in the neuronal population in the SNC; this decrease was equal to that described previously in Parkinson's disease (PD). However, the values of TH activity in the SN, the caudate nucleus and the putamen of these cases were at the lower limit of those of controls. In general, in cases with PD, the decrease in TH activity in the SN and the striatum is accompanied by nigral cell loss. In this sense, the present result is somewhat unique. Although the absence of parkinsonian symptoms in the present cases may account for fair preservation of TH activity in the nigrostriatal system, it is possible that the biochemical mechanism regulating and/or compensating for the TH enzyme in dopaminergic neurons in the present case differs from that regulating TH in PD.

4-09-22 PROTECTIVE EFFECTS OF BROMOCRIPTINE ON STRIATAL DOPAMINERGIC DAMAGE INDUCED BY 6-HYDROXYDOPAMINE

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Parkinson's disease (PD) is a slowly progressive disease due to several possible causes including toxins and free radicals. Bromocriptine, a potent dopaminergic agonist, is widely used for PD patients as monotherapy or combined therapy with levodopa. In the present study, we evaluated the protective effect of bromocriptine on striatal dopaminergic neurons with HPLC determination of dopamine (DA) and its metabolites as markers. Bromocriptine (5 mg/kg, ip, 7 days) strongly protected against the decrease in mouse striatal DA and its metabolites induced by icv injection of 6-hydroxydopamine (6-OHDA) with desipramine (ip), although levodopa/carbidopa (75/7.5 mg/kg, ip, 7 days) had no protective effect. Furthermore, in the *in vitro* system that generated •OH from FeSO4-H2O2, bromocriptine dose-dependently inhibited the generation of •OH. These findings clearly indicate that bromocriptine has a neuroprotective effect against neurotoxines such as 6-OHDA, probably due, in part, to its free radical scavenging activity, and that early introduction of bromocriptine to PD therapy is superior to the treatment with levodopa alone.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-09-24 LATE ONSET AUTOSOMAL DOMINANT CEREBELLAR ATAXIA WITH DEAFNESS

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Harding (1982) classifies late onset hereditary Autosomal Dominant Cerebellar Ataxias (ADCA) into four groups. Type IV is characterized by the association of ataxia , myoclonus and deafness. Recently several cases with this association have been reported showing a mitochondrial cytopathy. We have study a family whit late onset ADCA and deafness.

Eleven members of a three generation pedigree were examined. Three of them were affected; there was also available information of other 4 affected members. The pattern of inheritance was autosomal dominant. Symptoms begun at age 40-50 first with hearing loss and then appearing ataxia, ocular abnormalities and pyramidal symptoms. No dementia, myoclonus, epilepsy, extrapiramidal features or neuropathy were shown. Course was quite benign allowing deambulation up to very advance age. Audiologic and BAER studies showed sensorineural deafness and derangement of the brainstem auditory pathway. Cranial CT and MRI manifested cerebellar atrophy, specially the superior vermix. No mitochondrial or metabolic abnormalities were detected.

This form of late-onset hereditary ataxia is peculiar. It may be considered as a partial expressions of ADCA type IV, but apart from the absence of myoclonus it seems different to the other reported families.

4-09-25 SLOW-RELEASE LEVOPODA (MADOPAR HBS)(R) IN FLUCTUATIONS OF PARKINSON'S DISEASE

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Fluctuations of clinical responses in long term levodopa treatment of Parkinson's disease are fully recognized. 37 of the 92 patients treated at Ramathidbodi Parkinson Clinic encountered such therapeutic problems and that slow-release levodopa (Madopar HBS)(R) were prescribed as an add- on therapy. Hoehn & Yahr, Webster rating scale. Both akinetic and dyskinetic fluctuation scores were employed in monitoring drug effects. Madopar HBS(R) was found to be very useful, with 50% or more reduction of the scores in the following symptoms: end-of-dose akinesia (71.43%), *nocturnal akinesia (62.5%). Adverse drug effects and lack of* clinical response were found in 9 cases. One patient was lost to follow up whilst 27 patients have been doing well or fairly well, enjoying the positive clinical effects of this particular long acting levodopa.

4-09-26 HEREDOFAMILIAL SPINO-CEREBELLAR DEGENERATION (HFSCD) WITH SPECIAL REFERENCE TO SLOW SACCADE MOVEMENT OF THE EYE AND DYSAUTONOMIA.

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The object of study is to observe the clinical profile of Heredofamilial Spino-Cerebellar degeneration with special reference to slow saccade movement of the eye and evidences of dysautonomia.

25 cases of HFSCD have been studied and clinical profile observed; slow saccade movements of eyes have studied with help of video-tape recording; velocity of the saccade movement degrees/second. has been determined by a specially designed nystagmograph. For assessment of dysautonomia following tests are done, i.e. Sphygmomanometry, Standing Test, Valsalva Test, Reverse Standing Test, Cough Test. Dysautonomia was recognised when at least 2 of these tests were positive.

Slow saccade movements are seen in 6(25%) cases; the mean velocity is 108°/sec.

Dysautonomia are observed in 11 cases(44%). The clinical features of 4 cases are interesting in having cranial nerve palsies involving 3rd, 4th, 6th and 7th cranial nerves.

4-10-01 QUANTITATION OF DELETED MITOCHONDRIAL DNA (mtDNA) IN BRAIN TISSUE SAMPLE OF ALZHEIMER DISEASE PATIENTS BY COMPETITIVE P.C.R.

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A reduction in Cytochrome oxidase (COX) activity has been found in frontal and temporal cotices of Alzheimer Disease (AD) patients. Defects of mitochondrial energy metabolism could quicken degenerative processes already present in the neuronal cell. In order to evaluate a possible role of mtDNA mutations in reducing COX activity, we quantified deleted mtDNA (common deletion: bp 8470-13447) by competitive P.C.R. in frontal and temporal cortices of 3 AD patients and 2 aged controls. We didn't find any significative difference in the quantity of deleted mtDNA referred to total DNA between patients and controls. Because neuronal population is strongly reduced in AD cortices and because total DNA includes also glial cells, it is not possible to make precise conclusions. Morphological studies and in situ hybridisation will help in better understanding this data.

4-10-02 PRECURSOR PROTEIN GENE MUTATION IN ALZHEIMER'S DISEASE

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Some cases of familial Alzheimer's disease (FAD) were reported to have a point mutation in amyloid precursor protein (APP) gene. In Japan some FAD cases with the point mutation were reported, but the frequency of the point mutation is not yet uncertain. In this study we investigated the frequency of the point mutation to use the direct sequencing analysis.

We examined 19 sporadic cases of Alzheimer's disease (AD), 2 cases of FAD and 4 control subjects without dementia. The diagnosis of AD was made in accordance with the NINCDS-ADRDA and DSM-III-R criteria.

We extracted DNA from peripheral blood by the phenol-chloroform procudure and amplified the exon 17 by the asymmerical polymerase chain reaction (PCR). We performed the direct sequencing analysis by the dioxy method and decided the sequence.

No case of the FAD, AD and control group was found with the point mutation of APP717 Val-Ile, Val-Gly and Val-Phe or the other mutation. We suppose the frequency of the mutation associated with AD is not so much.

4-10-03 HAEMORRHEOLOGICAL PARAMETERS IN DEMENTIA.

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In an effort to determine whether some haemorrheological abnormalities are implicated in the pathophysiology of Dementia (Vascular=VaD and Alzheimer = AD), 3 groups of patients (24 controls, 12 VaD and 16 AD) comparable in age and sex and with no factors able to modify the haemorrheological profile, were examinated. Following parameters were determinated: 1.) Erithrocyte deformability; 2.) Erithrocyte aggregability at 5" by high (Ag-E-5) and low laminar flow velocity (Ag-E-5_1); 3.) Plasma viscosity; 4.) Plasma Fibrinogen (PF) and Haptoglobin. Results between groups were statistically compared (ANOVA).

Ag-E-5 was higher in VaD (X±SD = 9.94±2.03 MEA Units) compared with AD (8.52±2.05)(NS) and controls (8.44±1.71)($p<0.05$). Moreover, in the VaD group, but not in the other two, there was a positive correlation between Ag-E-5 values and PF.

These results show evidence of an increased erithrocyte aggregability in VaD. If such haemorrheological abnormalities are confirmed in a greater number of cases, their prompt detection and correction could be important to improve the clinical outcome in patients at early stages of VaD.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-10-04 MELAS MAY CLINICALLY RESEMBLE CREUTZFELDT-JAKOB DISEASE.

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We experienced a patient who was strongly suspected of suffering from Creutzfeldt-Jakob disease (CJD) on admission but finally diagnosed as MELAS after a series of investigation. This 50-year-old female patient had worked as usual until November, 1991. From early in December, disorientation, visual hallucination, paraphasia, alexia and agraphia emerged one after another. In January, 1992, as insomnia, excitement and soliloquy became uncontrollable, she was admitted to Keio University Hospital. Myoclonus was present. On brain CT, generalized mild brain atrophy was noted. In EEG typical "PSD" was demonstrated. These history, mode of onset, clinical signs and laboratory findings strongly suggested CJD. However, lactate and pyruvate levels in the serum and CSF were elevated. On T_2-weighted brain MRI, hyperintense signal area was noted, which disappeared on the follow-up MRI performed 2 months later. Muscle biopsy showed ragged-red fibers. On mitochondrial DNA analysis, the point mutation in the transfer $RNA^{Leu(UUR)}$ gene was detected and final diagnosis of MELAS was established. The clinical experience of the present case suggested that MELAS must be considered as one of the differential diagnoses of CJD, even if a patient shows typical CJD-like signs and PSD without any characteristic clinical signs of MELAS.

4-10-05 CSF METALS IN DEMENTIA

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The CSF concentration of the metals Al,Zn,Cu,Ca, Mg,Mn, and Cd were studied in dementing diseases using atomic absorption spectrophotometer. CSF samples were taken/ from 1o heathy controls and in 45 demented patients:28 Alzheimer's disease (AD); 10 vascular dementia; 4 Parkinson's disease; 1 multisystem atrophy; 1 normal pressure hydrocephalus and 1 korsakoff psychosis.

The results obtained were as follows: 1.Cu was / significanthy lower in AD patients than in controls - (p 0'001).2.We found no differences significant of othe metals in any group.3.There no relationship of CSF metals to age o degree of cognitire impairment.

Our findengs indicate an imbalance of CSF Cu levelsin AO:The significance of low CSF Cu in AD is not / clear, but the normal values from other dementing diseases imply that neuronal destruction per se is not sufficient to decrease CSF Cu concentration.The subject is yet open for further investigation.

4-10-06 LONGITUDINAL COGNITIVE FUNCTIONING IN ELDERLY WITH WHITE MATTER HYPERINTENSITIES

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The significance of white matter hyperintensities on MRI in the elderly is uncertain. It has been suggested that these white matter changes are associated with cardiovascular risk factors and may predict dementia. To examine this possibility, we longitudinally followed the cognitive functioning of 20 individuals enrolled in the Aging Process Study at the University of New Mexico. All 20 individuals had had an MRI in 1987/88 that showed moderate to severe white matter hyperintensities, and had mini-mental status examination (MMSE) close to the time of the MRI testing. They underwent repeat MRI and MMSE testing in 1991/92. The initial scores ranged from 26 to 30 (median 30), and they were unchanged on the second test. Fourteen of these individuals were available for extensive interview and examination. Cardiovascular risk factors occurred commonly in this subpopulation. Hypertension was present in 7/14. In addition, 8/14 individuals had a history of headaches, and 5/14 were found to have orthostatic hypotension. We determined that after 4 years of follow up, none of the individuals had developed cognitive impairment. Our findings suggest that white matter hyperintensities do not confer increased risk of developing dementia, but are associated with the presence of cardiovascular risk factors.

4-10-07 SCREENING OF THE MIS-SENSE MUTATION PRODUCING THE ^{717}VAL→ILE SUBSTITUTION IN THE AMYLOID PRECURSOR PROTEIN IN JAPANESE CASES OF FAMILIAL AND SPORADIC ALZHEIMER'S DISEASE.

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We investigated a C to T transition at base pair 2149 in the amyloid precursor protein gene in 41 Japanese cases of early-onset familial Alzheimer's disease (FAD), late-onset FAD and sporadic Alzheimer's disease (AD) by polymerase chain reaction and restriction enzyme polymorphism with BclI. Among 9 early-onset FAD patients, only one patient had the mis-sense mutation. Neither 5 patients with late-onset FAD nor 27 patients with sporadic AD had the mutation. Our result and the preveous reports from Japan indicate that this type of mis-sense mutation is present in several cases of Japanese early-onset FAD. On the other hand, our data suggest that this mutation is not a common cause of Japanese early-onset FAD. Because the mutation has been reported to be rare in Caucasian early-onset FAD and to be absent in Caucasian late-onset FAD and sporadic AD, the situation of this mutation in Alzheimer's disease may be common beyond the ethnic background.

4-10-08 THE SPECIFICITY OF CEREBRAL BLOOD FLOW CHANGES IN PATIENTS WITH FRONTAL LOBE DEMENTIA

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Frontal lobe dementia (FLD) is a degenerative condition characterized by changes in personality, breakdown in social conduct, disinhibition, impulsivity, unconcern, hyperphagia, and stereotyped and perseverative behavior. For this study, we carried out Tc99m-HMPAO SPECT scans in 8 patients with mild dementia and the psychiatric correlate of FDL, 8 patients with mild dementia and DSM-III criteria for Alzheimer's disease (AD) but no psychiatric changes, and 8 normal controls. A 3-way ANOVA with repeated measures (group x side x region) showed a significant group effect ($F(2,21)=15.3$, $p<.0001$) (patients with FLD had a significantly lower cerebral blood flow (CBF) than both AD patients and controls), and a significant group x region interaction ($F(12,126)=3.74$, $p<.0001$) (patients with FLD had a significantly lower CBF in the orbitofrontal cortex, temporal basal cortex, and basal ganglia than patients with AD and normal controls). Moreover, the FLD group also showed significant ventral-dorsal CBF asymmetries in both the frontal lobes (orbital < dorsolateral) ($p<.01$) and temporal lobes (basal < lateral) ($p<.01$). In conclusion, the present study demonstrated the specificity of regional CBF changes in the diagnosis of different types of dementia, and supports the importance of orbitofrontal, temporopolar, and basal ganglia dysfunction in the production of the psychiatric syndrome of FLD.

4-10-09 PROTON NMR SPECTROSCOPY IN SUBCORTICAL ARTERIOSCLEROTIC ENCEPHALOPATHY

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White matter hyperintensities (WMH) on MRI in subcortical arteriosclerotic encephalopathy (SAE) are thought to be due to vascular disease. Similar changes are seen, however, in normal elderly. To determine whether WMH in SAE are due to ischemia, 2 patients with SAE (65 and 70 y. o.) were studied using ^{1}H-MRS on a 1.5T GE Signa System with PRESS (TE=26,136,270 msec). Six asymptomatic elderly with severe WMH and 7 without WMH were controls. The patients had progressive gait difficulty, dementia, and small strokes. Tests for other causes of demyelination were negative; SPECT blood flow studies were compatible with vascular disease. Ratios of N-acetyl groups (NAG) to phosphocreatine/creatine (PCr) were calculated. Spectra from WMH in SAE patients had a reduced NAG/PCr ratio compared with both control groups and one patient had lactate. We conclude that ^{1}H-MRS is abnormal in WMH of patients with SAE and normal in asymptomatic elderly with WMH.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-10-10 CLINIC-INSTRUMENTAL CLASSIFICATION OF M.I. AND A.T. DEMENTIA

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Forty-four demented patients (29 males, 15 females, age range 53-83 years) were enrolled following the clinical classifications (DSM-III, Mc Kann) and scoring scales primary dementia and to further classify the various groups, the following examinations were carried out: routine blood chemistries, Vit.B12 and Folic Acid, VDRL & TPHA, T3-T4- FT3-FT4-TSH, Computerized EEG with Mapping, TC scan, Echodoppler of epiaortic vessels, Neuropsycological Tests battery, P300.
After such selection 15 patients were classified as MID (34% with high "vascular" scores and "focal" vascular symptoms); in these TC scans invariably showed lacunar infarcts, cortico-subcortical atrophy and leukoaraiosis. Moreover, Echodoppler in 12 cases evidenciated multiple non-stenosing plaques at the carotid bifurcation; Neuropsycological tests found a homogeneous deficit.
Twenty-nine patients were classified as DAT (66%). They included insidious evolution with focal pyramidal or extrapyramidal signs in 10 out of 29. TC Scan was normal in 6, while in the remaining it showed diffuse or focal atrophy and -in 6 patients- leukoaraiosis. Echodoppler showed plaques in 15 patients. Neuropsycological tests were disomogeneously and homogeneously altered respectively in 6 and 23 cases. EEG showed a significant decrement of "fast" vs "slow" rhythms in all the patients; such a decrement correlated with the cognitive deterioration. Alpha activity was more frontally represented than in normals and was less reactive. Alpha activity on the paricto-occipital leads was significantly asymmetrical in MID patients. No conclusive information was provided by the P300 with the exception of high degrees of delays and decrement in the cases of both classes.

4-10-11 PATHOLOGICAL VALIDATION OF CLINICAL DIAGNOSIS OF ALZHEIMER'S DISEASE (AD).

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Clinicopathological correlation in dementia populations show varying levels of accuracy (43-100%) for the diagnosis of AD. We evaluated the validity of NINCDS-ADRDA criteria for making accurate antemortem diagnoses of AD in a dementia research clinic population.

Cases were evaluated histopathologically (with Bielschowsky) using the Khatchaturian criteria for the diagnosis of AD.

From a dementia clinic population of 550 subjects, there were 95 deaths and 39 autopsies. From the autopsied population, 33 had a premortem diagnosis of possible or probable AD, 5 of other dementia and 1 of no dementia. In 25 cases the diagnosis of AD was confirmed at autopsy; the other 8 cases had a non AD degenerative dementia (3 Lewy body disease, 4 frontotemporal atrophy with neuronal loss and 1 multifocal encephalomalacia). Of the 5 cases diagnosed in life as other dementia, one had AD by histological criteria.

The congruence for the clinical (NINCDS) and the pathological (Khatchaturian) criteria for AD by histological criteria for AD was 76% in 39 cases evaluated from one centre. A clinical diagnosis of AD was most often confused with other degenerative dementias.

4-10-12 UBIQUITIN LEVEL IN CEREBRO-SPINAL FLUID: A DIAGNOSIS TEST FOR ALZHEIMER'S DISEASE ?

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The diagnosis of Alzheimer disease (AD), the most common cause of dementia, is made clinically and can only be confirmed by histopathological post mortem studies. At this moment, there is no specific and sensitive biological test for the diagnosis of this disease. A few studies try to evaluate in the cerebro-spinal fluid (CSF) of these patients concentration variations of proteins found in neurofibrillary tangles or amyloid plaques: A4 protein, tau protein or ubiquitin . Ubiquitin , a polypeptide present in all cellular compartment, participates in abnormal or short lived proteins degradation. Using a competition method and an ELISA test, we have evaluated concentration variations of free and conjugated ubiquitin in the CSF of 3 groups of patients: one with patients who had been clinically diagnosed as having AD (group 1) one with patients suffering from others neurodegenerative disease (group 2) and one with control patients, including patients with non degenerative dementia (group 3). Results demonstrate an ubiquitin concentration higher than 700 ng/ml in 88 % of patients with AD, in 63 % of patients from group 2 but in only 15 % of patients from group 3. To confirm and improve these results a bigger population is now studied and specific evaluation of conjugated ubiquitin is performed.

4-10-13 HIGHER CORTICAL FUNCTIONS IN DEMENTIA OF ALZHEIMER'S TYPE AND IN MULTI-INFARCT DEMENTIA

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In dementia of Alzheimer's type (DAT) modern imaging techniques (PET, SPECT) have revealed a specific metabolic dysfunction in the left temporo-parieto-occipital brain region. Lesions in this cortical region may cause the neuropsychological symptoms of acalculia, agraphia, right-left disorientation, ideomotor apraxia and aphasia. We investigated these symptoms in 23 DAT-patients (mean age: 79.3; SD=9.9), 19 multi-infarct dementia (MID) patients (mean age: 78.7; SD=6.2) and in 17 age-matched controls. Demented patients were diagnosed according to the criteria of the DSM-III-R (1987). 23 diagnoses were confirmed neuropathologically (15 DAT,8 MID).

MID- and DAT- patients did not differ in severity of dementia rated by the Mini Mental State Examination (MMSE) (DAT: MMSE: 11.6; SD=8.2; MID: MMSE: 14.8; SD=6.3; t=1.41; p=0.166). Controls differed from demented patients of both etiologies in all higher cortical functions ($p < 0.0001$). The pattern of neuropsychological deficits showed high intervariability between demented patients. The only significant difference between MID and DAT was found in right-left orientation, which was better preserved in MID (Mann-Whitney: $z=2.773$; $p=0.005$)[1].

4-10-14 CORRELATION BETWEEN SPET IMAGINGS AND NEUROPSYCHOLOGICAL DEFICITS IN ALZHEIMER'S DISEASE

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Until a few years ago it was commonly accepted that bilateral hypoperfusion of the posterior temporal and parietal areas is the typical SPET imaging of Alzheimer's Disease (AD). According to some recent studies, this is true only in advanced stages: earlier in the course of the disease, different patterns of SPET imagings, as well as different patterns of cognitive impairment, can be found. Consequently, a specific relationship should exist between site and extension of the SPET hypoperfusion imagings and neuropsychological profile of the appearing cognitive deficits. In order to verify this issue, we are studying 40 patients with probable AD (according to NINCDS-ADRDA criteria) and 60 patients affected by other degenerative disorders, with a more 'focal' pattern of brain involvement, either cortical or subcortical (e.g., Slowly Progressive Aphasia, Progressive Supranuclear Palsy, Parkinson-Dementia, Cortico-basal Degeneration, etc.). All patients have undergone neurologic and neuropsychological examination (this latter by means of a standardized Mental Deterioration Battery, providing an overall 'deterioration' score and different scores relative to different cognitive domains), CT-scan (or NMR) and brain SPET (Tc 99m HM-PAO, 740 MBq). Neuropsychological and SPET data - collected and evaluated independently, according to a blind procedure - will be matched in order to define and analyze all the possible correlations.

4-10-15 ORIENTATION IN ALZHEIMER PATIENTS (AD/pts).

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The term "disorientation" usually defines the impairment to demonstrate knowledge of temporal, spatial, and personal information. It is a feature of patients affected by global cognitive impairment. This study tests the hypotheses that in AD/pts residual orientation capability is dependent upon the "variability" or "invariability" of the information to be retrieved, and that changes in orientating ability are due to the difference in the amount of attentional resources required by "variable" or "invariable" information. By "variable" we mean an information needing continuous updating during life (e.g., age); by "invariable" an information that is not subject to modifications (e.g., birth date). An orientation inquiry made up by two sections, one "variable" and one "invariable", was administered to 112 AD/pts and 112 healthy subjects. AD/pts performed the "variable" section worse than the "invariable" one ($t=19.56$, $d.f.=111$, $p<.001$). Furthermore, 20 healthy young controls were tested in a dual-task condition, where the orientation inquiry was coupled with a continuous attention demanding reaction times (RTs) task. Results showed that difference between RTs in the two dual task conditions achieved significance ($t=2.12$, $d.f.=19$, $p<.05$). These findings may be fruitful in clinical practice in developing neuropsychological screening batteries to rate the severity of disorientation in cognitive deterioration.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-10-16 RISK FACTORS FOR DEMENTIA IN PARKINSON´S DISEASE.

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The cognitive deterioration and dementia are found in 10-40-% of patients with Parkinson´s disease (PD) and are related to: aging, severity of PD, treatment with L-Dopa or with anticholinergic agents. In a prospective longitudinal study of 70 consecutive PD outpatients we have investigated the risk factors for dementia. All cases had three clinical criteria of PD, CT scan and follow-up of 12 months or more. Dementia was stated according to DSM-III criteria in 15 patients, other 15 non demented patients scoring 4 in the Reisberg´s Global Deterioration Scale were labeled as "mentally deteriorated". The remaining 40 cases had normal cognitive functions. The data were compared by means of analysis of variance and Kruskal-Wallis test. In several linear and logistic multiple regression analysis only the three following variables significantly predicted the dementia: age, female sex, and time of anticholinergic intake (p 0.0001). This association of anticholinergic treatment with dementia could not be explained by an spurious effect of the tremor treatment (correlation between tremor and dementia r: 0,18 n.s.) neither of the disease duration (correlation between time of anticholinergic intake and disease duration, r: 0,12 n.s.).

4-10-17 SEROTONERGIC MECHANISMS IN ALZHEIMER'S DISEASE: PRELIMINARY RESULTS OF A CONTROLLED CLINICAL TRIAL WITH LISURIDE

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The functional significance of serotonergic neurotransmission in Alzheimer's disease remains poorly understood, but some preclinical studies suggested that interventions designed to decrease central serotonin levels may improve cognitive function. Lisuride has high affinity for the 5-HT_{1a} receptor and may inhibit central serotonergic activity. We evaluated the antidementia efficacy of lisuride in 16 patients with probable Alzheimer's disease in a randomized double-blind parallel group trial design. After a dose-finding phase of 4 weeks with lisuride (n=7) in doses of up to 0.3 mg/day or placebo (n=9), patients entered an efficacy phase of 8 weeks with treatment of their best-dose, defined as the optimal ratio between efficacy and tolerance. Outcome measures included tests of visual and verbal memory, attention, psychomotor function, and general cognitive function, as well as global clinical impression and mood assessment. Patients treated with lisuride significantly improved in a task of verbal memory compared to patients treated with placebo, however no consistent differences were observed in other outcome measures between both groups. Global clinical impression was in agreement with an apparent lack of clinical benefit of lisuride. It appears therefore unlikely that modulation of central serotonergic activity by lisuride will alleviate symptoms of Alzheimer's disease.

4-10-18 THE EFFECT OF ACETYLCHOLINESTERASE INHIBITORS ON ACETYL-CHOLINESTERASE IN SENILE PLAQUE

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A high specific activity of acetylcholinesterase (AChE) was detected in the senile plaque(SP)-rich fraction isolated from the brain of Alzheimer's disease (AD). AChE in SP possessed properties of type A isozyme, containing collagen like tail. AChE inhibitors including physostigmine, E-2020, THA, amiridin and nicergoline showed a poor effect on AChE present in SP fraction isolated from AD brain than that in the solubilized fraction of AD brain or in the control brain. However, AChE purified from rat skeletal muscle (type A) was more susceptible to AChE inhibitors such as E-2020, amiridin, THA or physostigmine than that purified from rat brain (G4 form). AChE purified from human erythrocytes (G2 form) was inhibited less effectively by E-2020, physostigmine or THA than AChE A form purified from rat skeletal muscle. AChE inhibitors exhibited a less remarkable effect on AChE extracted from SP than that in normal human or rat brain, human erythrocytes or rat skeletal muscle. These results suggest that the property of AChE present in SP is different from that in normal brain or skeletal muscle . AChE inhibitors would exert decreased effects on AChE in SP, due either to the abnormal property of the enzyme or to the impeded access of the drug to the enzyme present in SP.

4-10-19 LEWY BODY DISEASE IN PAMPLONA, SPAIN.

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Backgrounds and methods: Lewy body disease (LBD) as a separate nosologic entity causing dementia in the elderly is being firmly established. To know its prevalence and characterization, we reviewed 549 consecutive autopsied brains in our Department. The age of death was 60 years or older in 391 subjects. Immunohistochemical staining with antiubiquitin antibodies facilitated the identification of LB. Their specific density was measured (number per 100xfield) following a protocol in the predilection neocortical sites, entorhinal cortex, hippocampal gyrus, diencephalon and brainstem (12 different specimens were taken in each case). We assessed the clinical features according to LB findings. Classical pathology of Alzheimer's disease (density and distribution of mature/inmature senile plaques (SP) and neurofibrillary tangles (NFT), when present, demonstrated by modified Belchowsky technic and antitau serum) and Parkinson's disease were also studied.
Results: Twelve brains (2.1%) had neocortical LB. In 6 of them, it was most heavily concentrated in the temporal lobe, insular, entorhinal an frontal cortex without AD pathology (LBD, pure form). With fewer neocortical LB but with accompanying SP and NFT there were 2 brains (LBD, common form, concomitant AD). Two more brains had nigral and neocortical LB leading to a pathological diagnosis of PD. In the remaining 2 cases, the finding of neocortical LB seems to be either incidental or asymptomatic or preclinical.
Cognitive decline was mild to moderate in all brains which had neocortical LB in 4 or more lobes. However, the density of these LB does not correlate with the severity of dementia. Dementia was associated with minor parkinsonian symptons and psychiatric features in the 6 patients with pure LBD.
Thirty eight cases of the 391 (9.7%) older than 60 years in these series had been clinically diagnosed as senile dementia. Using accepted neuropathologic criteria, diagnoses were AD (63.1%), LBD (21.05%) and vascular dementia (13.1%).
Conclusions: These observations suggest that on consultant diagnosis of senile dementia, LBD must be taken into account. On the contrary, distorting results from clinical trials and epidemiological studies are likely to happen.

4-10-20 DISTINCTIVE NEUROPSYCHOLOGICAL FEATURES OF MILD DEMENTIA OF THE ALZHEIMER'S TYPE

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Patients affected by different forms of dementia - namely: Dementia of the Alzheimer's type (DAT: n=49), Multi-infarct Dementia (MID: n=43), Parkinson's Disease with Dementia (PDe: n=35), Depressive Pseudodementia (DPs: n=26) and Progressive Supranuclear Palsy (PSP: n=14) - were examined with a standardized neuropsychological test battery (Mental Deterioration Battery or MDB) described in previous studies from our laboratory. Thirty normal subjects matched for age and educational level to the dementia groups formed the control group of the study. The overall severity of dementia (as assessed by the MDB global score) was quite similar in the various dementia groups, but some neuropsychological features, obtained on the Rey's Auditory Verbal Learning Test (AVLT) and on a copying drawings (CD) test clearly distinguished DAT patients from all other patients. On the AVLT only DAT: (a) showed a clear prevalence of the 'recency' over the 'primacy' effect; (b) scored 0 on the Delayed Recall (47% of cases), thus suggesting rapid and complete decay of the memory trace; (c) made more than 2 'false alarm' errors on the Delayed Recognition (83% of cases). On the CD task, only DAT patients showed clear istances of the 'closing in' phenomenon (31% of cases). These results show that some neuro-psychological features can be considered as markers of Alzheimer's disease in mild forms of dementia.

4-10-21 SURVIVAL AND CLINICAL PREDICTORS OF MORTALITY IN ALZHEIMER'S DISEASE AND MULTI-INFARCT DEMENTIA.

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In order to examine survival and predictive risk factors for death in dementia, we followed-up prospectively 218 patients with Alzheimer's disease (AD) and 115 patients with multi-infarct dementia (MID) for 14 years. Patients were followed-up from Dec 31, 1976, to Dec 31, 1990 or until death.

Survival was analysed by the life table method. Significant predictive factors for survival were identified by using proportional hazard model and stepwise regression.

The 14-year survival rate in AD was 2.4% vs expected 16.6% (p< 0.001) and in MID 1.7% vs 13.3% (p< 0.001) By comparing survival distributions between AD and MID, the poorest survival was found among patients with MID (p< 0.05) In order to examine the correlation of survival in term of prognostic factors and clinical features, stepwise regression analysis picked up the following significant items, in AD group: age (p< 0.001), female gender (p< 0.001), occurrence of epilepsy (p< 0.01) or angina pectoris (< 0.05) and in MID group: age (p= 0.05), female gender (p< 0.05), disability (p< 0.01) and urinary incontinence (p< 0.05).

AD and MID carry a significantly increased risk of mortality, and the survival prognosis involves different features in each of the two diseases.

4-10-22 CSF IL-1β LEVELS ARE INCREASED IN SOME PATIENTS WITH ALZHEIMER DISEASE

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Inflammatory cytokines, for example, IL-1 and IL-6 have been suggested to play a role in the development of a local inflammatory reaction surrounding amyloid plaques in Alzheimer's disease (AD). Our object was to measure the levels of IL-1β in AD CSF and sera, and correlate them with severity of dementia. We used commercial ELISA kits to measure IL-1β levels in matching pairs of CSF and serum of 40 AD patients (age 51-81 years), 32 controls (44-82 years) and 13 patients with non-AD dementia (56-78 years). CSF IL-1β levels were significantly higher in AD and non-AD dementia patients compared to controls. The levels showed no correlation with age or severity of dementia. Serum IL-1β levels in three groups were similar. Increased IL-1β in the CSF in AD patients may be related to invasion of astrocytes and microglia in amyloid plaques. Because similar increase was also found in patients with non-AD dementia IL-1β can not be used as a laboratory marker to aid the diagnosis of AD.

4-10-23 THE ROLE OF AMYLOSOMES IN THE PATHOGENESIS OF OF ALZHEIMER'S DISEASE.

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We have shown that intraneuronal inclusions, present throughout the cortex, contain beta amyloid peptide which is not beta pleated. This was demonstrated by immunohistochemistry, amino acid analysis, PAGE, Western blotting and HPLC comparison and immunoblotting. All techniques showed identity between isolated inclusions, beta amyloid and isolated plaques. In view of the known metabolism of amyloid precursor protein and the single membrane of the intraneuronal structures we termed them amylosomes. Morphometric analysis of 120 brains showed that amylosomes are not present at birth but by age 10 years they reach a plateau in size and number which remains stable throughout life. Immunohistochemistry and congo red staining showed that beta amyloid is present in the choroid plexus of every brain after the age of 70 and can be demonstrated in some cases as early as age 40. We therefore propose that amylosomes are lysosomes filled with beta peptide which are transported along dendrites to the CSF where the peptide is released and appears in the choroid plexus or as congophilic angiopathy. We also propose that in Alzheimer's a decrease in microtubule function prevents this transport and amylosomes break into the neuropil with subsequent beta pleating and plaque formation.

4-10-24 THE CLINICAL PATHOLOGICAL CORRELATES OF LOBAR ATROPHY

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Objective To permit clinical pathological classifications in the syndromes of dementia of frontal lobe type (DFT). (13 brains), DFT and motor neurone disease (MND) (5 brains) and progressive aphasia (5 brains).

Results DFT is associated with bilateral symmetrical fronto-temporal atrophy. Two major histologies occur: large neuronal cell loss and spongiform appearance: astrocytic gliosis with and without tau and ubiquitin positive intraneuronal inclusion bodies (Pick bodies). Half the cases are familial.

DFT/MND is associated with bilateral symmetrical fronto-temporal atrophy and spongiform appearance in the absence of significant gliosis or Pick bodies. One case was familial.

A sub-group of patients (3 brains), having marked stereotypic behaviour and early extrapyramidal signs have striato-limbic involvement and features of both histological types. One case was familial.

PA is associated with two major distributions of pathology: asymmetrical left cerebral and bilateral symmetrical temporal lobe atrophy. The former is associated with non-fluent aphasia and the latter with fluent aphasia and associative agnosia. The histology is of spongiform appearance. Familial cases indicate an association with DFT.

Conclusions The topography of atrophy determines the clinical syndromes which are strongly familial. The histology manifests a spectrum of change including that of Pick's disease.

4-10-25 VERBAL LEARNING IN ALZHEIMER TYPE DEMENTIA (AD).

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The aim of this study was to examine the potential verbal learning abilities in AD as a function of severity of the disease and difficulty of the to-be-remembered material.

Preliminary data were obtained from 31 patients (mean age 68.6; SD:7.39; mean educational level 6;SD:4.15 and mean MMS:17.5; SD:4.66) using a paired associated learning task standardized for the italian population.ANOVA showed significant improvement for related and unrelated paired associates (p=.0007 and p=.0262 respectively), while the correlation between verbal learning and MMS was significant only for easy associations (r=.388; p=.0001). These results confirm that verbal learning is possible in AD, when the disease is not severe and cognitive demands of the task are reduced.

4-14-01 EVIDENCE FOR THE PRESENCE OF TRIPLE MOTOR ROOT OF TRIGEMINAL NERVE AND ITS CLINICAL SIGNIFICANCE

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Clinically the roots of trigeminal nerve are important for the management of intractable pain of trigeminal neuralgia. However the roots of trigeminal nerve at the pons do not follow a uniform pattern and several variations in the motor root of the nerve have been reported previously. In the present study carried out on 24 human cadavers on both the sides, the classical description of single motor root was found only in 8 cases (33.3%). In 12 cases (50%) double motor root at the pons was encountered. However on two sides on two different cadavers, the triple nature of the motor root was seen. The three motor rootlets have been named as inferior motor rootlets, superior motor rootlets, and accessory superior motor rootlets. The latter may be composed of sensory pain fibres, since previous workers have shown that some of the sensory fibres also run in the motor root. This can be clinically significant in the management of intractable cases of trigeminal neuralgia and the accessory superior motor rootlets should also be considered for the surgical intervention.

4-14-02 CHRONIC PAROXYSMAL HEMICRANIA OF 10 YEARS DURATION RELIEVED BY BROMOCRIPTINE THERAPY FOR A PROLACTINOMA

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Chronic paroxysmal hemicrania (CPP) is a rare condition, occurring mostly in women featuring brief episodes of acute pain in the periorbital region, accompanied by ptosis and tearing, recurring many times a day for many years. The mechanism is unknown and in only a few cases has structural pathology been reported.

A 50-year-old woman suffered for 10 years from typical CPP, with 10 minute episodes of intense pain around the right eye accompanied by ptosis and tearing, recurring 5 to 10 times each day. Elevated prolactin levels were found and MRI demonstrated a small adenoma. Treatment with bromocriptine resulted in a reduction in prolactin levels but also in a complete diappearance of episodes of headache, which has been sustained for over a year. This suggests that the mechanism for CPH may be found in the region of the pituitary gland or that it may be mediated by pituitary hormones. A trial of bromocriptine in other patients with this condition is suggested.

4-14-03 NORADRENERGIC NERVOUS ACTIVITY IN BENIGN COITAL CEPHALALGIA AND MIGRAINE WITH AURA

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It has been known that benign coital cephalalgia (BCC) sometimes occurs in patients with migraine, but the pathophysiology of BCC is obscure. The purpose of the present study was to investigate the autonomic nervous function in patients with BCC and migraine with aura (MA). Four patients with BCC, ten patients with MA and thirty age-matched control volunteers were studied. The autonomic nervous function was assessed both by measurement of the serum levels of norephinephrine and by hemodynamic functional tests. The plasma norepinephrine level in the steady state in BCC was not significantly different from that in controls, but the values in MA was significantly lower than that in controls. The changes in systolic blood pressure (BP) induced by standing from supine position were -13±5mmHg in BCC and -13±7mmHg in MA, which were significantly different from that in controls (-2±6mmHg, $P<0.05$). The time necessary for recovery of the BP from its peak to the steady state level following a bolus injection of 0.1μg/kg of norepinephrine (recovery time) was measured. Recovery time for the BCC and MA were 132±23s and 101±30s, respectively. These values were significantly longer than that in the control subjects (21±15s ,$P<0.05$). Since BCC shows similar autonomic nervous dysfunction as in MA, it is suggested that abnormal autonomic nervous function may be closely related to the pathophysiology of BCC.

4-14-04 VALIDATION OF A NEW INSTRUMENT FOR DETERMINING MIGRAINE PREVALENCE: THE UCSD MIGRAINE QUESTIONNAIRE.

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Prior survey instruments utilized for diagnosis of headache have been criticized for their poor predictive validity. With the hope of providing a more reliable instrument for use in large population surveys, we developed a short questionnaire based on existing International Headache Society diagnostic criteria and administered the questionnaire to 50 consecutive patients seeking evaluation at a University-based headache clinic. All patients subsequently were examined by a single neurologist, and their questionnaires were reviewed independently by a second neurologist, a non-neurologist physician and a non-physician graduate student. Based only on the questionnaires, the reviewers scored each patient as having migraine with aura, migraine without aura only or no migraine. In 47 (94%) of the 50 cases, all three reviewers agreed with the examining physician as to the presence or absence of migraine, and the concordance rates amongst any two of the three reviewers ranged from 98% to 100%. These data indicate high predictive validity and low interobserver variability and suggest the questionnaire may be quite useful as a survey instrument.

4-14-05 DRUG INDUCED HEADACHE : PHARMACOLOGICAL AND PSYCHOLOGICAL FACTORS

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Many physicians still seem unaware that large and repeated doses of these drugs can induce chronic headache.
Method - For the last ten years, we have regularly followed up 150 patients with this type of drug abuse problem . During the weaning period, we particularly studied two points of view.
1 - The pharmacological composition of the incriminated drugs
2 - The psychological state of the patients.
Results - 1 . Careful study of the composition of the drugs showed that these were almost never single analgesic.In the vast majority of cases, there was the addition of substances having a psychotropic action, barbiturate , codeine and particularly caffeine.
2 . Cursory psychological analysis often reveal an anxious and/or depressive component.More extensive psychopathological study shows that far from constituting the equivalent of depression or anxiety, drug addiction of headache sufferers often takes the form of as an alternative form of behaviour and a fight against anxiety and depression.
Conclusion - The pharmacological approach per se cannot adequately explain the pathogenesis of drug induced headache.
A dual pharmacological and psychological approach provides better understanding of this problem.

4-14-06 A RETROSPECTIVE ANALYSIS OF INTRAMUSCULAR DIHYDROERGOTAMINE (DHE) IN THE TREATMENT OF REFRACTORY ACUTE MIGRAINE HEADACHE

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The efficacy of i.m. DHE in the treatment of refractory acute migraine was assessed in the retrospective study of 137 acute migraine episodes (E) occurring in 91 pts. over 36 months. Pts. were treated 4-72 hr. after migraine onset after a variety of abortive medications failed to provide relief. The protocol treated 106 E in 82 pts. with a single i.m. injection of DHE (1.0 mg). For migraine unrelieved in 45-60 min. additional DHE (0.5-1.0 mg) was given. Pts. rated pain (P) relief 2 hr. and 24 hr. after DHE: Poor (<50%), Fair (50-75%), Good (76-99%), Excellent (completely P-free). Within 2 hr. of DHE treatment, 88% of E improved at least 50%; 57% were improved more than 75% and 20% were completely relieved. Overall, mean P relief was 73%. At 24 hr., 99% of E available for follow-up were improved at least 50%; 84% were improved more than 75% and 43% were P-free. Average 24 hr. P relief was 88%. Pts. receiving 1.0 mg DHE (84 E) reported 72% improvement at 2 hr. Injecting another 0.5 or 1.0 mg DHE (22 E) did not result in greater relief (76%). At 24 hr., improvement also was comparable: 87% and 92% for the respective dose groups. P relief achieved by 2 hr was sustained. The majority of E with "Good" relief at 2 hr continued to be >75% improved at 24 hr. (39/40). Recurrence of P was low: 11/12 E completely relieved at 2 hr. were still P-free at 24 hr. Very few E that had improved >50% at 2 hr. were worse at 24 hr. (3/79). P relief continued to improve after the 2 hr. evaluation. For E relieved <75% at 2 hr., 69% experienced "Good" or better relief (>75%) at 24 hr., with nearly half becoming totally P-free. Adverse events were few and mild. We conclude that i.m. DHE is effective and well tolerated in pts. with refractory acute migraine episodes.

4-14-07 DIFFERENT PROFILES OF PLATELET GRANULE SECRETION IN MIGRAINE WITH AURA (MA) AND WITHOUT AURA (MwA)

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We studied the platelet secretion of serotonin and PF4, in parallel with the platelet aggregation in PRP in 62 MA patients (39 M, 23 F), 42 MwA patients (29 M, 13 F), when headache free, and 21 controls (13 M, 8 F). We found no aberrances in platelet aggregation, but the PF4 secretion induced by 0.1 and 1.0 μM PAF was increased in both MA ($p > 0.01$ and $p > 0.0001$) and MwA ($p > 0.02$ and $p > 0.0001$). In MA, there was an increase in the basal intraplatelet serotonin levels ($p > 0.001$), and also the serotonin secretion induced by 0.1 and 1.0 μM PAF ($p > 0.003$ and $p > 0.002$) and by 0.5 and 2.0 μg/ml collagen ($p > 0.001$ and $p > 0.0001$). The increased basal and secreted amount of serotonin in MA may be realted to a particular aberrancy of serotonin turnover in this migraine group. The increase PAF sensitivity in migraineurs may be one factor behind the *in vivo* platelet activation in migraine.

4-14-08 REDUCED COLLAGEN-INDUCED AGGREGATION IN WHOLE BLOOD IN MIGRAINE: POSSIBLE RELATIONSHIP WITH INCREASED INTRAPLATELET L-ARGININE LEVELS AND THE NO PATHWAY

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We investigated the platelet aggregation and ATP-secretion induced by collagen (0.5 and 2.0 μg/ml) and PAF (0.1 and 1.0 μM) in whole blood in migraineurs and also we measured the intraplatelet levels of L-arginine precursor of NO in 61 MA patients, 42 MwA patients, in headache free, and 21 controls. The extent of collagen-induced platelet aggregation was decreased in MA ($p > 0.00001$) and MwA ($p > 0.006$). The platelet aggregation and ATP-secretion induced by PAF were similar in all 3 groups. The mean intraplatelet L-arginine levels were significantly increased in MA ($p > 0.007$) but not in MwA. The selective impairment of collagen-induced platelet aggregation together with high L-arginine levels in migraine, suggests a disturbance in the NO pathway. In MA this disturbance may be due to an increased platelet L-arginine availability, while in MwA the mechanisms remain abscure.

4-14-09 HIGH INTRAPLATELET LEVELS OF SEROTONIN AND 5-HIAA SUGGEST THAT TENSION HEADACHE IS A HIGH-SEROTONIN SYNDROME

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The platelet constitutes a useful peripherial marker of the study of serotoninergic function. There is, however, scarce data on serotoninergic function and metabolism in patients with tension headache (TH). Against this background we investigated the platelet levels of serotonin and its metabolite 5-hydroxyindole-acetic acid (5-HIAA) in TH. The study sample consisted of 27 patients with tension headache (14 M, 13 F) and 21 healthy volunteers (13 M, 8 F). We found that in TH there was a marked increase in platelet levels of both serotonin ($p > 0.006$) and 5-HIAA ($p > 0.001$). We postulate that this may reflect high plasma serotonin levels because increased platelet serotonin uptake has been found in TH patients. We hypothesize that the serotoninergic tone is increased in this form of primary headache, and that this may explain the generally mild and often short-lasting characteristics of the headache.

4-14-10 INCREASED PLATELET LEVELS AND BREAKDOWN OF SEROTONIN IN PLATELETS IN MIGRAINE WITH AURA (MA) BUT NOT WITHOUT AURA (MwA)

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We studied the intraplatelet levels of serotonin and its metabolite 5-hydroxyindole acetic acit (5-HIAA) in migraineurs. The study sample consisted of 61 MA patients (38 M, 23 F), 42 MwA patients (29 M, 13 F), and 21 healthy controls (13 M, 8 F). The patients were studied during the headache-free phase and all subjects disclaimed intake of drugs (except paracetamol) within 2 weeks. The values of MwA patients did not significantly differ from those of controls. In MA, however, there was a substantial increase in the intraplatelet levels of both serotonin ($p > 0.0001$) and 5-HIAA ($p > 0.01$). The high synthesis and breakdown of serotonin together with a major release from the platelet suggest that in MA the serotoninergic system is overactivated and may mitigate the frequency, duration and pain intensity of the attacks.

4-14-11 ENHANCED PLATELET SECRETORY RESPONSE *IN VITRO* IN TENSION HEADACHE (TH) PATIENTS

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In order to understand the role of platelet in TH we determined the *in vitro* platelet secretion of serotonin and PF4, in parallel with platelet aggregation, induced by collagen and PAF. The study sample consisted of 27 TH patients (14 M, 13 F) and 21 healthy controls (13 M, 8 F). Platelet aggregation was unaltered in TH patients. However, secretion induced by collagen (0.5 and 2.0 µg/ml) was significantly increased both with regard to serotonin ($p > 0.02$ and $p > 0.006$) and PF4 ($p > 0.004$ and $p > 0.0001$) in TH. Similar platelet responses in TH were induced by PAF (0.1 and 1.0 M), both in the secretion of serotonin (n.s and $p > 0.02$) and PF4 ($p > 0.006$ and $p > 0.0001$). The present findings that the secretion from both platelet granule types was similarly increased in TH suggests a generalized platelet hyperreactivity which may be due to plasma factor(s) causing "stressed" platelets.

4-14-12 EFFECTIVENESS OF SUMATRIPTAN IN TRIGEMINAL NEURALGIA

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The efficacy of carbamazepine, naproxen and sumatriptan as pain-relief agents was compared in the treatment of 10 patients, suffering from idiopathic, symptomatic or post-herpetic trigeminal neuralgia. In all patients, sumatriptan was found to be more effective than carbamazepine and naproxen in relieving spontaneous pain. Its efficacy was greater in patients with a brief history of neuralgic pain (less than two years). The hypothesis is suggested that the same 5-HT1-like receptors play a role in the mechanism of action of both vascular and somatic trigeminal pain (idiopathic neuralgia).

4-14-13 A randomized double blind placebo-controlled crossover study of subcutaneous sumatriptan in general practice.

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The aim of the present study was to evaluate the therapeutic response to sumatriptan (a selective 5-HT1 agonist) in the acute migraine attack. A random sample of 230 migraineurs with 1-6 moderate or severe migraine attacks per month diagnosed by their general practioners were included in the study. The patients treated 2 migraine attacks at home by subcutaneous injection using an autoinjector with sumatriptan or placebo for the first attack and the alternative medication for the second attack. Significantly more patients (209 evaluable) on sumatriptan than on placebo reported headache relief at 1 hour (56% v 8%, $p<0.001$) and 2 hours (62% v 15%, $p<0.001$) after the first injection. Nausea, photophobia and phonophobia also resolved in significantly more patients on sumatriptan than on placebo ($p<0.001$ for all comparisons). A neurological resident interview and examined 198 of the 209 patients and 188 (95%) patients had migraine according to the criteria of the International Headache Society. The adverse advents were usually transient and of mild or moderate severity, however, 3 patients withdrew due to adverse events.

4-18-01 SERIAL TRANSFER MAGNETIC IMAGING STUDY OF CHRONIC PROGRESSIVE MULTIPLE SCLEROSIS PATIENTS.

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The aim of this study was to compare multiple sclerosis disease activity on patients with primary versus secondary progressive MS during a 6-months period using serial magnetic resonance imaging (MRI) especially magnetization transfer (MT). This later technique is based on interactions between macromolecules and water proton. We hypothesized that MT ratio of white matter (WM) depends of the amount of organised myelin. Decrease MT ratio could be correlated to variable degree of demyelination but also other pathological changes.

Method: The study includes 3 imaging session (every 4 weeks during 6 months) for each patient: a spin echoaxial T2 sequence, a spin echo multiecho sequence allowing to calculate transversal relaxation time (T2), a MTI sequence allowing to calculate MT ratio and a T1 sequence with Gd. MT ratio and T2 values were calculated in lesions and normal appearing WM for MS patients and in WM of healthy subjects as control. A standardized clinical evaluation is performed the same day using Kurtzke'scales, ambulating index, and a codified neurological examination.

Results: 5 patients with primary progressive MS and 5 patients with secondary progressive MS have been included and have had the first session. The study will be completed by June 93 and detailed results will be presented at the congress.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-18-02 DEFINING PROGRESSION FOR MULTIPLE SCLEROSIS (MS) THERAPEUTIC TRIALS.

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OBJECTIVE: to determine the duration of an increase in Kurtzke's Disability Status Scale (dss) score sufficient for defining progression. METHODS: at each encounter between 1971 and 1991, we assigned a DSS score without recourse to prior scores. We compared follow-up to entry scores to determine the frequency of worsening of score and the percentage of patients who subsequently returned to baseline. We restricted the enquiry to visits wherein patients were classified in stationary or progression phase, had 3 or more visits, and were followed 3 or more years. RESULTS: With an entry DSS score of 1 to 6, 187/299 (63%) of the patients had an increase in score (simple worsening) within 3 years of entry. 72 of those worsening (39%) returned to their baseline scores within the 3 years after entry. If worsening was sustained for 3 months, 123/244 (50%) worsened and 22/123 (18%) returned to baseline. This is close to the reproducibility of our scoring (22-28% variation). If the worsening was sustained for 6 months, 103/232 (44%) deteriorated and 11/103 (11%) returned to baseline. CONCLUSIONS: We think an increase in the DSS score sustained for 3 months is sufficient for defining progression or treatment failure in a therapeutic trial.

4-18-03 HTLV-1 MYELOPATHY IN CANADIAN ABORIGINALS FROM B.C.

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We report 3 families of B.C. Natives with HTLV-1 Associated Myelopathy (HAM).Two had been diagnosed as multiple sclerosis.
Case 1: (E.J.) 59 y.o. woman of the Bella-Bella tribe. 10 months of back pain and spastic paraparesis and incontinence . CSF: high protein, lymphocytosis and oligoclonal banding (OCB). Normal MRI. Sero + (ELISA, Western blot). PCR + on blood lymphocytes (PBL). Received blood transfusions in the 50's.
Case 2: (N.G.) 44 y.o. woman (Squamish). Spastic paraparesis with bladder involvement. CSF findings: high proteins, lymphocytosis and OCB+. MRI shows one area of demyelination . HTLV1 + by Western blot. PCR + on PBL. Husband, healthy is sero+ and PCR + and received blood transfusions in the 60's.
Case 3: (E.M.) 38 y.o. woman from Nutkak. Progressive paraparesis starts age 14 (before sexual activity) with incontinence also nystagmus and saccadic pursuit. Inflammatory CSF and OCB+. MRI with 3 area of white matter abnormalities. Sero+ by Western blot. PCR pending. Patient was breast-fed by mother who had leukemia. Patient has a sero+ daughter; a nephew has leukemia.
Conclusion: HAM is often misdiagnosed as MS, is endemic in the aboriginal population of British Columbia, affects women more often than men. We confirm transmission through transfusion, sexual intercourse and by breast-feeding from a leukemic mother.

4-18-04 INCREASED GENERATION OF SUPEROXIDE RADICALS IN THE BLOOD OF MULTIPLE SCLEROSIS PATIENTS.

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It has been suggested that oxygen free radicals and lipid peroxidation may be involved in the pathogenesis of demyelination in multiple sclerosis (MS). In this study we evaluated: 1) superoxide radical(O_2^-) production in the blood, 2) plasma lipid peroxidation products, and 3) superoxide dismutase (SOD) activity in erythrocytes of MS patients. Blood was sampled during acute relapse of MS before and during treatment with prednisone (mean total dose: 666 mg per patient). Control group consisted of patients with other neurological diseases (OND). We have found significantly increased generation of the superoxide radical in the blood of MS patients after stimulation with phorbol myristate acetate (PMA) (51.3 ± 10.7 nmol/min. x ml) in comparison with control group (32.7 ± 7.4; $p<0.01$). In the MS group treated with prednisone O_2^- generation was lower than in untreated patients (44.8 ± 12.2),but was still significantly higher than in OND group ($p<0.05$). Plasma lipid peroxidation products and erythrocyte superoxide dismutase activity were at similar levels in all studied groups. These results suggests that increased generation of reactive oxygen species may occur in MS relapse.

4-18-05 THE EUROPEAN ISOPRINOSINE STUDY IN MULTIPLE SCLEROSIS.

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The aim of this multicenter double blind, randomized study was to evaluate the effects of Inosine Acedobene Dimepranol (IAD), versus placebo on the evolution of multiple sclerosis (MS). 97 patients with relapsing-remitting form and at least 3 relapses during the 2 years preceding the inclusion, were included and received 3 g/day IAD or placebo for 2 years. Both groups were remarkably homogenous concerning various clinical parameters. Effects on disease activity were appreciated with the Extended Disability Status Scale, the Functional Systems, the Incapacity Status Scale, the Ambulatory Index and the number of relapses. 81 patients were evaluable after 1 year and 66 after 2 years. No differences were observed between patients receiving IAD or placebo concerning progression of disease or number of relapses. Of note is that in both groups the number of relapses markedly decreased and the progression rate was unusually low during the observation period.

4-18-06 IMPAIRED SUPRASPINAL MOTOR CONTROL OF GAIT IN MULTIPLE SCLEROSIS (MS).

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Motor abnormalities apart from limb weakness are poorly characterized in MS. We identified eight patients with an "apractic" gait disorder,not previously described. All had definite MS (4 male,4 female,5 relapsing-remitting,2 relapsing-progressive, 1 chronic progressive). Ages ranged from 22-59 yr (mean 39). The mean duration of gait disorder was 3 years. In one patient this was only present during relapses. The presentation was stereotyped with difficulty initiating gait,poor limb sequencing and turning. Poor foot tapping, impaired ability to kick and draw circles were noted. Significant weakness,incoordination,sensory loss,upper limb apraxia, extrapyramidal and frontal lobe features were absent. 6/6 patients had right inferior parietal abnormalities on cerebral SPECT. The MRI images did not correlate with the SPECT images except in the relapsing patient who had a right parietal lesion and an abnormal SPECT. 5/5 patients were treated with Pergolide with benefit. The patient in relapse improved with corticosteroid treatment alone. We postulate that the right inferior parietal SPECT abnormalities account for the impairment of supraspinal motor control of gait in these patients. The response to Pergolide implicates involvement of D2-dopaminergic cortical pathways.

4-18-07 DECREASE IN IL-3 PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS IN PATIENTS WITH MULTIPLE SCLEROSIS

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The production of interleukin-3 (IL-3) by peripheral blood mononuclear cells was assessed in patients with relapsing multiple sclerosis (MS) in both the active and the stable states, and in healthy controls. IL-3 levels were compared to interleukin-2 (IL-2) , tumor necrosis factor (TNF) and gamma-interferon (γ-IFN) production levels. Lymphokine production was measured using bioassays. No significant differences in IL-3 levels were observed between stable-state patients and controls. When levels of cytokine production of patients in the inactive phase were compared to those of the same patients during relapse, there was a significant decrease in IL-3 levels as opposed to significant increases in γ-IFN and TNF levels, and an increase, though not significant, in IL-2 levels. The functional implication of decreased IL-3 production is unknown. However, these findings support the hypothesis of a highly complex interaction of overlapping regulatory influences in the cytokine network that parallels MS disease activity.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-18-08 CONTINOUS IMMUNOSUPPRESSION (CI) IN MULTIPLE SCLEROSIS (MS)

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In 176 MS patients with no clinical stabilization on corticosteroids CI with Prednisone (7.5-15 mg/day) and Azathioprine (50-200 mg/day) was initiated. Azathioprine was replaced by Cyclophosphamide (50 mg on alternating days-100mg/day) in patients with progressive objective neurological symptomatology following at least 4 months on Prednisone and Imuran.

In 45 patients in this series (27 females and 18 males) CI was applied longer than 3 years (range 3-10 years; median 75 months). At the beginning of CI the age of the patients was 38.5 ± 9.3 years and their average score using Kurtzke expanded disability status scale (EDSS) was 4.7 ± 1.7 (1σ).

Progression over 2 points of the EDSS was established in 2, over 1 point in 8 and off less than 1 point in 10 MS patients in this series. Because of abnormal liver tests and recurrent urinary tract infections CI was discontinued in 2 individuals. In 23 MS patients (51%) in this series no worsening in their EDSS was established.

Longitudinal immunophenotypic studies in 1-4 month intervals were helpful in adjusting the daily dose of immunosuppressive medications.

4-18-09 INTRATHECAL BACLOFEN FOR INTRACTABLE SPASTICITY: A DOUBLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED STUDY

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Intrathecal baclofen has shown to be effective in reducing muscular tonus in extreme, intractable spacticity. A very low dosage is required for the reduction of muscular tonus in comparison to oral application.

The effects of intrathecal baclofen are studied in patients whose spasticity of spinal origin had been refractory to oral medication, in a multicenter, randomized, multidisciplinary, placebo controlled, clinical trial. Up to now 12 of 33 expected patients are included. In a double-blind test phase intrathecal bolus injections (at increasing dosage) are administered and subsequent clinical changes are assessed. In contrast to the placebo group, the patients receiving baclofen responded with a marked reduction of spasticity lasting from 6 to 24 hours according to the dosage baclofen used. After this test phase all patients had a subcutaneously Synchromed programmable pump (Medtronic) implanted connected to an intrathecal catheter for continuous administration of placebo or baclofen (double-blind) during 13 weeks. Each patient was repeatedly tested with a battery of clincal, neurophysiological and urological tests. After 13 weeks the code was broken and each patient received baclofen. Thereafter the patients were followed up for a period of approximately one year. Besides the clinical effects, a cost-effectiveness (c.e.) study was performed. Moreover the quality of life was subject of study.

Preliminary results showed a subjective and objective, clinically significant improvement in parameters of spasticity, including muscle tone, frequency of spasms and pain in the baclofen treated patients in contrast to the placebo group. Long term follow up effects such as quality of life and c.e. aspects are still under study.

4-23-01 ANTIGANGLIOSIDE ANTIBODIES IN GUILLAIN-BARRÉ SYNDROME AND MILLER FISHER SYNDROME

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We studied antiganglioside antibodies in sera from 50 patients with Guillain-Barré syndrome (GBS) and 21 patients with Miller Fisher syndrome (MFS), both in the acute phase. Ganglioside antigens used were GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b and GQ1b. Antibody activities against at least one of these antigens were detected in sera from 31 out of 50 patients with GBS. Anti-GM1 antibody was seen in 17 patients and anti-GD1b antibody in 16 patients. Among them, 11 patients were with both anti-GM1 and anti-GD1b antibodies. Anti-GQ1b antibody was detected in 5 out of 6 patients with GBS with ophthalmoplegia and in 20 out of 21 patients with MFS. The titers of these antibodies decreased with clinical improvement. Monoclonal anti-GD1b antibody immunostained paranodal myelin in the ventral and dorsal roots of the spinal cord, whereas monoclonal anti-GQ1b antibody bound to that in the III, IV and VI of the cranial nerves. These results implicated the possible pathophysiologic role of anti-GD1b antibody in weakness and/or sensory disturbance in the limbs and that of anti-GQ1b antibody in ophthalmoplegia.

4-23-02 PROLIFERATION OF MICROGLIA BY INTERLEUKIN-4(IL-4)

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Various cytokines are produced in the central nervous system(CNS). They function as autocrine or paracrine mediators and form an unique cytokine network in the CNS. In this study, we have investigated the production and functions of IL-4 in the CNS. The mixed glial cell cultures, astrocyte- and microglia-enriched cultures were prepared as described(J.Neuroimmunol. 15:263, 1987). These cells did not produce IL-4 when assessed by bioassay using IL-4-dependent cell line and detection of mRNA by PCR method using the specific primer for murine IL-4. However, microglia and, to a lesser degree, astrocytes expressed IL-4 receptor mRNA. IL-4 dose-dependently induced proliferation of microglia in vitro when assessed by MTT assay and BrdU or ^{3}H-thymidine uptake, which was completely neutralized by addition of anti-IL-4 receptor antibody. On the contrary, IL-4 suppressed enzyme activity and cytokine production in microglia. Thus, IL-4 produced by invaded T cells may play a role for the proliferation of microglia in the pathological conditions.

4-23-03 SOLUBLE INTERCELLULAR ADHESION MOLECULE-1 (sICAM-1) IS PRODUCED BY CEREBROENDOTHELIAL CELLS AND BLOCKS CELL ADHESION

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Recently, we demonstrated that sICAM-1 is an indicator for an inflammatory blood CSF barrier dysfunction and that high levels correlated with poor disease outcome. In this study data on the function of sICAM-1 in CSF will be presented.
Immunohistological analysis of brain slices revealed that ICAM-1 is mainly expressed on capillary endothelial cells and small vessels. Some reactive astrocytes were also stained positive.
Stimulation of confluent monolayers of human cerebral endothelial cells with lipopolysaccharides or tumor necrosis factor-alpha (TNF-α) could induce secretion of sICAM-1 in a dose dependent manner. No sICAM-1 was detected in the culture supernatant from activated blood or CSF lymphocytes. Cerebral and meningeal endothelial cells are a likely source for sICAM-1 in the CSF.
In vitro adhesion assays revealed that sICAM-1 could block the adhesion of activated lymphocytes to brain endothelial cells. In addition, the same effect was observed with CSF from patients with high concentrations of sICAM-1 which was neutralized with an antibody against ICAM-1.Therefore, it can be hypothesized ICAM-1 plays a role in the regulation of cellular traffic across the blood brain barrier.

4-23-04 IMMUNOLOGICAL ASPECTS OF HTLV-I ASSOCIATED MYELOPATHY (HAM) PATIENTS, HEALTHY HTLV-I SEROPOSITIVE AND SERONEGATIVE BRAZILIAN FAMILY MEMBERS

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We analyzed the lyphocyte proliferation of 24 HAM patients, 9 healthy HTLV-I seropositive family members, 20 HTLV-I seronegative family members, 5 patients with myelopathy of unknown origin and 10 controls. Lymphocyte proliferation was measured in peripheral blood cells and whole blood cultures, with and without stimulation by mitogen or IL2. After 3, 5 and 7 days of incubation the proliferation was determined. With 3 days of incubation nearly 50% of HAM patients showed a spontaneous proliferation. This was not seen in the other groups, whereas within 5 days all HAM patients and some seropositive individuals showed such response. Similar results were seen with whole blood, but with a shift in the time curve. No supression of proliferation was observed. Some HAM patients either maintained the same rate of response or showed an increased rate when their cells were incubated with their own serum compared to fetal calf serum. Our results suggest that the difference observed between the groups was related to the presence of HTLV-I infection. This spontaneous proliferation could be due to multifactors such as dendritic cells, cytokines, the presence of proliferative clones and, finally, maybe to superantigens.

4-23-05 SERUM ANTI-GM_1 ANTIBODIES IN PATIENTS WITH GUILLAIN-BARRÉ SYNDROME AND CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

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Using an enzyme-linked immunosorbent assay, we measured anti-GM_1IgM and IgG levels in the serum of 33 with Guillain-Barré syndrome (GBS) and 46 with chronic inflammatory demyelinating polyneuropathy (CIDP) to correlate with clinical parameter, such as preceding infectious episodes, clinical symptoms and nerve conduction studies. When compared to the control group, anti-GM_1IgM was increased significantly in the both GBS and CIDP group ($p < 0.01$, 0.05). High anti-GM_1IgM antibodies were detected in 8 patients of GBS having previous infection of diarrhea in comparison with no-diarrhea group. In CIDP anti-GM_1IgM were elevated in 26 patients with motor dominant type ($p < 0.001$). The mononeuropathy multiplex type in CIDP had also high titers of anti-GM_1IgM antibodies in comparison with polyneuropathy type. There were no significant differences of anti-GM_1IgM titers between in patients with or without conduction block.

4-23-06 LONG-TERM THERAPY OF CIDP WITH HIGH-DOSE INTRAVENOUS IMMUNOGLOBULINS.

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High-dose intravenous immunoglobulins (Ivlg) have been recognised as a new therapeutic approach in chronic inflammatory demyelinating polyradiculoneuropaty (CIDP). Side effects are rare during short-time observation. In twelve patients with CIDP 400 mg immunoglobulin per kg body weight was given intravenously daily for 5 days. When symptoms increased again or at the latest after 4 weeks, a one-day dosage of Ivlg was repeated. Laboratory and clinical tests were done regularly. Two patients showed no reaction to the treatment. In 10 patients the symptoms ameliorated within the first 3 - 10 days. One of these patients had not responded to other immunosuppressive drugs before. Following 1 - 31 months of therapy, these patients now have no or very slight symptoms. Seven of them receive Ivlg on one day every 1 - 8 weeks, in three others no further treatment was necessary for 5 - 12 months. No correlation was found between duration or course of the disease and effects of therapy. Hardly any side effects were observed during 163 months of therapy. Even during long-term treatment, high-dose intravenous immunoglobulin therapy is an effective and safe therapeutic regimen in CIDP.

4-23-07 INCREASED ADHERENCE OF T CELLS TO HUMAN ENDOTHELIAL CELLS IN PATIENTS WITH HTLV-I-ASSOCIATED MYELOPATHY.

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We investigated the adherence of peripheral T cells to human umbilical vein endothelial cells (EC) in patients with HTLV-I-associated myelopathy (HAM). The adherence of T cells to EC increased significantly in all HAM patients when compared with the seronegative controls (1.3- to 2.8-fold), or anti-HTLV-I seropositive carriers (1.4- to 2.8-fold). To clarify this phenomenon, we determined the surface makers and expression of lymphocyte function antigen-1 (LFA-1) in T cells adherent or nonadherent to EC in HAM patients. The percentage of HLA-DR^+ T cells and the expression of LFA-1 in the adherent cell population were significantly higher than those in the nonadherent cell population. Moreover, the $CD4^+/CD8^+$ ratio of the HLA-DR^+ cells in the EC adherent T cells was significantly higher than that in the non-adherent cells. These results suggest that the increased active T-EC adherence may be related to the immunopathogenesis of HAM patients. Furthermore, $CD4^+$ HLA-DR^+ cells exhibited more adhesive activity to EC than $CD8^+$ HLA-DR^+ cells, suggesting that activated $CD4^+$ cells rather than activated $CD8^+$ cells may be important in the initial stage of lymphocyte migration from the blood to the central nervous system in HAM.

4-23-08 ANTINEURONAL ANTIBODIES IN EPSTEIN-BARR VIRUS INFECTION WITH NEUROLOGIC COMPLICATIONS

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The pathogenesis of Neurologic complications in Epstein-Barr virus (EBV) infections is obscure.

We examined serum antineuronal autoantibodies in two patients with acute cerebellar ataxia (patient 1) and with AIDP (patient 2), both following EBV infection and with no cancer. Wistar rat tissues were used for immunohistochemistry and immunoblotting.

In the cerebellar cortex, both cytoplasm and nuclear elements of Purkinje cells were stained. Some neurons in the hippocampus, the brainstem and the spinal cord were also labeled. Non-neural cells and tissues were not stained. Serum from one patient of infectious mononucleosis faintly stained Purkinje cells.

Immunoblotting revealed IgG binding to 34 and 29 kD bands and IgM binding to 44,37 and 29 kD bands in patient 1. Patient 2's IgG bound to 29 kD band and IgM bound to 37 and 29 kD bands. IgG and IgM from the infectious mononucleosis patient reacted with 29 kD band.

This is the first report of antineuronal autoantibodies, which suggest an autoimmune mechanism, in EBV infection with neurologic complications.

4-23-09 T CELL RECOGNITION OF MYELIN BASIC PROTEIN IN JAPANESE SUBJECTS.

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In experimental allergic encephalomyelitis (EAE), susceptibility to the disease and encephalitogenic regions of myelin basic protein (MBP) differ according to animal species and strain. Although several studies of MBP have been conducted in recent years in Caucasian subjects, much remains unknown regarding racial differences in the immunodominant epitope of MBP and the relationship with specific major histocompatibility complex (MHC). To clear up these questions, we evaluated the incidence of MBP reactive T cell line and the relationship between an MBP epitope and MHC class II antigen in eight Japanese volunteers. Among 34 MBP reactive T cell lines were established from the 752 T cell lines cultured, high MBP line response rates of 34.8% and 30.4% were obtained for MBP peptide 84-102 and MBP peptide 143-168, respectively. T cell lines were obtained in a majority of subjects, 5/8 of subjects for MBP peptide 84-102 and 4/8 of subjects for MBP peptide 143-168. These findings suggest that those two regions were the major T cell recognition sites of MBP in Japanese as Caucasians. Significant correlation was observed between T cell lines for MBP epitope 84-102 and DRw14, suggesting that multiple MHC antigens including DR2 previously reported in Caucasians may be associated with the immunodominant epitope of MBP 84-102.

4-23-10 **THE TRIAL OF PASSIVE TRANSFER OF PARANEOPLASTIC CEREBELLAR DEGENERATION.**

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The pathophysiological role of anti-Purkinje cell antibody (anti-Yo) seen in a group of patients with paraneoplastic cerebellar degeneration (PCD) and gynecological cancer has not been clarified yet. In this report, the trial of passive transfer of PCD to rodents was shown. IgG from anti-Yo positive serum (Yo IgG) or Yo IgG with complement or Yo IgG with Con A activated rat mononuclear cells were injected into the ventricles of rats which resulted no Purkinje cell loss nor ataxic symptoms though human IgG were proved to be taken up by Purkinje cells as long as 36 hours. To see the effects of long term exposure of cerebellum to Yo IgG, the mononuclear cells in the cerebrospinal fluid or in the peripheral blood of the PCD patient with anti-Yo antibody were injected into the cisterna magna or intraperitoneum of severe combined immunodeficiency mice (SCID), respectively. No change were seen in the SCID cerebellum sacrified 60 days after injection. The B cells in the peripheral blood of this patient were transformed with EB virus and injected into SCID intraperitoneum. The human IgG were seen in the Purkinje cells of SCID a week after injection with no neuronal degeneration.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-23-11 TUMOUR NECROSIS FACTOR AND OTHER CYTOKINES IN GUILLIN-BARRE SYNDROME.

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Guillain-Barre syndrome, GBS, is an acute inflammatory neuropathy characterised by demyelination of the peripheral nerves. In vitro experiments suggest demyelination can be induced by a proinflammatory cytokine, tumour necrosis factor, TNF. The pathogenesis of GBS, however, is not defined although humoral factors are implicated since plasma exchange significantly improves patient outcome. This retrospective study examined whether raised plasma concentrations of TNF are found in GBS. Stored plasma samples were obtained from 26 patients with GBS undergoing plasma exchange, 25 patients with other acute neurological diseases, and 40 healthy controls. Plasma concentrations of TNF, IL-1beta and IFN-gamma were determined by immunoassay using kits from Medgenix, Immunotech and Genzyme respectively. Raised concentrations of TNF (>25 pg/ml) were found in 7/26 GBS patients c.f. 0/23 disease controls, chi square 49 p=0.001. Raised concentrations (>260 pg/ml) of IL1 beta (2/26 GBS patients c.f. 0/23 controls) and Interferon gamma (11/26 GBS patients c.f. 7/25 controls) were similar. Raised levels of TNF showed a correlation with peak grade of deficit. R=0.6 P=<0.01. These data suggests that TNF might have a significant role in the pathogenesis of GBS.

4-23-12 EFFECTS OF IMMUNOADSORBENT TREATMENT ON SEVERAL AUTOANTIBODIES IN NEUROLOGICAL DISORDERS.

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Recently, many studies have suggested the efficacy of plasmapheresis, particularly immunoadsorbent treatment (IAT), as a therapeutic tool of autoimmune diseases. In this study, we investigated effects of IAT on plasma autoantibodies in 4 patients with several neurological disorders. Case 1: myasthenia gravis (MG) with anti-AChR antibody. Case 2: MG with anti-thyroglobulin (TG) antibody and anti-TSH receptor (TR) antibody. Case 3: Gullain-Barre syndrome with anti-nuclear antibody (ANA). Case 4: chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with ANA. IAT was carried out by means of either TR-350 or PH-350 (Asahi Medical Co.). The clinical symptoms improved in all cases after IAT with approximately 50% (TR-350) or 35% (PH-350) of decrease in IgG. In Case 1, anti-AChR antibody decreased to 85% of initial level after IAT. In case 2, anti-TG and anti-TR antibody decreased to 30% and 20% of initial level after IAT, respectively. They showed, however, rebound-like increase during course of IAT. The values of ANA decreased from 80x to 40x in both Case 3 and 4. Effect of IAT on autoantibodies in neurological disorders is attributed mainly to reduction of the total content of IgG rather than elimination of specific antibodies except anti-AChR antibody.

4-23-13 **CELLULAR IMMUNITY IN APPARENTLY IMMUNO-COMPETENT PATIENTS WITH TORULA MENINGITIS**

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Although torula meningitis (TM) usually affects the immunocompromised host, we have previously described TM in previously healthy subjects. In this study, we evaluated the cellular immunity (CMI) of 9 such TM patients, in whom there was an absence of prior illness immunosuppressive drug therapy, and HIV antibodies. T lymphocyte subsets, CD3, CD4, CD8, were evaluated by indirect immunofluorescence and flow cytometry. Lymphoproliferative responses to mitogens (PHA and ConA) were evaluated by tritiated thymidine uptake. 12 healthy controls were similarly evaluated. There was no difference in the CD3, CD4 and CD8 subset expression between patients, in both acute and convalescent phases, and controls. In contrast, lymphoproliferative responses to mitogens were impaired in the patients compared to controls. This impairment persisted into the convalescent period (PHA:$p<0.01$, ConA:$p<0.05$). Taken together, our results indicate the presence of impaired CMI, despite the normal T cell numbers, in this group of patients with TM.

4-23-14 BIASED EXPRESSION OF DISEASE-RELEVANT Vß GENES IN RATS WITH EAE

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To address the question to what degree the Vß gene biases reflect pathogenic T cells in EAE, we evaluated the expression of the EAE-associated marker Vβ8.2 and Vβ6 in the periphery, spinal cord (SC), and cerebrospinal fluid (CSF) during the course of EAE, in unselected, IL-2 expanded, and Gp-BP restimulated populations. In CSF cells, there was a strong bias of the marker Vβ prior to onset of EAE. In SC, the marker Vβs were expressed optimally during onset of EAE, even in unselected cells, and this bias could be enhanced by IL-2 expansion and Gp-BP restimulation. During the recovery phase, the marker Vβ8.2 bias was obfuscated by the appearance of a heterogeneous Vβ T cell population. These data suggest that peripheral T cells bearing the disease-relevant V genes appeared first in CSF prior to disease onset, and subsequently migrated to SC beginning on the first day of clinical signs. During the recovery phase of the disease, these cells were diluted by an influx of T cells bearing other Vβ genes, requiring restimulation with Gp-BP in order to observe the Vβ8.2 bias. Our data have important implications in the interpretation of Vβ gene biases that have been reported in human autoimmune diseases.

4-23-15 FUT-187,SYNTHETIC ANTI-COMPLEMENT DRUG,SUPPRESSES EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS (EAE) IN LEWIS RATS.

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The role of complement system in EAE was studied by using synthesized serine protease inhibitor, 6-amidino-2-naphthyl benzoate dimethane sulfonate (FUT-187), which has higher inhibitory activity on the enzymes in the complement system including $C1\bar{r}$ and $C1\bar{s}$. FUT-187 treatment (100mg/kg/day PO) suppressed clinical signs of EAE in Lewis rats sensitized with GPMBP: mean cumulative clinical score for FUT-187 treated rats was 8.7±1.6, saline treated controls 14.7±2.3 ($p<0.005$). Serum CH50 levels on the 10th days after sensitization were decreased in saline-treated controls than normal controls; mean CH50 was 40.4 and 48.3, respectively. Serum CH50 levels were not decreased, but rather increased in FUT-187 treated rats (mean CH50 54.1). FUT-187 did not suppress GPMBP-activated or Con-A-induced lymphocyte proliferation. The total amount of infiltrating cells in the spinal cord was not suppressed in FUT-187 treated rats compared to saline-treated control rats. Deposition of C3 around the vessels of the spinal cord was markedly suppressed in FUT-187 treated rats. These findings indicate that FUT-187 suppressed EAE through its anti-complement effect.

4-23-16 THE INCREASE OF NEUROVASCULAR PERMEABILITY DIRECTLY CORRELATES WITH CLINICAL SINGS OF CELL-TRANSFERRED EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS (EAE).

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Neurovascular permeability is quantitatively measured in spinal cord of Lewis rats with cell-transferred EAE by using dual isotope method. Abrupt increases in neurovascular permeability occurred in whole spinal cord one day prior to appearance of clinical neurological signs of EAE and in conjunction with initial detectable cell infiltration. Higher neurovascular permeability was consistently observed at the lower spinal cord than at the upper spinal cord. Maximal increase of neurovascular permeability was observed within the lumbosacrococcygeal segment of the spinal cord (LSC) on the first day of development of clinical signs, which was two days prior to maximum severity of clinical abnormalities. Returning of increased neurovascular permeability to normal levels was demonstrated prior to complete remission of neurological signs. The increase of neurovascular permeability in lower thoracic segments of spinal cords and LSC directly correlated with edema in spinal cord and clinical signs. These findings suggest that edema in spinal cord resulted by increased neurovascular permeability may cause clinical signs of EAE in this species of animal.

4-23-17 ANALYSIS OF ANTIBODY RESPONSE TO MAJOR CONFOMATION-INDEPENDENT EPITOPES OF THEILER'S VIRUS

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Using synthetic peptides corresponding to the regions of the major conformation-independent antibody epitopes, we have analyzed antibody responses to TMEV in susceptible SJL and resistant C57BL/6 and BALB/c mice. The major antibody epitopes defined by using synthetic peptides remain largely the same as those determined with fusion proteins, i.e. A1A(VP113-27), A1B(VP1145-159), A1Cb(VP1262-276), A2A(VP22-16) and A3A(VP324-27). A time course study with either pooled or individual sera idicate that susceptible SJL mice intracerebrally infected with TMEV strongly and selectively recognize the A1Cb epitope of the VP1 as compared to resistant BALB/c or C57BL/6 mice that preferentially recognize VP2 and A1A epitopes. A similar predominant recognition of the A1Cb epitopes was found with antibodies from cerebrospinal fluid of virus-infected, but not that of virus-immunized, SJL mice. When the epitope recognition pattern by antibodies from SJL mice immunized with the BeAN strain of TMEV (which induces a chronic demyelinating disease) is compared with that by antibodies from mice immunized with GDVII (which causes acute encephalitis), only the level of antibodies specific for the A1Cb epitope is significantly different from each other. Therefore the presence of a high level of antibodies to do this epitope and/or the lack of antibodies to VP2 and A1A epitopes may play a role in the pathogenesis of TMEV-induced demyelination.

4-23-19 INTRAVENTRICULAR ADMINISTRATION OF ANTI-ADHESION MOLECULES PROTECTS ADOPTIVE TRANSFER EXPERIMENTAL ALLERGIC ENCEPHALITIS

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Adhesion molecules play accessory roles in lymphocyte adhesion to target cells. Anti-LFA-1/anti-ICAM-1 mAbs have been reported to have beneficial effects on survivals of cardiac implants in mouse models and to have aggravating effects on some bacterial infections. To reduce adverse effects and to elucidate direct effects in the CNS, we have studied the effects of intraventricular administration of anti-LFA-1/ anti-ICAM-1 mAbs on adoptive transfer experimental allergic encephalomyelitis. MBP-reactive T-cells were obtained from Lewis rats immunized with guinea pig MBP . A 21 gauge needle was implanted into the lateral ventricule of naive Lewis rats. More than 2 weeks later, these rats were injected with MBP-reactive cells intravenously. On day 0, 1, 2, 3 and 4, 200μg of anti-LFA-1/anti-ICAM-1 or PBS were injected into ventricules via the inserted needles.

Treatment with anti-LFA-1/anti-ICAM-1 mAbs completely suppressed the clinical sings of the transfer EAE with reduced number of W3/25(+) cells and increased number of OX8(+) cells. In conclusion, intrathecal administration of antibodies against LFA-1/ICAM-1 may be useful for the treatment of demyelinating diseases.

4-23-20 INHIBITION OF MOTOR NEURON EXCITABILITY BY SERUM WITH anti-GM1 & GM2 antibodies and their monoclonal ones

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Recently Guillain-Barrè syndrome (GBS) & motor neuron disease (MND)[or MND-like disorder] with antibodies against gangliosides have been reported. Plasmapheresis is effective on the patients and antibodies decrease in time with clinical improvement. However, pathophysiological roles of these antibodies have been still unknown. We have recently established a heterotypic co-culture system using human muscle cells in monolayer and fetal rat spinal cord explants. In this early culture, miniature end-plate potential -s (mepps) & end-plate potentials (epps) were successfully recorded and in long-term culture spontaneous firings (spf-s), which was blocked by d-tubocurarine, were observed. We applied serums containing various anti-gangliosides antibodies (GM1,GM2,GD1a,GD1b,GT1b,GQ1b etc.) from 6 patients with GBS, MND-like disorder, Fisher syndrome etc. in this system. Two serums, which contained anti-GM1,GD1b & asyalo-GT1b,and GM1 alone, reversibly suppressed spfs and epps. Furthermore we applied monoclonal antibodies against GM1, GM2,GD1a,GD1b,GQ1b & GT1b in perfusion medium. Only monoclonal antibodies against GM1 & GM2 reversibly suppressed spfs. These results strongly suggest that humoral antibodies against GM1 & GM2 in patients cause the suppression of motor neuron excitability.

4-23-21 VIRUS INFECTION OF MOUSE BRAIN ENDOTHELIAL CELLS IN VITRO AND IN VIVO : A SUGGESTED MECHANISM FOR INCREASED BBB PERMEABILITY

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Endothelial cells can be infected with several viruses in vitro and in vivo. Increased vascular permeability is a feature of some viral infections, but the mechanism of this phenomenon is largely unknown. An avirulent mutant (A7) of neurotropic Semliki Forest virus (SFV) facilitates the development of both clinical and pathological signs in the Balb/c mouse model of experimental allergic encephalomyelitis (EAE). On the other hand, SFV infection leads to fibrinogen leakage from brain blood vessels.

We have established a method for culturing mouse brain microvascular endothelial cells (MBMEC) and infected them with SFV-A7. MBMEC are permissive for SFV in vitro, the infection is productive and leads to cell lysis. Further, capillary endothelial (EN) cells are infected in vivo as studied by immunohistochemistry of brains and spinal cords of infected mice.

We conclude, that infection of EN cells in vivo is at least one of the mechanisms, that may cause EN cell damage leading to the increased vascular permeability observed during SFV-infection.

4-23-22 γδ T-CELL REPERTOIRE IN BLOOD AND CEREBROSPINAL FLUID OF MULTIPLE SCLEROSIS PATIENTS.

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γδ T-cells that express Vδ1, Vδ2 and Vγ9 gene segments accumulate in acute demyelinating MS plaques. Using monoclonal antibodies and flow cytometry, we analysed the T-cell receptor (TCR) repertoire in paired blood and CSF samples from 25 patients with active MS, 8 patients with inflammatory neurological disease, 12 patients with non-inflammatory neurological disease (NIND) and blood from 25 normal subjects. In peripheral blood, no significant differences were observed in T-cell Vδ gene usage of MS patients compared with the control groups. However, in the CSF of MS patients compared with NIND patients there was a significant decrease in the percentage of total γδ T-cells (median [range]: MS, 2.9% [0.5-11.4]; NIND, 5.9% [2.1-15.7]; $P < 0.01$), Vδ1 T-cells (MS, 0.7% [0.2-5.9]; NIND, 3.2% [1.0-8.2]; $P < 0.01$) and Vδ2 T-cells (MS, 1.8% [0.1-6.2]; NIND, 2.9% [1.8-9.7]; $P < 0.01$) but not αß T-cells. This may be due to sequestration of both Vδ1 and Vδ2 subsets of γδ T-cells within the brain in active MS.
Expression of CD45RA and CD45RO was normal on γδ T-cell subsets in peripheral blood of MS patients. However, γδ T-cells in CSF of each patient group showed significantly increased expression of CD45RA without a concomitant reduction in CD45RO. This novel finding was not specific for MS but it may represent a feature of γδ T-cells migrating through the CNS.

Key words: Multiple Sclerosis, γδ T-cells, CD45.

4-23-23 TGF-ß, IFN-γ AND IL-4 mRNA EXPRESSING CELLS IN BLOOD AND CEREBROSPINAL FLUID IN MULTIPLE SCLEROSIS

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Previous observations indicate that IFN-γ, which is produced by the TH1 subpopulation of $CD4^+$ T helper cells, could be involved in multiple sclerosis (MS). Whether the TH2 cell related cytokine IL-4 or the immunosuppressive cytokine TGF-ß play any role is not known. We utilized in situ hybridization to detect and enumerate mononuclear cells from peripheral blood and cerebrospinal fluid (CSF) expressing mRNA encoding for IFN-γ, IL-4 and TGF-ß. Strongly elevated numbers of cells positive for these cytokines were detected in blood obtained from 20 MS patients, with median numbers of 1 per 5,000, 1 per 2,100 and 1 per 3,300 blood cells, respectively. IFN-γ positive cells predominated among blood mononuclear cells in 3 of the MS patients, IL-4 positive cells in 11 and TGF-ß positive cells in 6 patients. An enrichment of cytokine mRNA expressing cells was observed in the MS patients' CSF, with median numbers of 1 per 1,300 CSF cells for IFN-γ, 1 per 200 cells for IL-4 and 1 per 330 cells for TGF-ß. Larger patient groups must be studied to make possible correlations to clinical variables. The results indicate that an augmented production of IFN-γ, IL-4 and TGF-ß systemically and accentuated in the CSF compartment accompanies MS in most patients.

4-23-24 NEUROENDOCRINOLOGICAL EVALUATION IN MYASTHENIA GRAVIS (MG)

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The autoimmune character of MG involves dysfunction in Neuroimmunendocrinological System (NIES) studies the hypothalamic-pituitary-gonadal (HPG) axis of 33 MG patients. Steroid receptor was also evaluated in thymus cytosols in 15 MG patients, by dextran charcoal assay. Glycocorticoid receptor (GR) in peripheral lymphocytes of 39 and in thymus of 15 MG patients, by cell bynding assay. The peripheral GR of lymphocytes MG was higher than control, the thymus GR was lower than control. Mean estrogen (ER) and androgen (AR) receptor in MG thymus were higher than control estrogen receptor was found (ER) in 40%, progesterone receptor and AR in 53% and GR in 100%.

The HPG axis evaluated by seric levels of hormones was normal.

The expression of steroid receptor in thymus and lymphocytes of MG shows the involvement of NIES in MG.

4-31-01 LHERMITTE-DUCLOS: CLINICAL MANIFESTATION AND CRITICAL ASSESSMENT OF CT, MRI and H_1MR-SPECTROSCOPY

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The Lhermitte-Duclos'disease is an aetiopathiologically not clearly defined rare disorder of the cerebellum. Due to the insufficient neuro-radiological experience we intended to analyse the value of different methods: CT, MRI and H1-MR-spectroscopy.

On hospital admittance, a 22-year-old patient presented the signs of a raised intracranial pressure combined with a cerebellar ataxia and dysarthria. CT examinations exposed a huge, infratentorial growth with enhancement of contrast media. The MR images as well as angio-MRI yielded no further diagnostical informations.

However, the H1- MR-spectroscopy revealed that the solid portions of tumour were equivalent to atypical brain tissue.

In conclusion, the final and surgically confirmed diagnosis of the Lhermitte-Duclos'disease was only assured by H1-MR-spectroscopy.

4-31-04 DETERMINING NEEDS FOR NEUROLOGISTS IN SPAIN.

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There are now considerable controversy about the needs for neuro-logists in Spain. The number of neurologists employed full-time in the Health National Service in Spain is actually low. Based on data obtained from other countries, the Health National Service supports the opinion that the responsability for neurologists in Spain primarily includes consultative services to general physi- cians. According to those data the needs for neurologists ranged from 1 to 2 ones per 100.000 population. We did an adjusted need based model for determining the requeriments of neurologists in Alcoi (Alicante). Information was collected by a means of ques- tionnaire administered in a face-to-face interview with the general practicionners of the sanitary area. Total needs were esti- mated by means the method described by the GMENAC. The neuro- logist's time needed per annum for the more frequent neurological conditions were the following: M.S. 27.6 hours, T.I.A. 36.08 h., epilepsy 113.75 h., P.D. 46.92 h., dementia 49.0 h., migraine 430.5 h., polineuropathy 41.17 h., stroke 178.5 h. etc... The total neurologist's time requeriments were 3481.81 hours per 100.000 population that means that Spanish health service require a rate of 5.275 neurologists per 100.000 population.

4-31-05 DEVELOPMENT OF SUBDURAL HYGROMA/HEMATOMA DURING DELIVERY AFTER PERIDURAL ANAESTHESIA.

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We report on 3 cases.In the first case a subdural hygroma was found bitemporally, in the second case over the hemispheres. In the third case a subdural frontal hematoma was found on the left side and a small frontal hygroma on the right side. The examination was carried out by CT. or MR. These young women, 26 und 28 years of age, had had peridural anaesthesia during delivery. The reported complication developed immediately after delivery in 2 cases and a few days later in one case. So far this complication of delivery has not been reported in the literature.

4-31-06 CLINICAL STUDY ON TREATMENT OF NEUROSIS AND NIGHT-TERRORS OF CHILDREN WITH TRANQUILIZING-BRAIN TONIC FOOT THERAPY PAD

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The foot therapy pad is an innovative product for treatment of internal diseases with drugs applied on body surface. It is prepared by filling the natural medicines in the shoe-pad and is used for treatment by putting it in the shoes or slippers worn by the patient. It showed significant therapeutic effectiveness in clinical treatment of 226 cases of neurosis and 38 cases of night-terrors of children, and obviously improved the low urinary MGPG-SO_4 level in depression patients. The therapeutic effectiveness appeared after treatment for 3 days in most patients without side effect.

4-31-08 WHISTLING LANGUAGE (WHISTLE SPEECH)

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Whistling language is a communication system used by some human communities (Mexico, Cameroun, Caucasus). It is a prosodic or tonal language. Some natives from the island of La Gomera (Canary Islands) use a whistling language, so-called "silbo gomero". It is a language of prehispanic origin, later adapted to spanish. A number of linguistic studies have shown that itis a syllabic, non-tonal language, probably unique in the world. Since 1967 we have studied a series of patients from La Gomera affected by neurological diseases leading to loss of whistling speech. Thirteen of them had focal brain lesions (stroke, brain tumor, head injury). Other patients with diffuse brain lesions were discarded. Ten patients had a global whistling disturbance (both motor and sensory), the other three had only motor impairment. Six of the patients presented, in addition, a conventional aphasic disorder. Whistling disorder had no relationship with cerebral dominance. We think that this disorder could be the result of a brain lesion with no direct relationship with language areas.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

4-31-09 "ATYPICAL" HISTIOCYTOSIS OF THE CENTRAL NERVOUS SYSTEM - REPORT OF A CASE WITH FATAL COURSE.

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Involvement of the central nervous system by histiocytosis X is well known. However, there are several other, rare forms of histiocytosis differing from histiocytosis X.

We describe a case of "atypical" histiocytosis with predominant involvement of the central nervous system in a male patient who was healthy until he developed right sided hemiparesis at the age of 26 years. MRI revealed an intramedullary lesion localized at the level of the second cervical segment. Although additional disseminated lesions were found in the brain, the patient was operated on the cervical mass. Primary histological examination revealed a chronic inflammatory reaction and no evidence for neoplastic changes. After the operation the patient's neurological condition deteriorated and he was admitted to our hospital with marked tetraparesis and diabetes insipidus. MRI was found unchanged compared to the findings before the operation. Re-examination of the exstirpated cervical mass suggested an atypical form of histiocytosis. Treatment with chemotherapy, cortisone and radiation therapy showed only short-lasting improvement. The patient's condition deteriorated progressively and follow-up investigations by MRI revealed progression of the cerebral and spinal lesions. However, extensive investigations of other organs showed normal findings with exception of a few skeletal lesions. The patient died two years after onset of the disease from pneumonia.

Clinical data and post mortem findings will be presented in detail.

4-31-10 THE PATTERN OF NEUROLOGICAL DETERIORATION AND THE MECHANISM OF NEUROLOGICAL DEFICTT IN SYRINGOMYELIA

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Sixty-five cases of hind-brain related syringomyelia were evaluated. The progression of neurological deficits in these cases was classified into four stages. In the first stage, a dissociated sensory loss or motor weakness developed initially in one upper limb, then these symptoms were combined in the same upper limb at the second stage. At the third stage, dissociated sensory loss or motor weakness spread to the other side of the upper limb and eventually both dissociated sensory loss and amyotrophic motor weakness were present in both upper limbs at the final stage.

In stage two, the syrinx should be located on the affected side of the central gray matter, involving the anterior and posterior horn cells and the intraspinal decussating fibers of the bilateral spinothalamic tract. However, the dissociated sensory loss was unilateral in stage 2. Such a discrepancy has been reported, but no clear explanation has yet been advanced. We propose that the anterior and posterior horn cells and the intraspinal spinothalamic tract are equally compressed by syrinx dilatation, causing local ischemia. Under these circumstances, neuronal cells are injured but neuronal fibers are functionally intact at the margin of the syrinx because of decreased susceptibility to ischemia.

4-31-11 INTERVENTIONAL BRAIN IMAGING: IDENTIFICATION OF IDLING NEURONS WITH HYPERBARIC OXYGEN.

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Interventional brain imaging utilizing hyperbaric oxygen has recently been devised. Postulation is that in any type of brain injury, vascular traumatic or anoxic encephalopathies, certain areas of irreperable damage are surrounded by a penumbra of possibly recoverable, viable neuronal tissue (alluded to by the volume difference of CT and SPECT). Such areas are sustained by adequate oxygen to remain viable but not enough nutrient to fire electrically, or to be effective clinically. Because determination of most brain function has been electrophysiological; such areas have defied identification. With single photon emission computerized tomography (SPECT) scanning, it is possible to visualize metabolic brain functions. A protocol both with I-123 IMP and Tc-HM-PAO utilizing pre and post HBO exposures has been developed for brain injuries. Delayed imaging with I-123 and Tc-HM-PAO indicating more positive flow patterns have suggested viable tissue or prognostication of recovery. Scans will be presented along with clinical correlations.

4-31-15 A COMPARISON STUDY OF BLINK REFLEX BY SIGNAL AVERAGING METHOD BETWEEN PATIENTS WITH STROKES AND NORMAL CONTROLS

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In order to prevent the alteration of R2 component (onset delaying/amplitude decreasing), the conscious levels of subjects have to be kept alert. But the onset determination is often difficult to elicit due to many artifacts, then we developed the averaging method which makes its determination more clearly. The latency, amplitude and response pattern of R2 elicited in patients with strokes and in normal controls were studied by use of the averaging method. The subjects were 36 patients with strokes in chronic stage, 20 males, 16 females, ranging in age from 47 to 80 years (x = 65.8 years). The controls were 22 healthy, 13 males, 9 females, ranging in age from 19 to 54 years (x = 28.5 years). Procedure: Electrical stimulations consisted of squared pulses of 0.2msec and 80V and band pass from 20Hz to 3kHz were applied. The recordings were made by electronic signal averaging for 20 to 50 times. The stimulations were given manually at random. Conclusion: This averaging method is useful in determining the R2 responses in controls, however, in subjects who are in severe disabilities and use to become drowsy prone condition during testing, the alteration of R2 made this method difficult to apply.

4-31-16 ARYL ACYLAMIDASE ACTIVITY OF ACETYLCHOLINESTERASE FROM HUMAN CEREBELLUM AND ERYTHROCYTES

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The acetylcholinesterase (AChE) was purified from human cerebellum and erythrocytes by co-affinity chromatographies. The purified human cerebellum and erythrocyte AchEs showed one main band on SDS-PAGE under reduced condition with a molecular weight about 66000 dalton. The specific activities of cholinesterase and aryl acylamidase were 1299 and 143 μ/mg respectively for human cerebellum AChE, 4584 and 747 μ/mg respectively for human erythrocyte AChE. The optimal pH of cholinesterase and aryl acylamidase for human cerebellum and erythrocyte AchEs was close, between 7.5 and 8.0. Acetylthiocholine (ATCh), a substrate of cholinesterase competitively inhibited the aryl acylamidase activity of human cerebellum and erythrocyte AChEs. Its IC_{50} were 10.2×10^{-3} and 3×10^{-3} mol/L respectively. Soman (pinacolylmethyl-phosphonofeuoridate) showed inhibition for both cholinesterase and aryl acylamidase activities of human cerebellum and erythrocyte AChEs, which demonstrated that the serine in active center was essential for both types of enzyme activity.

4-31-17 NEUROLOGY OF PATIENTS WITH LIVER VERSUS CARDIAC TRANSPLANTATION

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A comprehensive neurologic evaluation was performed both before and after (up to 1 year) transplantation for 22 liver and 15 cardiac recipients. Preoperatively, the liver but not cardiac recipients showed icterus, muscular weakness and decreased mental functions. Both groups felt poor quality of life before and improved quality of life after the operation, but postoperative psychosomatic symptoms were less in cardiac than liver recipients. Transient side-effects of drugs were more severe in cardiac recipients who received heavier immunosuppressive medication. They included tremor, myopathy, neuropathy and seizures due to cyclosporin. The initially poor performance in some neuropsychological measures (Stroop and Trail-making tests) of liver recipients improved after the operation. MR and CT imaging of the brain were helpful. In three liver recipients treated for severe bacterial infection the development of silent multifocal white matter lesions were detected. Cerebral atrophy was prominent in some liver recipients, but not in cardiac recipients. The study shows different spectrum of neurological problems in liver and cardiac recipients and suggests that neurological assessments are needed both before and after organ transplantation.

4-31-18 END-STAGE LIVER DISEASE PATIENTS SHOW GOOD NEUROLOGICAL RECOVERY AFTER LIVER TRANSPLANTATION: A PROSPECTIVE STUDY IN 22 PATIENTS

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Seventy-two patients with endstage liver disease had liver transplantation in Helsinki, 54 were adults, of whom 19 died. We examined 22 of them before and 6 - 12 months after transplantation neurologically. Preoperatively the patients had muscular weakness, decreased mental ability and physical performance. Clinical investigation revealed jaundice, muscleatrophy and polyneuropathy. Neuropsychological tests showed preoperatively significantly decreased intellectual ability and memory. A significant improvement in most tests was seen after the liver transplantation. Furthermore, the patients were emotionally better adjusted postoperatively. MR imaging of the brain revealed new multifocal white matter lesions in three patients who had been treated for bacterial sepsis. Improvement in neurophysiological tests was seen in some patients but the changes were not significant.

4-31-20 SIGNIFICANCE OF DIAGNOSTIC PROCEDURES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND CNS INVOLVEMENT.

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The manifestation of central nervous complications in systemic lupus erythematosus (SLE) includes a wide spectrum of neurological and psychiatric disorders. Lacking specific features, the diagnosis of CNS involvement is based on clinical examination supported by laboratory investigations and brain scanning methods.We present a prospective study including 110 patients with SLE. Neurological examination, neuropsychological testing, magnetic resonance imaging (MRI) and a search for antineuronal and anticardiolipin antibodies was performed in all patients. Positron emission tomography (PET) of the brain and CSF studies were done in 50% of the patients. CNS involvement based on clinical judgement was observed in 42 %. The neuropsychological testing revealed marked impairment of cognitive functions on three test (Stroop Color 24%, Recurring Figures Kimura 22% and Kramer-Test 28%). So far no significant correlation between the clinical CNS involvement and the neuropsychological test scores was found. MRI brain scans showed pathological changes in 48%, predominantly white matter lesions in the T2 weighted images, whereas PET examinations (N=50) did not reveal any significant metabolic changes. Antineuronal antibodies were detected predominantly in SLE patients (20%). A serum binding titer to neuroblastoma lines (>1 : 20) was found significantly more frequent than in control groups and patients with rheumatoid arthritis. CSF studies showed oligoclonal bands in 8% and identical bands in serum and CSF in 38 %.
Our study disclosed distinct deficits of cognitive functions and a high percentage of pathological changes on MRI scans even in patients without clinical evidence of CNS involvement. The clinical importance and pathogenesis of antineuronal antibodies has to be further investigated especially in our prospective follow up in relation to the activity of the disease and changes in cognitive functions.

4-31-21 TWO NEW CASES OF KLEINE-LEVIN SYNDROME ASSOCIATED WITH CT SCAN ANORMALITIES

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Two new cases of periodic hypersomnia conforming to descriptions of the Kleine-Levin syndrome, are reported in two 14- and 17-year-old males. Diagnosis has been established after several hypersomnia and morbid hunger episodes. No sexual desinhibition has been observed. Clinical examination, serum growth hormone and cortisol levels were normal. Nocturnal polygraphic recordings during asymptomatic periods showed slow delta waves normal for the age. However, cerebral CT Scan showed in both cases, a hypodense lesion without contrast enhancement in the suprasellar cistern suggesting a lipoma. Such a lesion, with mood disorders, has already been described by S. Esposito. This relation will be discussed.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-03-01 EMBOLI DETECTION BY TCD MONITORING

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In a group of 60 patients with either symptoms of TIA or cerebral infarction thought to be embolic in nature, a bilateral simultaneous monitoring of the middle cerebral artery (MCA) was performed using transcranial Doppler sonography (TCD). Duration of the examination was between 15 and 30 minutes. Spontaneous emboli were identified by a short unidirectional high intensity Doppler signal and a characteristic brief sound. In 8 cases (13%) TCD was able to show spontaneous embolisation. As probable sources of embolic material, stenosis of the internal carotid artery (ICA, n=2), occlusion of the ICA (n=1) and a combination of extra- and intracranial arterial disease (n=2) were found. In 3 cases a cardiac pathology was thought to be the origin of embolism. TCD-monitoring represents a new method in the attempt to find a likely cause of cerebral ischemia in patients with TIA or stroke. The frequency of detection of spontaneous embolism by TCD however, should not be overestimated.

5-03-02 PROINFLAMMATORY CITOKINES IN PATIENTS WITH ACUTE STROKE: KINETICS OF SECRETION AND RELATION TO EXTENT OF BRAIN DAMAGE

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The release of the proinflammatory cytokines TNF-alpha, IL-6 and IL-1-ß in peripheral blood has been serially determined in patients with ischemic stroke presenting within 4 hours following onset of symptoms. In contrast to serum levels of IL-1-ß, TNF-alpha and cytokine levels in CSF which did not exhibit a consistent pattern of response, IL-6 showed a significant increase of serum levels already within the first 4 - 6 hours. Because of the demonstration of increase within the very early stage of disease the response of IL-6 is attributable only to the ischemic brain lesion. Values were maximal within the first day and returned to baseline after 2 - 3 days. Patients with severe disease and poor outcome showed highest levels which persisted. A significant correlation to the volume of brain lesion has been found by planimetric CT analysis. The large dilution of IL-6 in peripheral blood suggests considerable amounts at sites of ischemia. Because IL-6 is rapidly secreted and metabolized, monitoring of its serum levels may allow estimation of lesion extent within the first hours of stroke and provides new insights into the pathophysiologic sequelae of acute immune response associated with ischemic brain lesion.

5-03-03 INTERFERENCE OF STROKE PATTERN INTERPRETATION WITH VARIABILITY OF INTRACEREBRAL VASCULAR TERRITORIES

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Since the introduction of CT and MRI, mechanisms of brain infarction (e.g. hemodynamic, embolic and microvascular) have been attributed to the topography of vascular territories affected in the individual stroke patient (e. g. junctional/bordzone, territorial and lacunar infarcts). Analysis from large stroke bank data, however, has evidenced that infarcts within the anterior(ACA) and posterior (PCA) watershed zones of the middle cerebral artery (MCA) remain underrepresented with regard to the high incidence of severe carotid obstructions suggested to represent the key mechanism of hemodynamic infarction.

CT/MRI scans of 22 patients with severe carotid disease (>80% stenosis n=6 and occlusion n=16) were matched to reference 12 sections from the atlas of Talairach. Infarctions were standardized on computer templates constructed from these references. Composite lesions of all patients were superimposed on minimal and maximal territory maps of the MCA, ACA and PCA as recently reported in a postmortem study of 22 hemispheres. Taken the generally assumed large MCA area with narrow ACA/MCA and PCA/ MCA interzones only 3(19%)/16 patients with carotid occlusion had borderzone infarcts whereas consideration of the minimal MCA territory variation results in 13(81%)/16 correct diagnoses($p<0.01$). In contrast, only 1/6 patients with severe carotid stenoses displayed a junctional MCA/PCA infarction whatever territories were adjusted. Thus misinterpretation of CT/MRI patterns of infarction seems to be frequent and causes failure for the assessment of the underlying pathophysiology, if the physiological and functional variation of cerebral artery circulation areas are disregarded.

5-03-04 BW619C89 DECREASES GLUTAMATE RELEASE AND INFARCTION VOLUME AFTER MCA OCCLUSION IN THE RAT

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The pyramidine BW1003C87 is a potent anticonvulsant and anti-ischemic agent, but with limited use because of antifolate effects. BW619C89 lacks this toxicity but shares the property of its congeners in inhibiting veratrigine induced glutamate release *in vitro*. To determine *in vivo* if BW619C89 inhibits glutamate release and is neuroprotective, focal cerebral ischemia was induced in the rat by proximal middle cerebral artery (MCA) occlusion. Changes in extracellular glutamate were monitored by microdialysis. Infarct volume was determined at 24 hours. Pretreatment with BW619C89 decreased infarct volume in a dose dependent fashion maximal at 20 mg/kg compared to saline controls. Treatment 45 minutes after onset of ischemia was also effective. Microdialysate glutamate in drug treated animals was decreased in both caudate and rostral cortex. These results suggest that inhibition of glutamate release by BW619C89 may be protective in stroke.

5-03-05 ANTIPLATELET EFFECT OF ASPIRIN, NICORANDIL AND NICARAVEN ON PATIENTS WITH CEREBRAL THROMBOSIS - AN IN VITRO STUDY

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Nicorandil(N-(2-hydroxyethyl) nicotinamide nitrate ester) is known to dilate cerebral vessels. Nicaraven((±)-N,N'-propylene-dinicotinamide) captures hydroxyl radicals and improves cerebral blood flow. In the present study, the in vitro antiplatelet effects of those new agents on patients with cerebral thrombosis were compared with that of aspirin.

Thirty-two patients with cerebral thrombosis were enrolled in the study (male:18, female:14, mean age:62). Two aggregating agents were ADP and collagen, whose final concentrations were 2 μM and 2 μg/ml respectively. The final concentrations for aspirin, nicorandil and nicaraven were 0.1, 1, 10, 50, 100, 500 μg/ml which were added platelet rich plasma. Physiological saline was used as a control.

Nicorandil suppressed significantly the maximum aggregation by ADP at the concentrations 10 μg/ml or higher and by collagen at 100 μg/ml or higher. Nicaraven suppressed both ADP- and collagen-induced maximum aggregations at the concentration 500 μg/ml. Aspirin suppressed significantly the maximum aggregation by ADP at the concentrations 50 μg/ml or higher and by collagen at 10 μg/ml or higher.

The reason that nicorandil suppressed aggregation by ADP more strongly than aspirin did may be explained by the fact that nicorandil has a nitro group.

5-03-06 SEX DIFFERENCES IN THE BLOOD-CSF BARRIER (BCB) INTEGRITY IN PATIENTS WITH CEREBROVASCULAR PATHOLOGY.

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There are some indications that sex hormones, especially testosterone, might be directly responsible for modification of platelet aggregation (Hershey, 1991). The effect of sex hormones on TXA_2-PGI_2 imbalance and cerebral vessel walls in humans has not been extensively studied. In this three years study we evaluated the blood-CSF barrier integrity (Q_{Alb}) by radial immunodiffusion method in men and women with vascular headaches and ischemic stroke, matched for ages and duration of illness, which revealed a clear sex differences. In the group of patients with vascular headaches mean Q_{Alb} value was 199.48 ± 35.71 for men, and 262.29 ± 33.71 for women ($P<0.05$). We found that mild to moderate BCB impairment (Q_{Alb}: 170-70) occured in 50.0% of patients with stroke under 45 years of age, in 37.3% aged 45-60, and in 35.3% of patients older than 60 years. The BCB impairment occured in 45.6% of men and in 24.3% of women with stroke ($P<0.01$). These differences could be important in the observed phenomenon that aspirin reduced the risk of stroke for men but not women (Canadian Group,1978).

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-03-07 CORTICAL ALTERATION OF CATECHOLAMINE AND AMINO ACIDS RELEASE IN FOCAL CEREBRAL ISCHEMIA

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Recently, several investigators have demonstrated that a considerable amount of dopamine and glutamate are released in cerebral ischemia. The purpose of the present study was to investigate the changes in catecholamines(CA) and glutamate(GLU) simultaneously in the cortex following focal cerebral ischemia and to examine whether the relationship between CA release and GLU release existed.
METHODS: Ten adult cats were anesthetized and microdialysis probes (outer diameter: 220μm, length 5mm) were implanted into the cerebral cortex to measure CA and excitatory amino acids every 20 minutes by HPLC/ECD. The left middle cerebral artery at its origin was occluded by a Zen clip for 120 minutes. RESULTS: (1) Excessive release of norepinephrine(NE) (10.4± 21.3 pg/30μl perfusate) was significant compared with the preocclusion lebel (0.9±0.5 pg) ($p<0.05$) . Dopamine(DA) (3.2± 1.5 pg/30μl perfusate) was also significantly increased compared with the preocclusion lebel (2.3±1.0 pg) ($p<0.05$). (2) Cerebral ischemia induced the correlative extracellular levels between NE and GLU ($R=0.76$, $p<0.05$). COMMENTS: These results suggest that the augmentation in the release of extracellular NE and DA in the cerebral ischemic tissue is related with the extracellular GLU.

5-03-08 PATENT FORAMEN OVALE AND RECURRENT THROMBOEMBOLIC EVENTS.

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We studied 5 patients (mean age of 50.4 years) with ischemic stroke due to presumed paradoxical embolism. In all patients the presence of a patent foramen ovale (PFO) was evidenced by both transesophageal contrast echocardiography and transcranial contrast Doppler ultrasound.
Three patients showed also an atrial septal aneurysm. None had a left heart or carotid source of embolism, coexisting small-artery disease could not be excluded in one patient. During a follow-up of 2 to 30 months subsequent thromboembolic events were observed in all patients: second stroke (n=4) and pulmonary embolism (n=1). Events occurred in two patients while they were taking aspirin, in two patients receiving low-dose anticoagulant therapy (INR 1.5 and 2.7), and in one patient without treatment. Our observations confirm that there is no proven therapy to prevent reccurrent events in patients with cerebral embolism and evidence for a PFO. In some patients it may be appropriate to consider transcatheter or surgical closure of a PFO, especially if there is evidence of deep vein thrombosis.

5-03-09 MENTAL CONSEQUENCES FROM CEREBROVASCULAR DISEASES IN FORENSIC EXPERTISES

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It is known that the quality of life has been changed after cerebrovascular accidents. It is not because the diseased person becomes, most frequently, neurologically and psychically handicapped who has quite a different social treatment in micro- and macro-environment surrounding him, but also because he, in most situations, becomes a forensic problem in the following manner:

1/ In the criminal charges the patient diseased from cerebrovascular disease /CVD/, if he does a crime, he will be classified according to act 12 from the Criminal Statute of R. Macedonia as: responsible, irresponsible or basically impaired responsible person, and this has been done according to the "rest" of his psychic changes.

2/ In the legal procedures and out-of-court proceedings again depending on his psychic changes and when his acting capability is in question, the patient with CVD will be classified as professionally capable, partially professionally incapable or professionally incapable.

5-03-10 **MR-ANGIOGRAPHY IN VERTEBROBASILAR ISCHEMIA**

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Magnetic resonance angiography (MRA) was accomplished in forty-one patients with acute vertebrobasilar artery disease to determine its diagnostic reliability. **Methods:** Patients were examined by routine magnetic resonance imaging, extra- and intracranial Doppler ultrasound and selective intraarterial arteriography (DSA). MRA was accomplished using a three-dimensional time-of-flight gradient-echo technique. **Results:** Magnetic resonance angiography correctly identified all occlusions, stenoses and aneurysms within the distal vertebrobasilar system as revealed by conventional intraarterial arteriography but missed the diagnosis of vertebral artery dissection in one case. This results in a sensitivity of magnetic resonance angiography of 97% and a specificity of 98,9%. However, the degree of stenoses was difficult to evaluate by magnetic resonance angiography. Only the Doppler ultrasound studies provided the hemodynamic information for less severe degrees of stenoses. **Conclusion:** The combined use of magnetic resonance angiography and Doppler ultrasound findings may replace the invasive intraarterial arteriography examination in many patients with suspected macroangiopathy of the vertebrobasilar arteries.

5-03-11 **DETERMINATION OF INTRACRANIAL FLOW DIRECTION BY MR-ANGIOGRAPHY**

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To evaluate the accuracy of MR-angiography (MRA) with targeted presaturation for the determination of flow direction and vascular supply at the level of the circle of Willis, we examined 37 patients with high grade carotid artery disease and 9 patients with basilar artery obstruction. All patients were additionally examined by transcranial Doppler ultrasound (TCD) and digital subtraction angiograms (DSA). **Methods:** MRA was performed using 3 D time of flight FISP-acquisitions. For determination of blood flow direction targeted presaturation slabs were positioned to suppress the signal of selected arising vessel. **Results:** Out of 25 patients with collateral blood flow via the anterior communicating artery (AcoA) as diagnosed by DSA and TCD, MRA with presaturation study correctly identified 21 patients. Collateral blood flow to the anterior circulation over the posterior communicating artery (PcoA) was shown in four patients with bilateral vertebral or proximal basilar artery occlusion. All results correlated with both DSA and TCD. **Conclusion:** Our study shows, that the determination of flow direction by MRA using targeted presaturation is a little time consuming add-on examination to conventional and MRA imaging that delivers reliable results. To our opinion the question of intracranial collateral pathways via the AcoA and PcoA can be answered noninvasively by combination of MRA and TCD results.

5-03-13 **Prognostic value of combined motor evoked potentials (MEP) and cerebral blood flow velocity response (CBFVR) in lacunar stroke**

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The sensitivity of MEPs for the detection of cerebral lacunar infarction is low but may be increased by separate analysis of MEP amplitude and latency. In addition, combined use of early MEPs and evoked CBFVR improves the prognostic capacity of the test. We investigated 10 patients with MEP immediatedly after onset of stroke (< 24 h) and prospectively followed clinical outcome (day 1 to 60). Patients were selected for their symptoms corresponding with subcortical lacunar infarction involving the motor system. Topography and size as determined on MRI was projected on an anatomical atlas by using a computer system. MEP amplitudes were reduced (mean 33,2 ± 28%) compared with the nonaffected side and reduction corresponded with the size of the lesion and the involvement of areas with concentrated motor fibres, e.g. paraventricular. In these cases also latencies were increased (4/10). Furthermore CBFVR correlated with the size of infarction: the larger the area involved the smaller the response magnitude. Final functional outcome paralleled with early test's results: a poor outcome was found in areas of concentrated motor fibres and in larger lesions, in which amplitudes were strongly reduced, latencies increased and CBFVR were diminished. In summary, a combination of these diagnostic procedures could be a useful tool in evaluating the prognosis of lacunar infarction in the motor system.

5-03-14 **CEREBRAL BLOOD FLOW MEASUREMENT BY DYNAMIC CONTRAST ENHANCED T2-WEIGHTED MAGNETIC RESONANCE IMAGING**

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A paramagnetic contrast agent such as Gd-DTPA produces local magnetic field inhomogeneities when it passes through the brain tissue. This results in transient signal loss in and around blood vessels that correlates with local tissue perfusion and blood volume. **Methods:** We examined 17 patients with cerebral TIA or infarctions, 18 patients with cerebral neoplasms and 15 volunteers for assessment of cerebral blood flow. After routine MRI, a continuously acquired series of 30 FLASH 2D images (TR=47) ms, TE=27 ms, flip 15°) was obtained during bolus administration of Gd-DTPA to determine the dynamic contrast enhancement. **Results:** In ischaemic brain tissue no significant change in the signal intensities during bolus passage was measured because of complete loss of tissue perfusion. In 2 patients with grade II astrocytoma strong signal changes were observed due to tumour vasculisation in spite of an intact blood-brain barrier as demonstrated in T1-weighted images. **Discussion:** This method provides functional information about tissue perfusion and local blood volume not provided by conventional MRI. It has the advantage of high spatial resolution and is able to separate overlying structures.

5-03-15 **COMMON CAROTID ARTERY OCCLUSION: CLINICAL SIGNIFICANCE OF A PATENT INTERNAL CAROTID ARTERY**

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Scarce data exist about the clinical features and the neurological prognosis of common carotid artery (CCA) occlusion. In addition, the significance of a patent ipsilateral internal carotid artery (ICA) has not been investigated systematically. Over a ten-year period, we have performed a prospective study in 88 patients (57 men, 31 women; mean age 63 years) with CCA occlusion, which was diagnosed by standard duplex Doppler (n=88) or color Doppler flow imaging (CDFI) (n=29) and confirmed angiographically in 35 cases. 23% had a history of ipsilateral carotid endarterectomy. All patients had a neurological examination: 29 were followed for up to 9 years (mean follow-up 37 months). 51 % had strokes in the affected carotid territory, 22% had transient neurological deficits and 27% were asymptomatic. Among patients with a patent ipsilateral ICA (27%) stroke prevalence was significantly lower than in patients with ICA occlusion (33% vs. 58%; p=0.001). CDFI established patency of the ICA in cases with uncertain Doppler results and in 4 of 12 inconclusive angiograms.

CCA occlusion is associated with a high stroke risk which is significantly lower if blood flow is maintained in the ipsilateral ICA. CDFI is the most reliable diagnostic method for this condition. Carotid surgery is probably a relevant pathogenetic factor for CCA occlusion.

5-03-16 SYMPTOMATIC (TIA) AND ASYMPTOMATIC TIGHT UNILATERAL INTERNAL CAROTID ARTERY (ICA) STENOSIS AND ELECTRICAL BRAIN MAPPING OF EVENT RELATED POTENTIALS (P300)

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Unilateral ICA stenosis (> 80%) may be accompanied by wide spread arteriosclerosis of extra- and intracranial vessels leading to subtle cognitive disorders. We, therefore, applied electrical brain mapping of P300 in 28 patients (68.3 ± 8.1 y; 15 asymptomatic; 13 with a history of TIA) and compared them with an age and sex matched control group. All underwent a visual "odd-ball-paradigm". The potentials were derived from 16 electrodes according to the 10/20-system against linked mastoids. The amplitudes of N250 and P300 were mapped and their latencies measured. (1) There were no significant differences between the asymptomatic patients and those with a TIA history in all parameters of P300-complex. (2) In comparison to controls, the patients' maps of N250 revealed no amplitude reduction but significant ($p < 0.01$) restriction of its scalp distribution. (3) Patients' P300 showed normal scalp distribution but significant amplitude reduction ipsilaterally to the stenosis ($p < 0.01$) and contralaterally ($p < 0.05$). (4) The latencies were highly significantly ($p < 0.01$) prolonged in several electrodes not only ipsi- and but also contralaterally to the stenosis more for N250 than for P300. Altered P300 indicates electrophysiologically subclinical cognitive deficits in patients with unilateral tight ICA stenosis, preoperatively.

5-03-17 **Assessment of the neurological condition and the social rehabilitation of 172 patients with intercranial aneurysms : a 5-year follow up analysis**

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Although multiple investigations were iniated in order to control the outcome of patients after subarachnoidal hemorrhage there are only few informations available concerning the long-term social rehabilitation.

Therefore we reexamine 172 patients with the radiological diagnosis of one or multiple aneurysms. Due to the classification of Hunt and Hess 54 patients belong to grade I; 52 to II, 28 to III, 22 to IV and 56 to V. Meanwhile 50 patients respectively 29.06% died, 28 of them caused by complications of subarachnoidal hemorrhage.

As expected patients without surgery had the poorest outcome (14 of 17 died). The best neurological status was observed in patients with early aneurysm surgery (42 cases; 1st-3rd day) and in those with delayed operation (54 cases; after 24th day). Remarkably only slight differences were detected in cases which underwent surgery between the 4th-8th day, so that the benign initial neurological state, the lack of vasospasm and brain edema have a determining influence on the later outcome.

Correlation of the actual condition (after 2/ 5 years) to the results obtained after 6 months revealed a significant improvement in the neurological state, the social rehabilitation and professional life.

5-03-18 CISTERNAL INJECTION OF STREPTOKINASE IN CASE OF HYPERTENSIVE INTRACEREBRAL AND INTRAVENTRICULAR HAEMORRHAGE

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72 year-old Thai male was hospitalised with Lt. side weakness and numbness for 6 hours. Patient has been diagnosed as a case of hypertension for 20 years. 6 hours before admission, patient was found Lt. sided stroke in the toilet. Physical examination BP 180/110, pulse 72/min, R 24/min, Hypertensive retinopathy Rt. hemiplegia, and hypalgesia areflexia with Babinski's sign on the Rt., stiff neck, kernig signs are positive.

Treatment 1. Flunarizine 10 mg bid, 2. Glycerol 50gm q 6 hours, 3. Flurosemide 40 mg q a.m. 4. Dexamethazone 5 mg i.v. q 6 hours, 5. Streptokinase 300,000 units via cisternal injection.

Progression 24 hours decreased insize of 4th I.V.H..
48 hours No 4th I.V.H., decreased I.V.H. at 3rd ventricle
72 hours No I.V.H. decreased insize, and density at I.C.H. and I.V.H. at the body of lateral ventricles. Patient has improved about neurological deficits both consciousness and motor function.

Conclusion Thrombolytic drugs is indicated in I.V.H. to prevent hydrocephalus and ventriculostomy.

5-03-19 FAVOURABLE COURSE OF AN INTERNAL CEREBRAL VEIN THROMBOSIS WITH HEMORRHAGIC INFARCTION

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Isolated thrombosis of internal cerebral veins was rarely reported in adults and often associated with a poor prognosis.

We describe the case of an 18-year-old woman presenting with severe headache, vomiting and dizziness lasting for days who had been taking oral contraceptives since one year.

On admission neurological examination found a midbrain syndrome with stupor and decerebrate posturing. Analysis of CSF revealed a normal cell count with a markedly elevated protein content of 2.9 g/l due to a disturbed blood-brain barrier. Computed tomography without contrast showed increased density of internal cerebral veins ("cord sign") and bilateral hypodensities of the thalamus with hemorrhagic areas.

Angiography yielded nonvisualisation of the internal cerebral veins, Galen's vein and the straight sinus. The blood investigations were significant for an iron deficiency anemia (Hb 7.0 g/l) with reactive thrombocytosis (423,000/µl) as second risk factor for thrombosis. Coagulation and immunology parameters were normal.

Upon a high-dose heparin treatment, changed to phenprocoumon after two weeks, the patient recovered nearly completely. On MRI (flash sequence) after 4 weeks a partly recanalization of the deep cerebral veins and the straight sinus could be established, also sharply demarcated hemorrhagic infarcts in both thalami.

We conclude according to recent papers that early anticoagulation with heparin seems to be the treatment of choice in internal cerebral vein thrombosis, even when a pre-existing hemorrhage is evident.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-03-20 STROKE REGISTER IN SAUDI ARABIA: RESULTS OF A 3-YEAR STUDY IN THE EASTERN PROVINCE.

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Informations on stroke in the Gulf region are derived mainly from hospital-based studies. A study was designed to determined the incidence and natural history of stroke in a defined area in Saudi Arabia. All stroke patients admitted into hospitals in the study area(estimated population (750,000) were registered prospectively.Diagnosis of stroke types was on CT basis. A total of 755 cases were registered with an annual incidence of 34/100,000.Ischemic strokes were 66%,hemorrhagic 30%,and undetermined 3%.Lacunar infarcts accounted for 39% of ischemic strokes and an emboligenic cardiac diseases was found in 16%. Intracerebral hemorrhage (ICH) was twice as common as subarachnoid. Major risk factors were hypertension,cardiac disorders, diabetes mellitus and previous history of stroke. Stroke mortality increased with age, and was higher with ICH. The low incidence of stroke in the area probably reflects the age structure of the community although its pattern is similar to that in the Western countries.

5-03-21 TROMBOPHILIA TESTS IN YOUNG PATIENTS WITH IDIOPATHIC STROKE

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Among 204 patients (pts) under 40 years of age with cerebral infarction, we selected 36 pts (17 F, mean age 25, 19 M, mean age 28) with "idiopathic" stroke (IS), in order to find evidence of thrombophilia as potential cause of IS. All patients were studied with CT scanning or MRI, transthoracic echocardiography and cerebral arteriography. The following activity tests were carried out at least three weeks after stroke onset: Anti-thrombin III (AT-III), Protein-C (PC), Plasminogen (PIG), Tissue Plasminogen Activator (tPA), Plasminogen Activator Inhibitor (PAI) by means of chromogenic methods (Kabi-Vitrum), and Protein-S (PS) by the Laurell assay. The assays were performed both in pts and in 38 healthy subjects matched for age and sex. We found 25% (9 of 36) of cases with evidence of abnormal thrombophilia tests in our population with IS. The most frequent deficiency was related to PS deficiency (6 of 9), followed by PC (1 of 9), Plasminogen (1 of 9), and AT-III (1 of 9) deficiencies. We conclude that a decrease in the concentration of natural anticoagulants may be an important risk factor for stroke in young people, and must be performed routinely in young pts with IS.

5-03-22 CLINICAL PROFILE AND PROGNOSIS OF CEREBRAL VENOUS THROMBOSIS ASSOCIATED WITH PREGNANCY AND PUERPERIUM.

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The objective of this study was to analyze the clinical, and radiological findings in 67 women with cerebral venous thrombosis associated with pregnancy (5 cases) and puerperium (CVTP), compared with 46 patients (pts) with cerebral venous thrombosis no associated with pregnancy or postpartum (CVTNP), in order to disclose clinical and prognosis differences. Forty-one of 67 pts (61%) with CVTP had acute onset compared with 16/46 pts (35%) with CVTNP (p=0.005). Neurological symptoms reached a plateau within 10 days after onset in 47/67 pts (70%) with CVTP) versus 22/46 pts (48%) with CVTNP (p=0.01). Forty-three of 67 pts (64%) with CVTP showed anemia versus 12/46 pts (26%) with CVTNP (p=0.00006). There were no clinical and neurorradiological differences between both grupos. Although severity illness was similar in both groups, 55/67 pts (82%) with CVTP had favorable outcome versus 19/46 pts (41%) with CVTNP (p= 0.006). The clinical profile of CVTP was usually associated with acute onset and reached a clinical plateau in a short time resembling an arterial stroke. Anemia in CVTP deserve further studies. The CVTP has a better outcome than CVTNP probably due to a limited and transient effect of the occlusive process.

5-03-23 CLINICAL AND CAROTID ULTRASOUND STUDIES IN TRANSIENT GLOBAL AMNESIA.

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Although occlusive cerebrovascular disease is widely held as a major cause of transient global amnesia (TGA), a correlation of TGA with extracranial carotid disease has not been reported. Using a high-resolution Duplex ultrasound scanner (DRF 400), we have studied the extracranial carotid arteries (ECCA) in 16 consecutive patients with TGA. There were 10 men and 6 women with a mean age of 63±9 (range 37 ~ 76) years. The mean duration of attacks was 10 hours and 5 (31%) patients presented with more than one attack. Hypertension was found in 4 (25%) patients, diabetes mellitus in 1 (6%), and mildly increased serum lipid levels in 5 (31%). The results of ECCA study showed that 8 of the 16 patients had a stenosis less than 25%, 5 had a stenosis between 25 ~ 50%, and 3 had a stenosis more than 50%, including 1 with right internal carotid artery (ICA) occlusion. The patient with right ICA occlusion sustained a completed stroke 3 years after the first TGA. One patient with 63% stenosis at the right carotid bifurcation suffered from amaurosis fugax of the right eye later. None of the 13 patients with a stenosis less than 50% had transient ischemic attacks or stroke during a follow-up period of 2 months to 4 years. In conclusion, the majority of patients with TGA do not have significant ECCA disease. However, ultrasound study may be useful to identify a small subgroup of patients who may be at a high risk of stroke.

5-03-24 FAMILIAL YOUNG-ADULT-ONSET ARTERIOSCLEROTIC LEUKOENCEPHALOPATHY WITH ALOPECIA AND SKELETAL SYSTEM DISORDERS WITHOUT HYPERTENSION.

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In 1985, based on our three siblings and 4 reported patients, we proposed a new syndrome of young-adult-onset leukoencephalopathy, alopecia and lumbago without hypertension. We here summarize the total 19 patients of this syndrome including 5 of ours. All patients were Japanese and the illness seemed to be transmitted as autosomal recessive fashion. The male to female ratio was 3.8:1. The age of onset ranges from 25 to 30 years. Acute low back pain, spondylosis, dental caries, alopecia, and progressive motor and mental deterioration were common clinical features. Cerebral arteriosclerosis and diffuse white matter disease were demonstrated pathologically or radiologically. Both temporal artery biopsy from one patient and femoral muscle biopsy from another revealed arteriosclerosis and the former also showed abnormal intradermal structures, but none had apparent risk factors for cerebrovascular disease. This syndrome is differentiated from the classic type of Binswanger's disease by the following aspects: (1) familiality, (2) young-adult-onset, (3) absence of hypertension, (4) alopecia, and (5) skeletal disorders. Although the pathogenesis is still unknown, we think this is a new distinct clinico-pathological entity.

5-03-25 T-PA USE IN NONHEMORRHAGIC VERTEBRAL ARTERY DISSECTION: REPORT OF A CASE

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There is no general agreement on the best management of vertebral artery (VA) dissection without subarachnoid hemorrhage. Considerable literature has been accrued on use of thrombolytics in acute myocardial infarction and stroke but, thus far, none of these drugs have been applied to acute VA dissection.

We report a 49-year-old female who presented with the rapidly progressing basilar artery syndrome with decerebrate posturing and respiratory arrest six to eight hours after the onset of first symptoms. Thirty minutes after the intravenous dose of t-pa, dramatic recovery of the patient's consciousness and neurological signs were noted. A conventional cerebral angiogram revealed a dissecting aneurysm of the left VA which was occluded surgically proximally six months later. No postoperative complications were encountered and the patient has remained in the stable condition for the next six months following surgery.

To our knowledge, this is the first case of t-pa use in the acute VA dissection. The remarkable recovery justifies prospective trials on thrombolytics' utility in acute nonhemorrhagic dissection.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-10-01 THE EEG ANALYSIS OF BASIC AND ANTI-ISHAEMIC PROPERTIES OF AMIRIDIN - A NEW DRUG TO TREATMENT OF MEMORY DISFUNCTION.

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It was showed in EEG-testing of 28 healthy male subjects, that amiridin (two tablets each 20 mg orally with 45 min interval) lead to significant enhance of alpha stability and spectral power with decrease stability of deltha-activity compare with effects of placebo. These effects were more expressed in left hemisphere during rest conditions and in right hemisphere during mnestic activity.

During EEG-testing the propousal central mechanisms of amridin action (15 healthy male subjects), it was showed that this drug (40 mg orally) lead to disapear the EEG signs of transient hyperventilation ischaemia.

The results were discussed in terms of perspectives of clinical application of amiridin as antiamnesthetic drug.

5-10-02 FREQUENCY OF ALZHEIMER'S DISEASE (AD) IN A DEMENTIA CLINIC POPULATION

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There are many studies on the prevalence of AD in the general population, but few large studies on the prevalence of AD in populations referred to dementia clinics. Our objective was to determine the frequency of AD in a University hospital dementia clinic.

Patients referred by general practitioners (1985-1992) to a dementia clinic were examined using standardized evaluation and diagnostic criteria (DSMIII for dementia and NINCDS-ADRDA for AD). Half the patients were followed for > 1 year, and 20% for > 2 years. Data were analyzed and expressed as mean ± standard error of the mean.

The majority of patients (86%) had dementia. AD accounted for 74% (probable AD 59%, possible AD 15%), and non-AD dementia for 12% of the clinic population. In the AD population, 25% had severe Mini Mental State Exam < 13), 25% had moderate (MMSE 13-18), and 50% had mild (MMSE > 18) dementia. The age of patients at onset of symptoms was 68.9 ± 0.39 years, with a mean duration of 4.3 ± 0.13 years at initial evaluation. The most common complaints other than memory deficits were problems with calculation (>80%), language (>70%), orientation (>60%), and affect (>50%). MMSE scores decreased by 3.48 ± 0.34 per year. Over half (56%) of patients presenting to a dementia clinic have a diagnosis of mild to moderate AD. This information is useful in the planning of dementia clinics.

5-10-03 INFLUENCE OF PERCEPTUAL DEFICIT ON LEXICAL COMPREHENSION IN AD PATIENTS.

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Anomia and single-word-comprehension deficit in Alzheimer's Disease (AD) patients are interpreted in the context of a semantic memory disorder. Since the tasks adopted to explore naming and word-comprehension are often devised using pictorial material, we cannot exclude that some results could be influenced by subclinical visuoperceptual deficits. We selected 40 AD patients with pathological scores in lexical-semantic tasks, but without clinical signs of visuoperceptual disorders. The AD patients and 15 normal Controls (C) were given a 72-items word-picture matching (Chieffi et al., 1989). In 18 items the target was contrasted with two semantically related foils, in 18 items with two perceptually related foils , in 18 items with two foils sharing with the target semantic and perceptual features and in 18 items with two unrelated foils.
As expected, the AD patients produced more semantic (AD:$\bar{x}$=2.33; C:$\bar{x}$=.23) and unrelated errors (AD:$\bar{x}$=2.5; C:$\bar{x}$=.0) than Controls, confirming the presence of a lexical-semantic impairment. However, the AD patients also produced a larger number of perceptual (AD:$\bar{x}$=2.93; C:$\bar{x}$=.12) and semantic-perceptual errors (AD:$\bar{x}$=3.97; C:$\bar{x}$=.3). The findings suggest prudence in interpreting poor scores in lexical-semantic tasks as exclusively due to a semantic memory defect.

5-10-04 BASAL CORTISOL LEVELS IN DEMENTIA.

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The role of abnormal plasma levels of cortisol in demented patients is not universally accepted. The discrepancies found among the observed values in various works have streghened the controversy, but may be explained from methodological bias due to inadequate selection of the controls. We have studied all 157 aged-subjects older than sixty-years old living in a geriatric house and we have only excluded the persons who have an endocrine disease or take any medication that could interfere on cortisol levels. M.M.S.(<23), and Blessed test (>9) were used for evaluating the presence of dementia. Basal Cortisol levels were detected using an Fluorescence polarization immunoassay (FPIA). The values in the demented (n=39) patients were significantly decreased (mean 18.97 g %, S.D. 6.13, 95% Confidence limits 16.54 - 21.39, p=.008) than the levels found in the other subjects (mean 23.01 g %, S.D. 6.84, 95% Confidence limits 21.46 - 24.55), but any relation with the age was observed. Our study discards the existence of hypercortisolism but supports the possibility of an hypothalamic-pituitary-adrenal axis dysfunction in aged-demented subjects.

5-10-05 PRESERVED COGNITIVE SKILLS IN DEMENTIA OF THE ALZHEIMER TYPE.

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Five patients with probable Dementia of the Alzheimer type (DAT) and Mini-Mental State Exam scores ranging from 10-22 were studied. One patient continued to play the trombone in a Dixieland band although he could not name well-known numbers that he played. Another continued to solve adult jigsaw puzzles. The third retained skill at canasta, the fourth at dominoes. The fifth patient remained a skillful contract bridge player although he could not name the suits or articulate simple bidding rules. All patients were impaired on standard remote memory tests.

Together with previous studies of preserved piano playing or painting skills, the findings indicate that a broad range of complex cognitive abilities may be preserved in DAT patients who cannot perform simpler actions. This implies that the memories required to regulate many important behaviors may remain relatively intact but inaccessible in these DAT patients. An effort to devise therapies to foster access to stored knowledge may be warranted.

5-10-06 LANGUAGE ALTERATIONS IN DIFFERENTIAL DIAGNOSIS OF DEMENTIAS.

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Language functions of 26 patients with primary degenerative dementia (PDD) and 26 patients with multi-infarct dementia (MID) have been investigated by using a modified aphasia test for turkish citizen.

Language alterations differing from classical aphasias were found in all patients except nine. In patients with MID, remarkable alterations resembling non-fluent aphasia was observed. In PDD, speech fluency was preserved; but paraphasias and anomia were seen. The other language modalities both in PDD and MID were mildly or moderately impaired.

Aphasia tests should also be used routinely for the differential diagnosis of PDD and MID, in addition to other neuropsychological tests.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-10-07 MOTOR AND MENTAL EVALUATION OF PARKINSON'S DISEASE (PD) IN VERY OLD AGE

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To characterize the clinical features of PD patients (pts) in whom the disease started after 70y, 60 pts were selected from our data bank:- mean age: 76y, (range 71-87). Disease duration: 1-5y - 52 pts, >6y - 8 pts. Stage (Hoehn-Yahr) 2:16, 2.5:5, 3:33, 4:6; dementia (Folstein MMT) - 20 pts (1-5y - 17, >6 - 3); depression (Hamilton) >17 - 28 pts (10 pts also with dementia); motor fluctuations - 2 pts; dyskinesias - 5 pts; freezing episodes - 9 pts; frequent falls - 9 pts. Treatment: (mean daily dose in mg: levodopa with carbidopa (n=45), 455; bromocriptine (n=20) 7.5; lisuride (n=3) 0.7; selegiline (n+38) 8.8; amantadine (n=5) 200, trihexiphenidyl (n=7) 5.

Conclusions: 1) >50% PD pts (33/60) showed early axial symptomatology; 2) 1/3 pts (20/60) showed early dementia; 3) almost 50% showed depression (28/60), supporting our hypothesis (Biol Psychiatr 27:581-591, 1990) that both diseases may share a common neuroanatomical substratum; 4) the main dose-limiting factors were visual hallucinations and confusion (23/60 pts) which occurred far more commonly in demented pts (17/23).

5-10-08 AD BRAIN PROTEINS; 2-D ELECTROPHORETIC STUDY WITH IMMOBILIZED pH GRADIENT.

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Tampere Brain Research Center, Tampere Finland.

2-D gel electrophoresis with immobilized pH gradients in the first dimension was applied to study AD post mortem brain proteins.
Up to 800 spots could be detected. Total and buffer-soluble proteins were analysed Immunofixation to identify markers (albumin, enolase, GFAP, S-100) was used. GFAP immunepositive marker was markedly increased. Four proteins (22,6.5, 26,6.3, 28,6.5 and 43,6.8 KDa,PI) were constantly found in AD but not in the control brains Protein spots are microsequenced and compared with protein Data Bank for further identification.

Grant: Tampere Brain Research Center

5-10-09 PREVALENCE OF DEMENTIA, PARKINSONISM AND TREMOR IN THE ELDERLY: A DOOR-TO-DOOR SURVEY IN PAMPLONA, SPAIN

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Objectives: To investigate the prevalence of the most common forms of dementia, Parkinson's disease and other types of parkinsonism and any kind of tremor (specifically essential tremor) in a Spanish population older than 70 years.

Methods: Using a door-to-door two-phase approach, all survives as of March 1, 1991, within a random sample over the total population of the city of Pamplona identified in 1989 (N = 1,127) were examined using the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX), by one of three physicians specifically trained. Study neurologists using specified diagnostic criteria, investigated in a extensive way those subjects who screened positive for dementia, parkinsonism or tremor.

Results: We found 194 subjects affected by dementia. The overall prevalence of dementia was 8.8% for those of 70 to 79 years, 20.1% for those of 80 to 89 years and 34.7% for those of 90 years and over. The diagnosis of Alzheimer's disease was made on 61% of the cases. Within the whole number of individuals evaluated by neurologists, 184 (18%) of them were found to be affected by a tremor. The prevalence of tremor was 9.0% for those of 70 to 79 years, 18.1% for those of 80 to 89 years and 27% for those of 90 years and over. Essential tremor account for 13,7% among all types of tremor. We found 50 subjects affected by parkinsonism. The prevalence of parkinsonism was 3.3% for those of 70 to 79 years, 4,9% for those of 80 to 89 years and 6.7% for those of 90 years and over. The diagnosis of Idiopathic Parkinson's disease was made on 70% of all types of parkinsonism.

Conclusions: Our data are similar to those previously reported in Europe.

5-10-10 THE WISCONSIN ALZHEIMER DISEASE BRAIN BANK: PATOLOGICAL FINDINGS IN FAMILIAL AND SPORADIC CASES.

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We reviewed 209 consecutive autopsies to determine if pathological findings could discriminate Familial Alzheimer Disease (FAD) from Sporadic Alzheimer Disease (SAD). Dementia during life was diagnosed in 182 cases; of these, 134 were pathologically diagnosed as AD with the Khachaturian criteria. We further divided the AD patients in two subgroups depending on the sporadic or familial occurrence of the disease (Breitner 1988). The FAD and SAD groups (55 and 79 cases respectively) were matched for age, sex, duration of illness and cognitive impairment. Mean plaque count in each lobe did not differ between SAD and FAD, although on average plaque counts in the FAD group was 20% higher; this trend was more apparent in the occipital lobe ($p<0.06$). The same area in the FAD group, also showed a strong correlation between age and number of plaques ($r=0.41$; $p<0.03$). None of the premortem variables, such as age, sex duration of illness and degree of cognitive impairment were correlated to plaque count. In conclusion, using the Khachaturian criteria, FAD showed a trend towards a higher number of plaques than SAD. Additional techniques may be needed to confirm this difference.

5-10-11 CLINICAL-ELECTROENCEPHALOGRAPHIC CORRELATION IN NORMAL AGING AND DEMENTIA

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Neurologic, mental status exam and electroencephalography were performed on 93 people without evidence of organic disease of the central nervous system and on 79 patients with dementia (most of Alzheimer type). All examined were at age 90 - 100. Mini mental status exam, detailed neurologic examination, neuro-imaging studies (CT or MRI) and EEG were obtained in patients with dementia. Metabolic parameters (T3, T4, B12, folate acid levels, electrolytes) were obtained, and some of them underwent detailed neuropsychologic evaluation. Dominant background frequency during wakefulness in neurologically healthy adults was 8 - 11 hz. in 92.4%, 6 - 7.5 hz. in 6.4% and 12 hz. in 1.07%: mid amplitude delta activity in the left temporal region was noted in 4%, mid amplitude theta in left temporal region in 10.5%. Intermittent generalized theta activity was seen in 8.4%. Photic stimulation induced driving response in 10.5%. In contrast to the above data, dominant background frequency in 79 people with dementia was 5.5 - 7.5 hz. in 73% and 8 - 9 hz. in 26.5%. Intermittent generalized theta and delta activity was noted in 49.3%, and continuous generalized theta and delta activity was seen in 20.2% of people with dementia.

This study shows features of EEG in neurologically healthy nanogenarians, statistically signigicant differences in background rhythms, intermittent and continuous generalized slowing in people with dementia.

5-10-12 DOES LIPOFUSCIN DEPOSITION IN NEURONS PROTECT THE BRAIN OF ALZHEIMER'S DISEASE FROM NEURONAL LOSS AND BRAIN ATROPHY?

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Lipofuscin deposition in neurons is commonly seen in normal aging and Alzheimer's disease but it is rarely studied. In this study we examine the relationships of lipofuscin deposition in neurons with other neuropathological changes of Alzheimer's disease.

Fifteen cases of clinically and neuropathologically diagnosed Alzheimer's disease were studied. Histology slides of a specific coronal section of the hippocampus were obtained. Senile plaques per area, the percentage of neurons with neurofibrillary tangles and granulovacuolar degeneration, as well as neuron size, regional area and total neurons per region were measured and correlated with the percentage of neurons with lipofuscin deposition in CA1, CA4 and entorhinal/parahippocampal cortex.

We find that an increase in the percentage of neurons with lipofuscin deposition is associated with an increase in total neurons and regional area in the entorhinal cortex as well as an increase in senile plaques in CA1.

These findings indicate that an increase in lipofuscin deposition in neurons is associated with a decrease in the loss of both neurons and brain tissue in the hippocampus of Alzheimer's disease. The exact effect of lipofuscin deposition in neurons in Alzheimer's disease is not clear and requires further study.

5-10-13 TUBEROMAMMILLARY NUCLEUS IN PATIENTS WITH ALZHEIMER'S DISEASE AND PARKINSON'S DISEASE - A QUANTITATIVE STUDY.

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We studied the number of large-sized neurons and neurofibrillary tangles (NFT) in the tuberomammillary nucleus (TM) of the hypothalamus from cases with Alzheimer's disease (AD, 5 cases), Parkinson's disease (PD, 5 cases) and age-matched controls (5 cases). We also counted the number of Lewy body in TM of PD. Numerous NFT were found in TM of AD. However, NFT was never observed in this nucleus of controls. A few NFT were observed in TM of PD. The Lewy body was not observed in controls. Only one Lewy body was found in TM of a patient with PD out of 5 PD cases. The number of large-sized neurons was significantly reduced in AD compared to that in controls ($p = 0.004$, Mann-Whitney U Test). However, The number of large-sized neurons were not altered in TM of PD ($0.274 < p < 0.345$). Since the majority of large neurons in TM appear to correspond to histamine neurons, the loss of large neurons observed in TM may, at least partly, cause the histaminergic dysfunction in AD brain. In contrast, the central histaminergic system may be preserved in PD.

5-10-14 CEREBRAL VASOREACTIVITY (CVR) IN PATIENTS WITH MULTI-NFARCT DEMENTIA (MID) AND DEMENTIA OF ALZHEIMER'S TYPE (DAT)

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In order to analyze CVR impairment, 35 patients with MID and 55 with DAT were analyzed. All were classified by DSMIII-R and Hachinski ischemic score. CT scans, Color Doppler flow imaging of carotid and vertebral arteries, psychological rating scales (FMMS, GBS, SCAG), and Transcranial Doppler before and after stimulation of acetazolamide (AZT) were performed.

The results showed the impaired TCD findings in all MID patients before AZT stimulation, and in 26(47%) with DAT. After AZT stimulation the reduced CVR was observed in MID patients with moderate and severe mental deterioration, and in those DAT patients who had impaired TCD finding before AZT test ($p<0.001$).

In conclusion, AZT test with TCD is helpful in clarifying the hemodynamic origin of dementia, indicating the basic different pathogenety between MID and DAT.

5-10-15 ENDOTHELIN-1 IMMUNE-REACTIVITY IS EXPRESSED IN ASTROCYTES OF THE ALZHEIMER BRAIN.

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The distribution of endothelin-1 immune-reactivity was investigated in paraffin embedded sections of the formalin fixed human brain. The avidin-biotin-peroxidase method was applied to demonstrate the immune-reaction. Patients without history or signs of cerebral disease showed antigenic sites to endothelin-1 in neurons of the cerebral and cerebellar cortex, hippocampus and ventral horns of the spinal cord. Only exceptionally astrocytes were stained. Cases with Alzheimer' s disease showed numerous reactive astrocytes in the cerebral cortex and subcortical white matter with a strong immune-reaction. This reaction was entirely eliminated by preadsorption of the antiserumwith the antigen, endothelin-1.

This is the first investigation which demonstrates expression of endothelin-1 immune-reactivity in astrocytes of cases with Alzheimer's disease. Many functions such as marked vaso-constriction, promotion of mitogenic activity and diverse influences on the micro-environment of the brain, are attributable to endothelin-1. Therefore endothelin-1 may play many roles in the brain changes occurring in cases with Alzheimer' s and presumably also other cerebral diseases.

5-10-16 QUANTITATIVE MRI MESUREMENTS OF HIPPOCAMPAL, TEMPORAL AND PARIETAL LOBE ATROPHIES IN NEURODEGENERATIVE DISEASES WITH DEMENTIA.

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We evaluated the quantifying volumetric changes of the brains in demented patients with neurodegenerative diseases using magnetic resonance scans. The subjects were 22 cases of Alzheimer type of senile dementia (AD), 24 of vascular dementia (VD), 3 of Pick disease (PK), 3 of Huntington disease (HD), 14 of Parkinson's disease without dementia (PD), 5 of multiple system atrophy (MSA) as well as 15 controls (CTL). MRI was done with 0.5-tesla super conducting magnet. Coronal sections were used to measure hippocampus, temporal and parietal lobes. Hippocampus and parietal lobe were significantly reduced in patients with AD, VD, HD and PK. Temporal lobes were significantly reduced in patients with AD, HD and PK. Temporal atrophy correlated with parietal atrophy in all subjects. The ratio of hippocampus for temporal lobe were reduced in demented patients, especially in AD. These results show that MRI is useful to provide in vivo quantification of the brain atrophy in demented patients, and characteristic features of remarkably reduced hippocampus in AD.

5-10-17 TRH STIMULATOIN TEST IN THE HEALTHY ELDERLY:PARADOXICAL RESPONSE OF GROWTH HORMONE IS ABNORMAL IN NORMAL AGING.

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In patients with multi-infarct dementia and Alzheimer's type dementia, various changes of several neurotransmitter and neuropeptide systems have been reported. In addition to changes of their basal plasma level, abnormal TSH (thyrotropin), PRL (prolactin), GH (growth hormone) responses to TRH (thyrotropin-releasing hormone) stimulation test have been reported and discussed in this context. But these abnormalities are possibly due to aging process. And besides it is not clear which abnormality is the most specific to dementia. Then, we conducted TRH stimulation test in 40 healthy elderly subjects (37 male and 3 female, average 71.5 y/o) who lived normal daily life, and whose physical examination were negative, and compared the result with that of 8 young normal controls (5 male, 3 female;24-30 years). We analysed correlations between age, mental scores, depression score, free T3, free T4, TSH, PRL, and GH before TRH injection (Pearson correlation coeffecients by t-test), and tried to find out which " abnormal response " (delayed or hyperresponse of TSH, low or high response of PRL, paradoxical respone of GH) in TRH stimulation test was the most specific to dementia.

Paradoxical responses of GH were seen not in the oldest subjects, but in the worst mental-scale subjects. Paradoxical response of GH is abnormal in normal aging, and possibly is a part of reflection of neuroendocrinological abnomalities in dementia.

5-10-18 WHY VASCULAR DEMENTIA IS MORE COMMON IN JAPAN?

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We investigated lacunes and diffuse ischemic white matter lesion in 1,086 necropsy cases. Lacunes were found in brains from patients above the age of 40 years. The most common site of lacunes was the frontal lobe white matter, followed by the putamen, pons, parietal lobe white matter in descending order of frequency. The extent of arteriolosclerosis of the medullary arteries in the frontal lobe was measured and compared with the number of lacunes and diffuse ischemic white matter lesion. There were close correlations between arteriolosclerosis and lacunes, as well as diffuse ischemic white matter lesion.

Also investigated was the sclerotic rate of medullary arteries in 186 necropsy cases at UCLA, USA. Arteriolosclerosis is much less severe than that of Japanese cases. Vascular dementia is more common than Alzheimer's dementia in Japan. In our data, about 60% of vascular dementia is Binswanger's disease. It is suggested that Binswanger type lesion may contribute to the higher incidence of vascular dementia in Japan.

5-10-19 DEHYDROEPIANDROSTERONE-SULFATE (DHEAS) AND CORTISOL (CRT) PLASMA LEVELS IN ALZHEIMER'S DISEASE (AD)

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DHEAS was shown to block enzymatic effects of glucocorticoids, thus, a certain part in the progression of AD may be caused by the decrease of DHEAS and its anticlucocorticoid functions.

In our own series (Leblhuber et al., Psychopharmacology 1993) 24 drugfree patients with AD (11 females, aged 58 - 86; 13 males, aged 62 - 88) and 50 normal controls (23 females, aged 18 - 81; 27 males, aged 21 - 81) were studied. Blood samples for DHEAS (ng/ml) and CRT (µg/dl) plasma measurements were obtained after an overnight fast, stored at -20°C and tested in the same assay by RIA. The DHEAS/CRT ratio was calculated in all subjects studied. Data were analyzed by Student's t-test. Diagnosis of AD was established by DSM-III-R (290.00) and confirmed by X-ray CT. A strong negative correlation was found between age and DHEAS ($r = -0,8$ for females and $r = -0,7$ for males) (Leblhuber et al., Lancet 1990; Age 1991), but no significant correlation was found between CRT levels and age (Leblhuber et al., Age 1991), consequently, the DHEAS/CRT ratio dropped remarkably in older normal subjects (aged > 60) as compared to young individuals (aged < 45) ($p < 0.01$). Interestingly, a trend was found for a lower DHEAS/CRT ratio in AD patients compared to age and sex matched controls ($p < 0.1$), indicating that this ratio could be an appropriate measure for the effects of DHEAS as an antiglucocorticoid, by which subjects at risk for the neurotoxic effects of glucocorticoids could be identified.

These preliminary results suggest a possible relation of cognitive impairment to circulating corticoids, as mentioned by Wolkowitz et al. (Am J Psychiatry 1990).

5-10-20 THE LATERAL VESTIBULAR NUCLEUS IN DEMENTIA OF THE ALZHEIMER TYPE.

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Dementia of Alzheimer-type (DAT) is neuropathologically characterised by intraneuronal tangles, neuritic plaques and loss of neurons in numerous cortical and subcortical areas. Cholinergic nuclei in the basal forebrain are severely affected in DAT (Whitehouse et al 1981) whereas no loss of neurons is observed in the cholinergic pedunculopontine nucleus (Hirsch et al 1987, Jellinger, 1988). The lateral vestibular nucleus (LVN) was found to contain cholinergic neurons (Mizukawa et al, 1986) and impairment of balance and motor coordination observed in patients with advanced DAT might be related to vestibular lesions. We analysed the LVN in 4 brains of subjects without CNS disorder and 3 patients with DAT (clinical diagnostic criteria of the NINCDS-ADRDA 1984, neuropathological criteria of Tierney 1988). Mean age of the normal controls was 85 (range 76-91), of the patients with DAT 84 (range 75-91). Brainstems were fixed for 5 days in phosphate buffer containing 4 % of paraformaldehyde and 15 % of saturated picric acid, cryoprotected (5-20% sucrose) and deep-frozen. Five series of transverse 50 um cryostat-sections through the LVN were stained with HE, gallocyanin and silver impregnation (Palmgren) and immunohistochemically treated according to Grabiel et al 1987 with a polyclonal rabbit-antibody to human choline acetyltransferase (ChAT; Bruce et al 1985). In the DAT group moderate to high densities of tangles were observed in the LVN. In 2 of the 3 brains affected with DAT the number of ChAT-immunoractive neurons was markedly lower (24.1±2.8, 25. Mean±SEM, median; arbitrary units) than in the control brains (45.1±12.2, 51). These preliminary findings suggest that cholinergic neurons of the LVN might be affected in advanced DAT (grants of the University of Innsbruck and NIH AG05893).

5-10-21 MEMORY DYSFUNCTION IN HEALTHY AGED SUBJECTS: FREQUENCY AND RELATED FACTORS

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Over 900 volunteers in good social and economical conditions underwent (Programma Diamante/Genua, 1991-92) objective measurements of their health status, adjustement levels and cognito/affective status (Clifton Assessment Procedures for Elderly - CAPE/Zung' Anxiety and Depression Scales/memory tests). Within the subgroup of subjects classified as fully healthy and adapted (n 493: normal CAPE score, Zung' scales <45), 8.3% showed alterations of memory performance fulfilling the neuropsychological criteria for Age Associated Memory Impairment (AAMI), while over 70% had reported memory difficulties at the screening questionnaire, with a direct relationship with anxiety ($p<0.05$) and depression levels ($p<0.01$). Within the non-fully healthy subgroup (about 45% of the entire population), the frequency of objective memory dysfunction was increased up to 19%, with a positive correlation with ouvert depression, presence of psychosensorial deficits, previous surgical procedures and other age-related and non-related illness.

5-10-22 LOBAR ATROPHY IS NOT A PRION DISORDER

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We have previously described the clinical and pathological features of Dementia of Frontal Type and Progressive Aphasia, due to Lobar Atrophy. These degenerative dementias include patients who present with behavioural disturbance leading to mutism or with language disorder, and who have localized cortizal atrophy at autopsy. Approximately half of the patients have a family history of a similar disorder.

We have investigated possible relationships between these disorders and transmissable spongiform encephalopathies using morphometric analysis of regional brain atrophy, immunohistochemical staining of pathological sections, dot-blot immunoassays following limited proteolysis and sequencing of the prion protein (PrP) gene. Brains from 10 patients with lobar atrophy have been compared with those from 9 patients with Creuztfeldt Jakob Disease (CJD).

Lobar atrophy shows a characteristic distribution of atrophy and although neuronal loss and spongiform change is seen the pattern of associated glial change is different from that of CJD and no deposits of PrP are present. In addition protease resistant PrP was not detected by dot-blot in the 10 brains and PrP gene sequencing in 5 familial cases did not show any mutations.

These results imply that lobar atrophy is not a transmissable spongiform encephalopathy.

5-10-23 ANALYSIS OF APP GENE OF JAPANESE FAMILIAL ALZHEIMER'S DISEASE KINDREDS

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β amyloid deposition in the brain parenchyma is one of the characteristic feature of Alzheimer's disease(AD). Recent studies have shown several mutations in exon 16 and 17 of the amyloid protein precursor (APP) gene which are pathogenic for AD. To determine whether mutations of the APP gene are common, and if there are any mutations in other exons, we sequenced the entire coding lesion of the APP gene for ten unrelated families of Japanese familial Alzheimer's disease . The sequence was obtained from both strands by Taq DyeDeoxy Terminator Cycle Sequencing,using automated sequencer (ABI 373A).In exon 16 and 17, 50 cases of sporadic AD were also analyzed. Three of ten families showed the existence of the Val to Ile missense mutation at codon 717. We could not detect any other mutations. None of sporadic AD patients have any mutations in exon16 and 17. The results indicate possibility that 717 Val to Ile mutation is more frequent in Japanese FAD.

5-10-24 FOLATE AND VITAMIN B 12 LEVELS IN SERUM AND CSF OF PATIENTS WITH DEMENTIA DISORDERS --- RELATIONSHIP WITH MONOAMINE METABOLITES ---

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Folate and Vitamin B 12 levels were determined in serum and cerebrospinal fluid(CSF) of 15 controls and 35 patients with dementia.The dementias were classified as senile dementia of Alzheimer type(SDAT),vascular dementia(VD) and subcortical dementia(SD).At the same time, the CSF monoamine metabolites were measured by HPLC, and examine the relationship with CSF folate and Vitamin B 12 levels.The CSF folate levels in the VD group were 7.8±0.7ng/ml and those in the control group were 10.8±1.2, which exhibited significantly lower values($P<0.05$). In addition,compared to the control group,CSF folate levels in the SDAT group were significantly lower($P<0.01$). The CSF/serum folate ratio was 2.6 in the VD group,which was close to the 2.8 of the control group.On the other hand,compared to the control group,the 1.4 of the SDAT group was significantly lower.

The CSF Vitamin B 12 Levels were tended to be lower in the SDAT group only compared with values of the control group.However,there was no significant difference between the CSF Vitamin B 12 levels and the severity of dementia. The positive correlation was observed between the CSF folate levels and the CSF 5-HIAA and MHPG levels in the SDAT group.

It was noted that a reduction of the CSF folate and Vitamin B 12 levels somehow affected the appearance of dementia,which suggests that it is related to the metabolism of intracerebral monoamines.

5-10-25 REACTIVE MICROGLIA IN THE BRAIN OF SENESCENCE-ACCELERATED MOUSE (SAM): AN IMMUNOHISTOCHEMICAL STUDY

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We have developed Senescence-Accelerated Mouse (SAM)-P/8, which exhibits an age-related deterioration of learning and memory abilities. Pathological examinations have shown spontaneous spongy degeneration in the brainstem reticular formation. To test our hypothesis that some immunological process may be associated with the spongy state formation, we studied some markers for microglia (Mac-1, F4/80), astrocytes (glial fibrillary acidic protein), and lymphocytes (Ia, Lyt-2 and L3T4) in SAM-P/8 brain. We also studied SAM-R/1 and DDD mice as control strains. Mice were perfused transcardially with a Zamboni's fixative consisting of 4% paraformaldehyde, 0.2% picric acid in 0.1M phosphate buffer, pH 7.4, and fixed with the same fixative overnight. Frozen sections were stained in free floating immunohistochemical procedure, using Avidin-Biotin Complex and Nickle-Imidazol-diaminobenzidine (DAB).

Proliferation of Mac-1-positive microglia was observed in the spongy areas of the brainstem. The proliferation and cluster formation of Mac-1-positive microglia became more prominent with advancing age. The immune response and activation of microglia may play a role in the pathogenesis of the spongy degeneration in the brainstem of SAM-P/8.

5-11-01 LONG-TERM CHANGES IN VASOPRESSIN GENE EXPRESSION AFTER AMYGDALA KINDLING.

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We have previously reported elevation of resting plasma vasopressin (VP) after amygdala kindling (Greenwood et al., 1991). In this study we report the changes in VP gene expression in the supraoptic nucleus after amygdala kindling. Sprague-Dawley and Long-Evans rats and paired sham controls were kindled with amygdala stimulation to class 1 or 5 seizures. Rats were sacrificed 1 month after the last stimulation and 14μm coronal brain sections through the hypothalamus were processed for in situ hybridization using a [^{35}S]dATP-labeled 30mer oligonucleotide probe specific for VPmRNA. Analysis of autoradiographic silver grain density was done using an image analysis system(Bioquant IV). There was a significant (65%) bilateral increase in VPmRNA in magnocellular neurons of the supraoptic nucleus in both rat strains with each of 2 different kindling stimulus durations (1s and 2s). The increase in VP mRNA was only after class 5 kindled seizures suggesting that spread of the afterdischarge or repeated seizures are necessary for VP gene up-regulation. We conclude that kindling results in long-term up-regulation of VP gene expression in supraoptic nucleus magnocellular neurons.

Supported by NIH Grants NS13411 and NS30923.

5-11-02 PREVALENCE OF EPILEPSY IN NORTH EASTERN REGION OF INDIA: A HOUSE-TO-HOUSE SURVEY

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The objective of this study was to find out the prevalence of epilepsy and its relationship to age, sex, religion and ethnicity. The study was undertaken in an urban area of Guwahati city. Subjects included both male and female above the age group of 7 years. The survey was carried out by a group of medical graduates and the persons with positive symptomatology were reviewed by a neurologist. Between March 1990 to September 1991, 8010 people were surveyed, out of which 4180 (52.18%) were males and 3830 (47.82%) were females. 75% of the population were below the age of 40 years. 87.63% of the people were Hindu and 12.33% were Muslims. 92.55% of the people were Assamese, 5.69% Bengali and 1.39% were of Nepali community. Overall prevalence of epilepsy was 10/1000. This was 9.7/1000 in Assamese, 12.2/1000 in Bengali and 18/1000 in Nepali community. The prevalence was 10.4/1000 in Hindus and 7.1/1000 in Muslims. The most common type of epilepsy was partial epilepsy with impairment of consciousness (50%) followed by generalized convulsive siezure (43.7%).

5-11-03 THE RISK OF SEIZURE DISORDERS AMONG FIRST DEGREE RELATIVES OF EPILEPTIC PATIENTS IN LAGOS NIGERIA

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There are several studies which suggest genetic factors in epileptogenesis but there are few of such studies in African patients. This study therefore set out to determine the influence of genetic factors in genesis of epilepsy in Africans. 2104 sibs of 472 probands with epilepsy seen at a Lagos Hospital were evaluated for occurrence of seizures. Epileptic seizures occurred in 3.2% of the sibs which is more than twice the prevalence in Lagos area (1.3%). Epileptic seizures occurred in 3.6% of males sibs and 2.7% of female sibs. Similiarly, 3.6% of sibs of patients with generalised epilepsy and 3.0% of sibs of patients with partial epilepsy had seizures. However, the prevalence of epileptic seizures was significantly higher in sibs of probands aged 10 years or below (7.2%).

The result of the study suggest that the risk of epileptic seizures is higher in first degree relatives of epileptic patients, irrespective of the type of epilepsy, confirming in African patients, some influence of genetic factors in epileptogenesis.

5-11-04 AUDITORY EVOKED "P300" IN FOCAL AND GENERALIZED EPILEPSIES

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In order to determine focal abnormalities in epilepsies 38 patients suffering from epilepsy (aged 8 to 69 years) were investigated by auditory evoked cognitive P300 potential with a system capable of constructing potential maps of instant voltage and with 16 channels. 21 electrodes were placed according to the 10-20-electrode positions. Binaural presentation of 420 tones (frequent tone 1000 Hz, occurring at 86% of trials; rare tone 2000 Hz, occurring at 14% of trials) were applied to the patients. Latencies were compared to age-matched controls and local amplitudes were considered as abnormal when their average amplitude differed 30% as related to P300 at Pz.

In focal epilepsies (N= 25) P300 latency were significantly prolonged ($p < 0.05$) whereas generalized epilepsies (N= 13) showed no significant delay of P300 latency as compared to controls. 14/25 patients with localization-related epilepsies had focal reduction of P300 amplitudes.

Thus focal reduction of P300 amplitudes may provide further information about lateralization of functional disturbance, P300 latencies may reflect the influence of anticonvulsant therapy.

5-11-05 EPILEPSY AMONG CHINESE IN HONG KONG: A REVIEW OF 874 PATIENTS.

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Objective. To study the seizure characteristics and drug treatment response in Chinese epileptic patients.

Methods. A cross-sectional study of 874 epileptic patients was conducted in 2 regional hospitals in Hong Kong. The demographic factors, seizure types and possible causative factors of these patients were identified. The seizure control and mode of drug treatment were also reviewed.

Results. Of the 874 patients, 50% had generalized seizures, 48% had partial seizures and 2% had unclassified seizures. The causes of epilepsy were idiopathic in 71%, secondary in 28% and unclassified in 1%. Of the secondary causes, the commonest was infection (9.4%), followed by vascular (5.1%), trauma (4.5%) and congenital (3%). The control of seizures was unsatisfactory in 36% of patients with 19% having 1 to 2 attacks and 17% 3 or more attacks within last 3 months. 32% of patients were treated with 2 or more antiepileptic drugs.

Conclusion. A hospital-based, cross-sectional study of 874 epileptic patients in Hong Kong provided a database for future epilepsy study and health care planning in Hong Kong.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-11-06 SURVEY OF PUBLIC AWARENESS, UNDERSTANDING, AND ATTITUDES TOWARD EPILEPSY IN TAIWAN.

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A survey to evaluate public awareness, understanding, and attitudes toward epilepsy was conducted in Taipei city and Chin-San county, Taiwan. Of the 2610 adults, 87% had read or heard about epilepsy; 70% had known someone having a seizure; 56% had seen someone having a seizure; 18% would object to having their children in school or at play associate with persons with epilepsy; 72% would object to having their children marry a person with epilepsy; 31% thought that persons with epilepsy should not be employed in jobs like other people; 7% thought epilepsy to be a form of insanity; 34% did not know the cause of epilepsy; 13% did not know what an epileptic attack was like; and 18% did not know what to recommend if their friends or relatives had epilepsy. Younger, unmarried persons with higher education living in urban area tend to have higher awareness and understanding of epilepsy, have less prejudice against play and employment, but have more objection to marriage. Our survey showed that awareness of epilepsy in Chinese in Taiwan was the same as those in Western countries, and the attitudes toward epilepsy seem to fall between the Western countries and Mainland China.

5-11-07 PRELIMINARY DATA FROM AN OPEN MULTICENTRE TRIAL OF LAMOTRIGINE (LAMICTAL®) IN PATIENTS WITH TREATMENT-RESISTANT EPILEPSY ON ONE ANTIEPILEPTIC DRUG WITHDRAWING TO MONOTHERAPY.

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Lamotrigine is a novel antiepileptic drug (AED). This open, multicentre Pan-European study of lamotrigine was designed to assess withdrawal of concomitant AEDs in patients with treatment-resistant epilepsy who respond to add-on lamotrigine. The study consisted of 3 phases: the add-on phase - lamotrigine added on to phenytoin, carbamazepine or valproate; the AED withdrawal period; and a twelve week lamotrigine monotherapy period. Up to 340 patients will be entered into this trial.

We present preliminary data on 303 entered. Fifty six percent of patients completing the add-on phase experienced at least a 50% seizure reduction and entered the withdrawal period during which the concomitant AED was withdrawn over 10 weeks. Fifty-five percent of patients who entered the withdrawal phase achieved lamotrigine monotherapy.

This study demonstrated that Lamictal can be used successfully in monotherapy following withdrawal of concomitant antiepileptic therapy. The study has also provided preliminary evidence that decreasing the dose escalation rate reduces the number of patients being withdrawn from the study due to rash.

5-11-08 PROSPECTIVE INCIDENCE STUDY OF NEWLY DIAGNOSED UNPROVOKED SEIZURES IN ADULTS

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Studies of unprovoked seizures show great difference in age-specific incidence, especially in the elderly. While the majority of studies show a lower incidence in the elderly compared with other adults, 3 recent studies find the highest incidence in old persons. To avoid underrepresentation of the elderly, the present study was undertaken with a closer survey of the elderly compared to previous studies.

Method. Cases were ascertained through continous survey of all patients with a history of seizures or seizure-like events, referred to the only laboratory for electroencephalography or to the only dept of Neurology in the investigation area. All seizures and seizure-like events occurring in institutions of the elderly were reported monthly to the investigator.

Results. In the population of 104.100 persons, age 17 years and older, 53 cases with newly diagnosed unprovoked seizures were found during a period of 10 months. Total incidence was 61/100.000 inhabitants at risk. 29 were males, incidence 67, and 24 females, incidence 55. Age specific incidences were: 39 (17–29 years), 34 (30-39), 51 (40-49), 57 (50-59), 85 (60-69), 151 (70–79), 206 (80 and above).

Conclusion. Onset of unprovoked seizures are especially common in old age. Prognosis of seizures and treatment policies in this group need to be established and risk factors should be identified.

5-11-09 LACK OF TOLERANCE TO THE ANTICONVULSANT ACTIVITY OF THE NEW IMIDAZO-BENZODIAZEPINE IMIDAZENIL IN RATS

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The sensitivity to the i.v. infusion of convulsive agents acting on the $GABA_A$ receptor complex was assessed in rats undergoing chronic treatment with diazepam or the new imidazo-benzodiazepine imidazenil. Changes were measured in the anticonvulsant action of these benzodiazepines (BZs) against a slow i.v. infusion of bicuculline (0.11 µmol/min), pentylenetetrazole (PTZ) (54 µmol/min), or the ß-carbolin ester (ß-CCM) (0.28 µmol/min) to assess the functional state of GABA binding site and the coupling between the BZ modulatory sites with the GABA binding sites. Tolerance to anticonvulsive effects of diazepam against bicuculline, PTZ, and ß-CCM-induced seizures occurred 68, 35, 9 and 4 days, respectively in animals treated 3 times a day, p.o. with 8.75, 17.5, 35 and 88 µmol/kg. Conversely, no tolerance to anticonvulsive effects of imidazenil was shown when the above convulsive agents were infused in rats that received imidazenil (2.5, 12.5 or 25 µmol/kg) 3 times a day, p.o. for 150 days.

The results indicated that chronic imidazenil treatment is not accompanied by an alteration in the molecular mechanisms underlying sensitivity of the $GABA_A$ receptor complex.

5-11-10 CLINICAL AND EEG PICTURE IN 19 PATIENTS WITH NON-CONVULSIVE STATUS EPILEPTICUS

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Nineteen patients, aged 8-82 years, with confirmed non-convulsive status epilepticus (NCSE), are described. No previous history of epilepsy was present in 10 patients of whom 6 had a CVA while 4 had other systemic disorders. Nine patients had a history of epilepsy, of whom 6 were seizure free and on no treatment for between 7-47 years before the onset of NCSE while the remaining 3 patients were on treatment and had no convulsive seizure attacks for several months before their NCSE. The clinical presentation included acute confusion of varying degree, lack of spontaneous speech, psychiatric manifestations and occasional easily missed minor motor features. Their EEGs showed generalised (14) or lateralised (5) paroxysmal discharges of spike-and-wave (9), triphasic complexes (8) or delta waves (2). Both clinical and EEG improvement occurred shortly after i.v. Diazepam during the EEG recording (in 14 patients) or several days following oral anticonvulsant medication. Subsequent clinical and EEG follow up confirmed a favourable response to anticonvulsant medication in all the patients. We emphasise that NCSE can be easily missed and should be considered with unexplained clouding of consciousness or sudden psychiatric manifestations even in patients with no previous history of epilepsy. The condition is treatable and EEG plays a major role both in the diagnosis and in monitoring response to treatment.

5-11-11 TREATMENT EFFECTS OF FERTIFIED POLLEN TO BEHAVIORAL TOXICITY OF PHENYTOIN IN EPILEPTICS

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This study investigated the neuropsychological effects of phenytoin and fertified pollen in forty-six epileptic patients, before and after treated three months, neuropsychological evaluation at the third and the sixth month treated with phenytoin, included 15-WT, Cancellation Test, Index Finger Tapping and Revised Visual Retention Text. The concentrations of serum vitamin B_{12}, folic acid, free amino acids and the levels of trace elements in hair were examined.

The results suggested, after receiving PHT 3 months, the cognitive functions included memory, attention-concentration, motor speed and visual retention were impaired significantly. While the levels of vitamin B_{12}, folate, free amino acids of blood and the trace elements in hair had reduced severely. After administering fertified pollen 3 months, the impaired functions of cognition had recovered and the reduced levels of serum vitamin B_{12}, folic acid and free amino acids had increased and the abnormalities of trace elements of hair had recovered.

The correlations were analyzed between the fluctuation of cognitive functions and the alteration of serum vitamin B_{12}, folate, free amino acids and trace elements in hair. The conclusion revalued that the behavioral toxicities of phenytoin may be induced by the abnormalities of nutritive substances such as vitamin B_{12}, folic acid, free amino acids and the trace elements of the body. During this period the concentration of PHT was monitored, no significant altering had been found.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-11-12 SIMULTANEOUS DETERMINATION OF CARBAMAZEPINE, PHENYTOIN, PHENOBARBITAL, PRIMIDONE AND THEIR PRINCIPAL METABOLITES BY HPLC METHOD AND ITS APPLICATIONS

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Carbamazepine (CBZ), phenytoin (PHT), phenobarbital (PB) and primidone (PM) are commonly used antiepileptic drugs (AEDs). The use of several AEDs in combination is required sometime for the control of seizures. The most rapid and cost-effective approach to monitor AEDs level in epileptic patients with polytherapy is multiple drug analysis. An ideal method for the monitoring of AEDs should be able to simultaneously analyze these drugs as well as their principal metabolites, because some of the metabolites also have anticonvulsant and toxic activities as the parent drugs while other metabolites are essential in the pharmacokinetics studies on AEDs. A precise and accurate reversed-phase high-performance liquid chromatography (HPLC) method with isocratic elution and photodiode-array detection has been established for the simultaneous assay of CBZ, PHT, PB, PM and their principal metabolites in serum, saliva and urine samples. This method has the necessary sensitivity and linearity for routine therapeutic monitoring of both total and free drug levels and may be employed for pharmacokinetics study of drug interactions and metabolism as well.

5-11-13 TOTAL AND FREE SERUM CONCENTRATIONS OF CARBAMAZEPINE, CARBAMAZEPINE-10,11-EPOXIDE AND CARBAMAZEPINE-10,11-DIOL IN EPILEPTIC CHILDREN

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The major metabolic pathway of Carbamazepine (CBZ) yields CBZ-10,11-epoxide (CBZ-E) and 10,11-dihydro-10,11-trans-dihydroxy-CBZ (CBZ-D). CBZ-E has an independent anticonvulsant activity in various animal models. Abnormal serum ratios of CBZ-D to CBZ-E have been found to be useful indicators of noncompliance, and the CBZ-D/CBZ ratio to be a sensitive indicator of enzymatic induction. Analysis of free CBZ, CBZ-E and CBZ-D levels may be more indicative in epileptic patients. Serum total and free CBZ, CBZ-E and CBZ-D concentrations were simultaneously measured by an HPLC method in thirty children with epilepsy. The serum total CBZ, CBZ-E and CBZ-D concentrations obtained were 12.97±3.92, 2.37±0.71 and 6.26±3.56 (mean±S.D., μg/ml) respectively. Free CBZ, CBZ-E and CBZ-D levels were 2.59±0.77, 0.99±0.36 and 3.86±2.05 respectively. The free fractions were 20.28%±3.72, 41.88%±8.07 and 62.70%±7.03 for CBZ, CBZ-E and CBZ-D respectively. CBZ-D has the largest coefficient of variation (56.88% and 53.25% for total and free levels) in addition to the highest free fraction. CBZ-D was highly correlated with CBZ-E and free CBZ-D (r=0.6403 and 0.9862). CBZ-E showed significant correlation with free CBZ-E and CBZ-D (r=0.8267 and 0.6271). CBZ only correlated with free CBZ (r=0.8384). The free fractions of CBZ and its metabolites were highly correlated with one another. Analysis of both total and free CBZ and its metabolites simultaneously may provide more information for the therapeutic drug monitoring.

5-11-14 CHEMOSENSORY EVENT-RELATED POTENTIALS IN TEMPORAL LOBE EPILEPSY

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The aim of the study was to investigate chemosensory functions in patients with temporal lobe epilepsy to find out, whether both olfactory and trigeminal stimuli applied either ipsilaterally or contralaterally to the focus are processed differently.
METHODS: Twenty-two patients suffering from pharmacoresistent TLE were investigated (left-sided focus: n = 12; right-sided focus: n = 10). Investigation of the trigeminal nerve was performed by the use of CO_2. The olfactory system was tested using vanillin and H_2S as stimuli. Chemosensory functions were assessed by means of chemosensory event related potentials (CSERP) and a simple odor identification test.
RESULTS: In both groups of patients CSERP latencies were prolonged after left-sided stimulation with CO_2 when compared to stimulation of the right nostril. In contrast, prolonged latencies were found in patients with left-sided foci after left-sided olfactory stimulation, and, in patients with right sided foci after stimulation of the right nostril. Thus, it may be assumed that the neocortical processing of olfactory, but not trigeminally mediated information is affected by temporal lobe lesions. After olfactory stimulation in patients with a right-sided focus the distribution of ampitudes was different from normal. Moreover, analyses revealed non-overlapping 95%-confidence intervals for latency N1 when vanillin was applied to the right nostril. These results indicate that the right temporal lobe possibly plays a different role in the processing of olfactory information.

5-11-15 PREVALENCE AND TYPE OF EPILEPSY IN A RURAL COMMUNITY OF GUATEMALA

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The prevalence of epilepsy in a rural Guatemalan community (population 2,111) was assessed in a cross sectional study. Using the WHO questionnaire and standard neurologic examination, 1,882 (97.3%) individuals were surveyed; 16 cases of epilepsy were detected, eight (50%) had generalized tonic-clonic, six (37.5%) complex partial, one (6.25%) partial simple, and one (6.25%) atonic seizures. The crude prevalence of epilepsy was 8.5/1000 for the general population; 11 were active epileptics (prevalence 5.8/1000). Age-specific prevalence was highest among the age group of 20 to 29 years; however, all cases were younger than 40 years (prevalence 11.6/1000). Fourteen were treated but only five on an ongoing basis. Phenobarbital was the most common anticonvulsant. Most cases (56%) had symptomatic epilepsy; five (31%) had history of significant head trauma, four (25%) of CNS disease, while seven (44%) had family history of epilepsy. In this Guatemalan rural community, prevalence of epilepsy was greater in young adults, and most cases were symptomatic.

5-11-16 PATIENT ACCEPTANCE OF VAGUS NERVE STIMULATION (VNS) FOR TREATMENT OF REFRACTORY EPILEPSY

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The objective of this paper is to measure patient acceptance of VNS therapy for refractory partial seizures at the time of generator replacement. The devices are surgically implanted in a 2 hour procedure and last approximately 18 months with patients undergoing an 1 hour operation for replacement. Common side effects include hoarseness, paresthesia, throat pain and coughing. One-third of patients experience at least a 50% reduction in seizure frequency.

The method used to measure therapy acceptance was patient satisfaction and tolerability as determined by a patient's decision to continue or discontinue with VNS. Upon battery depletion, patients were asked if they wanted their device replaced, not replaced, or were unsure.

Results of 45 patients experiencing battery depletion reveal that 38 (84.4%) have opted for replacement, 3 (6.7%) are considering replacement, and 4 (8.9%) have discontinued therapy and opted for device explant.

In conclusion, 84% of patients experiencing battery depletion believed they derived enough benefit from VNS therapy to undergo replacement, while 9% chose to discontinue therapy.

5-11-17 ONE YEAR RESULTS OF VAGUS NERVE STIMULATION (VNS) IN 82 REFRACTORY EPILEPSY PATIENTS

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Our objective is to determine if acute phase efficacy seen with VNS for refractory partial seizures continues over a one year period. A 26 week double-blind controlled study has shown that VNS is effective in reducing refractory partial seizures. The results of the first 82 patients who received at least one year of VNS are presented here.

The methods included implanting 113 refractory epilepsy patients with vagus nerve stimulators at 17 centers in the US, Canada, Holland, Germany, and Sweden. Mean seizure frequency percent change (MSFPC) is compared to a 12 week baseline after 3, 6, 9, and 12 months of therapy for the first 82 patients to reach the one year mark. Patient response distribution is also analyzed.

After 3 months, there was a 22% decrease in MSFPC. At 6, 9, and 12 months, MSFPC reductions were 24%, 26% and 28% respectively ($p \leq 0.0001$ for all periods). At 12 months, 30 patients (37%) had $\geq$50% seizure reduction and 8 patients (10%) had $\geq$75% reduction. Side effects included hoarseness, coughing, throat pain, paresthesia.

Efficacy of VNS for treatment of refractory partial seizures is sustained over a 12 month period and appears to improve with time.

5-11-18 PRE-PREGNANCY COUNSELLING AND PREGNANCY MONITORING IN OVER THREE HUNDRED EPILEPTIC WOMEN.

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We have followed epileptic women for pre-pregnancy counselling and prospectively during pregnancy, and assessed the offspring of these women. A total of 319 patients, 105 of whom only for pre-pregnancy counselling, was ascertained. The remaining 214 patients had 287 pregnancies resulting in 228 offspring, including 165 children who were followed after birth. The frequency of major malformations (MJ) in the offspring was increased as compared to the normal population (17.9.% and 0.5% respectively, $p<0.05$). The frequency and type of MJ were associated with the anticonvulsant (AC) regimen and family history of MJ. Folate supplementation pre- or early during pregnancy was found to significantly reduce MJ. The frequency of minor anomalies was not increased in the offspring of epileptic women. Abnormal neurological development (AND) was not present in an increased frequency, but we could define high risk groups for AND according to AC regimen. The risks for complications during pregnancy, labour, delivery and puerperium were not increased. The occurrence of seizures during labour, delivery and early puerperium was significantly associated with discontinuation of AC. Eighteen percent of our patients had increased seizure frequency during pregnancy which was not associated with decreased blood AC levels; however, a significant correlation with poor pre-pregnancy seizure control was found. The most important risk factor for increased seizure frequency during pregnancy was failure to present for pre-pregnancy counselling.

5-11-19 SEIZURES INDUCED BY COCAINE ABUSE - A PROSPECTIVE STUDY

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From 177 drug abusers patients between may 1990 and december 1991, 22 cocaine abusers were selected in order to study the prevalence of seizures induced by this drug. These patients had no history of alchoolism or any other drug abuse, no trauma, no previous seizures and were HIV (-), VDRL (-). The cocaine induced seizures was stabilished when they had occured whithin 90 minutes after the cocaine use. All of them were male patients with a mean age of 23.4 years and the mean time of use was 8.27 years. The neurologic examination was normal and the CT scan did not show structural lesion. 7 patients (31.8 %) presented with seizures related with cocaine use. 5 presented generalized tonic-clonic seizures and 2 partial seizures. The EEG were abnormal in 12 (54.5 %), and fronto-temporal slowing was the main finding. Cocaine abuse play an important role in the development of seizures in acute intoxication of this drug and is an important differencial diagnostic in epilesy.

5-11-20 EFFECTS OF ANTIEPILEPTIC DRUGS ON THE PERIPHERAL AND CENTRAL NERVE CONDUCTION

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It has been reported that the antiepileptic drugs is known to affect the conduction in the peripheral and central nerve system, but the effect is disputable. The results of both peripheral nerve conduction volocity(NCV) and somatosensory evoked potential(SEP) in patients with antiepileptic drugs were presented in this paper. 20 patients were studied; male 11 and female 9 aged 18-58. All patients were primary epilepsy and the type of seizures was as followed; 16 tonic and clonic seizures, and 4 complex partial seizures. 2 patients showed the decrease of the motor conduction velocity(MCV) and 5 patients showed the decrease of sensory conduction velocity(SCV). 2 patients showed the increase in the somatosensory central conduction time(CCT)(N13-N20 interval). In one patient with the increase of CCT, the plasma concentration of antiepileptic drug showed the high dose level. The patients with the decrese of NCV were medicated with PHT or VPA. The NCV had the negative relation with the plasma concentration of PHT. The CCT had not the relation with the plasma concentration of antiepileptic drugs.

5-11-21 RESULTS OF SEIZURE REDUCTION AND GLOBAL IMPROVEMENT PARAMETERS IN THREE DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDIES OF GABAPENTIN AS ADD-ON THERAPY IN PATIENTS WITH REFRACTORY PARTIAL EPILEPSY

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Three double-blind, placebo-controlled, parallel-group, multicenter studies of 600, 900, 1200, or 1800 mg/day gabapentin as add-on therapy were conducted in 705 patients with refractory partial seizures. Measures of seizure reduction were percentage change in seizure frequency and response ratio. A secondary outcome measure was a global evaluation, performed both by patients and investigators, assessing the ability of the patient to perform activities of daily living at the end of treatment, compared to the ability at screening (improved, same, worse). In each study, the adjusted mean response ratio and median percentage change in seizure frequency was better for patients receiving any dosage of gabapentin than for placebo-treated patients. A dose-response trend was evident. Statistical testing of response ratio compared results for the placebo-treatment group and one gabapentin-treatment group in each study; significance was attained in two of the three studies. Results of global evaluations showed significant differences favoring gabapentin and correlated well with outcomes as demonstrated by measures of seizure reduction.

5-11-22 MUNICIPAL PROGRAM OF PREVENTION, CONTROL AND ACCEPTANCE OF EPILEPSY IN PRIMARY SCHOOL STUDENTS IN BUENOS AIRES CITY

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In our city, children and teenagers are the highest risk population for epilepsy. This disease is considered a fact of taboo and prejudice. Sometimes the patients have fear and feel inferior with poor adaptation in their social environment. An adequate knowledge of epilepsy is important to prevent it and to educate people for social acceptance of the illness. We have designed a program of prevention, control and acceptance of epilepsy in private and public primary schools of Buenos Aires City. This program has 3 stages: 1) a neuroepidemiological study on a school population. The purpose of it was to establish the prevalence and identify its possible risk factors. 4% was the prevalence. 12% had wrong diagnosis of epilepsy. Perinatal anoxia, head trauma, febrile convulsions and infections of CNS were significant risk factors; 2) a campaign in primary schools for kids, parents and teachers to divulge the basic knowledge of epilepsy was done. We used the dramatization of different types of crisis with actors showing inadequate behaviours of occasional spectators and exemplifying good attitudes with the person having a crisis. After a final debate didactic brochures were delivered; and 3) the program is being completed with the creation of a network of assistance services.

5-11-23 DETECTION OF CHANGES IN EPILEPTIC EEG CAUSED BY CARBAMAZEPINE USING QUANTITATIVE EEG ANALYSIS

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Quantitative EEG analysis was introduced in 32 new cases of epilepsy classified as simple partial and complex partial seizures. In all patients computed tomography and other morphologic methods showed no macrofactor. The analysis was performed 1 to 3 days after the first clinical manifestations. After that Carbamazepine was administered orally in two daily doses of 200 mg. Within a period of two weeks a stable serum level was reached in the lower part of the therapeutic range (5.3 ± 1.1 mg/ml) and the quantitative EEG analysis was repeated. All the results were compared using Z-score with the results from the control group consisting of 31 normal subjects and also they were compared among each other. The quantitative EEG analysis of the effects of Carbamazepine in a short-treatment showed stable changes in the decreasing of mean and peak alpha frequency as well as in the spectral power and the increasing of theta/delta spectral power ($p = 0.01$) and also showed some changes in band ratios. From the explanation written above we can make a conclusion that the EEG changes in the patients who suffer from epilepsy should not be mistaken for changes of the EEG activity elicited by Carbamazepine.

5-11-24 RECURRENT SEIZURES DUE TO UNDIAGNOSED SICK SINUS SYNDROME

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A 45 yr. old female was admitted to hospital with acute onset of "generalized seizures" preceded by epigastric discomfort and nausea. The left plantar response was extensor on admission. During the seizure EEG showed bitemporal sharp theta waves. ECG was normal. Remainder of physical examination and investigations were normal. She had similar attacks 12 months and 16 months later. 7.5 years later she was again admitted with seizures preceded by abdominal discomfort and loose bowels, and 9 years after onset she had similar episode when bradycardia was noted during seizure and pulse returned to normal after that. Diagnosis of Sick Sinus Syndrome was made and dual chamber pacemaker was implanted. She has remainder seizure free for six years.

Sick Sinus Syndrome consists of symptoms including dizziness, syncope which may progress to seizure, and fatigue and manifests as sinus bradycardia, sino-atrial block, or sinus arrest. As in this patient, ECG abnormalities may be intermittent and the underlying cause may go unrecognized for many years. This case illustrates the need for careful cardiac investigations in seizures on the background of episodic autonomic gastrointestinal dysfunction.

5-11-25 INTERIM REPORT ON AN OPEN MULTICENTRE LAMOTRIGINE (LAMICTAL®) VS CARBAMAZEPINE MONOTHERAPY TRIAL IN PATIENTS WITH EPILEPSY.

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Lamotrigine is marketed in a number of countries, and has shown efficacy as add-on therapy in patients with refractory epilepsy. Currently, there is an active programme to study the use of lamotrigine in monotherapy.

This is an interim report on an open multicentre trial comparing the monotherapy use of lamotrigine and carbamazepine in patients with newly diagnosed partial or generalised tonic-clonic seizures, or recurrence of those seizures. Patients are randomised to three Treatment Arms: Lamotrigine 100 mg (LTG 100), Lamotrigine 200 mg (LTG 200) or Carbamazepine 600 mg (CBZ 600) and treated for 6 months.

Two hundred and sixty six patients have enrolled, of which 113 are ongoing. The number of patients that completed the study period seizure free were: LTG 100: 27, LTG 200: 28, CBZ 600: 25. Another 31 patients completed the study after a seizure following the dose escalation phase. Ten patients on CBZ were withdrawn with adverse experiences (6 skin rashes); between the two LTG arms, 5 patients in total were withdrawn (3 skin rashes). Twenty seven patients were withdrawn for administrative reasons.

5-11-26 AN ANALYSIS OF 50 PATIENTS WITH HEADACHE EPILEPSY

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The EEGs in 50 patients with headache epilepsy were analyzed with encephalofluctuograph technique (ET). ET is a technique based on systemic theory, synopsis and dissipative structure to analyze cerebral super-slow encephalofluctuograph. The features of ET are the characteristics continuous spectra, of which the numbers are closely correlated to the severity of headache. The sterical distributions of the spectra on patient's head are corresponding to the localization of headache. It is practically useful in the differential diagnosis of the headache epilepsy.

China is a developing country with a huge population. Therefore there are alot of patient's chief complain of headache. ET is in turn a useful method to screen and detect patients with headache epilepsy, and a helpful tool to design a reasonable therapeutic protocal. ET is simple, noninvasive and valuable to be widely used.

5-11-27 DOES GADOLINIUM ADMINISTRATION IN MRI-TECHNIQUE LEAD TO MORE SENSITIVITY IN UNSELECTED PATIENTS WITH EPILEPSY ?

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Enhancement by contrast media in cranial computerized tomography (CT) leads to more sensitivity when detecting epileptogenic morphological lesions. Magnetic resonance imaging (MRI) already reveals this abnormality in standard noncontrast technique and is additionally superior to the CT-procedure in displaying heterotopias, schizenzephaly, low-grade gliomas and typical temporal mesial gliosis. Prospectively, we investigated 105 unselected patients with epilepsy by MRI with T2w, PDW and T1w transverse and coronary sections before and after gadolinium-DTPA administration to prove that additional information is available by applicating contrast media: 63,8% of the MRIs were normal. In 11,4% of the patients, we found ventricle and/or sculi asymmetries. 7,6% presented with temporal lobe hypoplasia with or without arachnoidal cysts. 16,7% of the patients showed other various abnormalities, but only in one of 105 cases, contrast enhancement revealed additional pathology by showing an isointense lateral sphenoidal meningeoma. In conclusion, our results suggest sufficient sensitivity of standard noncontrast MRI-techniqoe for detecting morphological lesions responsible for epileptogenic focus. Additional contrast media does not lead to more sensitivity; therefore it is not necessary in routine MRI-diagnosis concerning this patient collective. On the other hand, specitivity increases in MRI-techique by gadolinium-application when clearing e.g. the dignity of a neoplastic process, which has already been documented in standard series.

5-11-28 DOSE-RESPONSE RELATION OF CLONAZEPAM IN THE TREATMENT OF STATUS EPILEPTICUS

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Approximately 5% of all epileptic patients experience an episode of status epilepticus (SE) at some time in their lives. Generalized tonic-clonic SE is the most frequent type, and it is medical emergency because of possibility of permanent brain damage or mortality.

We studied 69 generalized tonic-clonic SE who were treated with clonazepam (CZP) initially, and investigated effectiveness of CZP.

In 21 cases SE lasts up to 1 hour, in 28 cases continues 2 to 6 h., in 6 cases persists 5 to 24 h., and in 12 persists longer than 24 h. After initial therapy with intravenous CZP, seizures were controlled within 5 to 15 min. by 1 mg CZP in 30 cases, within 15 - 30 min. by 2 mg CZP in 16 cases, and within 30 - 45 min. by 3 mg CZP in 8 cases. Eventually, in 54 of 69 cases (78.3%) with tonic-clonic SE, we controlled seizures by intravenous CZP (1 to 3 mg) within 5 to 45 min. In 15 cases we couldn't control seizures by CZP, and these patients were treated with barbiturate coma by using pentobarbital. Difference between plasma CZP levels of patients whose seizures ceased with CZP and of those that didn't, was not significant.

The aim of our study is to investigate effectiveness and dose-response relation of CZP in the treatment of SE and to compare our results with the other series reported previously.

5-17-01 LESCH NYHAN DISEASE: A CASE OF CHOREOATHETOSIS, DYSTONIA, NORMAL MENTATION, AND NO SELF MUTILATION.

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We present a 22 yr old man with a 20 yr history of progressive gait disturbance, movement disorder, and speech difficulties. Motor but not intellectual milestones were delayed, and at age 2 he developed gait change, flinging arm movements, and speech difficulties. At age 9 he had kidney stones and started allopurinol. Parents, 1 sister and her 2 daughters were unaffected, and 1 sister had kidney stones.

Physical exam revealed dysarthria, choreoathetosis, dystonic posturing, hyperreflexia, and Babinski signs. Mentation was intact, and there has never been self mutilation.

Lab evaluation revealed absent HPRTase activity in erythrocyte and cultured fibroblast lysates (Gottlieb et al. J Inher Metab Dis 5:183, 1982). Previous work has shown that this patient has an internal duplication of HPRT exons 2 and 3 (Yang et al. Somatic Cell and Mol Gen 14:293,1988). This duplication has a 100-1000 fold increased rate of spontaneous reversion to the normal gene structure in cells in culture, resulting in HPRT enzyme activity in vitro.

A mosaic cellular pattern of spontaneous reversion of the HPRT mutation in this patient's tissues may explain why, unlike typical Lesch Nyhan disease patients, this patient has normal mentation and no self mutilation.

5-17-02 TREMOR-MOVEMENT INTERACTION IN CEREBELLAR PATIENTS.

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Human subjects (9 cerebellar patients, 4 normals) pointed at visual targets under different speed and load conditions. Index fingertip position was recorded contact-free in 3-D at 200 Hz, using the Selspot^R system.

From the recordings, we calculated power spectral density functions for overlapping 2-sec segments, which allowed us to separate tremor and purposive movment by their frequency contents, and to compare their timing.

We found that purposive movments modify tremor amplitude but not frequency. Movements could initiate, amplify or terminate tremor, and different types of interaction could be found even for the same subject.

Standard tremor classification provides little help in understanding our data. We interpret the findings as dynamic coupling between two neuronal pools, one generating tremor and the other controling purposive movements.

Supported by NATO, DFG (SFB 194,A5), and the Ontario technology Fund.

5-17-03 WITHDRAWN

5-17-04 LIGHTS OUT NUCHAL MYOCLONUS

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A 46-year-old woman presented with a four year history of peculair twitching movements of the muscles of the right side of her neck provoked by sudden darkness. Examination revealed that, when room lights were extinguished, she developed from 2 to 10 clonic contractions of the muscles of the right side of the neck. This response showed fatiguability when she was repeatedly placed in darkness.

Simultaneous E.E.G. and surface E.M.G. recordings showed no change in the E.E.G. in association with the clonic activity. MRI scanning revealed several foci of increased T2 signal in the C2 through C4 levels of the cervical cord and a few tiny peripheral foci of increased T2 signal in the white matter of both cerebral hemispheres. A trial of carbamazapine produced a decrease in the frequency and intensity of this phenomenon. A video recording of the patient's unusual movement disorder will be presented. The mechanism remains unexplained.

5-17-05 BOTULINUM TOXIN IN CERVICAL DYSTONIA. A FOUR YEAR FOLLOW UP.

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140 patients with different features of cervical dystonia received local injections of Botulinum toxin A (Dysport^R). The severity of the movement disorder was assessed before and after treatment by rating scales. In addition psychological questionnaires were performed during follow-up. The BOTOX dose at the initial injection course (1 to 3 injections) ranged from 25 to 100 ng. 81% of patients reported substantial benefit (> 50% improvement). The mean score of the subjective 4-point scale fell from 3.65 to 1.8 ($p<0.001$). There was a high intercorrelation between all rating scales. The BOTOX effect lasted 14,1 weeks. 10% of patients developed mild dysphagia, in 2 cases severe dysphagia occurred. During follow-up in one group of patients the interval between injections grew longer and the abnormal movement became less severe. 9 patients did not require repeated injections because of a continuing acceptable head posture. 4 patients have been free of symptoms for more than two years. 2 patients failed to respond owing to the presence of antibodies against BOTOX. 15 patients with pathological "psychosocial patterns" prior to injection presented a normalization after the head posture had been corrected for more than two years by repeated BOTOX injections. BOTOX is a safe and effective treatment for cervical dystonia. The long-term benefit can be limited by development of antibodies. Psychosocial abnormalities in patients with cervical dystonia may be secondary to the abnormal head posture. Different types of long-term responders can be observed.

5-17-06 MENINGIOMA-INDUCED LOSS OF ANTIPARKINSONIAN RESPONSE TO DOPAMINERGIC AGENTS.

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We describe a case of Parkinson's disease with loss of antiparkinsonian response to dopaminergic agents, secondary to a frontal lobe meningioma. A 65 y.o. woman with Parkinson's disease complained with marked decrease in therapeutic response to oral levodopa, despite increasing dosage. Acute challenges with both levodopa and apomorphine produced no clinically significant improvement. CT scan showed a contrast-enhanced area in the left frontal lobe, surrounded by perilesional edema. Patient underwent surgery, and pathological exam disclosed a meningioma. 3 weeks after surgery, oral levodopa dosage could be reduced from 1400 to 750 mg/day, with optimal control of motor symptoms. Repeated pharmacological tests documented a markedly improved response: motor symptoms severity decreased by 76% after levodopa, and by 71% after apomorphine. Perilesional edema possibly caused striatal functional damage in this patient by impairing the postsynaptic compartment of the nigrostriatal pathway. Diseases other than MSA may cause unexpected decrements in antiparkinsonian treatment efficacy.

5-17-07 β_2 ADRENOCEPTOR AGONIST POTENTIATES L-DOPA TRANSPORT TO BRAIN IN AGED MPTP-TREATED MICE.

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Recent evidence in intact animal studies suggest that β_2 adrenoceptor agonists enhance the transport of large neutral amino acids, such as tyrosine and L-dopa, from blood to brain. This study was designed to elucidate whether β_2 agonist exerts its effect by increasing the transport of L-dopa into the brain in mice with damaged dopaminergic system. We used 34-week-old C57/BLmice treated with MPTP (20mg/kg i.p. 10 times) . L-dopa (5mg/kg) and carbidopa (1.25mg/kg) were injected i.p. to those mice. In one group, salbutamol (10μmol/kg),a selective β_2 agonist, was injected i.p. at the same time, and in the other group saline was injected as a vehicle. Concentration of dopamine(DA) and its major metabolites (DOPAC and HVA) in the striatum was measured up to 240 min using microdialysis method. Although concentrations of DA, DOPAC and HVA were increased in both groups, the amounts of increase were significantly greater in salbutamol-injected group during 120 and 220 min. This result suggests that β_2 agonist potentiates L-dopa transport into the brain in mice with damaged dopaminergic system.

5-17-08 PRAMIPEXOLE IN EARLY PARKINSON'S DISEASE: a SINGLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED, MULTICENTER, SAFETY AND EFFICACY STUDY

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A total of 55 patients with early Parkinson's disease (mean age: 63.1 years, range 37 to 86 years; 35 males and 20 females; mean duration of disease 2.3 years), who did not require levodopa, were randomized to either pramipexole or placebo and received at least one dose of study medication. All patients received 10 mg of deprenyl daily. Patients were titrated to their maximally tolerated dose and twenty of 28 pramipexole patients had no dose-limiting toxicity and reached the maximum daily dose of 4.5 mg. Change from baseline on the Unified Parkinson's Disease Rating Scale (UPDRS), part II (Act. Daily Living) and part III (Motor Examination) were the primary endpoints. The pramipexole patients showed a 47% mean improvement in the UPDRS part II score from baseline compared with a 21% mean improvement in the placebo group (p=0.002). For the UPDRS part III score, the patients had a 45% mean improvement from baseline compared with a 30% mean improvement in the placebo group (p=0.10). The overall adverse event profile was similar to other dopamine agonists. The trial provides evidence that pramipexole may be a useful agent in the treatment of early Parkinson's disease.

5-17-09 BOTOX TREATMENT OF HEMIFACIAL SPASM.

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There are now several series of hemifacial spasm (HS) treated with Botulinum Toxin (BT). This report concerns 79 patients who had from 1 to 9 Botox injections, using EMG guidance for injecting the lower half of the face. Of 60 patients available for follow up 48 had a better than 50% improvement, and 7 a better than 25% improvement. 6 patients had a previous Janetta Procedure, and 1 each had either an alcohol injection or peripheral nerve section which was unsuccessful. Side effects included facial weakness in 13, ptosis in 5 and diplopia in 3 patients. Of 9 patients who had an MRI 7 had evidence of an abnormal vessel.

An interesting feature was the presence of 8 patients of Chinese origin in the series. In 200 patients seen in the BT Clinic for Movement Disorders other than HS, only 3 were of Chinese origin. The explanation for this apparent preponderance of HS in the Chinese population is uncertain and requires further investigation.

5-17-10 HEMIBALLISM

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We study 50 consecutive patients with hemiballism. They are 16 men and 34 women. The age of onset ranged from 12 to 84 years (mean, 65.9). Unilateral limbs were affected in 44 patients (88%). Face was also involved in 16 of 44 patients. Only hand was affected in 5 patients and only leg in 1. Stroke was diagnosed in 47 patients including infarction in 41 and hemorrhage in 6. Other causes included tuberculous meningitis in 1, nonketotic hyperglycemia in 1, and undetermined in 1. CT and MRI scans demonstrated a contralateral lesion in 24 patients and an ipsilateral lesion in 1 patient. The contralateral lesion was located in putamen in 8 patients, both putamen and caudate 5, thalamus 3, subthalamus 3, caudate 2, cortex 1, cerebellum 1, and both subthalamus and thalamus 1. The ipsilateral lesion involved both caudate and putamen. The hemiballism disappeared spontaneously in 4 patients, and was improved by haloperidol in 40 mainly within 3 months. Two patients had persistent but less severe hemiballism and the remaining 4 were lost to follow-up. Either clinical pattern and severity of hemiballism or the size, location, and nature of the lesion are not related to the prognosis of hemiballism. In conclusion, lesions in striatum and thalamus are the main responsible locations for contralateral hemiballism which has a good prognosis.

5-17-11 CROSS-CULTURAL COMPARISON OF TRAJECTORIAL LEARNING IN GERMAN AND JAPANESE SUBJECTS.

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Isochrony, i.e. the invariance of movement time irrespective of movement amplitude is a prominent feature of overlearned motor activities. The present study examines how new spatio-temporal invariances are acquired in healthy volunteers. 12 right-handed Japanese and 12 German subjects were trained on new ideograms at five different sizes. After the trajectory had been overtrained with one hand, learning transfer to the contralateral hand was analysed in the same (CO) or reversed (CRe) direction of writing and as a vertical mirror image of the ideogram (MO; MRe). In Western subjects, trajectories learned under left hemisphere control were transferred to the right hemisphere (CO, CRe, MO) but not vice versa, and the trajectorial storage system had clear geometrical restraints (MRe). By contrast, Japanese revealed a significant learning transfer under right as well as left hemisphere control not affected by change in orientation or by switch between start-and end-point coordinates. Findings point to the relevance of Japanese *kanji* abound in figurative characters and have direct implications for the design of new rehabilitation programs.

5-17-12 THE QUANTIFIED NEUROLOGICAL EXAMINATION (QNE) FOR HUNTINGTON DISEASE (HD): DATA ON SENSITIVITY AND SPECIFICITY DERIVED FROM THE CANADIAN PREDICTIVE TESTING PROGRAM

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The QNE (Folstein et al., 1983) was designed to aid in diagnosing and monitoring disease progression in HD. To determine its diagnostic usefulness, the QNE's from participants in the Canadian National Predictive Testing Program were analysed. Normal values were assessed in 126 QNE's from 88 persons with a decreased risk and defined as the cut-off value that incorporates 95% of the sample. For the total score (TS) this value was equal to 4, 0 for the choreascore (CS) subscale, and 1 for both the eye-movement score (ES) and the motor-impairment score (MS). Using these criteria in 45 QNE's from 24 persons diagnosed upon entry as being symptomatic for HD, an abnormal TS was found in 43 instances (95.6 %). The CS was abnormal in 38 instances (84.4 %), the ES in 33 (73.3 %), and the MS in 35 (77.8 %). Of 93 QNE's from 61 persons with an increased risk, 19 (20.0 %) displayed an abnormal TS, 16 (17.2 %) an abnormal CS, 9 (9.7 %) an abnormal ES, and 13 (14.0 %) an abnormal MS. Thus, the QNE allows the definition of highly sensitive and specific criteria for diagnosing affected status in individuals with a family history of HD. Moreover, the total score is more sensitive than any of the subscales in detecting clinical abnormalities.

5-17-13 RELATIONSHIP OF TWO UNIQUE MONOAMINE OXIDASE B (MAOB) POLYMORPHISMS AND PARKINSON'S DISEASE (PD).

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BACKGROUND: Conflicting reports have supported (Neurology 1992;Suppl 3:379) or contradicted (Neurology 1992;Suppl 3:173) the association of MAOB alleles with PD. One polymorphism, in intron 13, is a bi-allelic single-stranded conformational polymorphism (SSCP) of a PCR product. SSCP allele 1 is associated with PD (Ann Neurol 1993, in press). The other polymorphism, in intron 1, is a multi-allelic dinucleotide repeat ($[GT]_n$) of a PCR product (Am J Hum Gen 1991;49:383-392). Conflicting results may be caused by statistical sensitivity differences and/or molecular evolution of the different MAOB polymorphisms. METHODS: DNAs from PD and control populations were analyzed using these two MAOB polymorphisms. Allelic frequencies using both systems were compared in control and PD populations. RESULTS: $[GT]_n$ allele 4 is associated with SSCP allele 1 (X^2-15.1, d.f.=5, $p<0.02$). $[GT]_n$ allele 1 is more frequent in PD, though not statistically significant. CONCLUSIONS: Multi-allelic polymorphisms require larger samples to achieve statistical significance due to increased degrees of freedom. Furthermore, dinucleotide repeat polymorphisms are known to evolve rapidly, and disease associations in random individuals can easily be lost. For small populations, the MAOB bi-allelic system is more sensitive, and shown an association with PD that was not statistically detectable with the multi-allelic $[GT]_n$ polymorphism.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-17-14 DYSKINESIA AND ELEVATED CREATINE KINASE

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Objective. To assess a possible relationship between elevated creatine kinase (CK) and dyskinesia.

Background. Adria Laboratories sponsored a dose-response study of cabergoline that enrolled 61 patients with Parkinson's disease at three centers. Eight patients had an elevated CK (≥ 300 U/L) on one or more occasions during the study (normal, 21-198 U/L).

Design/Methods. Serum chemistries including CK were measured and the patients were evaluated with the UPDRS weekly for the first five weeks and at least biweekly for the last eight weeks of the study.

Results. An elevated CK occurred in 24 out of 721 determinations. The elevations were not related to myocardial ischemia (ECG's were done in five patients) or to cabergoline (decreases occurred in all eight patients while the drug was continued). The frequencies of elevated CK in each dyskinesia category (item 32 on the UPDRS) were 2% at 0, 2% at 1, 4% at 2, 16% at 3, and 67% at 4.

Conclusions. Severe dyskinesias (more than 50% of the day) may cause muscle injury. Thus, an elevated CK may appropriately be attributed to dyskinesia in the absence of other suggestive signs or symptoms.

5-17-15 PET STUDIES ON THE DOPAMINE D1 RECEPTORS IN THE PARKINSONIAN BRAIN USING NOVEL LIGANDS (11C)SCH 39166 AND (11C)NNC 756.

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Studies on the role of dopamine D2 receptors in Parkinson's disease have shown upregulation in drug-naive de novo parkinsonian patients, whereas in the case of D1 receptors, this kind of change could not be found with (11C)SCH 23390. Recently, more specific ligands for D1 receptors have been developed including (11C)SCH 39166 and (11C)NNC 756. PET studies were carried out in 8 untreated parkinsonian patients with predominantly unilateral symptoms. Every patient was studied with both of these ligands and (11C)-raclopride for D2 receptors. 5 mCi of each ligand was injected i.v. (11C)NNC 756 caused a significantly higher striatum:cerebellum ratio than (11C)SCH 39166. The binding of (11C)raclopride was higher in the striatum contralateral to the patient's symptomatic side, whereas the binding of (11C)SCH 39166 and (11C)NNC 756 was symmetric. These results confirm our previous results implying that there may not be upregulation of D1 receptors in early Parkinson's disease as happens with D2 receptors. (11C)NNC 756 seems to be the ligand of choice because of its better accumulation in the striatum.

5-17-16 P.G.Bain L.J.Findley C.D.Marsden
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OBJECTIVE: To determine the phenotype of Hereditary essential tremor (HET). METHODS: 20 index cases with incontrovertible HET and their kindreds were studied (53 of whom were affected).

RESULTS: HET is autosomal dominant, with bimodal age of onset (median: 15yrs). Penetrance was virtually complete by the age of 65. The segregation ratio for affected/total kin was 0.46. There were no examples of the disease skipping a generation. Men and women were equally affected. The typical phenotype was a mild symmetrical action tremor of the upper limbs. No isolated tremors of the legs, head, face, voice, jaw or tongue were encountered and no dystonic postures occurred. There was a strong association with classical migraine but none with Parkinson's disease. Primary writing tremor and primary orthostatic tremor did not occur. 75% of head tremor was of a "no-no" variety. 50% of cases were alcohol responsive but in 20% of families heterogeneity of responsiveness was found. Tremor severity and disability increased with age and the duration of tremor but age of onset had no predictive value on outcome.

CONCLUSION: HET does not produce dystonia and differs in many respects from previous descriptions of "essential tremor".

5-17-17 ROPINEROLE: A DOUBLE BLIND PLACEBO CONTROLLED MULTICENTRE STUDY OF EFFICACY AND SAFETY IN EARLY PARKINSON'S DISEASE (MONOTHERAPY)

DJ Brooks, London; A Lees, London; R Abbot, Leicester; H Sagar, Sheffield; O Rascol, Toulouse; G Ebinger, Brussels; RAC Roos, London; D Philcox, Cape Town; G Nappi Pavia; G Murray, Reigate.

OBJECTIVE: To evaluate efficacy & safety of ropinirole vs placebo as "Monotherapy" in early Parkinson's Disease. BACKGROUND: Ropinirole is a novel, non ergot dopamine agonist with low dyskinetic potential from animal data. Efficacy/tolerability have been tested in open trials as adjunct to L-dopa & as early therapy. METHODS: Ropinirole or placebo were administered by dose-titration 0.5 mg - 5 mg bid in a study of 12 weeks duration. The primary efficacy criterion was ≥ 30% reduction from baseline in Total Motor Scores on the UPDRS. Secondary measures included CGI, Finger taps & ADL. RESULTS: Sixty three patients were randomised 2:1 to ropinirole (N=41, mean age 59.2) & placebo (N=22, mean age 56.5). Seventy percent of ropinerole & 40% of placebo patients showed ≥30% reduction on UPDRS Motor Scores (p=0.021) in the intention to treat analysis. Mild transient nausea and postural hypotension were observed but only 7% ropinirole & 4.5% placebo were withdrawn due to adverse events. CONCLUSION: Placebo controlled efficacy has been demonstrated for ropinirole in this 12 week study; a 1 year evaluation is completing.

5-17-18 WITHDRAWN

5-17-19 QUANTITATIVE ASSESSMENT OF PARKINSON'S DISEASE

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Optoelectronic camera systems provide a practical tool for truly objective and reproducible quantification of movement disorders in the clinic. The measurement system (MacReflex, Qualisys AB, Partille) is built upon an infra-red flashlight, reflective markers positioned on different parts of the subjects body and a videoprocessor-based camera which provides the Cartesian space coordinates of the markers to a Macintosh computer with a repetition rate of 50 Hz. Using a simple test movement (the PLM-test) where the subject is asked repeatedly to move a small object from a starting position on the floor a few steps forward and place it on top of a stand and an automatic computer analysis of the body movements, the degree of disturbance of postural (P), locomotor(L) and manual(M) reaching movements as well as their coordination into a smooth and purposeful movement can be quantitatively assessed. The movement time (MT) of the PLM-test is used as a simple measure of disability. With this technique it can be shown that patients display different PLM symptom profiles and that they respond differently to test doses of different treatments. Single-dose treatment with l-dopa has been used as a diagnostic procedure. All Parkinsonian patients responded with reduction of the movement time while this was not the case in some Parkinson-like degenerative diseases.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-17-20 BLOOD-TO-BRAIN IRON TRANSPORT IN PATIENTS WITH PARKINSON'S DISEASE (PD) MEASURED USING [52FE]-CITRATE AND POSITRON EMISSION TOMOGRAPHY (PET).

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Brain iron uptake in PD patients and in healthy subjects was measured using [52Fe]-citrate and PET. Iron is involved in the pathophysiology of PD. In particular, post-mortem studies of PD patients revealed specific increases of iron concentration in the substantia nigra. Fe-citrate binds almost completely to transferrin in the blood plasma. To date 6 PD patients (both levodopa treated and untreated) and 6 healthy controls were studied. Activity in the brain and in plasma was measured over two hours after tracer injection. Tracer influx constants (Ki) were calculated using multiple graphical plotting method for global brain, frontal cortex, striatum and cerebellum.

Little tracer uptake was found in healthy controls. No differences were found between various brain regions. Mean (SD) Ki for global ROI's were $2.96e^{-5}$ ($0.461e^{-5}$) in healthy controls. Ki values in PD patients were increased: mean $5.41e^{-5}$ ($1.64e^{-5}$).

These findings show increased iron transport across the blood brain barrier in patients with PD.

5-17-21 BROMOCRIPTINE-INDUCED DYSTONIA IN PATIENTS WITH APHASIA AND CORTICOSPINAL TRACT DYSFUNCTION

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Posthemiplegic dystonia is a rare complication of stroke, and is characterized by dystonic movements developing months or years after the acute event. During a drug-trial of bromocriptine in 7 aphasic patients, 5 patients developed a painful hemi-dystonia characterized by slow involuntary movements of the right arm and painful spasms of the right hand and foot. Dystonic movements started with a bromocriptine dosage of 34-40 mg, were most severe with 60 mg, and cleared away when bromocriptine dosage was tappered below 30 mg. All 5 hemidystonic patients had a moderate to severe hemiparesis, arm > leg. The dorsolateral, opercular, and parietal cortices were the only brain areas involved in all 5 patients, and only 3 patients had basal ganglia lesions. While the 2 patients that did not develop dystonia had a similar lesion location, they had less severe corticospinal tract dysfunction. In conclusion, this is the first report of bromocriptine-induced dystonia in stroke patients. This phenomenon may be related to bromocriptine stimulation of spinal motoneurons, either directly on dopaminergic receptors, or indirectly through the diencephalospinal dopaminergic system.

5-17-22 SUBJECTIVE UNSTEADINESS IN PARKINSON'S DISEASE

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Parkinson's disease (PD) patients frequently complain of unsteadiness. We studied the prevalence of subjective unsteadiness in patients with PD to determine if there is a correlation between the presence of this symptom and the presence of abnormalities of anteroposterior or lateral postural stability. Loss of postural response (retropulsion) and a tandem gait scale were utilized to assess stability.

We studied 47 parkinsonian patients, 34 males and 13 females, stages 1-3 Hoehn-Yahr scale. Twenty three patients (49%) reported subjective unsteadiness. There was no significant difference in age between those without unsteadiness and those with unsteadiness. The unsteady group had a higher proportion of females (43%) than the steady group (14.2%) ($p=0.02$). There was no significant difference between the groups with regard to falls, freezing, walking difficulties, or postural instability. Patients with tandem gait difficulties were significantly older regardless of group (60.6 vs 73). Subjective unsteadiness of gait did not correlate with an abnormality of tandem gait or postural instability.

We conclude that presence of subjective unsteadiness in PD does not correlate with abnormalities of postural stability. There is a strong association between abnormalities of tandem gait and age. Further studies are necessary to determine if abnormalities of tandem gait carry clinical consequences.

5-17-23 IS STOOPING A PREDICTOR OF PARKINSON DISEASE IN THE ASYMPTOMATIC SIBLINGS OF PARKINSON DISEASE PATIENTS ?

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Genetical predisposition in Parkinson disease has been debated. Whether classical Flexion Stooping Posture is present in the asymptomatic siblings of the Parkinson disease patient's is not known. To evaluate it the line of gravity for erect posture was estimated in 20 Parkinson disease patients and their siblings, 20 other movement disorder patient's and they were compared with the normal age matched controls. The results showed no increase in the stooping posture of the sibling as compared to the controls.

5-17-24 ELECTROCONVULSIVE THERAPY (ECT) IN PARKINSON'S DISEASE

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We examined the effects of right hemisphere ECTs on 15 patients, average age 63 years, disease duration 2 months to 16 years. Each patient received 4 ECTs, given separately over a one week period. Their clinical status was evaluated using the Unified Parkinson Disease Rating Scale, North Western University Disability Scale and the Hoehn & Yahr Staging System. Scoring was performed prior to, same day on and two weeks after completion of the course of ECT.

Average pre/same day post ECT scores for akinesia were 1.73/1.09, for tremor 1.82/1.09, for rigidity 2.00/1.27 and for Hoehn & Yahr staging 2.27/2.00. One patient developed levodopa dyskinesia. Corresponding values for pre/2 weeks post ECT scores were akinesia 1.79/1.00, tremor 1.79/0.79, rigidity 2.07/1.14 and Hoehn & Yahr 2.29/1.64. There were no significant changes in the disability score on walking, dressing, hygiene, eating, feeding and speech.

We believe unilateral right hemisphere ECT is particularly favourable in alleviating akinesia, tremor and rigidity in Parkinson's disease.

5-17-25 PROGNOSIS IN MULTIPLE SYSTEM ATROPHY AND PROGRESSIVE SUPRANUCLEAR PALSY - A PROSPECTIVE CLINICO-PATHOLOGICAL STUDY.

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Clinical studies indicate that prognosis in Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP) is less favourable than in the idiopathic Parkinson's disease but the literature on autopsy verified cases is sparse. We report our prospective observations in pathologically confirmed cases of MSA and PSP.

All patients were followed by one of us (AHR). Standard pathological criteria were used by a qualified neuropathologist (BR or LA) to make diagnosis of MSA and PSP.

13 MSA (M=8, F=5) and 4 PSP (M=4, F=0) cases were studied. The mean onset age in MSA was 51.5 $\pm$ 13.7 (range 21-77) and in PSP 62 $\pm$6.1 (range 55-68) years. On levodopa, 3 of 12 MSA cases had mild to marked syptomatic improvement but none of the PSP cases improved. The mean survival after onset in MSA was 9.9 $\pm$ 5.6 (range 6-23) and in PSP 7.3 $\pm$ 3.4 (range 4-12) years.

In summary, the age at onset is younger in MSA and comparable in PSP to IPD. The overall prognosis in both disorders is, however, worse than in IPD.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-17-26 DOES SLOW RELEASE LEVODOPA/CARBIDOPA BENEFIT COMPLICATIONS DUE TO REGULAR LEVODOPA/CARBIDOPA IN PARKINSON'S DISEASE?

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The slow release oral formulation of levodopa/carbidopa was developed to produce more constant levels of plasma levodopa/carbidopa, and hence, with the intention of reducing the number of of complications due to regular levodopa/carbidopa. In this study, we present our data of randomly selected 100 patients who were switched from standard levodopa/carbidopa to the slow release preparation for complications like wearing off, freezing, dyskinesias, psychosis, peak dose confusion and orthostatic hypotension. we will also discuss which of these needed patients needed standard levodopa/carbidopa in addition to the slow release preparation. This study should clarify if the slow release levodopa/carbidopa serves the purpose for which it was introduced in the management of Parkinson's Disease. Supported by the Parkinson's Disease Foundation, USA.

5-18-01 MULTIPLE SCLEROSIS IN NATIVE SAUDIS

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Ninety-eight cases of clinically definite or laboratory-supported definite multiple sclerosis (MS) were seen at a major referral center in Saudi Arabia. The mean patient age was 32.7 years (range 14-63) with a female to male ratio of 1.6:1. Familial occurrence was noted in only two cases. There was no history of migration or travelling abroad and geographic distribution showed no predilection to specific region. The case ascertainment per year increased significantly during the last four years. The course was relapsing-remitting in 54%, primary progressive in 18% and secondary progressive in 28%. Visual symptoms were the presenting complaint in 32%, limb weakness in 29% and sensory complains in 16% of patients. The disability was severe in 31%, moderate in 28% and mild in 49%. Eleven percent of patients were be-ridden in < 5 year.

MRI studies were positive in 94%. Oligoclonal bands were present in 66% and elevated IgG synthesis index in 92% of patients.

We conclude: (1) MS is under-reported in Saudis, (2) improved health standards and medical awareness leads to more accurate and earlier diagnosis, and (3) MS in native Saudis has: clinical and neuro-imaging features similar to other Caucasians.

5-18-02 T CELL RECEPTORALPHA CHAIN GERMLINE POLYMORPHISM IN MULTIPLE SCLEROSIS: AN ASSOCIATION AND LINKAGE STUDY

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Although the cause of Multiple Sclerosis (MS) is unclear, several epidemiological observations suggest that genetic factors may influence susceptibility to the disease. An association between the major histocompatibility complex and MS is well known, but pedigree analysis supports the hypothesis of polygenic disease control. Recently the potential role of other molecules involved in the immune reponse, such as T cell receptor (TCR) has been proposed.

To evaluate the role that TCR alpha chain genes may have in MS susceptibility, two constant and one variable alpha chain polymorphisms were evaluated, using RFLP, for associations in MS patients. No significant differences in allele and genotype frequencies between MS patients and healthy controls were observed. In addition, we studied 54 families, using the method of identity by descent in affected sibling pairs, to evaluate linkage between TCR alpha chain genes and MS. No significant increase in haplotypes shared by affected siblings over that expected by chance was found. Our results do not support a role for germline TCR alpha chain genes in the genetic susceptibility to MS.

5-18-03 CHANGING PATTERNS OF MULTIPLE SCLEROSIS IN SOUTH AFRICA

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In 1949, 84% of multiple sclerosis (MS) patients in South Africa (SA) were immigrants or had been out of the country (Dean). In 1967, although 158/281 (56%) MS patients were born in SA, (57/281 (20%) of Afrikaans origin), 169/281 (60%) were either immigrants or had been out of the country, none were black (Dean). This study demonstrates that MS is becoming more common in South African born patients especially those of Afrikaans origin.

METHOD: SA patients with definite MS completed a survey identifying home and school language, place of birth of self, parents, grandparents and visits out of SA.

RESULTS: Of 1000 MS patients who are presently members of the SA MS society (20/100,000 white pop.), 404 of all races responded. 394 were white patients (93 male, 301 female). 309 (75%) were born in SA, 204 of at least 2nd generation. 101/404 (25%) were 3rd generation SA born of exclusive English origin and 127/404 were "mixed" (2 or more parents or grandparents of Afrikaans origin). 151/394 (37%) were either immigrants or had been out of South Africa.

CONCLUSION: 253 (63%) SA white patients with MS have never left the country, 25% are 3rd generation Afrikaners, the disease remains rare in other racial groups especially black patients. SA has an unusual genetic, ethnic, racial and geographical status thus future country wide epidemiological accuracy is important to ascertain.

5-18-04 LYMPHOCYTE SUBSETS IN THE CSF OF MS PATIENTS DURING AND AFTER AN ACUTE RELAPSE

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T-lymphocytes which belong to CD8+CD11b+ and CD4+CD45RA+ populations are scarce in the CSF during an MS-relapse. Functionally, suppressor and suppressor-inducer cells belong to these two groups. Activated T-cells with CD3+HLA-DR+ phenotype have been reported as increased in the CSF compared to peripheral blood (PB) in MS patients during a relapse. We have now analyzed the relative number of these cells in the CSF and PB during and two months after a relapse and compared the results to those in patients with other neurological diseases (OND). Lymphocyte subsets were analyzed by flow cytometry using two colour immunofluorescence staining techique.

CD4+CD45RA+ cells are extremely rare in the CSF compared to PB both in OND and MS patients while their relative number is the same during and after an MS-relapse. The percentage of CD8+CD11b+ cells is also very small in the CSF both in MS and OND patients and particularly small during the relapse. The proportion of activated T cells is high in the CSF compared to PB. This is the case particularly in the CSF of OND and MS patients after the relapse while the percentage of activated cells decreases during the relapse.

5-18-05 HHV-6 LATENT INFECTION IN A MULTIPLE SCLEROSIS PATIENT. MOLECULAR ANALYSIS.

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In previous studies from our laboratory, we found serum antibody titres against HHV-6 significantly higher in multiple sclerosis (MS) patients than in normal controls. Nevertheless, the PCR performed in peripheral blood mononuclear cells (PBMCs) DNA showed HHV-6 specific sequences in only one out of 32 MS examined. This finding was confirmed by Southern Blot analysis, which revealed a considerable amount of HHV-6 genomic material, suggesting the presence of a viral latent infection in this patient. In order to gain some insights into the state of viral genome, we used pulsed field gel electrophoresis (PFGE) to separate the DNA directly from the PBMCs of the patient and from HHV-6 infected HSB-2 cells. Our study showed the presence of intact HHV-6 genome (170 kb) only in the HSB-2 DNA. The restriction analysis of the patient's PBMCs DNA, at variance with HSB-2 DNA, showed fragments higher than the 170 kb segment, indicating that the viral sequences are linked to the cellular DNA, and suggesting a latent infection in which HHV-6 is integrated "in vivo".

5-18-06 Pregnancy and multiple sclerosis.
A 5-year follow-up study.
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The controversy on whether the prognosis of multiple sclerosis (MS) in women is affected by pregnancy is longstanding. In January 1986, 39 women with definite MS were identified by reproducible selection to estimate the effect of pregnancy and childbirth on the long term prognosis. Impairment was estimated by the Kurtzke Disability Status Scale Score (DSS). On follow up 5 years later, four were dead and three declined participation. Of the 32 remaining, 9 had no children, 9 had onset of MS not less than 6 months after last childbirth and 14 had onset of MS before or in connection with childbirth. At the time of identification there was no significant variation in age or duration of illness. At follow up the condition was found to have deteriorated in that DSS had risen significantly, (p=0.017). The rise was found for women with no children, (p=0.012), and women with onset of MS before or in connection with childbirth, (p=0.021). It appears from this study and available literature that pregnancy or childbirth do not affect the longterm prognosis of MS in women.

5-18-07 Pain syndromes in multiple sclerosis.
A 5-year follow-up study.
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Recent studies have demonstrated that pain syndromes occur more frequently in multiple sclerosis (MS) than believed earlier. The Purpose of the 5-year follow up is to estimate the frequency of chronic and acute pain syndromes in 35 patients with definite MS (17 females and 18 males). At follow up it was found that 74% had chronic pain syndromes as against 40% at the start of the study; acute syndromes were registered for 69% at follow up as against 31% at the start. A total of 77% had pain, most had both acute and chronic syndromes. Eighty per cent of the patients with myelopathy had pain syndromes. The increase in frequency over time was independent of sex, signs of depression, cognitive deficits and deterioration according to the Kurtzke Disebility Status Scale. The most frequent form of chronic pain syndrome was tension and pain in extremities (80%) followed by spasms and tonic seizures, low back pain and dysaesthesia. The most frequent acute syndrome was tonic seizures (60%), followed by neuralgia, Lhermitte's sign and pain in connection with optic neuritis. Management and rehabilitation implications are discussed.

5-18-08 AN ATYPICAL MULTIPLE SCLEROSIS SYNDROME IN WOMEN WITH SILICONE BREAST IMPLANTS OR SILICONE FLUID INJECTIONS INTO BREAST.
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Eleven women developed at an average latency period of 5 years (range 3 months - 13 years) a multiple sclerosis syndrome after receiving silicone-gel breast implants (n=10) or silicone fluid injections into breast (n=1). All had a history and neurological findings compatible with multiple sclerosis. Additional symptoms included myalgia (n=10), morning stiffness (n=10), memory deficits (n=8), Sjogren's syndrome (n=7), arthralgia (n=5), joint swelling (n4), rash (n=3) and Raynaud's phenomena (n=4). All patients had oligoclonal bands in their spinal fluid. Ten patients had visual evoked responses taken, which were found to be delayed in all. Ten had multiple periventricular white matter lesions on MRI and 8 had autoantibodies. These women had developed symptoms and findings of multiple sclerosis along with the symptoms previously reported in women with silicone adjuvant breast disease. Further studies are needed to evaluate nervous system diseases in women with silicone breast implants or silicone fluid injections.

5-18-10 ACTIVATION OF BRAIN MAST CELLS (BMC) IN MONKEY EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS (EAE)
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As we found in our previous *in vitro* studies, mast cells can degrade brain myelin, while myelin basic protein (MBP) causes mast cell secretion. Both phenomena are more pronounced in strains of rats and mice which are susceptible to EAE, than in resistant ones. Our recent data also revealed increased level of tryptase, a proteolytic peptide specific only for mast cells, in cerebrospinal fluid (CSF) of patients with MS. Moreover, mast cell mediators are able to alter blood-brain barrier (BBB), which is crucial for MS pathogenesis. We investigated the ultrastructure of BMC after their natural *in vivo* exposure to MBP during the course of EAE. The disease was induced in *Callithix Jacchus* monkeys by single immunization with human brain homogenate in complete Freund's adjuvant. Additionally, a suspension of *Bordatella pertussis* was injected intravenously immediately after immunization, as well as two days later. Severe neurologic symptoms, including tetraparesis, were seen 22 days after immunization. Brain samples (white matter, as well as thalamus and hypothalamus) were removed within 20 min from the time of the animal sacrifice. The tissue was fixed in 2.5% glutaraldehyde with 0.5% tannic acid in 0.1 M phosphate buffer for 24 hours at 4°C. The samples were then washed, postfixed in 2% osmium tetroxide, dehydrated in graded alcohols, embedded in Epon and observed under electron microscope. Ultrastructural changes of BMC showed extensive loss of granular electron-dense contents, indicating secretion (40 - 70% of the granules were empty). Presented data confirm our other findings of BMC activation in demyelinating diseases.

5-18-11 OPPOSITE EFFECTS OF LIDOCAINE ON POSITIVE AND NEGATIVE *SYMPTOMS OF MULTIPLE SCLEROSIS*
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In the demyelinated part of nerve fibers, impulses are conducted with low safety factors, since action current generated at a node of Ranvier is shunted to demyelinated internodal membrane. If a Na channel blocker is applied to such a part, it would reduce action current and hence current reaching next node further, blocking conduction of impulses, at a dose which has no or little effects on conduction of normal fibers. Thus, it would unmask or worsen negative symptoms derived from silent or silent fringe of demyelinative lesions in multiple sclerosis (MS). On the other hand, it would ameliorate positive symptoms by blocking abnormal impulses. Furthermore, a demyelinated segment which produces abnormal impulses should be more depolarized and have higher firing rates, required dose of lidocaine which is a voltage-dependent Na channel blocker would be smaller for alleviating positive symptoms than for provoking negative symptoms.

Under this hypothesis, we applied lidocaine to MS patients intravenously (mean plasma concentration, 2.8 ug/ml). As the hypothesis predicts, lidocaine elicited subclinical symptoms or enhanced preexisting ones, both reversibly, in 23 of 28 MS patients studied; but it had no effect on control subjects (n=26). Further, it improved positive symptoms of MS patients (n=20): it abolished paroxysmal symptoms (and a sign) including painful tonic seizure (n=4), paroxysmal pain (n=3) and ithing (n=1), and Lhermitte's sign (n=10). Non-paroxysmal symptoms like persistent numbness and pain were also ameliorated. Lower doses were required for suppressing positive symptoms than provoking negative ones.

5-18-12 APOLIPOPROTEIN E INTRATHECAL SYNTHESIS (ITS) IN MS
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Apo E determination by EIA in serum and CSF of 108 neurological (41 definite MS + 30 VIH1 infected + 37 other neurological) patients compared to 9 controls lead to the following conclusions :
- Apo E is a normal constituant of the CSF (1.4 ± 0.3µg/ml)
- As suggested by blood/CSF ratio and CSF Apo E/CSF Albumin ratio, and calculated by an empirical formula, 85% of CSF Apo E derives from an ITS which is physiological (1.2 ± 0.3 µg/ml).
- In MS sera : no significant difference with the 2 other patient groups
- Apo E ITS : significant decrease ($p < 0.05$) correlated with the disability grade, but not with the age of the patient, the duration of MS or the type (remittent or progressive) of course.
Such a correlation is not found with other apos (AI, AII, B, H and (a)). Thus Apo E may be involved in myelin repair.

5-18-14 MYELIN ANTIGENS SPECIFICITY OF AUTOANTIBODIES FROM MULTIPLE SCLEROSIS AND OPTIC NEURITIS CEREBROSPINAL FLUID

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Myelin basic protein (MBP) and proteolipid protein (PLP) were purified from normal human brain tissue. Autoantibodies to MBP (anti-MBP) and PLP (anti-PLP) were detected in cerebrospinal fluid (CSF) of patients with optic neuritis and multiple sclerosis (MS) by a solid phase radioimmunoassay.

Anti-MBP was elevated in 47/53 optic neuritis patients. Anti-PLP was detected in the remaining 6 patients which did not have measurable levels of anti-MBP. Antibodies to both antigens were not found in any of the 53 optic neuritis CSFs.

369 clinically definite multiple sclerosis patients were clinically divided into 173 with acute relapses, 109 with progressing disease and 87 in remission.

- 169/173 acute relapses had increased anti-MBP, 3/173 had increased anti-PLP and 1/173 had no antibody
- 108/109 progressing's had increased anti-MBP and 1/109 had increased anti-PLP
- 15/87 remissions had somewhat elevated anti-MBP, none had anti-PLP

From an immunochemistry point of view there may be at least two forms of MS: a common form highly associated with elevated anti-MBP and a more infrequent form associated with detectable anti-PLP. To date, autoantibodies to these two myelin proteins were not simultaneously detected in any CSF of individual optic neuritis or multiple sclerosis patient.

5-18-15 PREVENTION OF CHRONIC RELAPSING EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS BY SOLUBLE TNF RECEPTOR I.

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The effect of soluble TNF receptor I (sTNFrI) of high neutralizing activity of TNF was investigated with a form of experimental autoimmune encephalomyelitis (EAE) in SJL/J mice induced by the adoptive transfer of myelin basic protein (MBP)-sensitized T lymphocytes, an animal model of the human disease multiple sclerosis. No mice sensitized for EAE and then treated with sTNFrI by intraperitoneal injections (every day or every second day) developed signs of CNS disease. Examination of CNS tissue from sTNFrI-treated animals showed no pathologic changes. CNS tissue from control animals demonstrated extensive inflammatory cell infiltration and demyelination. In experiment in which animals received only bolus sTNFrI injection the frequency and severity of EAE was significantly reduced. To test whether sTNFrI therapy is inhibiting to encephalitogenic cells, preincubation of MBP-sensitized T lymphocytes with sTNFrI in vitro prior to injection into recipient mice resulted in no dimunition of their ability to transfer EAE. The effect of sTNFrI treatment was long lived and sustained for 6 weeks. These findings suggest that sTNFrI may have important application to the development of new therapeutic strategies for MS.

5-18-16 T CELL VACCINATION AS AN IMMUNOTHERAPY IN MS

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Autoimmune mechanisms have been implicated in the pathogenesis of multiple sclerosis (MS). Recent advances in the treatment of experimental autoimmune encephalitomyelitis (EAE) by T cell vaccination have provided new prospect that MS may be amenable to treatment in a similar fashion. In this report, we conducted a phase one clinical trial that employed this approach in treatment of MS. Eight patients with MS were inoculated with irradiated myelin basic protein (MBP)-specific T cell clones isolated from their peripheral blood and were closely monitored for immunological and clinical effect for more than 16 months. Our studies suggest that this T cell vaccination induced a specific immune suppression. The immunological responses to the T cell inoculates and their association with specific immune suppression as well as clinical effect are discussed.

5-18-17 TOTAL LYMPHOID IRRADIATION(TLI) IN MULTIPLE SCLEROSIS(MS)

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Seven patients with definite MS (4 females and 3 males) who failed to stabilize their progressive neurological symptoms on oral immunosuppressive therapy (Prednisone, Azathioprine or Cyclophosphamide) underwent TLI. The average age of the patients at the time of TLI was 41.0 ± 4.8 and their average score on Kurtzke expanded disability status scale was 5.6 ± 0.9 (1σ). Prior, during and following the TLI immunophenotypic studies in peripheral blood inluding two color (four parameter) cytometric studies were performed. In course of the TLI 2400 cGy in 13 fractions were applied in two series starting with supradiaphragmatic and followed by infradiaphragmatic irradiation. The average lymphocyte concentration in the MS patients irradiated reached 117.1 ± 41.4 per cmm. In 5 of the patients studied transient improvement in their objective neurological symptomatology occurred during the weeks 2-10 from the beginning of TLI. Progression in objective neurological symptomatology started between 3-11 months from the beginning of TLI. Marked variations in the immunophenotypic profile, including delayed increase in the percentage of B cells, activated CD3 and/or CD2 cells and NK cells, were established in all patients studied.

5-18-18 IMPAIRED PROCEDURAL LEARNING IN NON-DEMENTED MULTIPLE SCLEROSIS PATIENTS

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The pattern of cognitive impairment in Multiple Sclerosis (MS) is similar to that of subcortical dementias. Aim of this study was to evaluate motor and cognitive procedural learning in MS patients. Twenty non-demented, mildly or moderately physically disabled (EDSS< 6) MS patients and 20 controls underwent a pure-motor procedural learning test (Tracking Learning Task - TLT) and two cognitive procedural tasks: one visuo-perceptual (Mirror Reading Learning Task - MRLT) and the other visuo-spatial (Puzzle Learning Task - PLT) . Each test was administered 3 (T2) and 24 hours (T3) after the baseline evaluation (T1). We performed repeated measure ANCOVAs with T1 performance as covariate, to eliminate the effect of baseline motor and cognitive impairment. This analysis revealed a group effect only on the two cognitive learning tasks (MRLT - T2: $F=6.59$, $p<0.005$; T3: $F= 7.27$, $p<0.0003$ and PLT - T2: $F=4.16$, $p<0.02$; T3: $F= 5.08$, $p<0.01$) .

In conclusion, also cognitive procedural learning is impaired in non-demented MS patients . This finding suggests that not only nuclear lesions like those occurring in Huntington's and Parkinson's diseases, but also neural fronto-subcortical disconnections can cause procedural memory dysfunction, increasing the similarities between these conditions.

5-18-19 MULTIPLE SCLEROSIS IN GORSKI KOTAR, CROATIA

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An epidemiologic descriptive and analytic investigation on multiple sclerosis (MS) in Gorski Kotar was carried out during the period from 1988-1992. It identified 139 potential MS patients. According to Poser`s criteria, 74 clinically definite and laboratory supported definite MS patients were ascertained. On 31 March 1991,the prevalence day,36 nature-born MS patients were still living in this area.The crude prevalence of MS in Gorski Kotar amounted to $117.86/10^5$ inhabitants (stand.prevalence $122.34/10^5$ inh.; 95% CI:85.66-162.60) The disease was more frequent in Čabar ($193.46/10^5$ inh., 95 CI: 15.26-88.85). The sex ratio (F/M) was 1.76. The mean age at onset was 24.56, SD 9.45 years. The age of MS patients on prevalence day was40.58, SD 12.53 years. The duration of illness up to prevalence day was 16.3, SD 9.2. Theannual mean incidence (1948-1991) was $3.98/10^5$ inhabitants.The clinical type of disease was remittent in 90.5%, and progressive in 9.5 MS patients. In a case-control study (method of odds ratio) MS patients consumed daily different quantities of fullfat unskimmed milk, potatoes with lard and fresh or smoked pork meat and new potatoes more frequently than controls, which was statistically significant MS patients more frequently than controls reported a history of trauma to head, neck or spine (OR=4.87, CI=1.48-15.9; $\chi^2=5.97$, p=0.014). Familiar clustering of MS patients (less in the eastern part: municipality of Vrbovsko, land of Severin, and more present in the western and southeren part:municipalities of Čabar and Delnice) strongly supports the hypothesis the genetic factors are fundamental in determining MS susceptibility in Gorski Kotar, Croatia

5-18-20 CORRELATION BETWEEN HLA ANTIGENS AND CLINICAL AND LABORATORY FINDINGS IN ITALIAN MULTIPLE SCLEROSIS PATIENTS

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A total of 161 Multiple Sclerosis definite patients, 68 of which with Chronic Progressive MS (CPMS) and 93 Relapsing Remitting (RRMS) and 128 ethnically homogeneous and no consanguineous healthy controls have been typed using microlymphocytotoxicity test.The frequency of HLA-Cw7 and DR2 antigens are significantly higher both in CPMS and RRMS compared with controls; on the contrary HLA-Cw1 and DR4 are significantly more frequent in the controls. The study of HLA distribution using cluster analisys showed the HLA-A2-Cw7-B7-DR2-DQ1 could be a characteristic phenotipe of CPMS patients because its frequency in this group (8.8%) appeared significantly higher ($p<0.05$) than in the controls (1.5%). The relationship between HLA distribution, Kurtzke's EDSS and some laboratory parameters (CSF oligoclonal bands, IgG Index, Tourtelotte) have been also evaluated.

HLA-Cw7 is significantly more frequent in MS patients with Oligoclonal Bands (OB+CSF) than in those with a negative CSF (OB-CSF) while HLA-DR4 is more frequent in OB-CSF compared to OB+ CSF patients. Similarly HLA-Cw1 antigen is significantly more frequent in OB-CSF RRMS than in OB+CSF RRMS patients.On the whole our results suggest a possible role of Cw7 antigen in the susceptibility to the disease and, on the contrary, a protective role for DR4 and Cw1 antigens.

5-18-22 CENTRAL PAIN IN MULTIPLE SCLEROSIS.

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The study investigated the characteristics of central pain in MS, and the other neurological symptoms of these patients, with an emphasis on sensory abnormalities.

255 patients with MS responded to a questionnaire regarding pain and sensory disturbances. All 172 who reported pain were telephoned by one of the investigators and those with suspected neurogenic pain were examined at the outpatient clinic and entered into the research program, which included clincial and quantitative sensory testing, neurography, SEP, CSF assays, MRI, evaluation by physiotherapeut, occupational therapeut and social worker, and psychological inventories.

64% of the 255 patients reported pain, of which 21% was nociceptive pain (back, neck, joints, etc), 21 % headache, and 22% neurogenic pain. 21% had central pain (including 5% with trigeminal neuralgia). Non-paroxysmal central pain had the following characteristics: in 88% the pain location included the lower extremities, in 18% the upper extremities; aching (60%), burning (52%) and pricking (33%) were the most common qualities; 78% had constant pain; 49% had no paresis, 63% no ataxia; the sensibility to temperature and pain was most severly abnormal, whereas touch and vibration were less abnormal; one patient had normal sensibility.

A majority of MS patients have pain, and about one in five have central pain, which is predominantly located in the lower extremities, and in the face as trigeminal neuralgia. Central pain is accompanied by sensory abnormalities dominated by abnormal pain and temperature sensibility.

5-18-23 PLACEBO EFFECT IN MULTIPLE SCLEROSIS (MS)?

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OBJECTIVE: to discover if and how much "placebo effect" there might be in patients with MS. METHODS: With Kaplan-Meier survival analysis, we compared the clinical course of patients taking placebos in two therapeutic trials with those taking standard of care treatments in a MS clinic. Worsening means a one step increase in Kurtzke's DSS or EDSS score sustained 3 or more months. RESULTS: For the clinic cohort (n=310) 24% worsened within one year; 33% in 2 years; and 47% in 3 years. For the azathioprine (aza) placebo cohort (n=33) 15% worsened in 1 year; 24%, 2 years; and 49%, 3 years. For the cyclosporine placebo group (n=272) 14% worsened in 1 year; and 25% in two years. The differences between the clinic and the placebo cohorts are significant (chi squared, $p<0.01$) except aza placebo vs clinic at 2 years. CONCLUSIONS: This study indicates a placebo effect, in the first two years of a therapeutic trial, which seems to disappear in the third year. The placebo effect could lead one to falsely attribute efficacy in an uncontrolled therapeutic trial. These findings should be taken into account when planning and interpreting therapeutic trials.

5-18-24 LATE ONSET MULTIPLE SCLEROSIS: CLINICAL AND LABORATORY FINDINGS IN 30 PATIENTS

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Objectives: The clinical features and CSF laboratory findings of 30 patients with late onset multiple sclerosis (LOMS) were studied.

Backround: Multiple sclerosis in the elderly gives frequently diagnostic difficulties, because well-accepted diagnostic criteria exclude this group of patients from diagnostic consideration.

Patients and Methods: A group of 30 patients (19 females) treated at the Department of Neurology between 1989 - 1991 was analyzed. Only patients with diagnosis of MS according to Poser's criteria with age over 50 at onset were included. Symptoms at onset, mode of onset, severity of disease according to Kurtzke's Expanded Disability Status Scale (EDSS) were analyzed, CSF and serum were determined as regards mononuclear pleocytosis, concentration of total protein, immunglobulin G as well as the serum/CSF ratios of IgG and albumin.

Results: The predominant initial signs and symptoms showed in 62.5% slow deterioration of motor function, especially spastic paraparesis, mode of onset was monosymptomatic in 66.7%, in 86.5% of the patients more severe and very severe neurological dysfunction was seen. In CSF 93.2% of these patients presented positive oligoclonal banding and IgG index was increased in 66.6%.

Conclusion: Our results suggest, that there are certain clinical features which characterize patients with LOMS and that CSF neuroimmunological techniques, including quantitative determination of IgG levels and detection of oligoclonal bands, are of high diagnostic yield in older patients presenting LOMS.

5-18-25 INTERLEUKIN-2 (IL-2) EFFECT ON CYTOTOXIC ACTIVITY IN MULTIPLE SCLEROSIS (MS).

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Incubation of peripheral blood mononuclear cells (PBMC) with IL-2 leads to the generation of lymphokine activated killer (LAK) cells. LAK cells can lyse not only tumor and virus-infected cells but also oligodendrocytes in vitro. Some authors found increased serum IL-2 level in MS and we hypothesized it could induce LAK cell generation in vivo.

Using Daudi cells (a B lymphoma cell line sensitive to cytotoxic activity of LAK cells) in 4-hour ^{51}Cr release assay we investigated the spontaneous and the IL-2 -induced cytotoxic activity of PBMC from MS patients and controls (NL).

We observed no significant difference in IL-2-induced and spontaneous cytotoxic activity between MS patients and NL (IL-2-induced cytotoxicity in MS=43±28.6%, in NL=42.7±17.6%; spontaneous cytotoxicity in MS=25.8±14.5%, in NL=26.2±8.2%) and between stable and active MS patients (IL-2-induced cytotoxicity in stable MS=48.6±36.6%, in active MS=38.5±10.7%; spontaneous cytotoxicity in stable MS=26.2±18.2%, in active MS=31.8±4.5%).

Our results suggest that in MS the significance of peripheral LAK cell function is unclear. Further studies of LAK cells in MS plaques or cerebral spinal flow are necessary to clarify whether LAK cells could contribute to demyelination and the development of a particular clinical form of MS.

5-18-26 IMMUNOSUPPRESSIVE TREATMENT OF MULTIPLE SCLEROSIS WITH 15±DEXOXYSPERGUALIN (DSG). EFFECTS ON CEREBROSPINAL FLUID PARAMETERS.

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DSG is a potent new immunosuppressive drug. A possible way of action may be depression of B-lymphocytes.

Therapy with DSG results in considerable longer survival of organ transplants and in chronic relapsing EAE a reduction of clinical symptomes was achieved. In autumn 1992, an early phase-II-study was started in Europe, which was placebo controlled, prospectively randomized and double blind. It contained three parallel groups treated either with placebo or 2 mg DSG/kg and 6 mg DSG/kg resp. Inclusion criteria were: age between 18 - 50 years, EDSS ≥ 1 focus in MRI with gadolinium enhancement within two weeks before commencement of therapy. In Hannover 24 patients were recruited who had agreed to lumbar puncture before entry into the study and immediately after the fifth course of treatment. The following CSF parameters were evaluated: cell count, subtypes of lymphocytes, intrathecal IgG synthesis, oligoclonal band pattern, concentrations of myelin basic protein and tumor necrosis factor α. These data will be correlated to MRI findings, i.e. integrated plaque volume and number of enhanced foci. At this time no final results can be given because of the blind character of the study.

5-19-01 AZT EFFECTS ON HUMAN MUSCLE CELLS AND IN ANIMAL MODEL

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Long-term administration of zidovudine (AZT) in AIDS patients induces a mitochondrial myopathy, associated with mitochondrial -DNA (mtDNA) depletion, probably due to AZT incorporation during the mt-DNA replication. Two experimental models of AZT-induced mitochondrial toxicity have been studied. 1) Primary human muscle cultures from normal adult and old controls, Alzheimer's Disease, and mitochondrial disease patients were evaluated during proliferative and differentiative stages, adding different AZT concentrations to the medium (range 5-250 uM). At the highest doses, proliferative rates were decreased starting from the third day. Cytoplasmic inclusions accumulated in differentiating myoblasts of AD and mitochondrial disease patients starting from the third day. Respiratory chain enzyme activity did not differ in treated and untreated cells. 2) Sprague-Dawley rats were given AZT (1 mg/ml) in drinking water for 35 days. Cerebral functions, such as total motor activity (Digiscan Animal Activity Monitor) and spatial memory (Morris task), were unaffected by treatment. Cortical cerebral mitochondrial activity evaluated by polarography and respiratory chain enzymology did not show any significant difference in treated (n=6) and untreated animals (n=6). Southern blot analysis of cerebral tissue mtDNA did not demonstrate qualitative and quantitative variations.

5-19-02 EXPRESSION IN HUMAN FIBROBLASTS AND MUSCLE CELLS OF A ACYL-CoA DEHYDROGENASES DEFICIENCY

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Acyl-CoA Dehydrogenases catalyze the first reaction in the fatty acid beta-oxidation spiral in mitochondria.Genetic defects of 3 Acyl-CoA DH with overlapping substrate specificities has been characterized:long-chain (LCAD), medium chain (MCAD) and short-chain (SCAD).The clinical phenotypes associated with these deficiencies are extremely variables. The clinical picture ranges from cases with neonatal onset,vomiting,hypoglicemia,metabolic acidosis and rapidly fatal outcome, to juvenile or adult cases that are much less frequent and have a heterogeneity of biochemical and clinical features such as muscle weakness and recurrent metabolic crisis.We report a case of a 27 year-old woman that had been complaining of muscle weakness since the age of 13.First muscle biopsy showed lipid storage myopathy and decreased levels of carnitine. A second muscle biopsy after riboflavin treatment was normal and the symptomatology rapidly improved.Muscle and fibroblast cell cultures did not show lipid storage in standard condition. Massive and clonal muscle culture and skin fibroblasts obtained from this patient showed a normal growth curve and a normal differentiation. Conversely in these cultures grown in a specific Medium without riboflavin an increase of citoplasmic inclusions has been observed. Sudan Black, Nile Red, Oil Red Oil demonstrated lipid storage in fibroblasts and in myotubes. Cultures were also characterized for activity of Acyl-CoA DH and type of deficit, and lipid storage was analyzed by gas chromatography.

5-19-03 CARDIOMYOPATHY, MENTAL RETARDATION AND VACUOLAR MYOPATHY ASSOCIATED WITH DESMIN TYPE INTERMEDIATE FILAMENTS.

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The clinical and morphological findings of a family affected by vacuolar myopathy, mental retardation and severe cardiomyopathy are reported. Several members of this three- generation family were similarly affected: all males had the complete phenotype, including a lethal hypertrophic cardiomyopathy, while all females only had mild signs of cardiomyopathy. This form is compatible both with X or autosomal dominant inheritance. The vacuoles found on skeletal muscle biopsy were of sarcolemmal origin. Accumulation of desmin-type intermediate filaments was documented using immunocytochemistry both in the skeletal and cardiac muscle. No evidence of polyneuropathy was found after detailed electrophysiological investigation. These findings are discussed in the light of all previous reports with related conditions.

5-19-04 REGULATION OF CELL CALCIUM IN DOG DYSTROPHIC MUSCLE

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The Golden Retriever Dystrophic dog is the only animal model which corresponds genetically and clinically to human Duchenne Muscular Dystrophy. In skeletal muscle samples from affected dogs we have analyzed three of the cellular systems involved in calcium homeostasis: the sarcolemmal calcium pump and dihydropyridyn receptor, and the sarcoplasmic reticulum ryanodine sensitive receptor. Preliminary results have shown a significant reduction of the total amount of the two calcium channels and alterations of the sarcolemmal calcium pump. Results on the latter enzyme suggest the possibility that an isoform of the pump, slightly lighter than the canonical 134 Kda enzyme, may be specifically enriched in the dystrophic muscle.
We have explored the Ca-dependent proteolysis of the plasma membrane calcium pump, which is a preferred calpain substrate however, the dystrophic samples analyzed did not show any preferential degradation of the pump by calpain.

5-19-05 LONG TERM DEFLAZACORT TREATMENT IN DUCHENNE MUSCULAR DYSTROPHY

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We have previously reported the benefits of Deflazacort (DF), an oxazolinic derivative from Prednsone, on muscle strength and function in Duchenne Muscular Dystrophy (DMD) (Neurom. Dis. 1: 261, 1991) and we have also shown that there is a dose response relationship (AAN 92). 95 patients are now under treatment, including 10 in advanced stage (wheelchair), 45 for over 1 year including 25 for more than 2 years. Side effects after 2 years continue to be moderate being increased appetite the most frequentt(70%); Cushingoid appearance 35%; mild hyrsutism 35%. No patient had to be withdrown from treatment because of side effects. Average weight gain after 2 years is in a lower percentile (30 to 26) than baseline. Myomertic strength/functional ability possitive ratio is mantained after 2 years. There is a decline in muscle strength after the 2 nd year but average values are still significantly higher than baseline. Younger patients (< 7.5 y) improve more than older ones. No significant improvement is obtained in weelchair bound patients. These data may suggest that more benefits could be achieved with early Steroid treatment in DMD. Adequate controls minimize side effects using DF as the therapeutic agent.

5-19-06 IMMUNOCYTOCHEMICAL STUDY OF DYSTROPHIN & RELATED CYTOSKELETAL PROTEINS BY QUICK-FREEZING AND DEEP-ETCHING METHODS

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Three-dimensional localization of dystrophin and its relationship with other cytoskeletal proteins such as spectrin, actin etc. were investigated on cultured mouse muscle cells immunocytochemically by quick-freezing and deep-etching (QF-DE) method. Dystrophin was localized granurally just underneath the plasma membrane and was close linked with filamentous networks with diameter of 8-10 nm, which were decorated with myosin subfragment-1 (S-1). They were considered as actin filaments. Some short cross linking filaments were inserted into these filaments. Another highly interconnected filamentous networks with various diameter were mainly localized in actin-poor regions. They were decorated by immunogold products of antispectrin antibodies. So there was less association of spectrin with actin filaments ,as compared with dystrophin, in cultured mouse myotubes.
The present studies show that in developmental stage of muscle cells, dystrophin and spectrin were differently organized and they might play an important role in the cell membrane stability against muscle stretch and contractions.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-19-07 "STICK-MAN"- REPORT OF FIVE CASES OF FAVORABLE EVOLUTION

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Congenital Muscular Dystrophy (CMD) is characterized by a variable clinical picture, including muscle weakness, neuropsicomotor developmental retardation, ocular anomalies and alterations of the Central Nervous System (CNS) white matter. Among the subtypes of CMD without CNS involvement, a form described as "Stick-man" is included (Goebel,1980). Here we report five cases, between ages 5-17, all of which present an absolutely skeletal phenotype. In spite of the generalized dystrophic appearance, the muscle weakness is subtle with diffuse but mild fibrotendinous retractions. The muscle biopsy shows a common finding that consists of the variation in muscle fiber diameter among fascicles. Angular fibers and small group atrophy are observed in the case aged 17, suggesting a mixed myopathic and neurogenic pathogenesis of the disease.
We stress the importance of recognizing this subtype of CMD because the clinical evolution of our cases was proof of a favorable prognosis.

5-19-08 THE ULTRASTRUCTURAL SPECTRUM OF MITOCHONDRIAL ABNORMALITIES IN HYPERTHYROID MYOPATHY.

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Hyperthyroid myopathy is a disease of unknown pathogenesis. Several studies suggest that mitochondria could be involved. Ultrastructural study of skeletal muscle biopsies from 32 hyperthyroid and 5 normal subjects was performed to assess qualitative and quantitative abnormalities in mitochondria and their relationship to the degree of myopathy. We found an increased number of mitochondria in 13 patients (40.6%), increase in mitochondrial mean area in 11 (34.3%), subsarcolemmal or intramyofibrillar clustering of mitochondria in 8 (25%), intramitochondrial edema in 4 (12.5%), disruption of cristae in 4 (12.5%), and intramitochondrial crystalline structures in one case (3.1%). This latter finding has not been previously reported in the muscle mitochondria from these patients. None of these changes was found in control cases. Increase in mitochondrial area was mild in patients without clinical myopathy(p 0.04), moderate in patients with clinical myopathy (p 0.003), and marked in patients with severe amyotrophic myopathy (p 0.001). Though most of these findings are non-specific, they seem to indicate that mitochondrial abnormalities are involved in the pathogenesis of hyperthyroid myopathy.

5-19-09 HYPERTHYROID MYOPATHY INDUCED BY AMIODARONE.

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Some patients treated whit amiodarone (Am) develop hyperthyroidism (HT). It is well-kwonw that HT induces myopathy (My). We studied 8 patients with Am-induced HT to evaluate the presence and characteristics of My and to compare it with classical HT-My. Results: 1.- Mild My appear in 8/8 of Am-induced HT. 2.- Clinical and ultrastructural abnormalities are related to thyroid hormone levels. 3.- EMG reveal mild myopathic changes and show good correlation with clinical status. 4.- Muscular biopsies (4 cases) showed the following changes: increase of lipid amounts (4/4), mild increase in glycogen amounts (4/4), focal dilatation of T-system (3/4), increase in mitochondrial number without increased in size (3/4), and abnormalities in sarcolemmal membrane (2/4). 5.- No differences between patients who developed My during Am treatment and patients who presented My after discontinuation of Am were seen. 6.- No clinical differences were found with classical HT-My, however Am-induced HT-My was associated with increased amount of lipid and glycogen, more severe sarcolemmal abnormalities and fewer mitochondrial alterations. 7.-The hormonal excess seems to be the main pathogenic factor in Am-induced HT-My as it is for classsical HT-My. However, the higher severity of pathological alterations in Am-induced HT-My suggest a particular role for Am.

5-19-10 CARDIAC FAILURE IN PATIENTS WITH BECKER MUSCULAR DYSTROPHY

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Patients with Becker muscular dystrophy (BMD) died more frequently of cardiac failure than those with Duchenne muscular dystrophy (DMD). We studied cardiac function in 19 BMD and 41 DMD patients using electrocardiography, mechanocardiography, and Doppler echocardiography. Findings suggestive of myocardial damage in the postero-lateral wall of the left ventricle were found on the electrocardiographis of 72.2% of BMD patients, which was comparable to that in DMD patients. The ejection time/pre-ejection period (ET/PEP), which is an index of left ventricular systolic function, was lower in BMD patients (2.87 ± 0.62, mean $\pm$ SD) than in DMD patients (3.60 ± 0.55). There was no apparent correlation between ET/PEP and the degree of motor disability in the lower limbs of BMD patients. Left ventricular dimensions and mitral annular size increased with age in BMD patients, but not in DMD patients. Mitral regurgitaion due to mitral annular dilatation was seen more frequently in BMD patients (26.7%) than in DMD patients (12.2%).

These data suggest that cardiac involvement in BMD patients is characterized by left ventricular dilatation and mitral regurgitation due to mitral annular dilatation. The high frequency of cardiac failure in BMD patients may be the result of exercise loading to the heart over the long clinical course of this disease, since it results in relatively mild muscle weakness, as compared with DMD.

5-19-12 OCULOPHARYNGEAL MUSCULAR DYSTROPHY (OPMD) AND CARNITINE DEFICIENCY IN A LARGE GERMAN FAMILY

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Oculo-pharyngeal muscular dystrophy (OPMD) is autosomally dominant inherited in a large northern german family since 6 generations. The age of onset is about 50 years and the symptoms, being slowly progressive, include dysphaghia, bilateral ptosis, an affection of eye muscles in a few cases, and muscular dystrophy of the limb girdle, which leeds to severe dysability.

We found mild peripheral neurogenic besides the prominent myopathic changes in some cases. The muscle biopsies exposed abnormal mitochondria, rarely ragged red fibers, and the pathognomonic ultrastructural intranuclear filaments of 10 nm in diameter. In addition, the estimation of carnitine in muscle showed abnormally low concentrations of free and esterified carnitine even in young family members, while carnitine levels were low, but mostly still within the normal range in serum and urine samples. A primary muscular deficiency of carnitine is suspected.

5-19-13 IDENTIFICATION OF Ca^{++} AND Na^{+}-K^{+} ATPase IN THE SKELETAL MUSCLE

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Identification of these organelles will be required. These organelles are thought to have characteristic ATPase including Ca^{++} ATPase on SR. The purpose of our study was to determine the active site of Ca^{++} and Na^{+}-K^{+} ATPase immunocytochemically and electron microscopically.

METHODS: Immunofluorescent staining; cryostat sections of rat hamstring muscles were treated with monoclonal anti Na^{+}-K^{+} ATPase mouse IgG and also isothiocyanate-labeled polyclonal rabbit anti-mouse antibody for 60 min. each at room temperature. Electron microscopy; after the same muscle specimen was fixed with 4% paraformaldehyde and 0.25% glutaraldehyde, 150 m thick sections were prepared with the microslicer. The sections were preincubated with EGTA for Ca^{++} chelation, then treated for Ca^{++} ATPase activity according to the method by Ando et al. The sections were post fixed with 1% OsO_4, embedded in Quetol 812 and then examined with JEM-100C electron microscope.

RESULTS: By the indirect immunofluorescent staining with antibody to Na^{+}-K^{+} ATPase, the plasma membrane was strongly stained, and scattered immunoreactivity was found in cross sections of the muscle fiber. The immunoreactivity was also found in longitudinal sections in a linear fashion. Since the t-tubules are transverse invagination of the plasma membrane, this would indicate the localization of Na^{+}-K^{+} Atpase in the t-tubules. Ca^{++} ATPase activity was detected in the membrane of the terminal and longitudical cisterna of SR, but not of t-tubules.

5-19-14 A NEW STRATEGY AND EQUIPMENT FOR MUSCULAR DYSTROPHY-PATIENTS TO TRAIN THEIR INSPIRATORY MUSCLES AT HOME.

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To train the inspiratory muscular system in patient with neuromuscular diseases, especially the important diaphragma at a rather early stage of disease, we developed a special apparatus. It is installed in a small suitcase and easy to handle for training at home.
By means of a sniff-trial the transdiaphragmal pressure of each patient is measured and therefore an individually adaptable programme can be set up to train the strength as well as the endurance of the inspiratory muscels.
When the patient has finished his exercises correctly, a stimulating video game is starting.
First therapeutic results of 6 patients (4 Duchenne MD, 2 spinal muscular atrophy) who trained during 6 month at home, showed, compared to an untreated control-group, a significant increase of transdiaphragmal pressure ($p = 0,01$).

5-19-15 EVOKED POTENTIALS IN Xp21 LINKED MUSCULAR DYSTROPHY.

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Experimental data provide evidence that dystrophin may play a physiological and structural role in cells in Central Nervous System (CNS). Some alterations in somatosensory evoked potentials (SEPs) have been reported in Duchenne muscular dystrophy (DMD). We performed SEPs by median nerve stimulation, brainstem auditory evoked potentials (BAEPs), visual evoked potentials (VEPs) in 9 DMD patients, 5 patients with Becker muscular dystrophy (BMD) and 6 carriers of DMD gene. In BMD patients and in carriers motor evoked potentials study (MEPs) by transcortical magnetic stimulation was also carried out. BAEPs and SEPs resulted normal in all subjects while VEPs revealed abnormalities in 3 DMD patients and MEPs in 3 BMD patients and in 4 carriers. These preliminary results furtherly confirm that CNS may be involved in Xp21 linked muscular dystrophies. Correlating the evoked potentials data with the genetic analysis may clear up the variability of CNS involvement in these subjects.

5-19-16 EXPRESSION OF CYTOSKELETON PROTEINS IN CENTRAL CORE DISEASE

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Diagnosis of central core disease (CCD) is based on the evidence of single or multiple regions within muscle fibers, lacking mitochondria, glycogen and reactivity for oxidative enzymes and phosphorylase. Pathogenesis is still unknown. The core areas have disorganized myofibrils and distortions of the anatomy of sarcoplasmic reticulum and t-tubules have been recently described. We studied 5 patients with CCD: 2 with onset at birth, 1 in the second decade and 2 in adult life. Muscle biopsy showed cores in 10-100 % of type 1 fibers, which were often atrophic and prevalent. Immunocytochemistry was done using monoclonal antibodies against several cytoskeleton proteins. Dystrophin, spectrin and vinculin were normally localized in the surface membrane. Desmin had a cytoplasmic distribution except in the core regions, which appeared negative and sometimes with a halo of increased binding. Vimentin was absent in muscle fibers and expressed only in connective tissue and vessels. Rare fibers exhibited developmental myosin only in one patient muscle. Cores were seen mostly in fibers positive for slow myosin. The absence of desmin in the cores is likely related to disrupted organization of the myofibrils. Altered expression of this cytoskeleton protein might have a role in the pathogenesis of CCD.

5-19-17 BENIGN MITOCHONDRIAL MYOPATHY WITH DECREASED SUCCINATE CYTOCHROME C REDUCTASE ACTIVITY.

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In the most cases previously described, the defect of complex II was suggested by low activity of succinate cytochrome c reductase (SCCR). Clinical pattern of the previous ten cases is heterogeneous and may be limited to one particular tissue or be of a more general nature.
We report a 22-year-old woman, daugther of consanguineous parents, with generalized muscle weakness and easy fatigability and benign course, who showed a decrease of SCCR activity in mitochondria of muscle fibers. The myoplasmic areas showed a mild variation in fiber size, subsarcolemmal aggregates with DPNH and excess of neutral lipids. On electron microscopy, we might observe mitochondria proliferation, abnormally large and with altered structure, showing packed parallel cristae and electron dense material.
An autosomal recessive pattern of inheritance is suggested.

5-19-18 **BIOCHEMICAL CHANGES IN RAT MUSCLE FOLLOWING CONSUMPTION OF L-TRYPTOPHAN AND DIFFERENT KINDS OF OILS**

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Recently an association between ingestion of L-tryptophan and eosinophilia myalgia syndrome (EMS) was shown. Similar clinical symptoms were found in toxic oil syndrome.The present study investigated the effect of L-tryptophan and different kinds of oils on biochemical and pathological changes in gastrocnemius muscle. 5 groups of 6 rats each (Charles River C.D) were fed 3 weeks on diet contains 12.2% casein and either 8% soybean oil (control a) or 8% cocconut oil with 1% cholesterol (atherogenic,b) soybean with 0.4% tryptophan (c),cocconut with 0.4% (d),and with 1% tryptophan (e). Muscle protein oxidation (PO) was determined by reduction of dinitrophenylhydrazine to dinitrophenylhydrazone. A significant increase has been shown in group c,d,e (2.2 ± 0.51, 2.1 ± 0.27, 4.3 ± 0.17, 8.16 ± 1.04, 13.43 ± 0.49 respectively). In contrary, no difference was shown in serum. Activities of Alkaline and Acid Phosphatase increased significantly in the treated groups.(4.75 ± 1.2, 8.79 ± 3.5, 8.38 ± 2.9, 7.48 ± 2.9, 15.0 ± 4.2) and (4.05 ± 1.5,11.75 ± 1.07, 13.34 ± 3.4, 15.8 ± 5.8,28.18 ± 9.9 respectively). Biochemical results were supported by histochemical and morphological observation that included increased fibrosis and proliferation of inflammatory cells along blood vessels and in perimysia. It thus seems that tryptophan alone induced muscle dammage as in EMS, along with elevated PO. Also,combination of atherogenic and tryptophan diet enhanced greater muscle dammage.

5-19-19 TIBIAL MUSCULAR DYSTROPHY. A NEWLY DESCRIBED LATE ONSET DISTAL MYOPATHY IN FINLAND

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Tibial muscular dystrophy (TMD) was recently described in 66 patients from Finland. Rimmed vacuoles were found in a minority of the patients. In a large consanguineous kindred with 26 TMD patients and severe proximal dystrophy in 8 homozygotes, vacuoles were not found at all. Epidemiology was updated and the significance of "rimmed vacuoles" in muscle biopsy was evaluated with genealogical investigation of families with and without this finding.

One family with 6 affected members and rimmed vacuoles in muscle biopsies of 4 of them proved genealogically linked to the large nonvacuolar family and to 4 other families with TMD patients. 21 new patients were discovered. These and the previously published 66 patients had reportedly 62 symptomatic relatives.

Rimmed vacuoles in muscle biopsy might be a nonspecific and not a distinctive finding in late onset distal myopathy, at least in TMD. At the moment there are 149 known patients in Finland making it one of the commoniest muscle diseases with a prevalence of about 3/100.000.

5-19-20 PRESYMPTOMATIC CLINICAL DIAGNOSIS OF MYOTONIC DYSTROPHY IN THE SAGUENAY-LAC-SAINT-JEAN REGION (QUEBEC, CANADA).

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The prevalence of myotonic dystrophy (DM) in the Saguenay-Lac-Saint-Jean region (189 per 100,000 pop.) is the highest prevalence reported in the world and an homogeneous mutation is presumed among this population.

From 1988 to 1992, 106 individuals at 50% prior risk of DM were assessed by neurological examination, electromyography and slit-lamp examination, and failed to show strict diagnostic signs. DNA analysis of these 106 asymptomatic individuals revealed 15 at high risk of carrying the DM gene. Four (4) patients considered at high risk on clinical grounds were found to be at low risk by DNA analysis. In our experience, the specificity of colored densities and myotonic discharges is respectively 97.8% (95% CI 94.8-100) and 98.9% (95% CI 96.8-100). The negative predictive value of normal results on clinical examination is 94.5%. When clinical examination is normal, the residual risk of carrying the DM gene is 6.9% (95% CI 0.4-13.4) for individuals aged from 20 to 39 years and 3.3% (95% CI 0-9.8) after age 40 years.

5-19-21 FREQUENT OCCURRENCE OF THYROID CYSTS IN PATIENTS WITH MYOTONIC DYSTROPHY.

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Myotonic dystrophy is a multi-organ disorder with a variety of clinical symptoms including muscle weakness, cataract and endocrine dysfunction. We studied the morphology and function of the thyroid gland in 19 patients with myotonic dystrophy using ultrasonography. None of the patients showed clinical symptoms of thyroid dysfunction. The levels of thyroid hormones were normal in all patients. Three patients had struma on palpation. We found thyroid cyst(s) in 10(52.6%) of 19 patients; i.e., in 2(28.6%) of 7 males and 8(66.7%) of 12 females. The existence of the thyroid cyst showed no apparent correlation with the severity of muscular symptoms, but did seem to correlate with the duration of myotonic dystrophy. There was no relationship between the existence of a thyroid cyst and other non-muscular manifestations, such as cataract, impaired glucose tolerance, frontal baldness, or dementia. Thyroid cysts may now be considered one of the diverse clinical manifestations of myotonic dystrophy. Moreover, further studies on the development of the thyroid cyst in this disorder may contribute to a better understanding of the mechanism of cyst formation in various organs.

5-19-22 EFFECTS OF CALCITONIN GENE-RELATED PEPTIDE AND EPIDERMAL GROWTH FACTOR ON MUSCLE CELL DIFFERENTIATION.

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The effects of human calcitonin gene-related peptide(CGRP) and human epidermal growth factor(EGF) on muscle cell differentiation were studied using rat myoblast(L6) cells in culture. CGRP was added at final concentrations of 1, 10 and 100nM, and EGF was added at a concentration of 1nM. During 10 days of cell differentiation, cell morphology, myoglobin(Mb) content, creatine kinase(CK) activity, DNA content and intracellular calcium concentrations were studied in the culture cells.

The number of the cultured cells increased steadily until day 6, when myotubes appeared in all groups. The number of myotubes then rapidly increased. At 8 day, the length (short axis) of the cultured cells in the groups which had been treated with CGRP, EGF or both was significantly greater than that in the control group.

In the CGRP-groups, Mb content per DNA, CK activity per DNA, and intracellular calcium concentration were significantly greater than those in the control group. In the EGF-group, these values were also significantly greater than those in control group. In the group which received both CGRP and EGF, Mb content per DNA was significantly increased compared to the other three groups (control, CGRP- and EGF-groups). The increase in CK activity per DNA and the intracellular calcium concentration in this group were also greater than those in control group.

These findings suggest that CGRP and EGF facilitate myoblast differentiation and accelerate protein synthesis in muscle cells.

5-19-23 MRI AND MRI GUIDED MUSCLE BIOPSY IN ADULT ONSET INFLAMMATORY MYOPATHIES

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Due to the low sensitivity of approximately 70% the histological diagnoses of dermatomyositis (DM) and polymyositis (PM) remains a problem. The value of MRI and MRI guided muscle biopsy for morphological diagnosis of DM and PM was subject to investigation.

17 female and 14 male patients age range 26-71 so far without antiinflammatory treatment were investigated.10 were classified as idiopathic, 8 were associated with malignancy, 4 had an inclusion body myositis, 4 had PM due to infection and 5 suffered from less common forms of PM. MRI including STIR images were performed for the lower extremities and in some cases for the upper arm followed by MRI guided biopsy from the muscle with maximal increased MRI signal.

STIR images of all patients showed a marked edema mostly localized symmetrical in proximal muscles. MRI also revealed fatty degeneration and atrophy in chronic courses. 28 biopsies showed the histological criteria of a myositis. In two biopsies only a vasculitis could be observed.

In conclusion MRI with STIR is a very powerfull technique with a sensitivity of 100%. The sensitivity of muscle biopsy is increased from 70% to 93% by MRI guidance. MRI can be considered as a new diagnostic tool in inflammatory myopathies.

5-19-24 VARIABILITY OF THE EXPRESSION. OF MUSCLE MITOCHONDRIAL DAMAGE IN OCULAR MITOCHONDRIAL MYOPATHIES

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In mitochondrial myopathies a threshold of mitochondrial proliferation is requested to induce the evidence of ragged red fibers (RRF), the most typical histological sign. Two groups of ocular mitochondrial myopathies, respectively with eyelid ptosis and ophthalmoplegia (CPEO: group 1 and with ptosis but without ophthalmophegia group 2) were evaluated for the distribution of muscle histochemical, biochemical and mitochondrial DNA alterations. RRF occurred in all but one patient of group 1 and in none of group 2. In 2 patients from group 2 single mitochondrial CNA deletion was detected in absence of RRF and cytochrome of oxidase-negative fibres. Variability of skeletal muscle involvement has to be taken into account in the interpretation of mitochondrial alterations in mitochondrial myopathies. The relative expression and complementation of wild-type and deleted mitochondrial population, possibly with an age-dependent effect can play a significant role at this regards.

5-19-25 PHYSIOTHERAPIC TREATMENT IN DUCHENNE MUSCLE DYSTROPHY

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METHODS: the study surveys 50 DMD patients ranging from 5 to 20 years of age. A group of patients underwent physiotherapic treatment, a second group was never treated. The following protocols have been applied:

a) muscle strength was evaluated using a scale modified from the Medical Research Council and dynamometric study were performed as well;
b) joint contractures measurement was calculated by goniometric analysis;
c) motor functional grade was based on the scale proposed by Vignos (1963); and,
d) timed functional tests have been performed following seven different tasks.

RESULTS: patients who underwent physiotherapy and orthesic treatment showed better results in functional testing, muscular strength, level of contractures, severity of scoliosis, stop walking did not correlate with treatment.

5-19-26 HISTOCHEMICAL FEATURES IN HETEROZYGOTES OF DUCHENNE MUSCULAR DYSTROPHY.

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Muscle biopsies of 10 heterozygotes in the families with Duchenne muscular dystrophy were made, previously identified by CPK tests performed at the Neurologic Clinic of the Medical faculty in Skopje. Histological and histochemical stainings like H & E, Gomori, ATP and NADH were used.

Changes of histochemical type were found in all patients, especially in younger individuals the changes were more marked, by what was stressed the Lyon hypothesis for the appearance of these changes.

The most frequent histochemical changes were the existence of the moth-eaten fibres and the predominance 1 muscle fibres.

5-19-27 **IN SITU HYBRIDIZATION OF MYOGLOBIN mRNA IN THE SKELETAL MUSCLES OF NORMAL SUBJECTS AND PATIENTS WITH NEUROMUSCULAR DISEASES**

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The localization of myoglobin(Mb) mRNA in the skeletal muscles of normal subjects and patients with Duchenne muscular dystrophy(DMD) or amyotrophic lateral sclerosis(ALS) was examined using light and electron microscopy by *in situ hybridization* using a biotin-labeled cDNA probe. Mb mRNA signals were quantified by measuring the optical density(OD) of the reaction products.

By light microscopy, Mb mRNA in normal muscles was stained homogenously as granular reaction products throughout the sarcoplasm, and the signals preferentially located over the A-band. In DMD muscles, degenerative fibers revealed a different signal distribution with much less stringent localization, opaque fibers showed apparent signals, and non-atrophic fibers showed a distribution similar to that in normal muscles. The OD of stained signals was higher in non-atrophic fibers, and lower in atrophic fibers, than in normal muscles. In ALS muscles, atrophic fibers revealed a heterogenous distribution, and the OD was lower than that in normal muscles.

At the subcellular level, Mb mRNA in the normal muscles was localized in the A-band more intensely than in the intermyofibrillar space or the I-band. However, this localization was different in degenerative fibers of DMD muscles or atrophic fibers of ALS muscles. In conclusion, Mb mRNA is localized predominantly in the A-band of normal muscles.

5-19-28 THE SPECTRUM OF MUSCLE DISORDERS IN SOUTH AFRICAN BLACK PATIENTS: ANALYSIS OF PATIENTS SEEN IN DURBAN, NATAL

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An analysis of muscle disorders in S.A. black patients over a period of 9 years at Wentworth Hospital was undertaken.

The most common disorders seen were inflammatory myopathies and myasthenia gravis. Duchenne and Becker muscular dystrophy were the most common of the muscular dystrophies. Limb girdle dystrophy was less common. Some of these patients may represent dystrophinopathies.

We describe the first black family with the typical clinical and histological features of FSHD, not previously noted in South African black patients.

Myotonic dystrophy has not been described in South African black patients. One black patient of mixed ancestry has been studied with myotonic dystrophy and is described.

The most common congenital myopathy was centronuclear myopathy. Mitochondrial cytopathies were seen in 7 patients. All had PEO except 1 with a pure limb girdle syndrome. Of note is the rarity of FSH and myotonic dystrophy.

5-19-29 STUDY OF A FAMILY WITH 17 CASES OF AUTOSOMAL RECESSIVE DISTAL MUSCULAR DYSTROPHY

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We report a clinical, électrophysiological and histopathological study of a large kindred with 17 cases (6 males and 11 females) belonging to a consanguineous Tunisian family with autosomal recessive distal muscular dystrophy similar to that described by Miyoshi (1967) as "autosomal recessive distal muscular dystrophy" (ARDMD). The age of onset was between 16 and 22 years. Muscle weakness and atrophy were mostly predominant in the distal and posterior muscles of the legs. In the first stage of the disease, are involved proximal muscles of lower limbs and proximal and distal muscles in the upper limbs in later stages. The EMG showed myopathic changes with normal nerve conduction. Serum creatine kinase (CK) activity was highly increased in the early stages of the disease. Muscle biopsies revealed myopathic changes similar to those of Duchenne muscular dystrophy in all patients with presence of normal dystrophin.

5-19-30 CARDIAC FAILURE IN DUCHENNE MUSCULAR DYSTROPHY : CLINICO – PATHOLOGICAL CORRELATION IN 29 AUTOPSIED PATIENTS.

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In Duchenne muscular dystrophy (DMD), cardiac failure is one of the most frequent causes of death next to respiratory failure. We retrospectively studied clinical and postmortem findings regarding the hearts of 29 autopsied DMD patients.

Eight DMD patients in whom cardiac hypertrophy was found at autopsy (hypertrophic group) died at a mean age of 17.9, and 21 cases with normal-sized or hypotrophic hearts (non-hypertrophic group) died at a mean age of 20.0. There was no significant difference between the age of initial gait in the two groups. However, the mean age at which patients in the hypertrophic group lost ambulation was younger than that in the non-hypertrophic group : 9.9 years vs. 10.7 years ($p < 0.05$). In the hypertrophic group, the mean cardiothoracic ratio (CTR) on chest roentgenogram was 50% at age 10, 56% at age 16, and 66% at age 20. In contrast, CTR remained at 50% throughout the clinical course in the non-hypertrophic group. Mean values of cardiac weight and the diameter of myocardial fibers in the hypertrophic group were twice as much as those in the non-hypertrophic group.

These data suggest that DMD patients with early progression of motor dysfunction and increased CTR tend to suffer more severe cardiomyopathy, and, therefore, are more likely to die of cardiac failure.

5-22-01 NEURORADIOLOGICAL FINDINGS IN MITOCHONDRIAL ENCEPHALOMYOPATHIES.

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Neuro-imaging studies on MELAS and MERRF syndromes have been rare. We studied the clinical features, neuroradiological findings and mitochondrial DNA analysis in 7 patients (3 men and 4 women). Four patients had MELAS and three had MERRF, but two MELAS patients had overlapping syndrome. CT scans from MELAS revealed cerebral hypodense lesions with relative sparing of the basal ganglia and thalamus. In MERRF, 2 patients had cerebral and cerebellar atrophies and one had basal ganglia calcification. MRI scans obtained during the recovery exhibited subcortical white matter lesions in 2 MELAS and 1 MERRF patients. The white matter lesions involving paraventricular areas, were not seen on CT. Mitochondrial DNA analysis showed point mutations at the 3243th nucleotide pair in 4 MELAS patients and at the 8344th nucleotide position in 2 MERRF patients. It is concluded that hypodense lesions tend to affect the cerebral hemispheres in MELAS, but involvement of the paraventricular areas may occur in both MELAS and MERRF.

5-22-02 PATHOPHYSIOLOGY OF ECLAMPSIA STUDIED BY CT, MRI AND SPECT

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Twenty-two patients (28.6±4.4years) were studied during the attack of eclampsia. Most frequent neurological findings were impairment of consciousness, headache, seizure and visual disturbance. Mean arterial blood pressure increased by 46mmHg (n=18) during the attack of eclampsia. Nine of 10 patients studied by brain CT and/or MRI showed abnormalities in the occipital cortex, basal ganglia, internal and external capsule. These findings were compatible with regional brain edema and were seen mainly in the white matter. They disappeared within 2~3 weeks. Cerebral blood flow was measured by SPECT method in two patients. One patient studied during an attack of eclampsia associated with visual disturbance showed the regional increase of blood flow in the occipital cortex. Another patient was studied one day after the cesarean section and showed regional reduction of blood flow in the occipital cortex. It was considered that the main pathophysiology of eclampsia was hypertensive-encephalopathy particularly during the early stage, but during the further progressing stage it was mainly brain edema which reduced flow and aggravated the pathophysiology of eclampsia.

5-22-03 THALLIUM-201 BRAIN SPECT IN A PROBLEM-SOLVING SETTING

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Aim of this retrospective study was to assess the sensitivity and specificity of Thallium-201 SPECT in the differential diagnosis of brain tumors. In 90 patients SPECT was performed because of clinical or radiological suspicion of tumoral invasion. For all tumors diagnosis was based on biopsy or autopsy. Other diagnoses were made only after clinical and radiological follow-up for at least 6 months. SPECT was performed immediately after i.v. injection of 4 mCi Thallium-201.

Tumors consisted of astrocytoma stage I or II (number of patients, n=5), astrocytoma stage III (n=7), glioblastoma multiforme (n=14), pons and optical nerve gliomas (n=2), brain metastasis (n=12), lymphoma (n=3), meningeoma (n=3), oligodendroglioma (n=3) and pituitary adenoma (n=2). False negative studies included pinealis tumor (n=1), craniopharyngeoma (n=1), pons glioma (n=1), the astrocytomas stage I or II (n=5) and stage III (n=2), 1 metastasis of brainstem and 4 additional metastases < 1.5 cm. A false positive study consisted of skull metastasis.

All 15 patients suffering from ischemic infarction, examined 9 till 28 days after the onset of symptomatology, had a normal SPECT study. Of 5 patients with hemorrhagic infarction, studied within 2 weeks, 4 were false positive. Of 6 patients with intracaranial hemorrhage, studied after 9 till 39 days, 1 showed focal Tl-201 accumulation. Two further false positive studies consisted of angioma and epidural hematoma. Finally, SPECT studies were normal in 6 patients with definite diagnosis of (reactive) gliosis (n=3), encephalopathy (n=2) and multiple sclerosis (n=1).

In the patient population presented, sensitivity of Tl-201 SPECT for brain tumors was 65 % and specificity was 83 %. Retrospectively, clinical information and control SPECT studies may improve on these figures. On the other hand it seems that apart from tumoral histology, the presence of tumors in the fossa posterior and a small volume contribute to the occurrence of false negative Tl-201 SPECT studies.

5-22-04 RELATIVE SENSITIVITY OF INTERICTAL SPECT AND BRAINMAPPING IN COMPLEX PARTIAL AND PRIMARILY GENERALIZED SEIZURES

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Aim of the study was to assess the relative sensitivity of interictal Tc-99m HMPAO SPECT and brainmapping in patients with complex partial and primarily generalized tonic-clonic seizures. Interval between 2 examinations was < 2 weeks. Brainmapping was performed using a Nicolet Pathfinder and SPECT using a single head system. Only regional SPECT asymmetries >13 % were considered abnormal.

Results in 10 patients with idiopathic grand mal epilepsy were concordant in 6, including no focus (2), matching of a right posterior parietal focus (2) and bifrontoparietal focus (2). All 4 discordant results consisted of a bifrontoparietal focus on mapping in the presence of a temporal perfusiondefect (3) or normal SPECT (1). In 4 patients with symptomatic grand mal epilepsy attributable to structural changes, concordance was found with extensive bilateral tumoral invasion (1), while in 3 patients with normal mapping, SPECT reflected ischemia (1), a temporal cyst (1) and focal frontal atrophy (1). In 9 patients with complex partial seizures (CPS) without demonstrated structural changes, matching of the epileptogenic focus was found in 2 patients, while SPECT remained normal in 4 other patients. Complete mismatching was found in 1 patient, while a temporal perfusion defect in the presence of a normal mapping was found in the 2 other patients. Finally, SPECT corresponded to the lesion in all 5 patients suffering CPS in the presence of structural lesions, while brainmapping was normal in one of them.

These preliminary results confirm the higher sensitivity for structural lesions of SPECT, when compared with brainmapping, due to better spatial resolution. On the other hand in CPS without structural lesions, brainmapping was more sensitive in detecting physiopathological alterations. The significance of SPECT defects in patients suffering from idiopathic grand mal epilepsy remains unanswered.

5-22-05 MR IMAGING OF THE ACUTE TRANSVERSE MYELOPATHY ASSOCIATED WITH MYCOPLASMA PNEUMONIAE INFECTION

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Chronological changes of MR imaging and autoantibodies to neural components of a 17 years old boy with acute transverse myelopathy at the level of the Th7 associated with serologically confirmed *Mycoplasma pneumoniae infection* were presented.The heterogeneously hyperintense lesion was detected in the spinal cord on T2-weighted MR image. Its distribution ranged from the level of the 7th thoracic vertebra to the first lumbar vertebra. Treatment with prednisolone improved his neurological symptom. The abnormal intensity and area of MRI decreased with his clinical improvement. IgM antibody to the gangliosides, GM1 and GD1b,was detected in his sera byELISA. Immunostaining of the human brain western blot with his sera detected antibody to the 40 and 44 kD molecules in the white matter. MR imaging was useful for detection, differential diagnosis and chronological observation of the lesion. Edema, demyelination, and/or gliosis were suspected as the causes of the hyperintensity of the lesion on T2-weighted MR image. Although the postulated mechanisms of neurological complication associated with this microbe remains controversial, the prodromal infection, effects of prednisolone and autoantibodies against neural components related with clinical course would favor an autoimmune mechanism.

5-22-06 MRI OF WILSON'S DISEASE : ANALYSIS OF 20 PATIENTS

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In all patients, diagnosis of Wilson's disease (WD) was biochemically proven.

MR (0,5 T) was performed in T2 weighted sequencies. In 5 asymptomatic cases MR was normal ; in 2 hepatic forms, unusual putaminal hypointensities due to paramagnetic effect of copper were observed. In 13 neurological patients, bilateral and symmetrical hyperintensities of putamina were the most common finding. Size of abnormal signals was related to the severity of neurological symptoms. Extralenticular nuclei were less frequently involved. MR was repeated in 5 patients treated with D-Penicillamine for several years. A complete disappearance of extralenticular and a decreased size of putaminal hypersignals were associated to good prognosis. MR was unchanged in chronic dystonic forms. In WD MR seems to be more sensitive than CT for location of lesions. Findings are not specific but may be reversible under therapy. MR may be useful to recognize atypical forms (psychiatrical, without pericorneal ring) and to prevent misdiagnosis and late therapy.

5-22-07 IMAGING CHARACTERISTICS OF AMYOTROPHIC LATERAL SCLEROSIS WITH CLINICAL CORRELATION

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Material and Methods: Head MRI's (GE Signa) were performed on 17 documented ALS patients and compared to 17 age-matched controls.

Results: Normal subtle increased signal similar to grey matter in the posterior internal capsule (corticospinal tract) was seen in 9/17 controls on two or more slices. Seven (7/17) ALS patients demonstrated sharp, well-defined, round symmetric high signal lesions of greater intensity than grey matter within the corticospinal tract, best seen at the mid or low thalamic level. The diameter of the abnormal corticospinal tract is often greater than in normal controls and often extends superiorly to the motor cortex. An additional useful finding is that of low signal within the motor cortex in 4/17 patients. Positive MRI findings were correlated with a younger age group and to rapid progression of the disease.

Conclusion: There are characteristic cerebral MRI findings in rapidly progressive ALS patients.

5-22-08 CEREBRAL BLOOD FLOW IN PURE AKINESIA, PARKINSON'S DISEASE AND PROGRESSIVE SUPRANUCLEAR PALSY.

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Pure akinesia (PA) is a rare extrapyramidal syndrome characterized by freezing when walking and poor response to L-dopa (Narabayashi et al, Adv Neurol 1986, 45, 593-602). Putative relationships between PA and other disorders of basal ganglia like Parkinson's disease (PD) or progressive supranuclear palsy (PSP) are poorly understood. PA could be a variant of PSP (Matsuo et al, JNNP 1991, 54, 397-400).

We measured cerebral blood flow (CBF) using single photon emission tomography (Tomomatic 64, ^{133}Xe iv) in 8 PA, 7 PD, 13 PSP patients and 20 aged matched controls. We calculated an anteroposterior (ANT/POST) CBF ratio to assess if we could observe in our patients the frontal hypoperfusion which has been previously described by others in PSP (D'Antona et al, Brain, 1985, 108, 785-799).

Global CBF was different between the 4 groups (ANOVA, $p < 0.003$), being smaller in PSP (43±8 ml/100g/min) and PD (47±13 ml/100g/min) than in PA (58±12 ml/100g/min) and controls (57±9 ml/100g/min) ($p<0.05$).

The ANT/POST CBF ratio was different between the 4 groups ($p < 0.0016$), being smaller in PSP (0.96±0.07) than in the 3 other groups (PD : 1.12±0.12 ; PA : 1.10±0.16 ; controls : 1.10±0.06) ($p<0.05$).

CBF patterns differ in PA, PD and PSP. This result suggests that the 3 diseases have different pathophysiological mechanisms.

5-22-09 AGING OF THE NIGROSTRIATAL DOPAMINERGIC SYSTEM: POSITRON EMISSION TOMOGRAPHY STUDIES.

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Positron emission tomography (PET) with [18F]-fluorodopa (FD) in aging of the nigrostriatal dopaminergic system has produced conflicting results despite the post-mortem findings of a decline in neuronal numbers. We have evaluated 4 studies performed at UBC - all showed a decline with age. The scans were analyzed by measuring total striatal FD uptake. This contrasts with reports that measure FD uptake as per concentration of striatal tissue and showed no decline with age. Recent MRI data has shown a marked reduction in striatal volume with age. This reduction would artificially increase the FD uptake when measured as a function of striatal concentration and would therefore obscure any age-related reduction of nigrostriatal dopaminergic function. In the fourth study from UBC, we have scanned 10 subjects and calculated FD uptake by both methods. There was a significant decline in total striatal FD uptake with age ($p=0.048$), and a non-significant decline when the concentration of FD uptake was measured ($p=0.15$). We conclude that nigrostriatal dopaminergic function, as measured by PET, does decline with age, and that striatal atrophy may confound results expressed as concentrations.

5-22-10 CEREBRAL GLUCOSE METABOLISM (rCMRglc) IN DEMENTED PATIENTS WITH FRONTAL LOBE FEATURES ASSESSED BY HIGH-RESOLUTION POSITRON EMISSION TOMOGRAPHY (PET).

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To investigate cerebral metabolic correlates of dementia with frontal lobe features (DFL), we studied 3 subjects (2 F, 1 M; 45, 56 and 58 yr/old, respectively) with slowly progressive dementia, characterized by early personality changes, and behavioral disinibition and later perseveration and apathy. PET examinations (Scanditronix PC1024-7B, Uppsala, Sweden; 6mm FWHM) were performed in the "resting state" (ears plugged/eyes covered, low ambient noise) with [18-F]2-fluoro-2-deoxy-D-glucose. Results were compared with two groups of 18 sex- and age-matched healthy controls (z-score analysis). Absolute rCMRglc values were measured in mg/100 g of tissue/min; moreover, to reduce inter-subject variability, rCMRglc values were "normalized" to mean globalCMRglc. In all patients rCMRglc was severely reduced ($p < 0.01$; mean average decrease greater than 50%) in frontal, prefrontal and cingulate areas; in addition, the 2 female patients showed a significant, although smaller, rCMRglc decrease also in association paricta1-temporal areas, along with a broader cognitive impairment. Hippocampus and amigdala, cerebellum, basal ganglia, and primary motor and sensory neocortical areas were unaffected in all patients. Distribution of rCMRglc abnormalities is consistent with behavioral impairment and further indicates DBF as a specific clinical entity.

5-22-11 A POSITRON EMISSION TOMOGRAPHY STUDY OF PATIENTS WITH ACUTE CARBON MONOXIDE POISONING TREATED BY HYPERBARIC OXYGEN.

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Seven patients with an acute and severe carbon monoxide intoxication were treated with hyperbaric oxygen at 3.0 ATA. They underwent a positron emission tomographic examination 2 to 5 days after the acute event, using the steady state technique with ^{15}O in order to evaluate regional cerebral blood flow, oxygen extraction rate and oxygen consumption. Although the final clinical outcome was good in all patients, ischaemic changes mainly in the cerebral cortex and in the white matter were observed in 4 of them. One of the latter patients had a moderate amnestic syndrome for 3 weeks and another developed delayed transient neurological deficits.
Although positron emission tomographic examination cannot predict the final outcome of patients with an acute carbon monoxide poisoning, it can define a group of patients "at risk".

5-22-12 CEREBROVASCULAR PATHOLOGY IN KLIPPEL-TRENAUNAY SYNDROME IS NOT A REPLICA OF THE STURGE-WEBER SYNDROME

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The Klippel-Trenaunay Syndrome (KTS) is a congenital hypertrophy of limbs or trunk with involvement of the skin, blood vessels, lymphatics, soft tissue, bone, and viscera. When the head is involved the findings resemble the Sturge-Weber Syndrome (SWS). This has given origin to the concept that the association of these two rare disorders is not uncommon. To test the validity of this notion we searched the Mayo Clinic files for records of patients with KTS and facial angiomatous nevus or symptoms or signs of cerebral pathology and patients with both diagnoses, KTS and SWS. We found that some patients with KTS have hemimegalencephaly whereas patients with SWS have hemispheric or lobar atrophy. Further, patients with KTS do not have the abnormal cerebral venous blood flow characteristic of SWS but quite the contrary, in KTS the deep cerebral as well as the internal jugular veins are occluded whereas the cortical veins remain patent. Thus, the venous blood flows through the superior petrosal sinus into the cavernous sinus, the orbital veins, facial and external jugular veins and superior vena cava, whereas in SWS venous return is by deep medullary veins, internal cerebral and galenic vein.

5-22-13 CENTRAL EFFECTS OF CALORIC VESTIBULAR STIMULATION

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Caloric vestibular stimulation (CVS) induces a temporary remission of spatial neglect suggesting that the vestibular system modulates the neural networks subserving the representation of space. We investigated the regional cerebral blood flow (rCBF) changes induced by CVS, with Positron Emission Tomography (PET).
Six volunteers underwent 12 consecutive measurements of rCBF, six of which immediately after cold CVS in the left ear. rCBF measurements were obtained with a CTI 953B PET scanner. A bolus of $H_2{}^{15}O$ was infused as a tracer of blood flow. Statistical analysis of the rCBF brain images, after transformation into a standard stereotactic anatomical space, was performed with Statistical Parametric Mapping. Comparisons of the two condition means (CVS+ versus CVS-) in all pixels were made using the t statistic (Bonferroni correction: $p<0.05$).
The maximal activation induced by CVS was detected in the right temporoparietal cortex and putamen.
These same cortical structures are the most frequently damaged in neglect patients. Our results suggest that the temporary remission of neglect induced by cold CVS in the left ear, could be due to the activation of perilesional areas. Our hypothesis will be examined with further PET studies using CVS in neglect patients.

5-22-16 MR IMAGING OF ESSENTIAL TREMOR

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Aim of study;We analyzed the responsible lesion of essential tremor with the high field MRI.

Patients and methods;We examined 44 cases,consisting 16 of essential tremor(77±6.25years) ,20 of Parkinson's disease(67.4±10.4 years) and 8 of healthy cnotrols(74.7± 4.23 years) by 1.5 tesla high field MRI(TOSHIBA MRT200, FX3).

Axial T2-weighted images (TR2000msec,TE100msec) were done. We compared the signal intensity of the most medial part of substantia nigra to that of the red nucleus. We visually classified restoration of signal intensity (RSI) in the red nucleus into four discrete rating for analysis.

Results;Although a few cases of Parkinson's disease and healthy controls revealed RSI of the red nucleus,it was more frequently(81.25%) and prominently observed in the cases of essential tremor. Our study disclosed RSI in the red nucleus in 81.25% of essential tremor.

It was suggested that RSI in the nucleus was caused by metabolic changes of iron.

5-22-17 AUTOMATIC EMBOLUS DETECTION WITH ARTEFACT SUPRESSION

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Transcranial Doppler ultrasound may now be used to detect cerebral emboli. However, monitoring over longer periods requires reduction in the amount of Doppler data which must be stored in the instrumentation. This may be achieved if emobli-related events are stored whereas Doppler signals due to artefacts are rejected.

We have carried out in vitro experiments which have shown that the spectral characteristics of emboli compared to normal blood flow velocities are independent of their position in the ultrasound beam. Furthermore that the power increase and shape of the spectral distribution caused by emboli may be clearly differentiated from that due to artefacts. This has allowed the development of an embolus detection system which significantly reduces the amount of Doppler data which must be stored during monitoring. Assessment of this system in vitro gave a specificity of 97.2% and a sensibility of 96.3% for embolus detection.

These results strongly suggest that automatic embolus detection should now be assessed using transcranial Doppler monitoring in the clinical situation.

5-22-18 THREE DIMENSIONAL ULTRASONIC COMPUTER ANGIOGRAPHY FOR THE BRAIN

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The three dimensional (3D) cerebral angiogram, which was reconstructed by a newly-developed ultrasonic computer angiography (UCA) based upon the transcranial color flow images (TC-CFI), was supplied to non-invasive diagnoses of the cerebral vascular diseases (CVD). The UCA used 2.25MHz electric sector scan probe of Ultramark 9 (ATL,USA), and a robot arm system which could support the probe and read automatically the 3D position & angle of tomographic plane given by a precise optical encoder settled at all six joints. The 3D image was reconstructed by a multi-projected image software including by whole cross sectional images, 3D bird's eye view images and rotation of these 3D images. All system was controled by a high speed micro- computer with memorized 64 TC-CFIs having the 3D co-ordinate data. The 3D angiogram such as the anterior, middle and posterior artery was obtained from 16 healthy young adults. It was verified that the rotation image of 3D vasculature by a new UCA had great advantage for early diagnoses of morphological CVD such as aneurysms, stenoses and arteriovenous malfunctions.

5-22-19 EXPERIMENTAL AND BIOLOGICAL VARIATIONS IN TIIREE DIMENSIONAL TRANSCRANIAL DOPPLER

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Transcranial doppler (TCD) is a non-invasive ultrasound method for measurement of blood flow velocity in the large cerebral arteries. A new transcranial doppler system (3-D Transcan,2MHz, EME), which allows the drawing of a three dimensional map of the large cerebral arteries, was validated in 60 healthy volunteers *in relation to age, sex, intersubject, interobserver and day to day* variation. Mean maximal velocities in MCA, PCA and ACA did not differ from values found in earlier studies. Mean maximal velocity was significantly higher in females compared to males and decreased within age in both genders. The coefficient of variation in the middle cerebral artery (MCA) was 26% between subjects, 20% between sides, 16% between days, 13% between observers and 7% during 5 minutes. The coefficient of variation was higher in the anterior and posterior cerebral arteries. Bruits were found more frequently in females than in males (12 of 15 females versus 5 of 15 males).The variations and differences in mean velocity between male and female in resting condition, emphasize the necessity of standardized conditions and of a very carefully matched control group. Most optimally, the patient must be her/his own control.

5-22-20 SPECT WITH THE LIGAND ^{123}I-IODOBENZAMIDE (IBZM) SHOWS CHANGES OF STRIATAL DOPAMINE D2 RECEPTOR IN FLUCTUATING PARKINSON'S DISEASE (PD) PATIENTS

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Long-term L-Dopa therapy often leads to fluctuating response. Whereas pharmacokinetic-pharmacodynamic changes have a role, evidence from pathologic and in vivo studies exists that alterations of striatal D2 receptors take place in patients with a complicated response to L-Dopa.

To evaluate if changes of caudate (C) and putamen (P) D2 receptors may contribute to a complicated/fluctuating response to L-Dopa in PD patients we used SPECT with the D2 receptor ligand IBZM to determine the relative uptake (C/P to cerebellum ratio) of the tracer in 3 groups of PD patients with diverse therapeutic behavior (6 untreated, 11 with a good response, and 7 with a complicated response to L-Dopa), and in 6 age-matched controls. SPECT scanning was performed 2 h. after i.v. injection of 185 MBq of the tracer.

IBZM uptake in C/P was similar to controls in the untreated and in the good responders PD groups, whereas in the complicated PD group (C:1.32 ± 0.11, P:1.43 ± 0.10) it was significantly reduced from the controls (C:1.61 ± 0.06, P:1.56 ± 0.07) and the PD responders (C:1.49 ± 0.12, P:1.60 ± 0.10) mean values. Furthermore, among various clinical features, only severity of the disease showed an effect on striatal IBZM activity in PD patients.

IBZM SPECT suggests that alterations of striatal D2 receptors may contribute to the altered response to L-Dopa in PD. Such changes appear due to disease progression and not to receptor down-regulation due to chronic L-Dopa therapy.

5-22-21 NEURORADIOLOGY OF FLUOROTIC SPINE

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Fluorosis is endemic in certain geographic regions of the world. It has been estimated that 25 - 30 million people in India are exposed to the risk of developing fluorosis. Eventhough radiological change in Fluorosis is well known there is hardly any information about application of CT and MR imaging technique.

We have studied 22 cases of Fluorotic spine (15 males and 7 females). Age range was 36 years to 65 years. MRI was done in all the cases and CT was done in 12 cases. In four cases MRI contrast Gadolinium was given which has no advantage.

In all the cases, Anterior Longitudinal Ligament (ALL), Posterior Longitudinal Ligament (PLL), Ligamenta Flavum (LF), Spinal Canal, Facet joints and subarachnoid space were measured and local abnormality noted. MRI signal intensities in the vertebrae and cord were also noted. The main values obtained were: ALL (Mean) 7 mm; PLL 5.8 mm; LF 5.75 mm. Spinal Canal 105 mm x 123 mm. Facet joints were fused in 9 cases.

We noted localized hypertrophy of the ligament compressing the cord on MRI in which surgery was beneficial.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-22-22 CONTRAST ENHANCEMENT AFTER TWO HOURS OF IODINE INJECTION IN CEREBRAL INFARCTION

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The relationship between the degree of blood-brain-barrier (BBB) damage and contrast enhancement (CE) and the volume of the infarction was analyzed in 10 patients with cerebral infarcts using the measurement of cerebral densities in HU over two hours after contrast media injection. The behavior of CE was similar in all patients. The density increased 15 and 30 minutes after the injection of contrast. Afterwards, the density slowly decreased. The standard deviation values also increased inmediately after contrast injection, and later on decreased progressively. The results suggest that CE in brain infarctions correspond to damage to the BBB: the contrast media flows easily through the endothelial junctions to the extravascular space, but the return to the endovascular space is obstructed.

5-22-23 DIFFERENTIAL DIAGNOSIS OF TUMOURS IN THE PINEALIS REGION BY CT AND MRI

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The rare tumours of the pinealis region or the quadrigeminal plate contribute to 0.6% of all brain tumours. The clinical manifestation is expressed by a parinaud´s syndrome or/ and consecutive hydrocephalus. Although these tumours are easily discerned by CT or MRI, the exact preoperative histopathological and neuroradiological diagnosis is often difficult.

Since January 1988, 23 patients with the CT/MRI diagnosis of quadrigeminal plate tumour underwent neurosurgical treatment. The histopathological investigation resulted in 9 germinomas, 3 astro-zytomas, 2 metastasis, 1 lipoma, 1 microangioma within an organised hematoma , 6 arachnoid cyst and 1 pineozytoma (grade II).

Special interest was focused upon the following radiological criteria: tumour surface, signs of in homogeneity (solid, cystic, focal necrosis, tumour bleeding and with calcification), reaction to contrast media and tumour metastasis.

The results of our diagnostical considerations are explained by examples.

5-22-24 Evaluation of different CT and MRI criteria in atypical and malignant meningiomas

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Meningiomas are predominantly of benign nature and constitute approximately 15% of the primary brain tumours. Atypical and malignant meningeomas are rarely and characterised by focal necrosis, mitosis cell and nuclear pleomorphism of different degree.

The aim of our study was to evaluate the benefit of CT in comparison to MRI in the preoperative diagnosis and post surgically radiotherapy.

Between October 1986 and 1992 21 patients in all - 12 women and 9 men - with the pathological diagnosis of atypical (n=11) and malignant (n=10) underwent neurosurgical intervention. In 8/3 cases the diagnosis was primary atypical respectively malignant meningioma.

As specific signs of atypical or malignant meningeomas we consider the following CT and MRI findings: in homogenous enhancement, signs of focal or intensive necrosis and irregularity of the tumour surface.

Routinely performed follow-up investigations revealed clear advantages of the MRI in the evaluation of relapsing tumours, strategy of neurosurgical intervention and radiotherapy treatment planning.

5-22-25 RADIOLOGICAL EVALUATION AND NEUROSURGICAL TREATMENT OF INTRAVENTRICULAR TUMOURS

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Although intraventricular tumours can be easily detected by CT and MRI the exact diagnosis according to histopathological and radiological criteria causes often difficulties. Therefore, we compared retrospectively CT and MRI findings of 40 patients with postoperatively confirmed histopathological results: 5 meningiomas, 2 plexus papilloma, 9 colloid cysts, 5 arachnoid cysts, 1 dermoid cyst, 2 subependymomas, 3 ependymomas, 4 astrocytomas, 1 only ventricular located craniopharyngeoma 1 neurocytoma 1 oligodendroglioma, 1 chondrosarcoma, 1 carcinoma, 1 granular cell tumour, 1 metastasis of a germinoma, 1 PNET and 1 ganglioglioma. For the exact radiological diagnosis and neurosurgical strategy we take the following features into consideration: topographical relation to the ventricle or choroid plexus, manifest hydrocephalus, delineation of the tumour, homogeneity res. inhomogeneity of the tumour. enhancement after application of contrast media. The results of our diagnostical considerations and neurosurgical treatment are explained by case reports.

5-22-26 IN VIVO ^{123}I-IBZM SPET IMAGING OF D_2 DOPAMINE RECEPTORS IN PATIENTS WITH NARCOLEPSY

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Autoradiographic investigations on central dopamine receptors found elevated D_2 dopamine receptor levels in human narcolepsy. We investigated the central dopamine D_2 receptor density in vivo in 3 narcoleptic patients with ^{123}I labeled 3'-iodo-6-methoxy-benzamide (IBZM) (a highly selective CNS D_2 dopamine receptor ligand) and single photon emission tomography (SPET). In human narcolepsy there was a higher ^{123}I-IBZM uptake in the basal ganglia compaired to the controls. The results indicate that narcolepsy may be associated with a dysfunction of the dopaminergic system.

5-22-27 HMPAO-SPECT IN THE DIFFERENTIATION OF DEMENTIA OF ALZHEIMER'S TYPE AND DEMENTIA SYNDROME OF DEPRESSION

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Dementia syndrome in old age depression (OAD) is the main differential diagnosis of senile dementia of alzheimer's type (SDAT). Previous investigations of cerebral blood flow (CBF) in SDAT revealed typical patterns of bilateral parieto-occipital, and temporal hypoperfusion. To test differentiating properties and because there was a lack of investigations of CBF in OAD, we performed CBF measurements with 99mTc-HMPAO and single photon emission tomography (SPET) in 13 patients with OAD (64.6±10.3 y), 13 patients with SDAT (67.9±11.8 y) according to criteria of NINCDS-ADRDA and 9 age matched controls, together with ratings for depression, Mini-Mental-Status-Examination (MMSE) and intensive neuropsychological evaluation. Semiquantitative analysis of different cortical regions to cerebellar ratios revealed, that no patient with OAD had his hypoperfusion focus in the parietooccipital region like most of the SDAT patients. Thus HMPAO-SPET seems to have good differentiating properties.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-29-01 SOMATIC & PSYCHOSOMATIC EFFECTS OF MINIMAL SPINAL CORD INJURY (SCI)

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Outcome from SCI is intuitively seen as benign proportionately to the degree of spared function. Yet care-givers note that "walking quads"often seem lesscomfortable with their disability than those who accept wheelchair mobility.

Retrospective analysis of 26 non-acute walking SCI patints, and age, education, duration and level of injury matched wheelers, focused on cognitive and personality psychometrics, out-patient clinic use, and life-style outcomes was performed.

Psychometrics were more often refused or endorsed more somatic complaints, distrust, and general anxiety by the walkers; a trend towards higher risk-taking and sensation-seeking was noted. Type of complaint (pain, social concerns) rather than frequency of out-patient visits and education/employment and relationship outcomes were less positive among walkers.

Stress proportionate to the incompleteness of SCI is suggested by this pilot study. Prospective exploration of ebcountered attitudes ("If you're an SCI, why aren't you in a wheelchair?") will be pursued. The unresolved association of sensation-seeking and SCI may be additionally problematic if those with incomplete SCI show this trait more frequently.

5-29-02 AUDITORY RHYTHMIC CUING IN GAIT REHABILITATION WITH STROKE PATIENTS

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We studied the effect of auditory rhythmic cuing (ARC) in gait facilitation and as a rehabilitation technique to entrian stride patterns and normalize muscle activity in hemiparetic gait of stroke patients.

To study gait facilitation, 10 stroke patients were evaluated over 3 trials. In each trial, a baseline walk without rhythm and a walk with rhythmic cuing, matched to the baseline gait cadence, were measured. For gait training, a control group received conventional gait training and a matched experimental group received supplemental rhythmic gait training. All subjects were pre and posttested without ARC. Computerized stride analysis, surface EMG, and videography were used to record and analyze data.

Results for ARC in gait facilitation show improved stride symmetry ($p<0.05$), increased amplitude and reduced variability in gastrocnemius EMG on the paretic side during pushoff and reduced gastrocnemius activity during swing phase ($p<0.05$). Results for ARC in gait training show significant increases in gait velocity, symmetry and reduction in double limb support over control group results.

5-29-03 POST-STROKE DEPRESSION TREATMENT WITH MOCLOBEMIDE

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Several stroke patients develop "post-stroke depression", which often is overlooked as reactive sadness or tiredness. Earlier treatment with conventional tricyclic agents have been found useful in some studies, but the anticholinergic side effects are often a problem in elderly patients.

In a prospective multicenter trial with moclobemide, a specific MAO-A enzyme inhibitor, 20 patients, 12 males and 8 females with age between 38-85 yr participated. All developed a major depression according to the DSM III criteria within one year after the onset of an ischemic stroke, where CT scan excluded tumours and hemorrhages.

The patients were treated at least 6 weeks with moclobemide. The maximal daily dose was 600 mg and all except two improved according to the Hamilton depression scale. More than half of the patients had a 50% reduction in the Montgomery-Åsberg depression rating scale. Ten patients had to continue with a supporting dose of 150-300 mg moclobemide daily. During the trial one patient died due to cardiac failure. Adverse reactions were mild, except insomnia in some cases.

Further studies of the post-stroke depression syndrome should lead to increased awareness of the cause and treatment of the disorder.

5-29-04 BODY ESTEEM IN CHRONIC PARAPLEGICS - FOLLOWING WAR INJURY.

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Body esteem was evaluated in twenty young paraplegic males (mean age 37.6 years, SD 5.51) with post traumatic spinal cord war injury. Body Esteem Scale (BES) and functional scoring of Barthel index (BI) were compared with 20 age and sex matched healthy controls.

No statistically significant difference was found in body esteem between the paraplegic group and the matched controls. This held true for all three subgroups (A - physical attractiveness; P - physical condition and U - upper body strength; P = 0.25, 0.22, and 0.24, respectively).

Using the Spearman Rank Order correlation to correlate the BES to BI, no significant statistical significance (0.82, 0.088, and 0.069, respectively) was found.

The results may be related to a high social esteem of war veterans in the Israeli society or to a bigger upper body development in wheelchair bound paraplegics with a high BES in subscale-U.

5-29-05 EXPERIENCES WITH LONG TERM INTRATHECAL BACLOFEN TREATMENT IN PATIENTS WITH SUPRASPINAL SPASTICITY

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Intrathecal baclofen application has proved to be also efficient in patients with supraspinal spasticity, who were non-responders to oral antispastic treatment. Nevertheless in this respect the efficiency of this therapy is discussed controversially. We report on 15 patients, who are under continuous long term intrathecal baclofen application and in whom not only a reduction of spasticity but also, in some cases, improved motor performances and bladder functions were documented. The latter seems to indicate a specific effect on the pontine micturition centre.

In order to achieve a good therapeutic response in these patients the intrathecal dosages exceed for approximately 100% those applicated in spinal spasticity. An increase risk of seizures should be borne in mind especially in patients with spasticity secondary to traumatic brain injury.

5-29-06 VISUAL FEEDBACK ON THE CONTACT PRESSURE OF STROKE PATIENTS

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Object: How the visual information effects on standing posture of hemiplegics was analyzed by the center of contact pressure(CCP).

Subjects and Methods: Seven hemiplegia, mean age 58 year-old, 6 right and 1 left hemiplegia, were studied as the stroke group. They were severe in 1 case, moderate in 4 cases and mild in 1 case. Age-matched 12 normal subjects were studied as the control group. Subjects stood on the measuring apparatus and gazed a target 1.5m in front of them (Prefeedback), and after that they looked at the TV monitoring their own foot pressure distribution pattern (during feedback). The foot pressure on each steel ball appears as the "first fringe", which diameter precisely defines the position of CCP and body-weight-loading ratio on each foot. They were analyzed for 60 seconds in each condition.

Results: (1) The number of the steel balls of the affected foot of the stroke group was significantly fewer before feedback($p<0.005$) but became almost the same during feedback as compared with those of the control group. (2) Body-weight-loading ratio of the affected foot of the stroke group was significantly fewer before feedback, but relatively increased during feedback($p<0.001 \rightarrow P<0.05$).

Conclusion: Hemiplegic patients can utilize visual information to maintain the upright posture, which suggests visual feedback training for standing in hemiplegics.

5-29-08 PELVIC MUSCULATURE REHABILITATION IN FEMALE PATIENTS

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Weakness of the female's pelvic floor musculature with ageing is not rare. This condition may be an important factor in the development of prolapses and urinary incontinence. We developed a rehabilitation protocol based on intravaginal bio-feedback with or whiteout electric stimulation and local contraction exercises to reinforce the pelvic musculature. This protocol allowed also the treatment of patients with pelvic floor problems aggravated or caused by hospitalisation after stroke. All the patients were examined by a gynaecologist before the beginning of the treatment. All the women did gladly adhere to the program exercises once fully informed about its nature. Most of the patients were able after few sessions to spontaneously contract their muscles at the start of an acoustic signal to reach the visual target on the computer screen with the cursor driven by the intravaginal probe. None of the patients with uterine prolapse for which a surgical therapy was suggested, which started the program in the meantime did finally necessitate surgery. All of the patients did improve and almost all did not have any urinary incontinence at an one year follow up. We suggest that use of bio-feedback techniques can safely be used to prevent tertiary damage in women with urinary incontinence due to pelvic weakness caused by age or stroke.

5-29-09 INTENSIVE REHABILITATION AFFECTS FUNCTIONAL STROKE OUTCOME

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The influence of intensive physical rehabilitation on stroke outcome has been debated. We compared the functional results of stroke rehabilitation in our non intensive program (physiotherapy provided 3 times per week) with those of a previously reported large cohort of stroke patients treated in the more intensive manner (daily physiotherapy) used in the U.S.(Uniform Data System for medical rehabilitation of 1990). We used the Functional Independence Measure (FIM) to follow patients progress. Our patient group did not differ from the American group in age, sex and admission FIM subscores and total score and the discharge from hospital FIM score. This reflects similar criteria for admission and discharge from an in-patient rehabilitation program. However the time required to reach the same final functional results was twice longer in our group. the opposite correlation between length of stay efficiency and intensiveness of therapy provided proves that intensive stroke rehabilitation is justified and cost-effective.

5-29-10 RESTORATIVE EFFECTS OF VARIOUS LOADINGS ON LOWER LIMB ATAXIA IN PATIENTS WITH SPINOCEREBELLAR DEGENERATION.

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This study was carried out to see the effects of various loadings on lower limb ataxia in patients with spinocerebellar degeneration and also to find clinical characteristics, if any, of those most likely to benefit from this treatment. Methods: Either weights (250g/500g around each ankle or 1Kg around the waist), elastic bands around both ankles or a wide waist-belt were used on each of 19 patients. The degrees of gait disturbance and hyperreflexia were assessed as clinical parameters. The sway areas of the center of gravity were measured while the patients were standing upright on a Gravicorder (Anima, Jpn) with eyes fixed on a point 3m ahead. The gait speeds and patterns were also evaluated on a force moment measuring plate (Anima, Jpn). The areas of the pons, the vermis and the posterior fossa obtained from midline sagittal MR images were measured using an image analyzer (PIAS, Jpn). Conclusions: Weights, particularly ankle loadings, were more effective than elastic bands or waist-belts. Patients with moderate gait disturbance, hyperreflexia ($p < 0.01$) and greater atrophy in the pons than the vermis ($p < 0.05$) were found to have gained the most benefit.

5-29-11 VERBAL TRAINING ON TRANSFER ABILITY OF STROKE PATIENTS WITH LEFT NEGLECT.

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Language and memory functions are preserved in stroke patients with left neglect. Twelve subjects (mean age 68 yrs), divided in comparable treatment and control groups, were assigned to learn transfering from wheelchair to chair and vice versa. Transfer was divided in 4 sequences -rising from wheelchair (RW), sitting down in chair (SC), rising from chair (RC), sitting down in wheelchair (SW)- in turn articulated in phases. Treatment patients had to memorize the sequences written in posters, and to execute them under verbal self-direction. There were 20 learning sessions in 4 weeks. Control group practised as usually. For statistics a model of repeated measures analysis of variance was used. Treatment group significantly improved in the sequences of RW ($p=.0029$), SC ($p=.0001$), and RC ($p=.0058$), with SW bounding significance ($p=.0786$). The effectiveness of a programmed learning of motor sequences by the language function is supported.

5-29-12 GAIT-ANALYSIS - A PREREQUISITE FOR GENERAL MOVEMENT ANALYSIS

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Objective: The exact analysis of gait is a prerequisite for understanding behaviour and is a way for measuring therapeutic effects in neurorehabilitation. Background: Gait is analyzed by determining the positional relationship between points on moving body parts over time and by measuring the forces exerted on the sole of the foot. Design/method: Pressure changes (50/sec) are measured by 8 piezoresistive, hydraulic sensors applied at each foot sole, calibrated as areas (N/cm2) changing over time during walking. Moving body parts are defined by spatial co-ordinates of infraredreflecting markers applied at 20 points near joints of extremities and trunk. Movement is measured as changes of angles (velocity and acceleration) between such points over time. These measurements are performed simultaneously and displayed graphically. Results: Exact measurements of pressure (N/cm2) at 8 points on each foot sole and of the changing position of moving body parts (°/sec) in three dimensions over time during walking are possible with this system. Conclusion: Movement analysis is important for understanding human behaviour. Furthermore, our precise, easy-to-handle and inexpensive system allows to quantify the effects of therapeutic interventions in patients with disturbed motor performance, e.g. in neurorehabilitation.

5-29-13 LONG TERM MANAGEMENT OF MULTIPLE SCLEROSIS: THE ROLE OF AN INPATIENT NEUROREHABILITATION UNIT.

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One of the major issues in the long term management of multiple sclerosis (MS) is the method of delivery of care which will address the diversity of problems seen in this condition. We have assessed the role of a multidisciplinary inpatient neurorehabilitation unit and have used outcome measures addressing impairment (Kurtzke's Disability Status Scale [DSS]), disability (Barthel Index [BI]) and handicap (Environmental Status Scale [ESS]) to assess efficacy. Seventy-nine patients with clinically definite MS were admitted for a mean stay of 15 days and were assessed on admission and prior to discharge by the same observers. Sixty-four patients had progressive MS and 15 were relapsing/remitting. The median DSS on admission was seven and improved in 16 patients. The median BI on admission was 14 and this improved in 51 patients by a median of two. An improvement in the ESS occurred in 23 of the 52 patients (44%). Changes in disability and handicap were most marked in the patients who improved neurologically ($p<0.01$) but also occurred in 65% of progressive patients.

This study suggests a useful role for an inpatient neurorehabilitation unit in the management of patients with MS including those with progressive disease.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

5-29-14 LONGITUDINAL P3 STUDIES IN STROKE PATIENTS

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Previous studies indicate that vascular lesions at the junction between temporal and parietal lobes either abolish or decrease the amplitude of P3 response, showing the affected hemisphere the clearest reduction. These studies were carried out in hemiplegic patients one year after stroke. The present research was aimed at monitoring auditory P3 response along the recovery period after stroke. 30 right-handed patients were followed for 7 months. The lesion was in the left hemisphere in 21 cases and in the right hemisphere in 9 cases. CT scan was always employed. Neuropsychological testing for aphasia was parallel to P3 recordings. It was observed that following a right hemisphere lesion P3 was always present, whereas following a left hemisphere lesion P3 was missed in 43% of cases. These patients suffered from global aphasia. The finding was confined to the first 3 - 4 months. Possible explanations are the following: i) anatomical impairment; ii) lack of comprehension; iii) other neuropsychological impairments, such as lack of attention or memory.

5-29-15 ISOKINETIC STRENGTH, MACRO EMG AND MUSCLE BIOPSY OF PARETIC FOOT DORSIFLEXORS IN CHRONIC, NEUROGENIC PARESIS.

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Ten ambulatory patients with different degrees of foot dorsiflexor paresis due to prior poliomyelitis or lumbar root (L V) lesion were examined with isokinetic strength measurement, macro EMG and muscle biopsy. Isokinetic strength measurement showed peak torques at 30^{o}/s angular velocity ranging 6-44 Nm; and at 240^{o}/s 1-10 Nm. Mean of individual median macro EMG motor unit potential amplitudes was 2020 μV (SD 1040), which was 5-10 times higher than suggested values in healthy subjects. Muscle biopsies showed a mean type 1 fiber proportion of 91% (SD 14) and a mean type 1 fiber area of 8561 μm^2 (SD 2773), which was about two times larger than observed in healthy subjects. Peak torque and both motor unit potential amplitude and area were inversely correlated at 30 ($p<0.01$ and $p<0.025$), 60 ($p<0.025$ and $p<0.025$) and 120 ($p<0.05$ and $p<0.05$) ^{o}/s angular velocity, as were peak torque and type 1 muscle fiber proportion at 30 ($p<0.05$) and 60 ($p<0.05$) ^{o}/s angular velocity. Peak torque or macro EMG parameters were not correlated to muscle fiber area. Our data suggest that with a chronic reduction of more than 60% of foot dorsiflexor motoneurons, there was a proportional reduction of muscle strength and increase of type 1 muscle fiber proportion.

5-29-16 COGNIVISION - A SOFTWARE PACKAGE FOR IDENTIFICATION OF NEUROPSYCHOLOGICAL DEFICITS AND REHABILITATION

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Some of the commonly used neuropsychological test and rehabilitation procedures have severe disadvantages. A modern neuropsychological test and training programme should meet the following requirements:

* tests should be unidimensional and measure cognitive performance;
* tests should be designed so that they can be carried out without prescribed time schedule:
* little time should be required for the solution of individual items;
* the answering mode should have no influence on the test result;
* the difficulty of items should be automatically adapted to the performance of the test person;
* processing should be done by a computer and results should be available immediately.

So far the following tests have been developed for Cognivision:

* OPS: a test for detection of cerebral organicity.
* Perception: a test for measuring perception and visual memory.
* Neglect: a test for evaluation and follow-up of visual neglect.
* Space: a test measuring spatial perception on the basis of optical illusions.

The tests are easy to perform. The perception test is an interesting alternative to the Benton test and can also be used for rehabilitation purposes. The test block "space" consists of several sub-tests and provides - contrary to test procedures currently used - direct information about spatial perception of the test person.

6-03-01 OUTCOME AND RECURRENCES AFTER CARDIOGENIC BRAIN EMBOLISM

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Functional outcome and recurrence rate were evaluated retrospectively among 566 consecutive patients with cardiogenic embolism. Source of embolism mostly was nonvalvular atrial fibrillation (NVAF; n=324), followed by nonrheumatic valvular heart disease (NVD; n=82), the acute (AMI; n=26) and chronic stage (CMI; n=36) after myocardial infarction, and prosthetic heart valves (PV; n=28). 75 patients had a TIA/RIND, 163 a minor stroke, 238 a major deficit, and 90 a fatal event. In a logistic regression analysis the probability of a disabling or fatal outcome was influenced by age (p=0.0023), a previous stroke (p=0.0262), concomitant carotid artery disease in Doppler sonography (p=0.0210), and the underlying heart disease (p=0.0001). Fatal or major strokes predominated among patients with NVAF, PV, AMI, and CMI. The cumulative risk of recurrent cerebral embolism was 2.9 % within three weeks. In a proportional hazards model only the underlying heart disease was significantly linked with the risk of recurrent embolism (p=0.021). In conclusion outcome after cardiogenic brain embolism depends on the underlying heart disease and is influencend by concomitant cerebral atherosclerosis. Early recurrence rate is lower than assumed previously.

6-03-02 OUTCOME AND LONG-TERM PROGNOSIS AFTER VERTEBROBASILAR ISCHEMIA

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Clinical, CT, Doppler, and angiographic findings of 630 consecutive patients with vertebrobasilar ischemia were evaluated with regard to the early outcome and long-term prognosis. 226 patients had a TIA (35.9 %), 169 a minor stroke (26.8 %), 160 a disabling event (25.4 %), and 75 patients a fatal stroke (11.9 %). In a logistic regression analysis diabetes (p=0.0145), initial somnolence (p=0.0001), tetraparesis (p=0.0001), dysarthria (p=0.0001), an infratentorial infarct in CT (p=0.0108), and bilateral vertebral artery stenosis or occlusion (p=0.0393) were independently linked with a fatal or disabling outcome. 381 of the 395 patients with TIA/minor stroke could be followed-up for 3.9 years in mean. Kaplan-Meier estimates revealed a cumulative stroke rate of 5.1 % within the first year and a risk of stroke, myocardial infarction, or death of any cause of 9.8 %. In a proportional hazards model increasing age (p=0.018), minor stroke vs. TIA (p=0.0005), hypertension (p=0.022), carotid artery occlusive disease (p=0.0065), and a previous stroke (p=0.0006) significantly increased the risk of a recurrent stroke.

6-03-03 WITHDRAWN

6-03-04 IS LEUKOCYTOSIS RELATED TO THE PROGNOSIS OF STROKE?

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It was well known that when leukocytosis exceeding certain level it would have a strong correlation with a poor clinical grade and poor outcome in subarachnoid hemorrhage. The relation between leukocytosis and intracerebral hemorrhage(ICH) in stroke has not been tested, to our knowledge. A retrospective study was made to 36 case of ICH who was admitted to Ho-Ping Hospital from July 1991 to June 1992. We selected 31 cases of cerebral infarct with age and sex matched as control. Thirteen out Of 36 cases in the ICH group were expired and 3 out of 31 cases in the CI group were expired. Complete peripheral blood cell count, differencial count of leukocyte, initial and final(appearance at discharged) neurologic state, and size and location of stroke (demonstrated by brain CT scan). Cases with obvious systemic complication were excluded. Cases who expired 14 days after onset were excluded also, for being afraid of die from nosocomial infection or other complications. The results of peripheral leukocyte counts showed significant difference between expired ICH group, survival ICH group, and control group (CI) who survived.

6-03-05 HEMOSTATIC MARKERS IN ACUTE REVERSIBLE CEREBRAL ISCHEMIA

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We assessed the activity of the coagulation system through measurements of selected markers in patients with acute TIAs.

Coagulation abnormalities have been shown previously in stroke patients but their potential role in the pathogenesis of acute reversible cerebral ischemia has not been fully investigated.

We measured Fibrinopeptide A (FPA), D-Dimer and Thrombin-antithrombin III (TAT) in 36 patients with acute TIAs within 7 days, at 1 month and 3 months. Markers were also measured in controls (n=65) and in patients with remote TIAs (n=26).

Acute TIA patient's median FPA levels at <7 days was higher than at 3 months (2.9 vs. 1.75ng/ml, p=0.01). TAT levels at <7 days were higher than at 1 month (3.65 vs 3.1ng/ml, p=0.02). FPA at <7 days was higher than in controls (2.9 vs 1.9ng/ml, p=0.03). D-Dimer levels at 3 months were higher than controls (640 vs 335ng/ml, p=0.008). Comparison of the remote TIA group to controls did not show any difference in marker levels.

Our data suggests that there is evidence for early transient activation of thrombogenesis and ongoing fibrinolysis after a TIA.

6-03-06 TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) IN CEREBROVASCULAR DISEASE.

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OBJECTIVE: The objective was to study cardiac emboli source in cerebrovascular disease in young adults. TEE was done in patients with complicated migraine and other transitory cerebral disorders. BACKGROUND: TEE complements examination of young adults with cerebrovascular disorders, but, its value in hemiplegic migraine has not been well established. DESIGN/METHODS: We studied 18 young patients who presented with hemiplegic migraine, or cerebrovascular syndrome who had no obvious cause. TEE detected embolic cardiac source in 3 of 18 cases. RESULTS: TEE was abnormal; one patient with hemiplegic migraine syndrome (papilloma), second with transient ischemic attacks (infectoma), the third with hemiparesis (myxoma). 3 of 18 abnormals is a slightly higher incidence than previously reported (approximately 12%). CONCLUSIONS: In our study the number of cases were rather small, and curiously enough, the papilloma and infective vegetation were not seen in surface 2D echocardiography. We conclude that TEE is extremely useful in workup of young patients with stroke syndrome, and complicated migraine (only TEE was diagnostic). In our small group no complications were noted and no bacteremia pursued following the procedure. Lesional video pictures will be shown.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-03-07 HEMOPOIETIC VALUES IN 500 SAUDI STROKE PATIENTS

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Hematological data on 500 consecutive Saudi stroke patients(342M; 158F)(mean age 63±17 yrs) were analysed to assess if high concentration of any of 3 parameters(RBC,Hb,Hct) is a risk factor for stroke. The composition of cases was: Large Infarcts 260(52%);Lacunar Infarcts 121(24.2%), intracerebral hemorrhage 107(21.2%) and subarachnoid hemorrhage 12(2.4%). Analysis of data showed that RBC(5.2±1.9x10^{a}/L),Hb(143±21g/l) and Hct (0.43±0.07)values were significantly higher (P<0.001) in patients with large infarcts as compared to other types of strokes.In all patients levels of above 3 parameters steeply arose at age 51 and fell at age 71. Highest values were in 61-70 yrs age group with males having higher than females(P<0.001). Our data suggested that CBC values were somewhat increased in our patients compared to normal Saudi values,especially in large infarcts.Since all CBCs were done in acute phase,it was difficult to ascertain if relative polycythemia was a primary event for stroke or was secondary to dehydration, stress or reactive hematopoeisis secondary to tissue hypoxia.

6-03-08 THE RESEARCH OF THE PERSISTANCE OF TXA_2-PGI_2 IMBALANCE IN RAT BRAIN WITH INCOMPLETE CEREBRAL ISCHEMIA AND REPERFUSION, AND THE CORRECTION OF THIS IMBALANCE BY CARTHAMIC XANTHOPHYLL

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In this study, we investigated the time course of TXB_2 (the stable metabolite of TXA_2) and 6-Keto-$PGF_{1\alpha}$ (the stable metabolite of PGI_2) for 24 hours in rat brain with incomplete cerebral ischemia and reperfusion. The result reveals the disorder of TXA_2-PGI_2 balance after incomplete cerebral ischemia and reperfusion is most obvious at 2 hours, and does not recover completely until 24 hours. So we suggest that the measurements achieved to correct the disorder of TXA_2-PGI_2 balance in patients with cerebral infarction should be maintained for at least 24 hours. We had researched the effect of Carthamic Xanthophyll on the level of TXB_2 and 6-Keto-$PGF_{1\alpha}$ in rat brain with incomplete cerebral ischemia and reperfusion. The result shows that the elevation of TXB_2 after incomplete cerebral ischemia is inhibited by Carthamic Xanthopyll; however, the level of 6-Keto-$PGI_{1\alpha}$ has little change. So it is believed that the disorder of TXA_2-PGI_2 balance can be alleviated by Carthamic Xanthophyll in incomplete cerebral ischemia. In reperfusion group, Carthamic Xanthophyll not only inhibits the elevation of TXB_2 but also increases the level of 6-Keto-$PGF_{1\alpha}$ making TXA_2-PGI_2 balance recover to normal 6 hours after reperfusion. So we believe that Carthamic Xanthophyll has the scientific basis to be used clinically for the treatment of ischemic cerebral vascular diseases.

6-03-09 THE DYSARTHRIA-HEMIPARESIS SYNDROME; A STROKE SYNDROME OF PARAMEDIAN PONTINE INFARCTIONS CAUSED BY ATHEROMATOUS BRANCH OCCLUSION OF THE BASILAR ARTERY.

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The purpose of this study is to elucidate the clinical features of paramedian pontine infarctions(PPI) caused by atheromatous branch occlusion of the basilar artery.

We defined PPI as a cerebral infarction in the whole territory of a paramedian pontine branch of the basilar artery. To elucidate the clinical features of PPI caused by branch occlusive disease, cases with large vessel occlusive disease in the vertebrobasilar system were excluded by conventional or MR angiography.

During the past five years, 21 cases of acute PPI were diagnosed by CT or MRI. There were 9 men and 12 women with a mean age of 65 years. All cases exhibited dysarthria and hemiparesis with varying degrees. Dysarthria was often prominent. Mild ataxia was noted in 6 cases and sensory symptoms in 7. In 16 cases, dysarthria and/or hemiparesis worsened in a stepwise fashion for 2 to 9 days after the onset.

In summary, progressing hemiparesis with prominent dysarthria(dysarthria-hemiparesis syndrome) was the most frequent clinical feature in PPI caused by atheromatous branch occlusion of the basilar artery.

6-03-10 BRAIN-STEM STROKE IN YOUNG ADULT

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Brain-stem stroke occurs mainly in the elderly and the cause is chiefly atherosclerotic and hypertensive. However, reports of brain-stem stroke in young adult are rare. We studies 39 patients, aged from 19 to 49, observed over a 8-year period (1985-1992) from about 4000 cases in Mackay Memorial Hospital. There are 24 infarction and 15 hemorrhage cases. The mean age in the hemorrhage group (43.9) is older than the infarction group (39.5). In the infarction group, 67% of these patients had associated disorders, for example hyperlipidemia, hypertension and diabetes mellitus. The sites of lesions were mainly in the medulla oblongata(11/24). The functional recovery was excellent in most of the cases (19/24, Rankin disability scale grade 1 and 2). In the hemorrhage group, there were 9 hypertensive, and another one proved to have cavernous hemangioma by MRI. The bleeding site was mainly in the pons. The initial presenting symptom was conscious disturbance in all cases with only one exception. There were 11 dead. In conclusion, hypertension remains the major cause of brain-stem stroke. The prognosis is good in the infarction group and poor in the hemorrhage group.

6-03-11 NEUROEPIDEMIOLOGICAL CHARACTERISTICS OF APHASIA OF VASCULAR ETIOLOGY

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Considering the patho-physiological mechanisms of the appearance of stroke and the mechanisms of recovery, neuroepidemiological investigations of vascular diseases and aphasias, open the prospects of solving the problem of the treatment of aphasias, which are not only an individual handicap, but also a professional, scientific, family and social problem.

This paper is a part of an extensive epidemiological study, carried out in the course of a two-year period, which comprised 384 patients with aphasia. The results of the investigation indicate a high mortality rate in aphasic patients, a high percentage of the presence of hemiplegia, thrombozis and hemorrhage as the most frequent etiological factor, and hypertension as the most frequent risk factor.

The other results, also obtained in this investigation, point out to epidemiological characteristics of aphasia of vascular etiology which programmes of the treatment of aphasia. By applying the results of these investigations, it is also possible to develop some of the aspects of the evaluative and diagnostic aspects of vascular diseases and aphasias.

6-03-12 THE STUDY OF THE RED CELLS AND FIBRINOGEN INTERACTION IN THE ACUTE PHASE OF ISCHEMIC STROKE

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In 36 patients with the acute phase of ischemic stroke a significant decrease of serum albumin /$p<0,05$/, IgM /$p<0,05$/, apo A_1 /$p<0,05$/ and HDL /$p<0,05$/ were indicated, whereas level of IgA was elevated /$p<0,001$/. In all studied subjects the value of yield shear stress /YSS/ demonstrating the red cells and fibrinogen interaction was also established by means of viscometric method. In patients the frequency of YSS higher than median was presented significantly /$p<0,05$/. YSS positively correlated with level of fibrinogen /in patients/ and with IgM /in controls/. The influence of fibrinogen on the thixotropic effect /value of YSS on 100 mg of a certain biochemical factor/ some of plasma constituents was analized and a high significant correlation /$p<0,001$/ regarding apo A_1 and albumin were indicated. These disturbances were noted only in patients, whereas in controls there were not any significant correlations. This observation might suggest a role of unknown factors connected directly with the ischemic process.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-03-13 LANGUAGE DISORDERS IN ANTERIOR OPERCULAR SYNDROME

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Anterior opercular syndrome (AOS) is characterized by labio-glosso-facio-pharingo-masticatory palsy. Aphasic disorders are of Broca's type, while impairment of comprehension is rare. We studied seven right-handed patients with AOS and bilateral perisylvian infarcts on the CT-scan. In four marked deficits of comprehension were observed. The CT-scan and the autoptic study in two of them revealed extensive involvement of the subcortical white matter or of the deep structures on the left side; besides both anterior and posterior opercula of the right hemisphere were extensively involved. In the cases without impairment of comprehension the lesions were circumscribed to the anterior opercular cortex. We suggest that disorders of comprehension in AOS may depend upon the extent of the lesions in the posterior opercular areas and subcortical structures of the dominant hemisphere. The minor hemisphere may also play a role because it may represent a functional reserve for recovery not only of articulatory, but also of receptive functions.

6-03-14 RISK FACTORS FOR ISCHEMIC STROKE IN THE ELDERLY

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We have conducted a nation-wide survey of the health status in the elderly aged 65 or over. The prevalence of cerebrovascular disease was 6290/100,000 in this age group. Among the post-stroke elderly, 74.3% of them were confirmed as cerebral infarction by CT of the brain. Therefore we evaluated the risk factors for elderly ischemic stroke. Factors possibly related to ischemic stroke were compared between post-stroke elderly who developed ischemic stroke after the age of 65 or over and non-stroke elderly. The percentage of elderly with a history of hypertension, smoking or diabetes mellitus was significantly higher in the post-stroke group than in the non-stroke group. Biochemical examinations at the time of survey revealed that mean level of high-density lipoprotein cholesterol (HDL) was significantly low and that of triglyceride (TG) was significantly high in the post-stroke elderly. But the percentage of elderly with abnormal level of TG was not significantly different between the two groups. On the contrary, mean level of LDL was not significantly different between the two groups, but a significantly higher percentage of elderly in the post-stroke group had abnormal level of LDL. Hypertension, diabetes mellitus, low HDL and high LDL are important risk factors for elderly ischemic stroke.

6-03-15 CLINICAL OUTCOME OF ACUTE ISCHEMIC STROKE PATIENTS WITH HEMORRAGIC TRANSFORMATION OF THE INFARCT

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In a continuous series of 124 patients hospitalized within 5 hours of their first ever ischemic supratentorial stroke, we investigated whether the hemorragic transformation of the infarct influenced 30-day clinical outcome. Of the 64 patients (53%) who developed an hemorragic infarction (HI), 15 (23%) died, 15 (23%) improved, 26 (41%) remained unchanged and 8 (13%) deteriorated, as opposed respectively to 8 (13%), 27 (45%), 18 (30%) and 7 (12%) of the 60 patients with no hemorragic infarction (non HI) (p=.07). The infarcts were cortical in 26 (41%), subcortical in 3 (4%) and cortico-subcortical in 35 (55%) HI patients as opposed respectively to 16 (27%), 35 (58%) and 9 (15%) non HI patients ($p < .001$). Infarct size (as detected by CT or by autopsy) was large (>1 lobe) in 37 (58%), medium (between 1/2 and 1 lobe) in 23 (36%) and small (<1/2 a lobe) in 4 (6%) HI patients, and respectively in 7 (12%), 19 (32%) and 34 (56%) [of whom 15 (25%) were lacunes] non HI patients ($p < .001$). Infarct size and site differed also in the subgroups identified by clinical outcome. These data suggest that both clinical outcome and hemorragic transformation of the infarct were strictly correlated to size and site of the lesion, with probably no clinical consequences of HI.

6-03-16 PROGNOSIS OF HYPERACUTE ISCHEMIC STROKE PATIENTS WITH CERVICAL INTERNAL CAROTID ARTERY OCCLUSION

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We evaluated retrospectively 19 consecutive ischemic stroke patients with congruous occlusion of the cervical internal carotid artery (CICAO) and compared them to 45 patients with no CICAO. Our aim was to assess whether early cerebral tomography (CT) findings may provide useful prognostic indications in this subset of acute stroke patients. CT scan and angiography were completed within five hours of the event. The CICAO group exhibited a very high 30-day fatality rate or severe neurological impairment (84% vs. 60%, $p<.05$). There was a trend for more frequent early hypodensity (EH) at first CT in CICAO (79% vs. 67%, $p<.2$). In particular, CICAO patients had far more cortico-subcortical EH in middle cerebral artery (MCA) territory than no CICAO ones (42% vs. .04%, $p<.001$). Among CICAO patients early cortico-subcortical EH defined a subgroup with very poor prognosis (44% case fatality rate and 100% severe impairment among survivors vs. no fatalities and 67% severe impairment in non EH patients). Hyperdense MCA sign did not influence the outcome. The poor prognosis of acute ischemic strokes with CICAO may justify aggressive treatments. CT findings may guide therapeutic decision making in individual cases and help for stratification in therapeutic trials of pharmacological or surgical reperfusion.

6-03-18 INDICES OF FREE RADICAL ACTIVITY IN THE CEREBROSPINAL FLUID IN ACUTE ISCHEMIC STROKE

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Only indirect evidence has been obtained indicating the generation of free radicals during and after cerebral ischemia because of the short half lives of the oxygen radicals. We investigated indices of free radical activity and lipid peroxidation in cerebrospinal fluid (CSF) samples obtained from 15 patients with acute ischemic stroke and 10 control subjects. Conjugated dienes (CD) and malondialdehyde (MD) concentrations were measured by using u.v. spectrophotometry. CD were assessed by the measurement of the absorbance at 235 nm of the chloroform layer against a pure chloroform blank using second derivative curves. MD was assessed by tiobarbituric acid (TBA) test and measurement of the absorbance at 460 nm. MD mean values were significantly increased in the patient group. ($P < 0.01$). CD mean values were also increased but the difference compared with the controls was not statistically significant.

It was concluded that the measurement of lipid peroxidation indices in CSF of patients with acute ischemic stroke by using TBA test is a practical and rapid way of determining free radical activity and could be used in the evaluation of lipid perosidation inhibitors which would be used clinically in the near future.

6-03-19 PROGNOSIS OF INTRACEREBRAL HEMORRHAGE IN CORRELATION WITH CT FINDINGS

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210 consecutive patients (98 men, 112 women; mean age 61 +/- 16years) with the diagnosis "Intracerebral hemorrhage" (ICH) were included in this study. All patients had cranial computed tomography (CCT) on admission. The volume of the ICH in ccm was estimated(mean ICH value 43.3+/- 53.1 ccm, range 0.5-288).The clinical prognosis - with respect to prognistic predictors during hospitalisation -was evaluated retrospectively.73/210 (35%) patients died during hospitalisation. The mean survival time was 10.3 days.Significantly associated with death during hospitalisation were: higher age (67 vs 58 years), larger ICH volume (67 vs 30 ccm), initial coma (37 vs 5%), initial severe neurological deficit (73 vs 29 %), coagulopathy (22 vs 11 %), previous stroke (22 vs 10 %). Hypertension was more frequent among survivors (80 vs 63 %). 26% of survivors were treated operatively, vs 12% of the patients who died during hospitalisation.In 115/137 surviving patients clinical follow-up was performed. The mean follow-up time was 30.3+/- 19.1 months. 40 % were completely independent, 33% slightly and 22% moderatly handicapped. 15% were completely helpless. 12% had developed vascular epilepsy.Prognosis was significantly associated with ICH volume size, initial level of consciousness, initial degree of neurological deficit and form of treatment but not with age,hypertension or sex.

6-03-20 CLINICAL AND LABORATORY INVESTIGATION OF PATIENTS WITH CEREBRAL ISCHEMIA UNDER PENTOSAN POLYSULFATE THERAPY

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I. *Acute effect of pentosan polysulfate* (PPS) an orally applicable heparinoid: Forty three patients with ischemic stroke received 4 mg/kg drug in one hour periode, *i.v.* Euglobulin lysis and Quick-time decreased significantly, prolongation of partial thromboplastin time (APTT) and thrombin time lasted for 2-4 hours. Anticoagulant effect of PPS related inversely to the level of high density lipoprotein (HDL). II. *Follow up investigation*: Seventy four patients with ischemic stroke received PPS continuously (200-400 mg/ day) orally over 2-6 years (mean=4.2 years). Control patients received no anti-coagulants during the observation period. In the treatment group significant decrease of initial hematocrit and increase of APTT was observed; however plasma fibrinogen, cholesterol and HDL level remained uneffected. The neurological condition of patients improved significantly in both groups after the acute stage of disease. Frequency of recurrent stroke and death in the control group was higher than in the teratment group by 32% and 25 % respectively. *Conclusion:* I.v. administered PPS proved to have strong fibrinolytic and heparin-like effect on the blood coagulation. Oral medication reduced the frequency of recurrent stroke and improved the life expectancy of patients.

6-03-21 THE OBSERVATION OF ENCEPHALOELECTRIC INDEX IN ISCHEMIC CEREBROVASCULAR DISEASES

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This article analysized encephaloelectric index of 249 cases ischemic cerebral vascular diseases verified by CT scan, and compared with that of 147 normal people. The findings were that, in encephaloelectric index, the slow wave in patient group more than control group, and α wave less than control group. These are similar in both lesion area and distant area.

This study shows that despite change, of encephaloelectric indexes in ischemic vascular disease is slowing down of encephaloelectric activities (α and θ wave index increase), the decrease in α wave considerable (compared between experimental and control group, the differences in both normal and abnormal are significant, $p < 0.01$ and $p < 0.05$, respectively). This is different from the results of Wang Tao's report. There is not significant difference in β wave band.

6-03-22 EPIDEMIOLOGICAL STUDY AND CLINICAL OUTCOME OF COMPLETE STROKE IN XINJIANG, CHINA: A SUMMARY OF 32 YEARS EXPERIENCE

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Shihezi is an urban and rural population of about 800,000. The incidence of stroke during the 1980s is gradually increasing. Three epidemiological studies during the 1980s were carried out and the clinical data were analyzed from 1960 to 1961 by us.

Results and Conclusions: (1) Stroke was increasing progressively from year to year. The incidence of complete stroke in Shihezi is at the highest level in China. The causes might be population aging and the dry and cold weather. (2) It is still at a lower level as compared with other data from China. (3) The fatality in our hospital also declined progressively (13% in the recent two years while in 1960s it was 30%). (4) Causes of death are various complications. An important means should be prevented. (5) Low mortality is synchronized with low fatality in hospital. The medical system and service attitude of Shihezi may be far superior to other areas. Many complications can be prevented and treated actively to increase survival rates.

6-03-23 MR ANGIOGRAPHY IN VERTEBROBASILAR ISCHEMIC STROKE

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Cerebral angiography can detect, localize, and quantify occlusive cerebrovascular lesion, but it is considered risky and seldom performed in vertebrobasilar artery(VBA) system. MR angiography(MRA) may provide an alternative way without invasive procedure to understand the lesions in these vessels. Twenty-one MRI-proved brainstem and/or cerebellum infart patients with MRA examination were retrospectively reviewed in 18 months periods(June,1991 to December,1992). The findings showed stenosis or occlusion of basilar artery in 11 patients, of vertebral artery in 3, of both vertebral and basilar arteries in 3 and unremarkable change in these vessles in 4. The MRA findings in these 4 patients may suggest the possibility of small vessel disease. The other 17 patients with stenosis or occlusion in VBA may related to thrombotic process or even related to embolism in some of them. Although the application of MRA to the diagnosis of VBA disease is largely unexplored, there are still several reports presenting good correlation in MRA and conventional angiography. Further data collection is needed for better understanding the pathogenesis of vertebrobasilar stroke and may provide a more scientific basis to use antiplatelet drug, anticoaguant therapy or even fibrolytic agent like tPA.

6-03-24 HETEROGENEOUS LOCALIZATION OF ENDOTHELIN-1 IN HUMAN STROKE BRAIN

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Endothelin-1 (ET-1) is a potent and long-lasting vasoconstrictor peptide. Present study is focused on localization of ET-like immunoreactivity in human stroke brain. Stroke brains with middle cerebral artery (MCA) occlusion were used for immunohistochemical study. Three micrometer paraffin sections were dewaxed, hydrated and washed in phosphate-buffered saline (PBS). After trypsinization, sections were incubated with normal swine serum in PBS. This was followed by incubation with rabbit polyclonal anti-human ET-1 antibody. On the following day, sections were rinsed with PBS and then incubated with biotinylated swine anti-rabbit immunoglobulin. After rinsing with PBS, sections were incubated with avidinbiotin complex, rinsed, then incubated with diaminobenzine, counterstained with hematoxylin. Immunohistochemical methods demonstrated a heterogeneous staining for ET-like immunoreactivity and the different intense immunoreactivity among center MCA, boundary MCA and non-MCA territory. We also compared these ET-1 localizations with that obtained from control brain without cerebrovascular disease. These data suggest that the immunohistochemical localization of ET-1 is closely related to the induction of ET-1 production in human stroke brain.

6-03-25 EFFECT OF MODERATE HYPONATREMIA ON THE LEVEL OF CONSCIOUSNESS IN PATIENTS WITH STROKE

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Severe hyponatremia(Na<110mEq/l) is well known to induce disturbance of consciousness. However, it remains uncertain whether moderate hyponatremia has an effect on the level of consciousness or not. The aim of the present study was to clarify the involvement of stroke in the disturbance of consciousness which derives from hyponatremia. We analyzed the clinical data of eight patients with moderate hyponatremia (120<Na<130mEq/l). Four patients (age,73.0±7.9years) were stuporous. They had suffered from thalamic hemorrhage, caudate hemorrhage, cerebral infarction or chronic subdural hematoma. They developed hyponatremia as a result of SIADH or a decreased Na intake at the subacute or chronic stage of stroke. They had become stuporous without any other evident causes except hyponatremia. The minimal plasma Na levels were 124.7, 121.7, 128.5 and 122.2 mEq/l, respectively (mean±SD,124.3±2.7mEq/l). The remaining four patients (age,71.5±4.7years) did not show any change in level of consciousness. CT scans revealed small lacunar infarctions in two cases. The other two cases suffered from diabetes and tension headache. The causes of the hyponatremia were SIADH, poor sodium intake or overhydration. The minimal levels of plasma Na were 121.3, 126.7, 127.4 and 123.1 mEq/l, respectively (mean±SD,124.6±2.5mEq/l). The severity of hyponatremia did not differ between the two groups. The present data suggest that moderate hyponatremia can lower the level of consciousness in patients with major stroke.

6-03-26 NONINVASIVE DIAGNOSIS AND FOLLOW-UP OF MIDDLE CEREBRAL ARTERY STENOSIS

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Transcranial Doppler (TCD) and Magnetic Resonance Angiography (MRA) were prospectively used to assess stenosis of the middle cerebral artery (MCA) in patients with stroke or TIA. Results were correlated with intraarterial DSA. In 26 patients 30 MCA stenoses were found. TCD was right positive in 29 cases and false negative in 1 patient. MRA findings were positive in all cases, however MRA tended to overestimate the degree of stenosis. Combined use of TCD and MRA allows noninvasive diagnosis of MCA stenosis with high accuracy.
TCD, MRA and transcranial color Doppler imaging (TCDI) were used for prospective follow-up examinations of patients with MCA stenosis. TCDI allows real time imaging of the MCA and enables exact velocity measurements within defined vessel segments. Asymptomatic progression to MCA occlusion could be demonstrated in 2 patients.
TCD, TCDI and MRA are ideal tools for follow-up studies of patients with MCA stenosis.

6-10-01 CEREBRAL BLOOD FLOW AND METABOLISM IN PATIENTS WITH MOTOR NEURON DISEASE WITH DEMENTIA

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This study was designed to investigate cerebral blood flow (CBF) and cerebral oxygen metabolism ($CMRO_2$) in patients with motor neuron disease with dementia. Two patients with motor neuron disease with dementia, 3 patients with motor neuron disease without dementia, 7 patients with clinically diagnosed Alzheimer's disease, and 5 patients with clinically diagnosed Pick's disease were studied. CBF and $CMRO_2$ were measured by positron emission tomography (PET) using $^{15}O_2$, $C^{15}O_2$ steady state inhalation technique. In one patient with dementia with motor neuron disease, CBF and $CMRO_2$ decreased in the whole cortex, and severely decreased in the frontal cortex. In another patient with motor neuron disease with dementia, CBF and $CMRO_2$ reduced slightly in the frontal cortex and the left temporal cortex. In patients with motor neuron disease without dementia CBF and $CMRO_2$ were preserved. In patients with Alzheimer's disease CBF and $CMRO_2$ decreased in the cortex, but there was no severe reduction in the frontal cortex in comparison to the posterior part of brain. In patients with Pick's disease CBF and $CMRO_2$ decreased markedly in the frontal cortex, but those values were preserved in the parietal cortex and the occipital cortex. A marked reduction in CBF and $CMRO_2$ in the frontal cortex was a common characteristic PET finding in both dementia with motor neuron disease and Pick's disease. These results suggested that there might be some relationship between motor neuron disease with dementia and Pick's disease.

6-10-02 EXPRESSION OF AMYLOID PROTEIN PRECURSOR AND CATALASE mRNA IN CANCER BEARING MICE BRAINS

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Although amyloid protein precursor (APP) in Alzheimer's disease has been attracting attention in recent years, the function of APP in vivo is not enough clear. The previous reports suggest that free radical may play a role in deposition of β-protein. To evaluate connection between APP and free radical, we measured mRNAs of APP and catalase in cancer bearing mice brains. Cancer (MKN28) bearing mice were classified into 4 groups on the basis of volume of cancer; normal group, stage 1 group defined as mice with cancer volume under $0.3cm^3$, stage 2 group from $0.3cm^3$ to $0.6cm^3$, stage 3 group over $0.6cm^3$. We extracted total RNA from whole mice brain and performed Northern blot analysis. *Expression of APP and catalase mRNA in stage 1 group increased more remarkably* than those of normal group, but decreased in correlation with enlargement of tumor size from stage 2 to stage 3. Expression of APP mRNA in cancer bearing state changed in parallel with them of catalase. Our study suggest that both APP and catalase may play a role in deposition of β-protein in Alzheimer's disease.

6-10-03 ELEVATED EXPRESSION LEVELS OF AMYLOID PROTEIN PRECURSOR (APP) mRNAS IN SKIN FIBROBLASTS FROM PATIENTS WITH DEMENTIA OF THE ALZHEIMER TYPE

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Deposition of amyloid β proteins in non-neural tissues, such as the skin, and intestine of patients with dmentia of the Alzheimer type (DAT) suggests that the disease may be a systemic disorder. In the present study, we investigated the *expression of APP mRNAs in cultured skin fibroblasts from demented patients.* Skin fibroblasts obtained from 12 DAT patients, 7 patients with multi-infarct dementia (MID), and 8 control subjects were cultured in media untill the passage of four or five. Cellular RNAs were extracted by acid guanidinium thiocyanate-phenol-chloroform method. APP mRNA was amplified by the polymerase chain reaction (PCR) technique primed reversetranscription (Golde et al.). Using two primers, three major fragments derived from mRNAs for APP695, APP751, and APP770 were purified by polyyacrylamide gel electro phoresis-autoradiogram. Their relative expression levels were measured by densitometry. In DAT patients, both the ratio of APP751 to APP695 (APP751/APP695) and that of APP770 to APP695 (APP770/APP695) were significantly increased than those in the other two groups. This result showed that the expression of the APPmRNA including Kunitz-type serine protease inhibitor (KPI) domain was enhanced in Alzheimer skin fibroblasts. Abnormally regulated APP metablolism may contribute to β amyloidogenesis in non-neural tissues of DAT patients as well as in the brain.

6-10-04 GROWTH INHIBITORY FACTOR mRNA IN PROGRESSIVE SUPRANUCLEAR PALSY

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The expression of the growth inhibitory factor (GIF) is dramatically decreased in Alzheimer's disease (AD) , especially in AD brains with numerous neurofibrillary tangles (NFTs) and curly fibers. To gain insight into the relationship between GIF and NFTs, we investigated GIF mRNA in progressive supranuclear palsy (PSP) which is another disease with NFTs except AD. Brains from 4 normal subjects and 7 PSP patients were examined. RNAs were extracted from both normal and PSP frontal brains and analyzed by Northern blot hybridization. A DNA fragment generated by PCR amplification of the specific 3' non-coding sequence of GIF cDNA was used as the probe. A case with NFTs in frontal cortex exhibited less expression of the GIF mRNA than normal brains.Six patients with no NFTs in frontal cortex showed normal expression of the GIF mRNA.These results suggest that GIF may have relation to the appearance of NFTs.

6-10-05 CEREBRAL METABOLIC ALTERATIONS IN DEMENTIA OF ALZHEIMER'S TYPE (SDAT) DETECTED BY PROTON MAGNETIC RESONANCE SPECTROSCOPY

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Proton Magnetic Resonance Sprectroscopy (HMRS) is particularly suitable for non-invasive in vivo measurement of metabolic alterations. The purpose of this study was to measure metabolic alterations in SDAT compared to normal aging. We investigated 8 patients (66.6±12 y) with SDAT according to NINCDS-ADRDA criteria, 6 of whom were drug free, and 6 age-matched healthy controls (mean 61.6 y). Integrated MRS and -Imaging was performed, and localized proton spectra of different volumes of interest were obtained. Semiquantitative analysis by ratios to the creatine signal (Cr), which is remarkably constant, revealed a significant ($p \leq 0.01$) reduction of NAA/Cr in the parietal grey and white matter in SDAT, whereas myo-inositol /Cr remained unchanged. This allows the conclusion, that in HMRS, NAA reflects neuronal cell damage in SDAT, as it could be shown under other conditions in previous studies.

6-10-06 REDUCED CEREBROVASCULAR RESPONSIVITY TO ACETAZOLAMIDE IN DEMENTIA OF ALZHEIMER'S TYPE (DAT)

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Previous studies in patients with DAT showed an impaired response to psychological stimuli in temporal regions, as measured by cerebral blood flow (CBF) and Glucose Positron Emission tomography (PET). Under the hypothesis of an underlying decreased general reactivity of cerebral vessels in DAT we performed CBF-measurements with 99mTc HMPAO and single photon emission tomography (SPET) before and 15 minutes after intravenous administration of 1 g acetazolamide in 8 DAT patients (71.5 ± 9.1 y) with various degrees of cognitive impairment (Mini-Mental-State-Examination (MMSE): 8 - 21, mean 15.1) and 6 age matched controls. We subtracted resting values two times from those values following stimulation and divided the result by the resting values. Thus, we obtained percentage values, which showed a positive correlation to MMSE-values, that means a negative correlation to severity of cognitive impairment. We conclude that neurodegeneration in DAT causes impairment of cerebrovascular reactivity.

6-10-07 EFFECTS OF CARBAMYLCHOLINE,THROMBIN ON AMYLOID PRECURSOR PROTEIN mRNA EXPRESSION

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The β /A4 protein,the major component of the amyloid depositions which characterize Alzheimer's disease,derives from the amyloid precursor protein(APP).

We investigated effects of carbamylcholine, m3 receptor agonist and thrombin,serum protease on APP mRNA expression using cultured human SK-N-SH neuroblastoma cells which possess m3 receptor.Total RNA was extracted from cultured cells with acid guanidium phenol chloroform methods and Nothern blot analysis was performed using 2.2kb APPcDNA probe to detect the general APP sequence.

Treatment of subconfluent cultured cell with carbamylcholine (1mM) result in approximately 3- fold increase of APP mRNA expression after 8 hr.The increased APPmRNA was turned out to be APP695 mRNA. Furthermore,treatment of the cell with thrombin (1U/ml) also enhanced the expression of APP mRNA after 24hr.However,other serum protease plasmin and tissue plasminogen activater did not change the level of the APP mRNA expression.

These results suggeest that carbamylcholine and thrombin regulate APP gene expression and may contribute to amyloidgenesis of Alzheimer's disease.

6-10-08 ABNORMAL DISSIMILATION OF PHOSPHOLIPID IN THE BRAIN WITH ALZHEIMER'S DISEASE

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We investigated phosphorus metabolites of the brain with Alzheimer's disease, applying in vivo ^{31}P magnetic resonance spectroscopic imaging (^{31}P-MRSI) using a 2 tesla whole body MR spectrometer.

We firstly measured spin-lattice relaxation time(T1) of phosphorus metabolites using inversion recovery and modified spin echo technique. As this result, we set 20 seconds as repetition time in this study. ^{31}P-MRSI study was performed under the conditions of echo time=4 msec., matrix=8×8, voxel size=3×3×4cm(36ml) and acquisition=1 time. We set a tube filled hexamethylphosphorustriamide (HMPT) as reference. ^{31}P-MRSI spectra were processed and each integrated peak areas were corrected referring to the signal of HMPT.

The phosphodiesters(PDE) of Alzheimer brain were longer in T1 (2.54±0.67 sec.) and larger in quantity(1.24±0.34 Mol/l) than those of normal controls(1.52±0.39 sec., 0.74±0.31 Mol/l). PDE are thought of intermediate metabolites of phospholipid dissimilation. These result suggest abnormal dissimilation of phospholipid in Alzheimer's disease.

6-10-09 AMYLOID PROTEIN PRECURSORS WITH KUNITZ-TYPE PROTEASE INHIBITIOR DOMAINS IN CSF OF DEMENTIA OF THE ALZHEIMER TYPE

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We examined the correlation of amyloid protein precursors with kunitz-type protease inhibitor domains (APPI) with acetylcholinesterase (AChE) and somatostatin (SRIF), and the correlation of APPI with the clinical course in patients with DAT.

The subjects consisted of 20 patients with DAT, 11 patients with multi-infarct dementia (MID) and 10 age-matched control subjects. Dementia was diagnosed according to the DSM-III-R diagnostic criteria and NINCDS-ADRDA criteria. We measured the APPI concentration by the trypsin-sandwich ELISA, the AChE activity spectrophotometrically using the thiocholine method, and the SRIF concentration by the double antibody RIA method.

We found the APPI in CSF of DAT to be significantly elevated compared with that of MID and controls. We could significantly correlate APPI with AChE, but not correlate APPI with SRIF. DAT patients showed symptomatic aggravation during the course, with decrease in the CSF level of APPI.

Our study shows that measurement of CSF APPI level may be useful for diagnosis of DAT and that CSF level of APPI reflects the condition of DAT well.

6-10-10 AN INITIAL STUDY OF CYTOSKELETAL PROTEINS ON ALZHEIMER'S DISEASE AND AGING BRAIN.

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Some reports showed some similar pathologic and chemical features in the Alzheimer's disease(AD) and non-dementia aging(NDA), but less severe in the latter. Is that same in the cytoskeletal proteins(CSPs)? The 160-200kd phosphorylated and non-phosphorylated neurofilaments(PNFs and nPNFs) monoclonal antibodies were used as probe to study the CSPs distribution inside cerebral neurons in 4 normal adults, 2 NDA and 2 patients with AD. Peroxidase anti peroxidase and low temporature embedding immunocolloidal gold techniques were performed. Normally, nPNFs was located in the perikarya and dendrites, wheres the PNFs mainly was enriched in the axon and peripheral of neuron's cell bodies. Interestly there were many PNFs and nPNFs in the cytonuclei of cortical neurons. It indicates CSPs was not only in the cytoplasm, but also in the cytonuclei and the phosphorylation was taken place in the cytonuclei as well. In AD, no significant difference was seen when nPNFs compared with normal adult brain, but PNFs was accumulated inside the neurons cell bodies, We did not find any immunoreactivity of above CSPs in the senile plaques. In NDA brain, there were less PNFs and nPNFs and more lipofuscins than in the normal adults, around lipofuscin there were more PNFs and nPNFs. It is significant different between AD and NDA.

6-10-11 DEMENTIA-PRONE LIFESTYLES; RISK FACTORS IN ALZHEIMER'S AND BINSWANGER'S DISEASE

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Case-control studies were made in Alzheimer's disease (AD) as well as Binswanger's disease/multifarct dementia (BD/MID).

In AD, significant risk factors included 1) psychosocial inactivity, 2) physical inactivity, 3) head injury, 4) loss of teeth, 5) low education. In BD/MID, they were 1) psychosocial inactivity, 2) physical inactivity, 3) head injury, 4) history of diseases (hypertension, diabetes, habitual constipation, etc.), 5) failure to participate in health examination. Many factors were in common with the two diseases, and they appeared non-specific promoters of dementing given each specific brain lesions. Hypertension, etc., were specific to vascular lesions leading to cerebral ischemia, but so far no factor including head injury was truly specific to AD. Loss of teeth was not significant in BD/MID who were much elder than AD, and the controls also lost their teeth.

Risk factors in senile dementias are not necessarily disease-specific or cause-specific.

6-10-12 GALANTHAMINE TREATMENT IN ALZHEIMER'S DISEASE: A PRELIMINARY EVALUATION OF FORTY PATIENTS

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A multicenter placebo controlled double blind enriched de-challenge efficacy, safety and tolerability trial of Galanthamine in mild to moderately severe Alzheimer's Disease (AD) was initiated. After a one week single blind placebo run-in period a three week single blind dose optimization and enrichment phase with a flexible dosage schedule was carried out. Responding patients were randomized and entered into a ten week double blind, de-challenge phase. Following titration of individual doses 40 patients who met NINCDS-ADRDA criteria for probable AD were enrolled. Results: 24 patients showed improvement in the cognitive subscales of the ADAS. The improvement of 8 patients in the constructional praxis was unexpected. Six patients learned to draw a three-dimensional cube. In the responder group the Mini Mental State increased from a mean of 19.29 (range 14 - 23) to 21.95 (16 - 27), and the Functioning Score increased from a mean of 53.58 (38 - 65) to 58.83 (43 - 68). Serious adverse events lead to two discontinuations. In the Global Evaluation we saw 24 responders (2 very much improved, 12 much improved, 10 minimally improved) and 15 non-responders (11 unchanged, 2 minimally worse, 2 much worse) and 1 drop out.

In summary, the results indicate that Galanthamine has overcome the pharmacokinetic limitations of the First Generation ChEI, and has therapeutic potential.

6-10-13 SENILE DEMENTIA OF ALZHEIMER TYPE (SDAT): LONG-TERM TREATMENT WITH DIHYDROERGO-KRYPTINE (DAVERIUM) VS PLACEBO.

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DAV.I.D.E. (DAVERIUM Italian Dementia Evaluation) is a long-term project consisting of a two-years study vs placebo on the safety and efficacy of dihydroergokryptine mesylate (DAVERIUM, Poli) in patients affected by SDAT (Senile Dementia of Alzheimer Type), diagnosed according to DSM-III-R criteria. 14 Geriatric and Neurologic centres are involved, each one enrolling 20 patients.
The study is divided into three phases: a) 1-month run-in with placebo; b) twelve months double-blind treatment with Daverium 40 mg/day or placebo; c) twelve months open treatment with Daverium 40 mg/day.
The efficacy of the treatment is measured with the IVC (Index of Global Mental Functioning), with the GBS, and with the Mental Deterioration Battery (MDB), that includes Word Fluency, Phrase Construction Test, Short- and Long-term Rey Memory Test, Immediate Visual Memory test and Constructive Functions test.
The tests are administered before the treatment period and every 3 months afterwards, and the results are logged and saved "on site" on a computer, using a custom-made program by Poli. We report here the data and the statistical analysis related to 210 subjects (70 males and 140 females, aged 63-83) who have completed 12 months of treatment. The MDB, the GBS and the IVC displayed good correlation, and indicated a clear difference in the target variables between the treated and the placebo group. The treatment was generally well tolerated.

6-10-14 CROSS-SECTIONAL STUDY OF COGNITIVE STATUS IN HYPERTENSIVE AGING OUT-PATIENTS WITH LEUKOARAIOSIS: PRELIMINARY RESULTS (49 CASES)

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Out-patients, 60 - 80-years-old, after written informed consent, with Mini-Mental-State of Folstein above 24, WAIS-R Intellectual Quotient and Memory Quotient (Wechsler Memory Scale) above 89, and with lucency score (LS) above 9 had nine neuropsychological tests. Demented and depressive patients were excluded. A second LS was performed by an independant evaluator as proposed by Rezek, 1987.

49 patients (72 ± 6 years) with hypercholesterolemia (43%), tabagism (39%), cardiovascular disease (20%), hypertriglyceridemia (20%), obesity (18%), hyperuricemia (10%), diabetes mellitus (8%), alcoholism (2%). Second LS = 22,7 ± 9,9.

Significant correlations ($p < 0.05$) were found between LS and auditory verbal learning test (Rey), visual retention test (Benton), paced auditory serial addition test (PASAT), trail making test, letter cancellation test, finger tapping test.

Leukoaraïosis intensity correlates with cognitive status in these non-demented out-patients.

6-10-15 CRANIAL COMPUTED TOMOGRAPHIC FINDINGS IN DEMENTED AND NON-DEMENTED ISCHEMIC STROKE

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We applied CT to understand the nature of cerebral infarcts, degree of brain atrophy, and white matter lisions (WML) in predicting the dementia following stroke.

All patients received mental state evaluation about 4 months following last stroke. Dementia was defined by DSM-III-R criteria and supported by Mini-Mental State Examination and Clinical Dementia Rating Scale and/or comprehensive neuropsychological test. Demented patients scored more than 6 in Hachinski Ischemic Scale. We consecutively examined 50 demented patients (M:32, F:18; age: 64.9 ± 11.7 y/o) and 50 non-demented patients (M:32, F:18; mean age: 65.1 ± 10.8 y/o).

The demented patients had more ($p < 0.01$) lacunes in basal ganglions and thalamus; larger ($p < 0.01$) infarcts in left cortex, especially frontal, temporal and parietal lobes. Periventricular and deep WML were more severe ($p < 0.01$) in demented group. The severity of atrophy showed no difference between two groups.

We concluded that several factors were important in developing dementia following stroke, in the order by logistic regression: left cortical infarct, severity of WML, left parietal infarct, left temporal infarct, numbers of basal ganglion and thalamic lancunes.

6-10-16 MITOCHONDRIAL DNA MUTATIONS IN PATIENTS WITH CEREBELLAR ATAXIA

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An A-to-G transition at nucleotide position 8344 of mitochondrial DNA (mtDNA), that is associated with MERRF, is reported in a patient with spino cerebellar degeneration without ragged-red fibers. On the other hand, a T-to-G transition at 8993 in the ATPase 6 gene is observed in a family with several neurological deficits including cerebellar ataxia.

We screened the nucleotide mutations at positions 8344 and 8993 in 34 sporadic cases of cerebellar ataxia. We also determined the total nucleotide sequences of mtDNA in two other patients (Patients 1 and 2) with cerebellar ataxia. The grandmother and the mother of Patient 1, and the mother of Patient 2 were affected by cerebellar ataxia.

No point mutations at nucleotide positions 8344 and 8993 were observed among 34 patients. Seven nonsynonymous mutations were observed in the protein-coding region of mtDNA of both of the two patients with hereditary cerebellar ataxia. These mutations, however, were frequently observed in control subjects. Three nonsynonymous mutations, which were observed only in Patient 1 but not in Patient 2, were frequently observed in control subjects. Three other nonsynonymous mutations, which were observed only in Patient 2, were rarely observed in control subjects. In addition, these three mutations would change the amino acids which were conserved among mammalian species. The contribution of the rare nonsynonymous mutations observed in Patient 2 in the development of cerebellar ataxia should be further evaluated

6-10-17 SILICONE BREAST IMPLANTS : ASSOCIATION WITH ABNORMAL SPECT SCANS AND MEMORY DEFECTS.

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Because patients with silicone breast implants complain of memory and thinking defects, we studied 15 implanted women with SPECT scans and psychological testing. Scans were digitalized at the mid-cerebellar transaxial plane and that region compared to 8 regions of the cortex at the midventricular transaxial slice. Occipital regions were normal (Ratio R=0.962, L=0.937), but other regions including bilateral temporal showed decreases which were statistically significant using paired t tests. On the California Verbal Learning Test, performance was below average for verbal learning, short and long delayed free recall, and delayed recognition. In contrast, performance on task requiring attention, language, and intelligence was average. We conclude that women with silicone breast implants can have selectively impaired memory and abnormal SPECT scans, the cause of which is not clear.

6-10-18 HETEROGENEITY IN DEMENTIA OF THE ALZHEIMER TYPE (DAT): NEUROPSYCHOLOGICAL AND CLINICAL EVIDENCES.

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Recent studies demonstrate the occurrence of an heterogeneity regarding the neuropsychological manifestations of DAT. Our purpose is to look for possible correlations between this neuropsychological heterogeneity and the clinical data in a group of 12 patients, six male and six female, aged between 48 and 66 years-old (mean age=59.1, SD=5.9), with educational level ranging from 5 to 19 years (mean=9.1, SD=4.1), following diagnostic criteria (NINCDS-ADRDA) for probable Alzheimer's disease. All subjects were between levels 3 and 4 of the Global Deteriorating Scale. Patients were submitted to serial neurological examinations over at least two years, being assessed mainly for the evidence of extrapyramidal signs and myoclonus. CT- scan of all patients were obtained. Neuropsychological evaluation consisted of the PENO, a detailed protocol that examines four main aspects of cognition (memory, language, gnosis and praxis).

As was expected, we found a marked neuropsychological heterogeneity in our population. The results show also an evidence of a neurological heterogenelty, namely, three patients presented extrapyramidal signs and another patient developed myoclonus during the course of the disease. These patients presented a faster progression. The discussion will address the correlations between both types of heterogeneity.

The identification of neuropsychological characteristics of distinct clinical subtypes of DAT is of primary importance both for clinicians and researchers.

6-10-19 LONG TERM FOLLOW UP OF PATIENTS WITH MULTI - INFARCT DEMENTIA TREATED WITH CITICHOLINE

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In previous studies from our department we have treated 146 patients with multi-infarct dementia with citi choline in a double blind placebo controlled trial with good results (J.Stroke, Cerebrovasc Dis 1992, 2, 232-33)The patients in this first trial were followed for ten months The author has now followed the patients from the first trial from January 1,1991 until July 1992 with 3 month interval examinations. (physical and Mini Mental State Examination (MMSE) 138 patients gave their consent. The results showed that the placebo group deteriorated further. The citi choline group showed the same results as during the first trial (mean MMSE 23). These results suggest that the improvement in the citi choline group lasted longer than two years

6-10-20 GLUTAMATE TRANSPORTERS VARY IN FORM IN PATHOLOGICALLY SUSCEPTIBLE CORTICAL REGIONS IN ALZHEIMER DISEASE.

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Brain damage in Alzheimer-type dementia (DAT) is area-specific. Thus, the temporal lobe is susceptible, whereas the primary motor and visual areas are relatively spared. Glutamate-mediated excitotoxicity may underlie DAT pathogenesis, through over-activated postsynaptic receptors. This would follow if the efficiency of glutamate reuptake were reduced. Glutamate transporters show differential regional sensitivity to antagonists in the cerebral cortex, cerebellum and hippocampus of rats, which suggests the existence of regionally variable glutamate transporter sub-types. This study looked at the binding profiles of D-[^{3}H]aspartate and the transport inhibitors *threo*-3-hydroxy-L-aspartate, dihydrokainate, and L-α-aminoadipate at the glutamate uptake site in synaptosomal membranes prepared from human brain tissue obtained at autopsy from DAT and control cases. Homogenate binding assays were carried out by standard procedures. Analysis of variance performed on log transforms of the affinity constants (K_A values) showed there was a significant difference in the affinity profile for the four ligands when the two case groups were compared, and also when areas susceptible to damage were compared with control areas. These effects were additive, and suggested that a different sub-type of glutamate transporter may be expressed in brain regions susceptible to damage in DAT. Pathologically non-DAT cases with similar clinical presentation had similar affinity profiles to DAT cases, which may imply there is a common underlying pathogenic mechanism in dementing illness.

6-10-21 MAGNETIC RESONANCE IMAGING PERIVENTRICULAR AND DEEP WHITE MATTER HYPERINTENSITIES IN SENILE DEMENTIA OF THE ALZHEIMER TYPE.

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Brain magnetic resonance imaging (MRI) of patients with senile dementia of the Alzheimer type (SDAT) frequently displays parenchymal signal abnormalities in addition to cerebral atrophy. The clinical significance of these hyperintensities is still controversial, however.

We therefore analysed the MRI scans of 24 SDAT patients (mean age 67+/-8 years) by measuring the total area of white matter hyperintensities (WMH), the width of periventricular hyperintensity (PVH) at mid-cella media and various indices of cerebral atrophy. These measures were correlated with dementia severity according to the *Mini Mental State Examination (MMSE)* and Mattis` Dementia Rating Scale (MDRS).

A highly significant correlation ($p<0.005$) was found between both dementia scores and the oblique diameter of the temporal horns. MMSE and MDRS scores were also significantly correlated with other atrophy measures but not with PVH width or the WMH area. Only the temporal horn diameter entered a multiple regression model with MMSE or MDRS scores as dependant variable.

Our results confirm the temporal horn diameter as single best determinant of dementia scores in SDAT but fail to substantiate a significant impact of MRI signal hyperintensities on dementia severity.

6-10-22 CORRELATION BETWEEN INTERLEUKIN-2 AND INTERLEUKIN-6 SECRETION BY MONONUCLEAR CELLS OF ALZHEIMER PATIENTS AND THEIR DISEASE STAGE

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Interleukin-6 (IL-6) and interleukin-2 (IL-2) secretion by mononuclear cells was investigated in 36 Alzheimer (AD) patients and compared to that of 10 severe multi-infarct demented (MID) patients and 10 age-matched controls. AD patients were divided according to severity of dementia into "mild" and "moderately severe" groups. IL-2 levels were measured by bioassay and IL-6 levels by using Elisa kit. No differences in IL-2 secretion were found between mild AD patients when compared to controls. However, there was a significant increase in IL-2 production both in the moderatly-severe AD group and in the MID group. IL-6 levels in AD patients of both groups were significantly higher than those of MID and controls. Between the latter two groups no significant differences were observed.

Our results suggest that increased levels in IL-2 production in severely demented patients may be the outcome of neuronal damage, whereas increased levels in IL-6 production seem to be specific to AD. IL-6 may thus have a role in the pathogenesis of Alzheimer disease.

6-10-23 ACCURACY OF CLINICAL CRITERIA FOR THE DIAGNOSIS OF DEMENTING DISEASES

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We have retrospectively applied clinical criteria to 137 cases of dementia with adequate antemortem clinical data from the State of Florida Brain Bank. The NINCDS-ADRDA criteria (McKhann et al., 1985) for Probable and Possible AD were used as well as *modified California criteria* (Chui et al., 1992) for vascular dementia. Neuropathological criteria used for AD were those of Khachaturian et al. (1984) and for vascular dementia were modified Fischer et al. (1991) criteria.

One hundred and four cases were diagnosed clinically to have probable or possible AD. Positive Predictive Rate of NINCDS-ADRDA criteria was 89% for Probable AD and 76% for Possible AD. Seven cases were diagnosed clinically to have vascular dementia of which four were diagnosed pathologically (Positive Predictive Rate of Chui et al. criteria was 57%). Refinements to criteria for vascular dementia that would significantly improve accuracy of diagnosis are: (1) gait disorder should be required on history and examination, (2) history of a stroke should be required, (3) initial symptom should be a non-memory problem (e.g., personality change, imbalance, etc.), (4) CT or MRI should have evidence of 2 or more infarcts.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-11-01 CHRONOPHARMACOLOGICAL INVESTIGATIONS OF A ONCE DAILY DOSAGE IN MONOTHERAPY WITH CARBAMAZEPINE (CBZ) RETARD - SHOULD A MORNING OR EVENING DOSAGE BE PREFERRED?

B. Zahner, H. Stefan

Antiepileptic drugs are frequently given several times a day. This investigation shows the levels of CBZ retard in a lower dosage range (up to 900 mg/day), being achieved in a once daily application, and the fluctuation in concentration during the day when morning dosage is compared to evening dosage.

12 patients suffering from epilepsies with focal seizures and secondarily generalized grand mal were examined. After six weeks of single-dose-therapy a neurological examination was performed and patients were asked for side-effects and seizure frequency. Blood was taken every three hours for one day, then the therapy regimen was changed in patients with a morning dose to an evening dose and vice versa.

All patients with newly diagnosed epilepsy became seizure-free and the condition of two patients with epilepsies refractory to medication did not deteriorate. The profiles in both morning and evening dosage regimen turned out relatively smooth, peaks were reached between 12am and 1pm in application of morning dose, and between 4pm and 7pm in evening dose. Thus we conclude that as long as there is some discussion in literature about possible cognitive side-effects of CBZ, patients working or attending school, if treated with one dose of CBZ, should take their medication in a single dosage at night. Further chronopharmacological investigations in comparison with neuropsychological tests are necessary.

6-11-02 SERUM PROLACTIN LEVELS IN EXPERIMENTAL STATUS EPILEPTICUS

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Transient elevation of plasma prolactin has been observed following epileptic seizures. However the effects of status epilepticus on endocrine function are still obscure.

In our study we assessed the changes in prolactin levels in two pathogenetically different experimental models of status epilepticus. Status epilepticus was induced in 10 rabbits by means of intracortical injection of 0.1ml $ZnSO_4$ 6% and in other 10 by intracortical injection of 0.1ml penicillin G.

All animals were continously monitored by EGOG. Two blood samples were collected from all animals, one just before the intracortical injection of the convulsant and the other 90 min later. Serum prolactin levels were significantly increased in 80% of our animals after 90 min of continous seizures of them. In 5 rabbits which served as normal controls, and received an intracortical injection of normal saline without developing seizures, plasma prolactine levels remained unchanged.

6-11-03 SINGLE PHOTONE EMISSION COMPUTERIZED TOMOGRAPHY (SPECT) IN EXTRATEMPORAL SEIZURES

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SPECT was shown to be valuable in detecting focal abnormalities in parital seizures. We studied its value as an accessible outpatient investigation, in comparison with EEG and CT scan, in confirming the clinical diagnosis of partial epilepsies especially extratemporal.

25 patients were classified on clinical basis according to the proposed international classification for epilepsies and epileptic syndromes. All had at least 2 EEGs, a CT and interictal SPECT. Although EEG was more sensitive, being positive in 84%, while SPECT 68%; SPECT was of more localizing value (56% to 48%), being the only confirmatory test in 9 patients. Its main value was noted in extratemporal epilepsies.

Data are summarized in 3 tables and details of 6 cases with their different investigations are presented as examples. One case illustrates the value of SPECT in clarifying secondary from primary generalized seizures, and another, frontal from temporal epilepsy.

We conclude that SPECT is valuable in confirming extratemporal epilepsies especially in differentiating frontal from temporal lobe epilepsy. It is complimentary to EEG and superior to CT scan and would be a reasonable second choice test in investigating epileptics.

6-11-04 RISK OF RECURRENCE AFTER SINGLE UNPROVOKED TONIC-CLONIC SEIZURE IN ADULTS

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The likelihood of seizure recurrence after a first unprovoked seizure has profound social, vocational, and emotional implications for the patients. Recurrence rates have varied between 27% and 71% in different studies, and the management of patients with a single unprovoked seiaure is controversial.

In this prospective study we investigated the influence of age, sex, family history, EEG patterns, and anticonvulsant drug (ACD) therapy on seizure recurrence after a first unprovoked tonic-clonic seizure in adults. For this purpose, between January 1989 and March 1991, we studied adult patients, who had experienced their first unprovoked tonic-clonic seizure within last one month before consultation, and followed them until December 1992. Finally, we included 147 patients who met the criteria for inclusion.

Overall cumulative recurrence rates were 32.7% by 6 months, 41.5% by 1 year, 43.5% by 2 years, and 45.6% by 4 years. Among the risk factors that we evaluated, only the time of the day at which the initial seizure occurred was associated significantly ($p < 0.001$) with seizure recurrence. In our series, 62 patients received ACD, and 85 did not. Difference in recurrence rates of ACD(+) and ACD(-) groups was not found statistically significant ($p > 0.05$).

6-11-05 INJECTION SITE REACTIONS FOLLOWING INTRAMUSCULAR ADMINISTRATION OF FOSPHENYTOIN VERSUS PLACEBO

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Fosphenytoin, a disodium phosphate ester prodrug that is rapidly and completely converted in vivo to phenytoin, may be a safer, more convenient method of administering phenytoin parenterally. The effects of IM fosphenytoin at the injection site were studied in patients taking oral Dilantin®QD at doses of 200-500 mg/day.

Patients were randomly assigned to 5 days of either IM fosphenytoin or a placebo injection. Patients rated pain, burning, and itching immediately after each injection, and again 5, 30, 60, and 120 minutes post-dose, and just prior to the next injection. Study personnel rated erythema, swelling, tenderness, and necrosis at the same time points. At the end of the study the investigator made global evaluations of all injection sites.

No differences in pain, burning, erythema, swelling, tenderness, or necrosis were found between fosphenytoin- and placebo-injected groups. The itching score was mildly elevated after fosphenytoin compared with placebo.

Multiple daily injections of IM fosphenytoin for 5 days were extremely well tolerated at the injection site and could not be distinguished from injections of placebo solution.

6-11-06 INTRACTABLE SEIZURES IN SAUDI ARABIA (WESTERN REGION) - OUR EXPERIENCE

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50 cases of intractable seizure were reviewed. The patients were seen, examined and investigated in the Neurology Department of King Abdulaziz University Hospital and King Abdulaziz Hospital. Patient population included both children and adults. EEG, CT scan and serum drug levels were done in all of the patients. All patients were on polytherapy. Specific problemsof the area were discussed in relation to the control of seizures. The study also includes six months' trial of a new anti-convulsant drug Lamotrigine. The intractable seizures were seen as a result of : birth injuries, post traumatic epilepsis, congenital abnormality and poor compliance. None of the known combination of anti-convulsant drugs made any difference in the control of seizures which made the choice of polytherapy arbitrary.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-11-07 EPILEPSY AND PSYCHIATRIC TROUBLES

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Temporal Lobe Epilepsy (TLE) is an entity commonly accepted by both neurological and psychiatric communities. However, the relationship between epilepsy and psychiatric troubles are yet in discussion, mainly due to the difficulty to establish the primary and secondary ethiology.

We present in this poster a year (1991) of survey into an Anti Epileptic Dispensary in a Psychiatric Hospital. We recorded 56 out and in-patients affected of a non-generalizated primary epilepsy, and studied also their kind of psychiatric affectation in relationship with the type of epilpesy.

The results of the whole year survey showed several interesting relationships between the focal seizure types of epilpesies and psychotic-like psychatric manifestations. Another results are also presented.

6-11-08 **REDUCTION OF ANTIEPILEPTIC DRUG DOSAGE FOR MONITORING EPILEPTIC SEIZURES**

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The recording of actual seizures with video-EEG telemetry is essential in order to localize epileptic foci for surgical treatment. If the seizures do not occur spontaneously during monitoring period, they must be precipitated. Eleven epileptic patients, candidates for surgical treatment, were examined. The daily doses of anticpileptic drugs (AEDs) were reduced by fifty per cent or less, and the reduced dosages were maintained until a seizure had occurred. The reduction resulted in seizures within five days among all patients, and the number of seizures increased significantly in comparison with the five-day period before AED reduction. The seizures so provoked were typical for each patient, as confirmed by clinical observation and video-EEG telemetry. The AED concentrations at the time of the seizures were generally within the reference values.

An ideal method for provoking seizures sufficiently but safely increases their frequency during a predictable time period, with the provoked seizures being typical of each patient. Comparative studies are needed to find the most pertinent method.

6-11-10 PREVALENCE STUDY OF EPILEPSY AMONG HIGH SCHOOL CHILDREN IN BURSA, TURKEY

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Although epilepsy is a curable disease and its prevalence is well-known in western countries, this is not the case in Turkey. For this reason, a population study was performed to estimate the prevalence of epilepsy in high school students in Bursa, the fifth largest city in Turkey. We used a mixed questionnaire and studied a sample of 20,105 students (aged between 12 and 18 years). We did not include the students receiving special education in our study. The probable prevalence of epilepsy in this age population in 1988 - 1989 was estimated to be 16.4/1,000 inhabitants. Comparison of our results with those of other studies for similar age groups in western countries showed some differences. Although most figures are between 2.5 - 9/1,000, our figure (16.4/1,000) is higher than these. We discussed the results.

6-11-11 PHARMACOKINETICS AND TOLERANCE OF FOSPHENYTOIN AND PHENYTOIN ADMINISTERED INTRAVENOUSLY TO HEALTHY SUBJECTS.

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The pharmacokinetics and tolerance of IV Fosphenytoin (F), a phosphate-ester prodrug of phenytoin (P), were compared to those of P in two crossover studies. Healthy subjects received 1200 mg P and molar equivalent doses of F. F infusion rates were 50, 100, and 150 mg P equivalents/min (N=12 each); P was infused at 50 mg/min (N=24). Serial blood samples for determination of F and P concentrations were obtained for 96 h postdose. F and P were well tolerated, with CNS symptoms most frequently reported. Injection site symptoms following F administration were reported less frequently and of lower intensity than those after P. Conversion of F to P was rapid. F displaced P from plasma binding sites, resulting in higher proportions of unbound P (the active moiety). During the 30 min following initiation of F administration at 50 mg/min, unbound P concentrations were generally less than those following P administration. However, following F administration at 100 or 150 mg/min, unbound P concentrations were similar to or slightly greater than those following P administration.

Mean (SD) Unbound P Pharmacokinetic Parameter Values (pooled across studies)				
Regimen	F at 50 mg/min	F at 100 mg/min	F at 150 mg/min	P at 50 mg/min
Cmax.	2.6 (0.53)	2.8 (0.61)	3.2 (0.90)	3.7 (1.2)
AUC(0-96)	66.2 (21)	79.8 (12)	85.5 (14)	80.4 (19)

In summary, F is well tolerated when administered at rates which yield unbound P concentrations similar to those obtained after administration of P at 50 mg/min.

6-11-12 STUDY OF CHROMOSOMAL ABBERATIONS IN EPILEPSY

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30 Epileptics were selected for finding out the chromosomal pattern. 18 were males and 12 were females. Family history was positive in 46.7% of cases. 19 cases were on antiepileptic treatment for varying periods and 11 were untreated. Chromosomal aberrations have been observed in 5 treated and 1 untreated cases. In the untreated case Mosaic Polyploidy was observed. In the treated cases Mosaic Polyploidy (1 case), dicentric chromosomes (1 case), chromatic breaks (1 case) and chromatid fragments (2 cases) were observed. The chromosomal damage in epilepsy was seen with all the four drugs. The chromosomal damage was seen only in treated cases and not in untreated cases. Thus it can be concluded that the chromosomal damage in epilepsy is due to the effect of antiepileptic drugs and not related to epilepsy itself. It may be due to direct effect of drug or due to its metabolites. The mosaic polyploidy (seen in both treated and untreated cases) in untreated cases can be because of epileptic state as such.

6-11-13 THE CHANGES OF P300 IN NEWLY DIAGNOSED EPILEPTIC PATIENTS RECEIVING ANTIEPILEPTIC DRUGS

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Reports in the literature suggest that a significant number of people with epilepsy experience cognitive difficults. Antiepileptic drugs(AEDs) might be one of the implicating factors in cognitive changes. Literature on the role of AEDs reveals conflicting findings and controversies.

We studied 20 newly diagnosed unprovoked epileptic patients who received monotherapy of phenytoin (DPH) or tegretol to investigate the drug effects on the cognitive function and P300. They received P300 and neuropsychologic tests before and after the drugs were taken. In 10 patients who took DPH, P300 latencies were prolonged after the drug levels reached the therapeutic range, but there were no changes in their neuropsychologic tests. Another 10 patients who took tegretol, the P300 latencies and neuropsychologic tests were unchanged.

P300 is a good tool for evaluation of auditory attention. Our study showed that cognitive function did't change after short term use of AEDs, but P300 latency might be prolonged. This might be a contributing factor for later cognitive dysfunction.

6-11-14 TRH INTENSIFIES LIMBIC SEIZURES INDUCED BY AN OPIOID PEPTIDE IN RATS

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Thyrotropin-releasing hormone(TRH) has been shown to counteract certain actions of opioid peptides such as induction of catalepsy in mammals. We investigated effects of TRH on limbic seizures induced by an opioid peptide in rats. Male adult Wistar rats were given icv. both TRH in the tartrate form (TRH-T) and [D-Ala^2-Met^5] enkephalinamide (DAME) at intervals of 15 min. Behavioral manifestations were scored using eight class scale (Tinel et al, 1978). Continuous seizures for longer than 30 min. were defined as status epilepticus. EEG was recorded from bilateral hippocampuses. Pulse density variation curves were made from spikes exceeding 300μV using a signal processor. Seizure scores (SS) in rats treated with DAME (50μg) or TRH-T (40μg) alone were not significantly different from that (0.2±0.2, mean±SE) of control rats with saline. SSs (6.2±0.5) were significantly increased in rats given both DAME and TRH-T ($P<0.001$). The effect of TRH-T showed dose-dependency. Incidences of status epilepticus were significantly larger in rats given both substances. DAME provoked seizure discharges at bilateral hippocampuses. They were increased in 4 out of 4 rats pretreated with TRH-T, while in 0 out of 3 rats with saline ($P<0.05$). TRH was suggested to intensify limbic seizures induced by an opioid peptide.

6-11-15 REFRACTORY EPILEPSY TREATED BY IVIG IN A DOSE FINDING, DUBBLE-BLIND STUDY.

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62 epileptic patients, from 2 to 51 years, were studied in 3 Centers and followed for 6 months after the 1st perfusion.
They received 7 perfusions of 100, 250 or 400mg/kg/perfusion of IgG or placebo, and for most of them a booster perfusion at the end of the study.
Seizures were counted for 1 month before and then during the follow-up. EEGs were recorded before the study, weekly during the first eight weeks and then monthly. IgG levels were analyzed before the study and then taken before each perfusion for a further blind analysis. Antiepileptic drugs levels were controlled monthly.
In some cases, seizures disappeared with normalization of EEGs. Preliminary results show some positive trend in favour of IgG treatment, but without significant dosage effect.

6-11-16 EPILEPTIC SEIZURES IN MENINGIOMAS

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This is a retrospective study to evaluate the causalities and occurrence of epileptic seizure before and after operation in the patients with intracranial meningioma.

Three hundred and twenty-three patients, aged 10 to 79, underwent surgery for intracranial meningioma. Ninty-eight (30.3%) of the 323 patients had different types of seizures before surgery and 32 of these 98 patients had recurrent seizures after surgery in spite of anticonvulsant treatment. Two hundred and twenty-five (69.7%) patients had no seizure preoperatively but 39 of them developed postoperative seizures. Thus, a preoperative history of seizure is a significant index(p 0.005) in predicting the occurrence of postoperative seizure. In the total 71 patients who had postoperative seizures, cerebral edema and hemorrhage at the surgical sites, and tumor recurrence were common factors precipitating the occurrence of seizure. In relation to the tumor sites, patients with parasagittal and convexity meningiomas had a higher incidence of seizure. There was no relationship between the histopathological features of tumor and the incidence of epileptic seizures.

6-11-17 CORRELATION OF INHIBITION OF VERATRINE EVOKED [^{14}C] GUANIDINE UPTAKE WITH INHIBITION OF VERATRINE EVOKED RELEASE OF GLUTAMATE BY LAMOTRIGINE AND ITS ANALOGUES

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Lamotrigine (LTG; [3,5-diamino-6-(2,3-dichlorophenyl-1,2,4-triazine]) is a new antiepileptic drug chemically unrelated to current therapeutic agents with a clinical profile similar to that of Phenytoin (Leach et al, 1991). LTG, like Phenytoin, inhibits both voltage-gated sodium currents (Cheung et al, 1992) and veratrine-evoked release of glutamate but, unlike Phenytoin, LTG does not block potassium-evoked release of glutamate nor does it block voltage-dependent calcium channels (Lang et al, personal communication). These results suggest that sodium channel function may play an important role in the regulation of glutamate release. We have, therefore, compared the ability of Lamictal and its analogues to both displace [^{3}H]batrachotoxinin binding and to inhibit veratrine-evoked uptake of [^{14}C]guanidine with their ability to inhibit veratrine-evoked release of glutamate. A highly significant correlation ($p > 0.001$, slope = 0.94, n=15) between inhibition of veratrine-evoked [^{14}C]guanidine uptake and inhibition of veratrine-evoked release of glutamate was found. These data are consistent with blockade of sodium channel function and consequent inhibition of glutamate release being the mechanism of action of LTG.

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6-11-18 REVERSIBLE REDUCTION OF BENZODIAZEPINE RECEPTORS IN TEMPORAL CORTEX DURING TREATMENT IN A CASE OF TEMPORAL LOBE EPILEPSY

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SPET investigations on central benzodiazepine (BDZ) receptor found reduced (BDZ) receptor levels in human epileptic tissue. We investigated the central(BDZ) receptor density in 1 patient with TLE. ^{123}I labeled Iomazenil (a specific lipophile central (BDZ) receptor marker) and single photon emission tomography (SPET) was performed before and after 2 month of sucessful treatment with carbamazepine (CBZ). First we noted a focal slowing of the EEG in the left temporal area and found a corresponding reduction of the (BDZ) receptor density of the left basal temporal lobe. After the treatment we found a normalized (BDZ) receptor density and no pathological EEG signs. The normalization in central (BDZ) receptor sites could possibly be due to the anticonvulsant effects of (CBZ) mediated through its known action on the so called peripheral (BDZ) receptor sites, which are localized on glia cells.

6-11-19 CLINICAL EVALUATION OF SPECT WITH N-ISOPROPYL-P-[^{123}I] IODOAMPHETAMINE IN EPILEPSY

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Single photon emission computed tomography (SPECT) with N-Isopropyl-p-[^{123}I] iodoamphetamine (^{123}I-IMP) was performed in 35 interictal epileptic patients (25 idiopathic and 10 symptomatic epilepsy), and compared with the findings of brain CT, MRI and EEG. We also evaluated relationship between findings on ^{123}I-IMP SPECT and the condition of control by antiepileptic drugs in idiopathic epileptic patients.

Abnormality of accumulation of ^{123}I-IMP was observed in 12 out of 25 idiopathic patients and 7 out of 10 symptomatic epileptic patients. On the other hand, in idiopathic epilepsy, the detectivity (1/24) of focal abnormality in brain CT and MRI was found to be lower than that of ^{123}I-IMP SPECT. On comparative study of relationship between the findings on ^{123}I-IMP SPECT and the condition of control by antiepileptic drugs in patients with idiopathic epilepsy, abnormality of ^{123}I-IMP SPECT findings was found to be higher in patients (71.4%) who were not controlled sufficiently than in patients (18.1%) who were controlled sufficiently. ^{123}I-IMP SPECT is useful for evaluation of treatment in epilepsy.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-11-20 STROKE-RELATED SEIZURES: THE ROLE OF CORTICAL AND SUBCORTICAL STRUCTURES

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Patients entered to study were 217 including 164 with ischaemic (embolic or thrombotic) and 30 with haemorragic stroke; in the remaining cases, CT-scan was "atrophic" in 18 and normal in 5. The types of seizures were: 16 heralding, 110 early and 91 late. In ischaemic strokes, cortical site of lesions was seen in 42 cases of late seizures, whereas it was subcortical in 14; in early seizures, on the contrary, the subcortical site of lesions was more frequent than the cortical one (34 vs. 30). In haemorragic strokes, the cortical involvement was predominant in either early or late seizures, more sharply in the former, The predominant involvement of cortical structures in late seizures is in agreement with the data of the literature; the pathogenesis is assumed to be the formation of "scars" with paroxysmal discharges. To explain the apparently major role of subcortical structures in producing early seizures, one can hypothesize that ischaemia of the basal ganglia, frequently involved in these cases, along with metabolic changes in perilesional areas such as an increase of excitatory aminoacids could both be responsible of seizures, their combined effect being that of withdrawal of the inhibition on the thalamus by its pallidonigral afferents and of a direct excitation of thalamo-cortical efferents.

6-11-21 SPECT AND PARTIAL EPILEPSY: COMPARATIVE STUDY WITH EEG, CT-NMR DATA AND PHARMACOLOGICAL TREATMENT

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We carried out a study to assess the value of the interictal SPECT examination in 57 subjects with partial epilepsy (PE) in relation to the results obtained through other techniques (conventional EEG, CT and NMR); moreover, we evaluated the possible correlation between SPECT abnormalities and antiepileptic drugs. In 15 patients with simple partial epilepsy (SPE) (26.3%) and in 29 subjects (51%) with complex partial epilepsy (CPE) we founded a significative correspondence between EEG data and SPECT results. On the contrary, in 9 SPE-patients (15.9%) and in only 3 CPE-patients (7%), SPECT images were partly different in relation to EEG abnormalities. In the correlative study between interictal SPECT study and CT-NMR images, we demonstrated in 13 SPE-patients (22.8%) and in 13 CPE-patients (22.8%) a significant similarity in the location and extension of abnormal perfusion and CT-NMR pathological areas. On the other hand, in 11 SPE-patients (19.3%) and in 20 CPE-patients (35.1%), we obtained a localized ipoperfusion area and a normal CT-NMR image. In all the patients treated with single antiepileptic drug, we don't identify significant differences of SPECT data in relation to pharmacological treatment. Nevertheless, in 14 drug resistant patients (24.5%) under politherapy SPECT examination showed ipoperfusion areas vs. normal CT-NMR images. The results of this study underline the ability of SPECT examination to identify cerebral pathological areas in epileptic patient responsible of the genesis and maintenance of epileptic discharges.

6-11-22 A COMPARATIVE STUDY OF INTERICTAL CERBRAL BLOOD FLOW (^{99m}Tc-HMPAO SPECT) AND MRI.

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Interictal regional cerebral blood flow (^{99m}Tc-HMPAO and SPECT) was compared with MRI scans in 32 patients with epileptic seizures. 23 patients had partial and 9 primarily generalized seizures. A blind visual evaluation of the MRI scans and the SPECT tomograms was performed.

Eight of the 23 patients with partial seizures had focal MRI abnormalities and 10 had multifocal changes, while five were normal. Five of the nine patients with primarily generalized seizures had focal and three multifocal MRI changes, while one was normal. Thirteen patients with partial seizures had localized SPECT abnormalities, one bilateral changes and nine showed normal CBF findings. Six of nine patients with primarily generalized seizures had localized and three had normal rCBF findings. A close correlation between MRI and rCBF was demonstrated in 11 of the 23 patients (48%) with partial and four of the nine patients (44%) with generalized seizures.

A considerable number of the patients showed a complex functional pathology with low concordance between SPECT and MRI findings. This was also the case for patients classified as having generalized seizures. Both MRI and SPECT should be studied in context in the evaluation of these patients.

6-11-23 NEUROMAGNETIC STUDY OF SPONTANEOUS AND SINUSOIDALLY MODULATED VISUAL EVOKED ACTIVITY IN TUBEROUS SCLEROSIS PATIENTS.

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This study is a preliminary multidisciplinary approach to a better understanding of the complex neurophysiological and behavioral disorders in children with Tuberous Sclerosis.

We have studied five patients with Tuberous Sclerosis and partial epilepsy (age ranged from 6 to 35 years). All the subjects had undergone MRI, regular EEG follow-ups and were on anticpileptic drugs.

Patients were selected on the basis of:

i) presence of more than one cortical lesion on MRI.

ii) location of at least one lesion in the occipital regions.

The magneto-encephalographic (MEG) recording was performed with a 28-channel neuromagnetometer in a shielded room, both during spontaneous and visually evoked synchronous activity. Six subsequent positions of the sensor were used, in order to achieve a complete mapping of the head.

The visual stimulus was a red light created by a Light Emitting Diode and delivered both full and half field via two optic fibers to plastic goggles. Light bursts were delivered at the subject's alpha frequency and at half that value.

The evoked response to sinusoidally modulated light presented a decreased amplitude and a less organized morphology on the affected hemisphere.

Preliminary analysis of the spontaneous activity showed that different morphologies of the interictal spikes corresponded to different locations of the equivalent current dipoles (ECD) which were well in agreement with the MRI location of the lesions.

6-11-24 FREQUENCY, MEDIAN TIME TO ONSET, AND MEDIAN DURATION OF ADVERSE EVENTS IN PLACEBO-CONTROLLED AND OPEN-LABEL STUDIES OF ADD-ON GABAPENTIN IN PATIENTS WITH REFRACTORY EPILEPSY

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In six placebo-controlled add-on therapy studies of gabapentin in 921 patients with refractory epilepsy, 543 patients received gabapentin and 378 patients received placebo, during an 84-day treatment period. For patients receiving gabapentin or placebo, the median time to onset of the first adverse event was 14 days vs 22 days, respectively, and the median duration of any adverse event was 14 days vs 13 days. For the ten most frequently reported adverse events, the median time to onset was generally shorter among patients receiving gabapentin, while the duration of specific adverse events was similar for the two groups. Among patients receiving gabapentin, frequent adverse events (>5% of patients) of early onset (median time to onset ≤5 days) included somnolence, dizziness, fatigue, and diplopia. Median time to onset for these events was longer among placebo-treated patients (8 to 23 days). Analysis of data from a total of 1460 patients who received gabapentin in controlled or open-label studies showed that with long-term treatment, the most frequently occurring adverse events remained the same.

6-11-25 CALCIUM CHANNEL BLOCKERS IN INTRACTABLE EPILEPSY TREATMENT: A CROSS-OVER STUDY WITH TWO CALCIUM ANTAGONISTS

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To assess the clinical relevance of CA in the treatment of intractable epilepsy 10 patients (6 males and 4 females) aged 22 - 47 years with drug-resistant partial complex epileptic seizures (DREPI) after ineffective treatment of average 13.7 years, free from general degenerative or dis-metabolic CNS or cardiovascular diseases, entered an open cross-over trial with two CA in a prospective study lasting 48 months.

Patients received firstly for six months a daily 10 mg flunarizine (F) administration and after a six month withdrawal (W) were treated for another six months with 90 mg nimodipine (N) daily administration. After another W patient received a second six month daily 90 mg N administration and after another W a second F administration.

The seizure free state (SFS), the EEG photosensitivity range (PSR), the psychic symptoms and cardiovascular status were considered prior, during and after each CA administration and W. SFS increased to 43.23% after F treatment with a slight reduction to 41.86% vs. basal values after withdrawal. SFS increased to 33.8% after N treatment with return to 11.3 vs. baseline values after withdrawal.

The PSR was reduced in 4 patients after F treatment, lasting for six months after W in 3 patients. PSR was reduced in 5 patients after N treatment, lasting for six months in 3 patients. A slight reduction in concomitant mood disorders have been observed after second F administration.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-11-27 MRI VOLUMETRIC STUDIES IN THE INVESTIGATION OF PATIENTS WITH INTRACTABLE EPILEPSY.

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MRI volumetric studies in patients with temporal lobe epilepsy (TLE) have been accurate in detecting volume reduction of mesial structures correlating with mesial temporal sclerosis in histopathology.

We performed MRI volumetric measurements of amygdala and hippocampus in 100 epileptic patients (76 with intractable TLE). We found significant atrophy of mesial structures, coinciding with the EEG focus, in 92% of the patients with TLE not having foreign tissue lesions. This volume reduction was more pronounced in those with a history of prolonged febrile convulsion (PFC) in childhood. No significant atrophy was demonstrated in the 24 patients whose seizures were not originated in the temporal lobe (usually they had frontal or generalized epilepsy).

Foreign tissue lesions, such as gangliogliomata and neuronal migration disorders, were found in the temporal lobe of 10 patients with TLE without antecedent PFC. In 8 of these 10 patients, the amygdalae and hippocampi were symmetrical and of normal volume. The remaining 2 patients, had mesial temporal atrophy ipsilateral to the lesion, suggesting 'double pathology'.

In conclusion, diminished and asymmetric volumes of amygdala and hippocampus appear to be specific for patients with TLE, since we found normal volumes of mesial temporal structures in patients whose seizures did not originate in the temporal region.

6-11-28 CEREBRAL VASCULAR MALFORMATIONS AND INTRACTABLE SEIZURES: SURGICAL OUTCOME IN 20 PATIENTS

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OBJECTIVE: To determine the long-term efficacy of surgical resection for cerebral vascular malformations (CVM's) in patients with medically intractable seizures.

METHODS: Restrospective review of 20 patients who underwent surgical resection of a supratentorial CVM for intractable seizures. All patients underwent a comprehensive presurgical evaluation. The surgical outcome was determined by medical correspondence, chart review, and direct patient contact.

RESULTS: The mean age at seizure onset was 22 years (range 4 - 52); seizure duration 14.8 years; duration of follow-up 3 years (range 6 months - 4 years). Eighteen patients had microscopic evidence of remote hemorrhage with hemosiderin deposition. MRI was superior to CT and angiography in demonstrating the CVM. Fifteen patients (75%) were seizure free without aura. Two patients were experiencing only nocturnal generalized seizures. The remaining three patients had a worthwhile reductin in seizure frequency (> 50%).

CONCLUSIONS: Excellent seizure outcome can be achieved after surgical resection of CVM's in patients with medically intractable seizures. The age at seizure onset and seizure duration did not appear to significantly affect outcome. Location of the CVM is less important than precise localization of seizure onset with appropriate cortical resection of surrounding gliotic or hemosiderin stained parenchyma. Subclinical hemorrhage may increase the epileptogenic potential of these lesions.

6-11-29 INFLUENCE OF TIME OF ONSET OF DRUG THERAPY ON PROGNOSIS OF EPILEPSY

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Two groups of previously untreated epileptic patients (Group A and B) were studied. Group A had anti-epileptic drugs immediately or within one year of onset of seizures Group B had seizures for over 3 years before reporting for treatment.

The result showed that 60% of group A patients were seizure free following treatment. Lower seizure remission rates occurred in patients with frequent seizures before treatment (41%) and interictal neurological abnormalities (45%). Higher seizure remission occurred in patients with generalized epilepsy (73.9%) Among patients in group B only 22.7% were seizure free following treatment. Lower seizure remission rates occurred in patients with partial epilepsy(17.5%), frequent seizures prior to treatment (16.7%), abnormal EEG (16.7%) and interictal neurological abnormalities (19.1%). Higher seizure remission occurred in patients with generalized epilepsy (30.8%), normal EEG (30%) infrequent seizures before treatment (38.9%) and normal interictal neurological signs (36.8%). However, these rates were still consistently lower than the seizure remission rates found in group A.

The study showed that late onset of therapy was associated with poorer prognosis of epilepsy.

6-11-30 HEALTH EDUCATION IN EPILEPTIC PATIENTS IN SURABAYA

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Epileptic patients from the Neurological outpatient clinic of the Dr. Soetomo Hospital already diagnosed and treated, get health education consisting of: explanation of the nature of epilepsy, healthy living, taking the drugs regularly, teaching the family and friends how to treat the epileptic patient.

At random we have 90 patients, mean age: 34,5 years consisting of 56 males and 34 females for health education.

As control group: 90 patients, mean age: 33,9 years consisting of 55 males and 35 females.

In the group with health education we have a better outcome with seizure frequency, which is significant: $p < 0,005$.

Conclusion: Health education in epileptic patients besides the regular treatment give better outcome.

6-11-31 EFFECT OF PROLONGED ANTICONVULSANT MEDICATION IN EPILEPTIC PATIENTS: COGNITIVE FUNCTION, SERUM FREE AMINO ACIDS, VITAMIN B_{12} AND FOLIC ACID

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Thirty-six epileptic patients, most from low socioeconomic groups and aged 14 - 62 years, were studied for effects of prolonged anticonvulsant medication. The intelligence quotient was above 50, and without systemic diseases. Besides reduced serum and cerebrospinal fluid (CSF) folate levels, significantly increased levels of vitamin B_{12} in serum were found in patients as compared with normal healthy volunteers. The bone marrow was normoblastic. Cognitive dysfunction was found (short-term memory, memory concentration and visuomotor tasks). The liver function was normal. Two patients showed signs of cerebellar atrophy, and 16 patients showed cerebral atrophy on CT scans.

6-11-32 INITIAL AND POST TREATMENT PLASMA CARNITINE LEVELS DURING VALPROATE MONO AND POLY THERAPY

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The reduction of free plasma carnitine levels during valproate therapy has been reported. Studies have not examined the plasma carnitine level prior to initiation of therapy. We compare the initial total, free and esterified plasma carnitine levels and acyl/free ratio with the lowest post treatment levels using the ANOVA procedure. Forty-one patients were on valproate monotherapy (VPAm) and 49 on valproate plus other antiepileptic (VPAp) drugs. The initial total and free plasma carnitine levels were significantly lower in the VPAp group versus the VPAm group. Post treatment total and free carnitine levels were significantly lower than the initial carnitine levels for both groups. The initial acyl/free carnitine ratio was significantly lower than the post treatment ratio for both groups.

6-15-01 CHARCOT - A PHILATELIC TRIBUTE

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All the persons mentioned are featured on stamps. Charcot is portrayed in front of the Salpêtrière, the institution he made into the world's center of neurology. He was preceded by Pinel who liberated the insane. Charcot's pupils included Bekhterev, Marinesco and Freud who even owed his concept of sexuality in the neuroses to his tutor. Charcot supported Pasteur in his claims for the rabies vaccine but opposed the venereologist Fournier's belief that tabes dorsalis was a syphilitic disease. Charcot's son, Jean Baptiste, followed his father into neurology but after the latter's death he pursued his first love - Arctic exploration - and became an even more famous public figure.

6-15-02 AN ICONOGRAPHIC APPROACH TO THE CLINICAL PICTURE OF HYSTERIA IN THE WORK OF J.M. CHARCOT AND P. RICHER

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Fidia France, Paris, France.

Jean Martin Charcot (1825 - 93), together with his pupil Paul Richer, formulated the differential diagnosis of epilepsy and hysteria and defined the clinical picture of major hysteria or "hystero-épilepsie". The multiform, intermittent, paradoxical "illness of impression" was thus crystallized into a general type, i.e., "le tableau classique de la grande attaque hystérique complète et régulière".

This "classical picture" was drawn by Richer in his synoptic illustration of 86 typical sequences and 9 variants; it was captured by the photographer A. Londe for the Iconographie de la Salpêtrière, and was reproduced by Charcot in his public sessions of hypnosis.

Furthermore, Charcot and Richer looked back to the representations of convulsions, diabolic possession and extasis in art history in order to prove that the "grande hystérie" is a perfectly well characterized morbid entity whose fundamental features were the same in the past as they are in the present.

Our presentation will focus on:

a) the visual character of Charcot's approach to nosology, analyzing the clinical picture of hysteria as an original art work and discussing its "natural" models, iconographic sources, copies, forgeries, criteria for authentification, etc.
b) the usually neglected role of epilepsy as a figurative model for hysteria, and more generally for the representation of "le mal" in its triple signification of illness, suffering and evil.

6-15-03 FOLLOW-UPS IN TWO CASES OF DR. HARVEY CUSHING

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One reason Dr. Harvey Cushing became preeminent among pioneering American neurosurgeons was his willingness to report adverse outcomes and mistakes as well as successes. These amusing follow-ups in two of his cases are in the tradition he established. Case 1 was a man of about 30 admitted to the Peter Bent Brigham Hospital with symptoms of a brain tumor, left-sided headache, progressing right hemiplegia, and papilledema. Dr. Cushing turned a large bone flap and found the dura "very tight;" he feared to open it and chose to probe the underlying brain, after several passes encountering a "rocky hard" mass 8 cm deep, surely an " inoperable malignant tumor." The flap was replaced and the patient sent home with the poor prognosis. Twenty years later I saw the patient at the Brigham because of other medical problems. He was intact neurologically and stated that recovery began within a few months of the brain surgery!

Case 2 was an elderly art school director seen at Positano. She related how, about 30 years earlier, she had developed a visual field loss, which the Neapolitan and then the Roman physicians thought to manifest a pituitary tumor. Dr. Cushing was recommended as the world leader in pituitary surgery, and an appointment was arranged for her under the clock at Grand Central Station, New York! She met him on schedule and was examined in the main concourse while sitting on one of the long benches! He opined that the trouble was not a tumor and she should return to Italy, expecting the symptoms to resolve. She did and reported to me that within months she was well again. So Dr. Cushing was very right in this case.

6-15-04 NEUROGERIATRICS IN ANCIENT INDIAN MEDICAL TREATISE-AYURVEDA.

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Ayurveda is the oldest still practised discipline of India which originated from Atharvaveda, the oldest scripture in the world. Ayurveda deals with disease prevention and health promotion. It is divided into eight parts. The 7th part, "Rasayan" (rejuvenation) deals with the retardation of aging process and treatment of degenerative disorders. Many neurological disorders, secondary to aging, as well as clinical symptomatology of neurodegenerative disorders including dementia have been well documented in Ayurveda. Most of these disorders are due to abnormalities in "tridosa" (three humors). The most prevalent dosa is "vata", which is synonymous with activities of the nervous system. The treatment of many neurodegenerative disorders are divided into preventive, good nutrition, exercise and "sansodhan" (elimination of toxic substances from the body by vomitting, emetics, sweating), particularly by the methodology of "kayakalp", total body rejuvenation. This very unique method is still practised. The symptomatic and specific therapy includes "shaman", utilization of herbs and other therapy to counteract "vata dosa". In spite of lack of modern technology, Ayurveda is still very useful integrated medicine to treat age-related neurological disorders.

6-15-05 ON THE NAMES OF BABINSKI

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Joseph (Jozef) Felix Francois Babinski, Charcot successor, became world-known for the sign that bears his name. His brother Henri gave up his name and abandoned engineering career to look after Joseph. Clovis Vincent, "father" of French neurosurgery and pupil of Joseph, stated: "Joseph Babinski lived for science, and Henri lived for his brother; without Henri Babinski, Joseph would not have accomplished that much." However, Henri's name became famous in all Paris for a cookbook *Gastronomie Pratique* written under the pseudonym of "Ali-Bab". Even though Joseph gave paternity to three daughters out of wedlock, he did not give them his name. Throughout Joseph's career his surname remained distorted despite his own efforts to spell and pronounciate it correctly. Several people can claim the name Babinski, but in neurology and neurosurgery there is only one, Joseph.

6-15-06 CONTRIBUTIONS TO HISTORY OF NEUROPSYCHOLOGY: AN UNNOTICED DESCRIPTION OF ANOSOGNOSIA WITH SOMATOPARAPHRENIA BY J.B.BOUILLAUD(1825).

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Unawareness of a deficit caused by brain damage is one of much discussed topics in cognitive neurology. It is said however that, following Seneca's notes on a case with lack of awareness for blindness in the antiquity(63 AD), "almost 2000 years were to elapse before von Monakow (1885) reported a similar observation"(Bisiach et al.1991), ca. 30 or 65 years more having been necessary before the classical description of denial of hemiparesis(anosognosia: Babinski 1914) or somatoparaphrenia(Gerstmann 1942) respectively. This paper calls attention to a case(J.B.Bouillaud 1825) which exhibited a "singulière illusion sensitive" that "il(the patient) croyait toucher la main d'une autre personne, sans pouvoir s'imaginer que ce fût la sienne (i.e. his left hand)"in the presence of left hemiparesis (haemorrhage in the right hemisphere at autopsy). A similar case was mentioned later also by Ch.Férét(1891) as "hallucinations altruiste".

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-15-07 THE SIGNIFICANCE OF BEEVOR'S SIGN

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Beevor's sign (an upward migration of umbilicus in the act of sitting up from supine position) is to be regarded as a reliable sign indicating the lesions at the level of Th_{10} spinal cord and/or roots.

Beevor described this finding in his 100 pages' monograph entitled "The Croonian Lectures on Muscular Movements and their Representation in the Central Nervous System" published in 1904.

The essential part of his description concerning the umbilical movements is appearing in the section of "Movements of the Spinal Column" at page 40.

He precisely stated the upward migration of umbilicus, but he also introduced two cases in which the umbilicus was drawn downwards due to weakness of the part of the recti situated above the umbilicus, one of whom had a myopathy.

There is no doubt that Beevor's sign can be seen in the cases of thoracic cord lesions around Th_{10} level. In addition, we could confirm this sign in some cases of myopathy, and also umbilical downward migration in two cases of syringomyelia and two cases of myasthenia gravis, respectively, as mentioned by Beevor.

The importance of Beevor's original description (only 27 lines) should be stressed in clinical neurology.

6-15-08 MARIN AMAT SYNDROME DESCRIBED BY PITRES AND ABADIE IN 1915

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Marin Amat syndrome is an involuntary contraction of orbicularis oculi muscle synergic with movement of the mandible. This phenomenon was described by Marin Amat in 1918 (in Spanish) and in 1919 (in French), and the term was suggested by Coppez in 1932. This phenomenon also was briefly described by Müller-Kannberg in 1894 and by Higier in 1902. However, no attention has been paid on the paper by Pitres and Abadie in 1915 which described explicitly the phenomenon and discussed the mechanism with impressive photographs.

The patient was a 40-year old woman, who developed left facial palsy in August 1903. In February 1905 her palpebral fissure was wider on the left side. When she opened her mouth, her left eye was almost completely closed. Photographs attached to their paper demonstrate the phenomenon clearly. The description and the photographs by Pitres and Abadie have not been cited by any author reviewing the Marin Amat syndrome.

6-15-09 NEUROMYCOTOXICOSIS IN THE SECOND WORLD WAR

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During the 2nd world war, several neurological diseases appeared in prisoners and ex-prisoners of war (PEW). Those cases showed a very interesting association with some foods such as maize and rice mostly.

On the other hand, those patients lived at the far east, mainly; and over there the humidity is high. With humidity, foods can produce molds. Some of them give rise to toxins called mycotoxins. Mycotoxins can produce immune disfunction, tumors, cardiovascular and liver disturbances, neuropathies and demyelinating diseases. These mycotoxins might explain why those patients' ailments were relieved when moldy foods were changed. Residual effects may exist and may allow us to understand other cases diagnosed as myelopathies with unknown aetiology some years later. Also, it may explain other neurological complaints with unknown aetiology, that appeared in the same region or in other places with similar climatic conditions.

This research suggests a new clinical entity which should be named human neuromycotoxicosis.

6-17-01 BOTULINUM TOXIN TYPE A INJECTIONS FOR CERVICAL DYSTONIA: A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Botulinum toxin type A, a powerful presinaptically active neuromuscular blocking agent, became the treatment of choice for a variety of spasmodic disorders. We now have carried out a double-blind, placebo-controlled study of the effectiveness of botulinum toxin type A (Botox) injections for the treatment of cervical dystonia. All entrolled patients (8female,4male) with idiopatic torticollis (pure rotational type or in combination with retrocollis-laterocollis) had failed to get substantial response from previous medications. Patients have been rated according to the Columbia Torticollis Rating Scale, as well as all of them were video taped before and 2 and 3 months after Botox injections. Botox was injected in 1,2 or 3 of the most affected muscle (sternocleidomastoid, trapesius, scalenus, splenius) in a total dose of 100-200 U.

Compared to placebo, Botox produced significant improvement in the severity of torticollis, pain and disability. There were no serious side effects. These patients as well as the others are now included in the open study. Results will be presented.

Study is supported by Ministry of Science, Republic of Croatia and by Allergan-Europe

6-17-02 EARLY LEVODOPA TREATMENT ENHANCES THE SURVIVAL OF PATIENTS WITH PARKINSON'S DISEASE.

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There is an inherent excess mortality involved in the natural course of Parkinson's disease. We have examined the effect of timing of levodopa treatment on the survival of patients with Parkinson's disease. Levodopa treatment was initiated during 1969 to 1975 on 83 patients at Hoehn and Yahr stage 1 or 2, on 158 patients at stage 3, and on 108 patients at stages 4 or 5. The patients were followed-up until April 30, 1992 or until death. The follow-up was complete.

The 22-years survival of patients with early treatment (stage 1 or 2) did not differ statistically from the expected, whereas in the two late treatment groups there was significant excess mortality. In age-stratified Cox proportional hazards regression model the most significant explanatory factor for survival was the stage of the disease at initiation of levodopa treatment; advancing stage relating negatively to survival. Also higher age at onset, prolonged duration of the disease at entry and male gender had a negative relationship to survival.

Early initiation of levodopa treatment is superior to later treatment in diminishing the excess mortality associated with Parkinson's disease.

6-17-04 THE CONTINUOUS DOPAMINERGIC STIMULATION: AN UP TO DATE.

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The alterations in L-Dopa responsiveness manifested by motor fluctuations and dyskinesias is one of the most important limiting factor in the management of parkinsonian patients. This problem reflects alterations in the therapeutic window and progressive reduction in the buffering capacity of the nigrostriatal dopaminergic neurons for levodopa. A continuous administration of the dopamine precursor may be the only therapy able to reduce fluctuations-induced disability.We administered the dopamine agonist lisuride by continuous subcutaneous infusion to 44 parkinsonian patients for up to 8 years, and another agonist, apomorphine, to 15 patients for at least 3 years. In addition, we administered levodopa methylester by continuous enteral infusion to 5 patients with extremely severe Parkinson's disease via a jejunostomy or a gastrostomy for up to 18 months .We have evaluated every six month all patients with UDPRS, AIMS, ON-OFF chart . We also considered l-dopa, lisuride, apomorphine dosage. A remarkable increase of ON period and improvement of dyskinesias was observed with each treatment.14 out of 44 pts in lisuride therapy, 4 out of 15 pts in apomorphine and 2 in enteral infusion dropped out of study mainly because of psychiatric side effects and poor compliance to the technique. Moreover, worsening of motor fluctuations over the years appeared significantly less rapid in patients treated with chronic lisuride infusion as compared with a matched population of parkinsonians receiving conventional oral treatment.

6-17-05 LAMOTRIGINE IN PARKINSON'S DISEASE

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Background: In animal experiments modelling Parkinson's disease (PD) several NMDA-antagonists such as MK 801 and CPP show clear locomotor stimulating effects. Since most NMDA-antagonists are not suitable in PD-patients due to their toxicity there is a rationale basis to investigate the anti-PD activity of other antiglutamatergic substances. The anticonvulsant Lamotrigine (LTG) might be of interest in PD, as it acts mainly as an inhibitor of presynaptic glutamate-release. In our present study we are evaluating anti-PD activity of LTG in man. Encouraging preliminary data from a preceeding open clinical observation in 5 PD-pats. have already been published. Design: 20 pats. with advanced PD and motor complications (fluctuations, dyskinesias, loss of drug-efficacy) are investigated in a controlled clinical trial under double blind conditions. LTG (max.400mg/day) is compared to placebo (PL) over a 5 months observation period. Standardized ratings of motor disability, fluctuations/dyskinesias and side effects are performed in 1-4 weeks intervalls.

Results: Interim evaluation of 13 pats. including data of 2 months observation shows slightly more pronounced improvement in the LTG-group:

(mean LTG/PL	week0	week2	week4	week8):
CURS-global	27/26	24/27	22/22	24/25pts.
P-Pegboard	158/173	141/154	147/173	151/142sec
Cumulative off	2.1/2.4	1.7/2.4	1.8/2.4	2.1/1.7pts.
Overall benefit	0.0/0.0	1.3/0.6	1.4/1.4	1.0/0.7pts.

Detailed results of final evaluation will be presented at the congress.

6-17-06 SEXUAL PROBLEMS OF PATIENTS WITH PARKINSON`S DISEASE.(PD)

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Sexual dysfunction is frequently seen in neurologic diseases and more common in the aged. Libido has been associated with the dopaminergic transmitter system. Consequently, sexual function is of interest in PD, but has only been studied to a limited extent as indicated in a recent review.

The aim of the present study has been to describe sexual function in the youngest PD patient. Twenty-five patients (15 males, 10 females) participated in a structurized interview on sexual function. The age interval: 36 - 56 years of age (mean age 50,3). Mean duration of treatment 5,4 years. Hoehn-Yahr stages I-IV.

Fifty-five percent had changes in sexual function. Seventy percent of females and 27 percent of males reported hyposexuality, while 2 males reported hypersexuality. Association with incontinence, depression, duration, and severity of illness will be presented. Implications for for association of sexual function and the dopaminergic system will be discussed and results compared to previous studies and other neurologic disorders.

6-17-07 LISURIDE-INDUCED MODIFICATIONS OF CENTRAL DOPAMINE METABOLISM IN PARKINSON'S DISEASE.

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The effects of dopamine agonists on central dopamine (DA) metabolism in Parkinson's disease have received little investigative attention. In an attempt to clarify this issue, CSF samples were collected on 3 different days in 5 patients with severe Parkinson's disease. Lumbar punctures were performed after overnight withdrawal of antiparkinsonian medications, and repeated at the end of 16-hour overnight i.v. infusions of levodopa and lisuride. Oral carbidopa (50 mg every 4 hours) was administered with levodopa, and oral domperidone (20 mg every 6 hours) with lisuride. CSF homovanillic acid (HVA), dihydroxyphenylacetic acid (DOPAC), DA and norepinephrine (NE) levels were determined by HPLC and electrochemical detection. As expected, a significant increase in CSF levels of DA, HVA and DOPAC with no effect on NE was observed after levodopa infusion. On the other hand, lisuride induced a rather selective increase in DA levels, dopamine catabolites being unchanged and NE decreased. These preliminary data suggest that multiple mechanisms may mediate the therapeutical effect of lisuride.

6-17-08 SERUM ELISA TEST FOR DETECTION OF BOTULINUM TOXIN ANTIBODIES

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Intramuscular injections of Botulinum Toxin A (BT), a double chain polypeptide with a molecular weight of 150 000 Dalton, are a new approach in the treatment of dyskinetic syndromes. Despite of their extraordinary clinical efficacy singular cases of therapy resistance have been reported and attributed to antibody production. To study this phenomenon development of an uncomplicated serum antibody test seemed necessary.

An Enzyme Linked Immuno Sorbent Assay (ELISA) was set up by coating microtiter plates with highly purified BT type A and incubating them with the test sera. After removal of surplus test serum antibodies were detected with peroxydase labelled anti human IgG. To quantify the results the extinction of the peroxidase catalyzed color reaction was measured photometrically. In 20 control sera extinction was below 0.4. Amongst 6 patients with BT therapy resistance extinction was between 0.8 and 2.2. In 10 patients successfully treated with BT for torticollis spasmodicus for more than 1 year extinction was not higher than in the control group. ELISA test results were confirmed by Western Blots.

BT antibodies in sera of patients with BT therapy resistance can be detected quantitatively with an ELISA test. This test allows screening investigations which might help to understand the development of BT therapy resistance.

6-17-10 AKINESIA: SYMPTOMS, DEFINITION AND DIFFERENTIALDIAGNOSIS

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The aim of the study is to point out symptomatologic variety (motor, affective, cognitive), ethiologic unspecificity and possible underlying pathophysiological mechanisms in akinesia.

Therefore we investigated 30 akinetic patients with different neuropsychiatric rating scales (BPRS,SEPS,AIMS, Rogers, AMDP,Columbia, SANS,GAS,HAMA), which measure beside motor symptoms also cognitive and affective alterations.

It is showen that akinetic states are accompanied by affective and cognitive alterations such that akinesia can not be regarded soleby as a motor disease.

Our 30 patients showed different diagnosis (Parkinson, Intoxication, Catatonia, Schizophrenia etc.) out which it is concluded that akinesia has syndrom character as a final common functional pathway into which different diseases run into.

6-17-11 NADH TREATMENT IN PATIENTS WITH PARKINSONS DISEASE.

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It has earlier been suggested that formation of L-dopa is stimulated by NADH. These suggestions have to be verified by measuring the in vivo and in vitro effects of the treatment.

Five patients with clinically moderate Parkinson's disease were treated with NADH, 25 mg, given intravenously once a day for four days. Then they were given 25 mg NADH intramuscularly after 2 and 4 weeks. Disability scores were determined before each treatment and two weeks after the final injection. A control group with comparable degree of Parkinson's disease obtained sodium chloride according to the same schedule as the study group.

According to the Unified Parkinson's Disease Rating Scale a tendency to clinical improvement was seen after the iv injections However, the changes were not statistically significant, No further changes occurred during the following weeks. No changes were found neither in the study nor the control group regarding cerobrospinal fluid concentrations of homovanillic acid, 5-hydroxyindole acetic acid, hydroxy-methoxy-phenyl glycol, dynorfin, met-enkefalin, and somatostatin.

The results indicate that a clinical improvement is possible during intravenous treatment with NADH, although not correlating to measurable alterations in biochemical parameters and not statistically significant. Intramuscular treatment showed no therapeutic effect.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-17-13 ASSESSING THE IMPACT OF ESSENTIAL TREMOR ON UPPER LIMB FUNCTION.

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We compared the impact of ET on the performance of 3 manual tasks: drawing spirals, holding a cup full of water and a joystick tracking test. Accelerometry was performed duing maintained posture, the joystick test and holding the cup. The inter-relationships between tremor amplitude, frequency and task impairment were then examined. The results showed that the amplitude and frequency of essential tremor changed with different activities. The amplitude of tremor decreased during the tasks and frequency altered by up to 4.5Hz. The smallest amplitude tremors altered most in frequency, the largest most in amplitude. The impairments in carrying out the tasks were highly correlated with one another and with the amplitude and frequency of postural tremor. The concept of tremor suppressability is introduced: the extent to which the amplitude of a particular tremor decreases during a specific task compared to posture.

6-17-14 INTERNAL TREMOR IN PATIENTS WITH PARKINSON'S DISEASE

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Although sensory symptoms were not classically described in Parkinson's disease (PD), in recent years it has been increasingly recognized that painful sensations and paresthesias occur in a significant number of patients. It has been our observation that PD patients often describe a sensation of internal tremor, a feeling of tremor inside the chest, abdomen, arms or legs that cannot be seen.

We investigated the prevalence and characteristics of internal tremor by administering a questionnaire to 100 consecutive patients with PD and 50 age matched controls seen in our movement disorder center. Each patient's symptoms and extent of motor impairment were documented with the Unified Parkinson's Disease Rating Scale.

A sensation of internal tremor was present in 44% of this sample of PD patients, and in 6% of the control population. Data describing the general characteristics and relationship of internal tremor to observable tremor, other sensory symptoms and severity of disease will be presented. The subjective sensation of internal tremor is very common in patients with PD and represents a new previously undescribed sensory symptom.

6-17-15 BEHAVIORAL AND HISTOCHEMICAL CHANGES IN MPTP-TREATED C57BL/6 MICE

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The effects of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine(MPTP) on behavioral and histochemical changes were investigated in C57BL/6 mice. For immunocytochemistry, one group of mice received a dose of 2X30mg/kg of MPTP given 12hours apart and the other group 30mg/kg/day of MPTP for 7days. Locomotor activity was measured during 120minutes after a single injection of 30mg/kg of MPTP. We compared the numbers of tyrosine hydroxylase(TH)-positive cell bodies using immunocytochemical technique in the substantia nigra, ventral tegmental area and locus ceruleus 10 days after the last injection of MPTP. There was a significant decrease in locomotor activity during 100minutes after injection of MPTP and the number of TH-positive cell bodies in the substantia nigra of the mice which received the dose of 30mg/kg/day for 7 days, but not in the ventral tegmental area or the locus ceruleus. But 30mg/kg of MPTP given 12 hours apart failed to produce a significant decrease in the number of TH-positive cell bodies in any three catecholamine nuclei examined. It is concluded that MPTP-treated C57BL/6 mice provide a useful model for studying characteristics of Parkinson's disease and the dose of 30mg/kg/day for 7 days is more effective in the animal model for Parkinson's disease in C57BL/6 mice.

6-17-16 LEVODOPA DOSE CAN BE MAINTAINED LOW WITH EARLY SELEGILINE THERAPY IN PARKINSON'S DISEASE

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In an earlier report of our placebo-controlled selegiline trial on de novo parkinsonian patients, we have shown that the need to start additional levodopa therapy is significantly postponed by using selegiline monotherapy. Now we report the two-year interim results of the double-blind continuation of the trial in 44 patients after the introduction of levodopa to the earlier therapy with placebo or selegiline (21 and 23 patients, respectively). The clinical disability was assessed by three rating scales. The daily dose of levodopa needed to maintain an optimal condition had to be increased progressively up to a 52 % higher level in the placebo group than in the selegiline group (524.9 ± 150.2 and 357.5 ± 117.3 mg, respectively, p=0.001). The respective numbers of daily levodopa dose were 4.5 ± 0.8 and 3.9 ± 1.0 (p=0.01). The combination of selegiline and levodopa was well tolerated, and there were no essential differences in adverse events between the two groups. In conclusion, early selegiline therapy allows a significant saving in the subsequent levodopa dosage and potentially offers beneficial effects in the long-term management of Parkinson's disease.

6-17-17 INJECTIONS OF BOTULINUM TOXIN-A FOR SPASTICITY

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Objective: We investigated the clinical usefulness and safety of botulinum toxin type A (BTX) in the treatment of spasticity.

Methods: 8 chronic subjects were treated: 6 multiple sclerosis (MS), 1 myelopathy, 1 head trauma. After injection, subjects were reassessed for 14 weeks. We injected with EMG guidance: hip adductors (3), hamstrings (2), quadriceps (1), wrist/finger flexors (1), tricep (1). Tone was assessed by the Modified Ashworth Scale (MAS, 0-4); Spasm Frequency (SF, 0-4) in the previous 24 hrs; and Pain during previous 24 hrs (0-100). Results: 4 patients received 1 treatment; 4 received a "booster" at 2 weeks. Average dose BTX was 260.0±42.1 Units. 1 subject (quadriceps) was excluded from analysis due to acute MS exacerbation 5 days after injection. The remaining 7 demonstrated improvement compared with baseline scores: MAS: 2.29±0.4 vs. 0.96±0.3, p= .0011; SF: 3.14±0.6 vs. 1.86±0.6, p= .018; Pain: 32.14±9.0 vs. 3.29±1.5, p= .007.

Maximum tone reduction was seen at 2-6 weeks s/p initial injection. A gradual increase in muscle tone was seen 10-14 weeks after initial injection. 2 subjects reported bruising at injection site; no other adverse reactions reported. Preliminary data suggest that "boosters" may not be warranted.

Conclusion: Our data support BTX injections as safe and effective treatment for spasticity. Further clinical trials are warranted to establish optimal dosing, long term efficacy and safety.

6-17-18 PAIN IN SPASMODIC TORTICOLLIS.

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Pain is commonly associated with spasmodic torticollis (ST). It is generally believed that successful treatment of motor symptoms with botulinum toxin (BOTOX) is followed by pain relief. We set out to investigate the matter in more detail.

21 patients (11 F/10 M, aged 24-72y) with established ST >6 months´duration participated in the study. The patients were seen before treatment and at 3 weeks, 3, 6, and 12 months after initiation of BOTOX therapy. Pain reports included visual analogue scales, verbal pain ratings, Finnish Pain Questionnaire, and Pain Chart. Muscle soreness was assessed by palpation and pressure threshold measurements. Motor symptomatology was rated by independent judges viewing standardized videotaped segments.

At entry, 16/21 patients reported constant or recurring pain in the neck and shoulders. Occasionally it radiated down the arms and up to the vertex. Tender points and lowered pressure thresholds were found in the primarily overactive muscles as well as in those contracting in a compensatory effort to oppose the turning of the head.

Improvement of neck posture was followed by reports of attenuation of pain; however, this took considerably longer to become apparent. When 13/16 patients undertaking repeat BOTOX injections were evaluated as a group, significant changes in pain parameters were not seen until at 6 months.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-17-19 DIET VITAMINS IN PARKINSON'S DISEASE.

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Although the evidence of oxidants in the pathogenesis of Parkinson's disease (PD) and the influence of antioxidant substances in prevention of PD has been stressed, there is still controversy about the role of these substances in the cause of PD. To elucidate this factor the influence of antioxidants vitamins, specially vitamin E, have been investigated with diverse procedures such as determination of serum or tissular levels, the presence of supplemental vitamin intakes or the intake of foods with high vitamin E content. However the relation of the daily vitamin intake in the usual diet with the development of PD had not been previously evaluated. We have conducted a community case-control study to determine the question, using a semiquantitative food frequency questionnaire and posterior quantification of nutrients intake by multiplying the reported amount of each food eaten by a weight representing its nutrient composition, assessing the intake of proteins, calcium, magnesium, zinc, and vitamin A,C and E. 50 PD patients and 50 age and sex matched controls were compared using unconditional logistic regression, divided in quartils based on the distributions among controls; the second and third quartil were grouped. No differences were observed in all the items evaluated, exception of vitamin E intake with a higher risk in the first quartil (OR=1.44-17.27) and a lower risk in the second-third quartil (OR=0.057-0.69). This study suggest a role of some aspects of the diet in the development of PD.

6-17-20 DHT - DIARY HANDY TERMINAL FOR EVALUATING FLUCTUATIONS IN PATIENTS WITH PARKINSON'S DISEASE

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It is well known that fluctuations of motor response - partly drug-induced - may occur in advanced stages of PD, which require a change of treatment strategies. Such flucuations, either corresponding to drug intake or occuring independently, are usually documented every hour or every fifteen minutes by hand written entries in a motor diary, which serves as a basis for treatment modification and better symptom control. The only disadvantage of this method is the limitation in time of such a form of documentation. In order to overcome this obstacle and to permit immediate evaluation of fluctuations and corresponding modification of drug administration we developed a software package running on an Epson Handy Terminal. The patient himself enters on this terminal all changes of motor response and drug intake with accuracy to the minute. We present a comparative study of 38 PD patients demonstrating the improved data evaluation and statistical evaluation of fluctuations registered by DHT as compared to hand-written entries as well as the resulting therapeutical consequences.

6-17-21 BENEFICIAL EFFECTS OF SUBTHALAMIC NUCLEUS STIMULATION IN PARKINSON'S DISEASE.

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In animal models of Parkinson's disease (PD), it is postulated that the excessive output from the subthalamic nucleus (STN) plays a critical role. Selective lesions or high frequency electrical stimulation of the STN can alleviate parkinsonian symptoms in MPTP-treated monkeys. We decided to carry out STN stimulation in PD.

After approval from the institutional ethical committee, we operated a parkinsonian patient aged 51, suffering for 8 years from a severe akineto-rigid form of PD, complicated with on-off effect (Hœhn & Yahr stage 5 in the worst off motor phase). Stereotaxic surgery was done under local anaesthesia on one side. The theoretical target was chosen according to stereotaxic atlases.

A spontaneous increase in neuronal activity was recorded in an area located 2 to 4 mm under the level of the intercommissural plane. Within the same place, a 130 Hz stimulation induced akinesia alleviation mainly on the contralateral limbs, comparable to that obtained with dopaminergic drugs. No dyskinesia was noticed. Then a long-term quadripolar DBS Medtronic electrode was inserted in that area.

Studies of the effects of chronic stimulation are in progress to determine the best temporal and electrical stimulation variables.

6-17-22 SIGNIFICANCE OF RESTING TREMOR IN ESSENTIAL TREMOR CASES.

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Essential tremor (ET) is characterized by postural or kinetic tremor of upper limbs or head. Resting tremor (RT) is the hallmark of Parkinson syndrome (PS), but has also been reported in some ET cases. The objective of this study was to determine the frequency and significance of RT in the ET.

Nine ET patients followed over 22 years came to autopsy. Additional diagnosis of PS was made only when unequivocal RT, bradykinesia and rigidity were present. Autopsy studies were performed by qualified neuropathologists. 6/9 ET cases had RT and in 3 additional diagnosis of PS was made. The substantia nigra neuronal population was estimated as normal for age in all cases and none had Lewy body inclusions.

In the 3 cases whose RT was a part of ET the onset age and duration of illness were similar to those without RT. However, the subgroup with RT had either medium or coarse upper limb ET while the three without RT each had fine or no upper limb ET. In 1/3 of these ET cases we believe RT represents a natural evolution which is related to age-related decline in striatal DA.

6-17-23 MEDIAN NERVE SOMATOSENSORY EVOKED POTENTIALS IN PATIENTS WITH DYSTONIA.

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Abnormalities in early frontal components of SEPs have been described in different movement disorders. The reduction in N30 amplitude in Parkinsonian patients has been referred to a dysfunction of Supplementary Motor Area (SMA). On the other hand N30 has been described to be increased in amplitude in patients with dystonia suggesting an opposite pathophysiology. We studied early median nerve SEPs in 10 patients with dystonia: 7 with focal dystonia, 1 with generalized dystonia and 2 with Dopa-responsive dystonia (DRD). Latency and morphology of N9,N13,N20-P25,P20-22-N30,N20/P25 and P20-22/N30 peak to peak amplitude and central conduction time (CCT) were analyzed. Latencies of all evoked potentials and CCT were normal as well as N20/P25 amplitude. Alterations of N30 amplitude were found in 4 subjects: both patients with DRD presented a reduction in N30 amplitude, while 2 patients with writer's cramp showed an increase in N30 amplitude. These conflicting results could reflect different pathophysiologic mechanisms underlying focal dystonia and DRD.

6-17-24 ORAL PULSE LEVODOPA THERAPY IN PARKINSON'S DISEASE

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Chronic levodopa therapy in Parkinson's disease (PD) is associated with the development of motor fluctuations related to the cumulative dose consumed by the patient. To reduce the cumulative amount of levodopa, we investigated in seven patients with mild PD (aged 59±10.5 years, Hoehn-Yahr stage I or II) the clinical efficacy of 15-days periods of treatment with levodopa plus carbidopa (ratio 10:1) scheduled at different dosages by a conventional design (62.5 mg t.i.d., 125 mg t.i.d., and 187.5 mg t.i.d.) compared to a treatment, defined oral pulse levodopa therapy (OPLT), in which 250 mg were given once every three days. The efficacy of each treatment was assessed by measuring the modifications of Movement Time detected by a computerized tachystoscope. OPLT was more effective than conventional treatment administering 62.5 mg and 125 mg t.i.d., and comparable to treatment with 187.5 mg t.i.d.. OPLT may be considered a new therapeutic approach in mild parkinsonism.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-17-25 PROGRESSION RATE OF PARKINSON'S DISEASE: A CLINICAL AND PHARMACOLOGICAL STUDY OVER A SIX MONTHS PERIOD.

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Istituto di Scienze Neurologiche, Facoltà di Medicina in Catanzaro, Università di Reggio Calabria, Italy.

We investigated the progression of Parkinson's disease (PD) in nine patients with mild disease (Hoehn-Yahr stages I to III) by measuring at a six months' interval clinical and Movement Time (MT) values before and after an acute 250 mg levodopa oral test. The results showed that clinical and MT values did not significantly change on the two different examinations, as well as the amplitude of MT response to levodopa. By contrast, on the evaluation at six months, the duration of MT response to levodopa significantly shortened, this being more marked in those patients presenting at the first examination a longer MT duration response to levodopa. These results suggest that over a period of six months the duration of MT response to acute levodopa test is the only detectable parameter to evaluate PD progression.

6-18-01 INTERFERON-BETA 1b IS EFFECTIVE IN RELAPSING-REMITTING MS

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A randomized, double-blind, placebo-controlled trial of interferon-beta 1b (IFNB, Betaseron® Berlex Laboratories) was performed at 11 centers in the United States and Canada. There were 372 ambulatory subjects with active, relapsing-remitting multiple sclerosis (MS), who received either placebo, 9 million international units (MIU) of IFNB, or 45 MIU of IFNB by subcutaneous injection on alternate days for 3 years. The primary outcome measures were differences in exacerbation rates and proportions of attack-free subjects in each group. Annual exacerbation rates were 1.21 in placebo, 1.05 in low dose, and 0.84 in the high dose groups, indicating a significant therapeutic effect (45 MIU vs placebo, p=0.0004; 9 MIU vs placebo, p=0.0087). More subjects in the 45 MIU group were attack-free at 2 and 3 years, and median time to first attack was nearly doubled compared to the placebo group. Significant changes in disability scores were not found in this short-term study, but serial MRI scans showed impressive reductions in number of active lesions and total disease burden during the trial in both groups of IFNB-treated subjects. Few serious adverse reactions were noted. Side effects were well-tolerated, and tended to diminish with time. IFNB is the only therapeutic agent that has ever been shown to substantially alter the course of MS in a properly controlled clinical trial.

6-18-02 PROGNOSIS IN ACUTE TRANSVERSE MYELOPATHY

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The use of magnetic resonance imaging (MRI) to help determine prognosis in idiopathic acute transverse myelopathy (ATM) has not been studied. We retrospectively studied 14 patients with ATM, all having had MRI studies of appropriate spiral levels, to look for correlation between MRI appearance and patient outcome. With abnormalities, seen as intraparenchymal increased signal intensity of T-2 weighting and cord swelling, correlated strongly with poor outcome (P .0009 by Fisher's exact test). Of four patients with these MRI abnormalities, all had severe weakness with little or no recovery over an average follow up period of 39 months. The ten patients with normal spinal MRIs had complete (n = 8), near complete (n = 2) recovery of function, regardless of the degree of weakness (5 severe) during the acute phase. Sphincter dysfunction was seen in all patients and improved in each. Unfortunately the timing of MRI studies varied from day 1 to day 21 after the onset of symptoms. MRI scan of the brain was performed in 12/14 of our patients, and was normal in all. Oligoclonal bands were not found in any of the patients examined (n = 8). These studies are possibly important in predicting which patients might develop MS. None of our patients developed MS over an average follow up period of 38 months.

6-18-03 HIGH DOSE RECOMBINANT-ALPHA-2A-INTERFERON (r-alpha$_{2a}$-IFN) IN RELAPSING-REMITTING MULTIPLE SCLEROSIS (RR MS).

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Immunologic and clinical effects of systemic high dose r-alpha$_{2a}$-IFN therapy in RR MS patients were studied in a double-blind pilot trial. Twenty MS patients received 9 milion U of im r-alpha$_{2a}$-IFN (Roferon,Roche) (n=12) or placebo (n=8) every other day for 6 months. Lymphocytes from MS patients were incubated with or without PHA (0.2 μg/ml) for 48 hours. Gamma-IFN production was determined in culture supernatants by RIA. Clinical relapse was defined as acute objective (ie, at least 1.0 point of EDSS) deterioration of neurologic status followed by stabilization or recovery. MRI (SE$_{2000/70}$ 8 mm slices) was performed and number and area of lesions analyzed. Baseline lymphocyte gamma-IFN production without PHA of 19.7±25.2 U/ml significantly decreased to 3.1±2.4 ($p<0.05$) in r-alpha$_{2a}$-IFN group, while was unchanged in the placebo group. Clinical relapses or new lesions at MRI occurred in 2/12 IFN-treated and in 7/8 placebo-treated patients ($p<0.005$). Fever, fatigue, and leukopenia were common side effects in the IFN-treated group. In conclusion, chronic systemic r-alpha$_{2a}$-IFN therapy downregulated lymphocyte gamma-IFN production in vitro, and was associated with fewer clinical relapses and new lesions at MRI than placebo in RR MS.

6-18-04 HETEROGENEOUS EXPRESSION OF CD4 AND CD8 MOLECULES ON MBP-SPECIFIC T CELL CLONES DERIVED FROM MS

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It is speculated that autoimmune reactions against CNS components might play an essential role for the pathogenesis of MS. CD4+ T cells restricted by HLA-DR appeared to represent such autoreactive T cells. However, we here report that T cells specific for MBP or PLP are heterogeneous with regard to the expression of CD4, CD8, CD3 and T cell receptors. The clones were established against MBP or PLP synthetic peptides. All the lines/clones expressed CD3, TCR and HLA-DR. Except for 2 clones with CD8 phenotype, all lines/clones were found to express CD4. Most interestingly, we found clones that contain at least 4 distinctsub-subpopulations (CD4+CD8-, CD4^{int}+CD8-, CD4-CD8^{dim}+, CD4-CD8+). Since this pattern was not altered after subcloning, it was indicated that the clone cells might not be terminally differentiated. This may imply that autoreactive T cells with different functional properties stem from a precursor population.

6-18-05 INCREASED INTERLEUKIN-1β LEVELS IN CEREBROSPINAL FLUID (CSF) IN PATIENTS WITH SUBACUTE SCLEROSING PANENCEPHALITIS (SSPE).

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Interleukin (IL)-1β and IL-6 are cytokines which mediate cellular immune responses during immune activation and inflammation. We measured IL-1β and IL-6 levels in matching pairs of CSF and sera from 25 patients with SSPE, 30 with definite multiple sclerosis (MS), and 26 with other neurological diseases (OND) by enzyme linked immunosorbent assay. Levels of IL-1β in SSPE CSF (median 151 pg/ml, range 23-250) were significantly increased compared to the MS CSF (21, 0-160) ($p<.0001$) or OND CSF (11.5, 0-130) ($p<.0001$). The IL-1β CSF/serum ratios were higher in the SSPE group than the MS group ($p<.013$) or the OND group ($p<.0006$). CSF and serum IL-6 levels in the three groups were similar. We conclude that there is an intrathecal synthesis of IL-1β in SSPE patients. The findings suggest that IL-1β may be involved in the pathogenesis of the disease.

6-18-06 MULTIVARIATE ANALYSIS OF PREDICTIVE FACTORS OF MULTIPLE SCLEROSIS (MS) CLINICAL COURSE

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Symptoms, phases, clinical events and course of the disease of 400 MS patients, were collected in a database structured according to the EDMUS (Confavreaux 1992), using standardized criteria (Poser 1979; Schumacher 1965; Confavreaux 1980). The inter-rater agreement, evaluated on a sample of 33 patients, was significant for all the considered variables (K range=0.53-1; Z range=6.7-12). A preliminary analysis of early prognostic factors was performed in a first series of 202 definite MS (Poser 1983). Hundred-eighteen had a relapsing-remitting (RR), 42 a relapsing-progressive (RP) and 42 a chronic progressive (CP) course of the disease. By means of logistic regression, the first interattack interval, the first event with sequelae and the disease duration were predictive factors for a severe disability (EDSS 6) and for a secondary progression in the RR and RP groups. A multivariate survival analysis (Cox's model) showed in the RP group that the time to reach progression and the time for a severe disability, were influenced by the first interattack interval (p=0.02; p=0.001), the first event with sequelae (p=0.008; p=0.04) and by the optic neuritis as symptom at the onset (p=0.02; p=0.07). When RP and RR were considered together, the first event with sequelae was the most significant predictor for a rapid shift to a secondary progression (p=0.04).

6-18-07 T CELL RECEPTOR ANALYSIS OF MS-DERIVED T CELL CLONES REACTIVE WITH PLP PEPTIDES: APPLICATION OF INVERSE PCR

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T cell receptor (TCR) gene usage by myelin autoantigen-specific T cells has become the focus of interest in MS. To investigate TCR usage by T cell clones derived from MS, we have developed a double-step and inverse polymerase chain reaction (PCR). After ligation of EcoR I adaptors to both ends, ds cDNA was circulated and subsequently amplified by two sets of C-region primers. Our method makes amplification of all kinds of TCR genes possible without preparing a panel of primers. So far we have sequenced TCR genes of 3 T cell clones/lines reactive with PLP peptides. Identical α-chain sequences resulting from a combination of Vα1.2 and JαHJCA and a β-chain sequences (Vβ6-Jβ2.3) were determined. This is the first report on the application of the double-step and inverse PCR for analysis of TCR genes utilized by human T cells reactive with myelin autoantigens.

6-18-09 TOTAL LYMPHOID IRRADIATION AND CORTICOSTEROIDS IN PROGRESSIVE MULTIPLE SCLEROSIS

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We have previously noted transient benefit from total lymphoid irradiation (TLI) in a double blind (DB) study of 45 patients with progressive multiple sclerosis (MS). Benefit was sustained for up to 4 years in patients with greatest initial lymphopenia.

In an open study of 27 progressive MS patients the effect of TLI combined with a one year course of low dose corticosteroids (TLI-LDC) was compared to the effect of TLI and sham TLI in our prior MS study. Eleven TLI-LDC patients received splenic irradiation (SI); 16 did not. Age, disease duration, sex and entry functional status were similar in all groups. The same radiotherapist administered TLI; clinical evaluations were performed by the same neurologist.

Significantly greater lymphocytopenia was seen with TLI-LDC as compared to TLI or sham TLI. Significantly more TLI-LDC patients were stable through 4 years of follow-up than sham controls ($P<0.01$) or TLI patients ($P=0.053$). Lymphocyte counts and clinical responses were similar with or without SI.

We conclude that TLI-LDC may result in significantly greater lymphocytopenia and longer stabilization in MS patients than TLI or sham TLI. A DB trial of TLI-LDC without SI is currently underway.

6-18-10 MYELIN BASIC PROTEIN INDUCES RESPIRATORY BURST IN LEUKOCYTES FROM MULTIPLE SCLEROSIS PATIENTS

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Increased spontaneous respiratory burst activity (BA) was recently reported in peripheral blood mononuclear cells of MS patients.

We have measured human myelin basic protein (hMBP)-induced BA in the leukocyte fraction of peripheral blood cells (mostly polymorphonuclear cells, PMNC) of MS patients and healthy controls. The cells were isolated by dextran sedimentation and BA was measured by luminol-enhanced chemiluminescence (CL). MS patients displayed significantly increased BA as compared with controls (mean responses : MS = 37mV, n=36; contr. = 9mV, n=20).

Pretreatment of control PMNC with anti-MBP antibody resulted in 4-fold increase in BA and the kinetics of the CL-production was similar to that seen in MS. Because also PMNC from herpes-positive donors displayed increased BA upon stimulation with herpes-antigen when compared to herpes-negative controls we postulate that this kind of antigen-specific activation of the oxidative metabolism is mediated by membrane bound antibody. The mechanisms underlying hMBP-induced BA are under study.

6-18-11 **Immunological monitoring in chronic progressive MS patients treated by cyclophosphamide boosters.**

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Induction cyclophosphamide treatment followed by periodical boosters has been proposed in chronic progressive MS (Hafler, 1991), although no clinical benefit versus placebo has been reported after CPH induction by the Canadian study (Canadian Cooperative Study Multiple Sclerosis Study Group, 1991).

19 patients with CP MS were treated with an induction CPH schedule (300mg/sqm/day for 9 days) followed by bi-monthly boosters (600mg/sqm/day for 1 day) for 12 months.

Immunological monitoring included WBC count and differential, PB CD3+, CD3-CD56+, CD4+, CD45RA+CD4+, CD45RA-CD4+, CD8+, CD8+DR+ before and after the induction and before every boosters.

CSF analysis included cells, total protein, IgG index and T-cell subsets (CD3+, CD4+, CD45RA+CD4+, CD45RA-CD4+, CD8+) at 0, 6 and 12 months.

WBC decreased after induction phase and progressively increased thereafter, reaching pre-treatment levels at month 8.

No significant changes were observed in any of the PB cell subsets during the 12 months.

A slight decrease in CSF cells took place after treatment but IgG, IgG index and CSF cell subsets were unaffected by treatment.

The majority of patients displayed slowing of disease progression.

2 patients dropped out, one because of serious leucopenia and the other for recurrent cystitis.

The lack of significant changes in immunological parameters is at variance with literature data (Hafler, 1991) and suggests that association with ACTH treatment and/or differences in the immune status of patients may influence treatment-induced effects.

6-18-12 SELF-DR REACTIVE T CELLS IN MULTIPLE SCLEROSIS PATIENTS

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We have previously observed that cloning myelin basic protein (MBP)-reactive cultures from multiple sclerosis (MS) patients resulted in the concomitant generation of not only MBP-specific clones but also of clones reacting to self lymphocytes in the absence of the autoantigen. In the present study, we have characterized these self-reactive T cells with respect to proliferative and cytotoxic ability and cell surface phenotype. T cell lines (TCL) were isolated from secondary-MBP reactive cultures of MS patients and healthy controls by limiting dilution. A large proportion of TCL from the patients but not from controls exhibited reactivity to autologous lymphocytes in the absence of MBP. This autoreactivity was directed against self-HLA-DR antigens as demonstrated by inhibition studies using monoclonal antibodies specific for class II gene products and in proliferation assays with HLA matched and mismatched cells. The self-DR reactive T cells did not have cytotoxic ability and were $CD3^+$, $CD4^+$, T cell receptor $\alpha\beta^+$. The finding that self-DR reactive T cells are generated in the response to MBP is novel. The role of these autoreactive T cells in the pathogenesis of MS remains to be elucidated.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-18-13 ANTI-ENDOTHELIAL CELL ANTIBODIES IN PATIENTS WITH MULTIPLE SCLEROSIS

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Objective: To determine the incidence of anti-endothelial cell antibodies (AECA) in a population of patients with multiple sclerosis (MS).
Background: Autoantibodies may participate in the pathogenesis of CNS-demyelinating diseases, and particulary AECA can play a role in the blood-brain barrier damage. There is evidence that AECA may injure vascular endothelium. AECA have been previously reported in sera from guinea pigs with acute and chronic relapsing EAE, as well as in sera from patients with MS.
Design/Methods: Sera from 50 patients with MS were examined for AECA by enzyme-linked immunosorbent assays (ELISAs) using cultured endothelial cells from human umbilical cord veins.
Results: IgM antibodies to endothelial cells but not IgG antibodies were detected in 7 out of 50 patients with MS (14%). No correlations were found between AECA and different clinical or laboratory parameters including the course of the disease, the presence of exacerbation and the score in the extended Kurtzke disability status scale.
Conclusions: These preliminary results show a low incidence of AECA in patients with MS. The determination of AECA using cultured brain endothelial cells can however be more sensitive as MS sera may have a organ-specific antibody to the cerebral endothelial cells.

6-18-14 INTERMITTENT SELF-CATHETERIZATION IMPROVES QUALITY OF LIFE IN MULTIPLE SCLEROSIS.

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Intermittent self-catheterization (ISC) was taught to 70 patients with multiple sclerosis (MS) between 1.9.1990 and 31.1.1992. All of them were interviewed in April 1992, and 89% returned the questionnaires. Bladder symptoms had been present for 7 years (mean), and the average time after the diagnosis of MS was 10 years. Altogether 28 patients discontinued the treatment after having catheterized for 11 months in average. The main reason (50%) for discontinuation was normalization of the bladder function. There was a statistically significant reduction in urgency symptoms, incontinence and difficulties in emptying the bladder. As many as 79% of the patients reported that their quality of life was improved by the ISC. The treatment allowed the patients to resume their personal and social activities of daily living. Significant improvement was reported in family life, marital relationships, sexual life and the quality of night sleep.

6-18-15 PERIPHERAL NEUROPATHY IN MULTIPLE SCLEROSIS

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To determine the frequency of neuropathy in multiple sclerosis (MS), we studied 22 consecutive patients using the Neuropathy Symptom Score (NSS) and electrophysiologic studies, including distal latency, F-response, MUP amplitude and motor conduction velocity (NCV), in ulnar, peroneal and tibial nerves. Sensory conduction velocities were obtained in ulnar, median and sural nerves. Abnormal electrophysiologic findings were found in 33 of 224 nerves examined (14.7%); in 10 patients (45.5%), 2 or more nerves were affected. The frequent abnormalities were prolonged NCV in the ulnar, sural and peroneal nerves. Neuropathic symptoms were mild and did not correlate with electrophysiological abnormalities; nor did age, disease duration or neurological signs evaluated by the Kurtzke Expanded Disability Status Scale (EDSS). Although MS is a central nervous system demyelinating disease, the present study showing frequent electrophysiologic abnormalities indicates peripheral neuropathy. We conclude that peripheral nerve involvement in MS, as demonstrated by electrophysiologic abnormalities, suggests the extension of the pathologic demyelinating process to the proximal nerve roots.

6-18-16 A NEW APPROACH TO AFFECTIVE SYMPTOMS IN RELAPSING-REMITTING MULTIPLE SCLEROSIS (MS).

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A variety of primary and/or secondary psychiatric impairments accompany MS; affecting the spheres of cognition, affect and personality and reflecting neurological damage and/or the functional distress associated with a disabling disease. We conducted a prospective study assessing the correlations of psychiatric symptomatology to neurological parameters: disease duration, disease activity (i.e., number of disease exacerbations per year) and disease severity (Kurtzke Expanded Disability Status Scale). 20 replasping-remitting MS patients were evaluated by a semi-structured psychiatric interview and the following rating scales: Hamilton Anxiety Scale; Hamilton Depression Scale; Hacket-Cassem Denial Scale; and Lubin Adjective Affective List. Results illustrated a high prevalence of anxiety (90%) and, to a lesser extent (50%), depression in relapsing-remitting MS patients. No association of depression or anxiety with disease duration, activity, or severity was found. The mechanism of denial plays a significant role in the psychiatric profile of the disease. We suggest psychiatric evaluation of MS patients to include phenomenologic and dynamic approaches to improve coping mechanisms with relapsing-remitting disease.

6-18-17 CHANGES OF VISUAL EVOKED POTENTIALS /VEPs/ IN MULTIPLE SCLEROSIS PATIENTS DURING 5 YEARS FOLLOW-UP STUDY

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The aim of our study was the evaluation of VEP changes during the course of multiple sclerosis /MS/. We evaluated VEPs in 48 patients with clinically definite MS, during succesive relapses and exacerbations. The diagnosis was based on clinical criteria according to Mc Alpine et al, CT and MRI.

We evaluated the latency to the first major positive component /P_{max}/, which is P_{100} in normal subjects. During 5-years follow-up period in most patients the P_{max} latency increased. The P_{max} latency did not increase in 4 patients, in 2 - remained normal, in 2 - increased P_{max} latency did not change.

We conclude that during the course of MS, irrespectively of the form of the disease and administered treatment the latency of P_{max} increases in majority of patients. There is no reduction of P_{max} latency during the course of MS. VEP measurement can be useful in the monitoring of the progression of MS.

6-18-19 HLA-Dw2 IN MULTIPLE SCLEROSIS: A CLOSE SEGREGATION WITH DISEASE IN MULTIPLEX FAMILIES.

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Introduction. Multiple sclerosis (MS) is associated with HLA-DR2, and genomic studies have specified this association to the haplotype *DRB*1501,DQA1*0102,DQB*0602*, equivalent to the cellular specificity Dw2. Cellular and genomic studies show that MS is associated with Dw2 also in American Blacks, Israelis, Gypsies, Chinese and Japanese. Sib-pair studies have suggested only a minor influence of HLA genes in MS, but such analysis is not ideal since 1) the Dw2-haplotype is the only haplotype with a confirmed role in MS, and 2) Dw2 is known to act dominantly in MS.

Methods. Nine Swedish multiplex MS families with 20 patients with clinically definite MS, were typed genomically for HLA-DR and -DQ by *Taq*I RFLP or PCR-SSP (sequence specific primers).

Results. In the 8 families where Dw2 occurred in MS patients, Dw2 was shared by *all* patients. In 48 published such families, only 3 of 107 individuals with MS were Dw2-negative, and in 2 of these 3 persons, only one DR-DQ haplotype was identified. MS segregated with the Dw2 haplotype (43 families) or to persons who had inherited the Dw2 haplotype from the other side of the families (5 families).

Conclusion. The Dw2 haplotype, when present in MS families, confers a very strong influence on MS susceptibility.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-18-20 **MULTIPLE SCLEROSIS: MYELIN BASIC PROTEIN AND PROTEOLIPID PROTEIN INDUCE TGF-ß mRNA EXPRESSION IN MONONUCLEAR CELLS**

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Transforming growth factor (TGF-ß) is produced by activated T cells, B cells and macrophages. It inhibits both cellular and humoral immunity, and has been proposed for treatment of immune-mediated diseases. TGF-ß also delays the onset of experimental allergic encephalomyelitis (EAE). We studied the possible involvement of TGF-ß in multiple sclerosis (MS) by separating mononuclear cells from blood and cerebrospinal fluid (CSF) from MS and control patients, followed by culture in presence and absence of the autoantigens myelin basic protein (MBP) and proteolipid protein (PLP). Both have been proposed as target for abnormal autoimmunity in MS. Production of TGF-ß induced in presence and absence of these antigens, was evaluated by in situ hybridization which allowed the detection and enumeration of cells expressing mRNA encoding this cytokine. We found that the patients with MS had MBP and PLP reactive TGF-ß producing cells in blood, and an about 10-fold increment in CSF. Patients with other neurological diseases showed no responses to MBP or PLP, while patients with MS showed no response to the myasthenia gravis-related control antigen acetylcholine receptor. We conclude that MS is associated with organo-specific autoantigen-induced TGF-ß production.

6-18-21 EXPERIMENTAL OPTIC NERVE DEMYELINATION

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We have shown that the microinjection of antibody to the myelin lipid Galactocerebroside can produce consistent focal demyelination in the rat optic nerve. Using small volumes (2-4 microliters) of antiserum, along with 20% homologous pooled serum, lesions covering 30-75% of the cross-sectional area of the nerve and extending 1-3 mm. from the injection site were demonstrated by light and electron microscopy. Primary demyelination was the principal change found along with increased cellularity due to an abundance of macrophages and reactive astrocytes. Occasional axons undergoing Wallerian degeneration were also found but no more than in the control nerve. Histopathologic and clinical studies have shown that a more diffuse optic nerve pathology occurs in multiple sclerosis than can be explained by the classic "plaque" model and they indicate that extensive axonal loss often occurs in the optic nerves of these patients. We plan to utilize this model to elucidate biochemical changes within the retinal ganglion cells to better understand this process.

6-18-22 INTERACTION OF MYELIN BASIC PROTEIN WITH MONONUCLEAR PHAGOCYTES: A POSSIBLE MECHANISM OF INFLAMMATORY DEMYELINATION.

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Myelin basic protein (MBP) is the major antigenic constituent of mammalian myelinated nerve fibers. In susceptible strains of animals, MBP is the crucial antigen responsible of experimental allergic encephalomyelitis (EAE), an autoimmune demyelinating disease which resembles multiple sclerosis (MS). Macrophages are the predominant inflammatory cell type in the CNS during EAE and MS. They phagocytize the myelin sheath and inflict myelin damage by releasing inflammatory mediators such as cytokines and reactive oxygen intermediates (ROI). The mechanisms by which macrophages release these soluble products in the CNS microenvironment are unknown. In this study we examined the effect of MBP on production of proinflammatory cytokines and on respiratory burst capability by human phagocytic cells. Cultured monocytes and monocyte-derived macrophages (MDM) were treated with purified bovine MBP protein. Northern blot analysis and specific ELISA demonstrated that MBP induced mRNA accumulation and secretion of Tumor Necrosis Factor (TNF), Interleukin-1ß (IL-1ß), Interleukin-6 (IL-6) and Interleukin-8 (IL-8). MBP did not stimulate ROI release from phagocytes but activated monocyte respiratory burst capability. Our findings demonstrate that a specific component of the myelin sheath is able to modulate macrophage gene expression and identify a possible mechanism involved in the course of inflammatory demyelination.

6-18-23 4-AMINOPYRIDINE IS SUPERIOR TO 3,4 DIAMINOPYRIDINE IN THE TREATMENT OF MULTIPLE SCLEROSIS.

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In a recent study we demonstrated that the potassium channel blocker 4-aminopyridine (4-AP) is superior to placebo in the treatment of multiple sclerosis (MS). To compare efficacy of 4-AP and the chemically related agent 3,4 diaminopyridine (DAP), 10 MS patients who in the previous trial had responded to 4-AP participated in a double blind, double cross over study. Their ages ranged from 26 to 52 years (mean 45.0 years). The mean Kurtzke Expanded Disability Status Scale was 5.9 (range 4.0-7.5). All patients were treated for 6 weeks. They always received 4-AP in the first and sixth week and were randomised to receive DAP during weeks 2 and 3, or weeks 3 and 4, or weeks 4 and 5. Neurological functions, symptoms and side effects were scored on a visual analogue scale using a diary which was filled in every day. The changes in weekly scores on both cross over points were compared to the occuring fluctuations in weekly scores during continued use of 4-AP. The mean daily doses of 4-AP and DAP were 23 mg (range 10-35 mg) and 46 mg (range 20-70 mg) respectively. Three patients discontinued the study because they felt that their overall neurological condition deteriorated. At that moment they all used DAP. Seven patients completed the study. During the cross over from 4-AP to DAP there were 9 changes in favour of 4-AP and 2 in favour of DAP. During the cross over from DAP to 4-AP there were 11 changes in favour of 4-AP and 1 in favour of DAP. These results indicate that 4-AP is more useful than DAP in the treatment of MS.

6-18-24 HLA-DQA1 AND -DQB1 ALLELES IN SARDINIAN PATIENTS FROM MULTIPLEX MULTIPLE SCLEROSIS FAMILIES

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Previous our studies showed differences in the distribution of HLA class II alleles between sporadic and familiar Sardinian multiple sclerosis (MS) patients (Marrosu et al. Neurology, 1988, 38, 1749-1753 and Neurology 1992, 42, 883-886). We studied the representation of HLA-DQB1 and -DQA1 alleles in 32 related Sardinian MS patients (RMS) and 86 healthy Sardinian controls. Allele identification was performed by dot-blot analysis with specific oligonucleotide probes after PCR amplification. In RMS, compared with controls, an increased frequency of the DQA1 * 0301 allele ($p < .003$) was found. This allele showed an increased frequency also in 46 healthy parents ($p < .005$) and 54 siblings ($p < .05$) of the RMS patients. On the other hand, no significant differences in DQB1 alleles were found. However, the analysis of the distribution of DQB1 alleles encoding for the aminoacid leucine in position 26 (Leu^{26}) showed that 48.5% of RMS, compared with 33.5% of 88 controls ($p = .04$), were found to be positive for DQB Leu^{26} residue. This is in accordance with an increased frequency of this residue in sporadic MS patients.

6-18-25 MULTIPLE SCLEROSIS IN THE FAROES: TRANSMISSION ACROSS FOUR EPIDEMICS.

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As of 1992 we have ascertained 45 native resident Faroese plus 12 non-resident "migrant" Faroese with clinical onset of MS in this century. The resident series comprised four successive epidemics beginning in 1943 and then at 13-yearly intervals thereafter, a separation of very high statistical significance (p 0.00001). We concluded that the first epidemic was the result of the introduction into the Faroes by British troops, during their occupation of World War II of a specific but unknown infection which we call the "primary MS affection" (PMSA). Clinical neurologic MS (CNMS) is then the rare late sequel of infection with PMSA. The first epidemic defined age of susceptibility to PMSA as age 11 to 45 at onset of exposure. Models of transmission used for the first three epidemics included the need for two years of exposure before PMSA acquisition and limitation of transmissibility of PMSA to age 13 to 26. With these conditions successive cohorts of susceptible Faroese were defined to account for the second and third epidemics, and they also predicted the occurrence of the fourth epidemic. Further consideration of the models suggests transmissibility is even more limited, perhaps to age 20 to 26 or so.

6-18-26 IMPAIRMENT IN MULTIPLE SCLEROSIS PATIENTS' BODY ESTEEM COMPARED WITH MATCHED CONTROLS

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A group of 35 remitting relapsing multiple sclerosis (MS) patients (23 females and 12 males) were evaluated for body esteem, compared with 35 age and sex matched healthy controls. We made use of the Body Esteem Scale (BES) for females (BES of sexual attractiveness, physical condition and weight) and for males (BES of physical attractiveness, physical condition and upper body strength). Psychiatric evaluation was carried out to exclude patients suffering from depression or hypomania. All examinations were performed during the remitting phase. Physical condition was significantly lowered, subjectively, in both sexes (P males=0.017; P females <0.001). Male's upper body esteem and female's weight concern were significantly impaired (P males=0.17; P females =0.028). Physical attractiveness in male and sexual attractiveness in female were not statistically different from the control group. This study emphasizes impairment of body esteem in MS patients even in the remitting phase. The absence of impairment of physical and sexual attractiveness may be due to the non-distinguishable outward appearance of the patients.

6-18-27 QUANTITATIVE BRAIN MRI LESION LOAD PREDICTS THE COURSE OF CLINICALLY ISOLATED SYNDROMES SUGGESTIVE OF MULTIPLE SCLEROSIS

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In order to dertermine their prognostic significance, semi-automated quantitative measurement of brain MRI abnormalities at presentation and at 5 year follow up were obtained in 84 patients presenting with an acute clinically isolated syndrome of the optic nerves, brainstem or spinal cord suggestive of multiple sclerosis (MS).

Patients who developed MS during follow up had a higher lesion load at presentation compared to those who did not ($p < 0.0001$). There was a strong correlation of the MRI lesion load at presentation with both the increase in lesion load and the development of clinical diability over the next 5 years ($p < 0.0001$). At follow up, disability and brain lesion load were strongly correlated in patients who had developed MS ($p = 0.0002$). These results establish that MRI at presentation with clinically isolated syndromes suggestive of MS is useful in predicting the subsequent clinical course, and the development of new MRI lesions. This suggests that quantitative brain MRI will be helpful in selecting patients with early clinical MS for treatment trials, and for subsequent monitoring of their response to treatment.

6-22-04 CRITICAL APPRAISAL OF CT - AND MRI - FINDINGS IN COLLOID CYSTS

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Colloid cysts are rare tumours of the third ventricle in the area of the foramina Monroi fixing on the velum interpositum or the plexus choroideus. The clinical manifestation is expressed by a consecutive hydrocephalus and raised intracranial pressure.

Colloid cysts are characterised on native CT and on T1- and T2-weighted MRI by primary hyperdense and respectively hyperintense representation. Some-times a hyperintense margin can be delimit from a central hypodense or hypo-intense content of the cyst. This imaging depends on the residue of leukocytes and cholesterol. Only few cases comparing CT and MRI findings have been published yet and therefore, we intended to analyse both methods.

Nine patients with CT and MRI were examined pre- and postoperatively. On MRI we consider the various sequences with special regard to differential diagnosis e.g. low grade glioma. In order to plan the access to the tumour we evaluated the multiplanar scanning direction. The size of colloid cyst varied from 8 x 8 to 26 x 48 mm in the latter case 17 ml of a glutinous fluid was intraoperatively aspirated.

In conclusion, because of some false negative CT findings, MRI is method of choice in the delineation of colloid cysts.

6-22-05 VARIETY OF LOW GRADE ASTROCYTOMAS IN CT AND MRI

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Low grade astrocytomas are characterised by a slow growth rate and mostly localised in the frontal and temporal lobe of the cerebral hemisphere. Despite their differentiation, low grade astrocytomas have the tendency to infiltrate the brain parenchyma. The usually solid tumours exhibit micro cystic and rarely macro cystic changes. We present five cases of low grade astrocytomas with an extraordinary appearance in CT and MRI. For example in one patient CT as well as MRI revealed only a diffuse hypodensity res. hypointensity in the frontal lobes. A clear delimitation between tumour and normal tissue was impossible. A later autopsy demonstrates an invasion of tumour cells in the whole brain with the exception of cerebellum and brain stem.

In another case CT and MRI exposed a great cystic formation similar to arachnoid cysts. Intraoperatively the tumour appeared as a solid mass.

The knowledge of their polymorphism facilitate an early diagnosis of low grade astrozytomas which results in a sufficient therapy.

6-22-07 EVALUATION OF VERTEBRAL ARTERY WITH ULTRASOUND

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The symptom of posterior circulation is not as clear as the anterior circulation, it is very amazing clinically. The best way to evaluate the condition of vertebral artery (VA) is magetic resonance imaging (MRI) and angiography, but the cost of MRI and the risk of angiography are very high. In this study, we tried to use the ultrasound to evaluate the VA, and compared it with angiography.

During the past year, we examined 100 patients (88 male and 12 female) who were admitted to our ward with ischemic stroke (n=70) or other neurological disorders (n=30) by both ultrasound (B-mode scanning) and angiography (Conventional angiography or Digital Subtraction Angiography (DSA).

According to the result of this study, the characteristic findings of stenosis or occlusion of VA as following: poor image, turbulent flow sound, lower systolic flow, lower diastolic flow, poor subclavian wave form, biphasic wave form, positive hyperemic test, reversed echoflow and no echoflow.

Owing to a lot of congenital variation and technical difficulty in examination of VA, the abnormal findings cannot be used as a definited proof of ischemic stroke of the posterior circulation, it may give us more information for the clinical interpretation of the VA.

6-22-08 ASSESSMENT OF BRAIN DEATH BY TRANSCRANIAL DOPPLER SONOGRAPHY

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Absence of cerebral blood flow is accepted as consistent with brain death. Transcranial Doppler (TCD) measures blood flow velocities in the basal cerebral arteries. We evaluated 40 clinically brain dead patients by TCD. Clinical diagnosis was intracranial hemorrhage (21); anoxic encephalopathy (12); massive cerebral infarct (3); trauma (3) and tumor (1). Thirty-six patients showed mean flow velocity of 10-15 cm/sec. or less with either reverberating, forward, backward flow or only systolic flow with no diastolic flow. None of these patients survived (specificity was 100%). In 2 patients (technical failure of 5%) insonation was unsuccessful. Two patients, showed false negative results (normal looking waveforms). Sensitivity was 94.7%.

In conclusion TCD is helpful in confirming clinical diagnosis of brain death and may save major expenses of management of hopeless cases and identify cases fulfilling criteria as donors in transplant surgery.

6-22-09 MULTIPLE SYSTEM ATROPHY: MAGNETIC RESONANCE IMAGING.

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By using magnetic resonance imaging (MRI), we studied 11 patients with multiple system atrophy (MSA) : 5 olivo-ponto-cerebellar atrophy (OPCA), 2 Shy-Drager syndrome (SDS), and 4 striatonigral degeneration (SND).The diagnoses of OPCA, SDS and SND were clinically made.

The MR images were performed on 1.5 tesla MRI unit (Siemens Asahi Medical, Magnetom H15), using a T2-weighted spin echo (SE) sequence (TR: 3000ms, TE: 80-90ms), a T1-weighted SE sequence (TR: 550, TE:15), and a proton density-weighted (PD) SE sequence (TR: 3000, TE: 12-22).

In the patients with OPCA, MRI revealed the cerebellar and brainstem atrophy and the degeneration of pontine transverse fibers more marked than in the patients with SDS and SND. T2-weighted images showed low intensity in the lateral putamina in one OPCA patient, two SDS, and all of SND patients. PD images demonstrated the abnormal slit-like high areas in the posterolateral putamina in three SND. The degree of cerebellar ataxia was relatively well correlated with the cerebellar and brainstem atrophy and the degeneration of pontine transverse fibers. In most of the patients with parkinsonism, MRI demonstrated abnormal signals in basal ganglia.

MRI is a useful adjunct in evaluating MSA. The abnormal slit-like high areas in the posterolateral putamina in MSA may suggest loss of neurons and/or gliosis of the putamina.

6-22-10 CHANGES OF MR IMAGING IN RADIATION MYELOPATHY

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Using MR imaging, we assessed the changes of the signal, size, and enhancing characteristics of the cervical cord in patients in whom radiation myelopathy developed after radiotherapy for nasopharyngeal carcinoma.

Seven patients, 2 men and 5 women, aged from 40-77 years, were included. First MR imaging was performed 1-4 months after onset of myelopathy. Follow-up MR scans were performed 2-22 months after onset of symptoms.

On the first imaging, all showed low signal intensity in a long segment of the cervical cord on T1-weighted images, high signal intensity on T2*-weighted images, and focal enhancement at C1-C2 area after intravenous Gd-DTPA injection. Five cases also showed swelling of the cord. When follow-up scans were performed less than 7 months after onset, there were no significant changes in signal intensity from the first. Focal enhancement at C1-C2 area remained the same in 3 cases; became larger and more dense in 1 case and less dense in 1 case. Subsidence of swelling was seen in 2 cases. Atrophy of the cervical cord at C1-C2 area without abnormal signal intensity and with faint enhancement at C1-C2 area was revealed when scan was performed as early as 10 months after onset.

6-22-11 HELICAL SCANNING CT FOR THE EVALUATION OF ARTERIOSCLEROTIC CAROTID LESIONS

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We examined 22 patients with arteriosclerotic carotid lesions using the helical scanning CT (HES-CT). A high speed slip-ring X-ray CT system was used. Following intravenous bolus injection of non-ionic contrast medium, continuous scanning of the neck for a 30 sec. period was performed, couch top rate of 2.0 mm/sec. From the continuous raw data, 59 axial images were reconstructed at a slice pitch of 1 mm and were used to obtain multiplanner reconstruction images (MPR image) and 3-dimensional surface images (3D image). MPR images were axial, coronal, sagittal of any ROI of the carotid arteries.

Excellent MPR and 3D images were obtained in most cases. In 8 cases, conventional angiograms were performed and a good correlation between HES-CT and angiogram was revealed on the detection of internal carotid stenoses and occlusions. In 3 cases, HES-CT images were superior to conventional angiogram for detection of the calcified plaques on the arterial walls. HES-CT detected the irregularities of the arterial walls which were indistinct by MR Angiograms in some cases.

These preliminary results suggest that HES-CT is useful as a non-invasive diagnostic method for the evaluation of the carotid artery.

6-22-12 MAGNETIC RESONANCE IMAGING OF THE LUMBO-SACRAL SPINE IN THE PATIENTS WITH CHRONIC BACK PAIN.

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Forty-five patients with chronic, recurring low back pain and sciatica out of 95 investigated by magnetic resonance imaging (MRI) were examined clinicaly and neurophysiologicaly by dermatomal somatosensory evoked potentials (DSEPs) to correlate the severity of symptoms with detected structural and functional lesions of the spine and nerve roots. MRI were performed on the RESONEX Rx HP, 0.5T in the sagittal plane in T1 (TR 600ms, TE 30ms) and T2 (TR 1800ms, TE 25ms, 80ms), also in the axial and coronal planes in T1. MRI estimated indepedently without any knowlege of DSEPs results disclosed: the normal spine in the 7% of patients, herniated disc in the 49% of cases at one level and in 44% at two or more levels. The spinal roots were compromised at one side in 70% of patients and bilateraly in 23%of cases. DSEPs derivated from stimulation of L3, L4, L5, S1 dermatomes were recorded from the scalp electrodes at Cz', refered to Fpz. DSEPs were false- negative in 20% of cases with herniated disc. An absent of DSEP, prolonged latency of first positive peak (P40) and/or pathological decreased amplitude of potentials of one spinal root and multiple roots were obtained in 16% and 64% of patients respectively. In the 71% of patients MRI and DSEPs results reveled the same levels and sides of spinal roots compression.

6-22-13 TRANSVERSE SINUS FLOW EVALUATION IN RIGHT-HANDED USING MAGNETIC RESONANCE ANGIOGRAOHY

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Magnetic resonance angiography (MRA) has been useful in investigating physiological aspects. Previous investigation to transverse sinus flow (TvSF) had been operated mainly invasive technique, using conventional angiograhy, and digital subtraction angiography. To determine the dominancy of TvSF noninvasively, we performed MRA for normal right-handed Japanese. 29 men (mean age 48.7 yr) and 31 women (mean age 47.8 yr) were interviewed and examiened. They had no neurological defecit nor abnormal intensity area in MR images without left-handed family history, were evaluated by MRA on a 1.5 tesla MR scan, using three dimensional fashion, time of flight technique with a standard head coil. The TvSF dominancy was evaluated from axial and coronal MRA images. The frequency of right side dominancy was 61%, left side dominancy was 15% in our TvSF observation. Under conventional technique for TvSF, right side dominancy had been reported 40-56% previously. These results suggested MRA is useful method for clinical evaluation to intracranial flow in vivo.

6-22-14 A CLINICO-MRI STUDY OF EXTRAPYRAMIDAL SYMPTOMS IN MULTIPLE SYSTEM ATROPHY (MSA)

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We did a clinico-MRI study concerning extrapyramidal symptoms and T2 weighted MRI findings of the putamen in 28 MSA patients and 25 Parkinson disease. In MSA, 15 cases showed extrapyramidal symptoms. And we could not observe cerebellar ataxia in two of these cases because of severe rigidity and akinesia. There was linear hyperintensity in the outer margin of the putamen of 17 patients, in which 14 showed extrapyramidal symptoms. The unilateral hyperinteisity was observed in 5 cases; 4 with contaralateral rigidity and one with bradykinesia. We could not find such abnormal intensity in any patients with Parkinson disease. On proton density MRI, the signal intensity in the lesion was higher than that in the gray matter, which leads the speculation that the hyperintensity reflects gliosis of the putamen or increased extracellular fluid space caused by severe shrinkage of the putamen. These MRI findings are useful to distinguish MSA with extrapyramidal symptoms from Parkinson disease.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-22-17 EFFECT OF CHELATING AGENTS ON ABNORMAL MRI FINDINGS IN WILSON'S DISEASE

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To clarify the pathologic lesions of tremor in Wilson's disease, serial MRI scans were performed in two patients with Wilson's disease who had tremor as a prominent clinical manifestation and were successfully treated with chelating agents.

Patient 1, a 22-year-old male, was admitted because of coarse resting tremor of the upper extremities and gait disturbance. T2-weighted MRI at admission (Feb., 1990) disclosed high intensity signals (HIS) in the lenticular nuclei, thalamus and midbrain. With D-penicillamine, the tremor completely disappeared and follow-up MRI (Aug., 1992) showed a marked decrease of HIS, especially in the thalamus. Patient 2, a 14-year-old girl, had noticed dysarthria and gait disturbance two years before. After admission on Mar. 1991, as tremor of her upper extremities worsened, she was treated with Trien which gradually ameliorated the tremor. MRI at admission showed HIS on T2-weighted MRI in the lenticular nuclei, lateral portion of thalamus and red nuclei. In follow-up MRI on Jan. 1992, a prominent decrease of HIS in the thalamus and red nuclei was observed.

Conclusion: Both of our patients showed marked improvement of tremor, accompanied with decrease of HIS on T2-weighted MRI in the thalamus and red nuclei. These observations suggest that the thalamus and/or red nuclei play an important role in the genesis of tremor in Wilson's disease.

6-22-18 CONTRAST ENHANCED DOPPLER EXAMINATION OF THE INTERNAL AND MIDDLE CEREBRAL ARTERIES

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A new ultrasound contrast agent Albunex (Nycomed, Oslo) was given i.v. to 10 healthy volunteers during continuous Doppler examination of the right internal carotid and middle cerebral arteries. Albunex consists of $4x10^6$ microbubbles per ml which have an average diameter of 3-5 microns. Each subject received two injections of contrast in doses of 0.08 and 0.22 ml/kg. The relative intensity of the Doppler signal was measured in decibels (dB).

Transpulmonary passage of contrast occurred and the intensity of the Doppler signal increased significantly ($p< 0.05$, Student's t-test) in both the internal carotid (dose 0.08 ml/kg: average intensity increase = 4.47 ± 2.47 (SD) dB, dose 0.22 ml/kg: increase = 4.76 ± 2.84 dB) and middle cerebral artery (dose 0.08 ml/kg: increase = 4.13 ± 3.04 dB, dose 0.22 ml/kg: increase 5.52 ± 3.09 dB).

These results strongly suggest that contrast enhancement will significantly improve the quality of both transcranial and extracranial Doppler examinations.

6-22-19 MRI AND CLINICAL FINDINGS IN SUPERFICIAL SIDEROSIS OF THE CNS.

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Superficial siderosis (SS) of the CNS is considered a rare disease characterized clinically by cerebellar ataxia, myelopathy, hearing loss, and dementia. MRI is the first diagnostic tool capable of detecting the pathognomonic hemosiderin deposits in the leptomeninges and subpial tissues. To accumulate further knowledge on this disorder, we reviewed our MRI database for patients with widespread hypointensity of the brain surfaces on T2-weighted scans.

Out of 8016 patients examined by brain MRI, 11 (4 males, 7 females) had SS. Their age ranged from 47 to 76 years (mean age 63 years). Hemosiderin deposits in the supratentorial meninges were present in all patients, but involvement of infratentorial structures predominated in 7. SS was most marked at the upper surface of the cerebellum in 6 individuals and extended to the spinal cord in 4. Only those two patients with the most extensive hemosiderin deposits presented with the above described clinical findings.

Our findings demonstrate the potential of MRI to display SS much more often than clinically suspected. However, SS does not appear to cause specific symptoms unless a certain amount of iron deposition has been accumulated.

6-22-20 MR AND CINE MR IMAGING OF NON-PROGRESSIVE JUVENILE MUSCULAR ATROPHY OF THE DISTAL UPPER LIMB (HIRAYAMA'S DISEASE)

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We report magnetic resonance (MR) and cine MR images of the cervical cord in 28 patients (27 males and 1 female) with non-progressive juvenile muscular atrophy of the distal upper limb (Hirayama's disease).

The most remarkable finding in both T1 and T2 weighted MR images was the appearance of a crescent-shaped high intensity mass behind compressed cord at the level of 6th cervical vertebra during neck flexion. This finding was present in 25 patients but absent in 3 patients who had past over 20 years from onset. A thickness of the crescent mass was inversely proportional to the length from onset and directly proportional to the severity of the disease. Pulsatile signal voids of round or linear shape were shown in the crescent mass with cine MR imaging.

Focal atrophy of the lower cervical cord even in neutral neck posture was present in 17 cases.

We suspect that the abnormal intensity behind the lower cervical cord represents congestion of the epidural venous plexus. Our results show that MR and cine MR imaging of the cervical cord is diagnostic and provide useful information to understand of the mechanism of this disease.

6-22-21 CEREBRAL ATROPHY IN COCAINE ABUSERS: A PROSPECTIVE PLANIMETRIC CRANIAL COMPUTORIZED TOMOGRAPHY (CT) STUDY

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We realized a prospective study in cocaine abusers through a planimetric and linear study of the CT between March and July 1992. We compared cranial CT of 8 cocaine abusers and 16 chronic headache patients. The criteria were: age 15 to 40 years, HIV (-), VDRL (-), no alcohol abuse (or any other drug) and no history of other neurologic disease. The mean age was 28.3 years between both groups. The mean time of cocaine abuse was 6.37 years. 87.5% of the patients used nasal route and 12.5% were intravenous drug users. Seizures found were in 5 patients, tics in 1, psychosis in 1 and autonomic disturbance in another. The planimetric measurement of cerebral atrophy were significantly different in cocaine abusers compared with headache patients, and a more severe frontal lobe involvement was suggested by linear measurement.

6-25-03 MR-Imaging of Radiation-Induced Brachial Plexopathy (RBP).

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Objective: The study aimed at determining the efficiency of MRI with regard to the diagnosis of RBP.

Patients and methods: Included were ten recurrence-free, mastectomized breast cancer patients of whom 6 had received a total radiation dose of 36.60 Grey (Gy) in 12 fractions and 4 a dose of 50.00 Gy in 25 fractions, who after a medium follow-up period of 66 months at neurological examination were characterized as having disabling RBP. Bilateral MRI of the brachial plexus was performed with coronal, axial and oblique sagittal T1 and T2 weighted Spin Echo sequences at 0.5 Tesla.

Results: At MRI studies six of the ten patients showed disintegration of the normal anatomy with shrinking of the branches of the brachial plexus and fibrous degeneration of adjacent structures located at its proximal/infraclavicular portion. There was a good correlation between severity of lesions at MRI and those of neurologic deficits.

Conclusion: MRI convincingly demonstrate disorganization of the structures in and around the brachial plexus in patients with RBP in comparison with the normal MRI-appearance of the brachial plexus.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-25-04 MYELOPATHY IN INTRAVASCULAR MALIGNANT LYMPHOMATOSIS

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Four autopsied cases of intravascular malignant lymphomatosis which developed myelopathy as the chief neurological symptoms, in which the pathological examination revealed spinal necrosis, were reported. In two cases, the onset was myelopathy with paraplegia and urinary disturbance and then the symptoms of encephalopathy developed. In one case, these symptoms occured at the same time and in one case, only the symptoms of myelopathy were observed.

Intravascular malignant tumor cells were immunohistochemically positive for B-cell marker in all cases. Autopsie exhibited most severe lesions in the lumbar and sacral cords and cauda equina, that both gray matter and white matter were damaged, and that fresh and old lesions were intermingled. Not only the circulatpry failure due to the tumor cells which filled the vascular lumen, but also thrombosis, thickning of the intima and angiitis were significant findings for the spinal cord necrosis and also the circulatory failure in the venous system was impotant as one of its etiological causes.

6-25-06 THE EFFECTS OF PHENYLACETATE AND RETINOIC ACID ON NEUROECTODERMAL TUMOR DERIVED CELL LINES.

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The aim of this study was to determine whether the differentiation agents phenylacetate (PA) and all-trans-retinoic acid (ATRA) affect the growth and differentiation of medulloblastoma and astrocytoma cell lines. Cell proliferation rate was determined using a thymidine uptake assay. PA and ATRA inhibited proliferation of the medulloblastoma cell lines Daoy and D283 MED in a dose dependent manner. PA and ATRA did not show additive growth inhibitory effects on Daoy cells. Human (U251 MG) as well as rat glioma (C6) cell lines also responded to PA. PA or ATRA did not change medulloblastoma cell morphology, whereas PA induced marked morphologic changes in the U251MG and C6 cells. PA-treated cells ellaborate more complex GFAP-positive processes. Preliminary studies of the molecular pathways suggest these effects are mediated by changes in TGFbeta and TGFbeta-receptor expression. Both PA and ATRA inhibit tumor cell proliferation at concentrations attainable in patients.

6-25-07 NEUROLOGICAL MANIFESTATIONS OF INTRAVASCULAR LYMPHOMATOSIS

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Intravascular lymphomatosis, also called neoplastic angioendotheliomatosis, is a rare, fatal neoplasm characterized by malignant cells of lymphocytic lineage in blood vessels. We studied 46 patients that fulfilled the criteria for intravascular lymphomatosis in order to define the neurological manifestations of this disorder. Three patients seen at our institution presented with progressive neurological deficits including dementia, paraparesis and hemiparesis. Review of additional 43 cases previously reported indicates that the most common manifestations were dementia, hemiparesis, and paraparesis. Brain imaging was abnormal in most of the cases. Cerebral spinal fluid exam detected pleocytosis and elevated protein in most of the cases; interestingly, no malignant cells could be detected in CSF, peripheral blood smears or bone marrow biopsy. In all of our three cases an occlusive angiopathy was found pathologically. In conclusion, further awareness of this rare neoplasm is needed in the differential diagnosis of progressive dementia. Our study also supports the lymphocytic B cell origin of the neoplasm.

6-25-08 SUPPRESSIVE EFFECTS OF INCREASED INTRACELLULAR CYCLIC AMP ON THE MITOGENIC RESPONSE OF GLIOMA CELLS TO GROWTH FACTORS

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The level of cAMP was known to be decreased in human malignant gliomas. On the other hand, various growth factors and their receptors were found to be overexpressed in these tumors. Thus, it is tempting to speculated that there might be some interplay between the two phenomena. In a basal medium consisting of 75% DMEM, 25% Ham's F-12 supplemented with 2% FBS, we showed that the mitogenic effects of PDGF, bFGF and EGF on human glioma cells were suppressed by dibutyryl-cAMP. Dibutyryl-cAMP alone neither potentiated nor inhibited the tumor cell growth. Since PDGF, bFGF and EGF receptors all possess tyrosine kinase activity, it is therefore tempting to speculate that cAMP may interfere the tyrosine kinase receptor pathway at a point common to these three receptors and the step of PLCγ tyrosine phosphorylation is the most possible locus.

6-25-09 PRIMARY NON-HODGKIN LYNPHOMA OF THE CENTRAL NERVOUS SYSTEM (PCNSL): TREATMENT RESULTS FOR 17 CASES

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17 patients (pts) with histologically proven PCNSL, 11 men and 6 women with a Karnofsky Performance Status (P.S.) > 60, were treated and followed longitudinally at Niguarda Hospital, in Milan, from January '79 through March '92. The histologic types were classified according to the Kiel classification and the Working Formulation; their ages ranged from 11 to 74 years (median 51.8). Pretreatment evaluation included HIV-1 antibody titers, total body CT, lumbar puncture, bone marrow aspirate, brain CT and contrast enhanced MRI, neurological examination. None had occult systemic lymphoma. All the pts had a surgical treatment: stereotactic biopsy in 5 pts, complete resection in 4 pts and partial resection in 8 pts. 15/17 pts received irradiation on the whole brain and a local boost on the lesion; the administered total dose was 45 - 55 Gy in 5 - 7 weeks. 3/17 pts are alive (17.6%) without evidence of systemic or local disease. The median survival of the whole group of pts was 13 months, of biopsied + RT pts 10 months, of total/partial resection + RT 13 months. Only biopsied pts had a 2 months median survival. Karnofsky P.S. > 70 was significant prognostic factor ($p < 0.001$); local recurrence at the site of the original disease remains the predominant cause of failure. Nobody had distant metastasis. Despite high dose irradiation, PCNSL still exhibits excessive mortality.

6-25-10 ZINC FINGER PROTEIN RECOGNIZED BY THE ANTIBODY FROM THE PATIENT WITH PARANEOPLASTIC CEREBELLAR DEGENERATION

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Autoantidodies against common molecules between cancers and Purkinje cells have been detected in some patients with paraneoplastic cerebellar degeneration(PCD). Here, we demonstrate a major 58kd protein antigen in an immunoblot of human cerebellum by serum from a patient with PCD. Immunohistochemically, the serum recognized neural cells especially Purkinje cells in a human brain. We isolated a cDNA clone from a human cerebellar cDNA library using the serum. Homology searches revealed a high similarity in nucleotide and amino acid sequences of this clone with the zinc finger sequence motifs. Recombinant protein was produced using expression vector (pET16b) constructed with the cDNA, and was recognized by the serum from the patient. PCD related protein reported here may be important to maintain neural cells especially those in the cerebellum.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-25-11 SENSORY NEURONOPATHY ASSOCIATED WITH SERUM ANTIBODIES TO PURKINJE CELLS AND DORSAL ROOT GANGLIA NEURONS.

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Anti-Purkinje cell antibodies (APCA), believed to be markers of paraneoplastic cerebellar degeneration, have been identified in the serum of 3 men with subacute sensory neuronopathies (SSN) and no evidence of tumors 5 years after the onset of the neurological signs. By indirect immunohistochemistry on sections of rat cerebellum and dorsal root ganglia (DRG) the patients' IgG bound to the cytoplasm of both Purkinje cells and DRG neurons.By Western blot analysis on whole human cerebellum and whole DRG homogenates, the IgG from 2 patients bound to a 62 kd protein in both homogenates while the IgG from 1 patient to a 110kd protein in the cerebellum homogenate only. Our study provides evidence that APCA may also be associated with SSN and are not necessarily markers of an underlying tumor. It also provides evidence that specific cerebellar antigens are also present in DRG neurons.

6-25-12 GRANULOCYTIC SARCOMA WITH MENINGEAL LEUKEMIA AND CHARACTERISTIC CEREBROSPINAL FLUID CYTOLOGY BUT NO BONE MARROW INVOLVEMENT

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Granulocytic sarcoma (GS) is a localized tumor of immature granulocytes that is usually associated with acute leukemia and myeloproliferative disorders. We report on a 52-year-old previously healthy male with mastoid GS and cerebrospinal fluid (CSF) involvement but no associated leukemia on presentation. Histological examination of the surgical specimen and the characteristic CSF-cytology revealed the diagnosis of a GS. The cytochemical staining of the immature cells by naphthol-ASD chloroacetate esterase (NASD) and myeloperoxidase was strongly positive, reflecting the myeloid nature. Immunophenotyping did not eloborate CALLA, Tdt, T or B cell antigens. The patient underwent intrathecal chemotherapy and radiation of the head and neuroaxis, and the CSF cytology returned to normal. The peripheral blood and bone marrow findings were normal in follow-up examinations.
This case emphasizes the value of CSF cytologic examination of tumor cells and the use of immunocytochemical marker for differentiating GS from malignant lymphoma.

6-25-13 SUPERIOR OPHTHLMIC VEIN THROMBOSIS WITH TAMOXIFEN

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Tamoxifen therapy is associated with ocular toxicity, which includes corneal opacification, retinopathy, optic neuritis and optic disc swelling with haemorrhages. Most of the ocular manifestations are bilateral. Tamoxifen is known to cause increased risk of thromboembolism in cancer patients. We report two women with breast carcinoma on long term Tamoxifen therapy who developed rapidly progressive mildly painful unilateral proptosis. No retinal involvement was evident in either of the cases. Plain and contrast enhanced CT scans of the orbits confirmed the presence of unilateral proptosis and showed enlarged, thrombosed superior opthalmic veins. An initial suspicion of metastatic deposits was belied by the rapid amelioration of ocular symptomatology and the return of CT scan findings to normal within three weeks of cessation of Tamoxifen therapy. The present report supports the tenet of increased incidence of thromboembolic phenomena associated with Tamoxifen and suggests that some of the ocular complications seen with this drug could have similar pathogenesis.

6-25-14 ENERGY METABOLISM OF BRAIN TUMORS: BIOCHEMICAL FINDINGS

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In spite of different therapeutical efforts the prognosis for malignant brain tumors is poor. It is striking that the ranges of survival vary despite an identical histolpathological grading and therapy. It is well-known that changes in energy metabolism may affect the sensitivity towards radio- and chemotherapy. Up to now we have investigated the energy metabolism of brain tumors (9 glioblastomas, 7 meningeomas, 5 metastases and 5 others) using conventional biochemical methods and HPLC (high-performance liquid chromatography). Glucose, lactate and adenine nucleotide levels were determined as well as important glycolytic enzymes (hexokinase, glucokinase, glucose-6-phosphatase, lactate-dehydrogenase). Large differences in the metabolic parameters were observed inter- and intraindividually and between tumor entities. The enzymatic activities for phosphorylation of glucose by hexokinase and glucokinase respectively were higher in all tumors than the dephosphorylation by glucose-6-phosphatase. In very large meningeomas with numerous mitoses and some metastases, however, we found an increased glucose-6-phosphatase activity. There was also an increase in the activity of the lactate-dehydrogenase in malignant gliomas. The large differences in energy metabolism of brain tumors may be one of the reasons for the very variable prognoses and therapeutic responses.

6-25-15 SPECT AND THALLIUM-201 IN DIFFERENTIATION OF RECURRENT GLIOMA AND RADIATION NECROSIS.

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Aim of the study was to evaluate the role of SPECT with ^{201}Tl in differentiating recurrent tumor from radiation necrosis in symptomatic patients who have previously undergone neurosurgery and radiotherapy.

Methods and patients: We studied 12 patients (7M, 5F,mean age 48.2 ± 11.6 ys) previously undergone neurosurgery and radiation therapy for cerebral tumor treatment. SPECT studies were performed with TOMOMATIC 564 (Medimatic, Denmark) with a high sensibility collimator, 25 ± 23 months after surgery. The rate of ^{201}Tl uptake was calculated as the ratios between the average counts of a region of interest (ROI) drawn on the lesion and both the average counts of a symmetrical ROI on the contralateral background (Lesion/Background) and a ROI positioned on the contralateral bone (Lesion/Bone).

Results: In the 8 patients, in whom visual evaluation of SPECT images showed an high ^{201}Tl uptake, the Lesion/Background and Lesion/Bone ratios were 2.7 ± .8 and 1.6 ± .6, respectively. In 5 of these patients the histologic diagnosis was of glioblastoma. One patient died without autopsy, the last 2 cases are waiting for histological diagnosis. In the 4 patients with a low ^{201}Tl uptake the Lesion/Background ratio was 1.6 ± .3 and the Lesion/Bone ratio was 0.8 ± .3. The histological diagnosis was available in one patients and it defined the lesion as radionecrosis. In the 3 remaining patients clinical status was unmodified after 12, 10 and 3 months.

Conclusion: Our preliminar data suggest that a high ^{201}Tl uptake is indicative of the presence of a recurrent glioma. Otherwise, our data are not conclusive in defining a low rate uptake as due to radiation necrosis, but the histological findings of radiation necrosis in 1 patients and the unchanged clinical status in the other 3 patients are suggestive for this hypothesis.

6-25-16 SURVIVAL RATE IN GLIOBLASTOMAS IS DEPENDANT ON THE EXTENT OF NEUROSURGICAL RESECTION AND RADIOTHERAPY

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The therapy of Glioblastomas – although different neurosurgical and radiotherapeutical concepts exixt – is still unsatisfying. The success of medical treatment depends on the time of diagnosis, tumour localization, extent of resection and the postoperative radiotherapy.

This study intends to demonstrate the effects of a new accelerated regime (two times daily / 3 times a week) in comparison to conventional radiotherapy. Special interest is focused on the extent of operation and early signs of recurrence visualized by MRI.

142 patients with an average age of 56.5 years underwent surgical intervention. MRI or CT controls with contrast media were performed within 48 hours after neurosurgery and led to the classification of the operative therapy in biopsy, extended biopsy, subtotal – and radical (> 95%) resection. Postoperatively, 36 patients were treated by the new regime whilst the majority was radiated conventionally.

To summarize, the new accelerated radiation regime facilitated short term stay in hospital without further complications. The efficacy of both radiotherapeutical concepts are nearly equal. To our preliminary data the extent of surgical therapy is a more important factor concerning the survival rate than different regimes of radiotherapy.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-25-17 **PROGNOSTIC FACTORS IN SPORADIC PRIMARY CEREBRAL MALIGNANT LYMPHOMAS.**

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Retrospectively, a series of 54 patients with sporadic primary cerebral malignant Non-Hodgkin's lymphoma (PCML) has been evaluated. In all cases a low-risk neuroimaging-stereotactic serial biopsy with histological and immunomorphological techniques was performed. The PCML were uniformly classified with the support of immunocytochemical data. In the series presented these tumours have been predominantly classified as high-grade blastic B-cell lymphomas. The evaluation of prognostic factors suggest that age at admission and morphological features of regression are relevant determinants of survival time. A correlation between gluco-corticoid administration and morphological signs of regression has been found. Thus, prior to CT-stereotactic brain biopsy, corticosteroids should not be administered in order to avoid or reduce tumor regression as well as to facilitate and to ameliorate lymphoma diagnosis and classification, unless herniation is imminent. The results of treatment in this series suggest that aggressive therapy improves life expectancy in younger patients (under 60 years), but not in older individuals. The same is true if morphological features exhibited only slight signs of regression.

6-25-19 CASE REPORT OF A SPINAL ASTROCYTOMA WITH ASCENDING CENTRAL NERVOUS SPREADING

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In 1979 the 42-year-old patient became aware of symptoms of a lumbar disc prolapse. In 1986 a pilocytic astrocytoma (grade 1) of the spinal cauda was removed. In 1989 a tumour recidive was partially removed from the same site. Histology showed a grade 2 astrocytoma. Two months later the patient developed symptoms of increased intracerebral pressure. Before this time he did not have any supraspinal symptoms. CSF cytology showed polymorphic giant tumour cells with hyperchromatic nuclei and a glioblastoma of the cerebral ventricles was diagnosed. The patient died from cardiovascular complications. The post-mortem investigation revealed an astrocytoma of the conus medullaris with an anaplastic ventral area (grade 4). This area had not been seen in the biopsy. It is believed that anaplastic parts of the tumour metastasised along the spinal cord and brain stem and finally invaded the brain and cerebral ventricles.

6-25-20 ISOLATION AND CHARACTERIZATION OF ACNU-RESISTANT SUBLINES OF C6 AND 9L RAT BRAIN TUMORS IN VIVO

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Two variant brain tumor cell lines (C6/ACNU and 9L/ACNU) resistant to a nitrosourea derivative, ACNU [1-(4-amino-2-methyl-5-pyrimidinyl) methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride], were selected *in vivo* from rat C6 and 9L brain tumors. Resistance to ACNU proved to be stable characteristics of the C6/ACNU and 9L/ACNU lines, whether the lines were grown *in vivo* or *in vitro*. These cell lines exhibited a different pattern of cross resistance to a wide range of chemotherapeutic agents with dissimilar chemical structures and mechanisms of action as compared with that of other ACNU-resistant cells established *in vitro*. Distinct cross resistance was observed in both C6/ACNU and 9L/ACNU cell lines to chloroethyl-nitrosoureas such as BCNU [1, 3-bis(2-chloroethyl)-1-nitrosourea], CCNU [1-(2-chloreoethyl)-3-cyclohexyl-1-nitrosourea] and methyl CCNU, and, additionally, to VCR (vincristine), VBL (vinblastine), ADM (Adriamycin) and Ara-C (beta-D-arabinofuranosylcytosine) but not to BLM (bleomycin), MTX (methotrexate), DDP (cis-platinum) and 5-FU (5-fluorouraci).

6-25-21 PURIFICATION OF A GLIA-GROWTH SUBSTANCE FROM A RAT GLIOMA

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Purification of a glioma-growth substance from a rat C6 glioma is reported. The final preparation of the glia-growth factor appeared homogeneous in Sephacryl S-200 gel chromatography and sodium dodecyl sulfate (SDS) polyacrylamide gel electrophoresis. The factor is a glycoprotein with a molecular weight of 22,000. The yeild of the factor was 1 mg from 10 g of glioma.

6-25-22 INTRATHECAL CHEMOTHERAPY WITH ACNU FOR MENINGEAL GLIOMATOSIS

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To test the feasibility of intrathecal ACNU in the treatment of meningeal gliomatosis, a rat model with meningeal gliomatosis (MG) was intrathecally treated with various doses (0.5 - 1.5 mg/kg) of ACNU and at various times (1 - 5 days after the tumor inoculation) according to its pathophysiological stages. The median survival time of the animals was significantly prolonged when ACNU (0.5 - 1.5 mg/kg) was intrathecally administered in the early stages of MG, i.e., within 3 days after the tumor inoculation, as compared to that of the control animals. However, intrathecal ACNU therapy failed to exhibit remarkable efficacy with comparatively high doses (1 or 1.5 mg/kg) in the late stage of MG, i.e., 5 days after the tumor inoculation. This points to the feasibility of intrathecal ACNU in the treatment of menigeal gliomatosis in its early stages, but not in its late stages in which the parenchyma has already been invaded by the tumor.

6-25-23 INTRATHECAL CHEMOTHERAPY WITH ACNU IN A NUDE MOUSE MODEL

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Intrathecal chemotherapy with ACNU [1-(4-amino-2-methyl-5-pyrimidinyl)-methyl-3-(2-chloroethyl)-3-nitrosourea hydrochloride] demonstrated a remarkable chemotherapeutic effect in a nude mouse model of meningeal gliomatosis. The therapeutic effect of intrathecal ACNU was evaluated in a nude mouse with meningeal gliomatosis induced by an intracisternal inoculation of human glioma cell lines. The median survival time of the rat treated with 1 mg/kg of intrathecal ACNU once on day 1 or day 3 after the tumor inoculation was singificantly prolonged by 45.0 to 52.9%, and 29.1 to 31.0%, respectively, as compared with that of the control animal. When the meningeal gliomatosis were treated intrathecally with 1 mg/kg of ACNU 5 days after the tumor inoculation or intravenously with 15 mg/kg of ACNU, both of these treatments failed to prolong the survival time of the animals. These findings suggest that intrathecal chemotherapy with a low dose of ACNU is effective in the early stages of meningeal gliomatosis, whereas intravenous chemotherapy with a high dose of ACNU is always ineffective.

6-25-26 THE ROLE OF CHEMOTHERAPY AS A FIRST TREATMENT IN IMMUNOCOMPETENT NHL-CNS PATIENTS

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Radiation therapy (TCT) has mainly been applied to treat cerebral lymphoma, but low cure rate and lack of enduring response has stimulated search for alternatives. In the aim of postponing TCT as long as possible, we tested the efficacy of a M-BACOD schedule administered immediately after diagnosis. 14 patients were recruited. The tumors found were of high or intermediate grade malignancy, according to the Working Formulation. After 2 M-BACOD courses objective response (CT) was: 71% of pts were apparently tumor free. In the 60% of responsive Pts, TCT was delayed 5 months (without recurrences after a follow-up ranging from 9 to 18 months). Moreover in 3 responsive pts, no recurrence took place (even without TCT) after a follow-up of 6 to 12 mts. We cannot draw definite conclusions about the validity of this therapeutic protocol. Nevertheless, our results seem very promising. Postponing radiotherapy until disease recurrence is an option worthy of continuing investigation

6-25-27 DIFFERENT SCHEDULES OF CARBOPLATIN, CARMUSTINE AND ETOPOSIDE IN GLIOBLASTOMA (GBM) PATIENTS .

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The aim of our study was to ascertain the tollerability and effectiveness of therapeutic protocols employing CDDP, CBDCA, VP16 and BCNU. 93 GBM Pts were admitted and divided into 4 different homogeneous groups. Group:(A) 14 Pts:BCNU 80 mg/m² x 3 d; (B) 27 Pts: CDDP 45 mg/m² + VP16 120 mg/m² x 3 d. (C)14 Pts: CBDCA 200 mg /m² + BCNU 60 mg/m² x 2 d.(D) 38 Pts:CBDCA 200 mg /m² + BCNU 60 mg/m² + VP16 150 mg/m² x 2 d. All Patients received TCT sandwiched between the second and third courses od chemotherapy. As tumor relapse, Pts belonging to group (A) had been treated symptomatically, but all other group of Pts received a second chemotherapeutic protocol PVC. Median TTP did not differ between the different protocols, being 9-11 months. At 18 and 24 months more than 50% and 33% respectively of the Carboplatin-treated Pts were alive. The Pts treated with platinum-based protocols had a significantly longer ST than those treated only with BCNU.

6-25-28 CONCURRENT CIS-PLATIN AND ^{125}I BRACHYTHERAPY FOR RECURRENT MALIGNANT BRAIN TUMORS

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14 patients (13-67 years of age) participated, diagnoses included: glioblastoma multiforme (8), anaplastic astrocytoma (3), ependymoma (1), oligodendroglioma (1) & metastatic adenocarcinoma (1). 13 patients completed treatment & are evaluable. Target volumes ranged from 5-73 cc (median: 29 cc). I^{125} sources gave minimum target doses of 45.2-51.0 Gy over 100-125 hours. Cisplatin, 20 mg/M²/day for 5 days, was given concurrently. Acute complications included headache (8), nausea/vomiting (3), transient worsening of neurologic deficits (5), & seizures (3). Steroid dependency (7), radionecrosis (8), and intellectual decline not attributable to tumor (1) were late complications. 6 patients died with recurrent tumor, 3 are alive with progressive disease and 4 are alive with stable disease. Local failure occurred in 7 & distant failure in 2 cases. Median survival was 15 months. Significant myelosuppression and post-operative infections were not observed. We conclude cisplatin can be given safely during brachytherapy for recurrent malignant brain tumors.

6-25-29 DTC 101 PHARMACOKINETICS WHEN ADMINISTERED EITHER INTRATHECALLY OR INTRAVENTRICULARLY

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DTC 101, a slow releasing formulation of ara-C, was given either intraventricularly or intrathecally in patients with leptomeningeal metastases. 4 patients received drug by intra-lumbar (7 courses) and 2 by intraventricular administration (5 courses). Simultaneous timed lumbar and ventricular CSF samples were obtained in both groups. Following intraventricular administration, the ventricular concentrations of ara-C decreased biexponentially with an initial half-life of 9.4 ± 1.6 hrs. and a terminal half-life of 141 ± 2.3 hrs. Lumbar concentrations of ara-C appear at 1.25 hrs. following intraventricular administration, with a 0.53 hrs. doubling time. Subsequently, lumbar and ventricular levels of ara-C decreased parallel to each other. Following intralumbar administration, the lumbar/ventricular concentrations of ara-C decreased mono-exponentially with a half-life of 38.0 & 22.4 hrs. respectively. In conclusion, intra-ventricular administration of DTC 101 resulted in sustained cytotoxic ara-C levels in the lumbar (14 days) and ventricular (9 days) CSF compartments whereas following intralumbar administration, ventricular (4 days) cytotoxic ara-C concentrations are abbreviated.

6-25-30 STEREOTACTIC RADIOSURGERY FOR RECURRENT GLIOMAS

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16 patients (7 - 60 years of age) underwent 19 radiosurgical procedures for treatment of recurrent malignant gliomas. Diagnoses included glioblastoma multiforme (4), anaplastic astrocytoma (9), astrocytoma (1); PNET (1); and juvenile pilocytic astrocytoma (1). All patients had failed conventional radiotherapy and at least 2 chemotherapy regimens. The median Karnofsky score was 80. Target volumes ranged from 3.2 - 53.5 cc (median, 21.4 cc). Minimum target doses of 294 - 2043 cGy (median, 1078 cGy) were delivered using 1 - 5 isocenters and 4 - 15 non-coplanar arcs. 7 patients experienced early complications attributable to increased intracranial pressure. Symptoms resolved after treatment with steroids in all but 1 patient. 3 patients required re-operation for radionecrosis/recurrent tumor. 8 patients died of recurrent disease with a median survival of 17 weeks. 7 patients, 4 with residual disease, are alive with a median follow-up of 15 weeks. In conclusion, radiosurgery demonstrated modest efficacy in patients heavily pre-treated with recurrent malignant gliomas.

6-30-01 CHANGES OF CREATINPHOSPHOKINASE AND ISOENZYME BB IN CEREBROSPINAL FLUID IN BRAIN INJURY

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CPK and its isoenzyme BB was investigated in 186 patients with brain injury (12-24 hour after injury). Depending on the heavinoss of the injury, the patients were divided in two groups: group A - with a minimal injury (brain concussion) and group B - with a severe injury (brain contusion).

24% of patients in group A and 33% in group B were with increased values of CPK. 87% of group A and 98% of group B were with increased values of isoenzyme BB. In 76% from group A were increased levels of isoenzyme BB with normal value of CPK and in group B - 67% which shows that the changes of CPK are predominantly on account of the isoenzyme spectrum and this specifies the greater diagnostic value of the isoenzyme analysis for the diagnosis and prognosis.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

6-30-02 HEADACHE IN MINIMAL BRAIN INJURY

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172 patients with a headache after a minimal brain injury (brain concussion) who had no complaind before the injury were investigated. The character and intensity of the headache were examined in the period 12th hour - 10th day after the injury.

Depending on the treatment the patients were divided in 2 groups. In group A the treatment was pathogenetic and symptomatic and in group B - only symptomatic. In the first group the headache faded away in 90% on the 3-4th day and in 16% on the 10th day and in the second group - in 54% on the 6-7th day and in 32% on the 10th day. These results define the greater effectivenesse of the treatment of the headache with an adequate scheme which includes besides a symptomatic treatment also an active influence on the changes in brain metabolism.

6-30-03 SEGMENTAL MYOCLONUS AND OLIVARY HYPERTROPHY IN PATIENTS AFTER SEVERE HEAD INJURY

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During the past four years, 150 patients with severe head injury have been examined on a 1.5 Tesla MR unit. In 14 of these patients, uni- or bilateral enlargement and increased signal of the inferior olives, suggesting olivary pseudohypertrophy, was detected as a sequelae to lesions within the dentato-rubro-olivary pathway. Clinically, four patients showed palatal myoclonus, ocular myorhythmia, and "wing beating" of the upper extremities; two patients had palatal myoclonus and occular myorhythmia, two had palatal myoclonus, and two had "wing beating" of the upper extremities, while in four patients no evidence of segmental myoclonias was present. The time interval between the occurrence of trauma, the onset of segmental myoclonia and the detection of olivary hypertrophy varied between four weeks and seven years. Our findings suggest that olivary hypertrophy can be detected by MR-imaging in some patients following severe brainstem and/or cerebellar injury. The exact localization of the lesions by MR offers new insights into the patho-anatomical basis of segmental myoclonias.

6-30-04 PROGNOSTIC VALUE OF QUANTITATIVE CT IN CEREBRAL TRAUMA

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We studied 110 patients with cranial trauma to evaluate the prognostic value of different quantitative parameters of the CT in a non selected sample of patients. The prognostic value of the Glasgow scale was also evaluated. The following CT parameters were measured: volume of the edema in ml, degree of the edema, ventricular collapse, volume of the hematoma in ml, collapse of the mesencephalic cisterns, blood in the ventricular system and in the subarachnoidal space. All these parameters were correlated with the mortality rate of the patients. All parameters had a highly significant correlation with mortality: volumen of the edema (R=0.73), collapse of the mesencephalic cisterns (R=0.71), ventricular collapse (R=0.54), blood in ventricles (R=0.48). The correlation between the Glasgow scale and mortality rate was 0.39. Significant negative correlation between Glasgow scale and CT parameters were also observed. We conclude that the quantitative evaluation of CT has a very high prognostic value in patients with cerebral trauma.

6-30-05 A NEW MECHANISM OF POST-CONCUSSIONAL SYNDROME — THE VERTEBRO-BASILAR ISCHEMIA.

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Cervical spine is usually in juried in head trauma. Thus 30 PCS pts with cervical spine instability were examined to find evidences of VBI.

RESULTS: VBI symptoms, mild brain-stem signs and abnormal neuro-electrophysiologic findings (BAEP, VEP and/or ENG in head-turning positions) were found in 28pts(93.9%). Doppler ultrasonography of external VA showed narrowed lumen in 12, with blood flow drop in 7. DSA of 17 pts showed various changes in 10 and focal spasm only at the site of dislocation in the extention-flexion position in 7 pts. After cervical traction and vasodilation therapy, 26 pts recovered or improved, basically parallel with the subsidence of clinical VBI features. The electophysiologic data normalized or the number of abnormal items decreased in 25 pts. The mean values of various data of the whole group shortened significantly ($p<0.01$) too. In the 4 pts of in-effectve group, however, clinical VBI features and abnormal electrophysiologic findings were unchanged and BAEP even deteriolated in 1 pt.

CONCLUSION: The mechanism of PCS is still of disputation. This study offers a possible but easily overlooked cause--VBI due to cervical spine injury.

6-30-06 PROSPECTIVE FOLLOW-UP OF OUTCOME IN ACUTE WHIPLASH INJURY

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100 patients with cervicocephalic syndrome and neuropsychological and/or vegetative disturbances following whiplash injury without neurological deficits were followed up over 6 months (< 14 days, 6, 12 and 24 weeks after accident). Clinical, test- and neuropsychological, algesimetric and electrophysiological examinations (spectral analysis of heart rate, HRV; EMG analysis of the antinociceptive inhibitory temporalis muscle reflex, ITR) were performed.

The mean posttraumatic headache duration was 15.7 days +/- 17 SD (max. = 71 days); neck pain duration was 20.6 days +/- 16.1 SD (max. = 67 days). Age, depressive mood, somatic factors, initial pain intensity and decrease of passive mobility of the neck correlated with pain duration. Sex, expected financial compensation, radiological findings in cervical x-rays (e.g. loss of lordosis) and clinical assessment of cervical muscle pain had no influence on posttraumatic pain duration. The HRV (0.05-0.15Hz) was diminished over 24 weeks. The ITR was altered with a shortened late exteroceptive suppression (ES2 = 34.4 ms), which recovered to 50.1 ms during the follow-up. Concentration, visual/verbal memory and cognitive functions were initially impaired and improved in 12 weeks.

Our results demonstrate that in whiplash injury a transient brainstem dysfunction, neuropsychological deficits and (cardio-)autonomic disturbances can be quantified by psychological tests and apparative diagnostics. They do not support the concept of a *pseudo*-neurasthenic syndrome and do not confirm the observation of long lasting time courses of recovery as reported in retrospective studies.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-03-01 BLOOD COAGULATION/FIBRINOLYTIC RISK FACTORS FOR ASYMPTOMATIC BRAIN INFARCTION

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The brains of 83 healthy adults were studied by 0.5-T Hitachi magnetic reasonance imaging. The blood coagulation/fibrinolytic factors including Factor VII, soluble thrombomodulin, fibrinogen, platelets, hematocrit, anticardiolipin antibodies, plasminogen activator inhibitor type-I, lipoprotein(a), tissue plasminogen activator, thrombin antithrombin complex and antithrombin III were studied. Eighty percent of subjects over the age of 40 showed the presence of spotty high intensity areas on T2 weighted images. The blood coagulation/fibrinolytic factors in those with the T2 high intensity spots represented the tendency of hypercoagulate with hypofibrinolytic state. Antiphospholipid antibodies were positive or lipoprotein(a) was also high in some of the subjects with T2 high intensity spots. Based on these data we concluded that the hypercoagulate with hypofibrinolytic state, observed in our subject, may have some roles for the development of high intensity spots in T2 weighted images which are regarded in part as a sign of small infarction or etát criblé.

7-03-02 PROTECTIVE EFFECT OF A LONG-LIVED SUPEROXIDE DISMUTASE DERIVATIVE DURING CEREBRAL ISCHEMIA IN RATS

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To elucidate the critical role of oxygen radicals in circulation during brain ischemia, we performed bilateral carotid artery ligation (BCAL) on rats and evaluated several effects of a long acting superoxide dismutase (SOD) derivative (SMA-SOD). T2 weighted magnetic resonance imaging (MRI) of the ischemic brain showed high signal lesions in the frontal lobe, and pre-administration of SMA-SOD prevented these changes. On microscopic examination, SMA-SOD effectively prevented ischemic changes in the frontal lobe. Analysis of cortical blood flow by a laser Doppler flowmetry (LDF) in BCAL rats revealed 55.9 ± 8.4% reduction of the blood flow in the frontal lobe, while occipital lobe blood flow increased to 119.6 ± 27.7%. Although pre-administration of SMA-SOD reduced the latter change, the former blood flow was unchanged. The chemiluminescence intensity of peripheral blood and the change of blood pressure transiently raised to high levels at an early stage of brain ischemia. In contrast, these changes attenuated in both polymorphonuclear cells (PMNs)-reduced and SMA-SOD-treated BCAL rats. These results suggest that superoxide radicals and their metabolite(s) may change systemic circulation as well as directly cause of ischemic brain damage.

7-03-03 PROTECTIVE EFFECT OF NITRIC OXIDE RADICAL ON RATS WITH BILATERAL CAROTID ARTERY LIGATION (BCAL).

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Bilateral carotid artery ligation (BCAL) to the rat has been commonly used as an animal model of brain ischemia. It is well known that, although ischemic changes in the frontal lobe of the brain and optic nerve edema and atrophy occur, the rats are alive after performing BCAL. However, intraperitoneal administration of N^G-monomethyl-L-arginine (LNMMA)(30 mg/kg) to the rats with BCAL revealed that 100% of the rats died within 8 h after challenging BCAL. In these rats, blood pressure was extremely increased (100 → 160 mmHg) and cerebral blood flow in the frontal lobe measured by laser Doppler flowmetry showed further decrease (simple ligation; 60% decrease, ligation + LNMMA; 70% decrease of normal flow). The rats without BCAL didn't die by the administration of the same dose of LNMMA. In these rats, no significant changes of blood flow and blood pressure were recognized. Moreover, DNMMA exhibited no significant changes of these parameters in both control and BCAL rats. These results suggest that increased NO radical generation may play a protective role for the ischemic brain induced by BCAL.

7-03-04 SYMPTOMATOLOGICAL ANALYSIS AND MRI FINDINGS OF ACUTE PHASE OF MILD CEREBRAL INFARCTION INITIALLY PRESENTING WITH VERTIGO OR DIZZINESS

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There are few reports on the cases in which cerebral infarction is initially accompanied by vertigo or dizziness. Here we present an analysis and evaluation of clinical features and MRI findings in a group of such patients. The subjects were 26 patients (18 men and 8 women) ranging in age from 40 to 85 (mean 61.7 years) who had been admitted with cerebral infarction beginning with vertigo or dizziness. Patients with a history of stroke were excluded. All cases were evaluated for neurological symptoms and signs for 7 days and compared in terms of MRI findings, which proved to be abnormal in 16 patients (61%).

The incidence of supratentorial lesions was 61% (16 cases), against 31% (16 cases) for infratentorial lesions. Three patients with vertigo had supratentorial lesions, and one such case had an infratentorial lesion. Among patients suffering from dizziness, there were 10 supratentorial lesions and 4 infratentorial lesions. Only 5 cases evidenced a correlation between neurological signs and MRI findings. Numerous patients with brain infarction complained mainly of vertigo or dizziness. In the present study, 13 cases (81%) had supratentorial lesions, and 10 cases (39%) were not proved by MRI findings.

7-03-05 SENSORY EXTINCTION

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Sensory extinction does not seem to be as outstanding as the manifestations of a stroke. The site of the lesion seems obscure, especially concerning cerebral dominance. In the present study, neurological and neuroradiological examinations were performed on 30 cases with sensory extinction caused by brain infraction. These examinations were performed in order to discuss the site of the lesion and to clarify the clinical significance of this phenomenon. Twenty-five patients had the lesion on the right side, while 5 patients had the lesion on the left. Four out of five cases with a left-sided lesion, however, were left-handed. Sensory extinction was long term in 26 cases in which the lesion included the parietal lobe. In all cases, elementary sensory disturbances were observed during the clinical period. Hemi-spatial neglect was commonly observed in the cases with a parietal lobe lesion. There were some patients who showed sensory extinction only as a neurological manifestation after the disappearance of hemispatial neglect. Inconclusion, sensory extinction was the phenomenon usually observed in the patients with a parietal lesion of the non-dominant hemisphere. Sensory extinction was considered to be an important sign of silent parital lobe syndrome.

7-03-06 CEREBROVASCULAR DISEASE ISCHEMIC RISK FACTORS

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Cerebrovascular risk factors initially centered in the platelet function, have been recently enlarged with other factors. The levels of fibrinogen (FBN) and Lp(a) are vascular risk factors that are related with stroke without a clear association of causality. The antiplaquetelet therapy (APT) modify the FBN and the effect over the Lp(a) is unknown.

We studied 42 patients with previous isquemic stroke confirmed with cranial CT, that have been examined at 48 hours of the stroke (acute phase) and after three weeks (chronic phase) with only APT. We analized plasma levels of glucose, cholesterol, triglicerids, HDL, LDL, VLDL, ApoA, ApoB, FBN and Lp(a).

We found differences in cholesterol *(200 ± 10,2 vs. 252 ± 7,7), triglicerides ** (114,7 ± 6,6 vs. 138,4 ± 12,2) HDL **(37,9 ± 2,5 vs. 44,6 ± 2,5), LDL *(139,3 ± 9,7 vs. 180 ± 5,7), FBN **(403 ± 48,9 vs. 362,3 ± 59,6) and Lp(a) **(64,3 ± 10,1 vs. 32,6 ± 6,5) *($p < 0,01$); **($p < 0,05$). Lp(a) and FBN had shown like independent factors from the others. The Lp(a) is reduced by APT.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-03-07 LONGITUDINAL EEG STUDIES IN STROKE PATIENTS

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Repairing mechanisms are known to occur after stroke and can, at least in part, account for favorable outcome. Very few data are reported so far on the use of computerized electro-encphalography (cEEG) in a rehabilitation plan. In the present study 40 patients affected by stroke were regularly followed for 7 months after the cerebrovascular accident. All parameters that could affect EEG were carefully controlled, such as medication, size and side of the lesion. Scales for motor abilities and activities of daily living were employed. All measures were taken every 2 weeks. Absolute and relative power, weighted mean frequency and coherence were calculated. Subgroups were then considered, in relation to either clincal severity or site of the lesion. Main results are: i) motor and ADL scales are strongly correlated; ii) cEEG is less favorable for prognosis than motor and ADL scales; iii) when clinical conditions appear to be stable cEEG still undergoes slight variations; iv) definite cEEg normalization never occurs at least in the 7 months after stroke; v) cEEG mapping might be a helpful support to neuropsychological studies as well as to the study of neuroplasticity in the human.

7-03-08 SPONTANEOUS INTERNAL CAROTID ARTERY DISSECTION PRESENTING AS MIGRAINE WITH VISUAL AURA - REPORT OF A CASE.

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Spontaneous dissection of the cervical internal carotid artery is an increasingly recognized cause of stroke. Recently there have been a few reports of stroke due to extracranial internal carotid artery dissection simulating acute migraine. Such similarity in the presentation of the two conditions can lead to considerable diagnostic confusion. We describe a patient with stroke in the territory of the right middle cerebral artery in whom the initial presentation was similar to that of migraine with unilateral pulsatile headache and positive visual phenomena. Doppler scan and carotid angiography demonstrated dissection of the cervical internal carotid artery.

Cervical internal carotid artery dissection may present in a similar way to the migraine-stroke syndrome. A high index of suspicion is needed in order not to overlook the diagnosis.

7-03-09 HEMORHEOLOGICAL DISTURBANCES IN CEREBROVASCULAR DISEASE

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The hemorheological disturbances in 117 patients(50 women,67 men,mean age 56,5 years)with cerebrovascular disease(CVD) were investigated. The examined 44 patients with transient ischemic attacks(TIAs) and 73 - with chronic cerebrovascular disease(CCVD) were without hemodynamically significant stenoses of the main neck arteries.Hematocrit(Hct),hemoglobin(Hb),fibrinogen(FIB) and plasma viscosity(PV) were evaluated in relation to the type of CVD,serum lipids CT findings,hypertension,smoking.

When compared to the control group of 80 healthy subjects PV was found to be increased in both patients' groups.The increase of FIB was marked in the patients with CCVD($p<0,001$).Significant correlations between the hemorheological parameters and serum triglicerides were established.Hct was also elevated in smokers.

Increase of PV in the patients with cerebral atrophy on CT was observed.

The variety of problems connected with the hemorheological disturbances in CVD is discussed

7-03-10 RISK FACTORS IN SYMPTOMATIC INTERNAL CAROTID DISEASE

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Carotid and coronary atherosclerosis have similar risk factors. To evaluate the specific risk factors of carotid occlusion, we performed a case-control study in ischemic cerebrovascular patients with carotid disease. 109 patients with carotid stenosis more than 30% or occlusion were included. 101 subjects without carotid disease were considered as a control group. There were 81 patients with moderate or severe stenosis (30-99%), and 28 patients with internal carotid occlusion. The degree of internal carotid stenosis was evaluated with Duplex scan ultrasonography. The analysis was based on multiple logistic regression; the statistical significance is showed as Confidence Intervals (CI). Comparing the control group with the whole group of patients, diabetes (CI = 1.2-6.3), high fibrinogen (1.0-1.1), low HDL-Cholesterol (0.9-1.0) resulted independent risk factors. The comparison between the two groups of patients (stenosis vs. occlusion) showed significant differences in gender (less women in the occlusion group, CI = 0.1-0.6), smoking (more smokers in the occlusion group, CI = 1.2-21.0) and fibrinogen levels (higher in the occlusion group, CI = 0.7-0.9). Among symptomatic subjects with carotid disease, patients with carotid occlusion have a different risk factors profile, where male gender, smoking and hyperfibrinogenemia seem to play an independent role. Our data could be relevant in programming primary and secondary prevention strategies.

7-03-11 EFFECT OF DURATION OF CEREBRAL ISCHEMIA ON PYRUVATE DEHYDROGENASE (PDH) ACTIVITY AND METABOLITES IN GERBIL BRAIN

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The purpose of this study is to determine the effect of duration of cerebral ischemia on PDH activity and the energy metabolism. Cerebral ischemia was produced by bilateral common carotid artery occlusion using Mongolian Gerbils. 20min (1) and 60min ischemic groups (2) were made. PDH activity and energy metabolites (ATP, PCr, lactate) were measured in the caudate nucleus and cortex at each time period.

(1) 20min ischemic group; PDH activity significantly increased after 20min ischemia in both the caudate and cortex , and decreased to the levels less than that of control after 20min reperfusion. At 60 and 120min reperfusion, PDH activity returned to the control levels. ATP and PCr concentrations were significantly depleted after the ischemic insult, returned to 60-80% of control level after reperfusion. Lactate concentrations increased significantly after ischemia, and reduced by reperfusion.

(2) 60min ischemic group; PDH activity significantly increased after 60min ischemia, and decreased but remained higher than control level after 20min reperfusion. At 60 and 120min reperfusion, PDH activity gradually decreased towards control levels or less. ATP and PCr concentrations were depleted after ischemia, and gradually restored after 20min reperfusion and recovered to 50% by 60min reperfusion. Lactate concentrations increased after the ischemic insult, and more elevated after reperfusion.

There is a significant difference in the PDH activities and metabolism depending on the duration of ischemia. The continuous elevation of PDH activities during reperfusion in prolonged ischemia that we observed could be implicated in impaired mitochondria allowing the influx of Ca^{2+}.

7-03-12 VASCULAR AND CARDIAC ETIOLOGY IN CEREBRAL ISCHEMIA

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The relative etiologic relevance of both cardiac and vascular factors in focal cerebral ischemia was evaluated. 258 consecutive patients, 101 women (39%) and 157 men (61%), mean age ± sd = 64.4 ± 12.8, with acute focal cerebral ischemia were studied by an exhaustive standardized protocol including cardiac evaluation (ECG, 24-hour Holter ECG recording, Transthoracic Echocardiography) as well as Duplex-scan and transcranial doppler examination of supra-aortic and intracranial arteries. An arbitrary score (from 0 to 3) was attributed according to the severity of cardiac and vascular alterations in each patient: the higher the score, the higher the probability of an etiologic role of the evaluated factors. The cardiac score was ≥ 2 in 110 subjects (43%). The vascular score was ≥ 2 in 97 (38%) subjects. The association of cardiac and vascular factors was quite common (126 subjects = 49%). This association was more frequent in patients with cerebral infarction than in patients with reversible ischemic attacks and lacunar syndromes (61% vs. 41%). A score ≥ 2 in both cardiac and vascular etiologies was seen in 41 cases (16%). No evidence of cardiac involvement was found in 46% of lacunar syndromes and in 17% of cerebral infarctions. A steady increase in association of cardiac and vascular factors with age was also shown. There was no evidence of either type of etiologic factors in a few cases (9%); in young subjects (age under 50) this figure rose to 21%. Finally the analysis of other etiologic and risk factors by multiple logistic regression showed an independent causal role of hypertension in lacunar syndromes in comparison with other patients.

7-03-13 CHANGES OF Mn SOD ACTIVITY IN MITOCHONDRIA FRACTION IN ACUTE PHASE OF ISCHEMIC GERBIL BRAIN

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We had investigated superoxide dismutase (SOD) activity of cerebrospinal fluid (CSF) by nitrite method in patients with cerebral infarction. Cu-Zn SOD activity was significantly elevated in acute phase of 36 hours and 72 hours after stroke compared with control values. While Mn SOD activity showed no elevation and significantly reduced compared with controls throughout the course. To clarify this discrepancy , we measured SOD activity in mitochondria fraction of Mongolian gerbil brain at 12 , 24, and 48 hours after common carotid artery occlusion.
The results showed that Mn SOD activity at 12 hours were significantly higher than that at 24 hours ($p < 0.05$) and 48 hours ($p < 0.05$). Also Total SOD and Cu-Zn SOD activities at 12 hours were significantly higher than those at 24 hours (Total SOD : $p < 0.01$, Cu-Zn SOD : $p < 0.01$) and 48 hours (Total SOD : $p < 0.05$, Cu-Zn SOD : $p < 0.01$).
It was concluded that Mn SOD activity in mitochondria fraction of Mongolian gerbil brain showed transient elevation at 12 hours after common carotid artery occlusion.

7-03-14 ALTERATION OF PLATELET AGGREGABILITY IN PATIENTS WITH MULTIPLE LACUNAR INFARCTS

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Platelet aggregation in patients with stroke has been extensively studied. However, the results are still controversial in the acute stage. The inconsistent results may partly be due to the heterogeneity of stroke patients in such studies. This study was therefore conducted to examine platelet aggregability in 30 patients with multiple lacunar infarcts (MLI) in the acute or subacute stage. The results were compared with those for 10 control subjects.
[METHOD] The patients with MLI were divided into 2 groups: acute (0-7 days after the onset) or subacute (8-28 days) group. No antiplatelet agents were administrated until the chronic stage (more than 29 days). Platelet aggregability to adenosine diphosphate (ADP) and collagen was assessed using a lumi-aggregometer early in the morning during the fasting state. ADP and collagen concentrations were between 0.25-5.0 uM / ml and 0.25-5.0 ug / ml, respectively.
[RESULTS] In the acute stage, no significant difference in platelet aggregability for ADP and collagen between the patients and normal subjects was detected. In the subacute stage, platelet aggregability increased markedly.
[CONCLUSIONS] In this study, platelet aggregability did not decrease even in the acute stage in patients with MLI, in contrast to the results of previous studies on patients with perforator thrombosis. Small ischemic insult would thus not likely to decrease platelet aggregability.

7-03-15 A RADIOLOGICAL AND CLINICAL STUDY OF CEREBRAL INFARCTION.

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In patients of cerebral thrombosis (except lacunar infarction) who were admitted to our hospital in the past 6 years (1987-1992), we studied radiologically [digital subtraction angiography (DSA) and single photon emission computed tomography (SPECT)] and clinically [activity of daily living (ADL)]. We divided them into 3 groups; 'cortical' (47 cases), 'subcortical' (82 cases) and 'combined' (66 cases), according to the findings of computed tomography. DSA shows us atherosclerosis of large cerebral arteries. There are normal DSA findings in 51% of 'cortical'. And in SPECT of 'cortical', we find decrease in cortical blood supply (51%). Abnormal DSA findings are shown in 62% of 'subcortical' and 89% of 'combined'. And SPECT shows us decrease in cortical and subcortical cerebral blood flow in 34% 'subcortical' and 85% of 'combined'. As for ADL, 85% of 'cortical' and 65% of 'subcortical' can live themselves, but only 32% of 'combined' can. Cerebral infarction in the subcortical area has high potential of large and serious cerebral vessel disease.

7-03-16 CEREBRAL CIRCULATION AND METABOLISM IN THE MOTOR FUNCTION WITH CEREBROVASCULAR DISEASE

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In order to investigate the relationship between motor function and cerebral circulation and metabolism, regional cerebral blood flow (rCBF) and cerebral metabolic rate for oxygen ($CMRO_2$) were measured by positron emission tomography, using ^{15}O steady state method, in 37 cases of cerebrovascular disease. Results were as follows; in the motor functions of upper extremity, both rCBF and $CMRO_2$ were significantly decreased on the motor cortex of upper extremity and internal capsule, and in the lower extremity, both rCBF and $CMRO_2$ were significantly decreased on the motor cortex of upper extremity, centrum semiovale and internal capsule. In the poor motality group as compared to the good modality group, both rCBF and $CMRO_2$ were remarkably decreased on each region. The results suggest that impairments of cerebral circulation and metabolism on the motor cortex, centrum semiovale and internal capsule, are reflected on the motor function.

7-03-17 PROGNOSIS IN ISCHEMIC STROKE PATIENTS WITH ANTICARDIOLIPIN ANTIBODIES

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We investigated the prognosis in 20 ischemic stroke patients with positive IgG ACA who had no collagen vascular diseases. We also examined the relationship between the prognosis and the chronological changes in the titer of ACA. The follow-up period ranged from 1 to 4.5 years, with a mean of 3.4 years. Among the 20 patients, recurrence of ischemic stroke occurred in 10 and myocardial infarction developed in 2 patients. As regards the number of ischemic episodes of stroke, the recurrence occurred twice in 4 and once in 6 patients. Seven patients (28.6%) died of vascular diseases during the follow-up period. Concerning the relationship between the prognosis and the changes in titers of ACA, the recurrence rate was high in patients with a continuously elevated titer of ACA (75%).

The prognosis was poor in patients with ACA and that the recurrence rate was high in patients with a continuously elevated titer of ACA.

7-03-18 ISCHEMIC LESIONS ON MAGNETIC RESONANCE IMAGING OF THE BRAIN: CORRELATION WITH COAGULATION AND FIBRINOLYTIC PARAMETERS.

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We studied coagulation and fibrinolytic parameters to clarify the usefulness of the parameters for the evaluation of the extent of vascular involvement. We analyzed ischemic lesions in the brain using magnetic resonance imaging (MRI), and correlation between the MRI findings and the coagulation and fibrinolytic parameters were investigated. We reviewed 98 subjects who were performed brain MRI and measured coagulation and fibrinolytic parameters. MRI were performed with a superconductive magnet at a field strength 1.5T. A small ischemic lesion (SIL) was defined as a patchy parenchymal area with increased signal intensity on T2 and proton density weighted images and smaller than 10 mm in diameter. We evaluated for the number of lesions at white matter, basal ganglia and brainstem, respectively. We identified SILs in 81 subjects (age range, 39 to 83 years; mean age, 67 years). The numbers of SILs in white matter were weakly correlated with the activities of coagulation factor VIII (FVIII) and von Willebrand factor (vWF) ($P<0.1$). The total numbers of SILs in the brain were significantly correlated with the activities of vWF ($P<0.01$) and weakly correlated with those of FVIII ($P<0.1$). These results indicate that vWF is a useful marker for the vascular damages of arterioles which cause small ischemic lesions in the brain.

7-03-19 NEW STRATEGY FOR SECONDARY STROKE PREVENTION USING HEMOSTATIC MOLECULAR MARKERS

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We indicated a new strategy for secondary stroke prevention according to a patient's hemostatic condition. Forty-four cases of acute ischemic stroke (mean age 75.5 y/o) were entered and followed for at least 8 (average 17.2) months. We examined 6 hemostatic molecular markers (HM) within 5 days of onset and evaluated their hemostatic condition. We selected antiplatelet therapy (P group: ticlopidine 200mg + ASA 100mg) for the 28 patients whose platelet function (beta-Thromboglobulin and Platelet Factor 4) was accelerated, and low-intensity anticoagulation therapy (C group: INR=1.47-1.81) for the 16 cases who had activated coagulation (Fibrinopeptide A and Thrombin-Antithrombin III complex) and secondary thrombolytic function (D-dimer and Plasmin-alpha 2 plasmin inhibitor complex) without platelet hyperstimulation.

In both groups, the alteration of HM was corrected after the appropriate therapy. Reattack occurred in 2 cases in the P group (5.1% / Y), and only in 1 case in the C group (4.5% / Y). All reattack cases were diagnosed as an atherothrombotic infarction. No cardiogenic embolism were observed. Three cases of gastrointestinal bleeding occurred in the P group. Neither subdural hematoma nor intracranial hemorrhage were documented. In three cases death occurred due to pneumonia or heart failure.

Our new strategy was safe and effective for secondary stroke prevention even in elderly patients, especially in cases of cardiogenic embolism.

7-03-20 MRA IS USEFUL FOR DETECTING THE STENOSIS OF THE MAIN TRUNK OF THE INTRACRANIAL MAJOR ARTERIES ?

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To determine the accuracy of magnetic resonance angiography(MRA) in detecting the stenosis of the main trunk of the intracranial major arteries, we compared the results of MRA and conventional angiography(CA).

Method: To 20 patients with ischemic cerebrovascular disease, we performed both MRA and CA. MRA was performed on a 1.5T Shimazu SMT-150X. We divided the findings of the main trunk of the intracranial major arteries into four categories based on stenosis: 0-15%, normal; 16-49%, mild; 50-99 %, severe, and totally occluded. Three neurologists read each angiograms independently without clinical data, and assessed the correlation of each findings. Basilar and vertebral arteries were excluded due to inadequate imaging by MRA.

Results: 40 internal carotid arteries(ICA), 35 anterior cerebral arteries(ACA), 37 middle cerebral arteries(MCA), and 31 posterior cerebral arteries(PCA) were examined. The accuracy of MRA in each categories was 98% in normal, 57% in mild, 50% in severe, and 100% in total occlusion. 4 vessels were overestimated and 3 underestimated.

Conclusion: Our study suggests that MRA is useful for the detecting the occlusion of the main trunk of the intracranial major arteries, but tends to mis-read the degree of stenosis.

7-03-21 STROKE IN YOUNG WOMEN: A HOSPITAL BASED STUDY

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This hospital-based study lasted for 4 years. Cases of young female stroke patients (20 to 44-years-old) diagnosed by WHO's definition and confirmed by CT-Scan of the brain ± cerebral angiography were admitted to Chulalongkorn Hospital. Risk factors among these patients were searched by using appropriate investigations.

Case recruitment during the study were 126. The mean age of case was 34 ± 7 years. The prevalence of subarachnoid hemorrhage, intracerebral hemorrhage, cerebral embolism and cerebral infarction were 21.4%, 23.8%, 21.4% and 25.4% respectively. Other type of stroke, e.g., intraventricular hemorrhage, hemorrhagic infarction, venous infarction were rarely detected. The major risk factor among these patients were pill user (24.59%), rheumatic heart diesease 17.46% and high blood pressure (15.87%). Other causes of stroke in this series were berry aneurysm, arteriovenous malformation moya moya disease, vasculitis, etc. The overall mortality rate was 7.4%.

7-03-22 UPDATING PERCUTANEOUS TRANSLUMINAL ANGIOPLASTY (PTA) OF CAROTID ARTERY STENOSES: LIMITS AND INDICATIONS

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Carotid artery disease has been recently pointed out as the main cause of further stroke in previously symptomatic patients. Carotid endarterectomy (CEA), however, involves not negligible risks, thus justifying the development of alternative techniques. PTA has shown interesting results in the management of the supra-aortic vessels. Our series of 53 carotid PTAs is here reviewed, with a success rate of 94%, average vessel dilation of 82±3%, major morbidity <4%, patency rate 79% at 2 years without clinical relapses. An auditing process aimed to improve quality of the procedure pointed out that: 1) the onset of ipsilateral neck pain at vessel dilation (carotidynia) is related to intimal dissection (OR=4.6 95%c.l.=1.4-14.8, p=0.0084); 2) cerebrovascular symptoms tend to occur when dilation lasts >10 sec (OR=6.6 95%c.l.=1.1-41.5, p=0.048); 3) a higher dilating pressure increases the risk of intimal flaps (R=0.324, p<0.01). In comparison with CEA, PTA shows: 1) minor invasivity, 2) feasibility in distal stenoses, 3) good long-term outcome. A multicentre randomized trial (CAVATAS) is ongoing.

7-03-23 LIPOPRTEIN (a) AND APOPROTEINS IN CAROTID ATHEROSCLEROSIS AND CEREBRAL INFARCTION

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In order to evaluate the roles of lipoprotein (a) (Lp (a)) and apoproteins in extracranial carotid atherosclerosis as well as cerebral infarction (CI), 207 consecutive patients during 20 months examined by doppler ultrasonic imaging were recruited for this study. 128 patients out of 207 patients were examined by X-ray computed tomography. 207 patients consist of 98 patients with plaque in extracranial carotid artery (PIECA) and 109 patients without PIECA. 128 patients consist of 50 patients with CI (14 patients ; cortical infarction and 36 patients ; deep subcortical infarction) and 78 patients without CI. Only when the patients younger than 60 years old were selected, the concentration of serum Lp (a) in the patients with PIECA was significantly higher than in the patients without PIECA. Significant elevation of the concentration of Apoprotein B and decrease of that of Apoprotein A-I in serum were observed in the patients with PIECA, as compared to those in the patients without PIECA. The concentration of serum Lp (a) had the tendency to be higher in the patients with cortical infarction than in the patients without CI. In conclusion, the same changes of serum apoprotein levels were observed in the patients with PIECA and in the patients with CI.

7-03-24 AUTORADIOGRAPHIC ANALYSIS OF [^{125}I]ENDOTHELIN-1 *BINDING IN EXPERIMENTAL CEREBRAL ISCHEMIA*

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In order to investigate the role of Endothelin-1 (ET-1) in cerebral ischemia, we performed in vitro receptor autoradiographic analysis with [^{125}I]ET-1 in ischemic gerbil brain employing two groups of Mongolian gerbils: the sham operated group (n=5) and the ischemia group (n=10). At 2 hours after the occlusion of the right common carotid artery, the local cerebral blood flow (lCBF) was measured by the [^{14}C]-iodoantipyrine method. Serial brain sections prepared in a cryostat were incubated with 1.16×10^{-10}M [^{125}I]ET-1 in the presence or absence of 8.03×10^{-7}M unlabeled ET-1 for 10 min at 25°C. The radioactivity was quantified to estimate the binding amount of ET-1. The ischemic side exhibited a significant reduction in lCBF ($p<0.05$-0.01). The binding amount of ET-1 increased in the medial nuclei of thalamus ($p<0.05$) and tended to rise in the hypothalamus on the ischemic side. On the other hand, the binding did not change in the hippocampus CA1 and CA3, in which a significant decrease was observed after 6-hour ischemia in our previous study. In summary, the regional alteration of ET-1 receptor binding may be closely related to the pathophysiology of cerebral ischemia.

7-03-25 THE EVALUATION OF VENOUS OCCLUSION IN PATIENTS WITH CHRONIC CEREBRAL INFARCTION.

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Endothelin (ET), a vasoconstrictive peptide produced by vascular endothelial cells, was discovered in 1988 by Yanagisawa et al. Since then, the association of ET with cerebrovascular constriction following subarachnoid hemorrhage and with the pathophysiology of hypertension has been clinically studied. We recently studied the response of vascular endothelial functions (in particular the response of ET) to extrinsic stress in patients with chronic cerebral infarction (CI). The subjects were 10 patients with CI and 10 healthy volunteers. Extrinsic stress was produced by experimentally inducing venous occlusion (VO). ET was measured by EIA. t-PA and fFAI-I were also measured. ET levels before induction of VO were slightly lower in the CI group than in the healthy controls. This difference seemed to reflect the state of the anti-thrombotic function in CI patients. After induction of VO, the ET level increased to a similar degree in both the CI group and the healthy controls, suggesting that the response of vascular endothelial cells to extrinsic stress is similar between CI patients and healthy individuals.

7-03-27 OPTIMAL SCREENING FOR CAROTID ARTERY STENOSIS: COMBINED TRANSCRANIAL AND CAROTID DUPLEX ULTRASOUND

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Recent studies demonstrated the need to identify patients with severe symptomatic carotid stenosis. Carotid Duplex ultrasound is an accepted screening test for severe carotid disease, while transcranial Doppler (TCD) identifies its hemodynamic consequences, providing an adjunct to Duplex. We compare three screening strategies for carotid stenosis: angiography without ultrasound screening, screening with Duplex alone, and screening with combined TCD and Duplex. Over 18 months, we identified all patients with ischemic symptoms who had angiographic, Duplex and TCD examination. We blindly measured angiographic stenosis using NASCET criteria, and identified criteria for Duplex and TCD that correlated with ≥ 70% carotid stenosis. Data were available for 84 total carotid bifurcations. The sensitivity/specificity were 100%/84% for Duplex; 100%/91% for combined Duplex/TCD. Retrospective application of each sreening strategy correctly identified all stenoses ≥ 70%. However, angiography without ultrasound screening resulted in 55 unnecessary angiograms (stenosis was < 70%); Duplex screening resulted in 9, and Duplex/TCD in only 5 unnecessary angiograms. Duplex/TCD improved the selection of patients for angiography compared with Duplex screening alone, correctly identifying all severe carotid stenoses and minimizing the number of angiograms performed. This diagnostic model requires prospective validation.

7-07-01 NEUROLOGICAL DYSFUNCTION IN OBSESSIVE-COMPULSIVE DISORDER: A PRELIMINARY REPORT.

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Some evidences of a neurological dysfunction in Obsessive-Compulsive Disorder (OCD) have been described in the last years. Our purpose was to evaluate a group of patients with OCD, using a neurological soft sign battery. Neurological soft signs (NSS) are nonlocalizing signs of altered performance on a motor or sensory task in the absence of a focal neurological disturbance. We examined 15 patients, six male and nine female, aged between 17 and 66 years (mean age=38.2, SD=15.0), following DSM-III-R criteria for OCD. Duration of illness ranged from 4 to 40 years (mean=14.9, SD=10.2); severity of symptoms was assessed using the Yale-Brown Obsessive-Compulsive Scale. Five patients were receiving clomipramine, the remaining ten were medication-free. The neurological battery included evaluation of fine coordination, sensibility, involuntary movements and visuospatial abilities.

Eleven patients (73.3%) presented NSS on examination, mainly palmomental reflex (n=6), mirror movements (n=5) and agraphestesia (n=3). We found no correlation between severity of symptoms and the number of NSS. Three out of the four patients who presented no abnormalities on examination were under medication. Nevertheless, no absolute conclusion about the effect of clomipramine over the NSS can be drawn. These results stress the interest of longitudinal studies in order to clarify the signification of the NSS and possible modifications under medication.

7-07-02 DO WE DREAM MIRROR-WISE?

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Steroscopic dream contents which were routinely sketched during the psychoanalysis of a lefthanded subjekt turned out as mirror image presentations of geographical reality. Four characteristic examples are described. In the discussion genesis and topography of this psycho-optic phenomenon are commented on, but leaves open the theoretical cognition question whether it is a psychological-psychodynamic or a neurological-physiological or a mechanism of origin associated with each other. Here might be the explanation for wrong-way-drivers (Geisterfahrer) and other phenomena of disturbed motor control, problems of handiness etc.

"Franzosen und Russen gehört das Land
Das Meer gehört den Briten.
Wir aber besitzen im Luftreich des Traums
Die Herrschaft unbestritten."

(Heinrich Heine)

7-07-03 IS THERE A DIFFERENCE OF CEREBRAL LANGUAGE ORGANIZATION BETWEEN HAN NATIONALITY AND WESTERN PEOPLE? A STUDY OF 972 STROKE PATIENTS

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Aphasia test was performed on 972 stroke patients of unilingual Han nationality from 1983 to 1992. More than 500 cases were examined with CT scanning at random. There were 235 cases with single lesion or normal results.

Results: There were no statistical difference of aphasia incidence among the sex, age and stroke types. There were 418 cases illiteracy and 554 of literacy. The incidence of aphasia of the former is lower than that of the latter ($X^2 = 6.56$, $P < 0.05$). The total incidence of aphasia, 42.4% (412/972), and the incidence of aphasia after damage in left brain, 58.5% (200/342), are lower than that of the Occidentals. The incidence of crossed aphasia, 13%, is at a higher level as compared with the western people. Motor aphasia is most common (66.8%) and the sensory (2.4%) and anomic (0.49%) aphasia are rarely seen. The correlation of aphasia and lesions in CT scan is not conformed with the classical theory of cerebral language organization in western world such as sensory aphasia can be seen in lesions of anterior hemisphere and motor aphasia may occur in posterior lesions.

Conclusions: The langage function of Han nationality does not only confine to the left brain but also localize in the right. The theory of dominant hemisphere in western countries might not be suitable for the Han. The ideographic language of the Han and low educational level of our patients might play an important role in these differences.

7-07-04 **PARKINSONISM, DEMENTIA AND OBSESSIVE-COMPULSIVE BEHAVIOR: A CASE REPORT.**

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This study reports a 62-year-old patient with a juvenile onset Parkinsonian syndrome. At the age of 60, she began to show signs of mental deterioration and polymorphic compulsive behavior, mainly consisting of the repetition of sentences and single words. Neurological examination showed severe akinesia and parkinsonian rigidity, mild inconstant resting tremor, more evident in the upper left limb. Neuropsychological testing revealed moderate mental deterioration with disproportionate impairment on tasks sensitive to frontal lobe dysfunction. Magnetic resonance imaging showed a small area of increased signal intensity in the anterior portion of the left putamen on T2-weighted images. 99m Tc HM-PAO single photon emission computerized tomography revealed hypoperfusion in the right parietal, frontal, sylvian and thalamic regions and in the left temporal, parietal and occipital regions. Possible correlations between the clinical picture and the neuroimaging data in this patient are discussed, also with reference to other reports of obsessive-compulsive behavior in patients with basal ganglia lesions.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-07-05 NEUROPSYCHOLOGICAL ASPECTS OF FAT EMBOLISM SYNDROME

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There have been few reports on characteristics of cognitive dysfunction in fat embolism syndrome(FES). We describe a case of classical FES with resulting serious cognitive dysfunction in detail.

A previous healthy 25-year-old physician was involved in a car accident and suffered from a closed fracture of right femoral bone. Following a lucid interval he developed disturbance of consciousness and respiratory failure. A diagnosis of FES was made and intensive care was initiated. After survival he remained unconscious for 3 weeks and gradually moved to apallic syndrome. In the subacute stage brain MRI disclosed multiple hemorrhages in the white matter with surrounding massive edema. In the chronic stage he showed marked cognitive dysfunction(WAIS verbal IQ:65, performance IQ:below 60). Lack of insight, flattening of emotion and loss of spontaneity were characteristic and most severely affected cognitive functions were abilities of writing and construction. Serial brain MRI revealed progressing diffuse brain atrophy.

In this case, according to the MRI findings cognitive dysfunction seems to be attributed primarily to multiple subcortical lesions of both cerebral hemispheres.

7-07-06 ANALYSIS OF NEUROPSYCHOLOGICAL FUNCTION IN DIABETIC PATIENTS: THE EFFECT OF HYPOGLYCEMIA ON BATTERY TESTS OF INTELLECTUAL AND COGNITIVE PERFORMANCE AND EVENT-RELATED POTENTIALS (ERPS)

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A variety of battery tests on intellectual and cognitive performance were performed and the latency of P300 in event-related potential (ERPs) was measured with reference to hypoglycemic episodes, glycemic control and daily fluctuation of plasma glucose level in 46 diabetic patients without cerbral vascular disease.

The latency was significantly more delayed in patients with than without hypoglycemic episodes. Among diabetic patients with hypoglycemic episodes, those under poor (HoA1 > 10) or labile glycemic control showed a lower score in attention (story recall). The patients having such 3 conditions as hypoglycemic episodes and poor and labile glycemic control showed a tendency for more delayed latency of P300 and significantly lower scores in tests including attention, learning and memory and abstraction than the patients having any two of the 3 conditions.

These results suggest that the neuropsychological function is deteriorated through not only hypoglycemia but also poor or labile glycemic control in diabetic patients.

7-07-07 CONSCIOUSNESS AND MEMORY DURING THE WADA TEST

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The Wada test is employed to assess memory during the pre-operative evaluation for epilepsy surgery, but the confounding effects of alterations in consciousness are unclear. The present study examines the effects of alterations in level of consciousness on memory performance during the intracarotid amobarbital procedure. Consciousness was assessed by a Modified Glasgow Coma Scale (altered to avoid verbal responses as a confound) while objects (8/injections) were presented for subsequent post-recovery memory recognition in 97 patients with intractable epilepsy. In dextral subjects with left cerebral language dominance, memory performance was significantly correlated with the Modified Glasgow score for injections on the right side ($r = .82$, $p \leq .002$) and ipsilateral to the focus ($r = .60$, $p \leq .006$), but not for injections on the left side ($r = .25$, NS) or contralateral to the focus ($r = .23$, NS). In contrast, these same subjects exhibited a significant effect of focus on memory for left side ($p \leq .006$) and contralateral to focus ($p \leq .01$) injections, but not right side or ipsilateral to focus injections. Further, a greater impairment in consciousness was noted on left vs. right injections ($p \leq .0002$). Alterations in consciousness do affect memory during the Wada, and these effects appear to interact with the side of focus and of injection relative to cerebral language dominance.

7-07-08 COGNITIVE DEFICITS IN MULTIPLE SYSTEM ATROPHY PATIENTS

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Multiple system atrophy (MSA) represents an ensemble of degenerative syndromes mainly characterized by motor and autonomic dysfunctions. Little is known about the cognitive manifestations of MSA partly because of the confounding motor handicap. The aim of this study was to examine the performances of MSA patients on neuropsychological tests when their motor handicap was taken into account.

Five MSA patients and six age matched control subjects were given a battery of neuropsychological tests which assess attention, language, visuo-spatial perception, verbal and visual memory, and executive functions. Tasks were used in order to control the motor demand of particular tests.

MSA patients had significantly inferior performances on all tests that are speed dependent. Once motor demand was accounted for, only the Trail Making Test part B and the Stroop Test showed significant differences ($p = .02$).

This study shows that a so-called frontal lobe deficit may best characterize the cognitive impairment of MSA patients and that this dysfunction is independent of the motor handicap. Further research is needed to elucidate the nature of these deficits.

7-07-09 REGIONAL CEREBRAL BLOOD FLOW DURING SIGNED AND SPOKEN LANGUAGE PERCEPTION

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Neurobiological research on language function has almost exclusively considered spoken language. In the present study signed and spoken language have been studied in parallel with the aim to attain an understanding of the total language competence and to separate visual and auditory components in language perception.

Nine bilinguals in sign and spoken language were tested with a comparable language perception test in spoken Swedish and Swedish sign language. Regional cerebral blood floow (rCBF) was measured by a xenon-inhalation method with 254 detectors. Further, three different groups with deaf or hearing-impaired persons were tested with sign language materials under similar rCBF-measurements.

Sign language in the bilinguals and in deaf with hearing parents gave a bilateral temporal activation, more pronounced than the activation during pure listening, but similar to a situation when the bilinguals watched a speaker. Deaf with deaf parents demonstrated a more right-sided activation.

The data shows that sign language perception is similar to a combined listening-watching situation with spoken language. Pure listening seems to be a different situation and further deaf that have grown up with sign language represent a special group with more activation in cortical areas responsible for spatial function.

7-07-10 LONG TERM FOLLOW-UP IN HERPES ENCEPHALITIS SURVIVORS: AN ANATOMO-FUNCTIONAL COGNITIVE AND BEHAVIORAL STUDY

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Among 23 cases of Herpes Simplex Encephalitis (HSVE) proved by biopsy or serology, 8 patients were followed during a mean of 7 years (2 y. to 13 y.). All had repeated (from 2 to 6 times) and complete investigations including EEG, CT scan, MRI, CBF (Xe133) and classical psychometric battery. Patients and relatives were submitted to a standardized questionnaire assessing daily behavior. CT and MRI showed sequellar foci typical of Acute Necrotizing encephalitis involving asymetrically temporal lobes with a predominance to the right side. In 2 cases only the right temporal lobe was involved. In the remaining 6, two had an extension of the lesion to the frontal and cingular areas. Outcome correlations were found between stages of severity in cognitive defects and inadequate behavior, specially Kluver Bucy and amnestic syndromes, and degrees of anatomo-functional deficits showed by CT, MRI and CBF.

We desperately need specialized departments or institutions able to adequately take charge of the most severely affected patients.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-07-11 NEUROPSYCHOLOGICAL STUDIES IN PATIENTS WITH BILATERAL OCCLUSION OF THE CAROTID ARTERIES (BCAO)

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BCAO has been linked with neuropsychological impairment (Miller Fisher Arch Neurol Psych, 1954). In order to analyze the neuropsychological functions of such patients, we have, prospectively, studied 16 cases of angiography-proved BCAO. All the patients underwent clinical examination, cerebral CT, rCBF study and neuropsychological tests. Normal results were found in 3 patients, abnormal slowness in 2 cases and focal neuropsychological signs not explained by the sole ischemic lesions in 11 patients. The importance of neuropsychological impairment was not statistically correlated to the presence of an ischemic lesion on CT or to a global impairment of cerebral vaso-reactivity on rCBF study. Finally, neuropsychological impairment is frequent in case of BCAO. It is not due to a sole cause but may be explained by several mechanisms (cerebral involvement due to arterial hypertension, diabetes mellitus, chronic renal failure, alcohol abuse, ischemic focal lesions ...).

7-07-12 CATASTROPHIC REACTION AFTER CEREBROVASCULAR LESIONS: FREQUENCY, CORRELATES AND VALIDATION OF A SCALE

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The Catastrophic Reaction (CR) was defined as a specific psychiatric entity produced by the inability of the organism to cope when faced with a serious defect in physical and cognitive functions. This disorder is characterized by anxiety, tears, aggressive behavior, swearing, displacement, refusal, renouncement, and compensatory boasting. However, since the frequency, mechanism, and correlates of the CR have never been examined, the possibility that the CR is no more than a manifestation of post-stroke depression cannot be ruled out. The present study examined the frequency and correlates of the CR in 62 consecutive patients with acute stroke lesions. The neuropsychiatric examination included a specially-designed CR scale, and scales of depression, anxiety, cognition, activities of daily living (ADL), and social functioning. The CR Scale showed a high internal consistency and inter-rater reliability. Twelve (19%) of the 62 patients had a CR. Patients with CR had a significantly higher frequency of familial and personal history of psychiatric disorders. Nine (75%) of the 12 patients with CR had a major depression, 2 (17%) had minor depression, and the remaining patient was not depressed. Patients with CR also showed significantly higer depression and anxiety scores, as well as significantly more deficits on ADLs. Finally, patients with CR had a significantly higher frequency of basal ganglia lesions ($X2=4.71$, $df=1$, $p<.05$). In conclusion, our study demonstrated that the CR is not a specific complication of brain injuries, but is a sub-type of post-stroke depression significantly associated with subcortical lesions.

7-07-14 HANDEDNESS IN MUSICIANS

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Several studies have shown an elevated rate of non-right-handedness in certain occupations, ie, those in which there is an increased use of spatial talents, such as artists. Amongst musicians it has been proposed that the left hemisphere is better equipped for dealing with local features of melody, and the right for arriving at global melody representations.

The handedness pattern of 382 members of 7 professional orchestras was assessed at rehearsals by two physicians using the short form of the Edimburgh Handedness Inventory Questionnaire.

Six percent of the musicians were left-handed and 4 per cent mixed-handed, the prevalence of non-right-handedness being 10% (95% CI: 7-14%).

The main outcome of this survey is that the prevalence of non-right handedness in these musicians was much the same as in the general population, a finding at odds with received wisdom. Although these data suggest independence of musical abilities and handedness, it has recently been shown on computed tomography (CT) that 18% of the normal population have reversed brain asimmetry.

We conclude that the clinical assessment of handedness may not be a good approach to study cerebral lateralization in musicians. Brain CT should ideally be performed for an analysis of cerebral asymmetry, though this may of course be difficult to justify.

7-07-15 MRI VOLUMETRY OF MEDIAL TEMPORAL LOBE IN AMNESIA FOLLOWING HERPES SIMPLEX ENCEPHALITIS

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To evaluate a relationship between amnesia and medial temporal lobe (MTL) damages, we studied five patients who had MTL damages following herpes simplex encephalitis (HSE) and memory impairment in the acute stage of their illness. When included, age ranged from 24 to 55 years, and time after onset of the illness from 12 to 52 months. Using a computer and image analyzing software with a combination of tracing and thresholding technique on 4-mm-thick T1-weighted oblique-coronal magnetic resonance images, volumes of the hippocampal formation (HF), parahippocampal gyrus (PHG) and anterior temporal lobe (ATL) were measured in the patients and ten age-matched healthy controls. Memory functions in the patients were evaluated by the Wechsler Memory Scale, Auditory Verbal Learning Task, Rey's Complex Figure Test, Benton Visual Retention Test and the length of retrograde amnesia.

HF, PHG, and ATL volumes normalized by intracranial volume (mean ± SD ml) were 2.63 ± 1.44 ($p<0.01$), 5.85 ± 2.84 ($p<0.01$), and 100.7 ± 29.1 ($p<0.05$) in patients; and 5.01 ± 0.52, 9.44 ± 1.13, and 121.4 ± 8.0 in controls. Memory functions in the patients were correlated with HF and PHG volumes. Three patients with a HF volume reduction up to 50 % from the normal had a significant recovery from the initial memory dysfunction. These results suggest that amnesia following HSE is related to MTL atrophy, and that there is a critical level of volume reduction for causing a lasting amnesia.

7-07-16 COGNITION IN RELAPSING-REMITTING MS PATIENTS WITHOUT NEUROLOGICAL SEQUEALE

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We have studied 48 patients diagnosed according to Poser's criteria as definite or probable MS, all with a R-R course and an EDSS less than 2. The patients were carefully matched for age, sex and education with 50 normal controls. The neuropsychological evaluation was carried out by means of the Luria Nebraska Neuropsychological Battery. As a group, patients with MS performed worse than normals on attention, visuospatial tasks, language comprehension, immediate and delayed recall and abstracting ability. Patients who showed cerebellar signs at disease onset scored worse than patients with either a visual or a sensory onset modality. There was no relation between cognitive performance and measures of disease activity. Finally, patients who after at least one year from testing did change their course inot R-R with sequelae or a C-P were more impaired than patients who remained stable. Cognitive testing may have prognostic implications.

7-07-17 IMAGE GENERATION IN BRAIN DAMAGED PATIENTS-WHAT IS THE INFLUENCE OF THE STIMULUS VERBALISATION?

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The neuropsychological models of image generation have received much attention in recent years There is a growing body of evidence in support of the view that the left hemisphere is specialised for image generation, a suggestion that has been put forward by Farah(1985,1986) and Kosslyn(1987) Still many authors disagree with this statement their main criticism falling on methods for evaluation image generation capacity.

This study was designed to test whether the degree of verbalisation of the stimuli would influence the lateralisation of image generation. Three experiments each with a set of stimuli differing in the degree of verbalisation from the others were performed. The Ist set requires mental images of letters, the IInd - of the angle between the hands of the clock when pointing to different hours. The IIIrd set is for object image generation, a new method that we devised especially as an attempt to diminish the overall verbalisation effect. Patients with damaged left or right cerebral hemisphere were investigated. The results are discussed in terms of Farah and Kosslyn computational model.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-07-18 NEUROPSYCHOLOGICAL DEFICITS IN DOMINANTLY-INHERITED OLIVOPONTOCEREBELLAR ATROPHY (OPCA)

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We reported frontal system cognitive deficits in patients from one large family (pedigree S) with dominantly-inherited OPCA, a degenerative cerebellar ataxia disorder (Ann Neurol 24: 200-206, 1988). To determine whether these deficits are specific to the pedigree S family, we administered a comprehensive neuropsychological battery to 44 patients, representing nine other OPCA families, and 24 control (C) subjects matched for age, education and sex. Generally mild, but highly statistically significant neuropsychological deficits were observed on tests of memory (mean WMS Memory Quotient: C, 115; OPCA, 97; $p<0.00004$), verbal and nonverbal intellectual ability (Peabody Picture Vocabulary: C, 159; OPCA, 146; $p<0.0005$; Raven's Coloured Progressive Matrices: C, 32.6; OPCA, 27.7; $p<0.002$), attention (Modified Continuous Performance test: C, 25.6; OPCA, 24.0; $p<0.04$), naming (Boston Naming Test: C, 56.5; OPCA, 51.5; $p<0.004$), visuospatial function (Hooper: C, 26.5; OPCA, 21.7; $p<0.0008$), and frontal system function (Wisconsin Categories: C, 8.4; OPCA, 5.6; $p<0.0007$). Our data suggest that the mechanisms underlying cognitive deficits in some OPCA subtypes may involve widespread neuroanatomical systems and are not limited to the frontal lobes. (Supported by U.S. NINDS 26034).

7-07-19 EVALUATION OF NEUROPSYCHIATRIC SYNDROMES IN NON-ALCOHOLIC PORTAL-SYSTEMIC ENCEPHALOPATHY (HE)

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PROBLEMS: Publications on this topic so far were either case reports or described essentially cognitive and vigilance impairment. Main focus of this prospective and interdisciplinary study was to examine systematically onset, characteristics and frequency of psychopathological symptoms in HE and to categorize findings.
METHODS: After clinical staging of HE according to HOLM and WIECK 20 patients graded HE 0-2 underwent a test battery to evaluate neurological symptoms, psychomotoric speed, cognitive functioning, personality traits and mood states including a semistructured diagnostic psychiatric interview (AMDP), additionally EEG was performed.
RESULTS: Anancastic personality traits seemed to be predominant. No close relationship between vigilance and cognitive disturbances, other psychopathological symptoms like mood changes and level of liver function assessed by conventional parameters could be observed.
CONCLUSION: Results indicate that neurochemical abnormalities associated with HE do not only determine vigilance and cognitive impairment but also induce changes of mood states.

7-07-20 A CASE OF PURE WORD DEAFNESS

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We report a case of pure word deafness caused by bilateral cerebral infarction. A 50-year-old female patient was unable to comprehend spoken language although she could read, write and speak in a normal manner. Comprehension of written language and nonverbal sound was relatively spared. Hearing threshold was around 40 dB on audiometry. Brain CT showed bilateral temporoparietal infarction. Cerebral angiogram demonstrated no occlusion in large arteries.

7-07-21 IMPAIRMENT AND RECOVERY OF MEMORY IN UNILATERAL CAROTID STROKES.

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An analysis of initial and eight weeks follow up quantification of memory functions forming part of a prospective study on strokes is presented. Seventy patients with C.T.scan confirmed unilateral carotid territory strokes were evaluated for memory function initially at onset of stroke, and later at eight weeks interval for recovery of function. All the patients were assessed using Wechsler memory scale form I for overall memory function and Bender visuomotor gestalt recall test for non verbal recall. Results were analysed using 't' test. It was observed that (1) there was a significant fall in memory function in unilateral stroke (2)Irrespective of the side there was definite impairment of verbal and non verbal memory in all (3) Immediate memory was most affected and showed the least recovery (4) Memory in right carotid strokes recovered better than in left.

7-07-22 VERBAL PERSEVERATIONS: TWO CASE REPORTS

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Two aphasic patients with frontal lesion and perseverative behaviour were submitted to a standardised language examination and to other different verbal and non verbal tests. Patient AB only persevered when he did not know the correct answer(failure in his Semantic System), this was evident in naming, writing and drawing. Two years later he persevered only in phonemic word-list generation. Patient MT showed marked perseveration in all the language tasks except repetition. Perseverative behaviour was also present in a gesture-imitation task and when using objects at the examiner's request. Improvement was soon apparent in gestural tasks but six months later perseverations were still present in a verbal fluency task and in a modified version of the Wisconsin Card Sorting Test. For both patients perseverations were not semantically related to the target; the most frequent case was that of repetition of a word or part of it and a correct response did not have any special status. MT still showed massive perseveration in verbal fluency when almost all perseverations had disappeared from naming, and word list generation was the only task in which AB persevered after two years of observation. Our data do not support the hypothesis that word-list generation is less likely to produce perseverations than a confrontation naming task.

7-07-23 **EFFECT OF TWO DOSAGES OF GINKGO BILOBA EXTRACT (EGb 761) ON THE DUAL-CODING TEST IN THE ELDERLY**

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The dual-coding test was used to compare the acute effect of two dosages of titrated and standardized Ginkgo biloba Extract (EGb 761) (320 and 600 mg), compared with placebo, in a group of 18 elderly subjects with slight memory impairment on inclusion. A randomized, double-blind, crossover study was conducted in order to assess, one hour after acute administration, the effect of the various test substances on picture and word coding at variable material presentation times. Both dosages significantly improved the presentation times allowing dual-coding. The values obtained with active treatment were better than those obtained with placebo and were similar to those observed in young healthy subjects.

7-07-24 SLOWLY PROGRESSIVE COGNITIVE DISORDERS WITHOUT GENERALIZED DEMENTIA CAUSED BY PREDOMINANTLY RIGHT HEMISPHERE ATROPSY: REPORT OF 3 CASES WITH SPECT & PET(FDG)-FINDINGS

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In recent years some cases have been reported presenting not only slowly progressive aphasia, but also slowly progressive agnosia, apraxia and other kinds of cognitive impairment without generalized dementia. The present paper details neuropsychological as well as neuroradiological findings(MRI,SPECT,PET-FDG) obtained in 3 cases of predominantly right-hemisphere atrophy that exhibited visual agnosia (Case 1: prosopagnosia & object agnosia), selective loss of memory for people (Case 2: not only prosopagnosia but also impaired recognition of voices and proper names of familiar persons), or visuospatial disabilities (Case 3) respectively in the absence of generalized dementia.

7-07-25 THE EFFECT OF SMOKING ON THE CORTICAL FUNCTION

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It has been noted that elderly persons who have been smoking almost more than 40 years around our community have good intelligence.

So, presumably smoking might be helpful to preserve cortical function and prevent dementia.

We analyzed 74 elderly persons (mean age 72.4) with short verbal test of HM that concerned general information, comprehension, arithmatic, memory, digit span and judgment.

Our result is that HM score is much better in smoking group (67.2/100) than non-smoking group (43.6/100).

7-07-26 COGNITIVE EVENT-RELATED POTENTIAL AND BRAIN MRI IN HTLV-1 ASSOCIATED MYELOPATHY (HAM)

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The study of cognitive event-related potential, P300, in patients with HAM has not yet been reported. The purpose of our research is to clarify the cognitive abnormality in HAM, using P300 and brain MRI. Fourteen HAM patients and 36 normal controls were studied. We used tone-clic sound (target 1000Hz tone/ non-target clic) and tone-tone sound (target 2000Hz tone/ non-target 1000Hz tone) as an auditory method, and colors (target red color/ non-target green color) as a visual method. As a result, abnormalities of P300 latency and amplitude were found in seven (50%) and three (21%) of the 14 patients, respectively. In brain MRI study, the abnormal T2-high-intensity lesions in white matter were observed in six (75%) , and the bilateral parietal lobe atrophy was found in one (13%) of the 8 patients. The incidence of abnormal cognitive event-related potentials was observed frequently, but its abnormality did not correlate with the brain white matter lesions.

7-07-27 DISORDER OF RETRIEVAL IN A CASE WITH RETROSPLENIAL AMNESIA

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A patient with retrosplenial amnesia who has shown a marked dissociation between very poor recall and relatively good recognition will be reported.

Patient M.K. : A 40-year-old right-handed man showed impairment of memory and other cognitive functions after successful radiation and chemical therapy of astrocytoma which originated from the splenium of the corpus callosum and invaded transcallosal fibers and retrosplenial regions of the both hemispheres. The patient showed personality change, impaired visual perception, dyslexia of verbal materials in the left visual field, and memory disturbance.

The patient's FIQ was 64 (VIQ: 77; PIQ: 57) on the WAIS, and his MQ was 62 on the Wechsler Memory Scale. The serial position curve of a word list task revealed lack of primacy effect with preserved recency one. Although he could not recall names and objects presented a few minutes previouly, multiple choice tasks of remembrance revealed that his recognition memory was not so poor as recall function. This suggests that his memory impairment results from disorder of retrieval. He seemed to have retrograde amnesia of about 10 years. His immediate memory was almost intact.

7-07-28 HETEROGENEITY IN PROSOPAGNOSIA.

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It was noticed that both nature of lesion and neuropsychological features were not always uniform in prosopagnosia (e.g.De Renzi, 1986), and some authors proposed to divide it into two types, apperceptive or perceptual and associative or mnestic. We report here detailed neuropsychological features of three cases with prosopagnosia resulting from occipital lesions of different site or nature (Table).

Patient	Age	Sex	Lesion	Prosopagnosia
1(M.Y.)	58	M	Occl.of the R.PCA	Transient
2(E.U.)	70	M	①R.O.H.infarct ②L.O.H.infarct	Absent Persistent
3(S.N.)	57	M	Occl.of the B.PCA	Persistent

R:right; L:left; B:bilateral; O:occipital; Occl:occlusion; H:hemorrhagic; PCA:posterior cerebral artery

In these cases, covert recognition of familiar faces they have failed to recognize overtly, ability to discriminate and learn unknown faces, visually perceptual functions, and others were examined exactly. Results provided some evidence that prosopagnosia is not so homogeneous.

7-07-29 KANJI AND KANA WORD READING PROCESS ANALYZED BY POSITRON EMISSION TOMOGRAPHY.

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Recent neuropsychological studies have revealed that reading and writing disturbances are sometimes dissociated between kanji and kana, i.e., kana reading is more impaired in alexia with agraphia due to an angular gyrus lesion, while kanji writing is more disturbed in alexia with agraphia by a posterior inferior temporal (PIT) lesion. We measured regional cerebral blood flow during kanji or kana reading and compared activation sites between them.

The subjects read aloud two-letter kanji words, three-letter kana words or kana non-words. Three-times intrasubject averaging analysis revealed that the kana tasks activated widespread regions including bilaterally the medial and lateral occipital gyri and the left PIT, while the kanji task activated only the bilateral PIT. Based on the fact that the kana word task activated the left PIT more than the kana non-word task and that the PIT is activated symmetrically by shape or face discrimination tasks, the left PIT was thought to play roles in both semantic and morphological processing in word reading.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-07-31 A NEW TYPE OF PARANEOPLASTIC SYNDROME WITH MYASTHENIA GRAVIS AND THYMOMA.

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Three patients with Neuropsychiatric symptoms(NPSs) associated with MG and thymoma are reported. The NPSs were antedated by several months to years before the onset of MG. They were also closely related to worsening and relapse of MG. The NPSs are as follows:(1)psychosensory symptoms of hallucinations, illusions and deja experience;(2)consciousness disturbance such as dreamy state with paramnesia;(3)psychotic symptoms such as secondary delusions developed from (1) and (2);(4)cognitive disturbances such as recent memory loss with compulsive behaviors;(5)emotional disturbances. These NPSs were rather homogeneous. One patient showed abnormal EEGs constantly. MG and the NPSs associated with thymoma and high titers of anti-acetylcholine receptor antibody represents a unique type of paraneoplastic neuropsychiatric syndrome. A possibility of autoimmune psychiatric syndrome and syndromegenesis of psychosis of MG are discussed.

7-07-32 NEUROBEHAVIORAL ABNORMALITIES ASSOCIATED WITH SUPRATENTORIAL ARACHNOID CYSTS: ANALYSIS OF TWO CASES

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We evaluated two individuals with behavioral disturbances in whom MRI studies revealed large arachnoid cysts unilaterally impinging on anterior temporal, opercular, and inferior frontal lobe areas. An elderly male, previously noted to avoid conflict, impulsivcly strangled his wife after she scratched his face in a domestic argument. Deficiencies in remorse, empathy and future-planning were evident by history and examination. MRI showed a left-sided arachnoid cyst severely distorting the anteromedial temporal and ventral frontal regions. A 44-year old woman complained of six years of right-sided headaches and suffered from medication-refractory depression. MRI showed a right-sided arachnoid cyst producing brain displacements which mirrored those described above.

Subtle neuropsychologic deficits indicative of frontal dysfunction were detected in each case, but in neither had these been attributed to structural brain disease. Both individuals underwent quantitative F^{18}-fluorodeoxyglucose Positron Emission Tomography (PET), which revealed statistically significant resting hypometabolism in multiple regions of the hemisphere adjacent to the cyst, including neocortical paralimbic areas involved in the modulation of emotional processing and executive functions. These findings suggest that brain compression secondary to long-standing extra-axial cysts in the perisylvian region can induce/release potentially serious comportmental and affective abnormalities.

7-07-33 UTILIZATION AND IMITATION BEHAVIOR ASSOCIATED WITH UNILATERAL DISCRETE SUBCORTICAL LESIONS

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Utilization and imitation behavior was first described by Lhermitte for neurobehavioral disorders due to frontal lobe damage. We observed five cases presenting these conditions resulting from unilateral discrete subcortical lesions. They comprised three cases of striatocapsular infarction (SCI) involving the putamen, caudate nucleus, and/or corona radiata (one left, two right), one case of small right putaminal hemorrhage, and one case of left tuberothalamic infarction involving the dorsomedial, ventral anterior, and ventral lateral nuclei, and the internal medullary lamina. All patients were alert, in terms of neurological response, although they were slightly apathetic and placid. Of these, three cases of SCI showed severe contralateral hemiparesis and mild dysarthria, and two cases had mild hemiparesis. There were contralateral spatial neglect in three cases of SCI, transcortical sensory aphasia in one case of left tuberothalamic infarct, and anomic aphasia in one case of left SCI. Electroencephalography and single-photon emission computed tomography strongly implicated dysfunction of the ipsilateral frontal lobe. Utilization and imitation behavior observed in these cases is considered to be resulted from the release of paricta1 lobe activities triggered by secondary impairment of frontal lobe inhibition due to lesion of the thalamus, basal ganglia, or corona radiata.

7-07-34 NEUROBEHAVIORAL EVALUATION IN PARKISON DISEASE - A STUDY USING EVENT-RELATED POTENTIALS AND MIDDLE LATENCY RESPONSE

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In order to evaluate characteristics of mental function in patients with parkinson disease, event-related potential (ERP) and middle latency response (MLR) were analyzed. The study was carried out on 10 normal individuals and 10 patients with Parkinson disease.

For the ERP and MLR components, latency, amplitude and topographical change on the scalp were determined. Various types of mental state scale such as Mini-Mental State were measured for evaluation of the mental impairment.

Parkinsonian patients showed abnormal ERP(P3) in latency, amplitude and topography on the scalp. Decreased amplitude or topographical abnormality of P1 in MLR was also seen in some patients.

These abnormal ERP and MLR findings tended to be correlated with the mental state scale, though, the correlation was not significant. In addition to that, they showed no correlation with the severity of disease and history length.

These data suggest that there is no relationship between cognitive impairment and severity and history length of disease Parkinsonian patients.

7-17-01 L-DOPA SERUMCONCENTRATION-EFFECT RELATIONSHIP IN FLUCTUATING PARKINSONIAN PATIENTS

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Background: L-dopa-serumconcentration(LSC)-effect relationships of conventional (CV) and slow release (SR) L-dopa have never been exactly described in fluctuating parkinsonian (PD) pats. Plotting LSC vs. motor-effects (ME) usually lead to hysteresis curves whereas relationships between CSF-concentrations and ME are probably linear (after CV L-dopa). Pre-ME lag and minimal effective (treshold) LSC were never quantified exactly. This study is conducted for precise decription of LSC-ME relationships for CV- and SR-preparations in fluctuating PD-pats. Design: 12 fluctuating pats. receiving oral L-dopa 100mg CV, 100mg SR, 200mg SR, 300mg SR in a 4-fold double blind crossover design were investigated. LSC-measurements (HPLC) and standardized clinical ratings (complete CURS + quantitative tests to gait/dexterity) were performed over 6hrs. in 15min. intervalls. Results: Plotting LSC vs.ME after 100mg CV L-dopa showed an hysteresis-curve with delay of ME. Treshold LSC ranged between 600-800ng/ml. Plotting SC vs. ME after 100mg or 200mg SR L-dopa showed delayed LSC increase not reaching treshold-LSC and no significant ME. Plotting LSC vs. ME after 300mg SR L-dopa showed a linear relationship SC/ME with long lasting ME after treshold-SC was reached. According to our data use of L-dopa SR might be advantagous due to linear LSC/ME relationships. To avoid subtreshold LSC use of large single SR-doses is suggested.

7-17-02 BACK ACHE AS A PRESENTING FEATURE OF PARKINSON DISEASE.

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Parkinson's disease has been traditionally described as a motor disorder. Complaints of sensory symptoms are unusual, but seen occasionally during the course of disease. Here we are presenting 18 cases of Parkinson's disease who were treated as "Failed Low Back Syndrome" and had undergone various diagnostic as well as therapeutic procedures for the relief of their back ache. In addition there were 11 cases who presented for their back aches without previous treatments and investigations, which on examination were found to have Parkinson's disease. Back ache as a presenting symptom of Parkinson's disease should always be remembered.

7-17-03 DEPRENYL EFFECTS ON SACCADES AND SMOOTH PURSUIT IN PARKINSON'S DISEASE

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Controversy exists as to whether deprenyl alleviates symptoms or exerts a protective effect in patients with Parkinson's Disease. Quantification of smooth pursuit gains or saccade metrics may demonstrate subtle changes in motor performance that could be missed by clinical motor rating scales. We investigated 13 subjects (ages 44 to 76,median 60, mean 60.9 ± 11.8) diagnosed with idiopathic Parkinson's disease to determine the effect of deprenyl on ocular motor performance. Eye movements were recorded by magnetic search coil technique prior to, and after starting deprenyl for up to 2 years (mean follow-up 5 months). The pursuit target moved horizontally in a sinusoidal pattern ± 10 deg. from midposition at 0.25, 0.5 and 1.0 Hz. Saccades to unpredictable horizontal target steps were recorded. We compared mean differences between pre-deprenyl and post-deprenyl pursuit gains, saccade velocities, accuracies and latencies using paired sample t-tests. Final horizontal pursuit gains showed improvement over the initial recording but the results were not significant (t-tests). We found no differences in saccadic metrics after deprenyl treatment.Our results to date, do not demonstrate a significant "symptomatic" effect of deprenyl on these motor systems.

7-17-04 RESPONSES OF PARKINSONIAN DISABILITY, PHARMACOKINETICS AND METABOLISM OF LEVODOPA TO COMT INHIBITION WITH ENTACAPONE.

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Currently dopadecarboxylase (DDC) is inhibited by DDC inhibitors (DDCI) in the treatment of Parkinson's disease (PD). Thus, methylation of levodopa (LD) becomes the dominant metabolic pathway and therefore inhibition of catechol-O-methyl-transferase (COMT) is important. The aim was to study effects of entacapone (OR-611) on clinical responses, pharmacokinetics and metabolism of LD.

12 patients with advanced PD associated with fluctuations in disability were studied. On day 0 they received only LD+DDCI and thereafter entacapone 800-1200 mg per day with LD+DDCI during 28 days. On day 0, 1 and 28 first dose of medication was taken at 8 a.m. and quantitation of motor response, plasma LD, 3-OMD, DOPAC, HVA, entacapone and its (Z)-isomer were determined in 30-60 min intervals during four hours or until the disability returned to baseline.

Entacapone increased significantly the bioavailability of LD, decreased the mean plasma concentration of 3-OMD and increased the mean plasma concentration of DOPAC. It also significantly increased the duration of clinical response to LD and the severity of involuntary movements.

Thus, peripheral COMT inhibition with entacapone significantly prolongs the antiparkinsonian effect of LD in advanced PD patients with fluctuations in disability.

7-17-05 INTERACTION OF THE COMT INHIBITOR ENTACAPONE WITH L-DOPA IN MPTP TREATED COMMON MARMOSETS

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A major portion of orally administered L-DOPA is metabolised by catechol O-methyltransferase (COMT) to 3-O-methyl-DOPA (3-OMD). The effectiveness and duration of action of L-DOPA may be prolonged by inhibition of COMT activity. For this reason, we have examined the effect of the novel COMT inhibitor entacapone on L-DOPA induced motor activity in MPTP treated common marmosets.

A dose response curve for the ability of L-DOPA (2.5-25 mg/kg plus carbidopa 12.5 mg/kg po) to reverse MPTP induced motor deficits was established to determine effective and threshold drug doses. Administration of entacapone (5.0-25 mg/kg po 30 min previously) potentiated the effect of L-DOPA (12.5 mg/kg) plus carbidopa by prolonging drug action. This effect was not dose related. Entacapone (25mg/kg) prolonged the duration of action of L-DOPA (2.5 mg/kg) without increasing the maximal response. Pretreatment of animals with entacapone (12.5 mg/kg) potentiated the effects of a range of doses of L-DOPA (2.5-18.0 mg/kg) by prolonging the duration of drug effect.

Entacapone is effective in prolonging the duration of effect of L-DOPA without increasing the intensity of response. As such it may be useful in the

7-17-06 ROPINIROLE, A PLACEBO CONTROLLED STUDY OF EFFICACY AS ADJUNCT THERAPY IN PARKINSONIAN PATIENTS NOT OPTIMALLY CONTROLLED ON L-DOPA

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Ropinirole is a novel, selective, non-ergot dopamine agonist with anti-parkinson activity. Preclinical data is predictive of less dyskinetic potential; in open label clinical trial of Parkinsonian patients it was efficacious both as adjunct to L-dopa and in early therapy. We have attempted to evaluate ropinirole as adjunct therapy in patients on L-dopa, exhibiting predictable "on/off" fluctuations and end-of-dose akinesia. Efficacy was sought primarily in terms of reduction in total daily dose of L-dopa with concommitant improvement or maintenance of clinical symptoms (CGI). During the initial incremental dose titration period of ropinirole, L-dopa had to remain constant (6 weeks). Over a second 6 weeks period L-dopa could be reduced. Responder criteria required at least 20% reduction in L-dopa daily dose from baseline, without deterioration of clinical state.

68 patients with a mean age of 63 years were randomized (2:1) to ropinirole (46) or placebo (22). Baseline daily doses of L-dopa were 675 mg (ropinirole) and 520 mg (placebo). Duration of illness was 5.6 yrs and 7.0 yrs respectively. Overall 62.9% of patients on ropinirole and 29.4% in the placebo group ($p = 0.010$) responded to treatment. Side effects were minimal. It is concluded that ropinirole is an efficacious drug in treatment of patients with complicated parkinsonism.

7-17-07 IMAGING OF DOPAMINE-RECEPTORS WITH IBZM-SPECT DURING NEUROLEPTIC MALIGNANT SYNDROME

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Neuroleptic malignant syndrome (NMS) is a severe akinetic-rigid syndrome induced by antipsychotic drugs. We performed IBZM-SPECT for imaging of D2-Dopamin-receptors during acute phase and remission in a 26 year-old patient with NMS. Basalganglia/frontalcortex ratio of IBZM-binding was markedly reduced (F/B 1,18) compared with normal subjects (F/B 1,45). 110 Days after onset of syndromes, during good clinical remission under treatment with Dantrolene, Lisuride and Bromocriptine the IBZM-binding was still reduced (F/B 1,20). With IBZM-SPECT the nearly complete Dopamin-receptor occupation with neuroleptic drugs during NMS can be demonstrated.

7-17-08 IMPAIRMENT OF DISPLACEMENT THRESHOLDS IN PARKINSON'S DISEASE REVEALED BY PSYCHOPHYSICS AND POSTUROGRAPHY.

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Spatiotemporal contrast vision is impaired in Parkinson's disease (PD) probably due to degeneration of amacrine and interplexiform cells. We have measured visual stabilization of posture by a force-measuring platform (Kistler) under four conditions: Eyes open, eyes closed, stroboscopic illumination of the visual surround by 1 and 4 Hz in a dark room. The latter condition caused the retinal image to displace in parallel with body sway. This discontinuous visual input was reproduced using a projector system and measuring psychophysically the lateral displacement thresholds (DT). In PD patients the postural stability significantly worsened by flickering with 1 and 4 Hz compared with controls ($p<0.05$):

Lateral postural sway	Continuous light		Flickering light	
Condition	eyes open	closed	1 Hz	4 Hz
Normals (n=20)	2.53±0.95	3.91±1.86	3.01±1.28	2.91±1.23
PD patients (n=12)	4.53±3.16	5.68±2.83	7.80±5.10	8.28±7.36

With simple background oscillation at 1 and 4 Hz psychophysically measured DTs remained within the normal range. However with synchronous flickering of the light we observed a slight increase of DTs in PD patients compared to normals with 1 Hz, and a marked difference with 4 Hz, which is significant at the 2% level (two-tailed t test). Normals seem to profit from faster flickering to lower their DTs, whereas PD patients don't.

DT (min. of arc)	Background oscillation		Synchronized flickering	
Displ. frequency	1 Hz	4 Hz	1 Hz	4 Hz
Normals (n=9)	2.87±0.86	3.44±0.86	21.8±12.8	9.03±3.65
PD patients (n=12)	3.15±1.23	3.87±1.49	25.0±8.01	23.5±14.7

We conclude that reduced postural adjustments in PD patients probably does not only result from impaired motor control, but from visual deficits in small displacement perception, especially if integration over time is required for successive stimuli.

7-17-09 SUCCESSFUL OXYCODONE THERAPY FOR THE RESTLESS LEGS SYNDROME: A DOUBLE-BLIND STUDY.

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Objective: To establish whether the opioid medication, oxycodone, successfully alleviates the sensorimotor and sleep problems of the Restless Legs Syndrome (RLS). **Background:** While a number of studies have suggested that various opioids may be useful for controlling RLS, no double blind study has found that they have a significant impact on both sleep and sensorimotor dysfunction. **Design/Methods:** 11 patients with symptomatic RLS were studied in a double blind crossover study (control measures, followed by randomized drug and placebo phases) of oxycodone. Patients rated symptoms daily with phone contact and were monitored polysomnographically three times (two nights each time for control and at the end of both phases). 8 subjects were also monitored with bilateral leg actigraphs during each phase. **Results:** Significant improvement was found with oxycodone. Specific measures improved included: subjective ratings of leg discomfort, motor restlessness, and daytime alertness; polysomnographic measures of sleep efficiency, arousal index, and periodic leg movement in sleep (PLMS) index; and actigraphic measures of leg activity. **Conclusion:** Oxycodone is a successful therapy for RLS. Multiple subjective and objective measures of therapeutic response may give a more complete picture of patient improvement.

7-17-10 *SUPPRESSION OF MAGNETIC MU RHYTHM* DURING PARKINSONIAN TREMOR

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We studied five patients with hemiparkinsonism by recording spontaneous magnetoencephalographic (MEG) activity and somatosensory evoked fields (SEFs) with a 24-channel planar SQUID gradiometer. The SEFs of the patients were within normal limits. During tremorless periods, the spontaneous activity over the somatomotor cortex had a frequency peak at approximately 10 Hz in all patients, and another at about 20 Hz in three. Tremor dampened consistently the 10-Hz activity: the effect was bilateral in three patients. MEG activity at the tremor frequency did not increase. The suppression of the mu rhythm by parkinsonian tremor resembled that seen during voluntary movements in healthy subjects.

7-17-11 DEBRISOQUINE HYDROXYLASE GENE POLYMORPHISM AND SUSCEPTIBILITY TO PARKINSON'S DISEASE.

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The cause of Parkinson's disease may be influenced by genetic and environmental factors. Cytochrome P450 mono-oxygenases help to protect against toxic environmental compounds, and individual variations in cytochrome P450 expression might, therefore, influence susceptibility to environmentally-linked diseases. The frequency of mutant CYP2D6 alleles was studied in 229 patients with idiopathic Parkinson's disease and 720 controls. Individuals with a metabolic defect in the cytochrome P450 CYP2D6-debrisoquine hydroxylase gene with the poor metaboliser phenotype had a 2.54-fold (95% CI 1.51-4.28) increased risk of Parkinson's disease. Determination of CYP2D6 phenotype and genotype may help to identify those at greatest risk of Parkinson's disease, and may also help to identify the environmental or metabolic agents involved in the pathogenesis of this disease.

Supported by the Medical Research Council, and Wellcome Trust (UK)

7-17-12 DYSTONIA, BASAL GANGLIA CALCIFICATION & ACANTHOCYTOSIS

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Progressive generalized dystonia demands an investigation for secondary causes. There are a variety of clues that can assist in making a correct diagnosis. Basal ganglia calcification on CT occurs in a limited number of conditions including Hallervorden-Spatz syndrome (HSS)(3 cases). Acanthocytes are commonly requested in the investigation of certain dyskinesias because of the association with neuroacanthocytosis. Additionally, there have been four reports of HSS with dyskinesias & acanthocytes. We report a patient with severe progressive dystonia, basal ganglia calcification & marked acanthocytosis (50%). We are unaware of any previous report of this association.

This 17 year old male, born to unrelated parents, had normal early milestones but was slow to walk independently and was initially thought to have cerebral palsy. At the age of 6 he developed right leg dystonia which steadly progressed to severe generalized dystonia. Additionally there is a supranuclear gaze palsy, generalized brisk reflexes and a yellow discoloration of the palms. His fundus & limb tone is normal. His blood smear shows greater than 50% acanthocytes, confirmed by EM, and the McLeod phenotype was not present. A lipoprotein electrophoresis was normal. Calcification on CT is limited to the globus pallidus.

This patient has characteristics of HSS & neuroacanthocytosis. We will present a discussion and differential diagnosis along with videotape recordings from early age to the present.

7-17-13 CEREBRAL MORPHOLOGIC AND FUNCTIONAL ALTERATIONS IN NEUROLOGICALLY ASYMPTOMATIC WILSON'S DISEASE (WD).

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Morphological (CT/MRI) and functional (PET/SPET) cerebral alterations were described in neurologically impaired WD patients, whereas incostant and aspecific changes were found in patients without neurological symptoms.

We evaluated 6 WD patients (4 neurologically asymptomatic and 2 with minimal symptoms) with MRI (1.5 Tesla) and SPET (two studies were carried out, 3 days apart: the first with the perfusion tracer ^{99m}Tc-HM-PAO, and the second with the dopamine D2 receptor ligand ^{123}I-IBZM). MRI alterations and SPET regional tracer activity deficits were compared with findings in 5 age-matched control subjects.

The two patients with minimal neurological symptoms showed hypointense MRI changes in basal ganglia or mesencephalon, and reduced striatal ^{123}I-IBZM uptake. ^{99m}Tc-HM-PAO SPET showed reduced putaminal perfusion in one case. MRI and SPET alterations were also found in two neurologically free patients. In a patient with severe cirrhosis (candidate for liver transplantation) ^{99m}Tc-HM-PAO uptake was reduced in the fronto-parietal cortex and MRI showed mild cortical atrophy. In the other one, hypointense alterations on MRI, and reduced ^{123}I-IBZM uptake in the basal ganglia regions were noticed.

These findings suggest that subclinical cerebral involvement may be present in otherwise neurologically asymptomatic WD patients. This observation may have therapeutic implications.

7-17-14 DIETETIC HABITS IN PARKINSON'S DISEASE.

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In recent years exist an increasing interest in the investigation of the influence of dietary habits in the etiology of Parkinson's disease (PD), mainly based on the evidence of a dietetic factor in ALS-parkinson-dementia complex and early reports about the role of specific foods with high content in vitamin E in preventing PD. However earlier works had evaluated only isolated foods and a whole dietary assessment has not been made. We have conducted a case-control study to evaluate the influence of dietary habits in the cause of PD, with a semiquantitative food frequency questionnaire that includes all the food items of the usual diet, including salt an other condiments. The study include 50 PD patients and 50 age and sex matched controls. PD patients and controls were obtained in a communitary survey. Only cases with a Hoehn and Yahr stage 2 or greater of the disease were included. The study revealed an increased frequency of intake of fish ($p < 0.024$) and capsaicin containing foods as pepper ($p < 0.027$) or sausage ($p < 0.04$). After Bonferroni correction no statistical significant differences were observed in these items. However, capsaicin is a mithocondrial complex I inhibitor and its possible role in the cause of PD deserves further attention.

(Funded by a grant from the FISS No. 89/743)

7-17-15 SELFMUTILATION IN NEUROPSYCHIATRIC DISORDERS

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Six patients with severe selfmutilation and neuropsychiatric disorders were analysed. One female patient with schizofrenia had perfured her eyes and taken off all her teeth with her fingers. Another female schizofrenic patient had eaten her lips. Two brothers with Lesh-Nyhan disease had injuried their faces using their hands. A mentally retarded child had take off her own hair and bitten her arms and legs. The sixth patient was a men with Pick's disease. He had eaten his own fingers. The selfmutilation is present in many neuropsychiatric diseases as Autism, Gilles de la Tourette syndrome, Cornelia de Lange syndrome, and is related with lesions at the cingulate gyrus although we could not find in our patients any radiological evidence of lesion in this area.

7-17-16 INVESTIGATIONS OF CLINICAL NEUROLOGY AND VOLUNTARY SACCADE ON TOURETTE SYNDROME (TS) SUGGEST HYPOFUNCTIONING OF THE DOPAMINE NEURON

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Hypofunction of dopamine neuron was suggested in some cases of TS.

Seventy cases of TS (64 males and 6 females) were subjected to this study. Their ages at onset were 6.8± 3.0 years and those at initial visit were 13.8 ± 5.7 years. Following neurological signs were quantitatively evaluated: diadochokinesis, muscle tone, including induced rigidity, tilting reaction and side of rotation when stepping with eyes closed. Voluntary saccades were estimated by Hikosaka's method. Neurological findings were reevaluated after levodopa given orally with dosis of 7 mg/kg with maximum dosis of 200 mg.

In 58 cases (83%) dysdiadochokinesis was observed with induced rigidity on the contralateral upper extremity. Mild scoliosis was observed in 58 cases, 45 concave to the right and 13 to the left. Usually, tilting reaction was poor on the convex side of scoliosis. When stepping with eyes closed, 20 of 58 rotated towards the side of concave and another 20 towards the side of convex, while 18 showed no rotation. Voluntary saccade towards the convex side was abnormal (hypometric, infrequent and/or long latency). Neurological signs improved with levodopa in most cases. These features suggested hypofunction of the nigrostriatal dopamine neuron in TS patients.

7-17-17 THE EFFICACY OF VERY SMALL DOSE OF LEVODOPA ON TOURETTE SYNDROME (TS)

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The efficacies of various therapeutic regimens on TS have been controversial.

Based on the neurological and neurophysiological analyses, we had speculated that the dopamine (DA) receptor supersensitivity plays an important role in the pathogenesis of TS. We have administered very a small dose of levodopa to modulate DA receptor supersensitivity.

Sixty-six (61 males, 5 females) patients of TS were administered with levodopa 0.5mg-1mg/kg of body weight, daily. The patients were divided to three groups according to the age of initiation of levodopa and to the duration of the illness before starting levodopa.The effectiveness of levodopa was graded to four from none to good.

The mean ages of onset, initiation of levodopa and duration of the illness before initiation of levodopa were 6.68± 2.96 yrs, 13.80 ± 5.69 years and 7.12 ± 4.71 years, respectively. Levodopa effect was better when started at younger ages and those who suffered from the disease for a shorter period. However no statistically significant differences were observed among groups.

These results support the existence of DA synaptic supersensitivity in the pathogenesis of TS and levodopa can be safely used for the management of TS, especially in younger cases.

7-17-18 THE USE OF MEDICATION IN CHILDREN WITH TOURETTE SYNDROME.

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Increasing numbers of children with Tourette Syndrome (TS) are being identified. Little data is available regarding how many of these patients require medication or for what purposes. TS is now recognized as a disorder that can cause tics, disordered behavior, or both.

We reviewed the charts of 172 patients ages 6 to 15 years to investigate their need for medication. Each had been treated or not based upon their individual needs. 98 of the 172(57%) were not receiving medication. Of the 74 being treated, 55(74%) were on only one medication (19 on a neuroleptic; 13 on clonidine; 23 on a behavior medication). Overall, 36(49%) were on a behavior medication since some were on more than one medication. Psychostimulants were being taken by 16, tricyclics by 19, and obsessive-compulsive medication by 3 patients.

Our experience emphasizes that more than 50% of TS children do not require medication. Of those that do, more require treatment of the associated behavior problems than of the tics.

7-17-19 COMPARATIVE STUDY OF LEVODOPA ABSORPTION AND GASTRIC EMPTYNG TIME IN PARKINSONIAN PATIENT.

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In 1979, Yokochi reported a difference in the time course of plasma levodopa level between early onset parkinsonism(E-PD) and late onset Parkinson's disease(PD) after oral loading of levodopa. In E-PD, the peak was reached much faster and higher than that in PD. A number of factors may influence absorption of levodopa, but among them the gastric emptying time may be one of the most important variables. This question prompted us to investigate the following research subject. We studied the peak time of levodopa absorption(Tmax) and the gastric emptying time(GET) using Acetaminophen in three patients with E-PD having a long history of the disease, three subjects with untreated PD in early stages, and four healthy adult control persons according to the HPLC-UVD and fluorometry methods following the oral administration of 500mg of levodopa or 500mg of Acetaminophen. The Tmax and the GET took different time courses. The Tmax in PD and the control subjects appeared earlier than the GET. While, the Tmax in E-PD was reached more slowly after the GET. By analyzing the backgrounds of those patients, it appeared that the absorption of levodopa was not only dependent on the type of parkinsonism and the GET, but also under the influence of the disease stage. Further studies are in progress.

7-17-20 ROLE OF PRIMARY AND SUPPLEMENTARY MOTOR AREAS IN COMPLEX FINGER MOVEMENT AS STUDIED BY PET.

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Studies of cortical potentials preceding voluntary finger movements suggested an important role of the primary hand sensorimotor area (HSMA) as well as the supplementary motor area (SMA) in the execution of complex movement. This study was aimed at testing the above hypothesis by measuring regional cerebral blood flow (rCBF) with PET using O-15 labeled water in 5 normal subjects. As the result of analyzing the PET data of each individual subject co-registered to his own MRI, the mean rCBF was found to be significantly increased in the contralateral HSMA in both the simple repetitive and complex sequential motor tasks, while the mean rCBF in the bilateral SMAs and the contralateral premotor area was increased only during the complex motor task as compared with the resting condition. However, when compared with the simple motor task, the mean rCBF was increased in the SMA and the ipsilateral HSMA during the complex task. Thus, not only SMA but also HSMA seems to play a critical role in the execution of complex finger movements.

7-17-21 PATHOPHYSIOLOGY OF ESSENTIAL BLEPHAROSPASM AND TORTICOLLIS.

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In the recent literature Benign Essential Blepharospasm (BEB) and Spasmodic Torticollis (ST) are considered under the heading of extrapyramidal movement disorders.

Thirty-five BEB and twenty ST patients were examined with the exteroceptive suppression (ES) test. ES was recorded from both masseter muscles after stimulation of each mental nerve at 20 and 80 mA, being 20 mA already supramaximal for normal subjects. Duration of early and late inhibition of voluntary electromyographic (EMG) activity was considered for each stimulus intensity.

ES could be seen in 100% of BEB and 85% of ST patients at 80 mA, while only 6% of BEB and 25% of ST patients had normal neurophysiologic responses at the usual stimuli of 20 mA.

Our data suggest an organic cause of BEB and ST. Reduced inhibition of the motor trigeminal nucleus by cutaneous afferents may be due to reduced activity of interneurons in the bulbopontine region.

7-17-22 ANALYSIS OF AUTOMATED HANDWRITING MOVEMENTS TO QUANTIFY DOPAMINERGIC EFFECTS IN DE NOVO PATIENTS WITH PARKINSON SYNDROME

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Amelioration of Parkinsonian signs following dopamimetic therapy supports the clinical diagnosis of Parkinson's disease. We studied the objective effect of the dopamine agonist apomorphine in the early stages of the disease on automated handwriting movements with a computer assisted system.

30 patients with previously untreated ("de novo") predominantly right sided Parkinson syndrome and 41 controls were investigated. Subjects drew 12 mm diameter circles fluently in a counter-clockwise direction with a high repetition rate for 3 seconds, using a special writing stylus connected to a digitizing board (TDS ZedPen). Analysis was repeated 30 min after injection of apomorphine s.c. We analyzed peak acceleration and acceleration changes per segment using a microcomputer. The results were compared to a clinical score (Unified Parkinson's Disease Rating Scale (UPDRS) part III).

Controls had acceleration changes (NCA) of 1.0 to 1.4 per segment. Before injecting apomorphine, 28 out of 30 patients had significantly higher NCA values up to 4.0. After the injection of apomorphine, 20 of these had clear improvement in UPDRS whilst 18 had clear improvement in NCA. 10 showed no such improvement, whilst 8 had no clinical improvement.

The improvement of automated handwriting movements, as shown by objective analysis with the computer assisted system, correlated well with clinical scoring (UPDRS).

7-17-23 SERUM DEHYDROEPIANDROSTERONE AND CORTISOL MEASUREMENTS IN HUNTINGTON'S CHOREA - A PRELIMINARY REPORT

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Serum levels of dehydroepiandrosteroncsulfate (DHEAS), known to antagonize metabolic effects of glucocorticoids in animals, and cortisol (CRT), already shown to be related to cognitive dysfunction in humans and animals (Leblhuber et al, Psychopharmacology 1993; Wolkowitz et al, Am J Psychiatry 1992), were measured in eleven drug-free male subjects (aged 39,4+/-13,8) with definite Huntington's chorea (HC) and in twentyfive age matched male normals (aged 37,8+/-10,2). Routine blood and urine parameters were studied in all patients. Blood samples for DHEAS and CRT were obtained after an overnight fast at 8 am, all samples were stored at -20°C and tested in the same assay, using commercial kits (DHEAS - Diagnostic Products corporation, CRT - Abbot, method tdx). Statistical difference was found between patients and controls with lower DHEAS serum levels in HC subjects ($p<0.01$). Similar to earlier studies (Heuser et al, Biol Psychiatry 1991), significantly higher CRT levels were found in HC individuals as compared to age matched controls ($p<0.01$), consequently, the DHEAS/CRT ratio differed significantly between the latter groups, revealing a lower mean ratio in HC patients ($p<0.01$).

These findings indicate a dysfunction of the hypothalamic-pituitary-adrenal axis and suggest a possible role of DHEAS as an antiglucocorticoid (Wolkowitz et al, Am J Psychiatry 1992) in the treatment of HC.

7-17-24 NIMODIPINE IN MOVEMENT DISORDERS

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The objective of this study is to assess the clinical efficacy of nimodipine in movement disorders. Nimodipine, a calcium channel block agent, readily crosses the blood brain barrier.

We have studied 30 patients, 16 males and 14 females with a mean age of 32 years (range 16 to 72). Seven patients had torticollis, 3 focal limb dystonia, 2 generalized dystonia, 5 tremors (3 cerebellar, 2 essential familial), 3 chorea, 3 tics, 2 spinal myoclonus, 2 hemifacial spasm, 2 painful leg moving toes and 1 large amplitude benign fasciculations. Nimodipine was administered 30mg orally 4 times daily for two weeks. The patient's movements were clinically rated and videotaped before and after administration if nimodipine. A neurologist unfamiliar with the patients rated the changes seen on videotapes.

All three patients with cerebellar tremor indicated improvement which in 2 of them was also clinically rated as significant. Nimodipine failed to improve focal, segmental or generalized dystonia. Patients with chorea worsened with nimodipine. These preliminary results suggest effectiveness of nimodipine in some patients with cerebellar tremor. The effect of nimodipine on cerebellar tremor deserves further investigation under a double blind protocol. A videotape showing these patient's response will be presented.

7-17-25 RELATIONSHIP OF ESSENTIAL TREMOR TO OTHER MOVEMENT DISORDERS.

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Controversy exists concerning the relationship of essential tremor (ET) and other movement disorders. It has been suggested that 20% of ET develop Parkinson' disease (PD) and that 47% have dystonia (Neurology 1991;41:234). However, others have not found such a strong association.

To further evaluate ET comorbidity, we prospectively collected data in the Movement Disorder Clinic on 276 ET patients (148 male, 128 female) with an average age of 67.6 yrs. A positive family history for tremor was present in 63.07% and alcohol reduced tremor in 35%. 25% of patients did not drink alcoholic beverages.

We found that 12 patients had PD (4.35%), 25 had a resting tremor without other PD signs which was thought to be related to ET. The frequency of dystonia was 2.97% (5 with spasmodic dysphonia, 2 with blepharospasm and 1 with torticollis). One patient had myoclonus and one patient had painful leg and moving toes syndrome.

It is concluded that the ET is only rarely associated with other movement disorders and that ET is not a risk factor for PD.

7-17-26 THE CHRONIC USE OF L-DOPA METHYL-ESTER IN THE MANAGEMENT OF PARKINSON'S DISEASE

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L-Dopa Methyl Ester is a less acid and more soluble prodrug of L-Dopa. In a number of studies had been demonstrated that L-Dopa M.E. is more rapidly absorbed and produce a more predictable clinical response than standard L-Dopa formulations.We tested the clinical chronic application of L-Dopa ME in different condition: single treatment, combined with DAagonists continuous infusion, Sinemet CR and standard formulation of L-Dopa.

As single treatment the ME was given with oral carbidopa, in 6 patients. The esther was more predictable in producing the clinical effect than conventional therapy. The drug was effective in all the pts.showing a very good tolerability.Combined with the slow release preparations of L-Dopa (6pts.) the Ester ensured a rapid clinical effect significantly reducing the long latency to "ON"and ensuring a more prolongod effect. L-Dopa ME was administered in 15 pts treated with subcutaneous DAagonist continuous infusion (15 pts) to ensure the minimal effective dose of L-Dopa .In 6 pts treated with standard preparation of L-Dopa the ME was given instead of the ineffective doses (i.e. the first dose in the afternoon).

In this condition the Ester was faster in action and more predictable than the standard formulation. The pts have been treated chronically for 6-24 months.The drug has been effective in all the condition showing a shorter latency to ON than the standard formulation.Another great advantage of this prodrug is that being liquid it can be easily administered at different dosages according to the patient needs.Moreover the drug is more predictable in action because more adsorbable.

Note: New number 7-17-27 see 8-17-22 for Abstract.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-18-01 NEUROMYELITIS OPTICA - A NOSOLOGICAL ENTITY ?

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Since the early times of DEVIC (1894) it has been disputed, if neuromyelitis optica (NMO; Devic's disease) should be considered a nosological entity among the group of demyelinating diseases, or solely as a special variant of encephalomyelitis disseminata (ED). Considering the clinical and relatively rare pathoanatomical criteria that have been reported so far, it is conceivable that NMO indeed shows similarities to both ED and inflammatory diffuse sclerosis.
We report two cases of NMO, one of which (case 1) has been reported already in the past (Neuro-ophthalmology 4:81-85(1984)) because of its fast and complete restitution from severe encephalomyelitic deficits. This total restitution was confirmed in a recent check that included MRT, spinal tap and evoked potential measurements. No signs of NMO or ED were found. Case 2 was a 33 years old man with sudden and severe initial deficits, such as paraplegia of the legs and complete visual loss due to acute bilateral optic neuritis. Whereas the visual loss was persistent, the spinal symptoms did resolve completely within three months. Results of MRT, spinal tap and evoked potential studies will be reported with special reference to the course of his recovery.
Considering both the characteristical clinical findings in NMO and in particular the complete remission over almost ten years in case 1 as well as remission of all spinal symptoms especially shown trough MRT in case 2, we suggest that NMO indeed is a nosological entity among the group of demyelinating diseases and not a variant course of ED.

7-18-02 NON-HERITABLE DEFICIENCY OF ERYTHROCYTE COMPLEMENT RECEPTOR /C3b/ IN MULTIPLE SCLEROSIS

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The study was carried out in patients with MS /n-121/ and in control group /n-519/. On the basis of haemagglutination intensity and results of radioimmunoassay three phenotypes of complement receptor were isolated: high HH, medium HL, and low LL. Considerable differences were observed in the distribution of these phenotypes between controls and MS in whom the low phenotype /$C3bR^1/C3bR^1$/ was more frequent. Family studies of controls suggested presence of two codominant alleles $C3bR^n$ and $C3bR^1$ with Mendelian inheritance while in similar studies in MS it was found that e.g. a child with MS whose parents had high C3bR phenotypes, that it were homozygotes for the $C3bR^n$ gene, had low phenotype. On the other hand, the high phenotype was found in a child of a female with MS with the low phenotype /$C3bR^1/C3bR^1$/. These observations suggest that reduced expression of the complement receptor on the erythrocytes depends in MS on the disease process in the first place, and not on genetic factors.

7-18-03 AN INVESTIGATION INTO THE CONTRIBUTION OF LEBER'S MITOCHONDRIAL DNA MUTATIONS TO MULTIPLE SCLEROSIS

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A small number of female patients presenting with optic neuropathy and harbouring a Leber's Hereditary Optic Neuropathy (LHON) mutation, 11778bp, later developed a neurological disorder indistinguishable from Multiple Sclerosis (MS). These observations may indicate a contributive role for mitochondrial genes in the genetic susceptibility to MS. We have screened 277 unrelated MS patients for the class I and most frequent LHON mutation, 11778bp and a class II LHON mutation at position 13708bp. Additionally, 21 of the MS patients whose initial presentation was a bilateral or unilateral optic neuritis were screened for the class I mitochondrial mutation at position 3460bp. Neither of the class I motochondrial DNA mutations occurred in these MS patients, although one harboured a mutation adjacent to 11778bp that was inherited in a matrilinear mode. The class II LHON mutation, 13708bp was also not present in MS patients at a significantly greater frequency than in healthy controls. Thus, it would appear that these LHON associated mtDNA mutations do not contribute to genetically determined susceptibility in most MS cases. However, a subgroup of female MS patients, whose primary presenting complaint is severe visual failure due to optic neuropathy, may harbour a LHON mutation and we suggest that mitochondrial DNA analysis should be performed in these patients.

7-18-04 AXONS INFLUENCE THE PROLIFERATION, DIFFERENTIATION AND GANGLIOSIDE EXPRESSION OF GLIAL PROGENITOR CELLS

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Oligodendrocytes synthesise myelin in the mammalian central nervous system; they are derived from progenitors which in vitro may also differentiate into astrocytes (Raff et al 1983). Maturation of the glial O-2A progenitor is influenced, in vitro, by astrocyte derived growth factors and by extracellular matrix molecules, some of which have been identified. We have investigated the effect of axons on glial development by co-culturing highly purified embryonic dorsal root ganglia (DRG) with neonatal glial progenitors. Axons produce signals, including platelet derived growth factor (PDGF) which cause progenitor cells to proliferate and, whilst allowing the normal process of myelination to take place, promote the differentiation of stellate cells which resemble type 2 astrocytes. Whilst most O-2A cells grown in the absence of neurons express complex gangliosides including GD3, their expression is down regulated and there is a slowing of galactocerebroside and myelin basic protein expression when progenitors are cultured under low serum conditions and in the presence of axons. The combined data indicate that myelination involves a complex interplay between glial progenitors, axons and growth factors and demonstrates that this aspect of central nervous system development cannot easily be studied in single cell culture systems. Studies such as these, which illuminate factors influencing the fate of glial progenitors have relevance to multiple sclerosis where a failure of remyelination is accompanied by astrocytosis.

7-18-05 THE COMBINED ROLE OF TCR BETA LOCUS AND HLA DR2 IN THE GENETIC SUSCEPTIBILITY TO MULTIPLE SCLEROSIS.

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The importance of genetic factors in susceptibility to multiple sclerosis has been clearly demonstrated by population based twin studies. We have adopted a candidate gene approach to identify the genes responsible. T cells are central to immune function and the genetic control of their antigen receptor has been studied in a number of autoimmune diseases including multiple sclerosis. We have studied 90 sibling pairs using the method of identity by descent and provide evidence for linkage to the TcR beta locus (7q 32-35). The maximum Lod score is > 2.7 ($p<0.001$).

Stratification of the patients to include those pairs who share the HLA haplotype DRw15/DQw6, increased the bias in haplotype sharing from 0.14, 0.40, 0.46 for sharing 0, 1, or 2 haplotypes to 0, 0.5, 0.5, each compared with the expected rates of 0.25, 0.50, 0.25. We conclude that the TcR beta locus contributes to disease susceptibility and we provide evidence for an additional role for the presence of DRw15.

7-18-06 THE ROLE OF IMMUNOGLOBULIN HEAVY CHAIN VARIABLE GENES IN SUSCEPTIBILITY TO MULTIPLE SCLEROSIS.

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There is a significant genetic component to susceptibility in multiple sclerosis, which involves more than one locus. Using the method of identity by descent in affected sibling pair we have studied 90 pairs in an attempt to prove or refute linkage of disease susceptibility to the variable region of the immunoglobulin heavy chain locus (chromosome 14q 32). We have used three polymorphisms from the proximal end of the variable region of the heavy chain and assigned haplotypes sharing of 0.09, 0.50, 0.41, compaired to expected rates of 0.25, 0.50, and 0.25. This gives a maximum Lod score of over 1.9 ($p<0.01$). The HLA haplotype DRw15/DQw6 is known to be associated withmultiple sclerosis in Caucasians, in 23 pairs both affected individuals carried this haplotype and an analysis of these families showed an increase in the haplotype sharing of 0., 0.44, 0.56 increasing the Lod score to 2.15. This study provides strong evidence for the linkage of the Ig heavy chain locus to disease susceptibility in multiple sclerosis especially in the context of HLA DRw15.

7-18-07 NEW ASSOCIATION BETWEEN MULTIPLE SCLEROSIS AND HLA IN CAUCASIANS OF SOUTH-SPAIN.

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Backgrounds and Methods: In the south of Europe many studies can not find any association between multiple sclerosis (MS) and HLA system or their results have demonstrated a weak linkage. In this study, HLA phenotypes (tested by alloantisera) of 60 MS cases (according to Poser's criteria) were comparated against 100 healthy controls. Cases and controls were caucasians living in Cadiz (south-west of Spain) and intragroup Hardy-Weimberg equilibrium was confirmed (ABO blood groups). Results were analized by different statistical tests (Yates correction X2, Fisher exact test, Bonferroni correction, etc.).
Results: Although in global cases DR6 (as protector) and DR2 (risk) seem to be significative, stratification by clinical-epidemiologic variables proved that DR6 was really associated with relapsing/remitting course (p=0,0015) and DR2 was really associated with relapsing/remitting males (p=0,000006).
Conclusions: New MS-HLA associations are described in a South-Spanish caucasian population. In these studies, stratification of cases by clinical-epidemiologic variables in proven to be very important in order to found the true specificity and the propoer linkage.

7-18-08 THE ASSOCIATION BETWEEN MULTIPLE SCLEROSIS AND HLA SYSTEM REFLECTS: A DYNAMIC AND HETEROGENEOUS PATTERN IN A SPANISH POPULATION

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Background and Methods: We have studied the association between multiple sclerosis (MS) and the HLA system by analyzing this linkage in relation with several epidemiologic variables (year of birth, year of onset and age of onset). HLA phenotypes (tested by alloantisera) of 60 MS cases (according to Poser's criteria) were compared against 100 healthy controls. Cases and controls were caucasians living in Cádiz (south-west of Spain) and intragroup Hardy-Weimberg equilibrium was confirmed (ABO blood groups). Results were analyzed by different statistical tests (Yates correction X2, Fisher exact test, Bonferroni correction, etc.). Results: Previously described associations (DR6 and DR2) were not related with year of birth and year of onset. But the analysis by year of birth discovered interesting findings in some HLA antigens: superpublic specificity Bw4 was protective of MS in patients born between 1950 - 59 (Odd Ratio = 0,23 p = 0,01). A2 antigen, that was not a risk factor for MS in the 1940 - 49 decade, had increased lineary as risk factor until today (Odds Ratio = 10,07 for people born between 1970 - 75). On the other hand, the analysis by age of onset demonstrated that protective effect of DR6 is maximum when MS onset occurs at 20 - 29 years old, independently of sex and clinical course.

Conclusions: MS-HLA association seems to be a very complex, heterogeneous and dynamic feature. Our results also suggest that possible factor acquired at very young age are more important than relapsing factors acquired at older age, as related to HLA-MS linkage.

7-18-09 IS GADOLINIUM ENHANCEMENT USEFUL IN MONITORING TREATMENT IN MULTIPLE SCLEROSIS?

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Serial unenhanced T_2-weighted brain MRI in multiple sclerosis (MS) detects many new asymptomatic lesions, which implies that MRI will be helpful in monitoring treatment. However, it is uncertain whether gadolinium enhancement detects more activity than what is seen on the unenhanced scan.

We therefore analyzed both the T_2-weighted and gadolinium enhanced scans obtained in twenty five patients with relapsing remitting or secondary progressive MS. Four consecutive monthly scans were reviewed. All new, enlarging or enhancing lesions were regarded as active.

A total of 106 active lesions were seen: 68 were seen only with enhancement, 16 only on the T_2 scan, and 22 were active on both sequences.

Thus gadolinium enhancement markedly increases the amount of activity seen on monthly brain MRI in relapsing remitting or secondary progressive MS, and its use should increase the power of MRI to detect therapeutic effects in such patients.

7-18-10 THE 'INVISIBLE' LESION LOAD IN MULTIPLE SCLEROSIS (MS) ASSESSED BY PIXEL-BY-PIXEL RELAXATION TIME (RT) MAPPING.

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We aimed (i), to define RT abnormalities in abnormal and normal appearing white matter (NAWM) in MS and (ii), to quantitate any abnormal white matter not visualized on conventional MRI.

We used pixel-by-pixel (1.5T, 256 x 256 matrix, resolution 0.94mm) mapping of T1 and T2 RTs in 5 patients with CDMS and 5 matched healthy subjects. Mean T1 and T2 values across all pixels in the NAWM of patients were prolonged (p <.04). This was due to averaging RTs from two subfractions of NAWM: pixels with normal RT averaged 54% (T1 estimates), or 63% (T2) of the total white matter in each slice ('normal NAWM', or NNAWM) whereas pixels with abnormal RT averaged 36% (T1) or 27% (T2). The latter were scattered randomly throughout NNAWM in areas of several pixels or less, comprising on average, 47% (T1) or 57% (T2) of all pixels with abnormal RT.

NAWM in MS contains both normal (NNAWM) and abnormal tissue. Discrete lesions 'invisible' to MRI constitute a significant proportion of the total lesion load. Their precise nature and relevance to the functional deficit need to be defined.

7-18-11 PROGRESSION AND CLINICAL PARAMETERS IN MULTIPLE SCLEROSIS.

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We tried to determine in a prospective study if clinical parameters indicating a good evolution are available in Multiple Sclerosis (MS).

Patients and methods.-Fifty-seven definite MS patients were studied along a 12-48 months period (47.5±26). The patients were 38±9 year-age average. The average age of onset was 27±9 years. A clinical follow-up rating onset and course type was made. We found 30 remittents, 19 remittent-progressives and 8 chronic-progressive forms.The Kurtzke scale was applied and the progression index (PI) computed

Results.-Nine of thirty patients labed as remittent forms at onset were considered remittent-progressives at the end of the follow-up. The global PI was 0.45±0.7 p/y and was only less in the non-evolutive remittents forms (0.14±0.6 p/year), in opposition of the other forms (Progressive forms 0.88±1.2, remittent-progresive forms 0.56±0.6 p/y), p=0.02. No sex or onset mode was a differential factor in the progresion index.

Conclusion.- The only prognostic factor of minor evolutive progression is for the patients to remain in the remittent phase.

7-18-12 CHANGES IN LYMPHOCYTE SUBSETS IN POSTINFECTIOUS ENCEPHALOMYELITIS

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In order to clarify the immunological abnormalities in postinfectious encephalomyelitis (PIEM), peripheral blood lymphocyte subsets were analyzed by 2-color immunofluorescence flowcytometry in 6 patients with PIEM.

In the active stage of the disease, the relative percentage of CD4-positive suppressor-inducer cells ($Leu3a^+$ $Leu8^+$) was significantly higher than that in healthy controls ($p<0.05$). No significant differences were found between patients with PIEM and healthy controls in CD4-positive helper cells ($Leu3a^+Leu8^-$) and CD8-positive suppressor/cytotoxic cells ($Leu2a^+Leu15^+$). However, the suppressor-effector cells ($Leu2a^{high+}$ $Leu15^{low+}$) in the active stage of PIEM were significantly lower in number than in healthy controls ($p<0.05$).

It is suggested that an aberration of the immuno-regulatory mechanism, such as failure to induce suppressor-effector cells in the active stage of the disease, might play a crucial role in the evolution of PIEM.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-18-13 **SERUM ANTIPHOSPHOLIPID ANTIBODIES IN PATIENTS WITH MULTIPLE SCLEROSIS**

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We measured serum antiphospholipid antibodies (APLA) in patients with multiple sclerosis (MS) using ELISA and examined the correlations between these antibodies and MS. The study included twenty patients with clinically definite MS, twelve patients with other autoimmune neurological diseases (disease control) and twenty-five healthy persons (normal control). IgG antibody against cardiolipin (CL) in the presence of cofactor (beta-2 glycoprotein I) was detected in 2, and IgM antibody in 10 of 20 patients with MS. This figure was significantly higher than that of the disease and normal controls. Results of antibodies against phosphatidylserine were found similar to CL, but antibodies against phosphatidylcholine were all negative. In addition, the APLA positive group in MS possessed at higher rate the other autoantibodies such as antinuclear antibody than the negative group.The serum autoantibodies in MS observed here may not link directly to the pathogenesis of central inflammatory demyelination. The higher incidence of APLA may, however, imply that a broad spectrum of autoantibodies might be produced in MS; some antibodies presumably related directly to MS pathogenesis are yet to be identified but APLA might be one of those antibodies which are to be tested for the capability of central inflammation and demyelination.

7-18-14 TOTAL LYMPHOID IRRADIATION IN MULTIPLE SCLEROSIS

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24 patients with chronic progressive multiple sclerosis were randomly assigned to receive 1980 cGy total lymphoid irradiation (TLI) or sham irradiation double blind and three patients were treated openly but assessed blind. The groups were well matched for age, Kurtzke expanded disability status score (EDSS) and deterioration in the year before entry. Change in EDSS score was the primary outcome measure. Patients were also assessed using magnetic resonance imaging (MRI) of the brain at 6 month intervals, psychometry and other measures of physical disability.

There was a small but significant difference in the rate of accumulation of lesions over two years favouring the TLI group. No major significant benefit was demonstrated on the EDSS, other physical scales or psychometry. The treated group had a higher incidence of infections, courses of antibiotics and amenorrhoea than sham treated in the follow up period.

The findings do not support the routine clinical use of lymphoid irradiation in chronic progressive multiple sclerosis.

7-18-15 A DOUBLE-BLIND RANDOMIZED STUDY OF ORAL PREDNISOLONE VERSUS PLACEBO IN PATIENTS WITH ACUTE OPTIC NEURITIS.

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During 5 years from August 1th 1987,128 patients with acute optic neuritis(ON),consecutively referred from neurologists and ophthalmologists from a well-defined catchment area(1.5 millions),were included in a single center treatment trial.Patients were randomly assigned to recieve oral prednisolone(50mg/day for 10 days tapered off during 15 days) or oral placebo. Patients with previous ON ipsilaterally were excluded. The patients(aged 18-57,median 32 years)were thoroughly examined immediately at referral(i.e. within 4 weeks from onset) and in 37 the ON was part of CDMS.In the remaining patients no known ethiologies of ON were revealed.Patients were followed with a battery of tests of visual function 1,2,4,8,12 and 52 weeks from referral.At onset ophthalmoscopy revealed a blurred disc in 41,a slight disc pallor in 12 and a normal disc in 75 patients.A relative afferent pupillary defect was present in 82% of patients.Median visual acuity was 0.2(NLP-1.0).As the visual function was assessed over a twelwe-month follow-up period,the study is still in progress,but results will be presented. At onset serologic studies,lumbar puncture,SEP,biotesiomotry and MRI were performed,too.

7-18-16 MULTIPLE SCLEROSIS AND MACROCYTOSIS: MEAN CELL VOLUME IN 63 PATIENTS

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A relation between Multiple Sclerosis (MS) and macrocytosis has been described in some recent papers. Although its pathophysiology is unknown, the last observations suggest that a B_{12} vitamin metabolic, binding or absortion disturbance may play an essential role on it.

A retrospective study of the Mean Cell Volume (MCV) as a parameter of macrocytosis, has been carried out in 63 patients with a definite MS (following the Poser's criteria), and compared with an age and sex-matched control group of 63 healthy, free of risk factors and unselected people.

For the statistical studies we applied a mean comparison by the Student-Fisher's test and two-tailed F test for homogeneity of variances, based on the Snedecor's law.

Our group did not find statistically significative differences between the MCV of the whole MS group and the control group. It is only possible to point out that, although there was not any difference between both groups of women, the male MS patients group had a MCV significantly lower than the control group.

Our study does not confirm the significant differences in the MCV between MS patients and a control group, previously described in similar studies. Further investigations will be necessary to understand the differences found only in males in our series.

7-18-17 A DOUBLE-BLIND RANDOMIZED STUDY OF PREDNISOLONE PERORALLY VERSUS PLACEBO IN PATIENTS WITH ACUTE OPTIC NEURITIS.

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During 5 years from Augustlth 1987,128 patients (69%F) with acute optic neuritis(ON),consecutively referred from neurologists and ophthalmologists from a well-defined catchment area(1.5mill) were included in a single center treatment trial Patients were randomly assigned to recieve oral prednisolone(50mg/day for 10days,tapered off during 15 days) or placebo.Patients with previous ON ipsilaterally were excluded.The patients(aged 18-57,median 32 years) were thoroughly examined immediately at referral(i.e. within 4 weeks from onset) and in 37 the ON was part of CDMS. In the remaining 91 no known ethiologies of ON were revealed. Patients were followed with a battery of tests of visual function 1,2,4,8,12 and 52 weeks from referral. At onset,ophthalmoscopy revealed a blurred disc in 41,a slight disc pallor in 12 and a normal disc in the remaining 75 patients. A relative afferent pupillary defect was present in 82% of patients.Median visual acuity was 0.2(NLP-1.0).As the visual function was assessed over a 12-month follow-up period,the study is still in progress, but results will be presented. At onset serology,lumbar puncture,SEP and MRI were done.

7-18-18 CYTOKINE EXPRESSIONS AND CLINICAL MANIFESTATIONS IN PATIENTS WITH HAM/TSP:STUDIES IN 15 PATIENTS.

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Recent studies indicated that the elevation of interleukin-6(IL-6) in the cerebrospinal fluid(CSF) of patients with HAM/TSP. We studied that if there is a correlation among cytokine activity of CSF,clinical manifestations, inflamatory findings of CSF and anti-HTLV-I antibody (serum,CSF) of HAM/TSP patients. Cytokine activity (IL1-beta,IL-6 and TNF-alpha) of CSF were studied by an ELISA, and clinical manifestations, inflamatory findings of CSF and anti-HTLV-I antibody(serum,CSF) of 15 HAM/TSP patients (9 men and 6 women, ages 31 to 67) were reviewed. An elevation of IL-6 was observed in CSF in 9 out of 15 patients. TNF-alpha and IL1-beta showed no significant difference between HAM/TSP cases and controls. There was no correlation between the value of IL-6 and clinical severerity, inflamatory findings of CSF and anti-HTLV-I antibody(serum,CSF). HAM/TSP patients with other diseases (Sjögren syndrome and thyroiditis,uveitis and HAB, mycosis fungoides, and psoriasis) showed an elevated IL-6 activity.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-18-19 COMPARISON OF CSF FINDINGS AND MRI WITH GADOLINIUM_ DTPA IN PATIENTS WITH ACUTE MONOSYMPTOMATIC OPTIC NEURITIS.

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We prospectively examined thoroughly 44 patients(3oF) with idiopathic acute monosymptomatic optic neuritis. Patients(18-57,median 32 years) were consecutively referred from neurologists and ophthalmologists from a catchment area of 1.5 millions.The interrelationships of CSF findings and MRI at 1.5 T(double SE and IR) were as folows:Of the 6 patients with Gd-DTPA enhancing lesions on MRI, 5 had OB,1 increased IgG-index and 2 pleocytosis in the CSF. Of the remaining 38 patients, these abnormalities were present in 39%,24% and 29%, respectively. Of the 19 patients with abnormal MRI prior to i.v. Gd-DTPA,68% had OB,26% increased IgG-index and 32% pleocytosis in the CSF as compared to 28%, 2o% and 28%,respectively, of the 25 patients with completely normal MRI.
In conclusion, OB(but not increased IgG-index and pleocytosis in the CSF) was more frequently observed in patients with lesions on MRI (with or without Gd-DTPA) than in those patients with acute monosymptomatic optic neuritis with normal MRI.

7-18-20 GENETIC SUSCEPTIBILITY TO MULTIPLE SCLEROSIS (MS) LINKED TO MYELIN BASIC PROTEIN GENE

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Objective. Genetic factors have been implicated in the etiology of MS, but the genes conferring susceptibility to the disease have not been identified.

Methods. We performed genetic association and linkage analyses by studying a multiallelic tetranucleotide repeat polymorphism 5' to the myelin basic protein (MBP) gene, a relevant candidate gene, in 21 MS families, in 72 non-related patients with definite MS and in 85 controls. Most of the families originated from an area with high prevalence and familial clustering of MS. Magnetic resonance imaging (MRI) was used to examine the asymptomatic members of the families.

Results. In the association analysis a 1.27 kilobase allele was found in 50.0% of the patients and in 23.5% of the controls (P=0.001, Relative Risk 3.3). In the linkage analysis, using autosomal dominant model, a maximum LOD score of 3.42 (θ=0.00) was obtained when patients with optic neuritis and asymptomatic subjects with abnormal MRI were classified as 'affected'. When they were classified as 'unknown' the maximum LOD scores ranged from 2.99 to 3.25 (θ=0.00).

Conclusion. The results provide evidence that genetic predisposition to MS is closely linked to the MBP gene. This further suggests that variation in the MBP gene or in its close vicinity has a role in the etiopathogenesis of MS.

7-18-21 HLA-DQA1 AND -DQB1 ALLELES IN UNRELATED SARDINIAN MULTIPLE SCLEROSIS PATIENTS

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Sardinian population differs from Caucasians in genetic characteristics. Regarding multiple sclerosis, in Sardinians the disease is associated with DR4 (Marrosu et al, Neurology, 1988,38,1749-1753), while with DR2 in Caucasians. We studied the representation of HLA-DQB1 and -DQA1 alleles in 116 unrelated Sardinian multiple sclerosis patients (UMS) and 86 healthy Sardinian controls. Allele identification was performed by dot-blot analysis with specific oligonucleotide probes after PCR amplification. In UMS, compared with controls, an increased frequency of the DQB1*0201 (p<.05) and *0302 (p<.01) (confirming our previous results, Marrosu et al., Neurology 1992,42,883-886) and DQA1*0301 (p<.001) alleles was found. On the other hand, DQB1*0502 (p<.05) and DQA1*0102 (p<.05) alleles showed a decreased frequency. Some differences were noted between groups of patients with different evolutive course. Moreover, the analysis of the frequency of DQB1 alleles encoding for the aminoacid leucine in position 26 (Leu^{26}) showed that 52.2% of 92 UMS, compared with 33.5% of 88 controls (p=.0002), were found to be positive for the DQB Leu^{26} residue.

7-18-23 HLA AND T CELL RECEPTOR POLYMORPHISMS IN THE BELGIAN MULTIPLE SCLEROSIS POPULATION

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There are compelling data to indicate that the susceptibility to Multiple sclerosis (MS), a disease of the central nervous system, is inherited. Particular HLA haplotypes may be associated with MS and recently also the T cell receptor (TCR) α and β chain complex has been reported to correlate with the disease. We investigated the TCR α and β chain genes of Belgian MS patients, with known HLA genotype, employing four DNA restriction fragment length polymorphisms (RFLPs) detected with TCR constant (Cα, Cβ) and variable (Vβ8, Vβ11) gene segments.

The frequency of these polymorphic α and β alleles was not significantly different between MS patients as compared to a panel of healthy control individuals. Although HLA-DR2 (DRw15) was significantly associated with MS, no interactive effects were seen with MS, DR2, Cα, Cβ and Vβ, implying that the combined presence of these polymorphic markers is not essential for increasing susceptibility to MS.

7-18-24 HICCUP: AN UNCOMMON PRESENTATION OF MULTIPLE SCLEROSIS

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Brain stem form of multiple sclerosis commonly presented with dizziness, vertigo, double vision and unsteadiness of gait. Hiccup is a rare and unfamilar initial symptom. Three patients presented with intractable hiccup lasting for weeks begore other brain stem symptoms and signs developed. MRI showed increased signal intensity at the medulla and upper cervical region on T2- weightied imaging. They subsequently ran an exacerbating and remitting course of illness typical of multiple sclerosis. Therefore, multiple sclerosis should be considered as a possible cause of intractable hiccup.

7-18-25 DOES GLYCOSYLATION CONTRIBUTE TO THE OLIGOCLONAL APPEARANCE OF INTRACEREBRALLY SYNTHESIZED IGG ?

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Despite the importance of an oligoclonal IgG band pattern for the diagnosis of multiple sclerosis, surprisingly little is known about its chemical basis. Even monoclonal IgG is split up into 3-14 bands after isoelectric focusing (IEF) on polyacrylamide gels, a phenomenon commonly attributed to postsynthetic deamidation and glycosylation. Similar effects might be working on oligoclonal IgG. Sera from 12 patients with IgG plasmocytoma were used directly for the investigation of monoclonal IgG, while oligoclonal IgG was isolated from the CSF of 12 MS patients with protein A. After IEF and Western blotting all mono- as well as oligoclonal IgG bands were found to be glycosylated as demonstrated by digoxigenin glycan detection. Digestion with N-glycosidase F or neuraminidase caused a shift of IgG paraprotein patterns as a whole, but only a few of the oligoclonal IgG bands were affected. Staining with lectins revealed peripheral sialic acid in half of both types of IgG and galactose in all oligoclonal IgGs. Although oligosaccaride chains are present on all IgG oligoclonal bands, they contribute minimally to charge heterogeneity.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-18-26 THE GROWTH PATTERN OF ENLARGING LESIONS IN MULTIPLE SCLEROSIS: OBSERVATION ON SERIAL MRI

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Objective: To describe the growth pattern of enlarging MS lesions seen on serial MRI. Method: 50 patients had MRI examinations every 6 weeks over 2 years. The pattern of growth of enlarging lesions (defined as increase in size of previously stable lesions) was determined by 2 radiologists who reviewed the scans together. Results: 63 enlarging lesions were identified. Of the 24 periventricular lesions, 11 enlarged predominantly away from the ventricle, 3 anteriorly, 2 posteriorly, 2 rostrally, 2 caudally, and 4 equally in all directions. Of the 29 non-periventricular lesions, 11 enlarged away from and 8 towards the ventricles, 2 posteriorly, 7 rostrally, 4 caudally, and 7 in all directions. Internal capsule lesions enlarged only rostrally or caudally. Lesions became smaller on the subsequent study in 70% (44/63). 41% (26/63) returned to their original size; 46% (29/63) were smaller but not back to baseline. Conclusion: MS lesions enlarge asymmetrically more often than concentrically.

7-18-27 DECREASED LEVELS OF BETA ENDORPHIN IN CSF OF MULTIPLE SCLEROSIS PATIENTS.

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Abnormalities in the immune function seem to be of particular relevance in the pathogenesis of Multiple Sclerosis (MS).
Together others neuroendocrine polypeptide hormones play an important role in the regulation of immune system.
For these reasons we have studied the Beta Endorphin (BE) levels in 22 definite MS cases and in 15 patients with other neurological diseases (OND).
The level of Beta Endorphin were measured using a radio-immunoassay, setted in our laboratory using specific antibodies against human BE.
The mean value of BE levels was of 29.7 pg/ml (SD=19.46) in the MS CSF and of 51.67 pg/ml (SD=25.05) in the control CSFs with a statistically significant difference (P<0.008).
The significant reduction of BE levels observed in CSF of MS patients in comparison to the OND seems of particular interest, its significance in the pathogenesis of MS is still to be cleared.

7-18-28 PHENOTYPICAL LYMPHOCYTE ANALYSIS OF PERIPHERAL BLOOD AND CSF OF MULTIPLE SCLEROSIS PATIENTS AND OTHER NEUROLOGICAL DISEASES

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Atypical pattern of lymphocyte subpopulation have been described in Multiple Sclerosis (MS) patients. These observations are a support to some of the mostly accepted hypothesis of a role of immune disfunction in the pathogenesis of MS. For this reasons we have studied, using two color cytometry, the lymphocyte subpopulation patterns in the peripheral blood (PB) and cerebrospinal fluid (CSF) of 40 Chronic Progressive Multiple Sclerosis (CPMS) patients, 23 Relapsing Remitting (RRSM) stable,21 RRSM acute and 17 with other neurological diseases (OND).
A significant increase of CD4+ in PB and of CD4+Leu8+, (suppressor inducer), subsets in CSF of all the MS patients compared with OND has been observed. As a further confirmation of the immune system activation in MS comes from the observation of significant increase of CD4+45- (helper inducer) cells observed in CSF of patient with active disease.
On the contrary CD8+ (suppressor/citotoxic) cells are significantly decreased in CSF of CPMS and RRMS patients and in PB of CPMS versus OND subjects. Moreover a significant increase of CD4+Leu8+ (suppressor inducer) has been observed in CSF of all MS patients studied.
On the whole our results seem to suggest that the immunosuppressive deficit observed in MS could be due not to a decrease of suppressor inducer cells but to a direct functional abnormality of CD8+ suppressor cells.

7-18-29 HTLV-I ASSOCIATED MYELOPATHY IN SALVADOR (NORTHEASTERN BRAZIL): A REVIEW OF 36 CASES

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Over a period of 22 months we studied 102 patients with non traumatic and non-tumoral myelopathies. All patients suffered from chronic and progressive paraparesis associated with neurogenic bladder and superficial sensitive syndrome. Mielography or magnetic resonance imaging (MRI) were carried out in order to rule out compressive diseases of spinal cord. CSF examinations as well as urodynamic and electrophysiological studies were carried out. CSF analysis to antibodies against HTLV-I were performed with ELISA. Positive cases were further confirmed by western-blot. It was found 36 positive patients. Urodynamic and electrophysiological studies were performed in 16 patients. Brain MRI was carried out in 22 patients.
None of the positive cases had CSF antibodies to syphilis, schistossomiasis, cisticercosis or toxoplasmosis. 72% of cases occured in females. There was previous blood transfusion in six patients and eight described TSP like diseases ocurring in blood relatives. 38% of patients had abnormalities in MRI and 45% had electrophysiological findings.

7-18-30 INTERFERON-BETA 1b IS EFFECTIVE IN RELAPSING REMITTING MS: MRI RESULTS (II) MRI EVALUATION OF A MULTICENTRE RANDOMIZED, DOUBLE-BLIND PLACEBO CONTROL TRIAL

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BACKGROUND: MRI has been shown to be an effective method of assessing MS disease activity with 5 times the sensitivity of clinical evaluation. Quantitative MRI can also determine an index of the disease burden in MS.

METHODS: 327 MS patients in a randomized clinical trial had measurement of the MRI burden of disease at baseline and at yearly intervals for 3 years. Fifty-two patients had MRI scans at 6 weekly intervals for 2 years.

RESULTS: Placebo patients had a 20% increase in burden of disease at 2 years and a 17% increase at 3 years. Patients treated with 45 mIU of IFNB had a 0.1% change at 2 years and -6.2% change at 3 years ($p = 0.002$). Serial scanning showed that placebo patients had a mean 30% rate of active scans compared to 15% active scan rate with 45 mIU of IFNB. Placebo patients had 2 new lesions/patient/year versus 0.5 new lesions in treated patients ($p = 0.0026$).

CONCLUSIONS: MRI measurement confirms the clinical results showing a significant decrease in disease activity and disease burden due to IFNB treatment. IFNB has a significant therapeutic impact on relapsing MS.

7-18-31 THE TREATMENT OF SPASTICITY WITH INTRATHECAL BACLOFEN.

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We studied 18 patients affected by different disorders (4 spinal cord injury, 6 familial spastic paraplegia, 2 acute myelitis, 5 multiple sclerosis, 1 primary lateral sclerosis) of different age and duration of the disease. They were all affected by severe spasticity refractory to any oral antispastic treatment. Patients were evaluated clinically and spasticity was scored according to the Ashworth scale. In the ambulatory patients we scored muscle strenght according to the Oxford scale. These evaluations were performed before and during a bolus administration of intrathecal baclofen (25 - 50 ugr) to test the efficacy of the treatment. Patients were then implanted with a drug administration system (Synchromed, Medtronic) connected with a catheter inserted into the lumbar CSF space. A continuous simple daily administration was programmed with different daily dosages according to te degree of spasticity and type of disease. A marked decrease of spasticity was obtained in every patient allowing a better nurse care and absence of muscle spasms in bedridden and wheelchaired patients while in ambulatory patients an increased global motor performance was achieved during treatment.

7-18-33 DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED STUDY OF HIGH DOSE IMMUNGLOBULIN 7S THERAPY IN MULTIPLE SCLEROSIS

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Intravenous Immunglobulin 7S (Ig 7S) is beneficial in immune mediated diseases. The efficiency in Guillain Barré syndrome and myasthenia gravis is well documented. In multiple sclerosis we get the impression that Ig 7S accelerates the remission. Ig 7S is said to promote remyelination in animal models and in stable optic neuritis. To prove the effect of Ig 7S on the course of exacerbation and the final outcome we started a randomised double blind placebo controlled study. Included in the study were patients with definitive MS (POSER criteria) and acute exacerbations. All patients were treated for three days with 1 g Methylprednisolone/day and Ig 7S (day 1 30 g, day 2 20 g, day 3 10 g) or 1 g Methylprednisolone/day and Placebo (0,9 % NaCl). The main criteria for evaluation were the endpoint of deteriation and begin of remission, the final outcome and the mean time until the next exacerbation. The neurological examination was done on day 0, 3, 10, 30, 90, 180, 270, 360 (neurostatus, EDSS (Kurtzke), ambulation index). On day 0, 4, 10, 30, 360 immunological monitoring including lymphocyte subpopulations and cytokines was performed. The first evaluation of the data showed an advantage of Ig 7S concerning the endpoint of deteriation and rapidity of remission. Concerning the corticosteroid pulse therapy Ig 7S seemed to cut off the rebound on day 10.

7-18-34 HLA MARKERS IN MULTIPLE SCLEROSIS IN A SPANISH POPULATION: CORRELATION OF CLINICAL COURSE

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We have studied 105 patients with definitive MS (Poser criteria 1983) and investigated their environmental, familiar and clinical aspects. The patients were divided into several groups according to their clinical course (relapsing-remitting and progressive), age at onset (before or after 30 years), rate of disability (benign or severe), and whether they have been affected by optic neuritis.

An increased frequency of the HLA-DR2 was found in the patients with definitive MS with a relative risk of 2.32 and etiologic fraction of 0.24 which are similar to other caucasian populations in our geographical area. We have also found an increased significative of the HLA-DR2 in the relapsing-remitting forms of MS and in patients who have begun the disease with optic neuritis. It was found that the phenotypic group B7, DR2, DQw1 are more frequent than the B18, DR3, DQw2 or B49, DRw6, DQw1 groups. In the progressive forms of the illness, the phenotypic groups B51, DR2 and DQw1 are more frequent than the B39, Dr4, DQw3 or Bw60, DR4 and DQw3 groups.

7-18-35 Suicide risk factors associated with multiple sclerosis.

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It has recently been demonstrated that there is an increased risk of suicide connected with multiple sclerosis (MS). The purpose of the study is to identify risk factors in 50 MS patients who commited suicide. A regional difference was noted. Fifty-eight% of the suicides were married. The majority were occupationally unskilled, i.e. 52%. At the time of the suicide 74% were in receipt of disablement pension. The majority of those on whom information was available had shown signs of depression. Almost half had expressed suicide intentions. Twenty-eight per cent had attempted suicide before. Most were in a progressive phase of the disease. The score of the Kurtzke Disability Status Scale (DDS) was 4-6 for 56%, 7-9 for 26% and 0-3 for 14%. Males most frequently used drastic methods (hanging, shooting etc.) while women most frequently took poison. A profile of males and females who commit suicide is presented and the implications for management of psychiatric patients are discussed.

7-18-36 SPINAL CORD IMAGING IN MULTIPLE SCLEROSIS

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While magnetic resonance imaging (MRI) of the brain has told us much about the pathophysiology of multiple sclerosis (MS) technical difficulties have prevented meaningful imaging of the cord. The recent introduction of fast methods of scanning (fast spin echo), coupled with multi array coils which scan the entire cord simultaneously has both reduced scanning time and improved resolution. Using these techniques we have examined 80 patients with clinically definite MS and 45 age matched controls in order to assess cord involvement in MS and define its relationship to disability. Intrinsic cord lesions were demonstrated in 59 of the 80 patients (74%) and in only one control. Of the 139 lesions seen, 86 were in the cervical cord and the remainder in the thoracic cord. There was no significant correlation between cord lesion load and disability and no difference in cord involvement between the clinical sub-groups of MS (benign, relapsing/remitting, primary and secondary progressive). Atrophy was seen in 32 patients (40%) and was associated with more severe disability ($p=0.006$).

Improved imaging techniques allow reliable detection of spinal cord lesions in MS and have the potential to increase understanding of the condition, improve monitoring of disease activity and enhance specificity of diagnosis.

7-19-01 CLINICAL STUDY OF 26 CASES OF CONGENITAL MUSCULAR DYSTROPHY

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26 patients (14 boys and 12 girls) with congenital muscular dystrophy were selected on the basis of clinical criteria. In 4 families there were 2 affected siblings. 23 had neonatal hypotonia and 3 had walking retardation. In all the cases muscle biopsy showed dystrophic pattern without necrosis nor regeneration. Psychometric tests, EMG, Serum creatine Kinase (CK) and CT scan were performed in almost all the cases. Three types were individualized. In type A (8 patients) intelligence was normal (IQ or DQ ≥ 80), in type B (14 patients) there was mental retardation and the 3 patients in type C had in addition Dandy walker malformation. CT scan showed hypodensities in white matter or cortical atrophy in 9 patients (1 of type A and 8 of type B). CK level was normal in 7 cases mildly elevated in 9 and high in 7 cases of type B and C. Thirteen patients had severe retractions. Improvement was observed in 6 patients, stabilization in 15 and aggravation. Intrafamilial clinical variability was noted.

7-19-02 DYSTROPHIN CONTAINING INCLUSIONS IN A CASE OF NEUROMYOPATHY

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The goal of this study was to determine the content of unusual sarcoplasmic inclusions found in two muscle biopsies from a patient with sporadic chronically progressive neuromyopathy involving both proximal and distal muscles. The inclusions were studied by light and electron microscopy and studied for dystrophin, spectrin, alpha actinin, desmin and vimentin content using immunological techniques. Up to 50% of fibers contained eosinophilic intracytoplasmic inclusions which displayed strong immunoreactivity for dystrophin (30kd and 60kd antibodies). Dystrophin positive deposits were found in both subsarcolemmal and central regions of myofibers. The inclusions were slightly positive for alpha actinin, but were negative for spectrin, desmin and vimentin. By ME the sarcoplasmic inclusions were devoid of organelles and varied considerably in shape and density. We conclude that these inclusions contain dystrophin, or a dystrophin-related protein which cross-reacts with multiple dystrophin antibodies. Possible explanations for the origin of the inclusions include a primary defect of the dystrophin gene causing overproduction or incorrect assembly of dystrophin molecules or dystrophin associated protein in the membrane cytoskeleton.

7-19-03 MUSCLE INVOLVEMENT IN MARINESCO-SJÖGREN SYNDROME: A CLINICOPATHOLOGICAL AND FOLLOW-UP STUDY OF SEVEN PATIENTS.

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Seven patients with Marinesco-Sjögren syndrome (MSS; 3 males and 4 females from 4 families, aged 6-40 years) had slowly progressive muscular weakness and were followed for up to 13 years. In 2 young patients, in whom mild to moderate muscular weakness was present and the cerebellar ataxia was non-progressive, their physical disability appeared to be improved during early childhood. In four of 5 adult patients, however, muscular weakness with predilection for lower extremities was predominant clinical feature and slowly progressive, leading to severe motor impairment in adulthood. Other clinical features of the patients were typical for MSS. EMG showed a myopathic pattern and serum CK was mildly elevated. Histochemical features of muscle biopsies were: 1) myopathic changes of variation in fiber size; 2) muscle fiber necrosis and regeneration; 3) changes in cytochemical architecture; and 4) type 1 fiber predominance and an increased number of type 2C fibers. We conclude that MSS is categorized as a form of congenital muscular dystrophies.

7-19-04 TOXIC ORGANOPHOSPHATES (CARBOPHOS) NEUROMYOPATHY: REPORT OF A CASE

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A girl aged 15 was studied. In the clinical picture pronounced muscle weakness and atrophy with polymyalgias of shoulder and pelvic girdle, trunk, arm and leg muscles more prominent in the distal parts of the arms were seen. EMG showed abnormal spontaneous activity, very short MUPs and increased polyphasic potentials. The peroneal nerves conduction velocity was 29 m/s. The activity of serum creatin kinase was increased and Erytrocyte and serum acetylcholinesterase was decreased. Biopsy of rectus femoris muscle showed many muscle fibres with multiple segmental necrosis and different size and form central and subsarcolemmal vacuoles. Treatment with plasma exchange and verapamil caused some increase of muscle strength and range of movement in joints and disappearance of polymyalgias. Toxic neuromyopathy was differentiated from acute polymyositis and acute polyneuropathy-Guillain-Barré syndrome.

7-19-05 DEFICIENCY OF DYSTROPHIN-ASSOCIATED PROTEINS: A COMMON MECHANISM LEADING TO MUSCLE CELL NECROSIS IN SEVERE CHILDHOOD MUSCULAR DYSTROPHIES.

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Dystrophin is associated with a large oligomeric complex of sarcolemmal glycoproteins, which provide a linkage to the extracellular matrix component, laminin. In Duchenne muscular dystrophy (DMD), the absence of dystrophin causes the drastic reduction in all of the dystrophin-associated glycoproteins (DAGs). In severe childhood autosomal recessive muscular dystrophy with DMD-like phenotype (SCARMD), the 50 kDa DAG is deficient despite the near-normal expression of dystrophin and the other DAGs. In Fukuyama-type congenital muscular dystrophy (FCMD), the DAGs are expressed abnormally despite the near-normal expression of dystrophin. These findings suggest that the dysfunction/disruption of the dystrophin-glycoprotein complex plays a key role in the cascade of events leading to muscle cell necrosis in three forms of severe muscular dystrophies, DMD, SCARMD and FCMD. K.P.C. is an Investigator of HHMI.
Supported by MDA, AFM and UMF.

7-19-06 MYOTONIC DYSTROPHY AND PAROTID GLAND TUMORS

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Genetic locus of myotonic dystrophy (DM) was recently mapped on the long arm of chromosome 19 at band 19q13.3. The gene product, most likely protein kinase which modifies membrane excitability through phosphorylation of ion channels, could be the basis of multisystem involvement of this disorder.

Among the list of multisystem involvement of DM, benign tumors are rare. Calcifying epithelioma is the only one that is known to have causal relationship to DM.

For the last 10 years, we experienced 22 cases of DM. Among them, 2 cases were found accompanied with parotid tumor. One is 43 y/o male and another is 38 y/o female. The similarites between 2 cases are both 1) maternally inherited DM, 2) adult onset and 3) unilateral benign adenoma, one of which was polymorphic and another was monomorphic adenoma.

Is the association of parotid tumor merely by chance? Is there any causal relationship? Silent small adenoma can often be missed.

7-19-07 A PATIENT WITH CONGENITAL MYOTONIC DYSTROPHY ASSOCIATED WITH PATERNAL INHERITANCE OF CTG REPEAT EXPANSION.

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We experienced a patient with congenital myotonic dystrophy (DM) born to normal mother and affected father. We analysed triplet repeat(CTG) expansion in this family.

A ten-year-old girl presented generalized muscle weakness, mental retardation and percussion myotonia. At birth, facial diplegia, hypotonia, pes equinovarus, neonatal feeding difficulty were noted. Her elder sister had DM with infantile onset. Their father had DM with onset of age 39. Their paternal grandfather had a gallstone and a cataract without muscle symptoms. Their mother and grandmother had no muscle symptoms.

Southern blot analysis showed expanded fragments which were 4kb, 2.7kb and 600bp greater than normal allele in the patient, her sister and her father, respectively. Her grandfather had 300bp and 200bp bands amplified by PCR using primers flanking the CTG repeat. Her mother and grandmother had normal CTG repeats.

Conclusion. The patient had clinical symptoms as congenital DM and had expanded CTG repeats inherited from her father and grandfather.

7-19-08 OCULOPHARYNGEAL MUSCULAR DYSTROPHY IN JAPAN: THE FIRST FAMILIAL CASES

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Oculopharyngeal muscular dystrophy (OPMD), an autosomal dominant disorder, is very rare in colored races. Recently, we have found and evaluated the first Japanese family including 5 patients with OPMD in 3 generations. The proband, a 62-year-old femal, developed bilateral blepharoptosis since at age 52. Seven years later, she noticed difficulty in swallowing. On admission, moderate blepharoptosis, nasal voice, dysphagia, and atrophy of the temporal muscle were observed. EMG on levator palpebrae showed myogenic pattern. The deltoid muscle biopsy revealed slight myogenic changes and a few small angulated fibers with rimmed vacuoles. However, the muscles obtained from cricopharyngeal myotomy showed marked dystrophic changes. Although rare, nemalin rods were found in a few necrotic fibers. Electron microscopy often showed aggregation of mitochondria with normal appearance in the subsarcolemmal spaces, but intranuclear tubular filaments were not shown. Immunohistochemical study did not show dysrophin abnormality. Her grandfather, mother, and two sisters also developed similar clinical features. The muscles including extraocular, cardiac, and distal limbs were spared.

In Japan, only several familial cases of oculopharyngodistal myopathy have been reported. Although this family is not French-Canadian origin, clinicopathologic features are compatible to OPMD, which appears to have a worldwide distribution.

7-19-09 OCULOPHARYNGEAL DYSTROPHY IN NATIVES OF THE CANARY ISLANDS

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Oculopharyngeal dystrophy (OPD) is an infrequent hereditary myopathy of adult onset that presents with progressive ptosis and dysphagia. There is a high incidence of this disorder in the Canary Islands (Spain), as we have previously reported. We report 33 patients from 15 families, consecutively admitted from 1975 to 1992. Age of onset ranges between 20 and 52 years (mean:42.15). First symptom was ptosis in 18 cases, dysphagia in 8, both symultaneously in 4, and dysphonia in 2. Enzymes (CK and/or aldolase) were elevated in 12 cases. EMG was myopathic in all the cases in which it was performed (16). Muscular biopsy was obtained from 12 patients, showing findings consistent with muscular dystrophy in 9. During the course of the disease we frequently observed ophtalmoparesis (11 cases) and proximal amyotrophies with limb-girdle weakness (11 cases). In two cases we observed a myopathic gait with Gowers sign and calf hypertrophy, together with the other typical symptoms. We conclude that OPD is a more frequent disease in closed communities, as ours is; that it is inherited following an autosomal dominant trail, with findings consistently myopathic, and with slow progression, during which symptoms can appear common to other myopathies.

7-19-10 SEQUENCING OF TCR TRANSCRIPTS IN PM SUGGESTS AN ANTIGEN-DRIVEN SELECTION OF CYTOTOXIC T CELLS.

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Polymyositis is an inflammatory myopathy in which mononuclear cell infiltrates composed of T cells, macrophages, and B cells are present within muscle tissue. CD8+ T lymphocytes are significantly more frequent at the endomysium than at the perimysium or at the perivascular site. RT-PCR analysis has revealed a restricted usage of TCR by these lymphocytes. Sequencing of the V-D-J regions of the TCR β chain has provided evidence of non random N addictions in the D region, and preferential rearrangement of Vβ15 with Jβ2.1 segments. These data favour the hypothesis of an antigen-driven selection of the T lymphocytes involved in the inflammation sites. Presence of activated cytotoxic T lymphocytes was confirmed by the correlation of CD45R0+, CD25+ staining with the molecular analysis of the IL-2R, perforin and granzyme A transcripts in the muscle tissues of PM patients. Furthermore, MHC class I and II antigens have been detected on the surface of muscle fibers nearby the cellular infiltrates. The immunological implications of these findings will be discussed.

7-19-11 LIPID STORAGE MYOPATHIES (LSM) DUE TO β OXIDATION DEFECTS.

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This study adresses the screening of β oxidation defects in (LSM). In our laboratory we use the radioisotopic measurement of $^{14}CO_2$ evolved from labeled substrates (palmitate, octanoate, butyrate, pyruvate) and their insoluble PCA intermediates to monitor for β oxidation defects. A 14 y old boy presented LSM, hereditary protein C deficiency, pulmonary emboli, low muscle and serum carnitine and abnormally low actanoate and butyrate oxidation. He responded to riboflavin and carnitine treatment. A 32 y old man had LSM, low muscle carnitine, low oxidation of octanoate and butyrate, decresed SCAD (short chain acyl dehydrogenase) before riboflavin treatment. This VO_2 max increased drammatically on riboflavin treatment. A 36 y old man had abnormal labeled substrate oxidation and was treated with steroids with benefit. Our data indicate that β oxidation defects are a common cause of LSM, susceptible to different types of treatment.

7-19-12 **Juvenile Leigh's disease. Antemortem diagnosis.**

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Subacute necrotizing encephalomyelopathy (SNE; Leigh's disease), though a defined entity in neuropathological and morphological terms, is characterized by high clinical heterogeneity. SNE of infancy can be defined and diagnosed on the basis of clinical symptoms more readily than juvenile forms.

A previously-well 15-year-old man presented urinary incontinence, diplopia and gait ataxia. In the course of his illness he became abulic and suffered recurrent episodes of severe headache, neck pain, loss of visual acuty, paraparesia, dysphagia, insufficient involuntary breathing. The clinical examination showed a bilateral optic atrophy and internuclear ophthalmoparesis; left facial palsy, bilateral ataxia and quadriparesis and generalized hypotonia.

CT scan and MRI showed bilateral symmetrical signal alterations (MR) or decreased attenuation (CT) of the brainstem. Laboratory investigations showed abnormal lactic and pyruvate metabolism. Evidence of mitochondrial myopathy was found in the muscle biopsy.

An antemortem diagnosis can now be suggested in juvenile SNE by the correlation of clinical and laboratory data with brainsten evoked potentials, computed tomography (CT) and/or magnetic resonance imaging (MRI).

7-19-14 MITOCHONDRIAL MYOPATHIES AND ENCEPHALOMYOPATHIES IN TAIWAN

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A multi-center registration program of mitochondrial myopathy and/or mitochondrial encephalopathy was conducted to the survey of mitochondrial disease in Taiwan. Till the end of 1992, a total of 76 cases were enrolled from 10 medical centers. All the cases met the definite criteria of clinical diagnosis, and 90% of the cases had histochemical and/or ultrastructural abnormalities of mitochondria. These include 22 cases of CPEO; 11 cases of MELAS; 8 cases of KSS; 7 cases of Leigh disease; 6 cases of MERRF; 6 cases of myopathy with or without cardiomyopathy or hepatopathy; 5 cases of encephalopathy with or without intracranial calcification; 3 cases of carnitine or fatty acid oxidation defect (FAOD); 5 cases of Menkes disease, and other types for 3 cases. Routine assay of complex enzymes of respiratory chain has been started in the recent two years and been done in some cases. During the past year, mitochondrial DNA point mutation with nucleotide position at 3243 had been proved in more than ten cases of MELAS, and at 8344 in the cases of MERRF. Mitochondrial DNA deletion of a large bands of 7.9 Kb had been observed in multi-system cells including muscles, hair follicle and blood cells. In Taiwanese cases, the behabivoral patterns of mitochondrial DNA show the racial differences as comparing to those of the Caucasian patients.

7-19-15 CORRELATION OF ENDOCRINE DISORDERS AND CENTRAL NERVOUS SYSTEM INVOLVEMENTS IN MYOTONIC DYSTROPHY

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The characteristic manifestations of myotonic dystrophy (MyD) are well known to be involved in the multi-systemic organs. Therefore, it is assumed that each organ is affected by the same cause. To elucidate whether the same extent of disease severity can be observed in affected organs, we performed the investigations of apnea index (AI), intelligence quotient (IQ) and Ellsworth-Howard (EH) test in 10 patients with MyD. A slight decline of IQ and a slight increase in AI were observed. To confirm whether the decline of IQ resulted from the increase in AI, the correlation between IQ and AI were examined. Because significant negative correlation between IQ and AI was shown ($p<0.02$), it was suggested that the increase in AI participates in decline of IQ as a contributing factor. In the EH test, the patients were divided into two groups according to the results of phospaturic response ($\triangle P$). In one group including 5 patients (Group I), normal phosphatuic response was observed. The other group consisting of 5 patients (Group II) showed negative phosphaturic response. Group II showed a significantly lower value in IQ and a significantly higher value in AI as compared with Group I. We then examined the correlations between $\triangle P$ and AI as well as between $\triangle P$ and IQ to investigate the extent of disease severity. Significant positive correlation between $\triangle P$ and AI ($p<0.01$) and negative correlation between $\triangle P$ and IQ($p<0.1$) were observed. From the above results, it was suggested that the extent of disease severity in affected central nervous systems was similar to that of endocrine organs.

7-19-16 LOCALIZATION OF HEAT SHOCK PROTEIN hsp72 TO RIMMED VACUOLE IN MYOPATHIES

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Heat shock proteins (hsps) are a group of proteins whose expression is profoundly induced under stress conditions such as heat, cold, glucose deprivation or various chemical agents. They are generally considered to protect cells under stress conditions. Hsp72 is a member of hsp70 family and has been regarded as non-constitutive in ordinary cells. We generated an affinity purified antibody against human recombinant hsp72 and examined expression of this protein in normal and pathological skeletal muscles by immunocytochemistry. In control muscles hsp72 antibody intensely recognized smooth muscles in perimysial arteries and nuclei of skeletal muscles. Cytoplasm of skeletal muscles was mildly labeled. This antibody intensely labeled rimmed vacuoles in various myopathies including distal myopathy with rimmed vacuole, inclusion body myositis, oculopharyngeal dystrophy, colchicine myopathy. Immunoelectron microscopy using indirect immunogold procedure revealed labeling of myelin figures of autophagic vacuoles. In immunoblotting single band of 72kD was shown both in control and rimmed vacuole containing muscles. Hsp70s have been known to assist movement of a protein across organella membranes. Hsp72 may be, accordingly, involved in translocation of substrates into lysosomes in rimmed vacuole myopathies.

7-19-17 EXAMINATIONS IN THE REANAL TUBULAR FUNCTIONS WITH ELLSWORTH-HOWARD TEST IN MYOTONIC DYSTROPHY.

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The characteristic manifestations of myotonic dystrophy (MyD) are well known to be involved in the multi-systemic organs. As abnormalities are ubiquitous, some disorders of signal transduction pathway in each organ are considered to be important in the pathogenesis of this disease. To examine the abnormalities of signal transduction, we performed Ellsworth-Howard (EH) test in 12 patients with MyD. All patients met the criteria of the EH test. Those patients were divided into two groups according to the results of phosphaturic response. Six patients (Group I) showed positive phosphaturic response ($\triangle$P; 42.6 $\pm$ 7.9mg/2hrs), the other 6 patients (Group II) revealed negative phosphaturic response ($\triangle$P; 4.6 $\pm$ 19.2mg/2hrs). Urinary cyclic AMP (cAMP) response was evaluated with $\triangle$cAMP and after/before cAMP ratio. $\triangle$cAMP in Group I and II was 2.50 $\pm$ 0.94 and 3.48 $\pm$ 1.19 μ mol/hr, respectively. After/before cAMP ratio in Groups I and II was 23.6 $\pm$ 7.5 and 67.1 $\pm$ 50.6, respectively. Urinary cAMP response was positive in both groups. In Group II, serum calcium and high sensitive PTH (PTH-HS) were 8.15 $\pm$ 0.58mg/dl, 921.8 $\pm$ 380.6pg/ml, respectively. Group I showed 8.68 $\pm$ 0.62mg/dl in serum calcium and 625.2 $\pm$ 258.9pg/ml in serum PTH-HS. From the above results, it was suggested that the patients in Group II were accompanied with pseudohypoparathyroidism type II. In the patients of Group I, the response of the EH test and serum calcium were normal, although serum PTH-HS was slightly elevated. Our results indicated that, in some cases of MyD, abnormality lies in the intracellular signal transduction, especially adenylate cyclase pathway of renal tubular cells.

7-19-18 CICLOSPORIN INDUCED MYOPATHY
- AN EXPERIMENTAL STUDY -

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Ciclosporin(Cs) has been widely used in organ transplantation and some immune-mediated diseases. Recently we have experienced three cases of reversible myopathy to whom Cs and Colchicine were concomitantly administered. By cessation of either drug myopathy rapidly improved in all. This observation prompted us an experiment to investigate whether myopathy was induced by Cs or Colchicine.

Method: The experimental design was as (1) A group of large dose Cs (25mg/Kg/day) (2) A group of large dose Colchicine. (2.5mg/Kg/day) (3) Control group. Rats were sacrificed at 2, 4, 6 and 8 weeks respectively. Skeletal muscles obtained from femoral muscles and myocardium were fixed and processed for microscopic and electron microscopic observations.

Results: (1) In a group of large dose Cs myopathic changes were invariably observed in skeletal and myocardial muscles at 6th and 8th week. Findings compatible with myocarditis were observed in 4 of 7 rats. (2) A large dose Colchicine yielded a mixed type of myogenic and neurogenic changes in skeletal muscles at 6th week.

Conclusion: A large dose Cs was found to induce toxic myopathy in skeletal muscles and myocardium in rats.

7-19-19 EFFECT OF CHRONIC ETHANOL ADMINISTRATION ON THE RAT SKELETAL MUSCLE.

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In order to clarify the mechanisms of myopathy seen in alcoholic drinkers, we studied the morphological changes on the skeletal muscle of rats loaded with ethanol.

Rats of SD-strain were subjected to isocalolic pair feeding with synthetic liquid diet for 6 weeks.The contents of diet were as follows. Group A: Lieber's diet. Group B: 36Cal% of carbohydrate of Lieber's diet was replaced with ethanol. Group C: 8Cal% of protein, 20Cal% of fat and 72 Cal% of carbohydrate. Group D: 36Cal% of carbohydrate using in Group C was replaced with ethanol. Histochemical studies were carried out on soleus and tibialis anterior muscle.

Results: There were no necrotic and regenerating fibers in all groups. Disorganized intermyofibrillar networks were seen only in Group D. Variation in fiber size was evident in Group D on the histgram. Mean diameter of type 1 and 2 fibers in Group D was about 80% of the diameter in other groups.

Conclusions: Morphological changes on the skeletal muscle were obtained from rats maintained on a diet using in Group D. The nutritional factors is important to develop alcoholic myopathy.

7-19-20 INJECTION OF NORMAL MYOBLASTS INTO DYSTROPHIC MUSCLES: RELATIONSHIP BETWEEN THE NUMBER OF MYOBLASTS INJECTED AND DYSTROPHIN-POSITIVE FIBERS

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Recently,attempts have been made to normalize the nature of dystrophic muscles by injecting normal myoblasts into them. We injected different numbers of myoblasts into dystrophic muscles and analyzed the frequency of dystrophin-positive fibers.

Cultured muscle precursor cells(mpc) were injected into the Extensor digitorum longus muscles(EDLs)of mdx mice at doses of 3 x 10^6 cells one to three times. The mice were divided into three groups: group 1 received one injection; group 2 received two injections;and group 3 received three injections. To prevent rejection,host mdx mice were exposed to 450 rad of X-ray 24 hours before the first injection. EDLs were removed from mice one month after the last injection,and were immunostained with anti-dystrophin antibodies to analyze the frequency of dystrophin-positive fibers.

The percentage of dystrophin-positive fibers in group 1 was 2.0 $\pm$ 1.1%. It was significantly higher than 0.7 $\pm$ 0.6% of the control group. The percentage of dystrophin-positive fibers in group 2 was 2.1 $\pm$ 0.4%,and that in group 3 was 2.9 $\pm$ 0.9%. There were significant differences between groups 2 and 3.

7-19-21 "RIPPLING MUSCLE DISEASE": EVIDENCE FOR A MUSCLE BIOENERGETIC DEFICIENCY.

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"Rippling muscle disease" is a rare muscular disorder first described by Torbergsen in 1975. We report here the case of a 50-year-old man whose major complaint was muscle stiffness mainly in the upper limbs with some difficulty in starting movements. Such impairment was more evident after a period of rest and was reduced by prolonged physical activity. Sudden stretching or percussion induced "rippling waves" in the muscles. CK values always resulted mildly increased. CNEMG excluded myotonia and revealed slight myopathic changes in quadriceps muscle, and doublets and triplets after ischemia in I interosseus dorsalis muscle. Muscle biopsy only showed few ragged red and COX-negative fibers. Mitochondrial respiratory chain activities were all slightly reduced. On 31P-NMR spectroscopy the PCr/Pi ratio was found abnormal in all conditions tested, especially in post-exercise recovery, suggesting an oxidative pathway deficiency in the skeletal muscle.

7-19-22 NON FAMILIAL HYPOKALEMIC PERIODIC PARLYSIS WITH SEASONAL PREDILECTION FOR ATTACKS IN SUMMER MONTHS

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Thertyseven cases of idiopathic hypokalemic periodic paralysis were reported from the Telengana region of Andhra Pradesh a state in South India. In 78% of the cases the onset was in the third and fourth decade and the mean age at onset was 29.2 years. There were 28 males and 9 females. Familial to non familial ratio was 1:18:5. There were no definite precipitating factors. A definite seasonal occurence was noted. In 32 cases the first attack occured in the summer months and in 28 the attack occured in the summer months. In one patient all the attacks occured in the month of May. Most of the patients had very few recurrent attacks, and the frequency of attacks were once in a year to thrice in 8 to 10 years. These are the distinct clinical features when compared to familial hypokalemic periodic paralysis. There seems to be clustering of these sporodic cases in this region of India.

7-19-23 THE HUMAN DYSTROPHINOPATHIES - A NEWLY DEFINED GROUP OF NEUROMUSCULAR DISORDERS

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The Duchenne muscular dystrophy (DMD) gene product is a membrane cytoskeleton protein termed "dystrophin". Animal homologues of DMD are the mdx mouse and muscular dystrophy in the cat, Golden Retriever and Rottweiler dogs. The term "dystrophinopathy" was first coined to describe this group. With the advent of molecular genetic diagnosis it became apparent that other neuromuscular diseases previously considered to be unrelated to DMD or Becker muscular dystrophy were due to abnormalities of the same gene. These were males with spinal muscular atrophy, limb girdle muscular dystrophy and less frequently quadriceps myopathy, congenital muscular dystrophy (Fukuyama) , myocardopathies, myalgia cramps and "CK aemias". These and manifesting DMD carriers may now be termed the "human dystrophinopathies" and classified accordingly.

7-19-24 **CARDIAC FUNCTION AND SKELETAL MUSCLE PATHOLOGY IN FEMALE GENE CARRIERS OF DUCHENNE MUSCULAR DYSTROPHY WITH CARDIAC MANIFESTATION.**

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We evaluated cardiac function in two female gene carriers (case 1 and 2) of Duchenne muscular dystrophy (DMD), who had cardiac manifestation, but no motor dysfunction, by electrocardiography (ECG) and ultrasonic cardiography (UCG). Skeletal muscle histology was examined by H-E stain, and NADH-TR stain. Dystrophin (Dys) and dystrophin-related protein (DRP) were studied immunohistochemically on the muscle fibers.

ECG revealed ST depression in case 1, and ventricular extrasystole in case 2. UCG revealed left ventricular dilatation and diffuse hypokinesis of the ventricle resembling dilated cardiomyopathy respectively.

Muscle pathology showed mild scattered atrophy of the muscle fibers, and a small number of necrotic and degenerative muscle fibers. Immunohistochemistry of dystrophin showed normal staining in 60% of the muscle fibers, but patchy staining in 30%, and negative staining in 10%, in both cases. Among the dystrophin-negative fibers, 4.7% and 29% were DRP-positive in cases 1 and 2, respectively. These DRP-positive fibers were comparatively small and shown to be basophilic with H-E , indicating that they were regenerative.

These two cases had cardiac dysfunction in spite of minimal skeletal muscle change, suggesting less expression of dystrophin and its related proteins in their cardiac muscles than in those of DMD carriers without cardiac manifestation.

7-19-25 **MITOCHONDRIAL MYOPATHY WITH AUTOSOMAL DOMINANT INHERITANCE: REPORT OF A FAMILY AND REVIEW OF THE LITERATURE**

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We report a family with mitochondrial myopathy which showed autosomal dominant inheritance. The proband was a 58-year-old Japanese male who presented with bilateral ptosis, chronic progressive ophthalmoplegia, dysphagia, and atrophy of proximal muscles in the upper extremities. Muscle biopsy revealed ragged red fibers at a frequency of 7%. Cytochrome oxidase activity in the muscle was 50% of the control value. PCR analysis of muscle mitochondrial DNA revealed 3 large-scale deletions in the non-D-loop region, ranging from 4.2 kb to 5.2 kb . This patient's father, three siblings, son and daughter all, had similar symptoms.

We also reviewed 45 individuals from six families, including our family with mitochondrial myopathy which showed autosomal dominant inheritance. Primary clinical manifestations included ophthalmoplegia (91.2%), ptosis (95.6%), hearing loss (72.7%), dysphagia (60.0%), limb weakness (74.1%) and respiratory muscle weakness (75.0%). Muscle biopsy showed ragged red fibers and cytochrome oxidase-negative fibers. Multiple large-scale deletions of mitochondrial DNA were found ,all of which were in the non-D-loop region.

Since nuclear DNA reportedly plays a role in the replication of mitochondrial DNA, multiple mitochondrial DNA deletions may be due to a mutation in nuclear DNA which is inherited as an autosomal dominant trait.

7-19-26 DETECTION FOR A C1840 ->T POINT MUTATION IN THE RYR GENE IN MALIGNANT HYPERTERMIA (MH) SUSCEPTIBLE INDIVIDUALS

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1. In humans the corresponding alteration of the sequence CTAC1840 to CTAT1840 in RYR gene deletes an RsaI site, providing the application of PCR procedure for a straightforward detection of the mutation in the genomic DNA. Analysis of 17 members belonging to 4 families predisposed to MH has revealed the presence of the corresponding substitution in a single family. In this large pedigree (55 components of four different generations), 2 siblings of the second generation died from MH during anaesthesia. Caffeine-halothane *in vitro* contracture test (CHCT) has been performed, following the European Protocol, in 16 components: 2 were diagnosed as MHS, 3 were MHE, and 11 were MHN. The pedigree of the family suggests an autosomal dominant pattern of transmission of MH susceptibility. 1 out of 3 members investigated for RYR point mutation showed C1840 ->T mutation and CHCT results was consistent with MH susceptibility. The other 2 members, without point mutation, were diagnosed as MHN. In this familial group, preliminary results suggest a correlation between the presence of C1840->T point mutation and MH susceptibility.

7-19-27 IMMUNOREACTIVE CuZn-SOD AND Mn-SOD OF SKELETAL MUSCLES IN NORMAL SUBJECTS AND PATIENTS WITH NEUROMUSCULAR DISEASES

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Superoxide dismutase (SOD) is an enzyme which catalyzes the dismutation of the oxygen radical superoxide anion, and protects cells against reactive free radicals. However, it was not well known that CuZn-SOD and Mn-SOD are involved in neuromuscular diseases. The aim of this study was to investigate the distribution and localization of CuZn-SOD and Mn-SOD of skeletal muscles in normal subjects and patients with neuromuscular diseases. We have previously developed monoclonal antibodies to human CuZn-SOD and Mn-SOD. The standard methods of immunohistochemistry were applied to the frozen sections of skeletal muscles in normal subjects and patients with neuromuscular diseases (Duchenne, limb girdle, myotonic dystrophy, polymyositis, dermatomyositis and ALS). In normal muscles, immunoreactivity of Mn-SOD was present in the type 1 fiber, but CuZn-SOD reactivity was not found. In diseased muscles, Mn-SOD immunoreactivity in polymyositis was demonstrated very strongly and was weakly contained in dermatomyositis, whereas CuZn-SOD immunoreactivity was not little detected . These results suggested that the functional role of CuZn-SOD and Mn-SOD may be different in human skeletal muscles and also high Mn-SOD immunoreactivity in polymyositis may play some protective roles in the muscle fibers against the superoxide anion.

7-19-28 APPEARANCE OF DYSTROPHIN AND DYSTROPHIN RELATED PROTEIN IN BUPIVACAINE HCL INDUCED DEGENERATION AND REGENERATION IN mdx MOUSE MUSCLES

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Dystrophin related protein (DRP) has been reported to present at the motor end-plates of the mature skeletal muscles and at the muscle membrane in the early stage of the regenerating muscles in mutant strain mice (mdx). The role of DRP, however, is not yet settled. This experiment was designed to examine if DRP is appeared at the extrajunctional acetylcholine receptor (AChR). We also examined the dystrophin on the degenerating and regenerating muscle membrane. Mdx and B-10 mice were used for this study and bupivacaine HCl was injected into extensor digitorum longs muscles (EDL). EDL were biopsied at 5 minutes and on day 6,9,12,15, and 30 after injection. Frozen sections were stained immunohistochemically using monoclonal antibodies against dystrophin (NCL DYS1 and DYS2, polyclonal antibodies for DRP (LDP) and peroxidase-labeled α-BGT.

LDP, DYS1 and DYS2 were positive on the muscle membrane of mdx on day 6 and 9 when are consistent with the appearance of the extrajunctional AChRs. Further study is necessary to clarify relations between DRP and AChR or other cytoskeletons.

7-19-29 NEUROPSYCHOLOGICAL IMPAIRMENT OF DUCHENNE MUSCULAR DYSTROPHY (DMD) CARRIERS AND THEIR AFFECTED SONS: A POSITIVE CORRELATION

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BACKGROUND: Non progressive MR is present in about a third of DMD patients. Dystrophin is localized in post-synaptic regions of mammalian central nervous system. METHODS: Fifteen women were diagnosed as obligate carriers. Clinical, laboratory, EMG, ECG and neuropsychological assessment were carried out in DMD carriers and DMD patients. Immunohistochemistry and Western blot analysis were performed on muscle samples of DMD patients and DMD carriers. RESULTS: Carriers' clinical features were unremarkable. Serum levels of CK were increased in six carriers. DMD carriers IQ and DMD patients IQ were lower than controls. Specific neuropsychological defects have been found. A statistically significant correlation was found for these items and for impaired mental performance between carrier and her affected boy. CONCLUSION: DMD carriers and DMD patients present common neuropsychological defects with a direct correlation between mother and her affected boy. X-linked MR appears also in heterozigous carriers.

7-19-30 SEVERE AUTOSOMAL RECESSIVE MUSCULAR DYSTROPHY (SCARMD) CHARACTERIZED BY DEFICIENCY OF 50kDa DYSTROPHIN-ASSOCIATED GLYCOPROTEIN (50DAG) EXISTS OUTSIDE NORTH-AFRICAN COUNTRIES.

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SCARMD, a disease with Duchenne/Becker muscular dystrophy (DMD/BMD) phenotype, first described in Tunisia, has been reported until now only in Southern and Eastern Mediterranean countries.

Deficiency of 50DAG (a component of a large oligomeric complex of sarcolemmal glycoproteins associated with dystrophin) was demonstrated to be specific of SCARMD (Nature, 359:320, 1992).

Immunocytochemical studies of muscle biopsies from sporadic patients with DMD/BMD-like phenotype, but no dystrophin deficiency, has allowed the identification of SCARMD in European patients. This suggests that the mutation responsible for the SCARMD may also exist in other parts of the world. Such cases are either undiagnosed or mis-diagnosed as DMD/BMD or limb girdle muscular dystrophies. K.P.C. is an investigator of HHMI. Supported by AFM and MDA.

7-19-31 DERMATOMYOSITIS ASSOCIATED WITH CHOLESTEROL LOWERING AGENT SIMVASTATIN.

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Myopathies, polimyositis and dermatomyositis (DM) associated with D-penicillamine, penicillin and cimetidine therapy are well known. Recently however cholesterol-lowering- agents have also been implicated in myopathic syndromes.

A 66 year old housewife is described who was ospitalized for weakness of the proximal limbs after two years' treatment with simvastatin(SV). She also presented an erythematous rash on the face, neck and forearms.

Based on high serum CK, CK-MB, GOT, GPT and LDH levels, and the results of EMG and muscle and skin biopsy, a DM was diagnosed.

Other tests excluded malignancy and connective tissue disorders.

After suspension of SV and two months' treatment with 75 mg of Prednisone per day the patient made a good recover and was dismissed.

The possible role of anticholesterol agents in inducing DM is discussed.

7-19-32 TONGUE FUNCTION AND "DYSTROPHIC CHANGES" IN DUCHENNE MUSCULAR DYSTROPHY

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BACKGROUND: Dystrophin has been identified as the missing protein in DMD but the mechanisms of weakness and necrosis are still controversial. Progressive weakness involves all skeletal muscle but extraocular muscles are never affected and others like the tongue are minimally involved and functionally preserved. METHODS: We performed tongue biopsies in 3 DMD severely affted patients with normal tongue function. Tongue extrussion strength (TES) was myometrically measured in 10 DMD patients and in normal subjects. RESULTS: TS values were reduced 18% as compared with normals whereas in the limbs the differences reached 90% DMD tongue muscle showed Dystrophin deficiency and were indistinguishable from a regular muscle biopsy showing typical dystrophic changes. CONCLUSIONS: Repetitive contractions cannot explain necrosis and weakness. Dystrophin deficiency may be necessary but not enough to develop weakness in DMD. Dystrophin related proteins or other substances may play a different role in tongue or eye muscles. Lengthening contractions may trigger necrosis (as suggested by others) and also induce weakness. Pathologically defined "Dystrophic changes" do not necessarily correlate with the degree of weakness. The study of "non traditional" muscle may give some clues for the mechanisms of necrosis and weakness in DMD.

7-19-33 NEMALINE MYOPATHY: FATAL NEONATAL VARIETY

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A three-year-old boy was born with hypotonia, sucking difficulties and with dysmorphic features. During the first months of life, he developed progressive generalized muscle weakness and recurrent respiratory infections. In February 1992 he was admitted to the hospital because of repiratory insufficiency requiring mechanical ventilation. CK levels were normal as well as a carlotype. A muscle biopsy showed prominent nemaline bodies with their characteristic aspect on histochemistry which were confirmed on electron microscopy. Both parents underwent muscle biopsies which did not show nemaline bodies either on the trichrome staining nor on electron microscopy.

At the present time, this patient is still ventilator dependent and his strength has not improved.

This case illustrates a severe clinical presentation of Nemaline Myopathy which is usually a mild muscle disorder. In addition, this case shows that it is possible to suspect the clinical diagnosis in a newborn with hypotonia and dysmorphic features.

7-21-01 MIGRAINE PREVALENCE IN STUDENTS: A PILOT STUDY

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There is a dearth of published studies of the prevalence of migraine in Australia.

A self-report questionnaire based on the criteria of the International Headache Society for the diagnosis of migraine was administered to 400 Australian University undergraduates. Overall, the prevalence of migraine was 18% (95% confidence intervals (c.i.) 14-21%); the prevalence in females was 21% (95% c.i. 18-23%) whilst the prevalence in males was 11% (95% c.i. 6-16%). The female : male ratio of migraine sufferers was 1.9:1.

The frequency, severity and impact of the migraine attacks will be outlined and self-medication described.

7-21-02 STROKE SUB-TYPES IN KARACHI, PAKISTAN.

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OBJECTIVE: Compare pattern of strokes in our urban population with that in Western countries.

BACKGROUND: Cerebrovascular Accidents are a major cause of morbidity and mortality in our population. No study has been undertaken to define the stroke sub-types and the major risk factors associated in this population.

DESIGN METHODS: All patients admitted in Aga Khan University Hospital between June and October 1992, with CVA were evaluated using history, physical examination, neuro-imaging and necessary investigations. Cases in which evaluation was incomplete or inadequate were excluded from the study. Strokes were divided into: a) Thrombotic; b) Embolic; c) Hemorrhagic; d) Lacunar; e) Subarachnoid Hemorrhage; f) Unknown.

RESULTS: Of the 60 cases that were evaluated, we found that large vessel disease predominates (43%), with thrombotic (25%) and embolic (18%), but as a single category hemorrhagic strokes were the most common (30%). Lacunar strokes were 6% but 16% were in unknown category.

CONCLUSION: We conclude that as a single category, hemorrhagic strokes are most common in our part of the world. In majority of these hypertension was felt to be the etiology. This high incidence of hemorrhagic strokes has not been reported in Western Literature.

7-21-03 EPIDEMIOLOGY OF MENTAL SUBNORMALITY (MS) IN UPPER EGYPT

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The studied population consisted of 3000 subjects whose age ranged between 2 - 18 years, from Assiut City and 2 villages. Stanford-Binet test was done for each individual. MS was ascertained by complete etiological sheet including neurological and psychiatric evaluation, anthropometric measurements, dermatoglyphics, photographs, pedigree chart, cytogenetic and biochemical studies for inborn errors of metabolism. 116 cases of MS were ascertained with prevalence of 3.9%. The clinico-etiological classification showed: 24% syndromes identified by MS, 12% primary CNS defects, 10% fragile X-syndrome, 10% inborn errors of metabolism, 5% teratogenic and environmental causes, 4% MS associated with epilepsy, 3% chromosomal disorders and 31% idiopathic MS. Male to female ratio was 2:1. The mean age of mothers was higher than control by 2 years, in severe MS by 3 years and in mogols by 8 years. Consanguinity was 66%. Family history of MS reported in 57%. MS was correlate with low birth weight, prematurity, complicated pregnancy and delivary, diseases occurred in first year of life and low socio-economic state.

7-21-04 PATTERN OF NEUROLOGICAL DISEASES IN SAUDIS

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The pattern of neurological diseases in a general hospital in Saudi Arabia was analysed. All neurological inpatients, outpatients and those seen in consultation from other disciplines were classified according to the Abridged Version of ICD-9 and regrouped in the classes listed below. In the period from 1988 to 1992, the total number of neurology patients was 7,702. 1,272 (16.5%) had epilepsy, 1,193 (15.4%) cerebrovascular disorders, 1,025 (13.3%) peripheral and 387 (5%) cranial neuropathies, 641 (8.3%) headache and migraine, 651 (8.4%) spine and spinal cord diseases including intervertebral disc prolapse, 417 (5.4%) nervous system infection, 303 (3.9%) Parkinsonism and extrapyramidal disorders, 260 (3.4%) dementia, 327 (4.2%) mental retardation, 206 (2.7%) myasthenia and neuromuscular disorders, 182 (2.4%) cerebellar and other degenerative disorders, and 156 (2%) vertigo, syncope and tinnitus, 164 (2.1%) brain tumours, 110 (1.4%) demyelinating disease and multiple sclerosis, 86 (1.1%) pseudotumour cerebri and 322 (4%) had other neurological diseases. The pattern of neurological diseases differs from that reported in the west. Nervous system infections and pseudotumour cerebri were more frequent, demyelinating disease and headache less frequent, cerebrovascular disorders and epilepsy had the same frequency.

7-21-05 EPIDEMIOLOGY OF DEMENTIA IN ROCHESTER, MINNESOTA

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A community-based diagnostic index that is continually updated provides access to detailed medical records from clinics, hospitals, and nursing homes for the population of Rochester, Minnesota. Our ability to retrieve health care information in a uniform and objective manner has enable us to provide age/sex-specific incidence and prevalence rates, trends, outcome, and risk factor assessment in this delineated population over several decades. Incidence rates for dementia show sharp increases with advancing age to 3,000 per 1,000,000 (3%) per year in the age group 85 and over. There are no significant differences in rates for men and women. Through the five quinquennia, 1960 - 1984, the rates have been stable with a trend for increase recently in the most elderly groups; this may reflect continuing improvement in diagnosis of the very old. Prevalence rates also have been calculated. These indicate a prevalence rate of dementia which follows the age trend, so that almost 20% in those 85 years and over were affected on the prevalence dates of January 1, 1975, and January 1, 1980. Case-control studies have yielded mostly negative results. In our studies, head injury with loss of consciousness, therapeutic radiation exposure, or thyroid disease, including Hashimoto's thyroiditis, do not appear to be significant risk factors for subsequent development of Alzheimer's disease. A multitude of systemic medical conditions also have been evaluated, but no significant association with dementia has been noted. We found a lack of association between Alzheimer's disease and education, occupation, marital status, or living arrangement. However, more patients with Alzheimer's disease than controls have episodes of depression prior to the index year.

7-21-07 NEURAL SHIFT THEORY OF MIGRAINE: A CASE-CONTROL STUDY

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A neural shift theory of migraine has been advanced suggesting that instability of central neurotransmission in migraineurs may result in impairment of neural responsiveness to environmental stimuli and, specifically, sudden environmental change. This impairment may be reflected in behavioral abnormalities such as difficulty moving from sleep to wakefulness, and vice versa. We have evaluated this particular "neural shift" behavior in a case-control study utilizing a questionnaire that included the Pittsburgh Sleep Quality Index (PSQI). Cases (n=150) were selected from a single neurologist's clinical migraine registry. Cases completed a questionnaire based on the criteria for diagnosis of migraine of the International Headache Society. Controls (n=150) were matched on the 3-digit telephone prefixes of cases to control for socioeconomic status and then randomly selected by the Mitofsky-Waksberg method. The PSQI is a validated instrument for research that allows analysis of "good sleepers" versus "poor sleepers" on a global PSQI score. The instrument also separately scores 7 major categories of sleep: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Odds ratios and 95% confidence intervals will be estimated for scores of global and separate sleep categories, specifically sleep latency.

Sleep latency allows testing and potential validation of the neural shift theory of migraine. These data may be helpful in understanding underlying biochemical abnormalities in the migraineur.

7-21-08 AN EPIDEMIOLOGICAL STUDY OF COMPLETE STROKE IN HUABEI REGION OF CHINA

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Summary: The population of nearly 87 million was investigated by an epidemiological study of complete stroke by door to door in Huabei region of China. This investigation involved the capital city of Beijing, the municipality city of Tianjin, and the three provinces of Hebie, Shanxi, and Inner-mongolia.

948 incidence cases were found from this population which were the first strokes in the year of 1986 (from Jan. 1st to Dec. 31st). The crude incidence was 109.2/100,000. It was 127/100,000 in males and 92/100,000 in females (547 male and 401 female). 645 cases died. The crude mortality was 74.13/100,000. Prevalence at Dec. 31, 1986 was 379/100,000.

Authors compared each of the cases with the region of Huabei and the whole country.

7-21-09 PREVALENCE OF EPILEPSY: COMPARISON OF THREE SCREENING QUESTIONNAIRES (SQ) AND DEFINITIONS.

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The prevalence rates obtained using 3 different SQ for epilepsy (WHO, ICBERG, POA) and 3 different definitions of epilepsy were compared in a door-to-door study in Porto Alegre, Brasil. Of the 3,153 persons interviewed in the screening phase 74 cases of epilepsy were diagnosed by the neurological interview plus 3 false-negative cases.

The prevalence rates found for one of the definitions of active epilepsy were 9.2/1,000 of population (WHO), 11.4/1,000 (ICBERG) and 13.9/1,000 (POA). There were significant statistical differences among them as well as for the other definitions of active and inactive epilepsy used.

This study shows the importance of methodological issues in epidemiological studies of epilepsy. The different prevalence rates of several studies might be due exclusively to distinct methodology.

7-21-11 EPIDEMIOLOGY OF PARKINSON'S DISEASE IN VARIOUS GEOGRAPHICAL AND ECOLOGICAL REGIONS

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Our investigations performed by the method of random selection in the forest-steppe zone of the Ukraine, Alpine and low-mountain areas of Kirghizia have shown significant differences in the incidence of Parkinson's disease in the above regions. The highest incidence of 90 - 91 per 100,000 people was observed in big industrial cities of the Ukraine - Kharkov and Sumy. In the Alpine Kirghizia this disease was very rare (3 : 100,000). In the low-mountain areas of Kirghizia the incidence was 19 : 100,000. The highest incidence was observed at the age of 55 - 65. It should be taken into consideration that in the food of the residents of the Alpine Kirghizia there were a lot of antioxidants and tryptophane. Among risk factors of the disease development the prevalence belonged to medicamental intoxications, brain injuries and emotional stress. Our data show that the development of Parkinson's disease can be influenced by various climatic and ecological factors.

7-21-12 A CASE-CONTROL STUDY OF THE ASSOCIATED FACTORS WITH *MULTIPLE SCLEROSIS IN ALCOI*

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Previous studies of MS in Alcoi, eastern Spain, found the highest prevalence and incidence rates published on a Spanish population and the existence of a relationship between MS and migration. To evaluate potential risk factors associated with MS in Alcoi, we carried out a matched case-control study. MS patients were classified according to the Rose's criteria. Only patients who fulfilled the criteria of clinically-definite MS were included in the study. Controls were randomly based on the census. Information was collected by means of a questionnarie administered by a medical trained interviewer in a face-to-face interview. The Mantel-Haenszel test was used to carry out statistical analysis. The study included 40 patients, 11 males (27.5%) and 29 females (72.5%) and four sex, age and birth place-matched controls (160). Our results show that a low social class (OR=2.94; 95% CL 1.47-5.89), a contact with dogs (OR=1.96; 95% CL 1.09-3.51) and working on textile industry (OR 2.39; 95% CL 1.4-4.95) are associated with MS. Our study suggests the existence of a genetic susceptibility and exogenous factors related with the MS risk. However, in our opinion, the evaluation of this association requieres further studies.

7-21-13 EPIDEMIOLOGY OF EPILEPSY IN SINGAPORE

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Though Epilepsy is recognised as a major medical and social problem in Singapore, there is no epidemiological survey to realise the size of the problem.

We studied this problem from data collected from hospitals, school health clinics and from military statistics. The prevalence varied in the 3 sample population studied. The most accurate data for prevalence study was obtained in Army recruits. A life time prevalence of 3.8 per 1000 was noted. The prevalence variation with age, sex and races is discussed.

The mortality from epilepsy was 0.5 per 100,000.

The types of epilepsies and the treatment patterns are discussed.

7-21-14 A TOTAL POPULATION SURVEY FOR NEUROLOGICAL DISORDERS IN SAUDI ARABIA: THE THUGBAH STUDY.

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Informations on epidemiology of neurological disorders in the Arabian peninsula are scanty.The available data are derived from hospital-based studies only. A study was designed to determine the prevalence of neurological disorders in the Saudi community. A door-to-door survey in Thugbah town was conducted using a pre-tested questionnaire. Individuals with abnormal responses were evaluated using defined criteria to find cases. A total of 23,219(98% of eligible subjects) were screened; only 1.5% were>60 y.o. Consanguineous marriages were present in 55%.The prevalence ratio per 10,000 population for headaches,seizures, mental retardation and crebral palsy were 120, 47.3, and 27.0 respectively.Strokes(18),Parkinson's disease(2), and Alzheimer's disease(2) were uncommon, and multiple sclerosis rare(0.4).Neurological disorders were common. The rarity of conditions commonly associated with old age probably reflects the age structure of the community and the high prevalence of degenerative disorders in children could be due to the high consanguinity rate.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-21-15 EPIDEMIOLOGY OF IDIOPATHIC INTRACRANIAL HYPERTENSION

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An epidemiologic survey of idiopathic intracranial hypertension (IIH) in Benghazi, Libya, over a period from September 1982 through August 1989 ascertained 81 patients. The group was comprised of 76 females and 5 males. Ages ranged from 8 to 55 years; the mean ± S.D. was 28.6 ± 7.9 for women and 21.0 ± 14.5 for men. The average crude annual incidence rates for IIH per 100,000 persons were 2.2 for the total and 4.3 for females for all ages (3.2 for the total and 5.9 for the females when adjusted to the 1980 United States population). In females aged 15-44 years, IIH occurred at a rate of 12.0 per 100,000 per year; for those defined as obese, the rate rose to 21.4. Moderate to severe visual loss occurred as a sequelae in 20 percent of our patients. The extent of the visual loss did not correlate with age at diagnosis, duration of symptoms, degree of obesity, use of oral contraceptive pills, cerebrospinal fluid (CSF) opening pressure, steroid treatment, or recurrence. We found no correlation between CSF protein and opening pressure. Interesting associations of IIH occurred with Addison's disease, hypoparathyroidism, hypothyroidism, and Weber-Christian disease. A case-control study was conducted on 40 consecutive female incident IIH patients and 80 age-matched female control subjects. Obesity and recent weight gain occurred more frequently in patients. More patients were married and more had irregular menses. We believe the present study provides the most comprehensive epidemiological data on IIH reported to date. The incidence rate for IIH described in our study is three to four times higher than that reported from the United States.

7-21-16 FACIAL (BELL'S) PALSY IN EIGHT MALES AT A SINGLE JOB SITE DURING A PERIOD OF TWO WEEKS.

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Eight cases of classical Bell's palsy occurred in construction workers engaged at a single job site where the workers were constructing a storage shed. All eight subjects had either a left or right facial palsy which cleared within six weeks of onset without any residual paresis. The workers ranged in age from 21 to 35 and all enjoyed good health prior to the development of the palsy. The only common factors at the job site were the water supply and the fact that they were working within a few hundred yards from a manufacturing plant which was engaged in the manufacture of biological agents. All the workers afflicted deny ever entering the main plant or being involved with the main plant workers. No cases of Bell's palsy were noted in the manufacturing plant during this time. This is the first reported cluster of classical Bell's palsy cases at a single site during such a brief period as two weeks. The possible etiology or etiologics for this penomenon shall be discussed.

7-21-17 THE PREVALENCE OF NEUROMUSCULAR DISEASE AND THE POST-POLIO SEQUELAE IN A SWEDISH COUNTY AND HEALTH CARE UTILIZATION.

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The prevalence of neuromuscular disease and the post-polio sequelae (PPS) was studied in the county of Örebro, Sweden (study population 270,000). Nine sources of data were utilized and validated, and 474 patients were identified.

On the prevalence day (Jan. 1st 1988) the rate per 100,000 was 92 for the PPS and 84 for the other neuromuscular diseases (motor neurone diseases 9, hereditary neuropathies 9, myoneural disorders 16, myotonic disorders 19, muscular dystrophies 20 and myositis 11). Out of the patients with PPS, 80% reported late-onset symptomes. On the basis of an expanded survey including all medical records in one health care district the prevalence of the PPS was estimated to 186 per 100,000.

With regard to the patients with neuromuscular diseases 76% of the patients had received institutional care on one or more occasions. The care was necessitated by the neuromuscular disorder in 60%, by respiratory disorders in 8%, by trauma in 5% and by miscellaneous in 27%.

7-21-18 PREVALENCE OF ADULT-ONSET COGNITIVE DISORDERS (AOCD): A DOOR-TO-DOOR SURVEY IN AN ITALIAN ELDERLY POPULATION.

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The prevalence of AOCD was investigated in an Italian elderly population. Two interviewers administered the Mini-Mental State Exam (MMSE) test and the Global Deterioration Scale (GDS) to all persons over age 59 (N=537) who, on January 1, 1991 were resident in the municipality of Faenza-Granarolo, Ravenna Province, Italy (door-to-door screening phase). We classified subjects as affected by AOCD if they scored less than 28 on the MMSE and/or 2 or more on the GDS. Then, all subjects we classified in screening phase (belonging stage 2 or more of the GDS, and performing a score less than 28 on MMSE) were further investigated by means of a clinical examination (2nd phase of the study design). In addition, on the basis of the performance on MMSE and GDS tests, we defined five stages of impairment severity: normal, Age-Associated Memory Impairment (AAMI), Mild Neurocognitive Disorder (MND), Mild Alzheimer's Disease (MAD), and Moderate-Severe Alzheimer's Disease (MSAD). The prevalence of AOCD subjects was found to be equal to 39,8%; an high correlation was found between MMSE and GDS (ρ = - 0,79). Age-specific prevalence increased steeply with age and was similar in men and women. Prevalences at different impairment stages were as follows: 15.1% for AAMI, 14.3% for MND, 4.2% for MAD, and 6.2% for MSAD. Severe impairment (MAD and MSAD) was more common in older and poorly educated subjects. At our knowledge, this is one of the first population-based study of AOCD prevalence on an elderly population. Nevertheless, our findings are consistent with those obtained in different populations and using different tests.

7-21-19 PREVALENCE OF DIFFERENT TYPES OF PARKINSONISM IN A RURAL GERMAN POPULATION OVER THE AGE OF 65 (The Stamberg Trial of Epidemiology of Parkinsonism and Hypertension, STEPHY)

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The prevalence of idiopathic parkinsonism (IPS) is estimated to be about 350- 800/100 000 in the elderly (>65 years). We investigated the prevalence of IPS and other types of parkinsonism (PS) in two representative rural german villages.

Two trained physicians examined the total population >65 (1190 residents) by a cross-sectional survey with a response rate of 82.5% (982 residents). Residents were asked according to the screening questionnaire for Parkinsonism of Mutch et al (Neuroepidemiology,1992). In addition each person was investigated for bradykinesia, gait disorder, posture, writing and tremor. Residents presenting a moderate to severe deficit in one of these items were preliminary classified having PS (Pre PS).

This group (PrePS) comprised 45 (23 male, 22 female) of 982 residents and 24 of 45 revealed action or rest tremor, 22 axial bradykinesia and 26 writing deficits. These patients were reevaluated and diagnosed by two trained neurologists, if necessary with the aid of a CT scan. The diagnoses were as follows: 9 IPS, 5 PS probably due to vascular lesions, 3 normal pressure hydrcephalus (NPH), 4 neuroleptic induced PS, 9 PS of other etiology, 11 essential tremor, 1 physiolog. tremor, 3 no movement disorder. All NPH patients and 4 of the vascular PS were newly diagnosed.
The prevalence of IPS with 900/100 000 agrees with previous studies. The high prevalence of NPH, vascular PS and PS of other etiology has not been reported previously. These data show the importance of neurological care in the elderly presenting with extrapyramidal symptoms.

7-21-20 STUDIES ON PRESENT STATE OF SUBACUTE MYELO-OPTICO-NEUROPATHY (SMON) PATIENTS

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SMON is an iatrogenic neurologic disease caused by intake of clioquinol for gastrointestinal symptoms. A new occurrence of the disease ceased in 1970 in Japan by prohibition of production and use of the drug.

We analized the present state of total 2189 SMON patients (537 males and 1652 females) studied from 1988 through 1991 by the nationwide SMON research group of the Ministry of Health and Welfare of Japan, with special reference to the SMON patients who had blindness and impossible gait at a time of the severest symptoms usually during the initial stage of the clinical course.

Out of 88(100%) blind patients 31(35.2%) were still blind, 23(26.1%) could read large letters of the newspaper and 3(3.4%) had almost normal vision.

Out of 1039(100%) patients who were unable to walk, 89 (8.6%) were still unable to walk or use a wheelchair, 82 (7.9%) used a wheelchair, 205(19.7%) could walk with a stick and 216(20.8%) had a slightly unsteady gait.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

7-21-21 NEUROLOGICAL ASPECTS OF POLIO EPIDEMICS ON SHANDONG PROVINCE OF CHINA

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In late 80's acute anterior poliomyelitis broke out in central-eastern China. The number of cases has been diminishing due to strict applications of expanded programs of immunization (EPI). In Shandong Province (population of 80 million), differentiation of "true" polio from suspected polio cases according to WHO criteria of acute flaccid paralysis (AFP) was done. In '91-92, totally 135 children with suspected polio were clinically examined. Results: Mean age at onset of polio-suspected cases was 24.6 months, and vaccination was given 2.4X. Clinically confirmed polio in 39 cases (28.8%, 16.4M, 1.6X). Guillain-Barré syndrome 12 cases (8.9%, 47.8M, 2.9X), non-polio myelitis, mostly acute viral and some presumably post-infectious, in 20 cases (14.8%, 22.4M, 2.7X). Twenty-four had yet another disorder (viral myositis, injection paralysis, acute arthritis, intracranial events, etc.). Forty cases (29.6%) had no neurological disorder at the time of examination and were thought to have been in "polio-panic" state. Isolates of polio viruses were all vaccine strains in '91-92. Thus, diverse disorders, many of which gave rise to acute paralysis or painful states, came to attention as polio, as the epidemic declined. Neurologists serve a major role in supporting EPI during the resolving stages of polio-epidemics.

7-21-22 DIET, ACTIVITIES OF DAILY LIVING AND COGNITIVE FUNCTIONS IN THE ELDERLY. CROSS SECTIONAL STUDY IN A RURAL POPULATION OF SOUTHERN ITALY.

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Nutrition plays an important role in preserving neurological functions in elderly people. Experimental data indicate a protective action of natural antioxidant agents of the diet (vitamin A,C,E) on brain functions. The aim of this study was to evaluate whether subclinical malnutrition might be associated with age-related functional changes (cognitive decline and decrease in motor performances). Mini Mental State Examination, Activities of Daily Living, Instrumental Activities of Daily Living, Geriatric Depression Scale, Motor Performance Scale were carried out on random sample of 704 free-living elderly people (88 subjects for each sex and age class: 65-69,70-74,75-79,80-84 years). A diet assessment was obtained with a validated self administered, semiquantitative food frequency questionnaire. Serum levels of vitamin A,C,E and selenium were assayed in a limited number of subjects. Multiple and logistic regression models were used for statistical analysis. The role of sex, educational level, number of chronic diseases, income, smoking as confounding factors will be discussed. C.N.R. grants P.F. 40.92.00314.

7-21-23 SUBACUTE SCLEROSIS PANENCEPHALITIS (SSPE) – REGIONAL DIFFERENCES

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A joint Japan (JP) - Pakistan (PK) study in the years 1983 - 1992 has revealed that (1) SSPE incidence in 50 - 100 fold, (2) ratio of late measles among SSPE patients is 2 fold, (3) SSEP incidences among early and among late measles sufferers are 15 and 75 fold, respectively, (4) ratio of fulminant form is 2 fold, (5) frequency of fever associated with SSPE onset and (6) efficacy of inosiplex are definitely, all higher in PK than in JP. The situation in USA seems different from both PK and JP.

Some, but not all, of these differences may be derived from the regional difference in vaccination coverage. We suggest that some other regional factors intrinsic to each region may be operating for the development of SSPE. Repeated injuries against host immune system may be one of those factors in high risk regions.

7-21-24 **EPIDEMIOLOGICAL EVIDENCE FOR AN ETIOLOGICAL ROLE OF CYANIDE IN KONZO, A NEW UPPER MOTONEURON DISEASE FOUND IN AFRICA**

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Konzo is a distinct form of upper motoneuron disease, characterized by abrupt onset of a permanent, non-progressive spastic paraparesis, mainly affecting women and children. During the last decade outbreaks of konzo have been described from six widely separated rural areas in four African countries: Mozambique, Tanzania, Zaire and Central African Republic with prevalences up to 7%. All studied cases are seronegative to retrovirus.

The epidemiological studies in these areas have attributed konzo to dietary cyanide exposure from insufficiently processed cassava and newly developed biomarkers of cyanide exposure are supportive. We review the findings that indicate a causal role in abrupt upper motoneuron damage of sustained high blood cyanide concentrations maintained by a deficient sulphur intake impairing cyanide to thiocyanate conversion. Further investigations of the causative mechanisms in konzo may contribute to the general understanding of neurodegeneration.

7-21-25 INFLUENCE OF GENDER ON SUSCEPTIBILITY TO MULTIPLE SCLEROSIS (MS) IN SIBSHIPS

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Research has given conflicting results about whether there is an excess of like-sexed pairs among concordant MS sibships. This study's purpose was to provide additional information on the issue. Patients with an MS sibling were sought through the files of a university MS clinic. The clinic neurologist either reviewed relevant clinical/autopsy material or assessed relatives of index cases prior to accepting the relative as having MS. Pairs of siblings (excluding twins) were divided into (1) male-male pairs; (2) female-female pairs; (3) female-male pairs. A total of 51 concordant sibling pairs were identified. There were 27 like-sexed pairs (6 male-male/21 female-female) and 24 unlike-sexed pairs. The observed number of like-sexed pairs was not significantly different from expected using 2 x 2 X^2 analysis, where expected values represent the binomial distribution predicted from the frequency of each sex as determined by total number of males and females. The age at onset intraclass correlation coefficient was -.15 for like-sexed pairs and +.48 for unlike-sexed pairs. This study does not provide evidence for an association between disease susceptibility and gender in siblings concordant for MS; it does suggest that genetics partially determines age at onset in unlike but not like-sexed MS sibling pairs.

7-21-26 ALCOHOL AND HEMORRHAGIC STROKE: A CASE CONTROL STUDY IN CHILE – PRELIMINARY RESULTS

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OBJECTIVE: To study in Chileans whether alcohol intake is a risk factor in Hemorrhagic stroke (HS).

DESIGN: Case-Control study. Assuming RR = 2, Alfa = 0,05, Beta = 0,10 30% the prevalence of alcohol consumed in the control group, A required sample size is 136 cases and 136 controls.

The cases were prospective hemorrhagic stroke inpatients to JJ Aguirre Hospital from August 1991 to October 1992. The Controls were inpatients from other units: matched by age and sex with the cases. Alcohol was measured in weekly intake, number of heavy drinking, types of alcohol consumed and alcoholic symtoms. Patients were classified in non drinker, normal drinker, moderate drinker, excessive drinker and alcoholic.

RESULTS: 70 conceccutive patients were studied, 36 female and 34 male. The control group were 39 female and 31 male. The mean age 64.9 years old for cases and 63.9 for control group. The hipertension appears the most important risk factor with Odds Ratio (OR) = 6,44, 95% CI (2.75 , 15.3), p-value = 0.00003. Using as a reference non drinking condition, high alcohol intake has OR = 3.76, 95% CI (0.98, 15.5). For the alcoholic condition, OR = 4, 89, 95% CI (1.42, 18.5); p = 0.04. Diabetes high cholesteral level, medication use and cigarette smoking were not statistically significantly related to hemmorrhagic stroke. The OR for hypertension stratified on other factor showed non interation and non counfounder with smoke, diabetes, alcohol excess, cholesterol, sex and chronic use of medication. OR for alcohol excess stratified on other variables showed only interaction with smoke condition. Step wise logistic regression with all main effect select hypertension, alcohol excess, and liver disease.

7-21-27 EPIDEMIOLOGY OF PARKINSONISM IN UPPER EGYPT

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In our door to door field study carried out on a population of 42,000 subjects in Assiut Governorate, the total prevalence of parkinsonian syndromes due to different aetiologies was 226/100,000 population and that of Parkinson's disease was 102/100,000 population which is a midway prevalence between Western countries, on one hand and Eastern & African coutries on the other hand. Atherosclerotic parkinsonism has a prevalence rate of 66.6/100,000 population which is higher than that recorded in other countries. Encephalitis was more common in Upper Egypt (33/100,000) than in population of European countries and U.S.A. (Esam et al., 1991). Parkinson's disease mainly affects people over 50 years, both the incidence and prevalence being low before that age. The age specific prevalence appears to increase up to the age of 80 years. In cases of atherosclerotic parkinsonism, a lower peak of age specific prevalence was observed at age of 70 years. All cases of encephalitic parkinsonism and drug induced parkinsonism were recorded in younger age group between 30 - 40 years. Sex prevalence in parkinsonian syndrome was significantly more common in males than females (P 0.05). A steady increase in the prevalence rate of all subgroups of parkinsonian syndromes was noted between urban, suburban and rural localities.

7-21-28 MORTALITY IN PATIENTS WITH PARKINSON'S DISEASE

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In recent reviews of the literature concerning mortality in Parkinson`s disease a change mortality has been reported. Before introduction of levodopa in the late 1960-ties, patients with Parkinson`s disease had a 2,9 times *increased mortality ratio compared to an age and sex standardised* normalpopulation. A decrease in mortality ratio has been reported. The aim of the present study has been, in a representative population of patients with Parkinson`s disease, to calculate standardised mortality ratioes (SMR) for causes of death. The study involved 458 patients, who in the period 1.4.1973 to 31.10.1991 were treated to Odense University Hospital with the diagnose Parkinson`s disease. In the period 254 patients died, 135 men and 119 females. Mean age at death was 74,33 and 75,56 years for males and females respectively and mean age in the general population at death was 71,8 years and 77,6 years for males and females respectively. The most important causes of death were for males infections 31,3%, heart diseases 31,3%, and malign neoplasm 4,5%, for females infections 23,1%, heart diseases 24,8%, and malign neoplasm 17,1%. Standardised mortality ratios for various causes of death will be presented and discussed.

7-21-29 SUICIDE IN PARKINSON`S DISEASE. A EPIDEMIOLOGICAL STUDY.

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A recent review of the literature on suicide in neurological diseases has shown that no proper studies concerning the suicide risk in Parkinson`s disease exist.
The aim of the present study has been, through an epidemiological study to assess whether patients with Parkinson`s disease are at an increased suicide risk.
The study involved 458 patients who in the period 1.4.1973 to 31.10.1991 were treated at Odense University Hospital with the diagnose Parkinson`s disease. In the study period 254 patientsdied, 2 patients committed suicide. The number of expected suicides was 1,06 for males and 0,55 for females, a total of 1,62. Neither for males nor for females the difference between expected and observed suicide was statistically significant.
The results will be discussed in relation to mortality of suicide in other neurological diseases.

7-24-01 DIDACTIC COURSES FOR NEUROLOGY RESIDENTS: HOW IS SUCCESS OR FAILURE EVALUATED?

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Formal instruction in basic sciences is requisite to graduate neurological education. As service commitments increase, efficiency for faculty and compliance/adherence by students are increasingly prized.

Two recent courses for Neurology and Psychiatry residents are contrasted in terms of goals, resident reactions, and opinions of faculty, both participants and non-contributors. Course A was formulated conceptually (blocks titled "Movement", "Learning" ...); Course B serially presented disciplines ("Neurochemistry", "Imaging" ....)

Faculty were reluctant to participate in A citing lack of evident cooordination; non-contributors however enjoyed the holistic and speculative presentations. Residents attended only those sessions pertinent to their current interests. Course B was easily recruited ("canned talks"), often avoided by other faculty, and routinely attended by residents as a boards preview. In-service exam scores under both A and B correlated with students' prior exams rather than course type.

Further studies on promulgation of "life-long learning" will clarify whether student-defined or teacher-defined patterns of content and attendance are preferable.

7-24-02 KURU, MOTH MADNESS, AND QAT: CAN ETHNOLOGY HELP INTEGRATE BASIC AND CLINICAL NEUROSCIENCE EDUCATION?

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Too often "Red eardrum...ampicillin" is the model for medical practice; a sign is identified and a therapy prescribed. Lip service only to basic science is unfortunately pervasive among non-academic practitioners and compelling models of its utility or necessity seem scarce.

Three "exotic" ethnological clinical examples are considered: kuru (locally ascribed to sorcery but pathologically to prion transmission), "moth madness" (the Navajo name for epilepsy believed due to sibling incest but treated by western medicine with cell-membrane stabilizers) and the consumption of qat, a phenylethylamine, by East Africans who assuage hunger and diarrhea and gain quasi-religious ideation through its use (all reducible to pharmacological explanations.)

The subliminal nature of basic science in these settings is evident; further analysis is exemplified by the initial ascription of prion transmission to cannibalism but when oral transmission proved rare, ritual rubbing of body parts was noted retrospectively. Such interplay between physical, social, and clinical sciences are perceived by students as intriguing, and parallels to their own cultural settings are volunteered. Formal measurement of such transfer of awareness needs to be pursued.

7-24-04 AMBULATORY CARE EDUCATION IN NEUROLOGY.

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U.S.Health care education has evolved into various phases parallel to U.S.health care delivery. Undergraduate and postgraduate education in North America is undergoing transformation due to cost, access and equity of medical education. Changes are taking place in many medical disciplines. In spite of changes in neurological education at undergraduate and postgraduate levels, there is much to be desired in the role of ambulatory care education in neurology. This paper deals with the unique role of ambulatory care education in neurology. A comprehensive, collaborative education program for neurology staff and students along with other ancillary services and medical disciplines is in progress at the Los Angeles Outpatient Clinic, largest VA ambulatory care center closely affiliated with the Dept. Neurology at USC. The concept of ambulatory day care treatment center is proposed where neurological patients are seen with active discussion with staff and providing consultation to other needed services. Subject review handout sheets and audiovisual aids are used to reinforce case studies. It is proposed that 50% of neurological training care can be provided from ambulatory care setting. An outcome analysis will be presented.

7-24-05 WITHDRAWN

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

8-08-02 LIMITATIONS OF ISOFLURANE ANAESTHESIA IN STATUS EPILEPTICUS -REPORT ON TWO CASES.

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The effectiveness of isoflurane, a volatile anaesthetic, in prolonged convulsive status epilepticus (Hilz et al., 1992) seems to depend on an early onset of therapy and seizure etiology:

In a 35-year-old female with a history of partial and tonic clonic seizures, status epilepticus with tonic clonic seizures evolved due to irregular medication. Diazepam, phenytoin, thiopentone sodium (50 mg/h) did not interrupt the status. After 24 hours, isoflurane was administered for 3 hours (0.5-1.5 vol.%). Status discontinued, but reappeared within 48 hours. Another 4 hours of 1.5 vol.% isoflurane insufflation terminated the status.

In a 28-year-old schizophrenic female, unknown heavy metal intoxication induced convulsive status epilepticus. Clonazepam, phenytoin and thiopentone sodium were not effective. 10 days after status onset, isoflurane was first applied (1.5-2.0 vol%). Seizures discontinued, but reoccured with 1.2 vol % isoflurane. After 7 days, isoflurane was discontinued, since there is no experience with its long-term application in seizures. Seizures reappeared. A suicidal heavy metal intoxication was diagnosed. The patient developed a vegetative state. The poor outcome is due to the etiology. Beyond, isoflurane's effect seems to be impaired by its late application.

8-08-03 EFFECTS OF 10-SECOND VENTRICULAR ARRHYTHMIA ON THE CEREBRAL BLOOD VOLUME IN CATS: TACHYCARDIA VERSUS FIBRILLATION.

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Studies that have monitored the cerebral circulation during ventricular arrhythmia are rare. We compared the cerebral microcirculatory changes elicited by experimental ventricular tachycardia (VT) and fibrillation (VF) in anesthetized cats. Thoracotomy was first performed. In 7 animals, the left ventricle was electrically stimulated (5-6 V, 10-20 ms, 300/min) for 10 s through a bipolar needle-type electrode (a model of VT; J Neurol Sci 1992;111:153). In another 7 animals, 10-s VF was induced by stimulating the left ventricle with an electric fibrillator (a model of VF). The cerebral blood volume (CBV) in the cerebral cortex was measured continuously with a photoelectric apparatus (Am J Physiol 1978;235:H56). The CBV was significantly decreased (-4.12±0.57 vol%, $p<0.01$) during VF, but exhibited an increase (reactive hyperemia; +1.51±0.39 vol%, $p<0.01$) immediately after conversion to the sinus rhythm. The CBV gradually declined thereafter. MABP was markedly reduced (-105.4±13.6 mmHg, $p<0.01$) during VF, followed by a mild overshoot after the termination of VF. Although the CBV reduction during VT (-0.63±0.12 vol%, $p<0.01$) was smaller than that during VF, a minimal reactive hyperemia (+0.26±0.06 vol%, $p<0.01$) was also observed just after restoration of the sinus rhythm. In conclusion, both VT and VF of 10-s duration significantly affected the cerebral microcirculation in cats. The present results support the widely believed but poorly proved hypothesis that the cerebral ischemic symptoms observed during ventricular arrhythmia are caused by a reduced cerebral blood supply.

8-08-04 PHILOSOPHY AND STRATEGY OF EMERGENCY NEUROLOGY

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In the past decades four major occurrences demand to be reviewed in DIAGNOSTIC, therapeutic as well as prevention program: 1. decrease in mortality and incidence of stroke; 2. significant improvement in NEW DIAGNOSTIC METHODS: CT, MRI, MRS, SPECT, EPs, USG...; 3. development of modern epidemiology; 4. antiaggregation and antithrombotic agents. To these facts should be added new knowledge in dg and pathophysiology of DAT, PD, headache, etc. For effective management of neurological diseases, mainly in emergency neurology it is necessary to have new philosophy and strategy for early, precise and definite diagnosis. The authors present DIAGNOSTIC PROGRAMME which allows to finish definite dg within 2 - 3 hrs after admission of pts to the hospital.

8-08-06 BILATERAL STRIATAL NECROSIS ASSOCIATED WITH ACIDEMIA

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[**Purpose**]The pathogenesis of the bilateral striatal necrosis in acute encephalopathy associated with methanol or cyanide intoxication, hemolytic-uremic syndrome or hypoxemia has been unclear yet. This is the first report of the radiological findings in aspirin intoxication with this type of necrosis and of it's serial neuroradiological follow up. We attempt clinicoradiological correlation in two patients with this type of necrosis.

[**Materials and methods**]The materials consisted of two patients of acute encephalopathy with bilateral striatal necrosis which were confirmed by serial examinations of cranial computed tomography and magnetic resonance imaging; a 24-year-old female patient with aspirin intoxication and a 42-year-old female patient with diabetic ketoacidosis, both in chronic alcohol dependence. We studied the history, the neurological and neuroradiological findings, biochemical data and clinical sequelae to look for similarities in both patients.

[**Results**]The serial neuroradiological findings were very similar. On early stage, the lesion distributed over frontal white matter and striatum. On later stage (3 months or more after onset), this distribution was localized in striatum. The clinical similarities were as follow; deep coma and severe lactic acidemia on admission, optic atrophy as sequelae, and heavy alcohol drinking just before onset.

[**Conclusion**]The acute bilateral striatal necrosis might have been introduced by the metabolic derangement of neural cells associated with lactic acidemia. The striatum might be one of the target areas of TCA cycle blockade.

8-08-07 FATAL CEREBRAL AIR EMBOLISM FOLLOWING ESOPHAGOGASTRODUODENOSCOPY AND ESOPHOGEAL STRICTURE DILATION

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We report a patient who experienced fatal cerebral air embolism following esophagogastroduodenoscopy (EGD) and esophageal stricture dilation. This complication of these common procedures has not been previously reported.

A 70-year-old man with acute upper gastrointestinal bleeding underwent emergent EGD. A bleeding distal esophageal ulcer was cauterized. EGD with esophageal dilation was performed two days later for esophageal stricture. Subsequently, the patient became diaphoretic and hypotensive. Neurologic exam revealed unresponsiveness, roving conjugate eye movements, extensor limb posturing, hyperreflexia, and Babinski signs. Head CT showed multiple low attenuation areas consistent with air emboli.

Despite hyperbaric oxygen, hyperventilation, and hyperosmolar therapy, the patient developed cerebral edema, leading to uncal herniation and death five days later. Autopsy demonstrated cerebral edema and infarction. There was no evidence of esophageal rupture, varices, or esophagovascular fistula. Cardiac exam revealed a patent foramen ovale.

We suggest the possiblity that air insufflated into the esophagus during balloon dilation of the stricture, reached the venous circulation through esophageal mucosal lesions, and then the cerebral arteries via the patent foramen ovale. Although rare, cerebral air embolism should be recognized as a potential complication of EGD and esophageal dilation in patients with patent foramen ovale.

8-08-08 REDEFINING BRAIN DEATH FOLLOWING CARDIAC ARREST

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Approximately 350,000 American patients experience a cardiac arrest each year. There is an urgent need to develop reliable criteria to predict neurologic outcome following cardiac arrest. An initial step is to identify patients with a hopeless prognosis regardless of how well they were managed.

We performed a prospective analysis of 40 patients with cardiac arrest in whom coma exceeded 6 hours duration. All had preserved brainstem function. Twenty-six patients died without awakening. Median nerve somatosensory evoked potentials (SEP) were the most useful guide to predicting outcome and, when absent bilaterally, always predicted death without awakening. Neuropathological study was obtained in 8 patients. The absence of cortical potentials correlated with global cortical necrosis.

There is sufficient scientific evidence now available to revisit the definition of brain death. It should include patients who are cortically dead as defined by the bilateral absence of cortical SEP. Greater utilization of SEP in comatose patients following cardiac arrest would avoid costy and dehumanizing care that is ultimately to no avail.

8-08-09 OUTCOME AFTER CARDIO-RESPIRATORY ARREST.
Treatment with Monosialoganglioside GM1.
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National University of Cuyo. Mendoza. Argentina.

Case history: A 29 year-old woman suffered a cardio-respiratory arrest during a gynecological operation in general anesthesia. During 15 days she remained in deep coma (Glasgow coma scale O1 V1 M2).
Follow up: 2 months later she was confused, desoriented, with attention and memory disturbances. Midriasis right. Upward gaze paresis. Hypertonic right limbs. Extensor response right. Visual agnosia.Apraxia. Acalculia. Alexia with agraphia.
Treatment: Repeated series of Monosialoganglioside GM1 40 mg daily (3 weeks each) and then 100 mg daily (2 weeks each).
Results: Progressive improvement of higher functions. Clearness of the state of consciousness. Better motility. She is independent in daily activities.
Effect of GM1 on association pathways and neuroplasticity?

8-08-10 PERSISTENT VEGETATIVE STATE AFTER 9 YEARS.
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A 67 year-old female patient suffered a traffic accident in 1984 with an indirect cranio-cervical trauma consisting of a side-to-side brisk head movement. She developed initially a deep state of unconsciousness (Coma III, Glasgow scale M2 O1 V1).
Neuroimaging studies showed a small cerebral hematoma in the left parietal region and signs of subarachnoid hemorrhage. E.E.G. and brain mapping with diffuse slow activity. Prolongation of central conduction time in evoked potential studies. Bilateral hydrocephalus followed by a ventriculo-peritoneal shunt in 1985. Two epileptic fits in 1986.
With intensive and continued support and care the patient remains with few changes in the neurological condition and is clinically not impaired.
The final outcome is still uncertain.

8-12-01 NEUROETHICAL DILEMMAS AND PERMANENT VEGETATIVE STATE (PVS).
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PVS is characterised by complex, stereotyped repetitive patterns, related to relatively fixed neuronal circuitry in the absence of functional cerebral hemisphere, that do not require awareness. Though certain aspects of the care and management of the PVS patient are known, there is no broadly accepted set of specific medical criteria for diagnosis of PVS. The clinical prognosis and meaningfulness of life in PVS remain questionable. EEG, MRI, CAT scan and cerebral blood flow, which are very useful in the diagnosis of brain death, are not always helpful in the evaluation of PVS. This paper provides comprehensive suggestions regarding neurological, legal, social and political issues pertaining to neuroethical dilemmas in PVS. An attempt is made to suggest implementable recommendations in controversial cases, such as the use of PET scan to augment diagnosis, change the definition of death by legislative action to encompass PVS as a state of being already dead, educate the public about cognition, condone the use of passive and in some cases active euthanasia for resolving the issues related to PVS.

8-12-02 ETHICAL ISSUES PERTAINING TO THE CARE OF THE PATIENTS IN PERSISTENT VEGETATIVE STATE (PVS).
C.A. Defanti, on behalf of "The Bioethical Commission of the Italian Society of Neurology".

This Commission analysed the Statement of the American Academy of Neurology (1989) on certain aspects of the care and management of PVS patients. It found it flawed, in so far as it assumes that artificial hydration and nutrition are medical treatments and, as such, can be withdrawn or withheld if the patient so decides through an advance directive. In fact some patients can be fed by mouth, and for this reason we think that feeding is part of normal nursing care. The treatment of PVS needs to be viewed in a broader ethical and philosophical framework. Most members of this Commission think that, morally, PVS is basically equivalent to Brain Death (BD) or, more precisely, to BD when the homeostatic functions of the brainstem are supported (as it happens during the process of its ascertainment). Being PVS equated with the death of the human being, nutrition and hydratin are redundant treatments and can be withdrawn. A few members, however, argue that BD and PVS are different conditions and don't accept the suggested equivalence. In any case this Commission prompts a public debate upon the new concept of death and the obligations towards the dead and the dying.

8-12-05 "ADVANCE DIRECTIVES" (ADs) AS PERCEIVED BY SPINAL CORD INJURED (SCI) PATIENTS AND THEIR CARE-PROVIDERS
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Technological advances and patient-centered ethics led to ADs: the living will (LW) and durable power of attorney for health-care (DPOAH); acceptance has been problematic.

Eighty-six SCI patients and sixty-two care-providers (physicians/assistants, nurses, therapists) responded to separate questionnaires. All patients recognized ADs; 40% had discussed them with providers cf. 66% with family. A LW was implemented by 85%; a DPOAH by 38%. Only 15% felt SCI had altered their subsequent attitudes towards death.

Care-providers endorsed competent patients as decision-makers; nurses uniformly wouldn't question patients' ADs, but most physicians and therapists would. Young physicians believed with non-physicians that a desire to save lives prevents providers from promoting ADs; older physicians cited time constraints. Despite 78% believing "everyone should have ADs," only 28% did. Age didn't correlate; ethics committee membership increased liklihood to 55%.

Patients express less discomfort regarding ADs than care-providers, whose low prevalence of ADs implies denial rather than interpersonal discomfort. Exploration of SCI patients' rejection of injury-related attitudinal changes may enlighten care-providers' own fears.

8-17-01 DOPA-UNRESPONSIVE PURE AKINESIA OR FREEZING: A CONDITION WITHIN A WIDE SPECTRUM OF PSP?
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Barbeau (1972) first described "pure" akinesia without rigidity and tremor responsive to L-dopa therapy. Since 1974, Imai and Narabayashi described cases with pure akinesia unresponsive to L-dopa treatment as a new condition. This condition exhibits only freezing symptom, which is a breakdown of repetitive voluntary movements emerging through festination or suddenly, e.g. freezing of gait, micrographia and inaudible speech. Kinésie paradoxale is always accomanied by this type of akinesia. The authors would like to report on our own 35 cases with this condition, and to review the subsequent development of clinical, pharmacological, neuropsychological and pathological investigations of this condition.

All cases were sporadic and slowly progressive, with some having been followed for more than 10 years, still without rigidity and tremor. L-threo-DOPS, a synthetic norepinephrine precursor, had a mild-to-moderate effect on some cases with freezing, but not persistent. Slight muscular hypotonia was observed in the extremities in two-thirds of the cases with no signs of cerebellar ataxia. Slowly progressive supranuclear ophthalmoparesis with MLF syndrome appeared later in some patients whose clinical diagnosis were changed to having progressive supranuclear palsy (PSP) despite no nuchal dystonia. Autopsy cases associated with this condition have been reported from several institutions in Japan and pathologically revealed PSP or pallido-nigro-luysian atrophy. The nosological position and responsible lesion sites of this condition are discussed.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

8-17-02 PRAMIPEXOLE IN ADVANCED PARKINSON'S DISEASE: A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED MULTICENTER TRIAL.

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This trial was performed to assess the efficacy, safety and tolerance of Pramipexole, a new dopamine agonist, in advanced Parkinson's disease. 78 patients were enrolled and treated either with Pramipexole or matching placebo tablets (q.i.d) for three months, as add-on therapy to levodopa/decarboxylase inhibitor. The maximal daily dose of Pramipexole was 5 mg using an ascending dose schedule, and a maintenance dose interval of at least 4 weeks. The effects of treatment were evaluated weekly or bi-weekly by the Unified Parkinson's Disease Rating Scale. Patients also kept a daily record of the occurrence of "on" and "off" periods 1 week before and at the end of the trial. Safety was assessed by the electrocardiogram, laboratory investigations, measurement of blood pressure and pulse, and by recording of spontaneously reported adverse events. After the end of the trial 32 patients entered long-term, open-label treatment with Pramipexole.

8-17-03 ANALYSIS OF SYMPTOMS IN PARKINSONISM WITH LESIONS IN WHITE MATTER AND/OR BASAL GANGLIA

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Pathophysiology of the parkinsonism attributable to the cerebrovascular lesions has not been elucidated. In order to clarify this issue, the relationship between symptoms and lesions detected by MRI was investigated. A total of 46 patients of parkinsonism with cerebrovascular lesions were studied. They are divided into three groups according to MRI findings, i.e., with lesions only in the white matter (group1; n=23), in the basal ganglia (group 2; n=3) and in both of them (group 3; n=20). The severity of five symptoms of those patients, i.e., tremor, rigidity, bradykinesia, petit pas gait and frozen gait, were evaluated as three degrees, i.e., mild, moderate and severe. The rigidity in the most severe grade was observed in group 1, while the tremor was prominent in group 3. It is notable that rigidity was remarkably mild in the most of cases in group 3. No relationship between other three symptoms and topography of lesions was observed. The neuronal interaction between white matter and basal ganglia might reflect the appearance of symptoms in parkinsonism such as rigidity and tremor.

8-17-04 TREATMENT OF FOCAL MOVEMENT DISORDERS WITH BOTULINUM TOXIN A.

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We report the results of botulinum toxin A (BTA) (Dysport, Porton Products, UK) treatment over a 4 year period in 75 patients with blepharospasm (BS) (n=13), Meige's syndrome (MS) (n=7), hemifacial spasm (HFS) (n=24), cervical dystonia (CD) (n=25), and writer's cramp (WC) (n=6). Criteria for inclusion in the study comprised adequate diagnostic work-up and follow-up and a negative response to preliminary placebo treatment (saline injections). EMG was used to localize dystonic muscles and guide BTA treatment in CD and WC. Composite scores, derived from standardized subjective, objective, and video scores, were used to calculate % improvement at the end of each treatment cycle.

	% improvement	# of sessions	time window	neurotoxin dose (pg)	relapse interval (months)
BS	76±16	1	3-8d	176±37	2.8±1.0 (1.5-4)
MS	50±13	2-4	4-8wks	884±413	4.0±1.6 (3-6)
HFS	85±10	1-2	1-8wks	242±118	4.4±2.4 (2-10)
CD	66±19	1-10	2-26wks	1774±1252	3.8±2.3 (2-10)
WC	44±11	1-5	4-32wks	560±267	------

Side effects were transient and included ptosis, moderate in BS (n=4) and mild in BS (n=3) and HFS (n=2), mild lower facial weakness in HFS (n=7), and mild dysphagia (n=2) and diplopia (n=1) in MS. We conclude that BTA is a safe and effective treatment for focal movement disorders.

8-17-05 NEUROPATHOLOGY OF MCLEOD PHENOTYPE IS LIKE CHOREA-ACANTHOCYTOSIS (CA)

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McLeod phenotype red cells (RCs) are acanthocytic, with reduced Kell blood antigens (autosomal), and absent X-linked Kx antigen. The phenotype includes mild myopathy, elevated serum creatine phosphokinase (CK), occasional cardiomyopathy or neuropathy.

WA had McLeod phenotype: neurological exam at 34 was normal. At 41, he had choreiform limb movements and cardiomyopathy. He developed severe generalized chorea, widebased gait, proximal myopathy, fasciculations, absent deep tendon reflexes, mild distal vibration loss. Lipids were normal, CK was 788, and 33% of the RCs were acanthocytes. He died at age 50 of unknown cause.

Autopsy: markedly atrophied caudate; cerebellum & brainstem normal and pigmented. There was severe neuronal loss & astrocytosis of caudate; moderately severe in putamen. There was mild diffuse astrocytosis in globus pallidus, but focal in a small region of SN. These findings are the same we and others have reported in CA. This case of McLeod is unique in developing gross neurological signs and pathology suggestive of CA, and may represent a link between these two disorders.

8-17-06 MANGANESE TOXICITY FOR STRIATAL GABA NEURONS IN CULTURE.

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Chronic Manganese (Mn) intoxication has often been linked to parkinsonism. However, close analysis reveals that dystonia is the predominant symptom. Accordingly, pathological studies in humans, rabbits and monkeys demostrated basal ganglia (BG) rather than substantia nigra lesions (for review, see Barbeau A., Neurotoxicology, 1984). To identify the neuronal target of chronic Mn intoxication, MnCl2 was added to serum-free dissociated mesencephalic and striatal cultures on day 4 in vitro. Twenty four hours later, dopamine (DA) and GABA uptakes were assessed as specific functional markers of DA and GABA neuron viability. MnCl2, at concentration ranging from 1.6 to 16 uM, reduced specific GABA uptake in striatal culture without affecting DA and GABA uptakes in mesencephalic culture. MnCl2 concentration up to 16 uM reduced uptake parameters in both cultures systems. Our data confirm and extend previous reports indicating BG as the main target of chronic Mn intoxication. The involvement of cholinergic striatal neurons remains to be established.

8-17-07 A computerized TV-method for three dimensional multi-segmental kinematic analysis of tremor.

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We used a stereophotogrammetric system (ELITE-BTS) to evaluate tremor characteristcs. A rigid plate with four retroflective markers was straped in 8 body segments (hand, forearm, arm, trunk, pelvis, thigh, leg, foot). Two infrared TV-cameras were placed laterally to the subject. The angles between 2 consecutive plates in the 3 planes were calculated using the Eulero's angles computation. Preliminary studies were performed in 6 patients with postural tremor. The tremor was analyzed for 10 sec with the patients standing with arms outstretched in the horizontal plane. Measurements of the raw kinematic data records were supplemented with spectral analysis to determine the principal components of the tremor. Quantitative analysis identified the presence of tremor in all patients. It localized the tremor mainly distally in the upper limbs, with a frequency between 4.5 and 6 Hz.

8-17-08 AMANTADINE TREATMENT IS AN INDEPENDENT PREDICTOR OF IMPROVED SURVIVAL IN PARKINSONISM.

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Amantadine has been used for 20 years in the treatment of parkinsonism. Several discoveries suggest that amantadine may be neuroprotective in parkinsonism. We studied survival in parkinsonism, employing standard survival curves and a Cox regression model to identify independent predictive variables for survival (while taking into account factors associated with treatment selection bias).

Survival data was established in 934 patients. 250 received amantadine (100mg bid) for a mean duration of 79mo; amantadine treated patients did not vary from those untreated with amantadine by age, gender, Hoehn & Yahr (H&Y) stage at initial visit, or dementia status. Amantadine use was identified as an independent predictor of improved survival ($p<0.01$), as were younger age, absence of dementia, and low H&Y stage at initial visit (all $p<0.01$). Levodopa use showed a trend toward improved survival.

The association of improved survival with amantadine use may stem from ongoing symptomatic benefit/selection bias. Additionally, amantadine may be providing neuroprotection. We speculate that such action may be mediated through NMDA receptor antagonism, dopamine uptake blockade, or other mechanisms.

Please Note: 8-17-08 is changed to 2-13-11.

8-17-09 CRITERIA FOR CLINICAL AND INSTRUMENTAL DIAGNOSIS OF MSA

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The term MSA describes three syndroms : striatonigral degeneration olivopontocerebellar atrophy and Shy-Drager disease which are characterized by frequent coexistence of extrapyramidal, pyramidal, cerebellar and autonomic symptoms and signs. MSA is the most difficult differential diagnosis with P.D., infact about 15% of pts diagnosed as PD at the beginning develope signs of MSA during the course of the disease.

We studied 35 pts , 18 female and 17 male with clinical diagnosis of MSA. In all pts we evaluated clinical symptoms at the time of the diagnosis and during the course of the disease and the response to L-Dopa with pharmacological test (subcutaneous apomorphine 4mg, L-Dopa 250 mg plus IDD). Moreover CT scan, complete urodynamic evaluation, perineal needle electromyography and cardiovascular evaluation were performed. The majority of the pts (32 out of 35) had an akinetic-rigid syndrome at the onset of disease. At the time of the diagnosis 20% of pts had pyramidal signs ,30% cerebellar and 90% had signs of autonomic failure. 15% of the pts had a full response to L-Dopa, 40% had a partial response and the rest never responded to drug. 30% of the pts showed cerebellar atrophy at the TC scan.

At the urodynamic evaluation all pts showed the pattern of iperreflexia with sinergia. This evaluation was performed also in 33 pts with PD and pattern of iperreflexia with sinergia was found only in 26.7% of parkinsonian pts with duration and severity of disease significantly higher compared with the remaining.

Perineal electromyography showed in 95% MSA pts poliphasic and longer potentials. We conclude that important MSA diagnostic criteria were the response to L-Dopa, the evidence of cerebellar or disautonomic failure , the results of urodynamic evaluation and EMG of the perineal floor.The cardiovascular test most of the time do not give clear answer.

8-17-10 ANALYSIS OF THE DYSTONIA GENE (DYT1) IN RUSSIA

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Torsion dystonia is a genetically heterogeneous disease involving over three dominant autosomal loci. Mutations in the DYT1 gene on chromosome 9q34 appear to underlie most cases of early onset, generalized dystonia. The high frequency of this form of dystonia in the Ashkenzic Jewish (AJ) populations results from a single mutational event in that ethnic group about 10 to 20 generations ago, probably in Lithuania/Russia. This particular mutation in the DYT1 gene is marked by a distinctive haplotype defined by allelic variations at three of four loci surrounding the gene. Affected AJ individuals with early onset distonia from 7 families in Russia all manifest this haplotype, while AJ individuals with essential tremor from 5 other families did not. In addition, one non-Jewish individual with early onset dystonia potentially manifests this haplotype. By comparison, in the U.S.A. about 90% of AJ individuals affected with this form of dystonia have this haplotype and it has not yet been observed in any non-Jewish individuals. The presence of the classic AJ haplotype in a non-Jewish individual is most likely explained by an AJ ancestor, although historical introduction of the mutation into the AJ population from a non-Jewish source is also a (less likely) possibility. Benign essential tremor in this population is not caused by this same mutation.

Please Note: 8-17-10 is changed to 2-13-12.

8-17-11 DIFFERENCES IN CSF BIOPTERIN AND NEOPTERIN LEVELS AMONG PATIENTS WITH PARKINSON'S DISEASE, JUVENILE PARKINSONISM, AND DOPA-RESPONSIVE DYSTONIA

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Generally, patients with juvenile parkinsonism (JP) respond to L-Dopa very well and are more prone to develop severe dopa-induced dyskinesias and motor response fluctuations than those with classic Parkinson's disease (PD), and sometimes they are accompanied by dystonia prior to L-Dopa therapy. In contrast, although patients with dopa-responsive dystonia (DRD) develop parkinsonism, they are never followed by these adverse effects. We measured biopterin (BP) and neopterin (NP) levels in CSF of PD, JP, and DRD patients. The BP levels in the JP and DRD patients were markedly lower than in the PD patients. However, there was no significant difference in the mean NP levels between the JP and PD patients, while the NP levels in the DRD patients were substantially reduced. These results seem to indicate that there are two different patterns for the involvement of the nigrostriatal dopaminergic neurons, resulting in markedly reduced CSF BP content. One occurs in JP, and that may be more severe injury of the terminals (where BP is highly concentrated) than occurs in PD, or poor neuronal maturation of the neurons. The other occurs in DRD, and that may be a congenital functional abnormality including the BP biosynthesis.

8-17-12 CHARACTERIZATION OF FETAL HUMAN AND FETAL PIG VENTRAL MESENCEPHALON AS POTENTIAL CEREBRAL GRAFTS FOR PARKINSONIAN PATIENTS

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In order to obtain an optimal graft which is well characterized before clinical implantations, in our hospital a research program was started. Because of the low availability of human fetal VM tissue (gestational age 6 - 16 weeks), also fetal pig VM (gest. age 3 - 10 weeks) was studied on its potency as dopaminergic graft.

Characterization of both possible transplants was done by:

- examining the catecholamine (CA) contents by using high performance liquid chromatography (HPLC) with electrochemical detection.
- determining the cellular composition by culturing of the tissue with subsequent immunohistochemical staining.
- testing their functional effect and histological behaviour after implantation in rat host striatum, using the Ungerstedt rotational model.
- anatomical study of the development of the fetal VM's by immunohistochemical staining.

Preliminary results showed the presence of DA as detected by HPLC; the cell cultures yielded besides DA positive cells especially GABAergic (gamma aminobutyric acid) cells. The results of implantation and the anatomical results are still under study. We believe that besides human fetal VM, also pid fetal VM can be regarded as a potential alternative for dopaminergic donor brain grafts in parkinsonian patients.

8-17-13 **BOTULINUM TOXIN THERAPY IN THAI PATIENTS WITH HEMIFACIAL SPASM : THE RESULTS OF DOSE REDUCTION.**

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Hemifacial spasm (HFS) is characterized by involuntary, episodic twitches of muscles innervated by the seventh cranial nerve. We have reported elsewhere that botulinum toxin (BTX) was effective and safe in Thai patients with HFS. Because BTX is very expensive, we started a single blind, prospective clinical trial to study whether it is possible to reduce the dosage of BTX in subsequent injections.

BTX supplied by the PHLS, UK. HFS patients were injected for the first time with 0.2 ml (20 units) of BTX in two sites in the lower eyelid and 0.1 ml (10 units) of BTX in the lateral part of the upper eyelid as a recommended dose (total of 50 units). After the facial contractions resumed, the patients were given reduced dosage of 0.1 ml in the same sites without knowledge of the reduction (total of 30 unit). Patient improvement was subjectively assessed by using the visual analog scale and reported in percentages (0-100%). Duration of improvement was also measured in months (ms) as assessed by patients.

Results :There were 34 HFS patients, 7 male and 27 female. Ages ranged from 29-74 years (yrs) (mean 48.7 yrs). The range of duration of disease was 0.6-25 yrs (mean 5.5 yrs). At the recommended dosage treatments all patients improved. Improvement ranged from 50-100% (mean 84 $\pm$10%) and lasted for 2-5 months (mean 3.2 $\pm$ 0.8 ms). At lower dosage treatments all but one improved, ranged from to 0-100% (mean 80.6 $\pm$ 17%) and lasted for 0-8 ms (mean 3.2 $\pm$ 1.3 ms). Side effect was transient ptosis in 13 and 11 patients respectively. There was no statistically significant difference between the two treatments in terms of percentage, duration of improvement, and side effects. (P=0.28, 0.91, 0.5 respectively).

Conclusion : The dosage of BTX can be reduced as much as 40% in subsequent injections without compromising the efficacy of treatment and so the cost of treatment can be reduced.

8-17-14 THE USEFULNESS OF FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN THE DIAGNOSIS OF HUNTINGTON DISEASE

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To determine the diagnostic usefulness of positron emission tomography with ^{18}fluorodeoxyglucose in Huntington disease, we retrospectively studied the scans of 70 patients and 33 controls and quantified their positive and negative predictive value. Different analytical procedures to determine caudate hypometabolism were compared, including absolute metabolic rates, normalized values, combinations of normalized values, and analysis of residuals from prediction-equations. Nomograms of age-dependent confidence limits for prediction that defined sensitivity for different levels of specificity were constructed. Comparison of receiver operator characteristics curves showed that the caudate (circular ROI) / whole brain ratio, which correctly classified 97.1% of the HD scans at a 95% level of specificity, gave the highest overall sensitivity. However, the diagnostic yields of the normalized values and the prediction equations were similar. The high sensitivity of PET was apparent at all stages of the disease: in persons with only minor motor abnormalities but no chorea (n=9), in persons with rigidity (n=3), in persons over age 60 (n=11), and in persons without caudate atrophy on CT (n=18).

8-17-15 INVOLVEMENT OF CENTRAL DOPAMINE D-1 AND D-2 RECEPTORS IN MPTP-INDUCED BEHAVIORAL PARKINSONISM OF CYNOMOLGUS MONKEYS

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To address the role of dopamine (DA) D-1 and D-2 receptors in Parkinson's disease, behavioral effects of dopamine agonists were investigated in MPTP-induced parkinsonian monkeys, using irritability and aggressiveness as criteria. Both the D-1 agonist, SKF 82958 and the D-2 agonist quinpirole, improved the parkinsonism in a dose-dependent manner. Apomorphine, a non-selective DA agonist, also exhibited antiparkinsonian effects but induced marked hyperactivity. Pretreatment with D-1 antagonist, SCH 23390, or D-2 antagonist, sulpiride, completely suppressed the apomorphine-induced hyperactivity, and this was associated with a slight attenuation in its anti-parkinsonian effect. Combined treatment with SKF 82958 and quinpirole augmented both the antiparkinsonian effect and hyperactivity. Thus, stimulation of central D-1 or D-2 receptor causes hyperactivity, which may reflect psychotic side effects.

8-17-16 *STUDIES ON THE PATHOGENESIS OF PARKINSON'S DISEASE:* **An Immunohistochemical Study on α-Ketoglutarate Dehydrogenase Complex in Substantia Nigra.**

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Since the discovery of MPTP-induced parkinsonism, a number of abnormalities have been reported on mitochondria of Parkinson's disease (PD) including loss of complex I activity and subunits, and presence of deleted mitochondrial DNA. Now we report an immunohistochemical study on α-ketoglutarate dehydrogenase complex (KGDHC) in PD. The KGDHC is an interesting enzyme complex in that it is the rate-limiting enzyme of the TCA cycle, and its activity is inhibited by MPP^+.

We studied 11 PD patients and 6 control subjects. Paraffin-embedded nigral specimens were used. The immunohistochemistry was performed according to the ABC method using an antibody raised against KGDHC. In the control subjects, most of the melanin-containing nigral neurons showed intense immunostaining, although some of the neurons showed reduced staining. In PD, the proportions of poorly stained neurons were increased, but well stained neurons were also seen. The nigral neurons appeared to be a mixture of well stained to poorly stained neurons. Similar mixed patterns were also observed in our previous study on complex I in PD. Parallel changes between complex I and KGDHC in MPTP-induced parkinsonism and PD suggest the presence of degenerative process similar to MPTP-induced parkinsonism in PD.

8-17-17 RELATIVE INCREASE IN STRIATAL DOPAMINE D2 RECEPTOR DENSITY IN EARLY PARKINSON'S DISEASE: A PET STUDY.

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Striatal dopamine D2 receptors were investigated with (11C)-raclopride in two groups of patients with early PD. The first group "strictly unilateral" (SU) showed parkinsonian signs only on the other side of the body together with axial rigidity. The other group, "relatively unilateral" patients (RU), had bilateral symptoms, but still with clear asymmetry.

Two (11C)-raclopride scans were performed in each individual and the maximal number of receptors (Bmax) and their dissociation constant (Kd) was calculated by Scatchard analysis. In the SU group the Bmax of (11C)-raclopride binding was 36.6 pmol/ml in the striatum contralateral to the symptoms as compared to 27.2 pmol/ml in the ipsilateral striatum (P = 0.004, t-test). In the RU patients the Bmax value in the striatum contralateral to the predominant symptoms was 28.3 pmol/ml, not different from the value in the ipsilateral striatum (25.9 pmol/ml). No significant differences were seen in Kd values.

Thus, in early PD there is a relative increase in the number of striatal dopamine D2 receptors contralateral to the symptoms, if the disease shows a clear-cut asymmetry.

8-17-18 PET STUDIES ON (18F)FLUORODOPA UPTAKE AFTER COMT INHIBITION WITH ENTACAPONE IN PARKINSON'S DISEASE.

U.K. Rinne, J. Bergman, M. Haaparanta, A. Laihinen, V. Oikonen, J.O. Rinne, U. Ruotsalainen, H. Ruottinen, O. Solin.
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The aim was to investigate the effects of COMT-inhibition with entacapone (OR-611) on the peripheral methylation and the striatal accumulation of (18F)6-fluorodopa (6FD). As we have shown earlier with nitecapone, peripheral COMT inhibition increases the access of 6FD into the brain. 16 advanced parkinsonian patients had a 6FD PET scan both at baseline and 1 hr after the oral administration of 200 mg, 400 mg or 800 mg of entacapone, respectively. There was a significant and dose-dependent reduction of methylation in the arterial plasma after the administration of entacapone. The accumulation of 6FD in the striatum studied with PET was significantly increased after the administration of entacapone when compared with the baseline. Thus, entacapone increases the bioavailability of 6FD into the brain and improves the quality of PET imaging. Entacapone may be used as an adjuvant of levodopa in the treatment of PD.

8-17-19 *PRESYNAPTIC AND POSTSYNAPTIC STRIATAL DOPAMINERGIC* FUNCTION IN MANGANESE INTOXICATION STUDIED BY POSITRON EMISSION TOMOGRAPHY

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The neurochemical alterations resulting from chronic manganese (Mn) intoxication have not been established. We studied pre- and postsynaptic striatal dopaminergic function in 4 patients with chronic industrial Mn intoxication. We used high resolution positron emission tomography (PET) with 6-fluorodopa (6FD) and C-11 raclopride (RAC). The duration of Mn exposure ranged between 3 and 13 yrs, and the period of illness ranged between 5 and 7 yrs. All patients had a rigid-akinetic syndrome (15 to 28 on Modified Columbia Rating Scale), which had not been or only temporarily been improved with previous l-dopa therapy.

All 6FD scans were normal. There was a significant 16% mean reduction in the equilibrium striatum/occpital cortex RAC uptake ratio in the patients compared with controls (n=6) (Wilcoxon's rank-sum test: $p<0.025$). The results suggest that parkinsonism in chronic Mn intoxication is, at least partly, attributable to a loss of striatal D2 receptors. The normal nigrostriatal dopaminergic pathway and the loss of D2 receptors might explain the inefficient response to l-dopa therapy in these patients.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

8-17-20 AUTOLOGOUS INTRASTRIATAL ADRENAL MEDULLA/NERVE COGRAFTS IN PARKINSON DISEASE (PD).

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OBJECTIVE: To determine the safety and efficacy of intrastriatal adrenal medulla/intercostal nerve cografts in PD. BACKGROUND: Studies in nonhuman primates with experimental parkinsonism have shown that cografts of autologous adrenal medulla and peripheral nerve yield greater behavioral improvement and graft survival than do adrenal grafts alone. DESIGN/METHODS: 3 male and 2 female patients ages 45, 47, 53, 55 and 64, with advanced PD (Hoehn & Yahr Stage 3 to 5) were selected and evaluated using the Core Assessment Program for Intracerebral Transplantation (CAPIT) protocol. They were maintained on an optimal medication regimen and 3 baseline evaluations were performed over 3-6 mos. before surgery. Following right flank adrenalectomy, cografts consisting of small fragments of adrenal medulla and minced nerve were stereotaxically implanted into 3 targets in the right striatum (caudate/putamen) using MRI guidance. RESULTS: Surgery was uneventful and post-op MRI scans revealed accurate placement of the grafts. No morbidity was encountered. Three of the 5 patients showed improvement; two did not. In those that improved, post-op UPDRS motor disability scores in the "off" state decreased on average by 16% at 3 mos., 42% at 6 mos. and 27% in the two followed for 12 months. CONCLUSIONS: Autologous intrastriatal adrenal medulla/nerve cografting can be performed safely and early results are encouraging, but longer follow-up is needed.

8-17-21 **THE USE OF MADOPAR HBS IN PARKINSON'S DISEASE WITH SPECIAL REGARD TO NOCTURNAL DYSTONIAS AND RESPONSE FLUCTUATIONS**

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Madopar HBS has been used in 126 patients controlled by rating scales elaborated in our institute since 1987. We paid special attention for parkinsonian patients with nocturnal problems and response fluctuations. 80 patients with painful nocturnal dystonia causing sleep disturbances were given 250-375 mg Madopar HBS in the evening. The number of awakenings, the degree of nocturnal immobility and that of dystonias were registered. We have found a significant improvement in all parameters. Madopar HBS was administered to 46 patients with response fluctuations. In "wearing off" (N=26) a remarkable improvement was detected in 20 patients compared with the earlier standard Madopar therapy. In "on-off" patients (N=20) Madopar HBS proved to be effective in 8 cases. In 4 patients the alternating administration of standard and HBS Madopar resulted in the decrease of fluctuations. We have some preliminary experiences with Madopar HBS monotherapy in de novo patients, as well.

8-17-22 TREMOR CHARACTERISTICS AND FAMILY HISTORY IN PATIENTS WITH ESSENTIAL TREMOR VS. CERVICAL DYSTONIA ASSOCIATED WITH TREMOR

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We have shown that cervical dystonia (CD) patients commonly have a history of relatives with essential tremor (ET) and possess elevated titers of the antinuclear antibody (ANA), rheumatoid factor (RF), thyroid antibodies (THy Ab). To clarify the biologic relationship between ET and CD, 230 CD patients were assessed by protocol between 1/88 and 9/92. 116 (26M/90F) had accelerometer documented tremor of head and/or hands or audio recorded vocal tremor. 34 (16M/18F) patients with isolated tremor presumed to be essential were evaluated by similar protocol. Comparisons included: age at tremor onset, tremor distribution, handedness, family history: ET, dystonia (Dys), scoliosis (Scol), PD; ANA > 1:80, Thy Ab and RF. In 76 patients with CD and tremor (ET/CD) the neck was the solitary dystonic site. Mean age tremor onset: ET/CD-46 yr; ET 54 yr. Left Handedness: ET/CD - 8%; ET 6%. Family History: ET/CD - ET 45%, Scol 12%, Dys 8%, PD 6% (57% more than one of these disorders per family); ET - 53% ET, none of the others. Autoantibodies: ET/CD-thyroid 12%; ANA 26%, RF 8%; ET-Tyroid 9%, ANA 21%, RF 3%. Tremor distribution: ET/CD-64% head only, 89% head plus another region; 1 voice only, 7 voice plus another region; 10% hands only, 29% hands and another region, 6 asymmetric hand tremor. ET - 6% head only, 27% head and another region; 3% voice only, 21% voice and another region; 56% hands only, 29% hands and another region; 7 asymmetric hand tremor (only 1 left worse than right, patient left-handed). Tremor rates in the two groups were similar for age. The data suggest the mechanism underlying essential tremor and tremor in focal dystonia may be similar with a separate familial mechanism producing dystonia.

Please Note: 8-17-22 is changed to 7-17-27.

8-17-23 NON-MOTOR SYMPTOMS IN PARKINSON'S DISEASE (PD) AND ESSENTIAL TREMOR (ET)

R Pahwa, K Busenbark, K Miner, P Barnes, J Hubble, W Koller, University of Kansas Medical Center, Kansas City, KS

To compare the non-motor symptoms in PD and ET.

There is controversy if ET is a risk factor for PD. Non-motor syptoms associated with PD often antedate the motor signs by many years. If ET is a risk factor for PD we would expect these non-motor symptoms to be present in ET.

We compared 3 subject groups: PD (< 3 yr duration), ET (age > 50 yrs) and controls (age > 50 yrs). There were 20 subjects per group. All were questioned regarding: constipation(defined as bowel movements less often than 3 times/week or hard stools or the use of laxatives), presence of dermatitis (scaling, flaking, redness or oily skin), sensory complaints without known cause (burning, tingling or pain) and decreased sense of smell. All subjects were also administered Beck's Depression Scale.

The average age in the groups did not differ. The symptoms were present in the following subjects: decreased sense of smell 3/20 controls (1 current smoker), 12/20 PD (1 current smoker), 7/20 ET (6 current smokers); constipation 3/20 controls, 13/20 PD, 5/20 ET; dermatitis 3/20 controls, 3/20 PD, 5/20 ET; sensory complaints 3/20 controls, 7/20 PD, 6/20 ET; depression 0/20 controls, 2/20 PD and 2/20 ET (Beck's scale > 11).

Our data suggests that the non-motor symptoms of PD may have a similar incidence in ET.

8-17-24 BOTULINUM TOXIN TREATMENT IN VARIOUS MOVEMENT DISORDERS: AN EXPERIENCE OF 610 PATIENTS AT SIRIRAJ HOSPITAL

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DESIGN: Prospective double-blind controlled study of botulinum toxin in hemifacial spasm and prospective open study of other various movement disorders were analyzed.

SUBJECTS: The grand total of 610 patients with various movement disorders were analyzed. They were comprised of a) 429 patients (70.66%) with hemifacial spasm; b) 55 patients (9.02%) with writer's cramp; c) 50 patients (8.20%) with blepharospasm and Meige syndrome; d) 38 patients (6.23%) with spasmodic torticollis; e) 15 patients (2.46%) with hemidystonia; 10 patients (1.64%) with spasmodic dysphonia; f) 11 patients (1.80%) with miscellaneous types (e.g., tics, Gilles de la Tourette, facial myokinia, etc).

RESULT: The results of treatment for hemifacial spasm were classified as excellent in 81.2 percent, moderate improvement 10 percent, mild improvement 6.8 percent and no improvement or worse in 2.0 percent. There were complications of mild transient facial weakness in 10 percent and mild ptosis in 2 percent. The effect of botulinum toxin treatment lasted for 3 - 6 months duration. In writer's cramp and spasmodic torticollis the response rates were around two-thirds of all patients whereas blepharospasm, spasmodic dysphonia and tics were reponsed in 75 - 85 percent of the patients.

CONCLUSION: Botulinum toxin injection is a simple and effective out-patient treatment for patients with various kinds of movement disorders but it is a costly therapy.

8-17-25 APOMORPHINE (APO) s.c. by continuous infusion in the treatment of Parkinson disease with long term L Dopa syndrome (LTDS)

L. SCARZELLA, B. BERGAMASCO, M. DELSEDIME, C.GIANGRANDI, M. RIZZONE - CLINICA NEUROLOGICA TORINO - ITALY

Is treatment with APO s.c. useful during the L Dopa Drug Holiday in Parkinson patients with LTDS?

The L Dopa Drug Holiday and the APO s.c. treatment are two of the therapies for Parkinson disease with LTDS.

20 Parkinson patients 5IV-V Hohn-Yahr Stage in off fase) with LTDS. They underwent the L Dopa Drug Holiday for an average of 15 days (range 10-17 days). During this period 10 of the 20 patients were treated with APO s.c. with an average infusion of 4 hours (range 3-6 hours) with a variable dosage correlated to the response obtained from the Test with APO s.c. in acute phase and with Domperidone (30 mg. b. i.d.) to avoid the side effects of APO.

A quick clinical effect was notices in all patients treated with APO; this effect showed an improvement of 20% compared to the control group after having stopped the L Dopa Drug Holiday for 6 months.

The data obtained recommends the usage of APO s.c. during the L Dopa Drug Holiday as a new strategy for Parkinson disease with LTDS.

8-17-26 THE PREMORBID HANDWRITING OF PARKINSON PATIENTS

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Handwriting might serve as a source for retrospective analysis of movement patterns which could be related to physical and mental characteristics. In a blinded experiment 30 premorbid handwritings (22 of patients with Parkinson disease, 8 of patients with essential tremor) written mean 23 years before onset of motor symptoms and corresponding handwritings of 21 normal controls were analyzed for indices of hypokinetic and hypertonic movements, such as regularity, lack of rhythm, and elevated tension. In study one 73 and in study two 77 percent of the handwritings were correctly identified. In study three the 3 groups were correctly classified. The differences of proportion were significant. The study suggests that the changes in the movement patterns of the Parkinsonian patients can be identified long before the clinical onset of the disease. Differentiation between handwritings of patients developing essential tremor or Parkinson's disease, is, however, difficult.

8-17-27 PRAMIPEXOLE - A NEW DOPAMINE AGONIST: A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMIZED STUDY IN ADVANCED PARKINSON'S DISEASE.

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69 patients with advanced Parkinson's disease (mean age: 63 years; mean duration of illness 10.5 years; 40 males and 29 females) were randomized to either Pramipexole or matching placebo tablets as adjunct to treatment with levodopa/decarboxylase inhibitor. The maximal daily dose was 5 mg Pramipexole using an ascending dose schedule. Efficacy was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS). UPDRS baseline values were: 51.9 for Pramipexole and 56.7 for placebo. At the end of the treatment phase there was a significant difference in change of total score of the UPDRS between the groups (final values: Pramipexole: 34.8, placebo 47.7; $p=0.0048$). The scores of parts II and III of the UPDRS decreased during the treatment of three months indicating an improvement of the Activities of Daily Living and of the Motor Examination. The adverse event profile was similar to other dopamine agonists. Four patients in the Pramipexole and three patients in the placebo group were prematurely discontinued. Overall the efficacy and safety results indicate that Pramipexole will be a useful drug as adjunct to levodopa in the treatment of advanced Parkinson's disease.

After the end of the study 41 patients entered a long-term, open-label treatment with Pramipexole.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

9-02-02 IMMUNOLOGICAL AND ENDOCRINOLOGICAL ABNORMALITIES IN PARANEOPLASTIC DISORDERS WITH INVOLVEMENT OF AUTONOMIC NERVOUS SYSTEM

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The incidence of neurological paraneoplastic diseases is reported to be around 1%, but this figure could be underestimated. Furthermore, the diagnosis and treatment of the primitive cancer is often delayed because of the relative diagnostic difficulties. We report a series of 5 clinical cases in which the onset of a cancer was a neurologic non metastatic complication and dysautonomic symptoms. Pt. 1 (Eaton-Lambert syndrome and polyneuropathy): autoantibodies (IgG) against calcium channels (Ab-VOCCs), elevated values of ADH and dry mouth and impotence. Pt. 2 (limbic encephalitis, documented by MRI): monoclonal IgG/k chain myeloma, serum antineural nucleoprotein reactivity, and postural hypotension and severe constipation. Pt. 3 (poliradiculoneuritis): IgM against myelin components (anti MAG), myelodysplastic syndrome, pupillary abnormalities and postural hypotension. Pt. 4 (hypercalcemic encephalopathy): PTH-like serum activity, elevated urinary AMPc values and gastroparesis. Pt. 5 (pontine myelinolysis): the MRI and autopsy confirmed the osmotic demyelination syndrome but also discovered a cerebellar astrocytoma, whereas his EEG disclosed cardiac arrhythmias. The etiopathogenesis of neurelogical paraneoplastic disorders may include autoimmune and endocrinologic mechanisms.

9-02-03 SYMPATHETIC SKIN RESPONSE IN PARKINSON'S DISEASE.

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Sudomotor function was evaluated by using the sympathetic skin response (SSR) and the sweat response to intradermal acetylcholine (ACh) injection in 83 patients with Parkinson's disease (PD). The incidence of SSR abnormality (36.1%) was increased and the SSR size was reduced with the severity of the illness. Moreover, the incidence of SSR abnormality was not influenced by the anti-parkinsonian drugs, levodopa and anticholinergic agent, neither was the amplitude of those responses. Therefore, the SSR is useful in evaluating sudomotor efferent pathway in PD patients.

In all patients with absent SSR, the local sweat response to ACh showed a reduced number of excitable sweat glands and a low volume of sweat. In a patient in whom the local sweat response to ACh was markedly impaired, however, the density of acetylcholinesterase-positive unmyelinated fibers in the biopsied sural nerve was in normal range. Therefore, the abnormal results of sweat response to ACh are considered to reflect the dysfunction of the postganglionic sympathetic fibers in PD patients.

9-02-04 PUPILLARY ALTERATIONS IN MIGRAINE PATIENTS

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Pupillary responses to tyramine (T) (5%) and phenylephrine (P) (1%) eye drops were studied in 17 headache free migraine patients and in 17 controls. Pupillary diameter was evaluated in the basal condition and 15, 30 and 45 min after instillation. T and P tests were repeated after 3-6 months in both patients and controls. Pupillary asymmetries were apparent in basal conditions only in patients. They persisted during the test in 10 out of the total 68 evaluations (15%). Unilateral oculosympathetic hypofunction was found in 15 (44%) and 3 (9%) out of the 34 T tests, respectively in patients and controls. This alteration was associated with sympathetic receptor hypersensitivity (P test) in 2 patients. The test repetition confirmed the previous findings only in 5 patients. Unilateral oculosympathetic hypofunction seems to be temporary and not related to the presence and side of the pain in migraine patients.

9-02-05 THE RELATIONSHIP BETWEEN EEG CHANGES AND AUTONOMIC NERVOUS FUNCTION DURING DROWSINESS.

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In a previous study, we have analyzed the cyclic nature of heart rate changes during drowsiness period. In this study, we examined the relationship between electrencephalographic(EEG) activities and the hemodynamics (heart rate, blood pressure, and peripheral blood flow) during drowsiness period. EEG, continuous blood pressure, finger blood flow, respiration and electrocardiogram were monitored in six normal subjects. During drowsiness period, the abrupt increase of the heart rate, accompanied by decrease of the skin blood flow and increase of the blood pressure from the baseline, were frequently observed but the abrupt decrease of the heart rate from the baseline could not be found. There were no significant changes in the respiratory patterns. Immediately before the changes of the heart rates, however, the increased amplitude of alpha wave or the burst of the slow wave could be observed. In one subject without heaving respiration showed cyclic changes of heart rates accompanied by EEG changes. We suspect that the internal stimulus produced the EEG changes and autonomic nervous tone (mainly increase of the sympathetic tone) simultaneously.

9-02-06 DIABETIC AUTONOMIC SKIN'S NEUROPATHIES: A NEW METHOD FOR QUANTIFICATION

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50 patients suffering from non insulin dependent diabetes mellitus (NIDDM) since more than 10 years and 50 age-matched healthy volunteers were studied. The hyperthermal Spectral-analysis was developed for economy-priced and fast diagnosis in ambulatory routine use of autonomic skin's neuropathies. The basic consideration of this new method is that a healthy autonomic nerve-function reacts to hyperthermia with an increase of microcirculation in the heated area after a well defined time. This time-interval is called "hyperthermal perfusin latency" (HTPL) and is described in seconds, measuring the time-interval from the onset of heating until the first increase of perfusion. With a special developed probe for temperature it is possible to measure the change of skin-temperature as a correlate to microcirculation's elevation. By analogy to HTPL the measure time interval is called "Hyperthermal temperature latency" (HTTL).

In the neuropathic group the HTTL were significantly higher than in controls (203 against 78 seconds). It was possible to quantify the severity of pathology.

9-02-07 PANDYSAUTONOMIA: A CASE CLINICO-PATHOLOGICAL REPORT OF 5 CASES

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Five cases of pandysautonomia were reported. Pupils, salivary glands, sweat glands, gastro-intestinal tract, urinary bladder and heart were mainly impaired in all cases, indicating the peripheral part of both sympathetic and parasympathetic nervous systems being involved, especially the cholinergic post ganglionic efferent fibers. Besides, 2 cases showed sensory impairment of distal parts of extremities, slight atrophy of small hand muscles and weak or absence of deep tendon reflexes. Three cases showed elevation of CSF protein without cellular reaction. Sural nerve biopsy was performed in 3 cases. Neuropathological changes included the reduction of myelinated neurofibers, Schwann's cells atrophy and containing degeneration products and myelinlike structures.

It seems that the disease entity is a result of autoimmune dysfunction, which may be due to a varient type of Guillian-Barré syndrome or an independent disease. The prognosis of pandysautonomia in the present group is good.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

9-02-08 ASSESSMENT OF SUDOMOTOR DYSFUNCTION IN EARLY PARKINSON'S DISEASE

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We studied sudomotor function in 10 patients with early PD and 11 age-matched controls. Local sweat rate were performed using the ventilated capsule method on both the left forearm and thigh. The sudomotor function was studied by measuring sweating in response to rising body temperature and administering Thyrotropin-releasing hormone (TRH). There was no significant difference in the sweat rate of the forearm between early PD (0.17+0.03 mg/cm2/min; mean+SE) and controls. Sweat rate in the thigh was not significantly different between early PD patients (0.14+0.04) and controls (0.22+0.05). There was no difference in frequency of sweat expulsion (Fsw) which is determined as synchronous sweat expulsion at the two test area. There was also no difference in sweat rate between forearm and thigh in controls and early PD. In control subjects, TRH increased sweat rate 170% and 136% ($P<0.01$) at the forearm and the thigh, respectively. TRH also increased Fsw by 170% ($P<0.01$). Early PD patients, however, responded to TRH in a very different fashion. They did not undergo changes in either areas of sweat rate or Fsw. These results suggest that sudomotor dysfunction in early PD is minor, but that there may be an impairment of TRH-induced sympathetic response in the early stage of PD.

9-02-09 SYMPATHETIC DYSFUNCTION MEDIATING CARDIOVASCULAR REGULATION IN ALCOHOLIC NEUROPATHY

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We used noninvasive hemodynamic studies to evaluate autonomic function in 16 patients with alcoholic neuropathy. Pulsatile arterial pressure was measured by a servoplethysmomanometer, while cutaneous microcirculation was examined by a laser Doppler flowmeter. In the alcoholic patients compared to age-matched healthy controls, 1) the magnitude of responses to phase IV of the Valsalva maneuver, cold pressor test and isometric exercise significantly decreased, 2) during cold pressor test paradoxical depressor response of blood pressure was elicited (5/16), 3) cutaneous blood flow changes of the right first toe to local warming of the right foot and submergion of the left hand into cold water decreased significantly, while blood flow changes of the right thenar did not differ, and 4) reflex bradycardia in pahse IV of the Valsalva maneuver and the variation coefficient of R-R intervals during resting 100 R-R intervals were lower. Our results indicated not only parasympathetic (vagal) but sympathetic dysfunction mediating cardiovascular regulation in patients with alcoholic neuropathy.

9-02-10 AUTONOMIC NERVOUS SYSTEM ACTIVITY IN SUBARACHNOID HEMORRHAGE PATIENTS.

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In order to assess the function of the autonomic nervous system (ANS) in subarachnoid hemorrhage (SAH) patients, ECG for spectral analysis of heart rate variability was recorded daily in 22 patients within the first seven days after SAH. On days 1, 3 and 7 after SAH blood samples for the determination of norepinephrine (NE) concentration were taken as well. The procedures were repeated no less than 60 days after SAH in order to obtain control values. Six patients were treated conservatively and 16 surgically.

Spectral analysis of heart rate variability showed no sympathetic hyperfunction after SAH, but, contrary to expectations, this method indicated an increased vagal activity during days 4 to 6 after SAH. No correlation between the results of spectral analysis and NE levels was found.

This study failed to confirm the occurrence of a significant sympathetic hyperfunction immediately after SAH. The demonstrated transient vagal hyperactivity several days after SAH will require further confirmation and elucidation.

9-02-12 NEW TECHNIQUE FOR PARASYMPATHETIC ACTIVITY MEASUREMENT

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To enhance the accuracy and sensitivity of the early parasympathetic abnormalities assessment we have developed a simple technique for digital measurement of HR changes. The photopletysmographic signal pulses are combined with 1 ms clock pulses, of a timebase clock in order to measure duration T of 8 successive pulses. HR was calculated as follows: 480/T. Six set of measurements were made and the mean HR ± SD in resting condition were determined for each subject in 55 diabetes, randomly selected, age 47 ± 17 yrs., duration of illness 12 ± 7.5 yrs., and in 54 control subjects. Reduced heart rate variations, associated with reduced parasympathetic activity were found in diabetic patients for STD. DEV. (1.77 ± 1.15) compared with nondiabetic control subjects (3.19 ± 2.36); $p<0.0001$.
In conclusion it appears that the technique may be a useful screening instrument; since the method of mean of HR beats is performed under resting conditions, it has the advantage that active cooperation of patient is not required.

9-02-13 COLD PRESSURE TEST IN A NORMAL POPULATION

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Cold pressure test (CPT) in healthy subjects has seldom been analyzed. We present the results of a group of 169 healthy subjects [64(40%) men, 105(60%) women, mean age 45.5±15.66, range 22-83] in whom we analysed the response of blood pressure (BP) to the immersion of left hand in ice-cold water (0º-4ºC). BP was measured at rest and after 30, 60, 120 and 180 seconds from the beginning of the test. Highest rise of sistolic (HRS) and diastolic (HRD) BP were calculated. Our results were (mean±standard deviation, mmHg): sistolic BP at rest: 120±24, diastolic BP at rest: 76±14, HRS: 19±12, HRD: 16±9. The HRD was coorrelated with the patient age (p:.001) and the diastolic BP at rest (p:.01) but not with sistolic BP at rest. The HRS was coorrelated with any parameters. Our data suggest that the response of BP to CPT is relatively constant and independent of other factors.

9-02-14 INDIRECT PREDICTION OF CARDIAC AUTONOMIC INVOLVEMENT IN DIABETIC PATIENTS

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In 43 patients with diabetic distal-symmetric polyneuropathy a series of neurophysiological tests was performed. 20 patients had definite cardiac autonomic neuropathy (ADN+), 23 diabetics were classified as ADN-. We measured thresholds of warm-, cold-perception at the dorsum of the foot, nerve conduction velocities (NCV) and sympathetic skin response (SSR). Additionally quantitative sudomotor axon reflex test (QSART) was performed. Sensitivity and specificity were assessed for ADN+ and ADN-. Significant p-values (Fisher) were found for SSR (hand and foot), QSART, motor amplitude of tibial and peroneal nerve, warm- and cold-threshold. In diabetic patients with ADN+ electrophysiological signs of axonal damage and efferent sudomotor failure are common. No relationship between reduced nerve conduction velocities and autonomic involvement was found. Supported by a BMFT grant (0701502 3).

9-02-15 CLINICAL STUDY ON TREATMENT OF NEUROSIS AND NIGHT-TERRORS OF CHILDREN WITH FOOT THERAPEUTIC PAD FOR NEUROSIS

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The foot therapeutic pad is an innovative product for treatment of internal diseases with drugs applied to body surface. It is prepared by filling the processed natural medicines such as root of American ginseng and Semen zizyohi spinosae in the shoe-pad and is used for treatment by putting it in the shoes or slippers worn by the patient. In clinical treatment of 266 cases of neurosis an 38 cases of night-terrors of children, it showed significant therapeutic effectiveness for symptoms such as depression, low spirits, mental stress, dysphoria, delayed falling asleep, nightmare, poor recovery of vigour after sleep, chest distress, foreign body sensation in throat, belching, headache, dizziness, night-terrors of children. The therapeutic effectiveness appeared after treatment for only 3 days in most patients without side effect.

The low urinary MHPG-SO4 level in depression patients was also improved obviously after treatment. Its level was measured to be 1021.6±501.2 μg/24hr in 20 patients before treatment and increased to 1368.4±476.3 μg/24hr after treatment, while it was 1420.3±402.6 μg/24hr in 20 healthy persons.

9-02-16 INTRAVESICAL CAPSAICIN FOR TREATMENT OF DETRUSOR HYPERREFLEXIA

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An intravesical instillation of 100 mls of 1 mmol capsaicin has been used to treat detrusor hyperreflexia in 12 patients with spinal cord disease and intractable urinary incontinence. Nine patients showed some improvement in bladder function: in 4 the benefit was only partial and short lived but 5 patients achieved complete continence whilst performing intermittent self catheterisation. The response was best in patients with the least severe neurological deficit who were still ambulant. There appear to be no short term ill effects from the procedure and the improvement in bladder function lasts for between 3 weeks to 6 months. The instillation can then be repeated with the same benefit. The intravesical administration of 1 mmol capsaicin, although uncomfortable for the first 5 minutes of the instillation is never so painful as to necessitate analgesia.

The improvement in bladder behaviour of these patients can be interpreted as showing that as in experimental spinal animals capsaicin sensitive afferents play an important role in the pathogenesis of the detrusor hyperreflexia which follows disconnection of the sacral cord from the pontine micturition centre.

9-02-17 MICTURITIONAL DISTURBANCE IN PROGRESSIVE SUPRANUCLEAR PALSY

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Micturitional disturbance in progressive supranuclear palsy (PSP) has seldom been described in textbooks of neurology or neurological articles. The purpose of this study is to describe the results of our detailed micturitional histories and urodynamic studies in PSP.

Eight of 9 patients (89%) had micturitional symptoms including urinary incontinence in 7. Urodynamic studies were performed in 6 patients and 3 had residual urine of 100ml on average. Four had detrusor hyperreflexia and 1 had a low compliance cystometrogram. One had detrusorsphincter dyssynergia. Two of 4 patients had neurogenic changes in sphincter motor unit analysis. The results were compared with our previous findings in Parkinson's disease (PD) and in striato-nigral degeneration (SND), and we found that the voiding dysfunction in PSP seemed to be severer than those of PD and SND especially in urine storage phase. The responsible sites of lesions seemed to be located at central as well as peripheral parasympathetic and somatic nervous systems regulating lower urinary tract.

9-02-18 AUTONOMIC FUNCTION AT ALTITUDE: EFFECTS OF AGE AND ETHNICITY

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Central autonomic function is affected by ethnicity and ages transiently in sojourners(S) at altitude. We report these influences on sustained hand grip (SHG), diving response (DR) and cold pressor (CP) tests. Nineteen well-trained S (age range 19-68) and 6 natives (N) (age range 23-58) were tested at 1500m, 3700m, 5100m and after 14 days again at 3700m using accepted methods. Each heart beat and accompanying systolic, diastolic and mean arterial pressures were recorded on a Colin® monitor using software (Dr. K. Bergmann) and a computer. Spectral analysis was performed on SHG. The other tests were analyzed for maximum responses. t-test, ANOVA and ANCOVA were used where appropriate. SHG showed sympathetic activation at altitude but a reduction on first exposure. DR was absent at 5100m in S and N. Latencies were unaffected by altitude. CP was absent in S and N at 5100m. Baseline heart rates increased with altitude but could not explain the results. Age had no effect. Unlike central autonomic function, predominantly peripheral autonomic function is affected by altitude, but not age or ethnicity.

9-02-19 IMMUNOHISTOCHEMICAL STUDY OF SUBSTANCE P IN THE DORSAL MOTOR NUCLEUS OF THE VAGUS AND THE NUCLEUS OF THE SOLITARY TRACT OF MULTIPLE SYSTEM ATROPHY.

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Substance P (SP) is a tachykinin neuropeptide and found rich in the dorsal motor nucleus of the vagus (DMV) and the nucleus of the solitary tract (NTS) as the projected nerve fiver terminals, and both nuclei are important medullary center related to the various autonomic nervous functions including baroreceptor reflex. By the way, autonomic dysfunction is one of main clinical symptoms of multiple system atrophy (MSA). In the present study, the distribution and the density of SP in DMV and NTS, obtained postmortem from four cases of MSA and eight cases of control were studied immunohistochemically with the avidin-biotin-peroxidase complex method. SP nerve terminals were seen densely throughout DMV and NTS of all control cases. As compared to control brains, MSA brains exhibited an obvious decrease of SP nerve terminals in both DMV and NTS. So, our results strongly imply that SP-containing visceral sensory afferents via vagal and glossopharyngeal nerves to DMV and NTS may be involved in MSA, and provide a new key to the pathophysiology of autonomic dysfunction of MSA, particulary cardiovascular dysfunction including orthostatic hypotension.

9-02-20 CHANGES IN AUTONOMIC NERVE FUNCTIONS ASSOCIATED WITH EVENT-RELATED POTENTIALS -WITH SPECIAL REFERENCE TO EFFECT OF CIGARETTE SMOKING-

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The purpose of this study is to investigate the relationship between autonomic nerve functions and higher brain functions during event-related potentials(event-related responce: ERR) and to evaluate the effect of smoking.

Studies were carried out on healthy subjects and patients with various neurological deficits. CNV was induced by the S1-S2 paradigm, and P3 by the oddball paradigm.

When provoked by the S1-S2 paradigm, the healthy subjects first presented S1 and then showed an increase in heart rate, blood pressure, skin blood flow, and electrodermal activity with the appearance of CNV. These changes declined toward S2 with time. When provoked by the oddball paradigm, they first presented P3 and then an increase in heart rate, skin blood flow, and electrodermal activity. ERR tended to be reduced or disappeared depending on the severity of disorders in the patients with dementia and autonomic disorders. After smoking, some of the subjects showed decreasing CNV amplitude and prolonged P3 latency. However, these changes were not significant. Increased CNV amplitude and decreased P3 latency was observed in one case.

The possibility is suggested that the autonomic nerve functions during ERR may be disturbed by not only peripheral autonomic nervous disorders but also higher brain function.

9-02-22 EFFECTS OF YOHIMBINE ON AMBULATORY BLOOD PRESSURE IN PARKINSON'S DISEASE WITH ORTHOSTATIC HYPOTENSION.

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Yohimbine, an alpha2-adrenergic antagonist, has sometimes been proposed for the treatment of orthostatic hypotension (OH). We investigated in a double blind placebo-controlled cross-over trial the effects of yohimbine (2 mg t.i.d) on ambulatory blood pressure recording (AMBP) in 17 patients with Parkinson's disease (PD) suffering from non iatrogenic OH. At the end of each sequence of 4 weeks, mean blood pressure (BP) and heart rate (HR) (± SD) and BP variability (coefficient of variation of the mean) were calculated for day-time (09-19 h) and night-time (23-06 h) using AMBP. A normal nychtemeral rhythm for BP and HR was considered when the night/day ratio was <0.9 and post-prandial hypotension was defined as of fall of at least 25 mmHg within 90 min after meal.

OH related to PD was characterized by : (i) loss of the nychtemeral rhythm of BP (night/day ratio: 1.18±0.14) but not of HR (night/day ratio: 0.87±0.04), (ii) high variablity of BP during day-time and (iii) post-prandial hypotension (71%).

There was no significant difference in AMBP parameters between baseline, yohimbine and placebo periods.

In conclusion, this study shows that AMBP is a simple and reproductible method to assess drugs effects in the management of OH and that yohimbine is not effective to correct OH of PD.

9-02-23 COMPARISON OF ORTHOSTATIC TOLERANCE PRE AND POST SPACEFLIGHT.

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Lower body negative pressure (LBNP) produces a hypovolemic stress that can provide a pre and postflight comparison of an astronaut's orthostatic tolerance. METHODS: Transcranial Doppler (mean flow velocity, MFV), electrocardiogram (heart rate, HR), mean arterial blood pressure (Finapres, MABP), were recorded beat-to-beat onto digital tape for off-line analysis from eight astronauts, preflight and within two hours after spaceflights of five to nine days, during a ramp LBNP protocol. LBNP pressures ranged from zero to -60 mmHg and were decreased by 10 mmHg in five minute intervals. *RESULTS*: Six of eight subjects performed less well postflight than preflight. The Tolerance Index (T.I.), devised to compare performance, revealed a definite difference in the overall response. T.I. values measured at the -60 mmHg endpoint preflight were achieved much earlier in the test postflight (e.g. at -30 or -40 mmHg). Low T.I. values of approximately 0.35 were associated with presyncope. CONCLUSIONS: Beat-to-beat analysis of HR, MFV, MABP provide time-locked segments for precise assessment of orthostatic responses to an environmental challenge such as LBNP. Using a tolerance index derived from and defined by these data, one can evaluate, consistently, an individual subject's or group of subjects' performance pre and post treatment.

9-02-26 PURE AUTONOMIC FAILURE: A CASE REPORT WITH CLEAR EVIDENCE OF A POSTGANGLIONIC DISORDER

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A 53-year-old woman complained of progressive postural hypotension with dizziness and fainting since three years. The clinical examination showed no signs of a sensory-motor neuropathy or hints of central nervous system disturbances. Computed tomography, magnetic resonance imaging, single photon emission computed tomography, EEG and cerebrospinal fluid showed no brain abnormality. Electroneurographic and electromyographic examinations were normal. Autonomic function tests were performed: heart rate variation at rest, deep breathing (E/I-Index, mean circular resultant, coefficient of variation) and VALSALVA-Index were highly reduced and gave evidence of a parasympathetic disorder of heart innervation. As sympathetic function showed remarkably excessive drops of systolic and diastolic blood presure, also documented by 24 hour ambulatory blood pressure monitoring. The sympathetic skin response was absent at feet. Cutaneous histamine prick tests were performed. No vascular reaction could be observed showing the absence of axon reflexes. Furthermore, basal blood norepinephrine was markedly reduced. Finally, histological examination of nerve tissue (N. suralis) demonstrated clearly reduced numbers of myelinated and unmyelinated axons. These data indicate an uncommon neuropathy as cause of pure autonomic failure in this patient.

9-02-27 DIABETIC AUTONOMIC NEUROPATHY: CLINICAL AND ELECTROPHYSIOLOGICAL DATA OF 80 CASES

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The peripheral autonomous nervous system can be involved in patients with diabetes mellitus. The so-called autonomic neuropathy appears to involve any organ system to different degrees. The earliest and most common manifestation is in the cardiovascular system, and finds expression as orthostatic hypotension, resting tachycardia, painless myocardial ischemia and "rigid pulse". Simple, non-invasive tests permit accurate quantification and follow-up. To assess the validity of different tests proposed in literature the impairment of cardiorespiratory reflexes and sympathetic skin responses were measured in 80 cases with somatic neuropathy due to diabetes mellitus, 35 insulin dependent and 45 non insulin dependent. Heart rate reactions to normal breathing, to deep periodical breathing (E/I-ratio, coefficient of variation, and mean circular resultant), to VALSALVA-manoever and to standing up were determined. In addition, the change in systolic blood pressure to standing up was measured. All data were correlated with the age, gender and duration of diabetes, and compared with age-matched normal subjects. In 76% two or more parameters showed impairment of autonomic activity, in 22.5% five or more tests assessing autonomic function were abnormal. RR- variation during deep breathing was most frequently abnormal, but reliance on this test alone to examine autonomous function would have missed 9 to 61 abnormal subjects.

9-03-01 PLATELET ACTIVATION AND ERYTHROCYTE AGGREGABILITY IN PATIENTS WITH CEREBRAL INFARCTION

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We previously reported that activation of platelet induced enhancement of erythrocyte aggregation in an *in vitro* study (Biorheology 1991;28:551). The purpose of the present study was to examine the relationship between platelet activation and erythrocyte aggregation rate (aggregability) *in situ* in patients with cerebral infarction.

MATERIALS AND METHODS: The subjects comprised 104 patients with cerebral infarction (85 males and 19 females; 61±8 YO (mean±SD)). The platelet activation and erythrocyte aggregability were measured simultaneously employing anticoagulated venous blood from the subjects. The degrees of platelet activation were estimated from the levels of plasma β-thromboglobulin. The erythrocyte aggregability was examined using the whole-blood erythrocyte aggregometer developed by us previously (Am J Physiol 1986;251:H1205) with concomitant measurement of the fibrinogen concentration.

RESULTS: The mean±SD values for the plasma β-thromboglobulin, erythrocyte aggregation rate and fibrinogen were 36±27 ng/ml, 0.150±0.021/s, and 320±74 mg/dl, respectively. There were statistically significant linear correlations among each of the parameters (β-thromboglobulin vs. erythrocyte aggregability, r=0.54 ($p<0.01$); β-thromboglobulin vs. fibrinogen, r=0.50 ($p<0.01$); and erythrocyte aggregability vs. fibrinogen, r=0.71 ($p<0.01$).)

CONCLUSION: The platelet activation, erythrocyte aggregability and fibrinogen concentration were closely correlated with each other in our patients with cerebral infarction.

9-03-02 DIABETES MELLITUS AS A RISK FACTOR OF WHITE MATTER LESIONS ON MAGNETIC RESONANCE IMAGING

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We examined 38 diabetic patients and 60 non-diabetics with magnetic resonance imaging (MRI) to evaluate the importance of diabetes mellitus as a risk factor of a small brain ischemic lesion. MRI were performed with a superconductive magnet at a field strength 1.5T. A small ischemic lesion was defined as a patchy parenchymal area with increased signal intensity on T_2 weighted and proton density images and smaller than 10 mm in diameter. We counted the number of lesions at white matter, basal ganglia and brainstem, respectively. The number of the small ischemic lesions in white matter was significantly higher in diabetic patients than non-diabetics($p<0.025$). In diabetic patients, the number of small ischemic lesions in white matter and basal ganglia were weakly correlated with HbA1c and inversely correlated with insulinogenic index ($p<0.1, 0.1$). The number of small ischemic lesions in white matter was significantly correlated with sex, age and hypertension ($p<0.05, 0.05, 0.05$), but not with diabetes mellitus in multivariate regression analysis. It was suggested that arteriosclerotic change of the small vessels in white matter is severe in diabetic patients than non-diabetics but the contribution of the diabetes mellitus as a risk factor to white matter lesions is smaller than sex, age, and hypertension.

9-03-03 SHEAR-INDUCED PLATELET AGGREGATION IN PATIENTS WITH ISCHEMIC CEREBROVASCULAR DISEASES.

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Recent evidence suggests that shear-induced platelet aggregation (SIPA) plays an important role in thrombogenesis at arterial bifurcations or stenotic lesions. Thus we determined SIPA using a newly-developed equipment (J. Clin. Invest. 87:1234-1240,1991) in 50 patients with cerebral infarction or transient ischemic attacks (TIA) as well as 26 control subjects. The extent of SIPA was expressed as the percent maximum change of light transmittance induced by high shear stress (108 dyn/cm^2). SIPA was increased in patients with atherothrombotic stroke (53.1 ±8.5%, p<0.01) and TIA (54.6 ±6.0%, p<0.01) but not in those with lacunar stroke (49.0 ±9.0%) in comparison with controls (45.6 ±10.1%). There was a significant correlation between SIPA and plasma levels of larger von Willebrand factor multimers analyzed by SDS agarose gel electrophoresis (r=0.57, p<0.01). SIPA was reduced from 50.8 ±5.9% to 34.8 ±6.3% (p<0.01) with 200mg/day of ticlopidine, while it remained unchanged (from 50.1 ±3.6% to 49.6 ±3.5%) with 81mg/day of aspirin. The results suggest that the increase in SIPA is associated with the large arterial diseases and the increase in von Willebrand factor multimers, and can be corrected with ticlopidine but not with aspirin.

9-03-04 VASCULITIS OF THE CENTRAL NERVOUS SYSTEM:A SURVEY OF 20 CASES.

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Cerebral angiitis is characterized by clinical polymorphism and an almost invariably fatal outcome . From 1989 to 1992,20 patients with cerebral angiitis were identified. Nine of them had the isolated form and 11 disclosed secondary cerebral involvement from systemic vasculitis:Takayasu's arteritis,4;systemic necrotizing vasculitis,2;Behçet's disease,1;systemic lupus erythematosus,1; cocaine abuse,1; acquired immunodeficiency syndrome,1; pheochromocytoma,1 . Corticosteroids were used in 17 patients and associated cyclophosphamide was utilized in 5. From 18 followed patients, 8 improved,7 were unchanged and 3 deaths occurred.Our patients responded partially to immunosuppressive therapy,probably indicating the heterogeneity of the group.

9-03-05 RISK FACTORS FOR CEREBROVASCULAR DISEASE IN THE ELDERLY PATIENTS OVER 80.

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The characteristics of cerebrovascular disease (CVD) in the elderly were analyzed, paying particular attention to the presence of risk factors (RF) such as hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), hyperuricemia (HU), heart disease (HD), atrial fibrillation (AF), smoking and drinking. We examined 170 patients with cerebral thrombosis, 60 with cerebral embolism and 55 with cerebral hemorrhage. We compared the incidence of each risk factor in cases under the age of 80 with that over the age of 80. In cerebral thrombosis, HT, HL and DM were major RF. However, arrhythmia and HD became important over the age of 80. Among the embolic cases, AF was the most important factor; however, HD also constituted a large part of the RF over the age of 80. In hemorrhagic cases, HT was the most important RF but the incidence of arrhythmia was increased and the significance of HL and DM as risk factors was decreased over the age of 80. Thus, in CVD in the elderly, not only risk factors for atherosclerosis but also hemodynamic factors such as circulatory dysfunction may contribute to the occurrence of ischemic and hemorrhagic CVD. It is suggested that the pathogenesis of CVD in the elderly could be different from that of other age groups.

9-03-06 ACUTE SUBDURAL HAEMATOMA AND VASCULAR MALFORMATIONS

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Acute Subdural Haematoma (ASH), is generally related to a ruptured dural vein due to craneoencephalic trauma. Association between ASH and ruptured artery aneurism (0,5 - 8%) or other arterial malformations is very uncommon or has been very rarely described (fewer than 100 cases).

We report three cases of non-traumatic ASH. One of them was associated to subaracnoid haemorrage and ruptured carotideal saccular aneurysm, close to the posterior communicating artery. The 2nd patient, previously diagnosed of a complex arterial malformation, suffered simultaneously an intracerebral and intraventricular haemorrage and an ASH. This association has been also very infrequently described. In the 3rd patient, an occipital intracerebral haematoma, associated to an ASH, lead to the diagnosis of an occipital angioma. Urgent craniotomy was not considered necessary in either of our cases, after the assessment of a clinical improvement.

We call attention to the diagnostic importance of angiographic studies in every case of ASH in the absence of any known head injury, delaying, if possible, the performance of an urgent craniotomy.

9-03-08 CEREBRAL VENOUS THROMBOSIS: COMMON CAUSE OF STROKE IN YOUNG

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In the young, aged below forty-five years, puerperal cerebral venous thrombosis causes ischaemic and haemorrhagic stroke and accounts for 20% of the cases. Mortality is 15 to 30% but quality of survival is excellent.

Our experience includes study of over 500 cases well investigated.

Cardiac causes, infections, Hypertension, Angiomas, Aneurysms, Mucoid vasculopathy, Collagen diseases all together account for 30 - 40% and in the rest cause is not known.

9-03-09 A BASIC STUDY ON MOTOR EVOKED POTENTIALS USING TRANSCRANIAL MAGNETIC STIMULATION: A CLINICAL APPLICATION TO HEMIPLEGIC STROKE

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We experimented with mapping of the normal human motor cortex and investigated the clinical application to hemiplegic stroke.

The experimental group consisted of 30 patients with hemiplegic stroke and 24 healthy adult volunteers. Both clockwise and anticlockwise stimuli were delivered at the cubital fossa, Erb's point, the 5th cervical vertebra and the scalp. The motor evoked potentials (MEPs) were recorded over both relaxed and voluntarily contracted abductor pollicis brevis (APB) and abductor hallucis (AH) muscles.

The most effective sites of stimulation on the scalp over the motor cortex to evoke MEPs from the AH muscles were Cz and from the APB muscles were F3' and F4' (2 cm anterior and 7 cm lateral to Cz), and clockwise stimulation tended to evoke MEPs in muscles on the left and anticlockwise stimulation on the right. Especially, this tendency was large in MEPs recorded from the relazed AH muscles. However, there were no differences between clockwise and anticlockwise stimulation in the frequency of MEPs elicited from the facilitated APB muscles. In patients with hemiplegic storke, the MEPs recorded from both the affected APB and AH muscles following motor cortical stimulation showed significant differences in latencies and amplitudes compared with those of healthy controls, and a relationship was detected between MEP abnormalities and the degree of each motor disturbance.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

9-03-10 A NEW MODEL FOR GLOBAL CEREBRAL ISCHEMIA IN PIGS

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Models for global brain ischemia in current use either require extensive surgical preparation or induce extreme systemic hypotension. We have developed a simple method to induce global brain ischemia by controlling the cerebrospinal fluid (CSF) pressure and the systemic blood pressure.

Eight piglets (18-28 kg) were used. Arterial and intracranial pressures were continuously monitored. Continuous laser Doppler flowmetry (LDF) was performed with a Periflux PF2B laser Doppler flowmeter. Brain blood flow was also measured at three intervals with a dose of 1 million 15 µm radioactive microspheres. Increased intracranial pressure (100 mmHg) was induced by infusion of artificial cerebrospinal fluid into the cisterna magna. Arterial pressure was reduced by withdrawal of arterial blood.

High CSF pressure and rapid arterial bleeding of 15-30 % of the total blood volume caused a drop in cerebral perfusion pressure to zero and a LDF signal of zero. Reduction of CSF pressure to normal and rapid blood reinfusion immediately normalized the LDF signal. Absence of intracranial circulation was confirmed by a microsphere count close to background. The advantage of this model lies in it's simplicity. In addition, the duration of ischemia is easily controlled, the systemic blood pressure can be kept within physiological limits, and access to the carotid or vertebral arteries is unnecessary.

9-03-11 APOMORPHINE TEST IN PRIMARY AND NON-PRIMARY PARKINSONISM: CHANGES OF FRONTAL SOMATOSENSORY EVOKED POTENTIALS TO MEDIAN NERVE STIMULATION (MN-SEP)

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MN-SEP were recorded during stimulation of the most clinically affected hand before (time 0) and after (times 10', 20', 30', in all; 50', 60' in few cases).

Acute subcutaneous administration of 3 to 5 mg of Apomorphine in 53 patients. SEP control values were prevously obtained by a sex-age matched population of 35 healthy volunteers. Following the test and the clinic-instrumental diagnostic selection, 38 cases were classified as primary - idiopathic - parkinsonians and the remaining 15 as non-primary parkinsonians. The frontal waves N30 and P40 were absent or significantly reduced in about 65% of the primary and 35% of the non-primary groups.

Following apomorphine administration about 70% of primary cases recognized a clinical amelioration, while none of the non-primary group showed a clearent clinical improvement. The frontal responses showed a clearent amplitude potentiation in nearly all the "responders" and in about 1/3 of the "non-responders" as well as in the non-primary group. Such an amplitude increment started at about 10' and decayed after 30' toward baseline levels.

We suggest that clinic-neurophysiological testing of the apomorphine effects can help in clinical diagnosis of Parkinson's disease.

9-03-12 SNEDDON'S SYNDROME: DIAGNOSIS BY SKIN BIOPSY AND MRI IN 17 PATIENTS

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We evaluated clinical, laboratory, histological and neuroradiological findings in a series of 17 patients in order to improve diagnostic criteria for Sneddon's syndrome.

Patients with generalized livedo racemosa and cerebrovascular events were included in the study.

Completed stroke was present in 8 patients and 15 reported transient neurological deficits. Magnetic resonance imaging yielded cerebral abnormalities in 16 of 17, while computerized tomography was abnormal in only 12 of 16 patients. Magnetic resonance imaging revealed more lesions in individual patient than computerized tomography. Magnetic resonance angiography demonstrated patent intracranial vessels in 16 of 17 patients. Skin biopsy showed distinct histopathological findings in all patients. The involved vessels were small- to medium-sized arteries at the border between dermis and subcutis. Early inflammatory reactions were followed by subendothelial proliferation and a late fibrotic stage. Laboratory examinations showed impaired creatinine-clearance in 8 patients, whereas all other laboratory tests, including, antiphospholipid antibodies, were normal.

9-03-13 CARDIAC SURGERY UNDER CARDIOPULMONARY BYPASS (CS-CPB) AND THE CLINICAL SCREENING OF NEUROPROTECTIVE AGENTS (NPA) FOR PRE-TREATMENT OF PATIENTS AT RISK FOR ISCHEMIC STROKE (IS)

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Objective: To study the use of CS-CPB for the screening of NPA for pre-treatment of patients at risk for IS.

Cognitive deficits (CD) are seen after CS-CPB: 77% of 47 patients (pts) of Harrison et al. scored worse vs. baseline on neuropsychologic testing (NPT) 8 days after CS-CPB (Stroke 1989; 20: 235-237).

We sought NPA effect by giving GM1 ganglioside 600 mg i.v. or placebo (unbalanced randomized, double-blind protocol) to pts just before CS-CPB. We looked for reduction in severity of CD as evidence of benefit from pre-treatment. One week after CS-CPB 76% had worse composite NPT scores and 24% scored better vs. baseline: net 52% worse; no difference between 18 GM1 and 11 control pts.

Discussion and Conclusions: A large number of ischemic events in a pool of pts in a short observation period would facilitate recognition of benefit from pre-treatment in NPA studies. Compared with the stroke end-point yeild in TIA pts (13% in 3 years on aspirin per Hass et al.: N Eng J Med 1989; 321: 501-507) the apparent cerebral ischemic phenomenon yield at 1 week after CS-CPB (50% or greater) is striking.

9-03-14 DIFFERENT STRATEGIES OF FUNCTIONAL REORGANIZATION AND ASSOCIATED MOVEMENTS IN RECOVERY FROM STROKE.

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In the process of recovery from stroke due to ischemic infarction, associated movements of the healthy hand, when moving the previously paretic hand, are relatively common. This study was conducted to investigate whether this phenomenon is related to the pattern of cortical reorganization.

We studied 13 patients after recovery from hemiparesis due to ischemic infarction (5 cortical, 3 subcortical and 5 brainstem). Eight exhibited associated movements, five did not. Regional cerebral blood flow was measured with PET using an integral O-15 CO2 inhalation technique during rest and during sequential finger opposition of the previously paretic hand. After transformation into a standard stereotactic space and removal of global flow differences, a planned comparison on a pixel by pixel basis between conditions was performed.

In both groups, the sensorimotor cortex, the parietal association cortex, the supplementary motor area and cingulate gyrus were activated. In patients with associated movements, in addition, an activation of the ipsilateral sensorimotor cortex in the area normally associated with finger opposition (44-52 mm above AC-PC line) as well as of a more lateral and slightly more frontal extension (24-36 mm) was seen, and activation in supplementary motor area and cingulate gyrus was more prominent.

We suggest that in recovery from stroke, different patterns of functional reorganization are possible, partly reflected in the presence or absence of the clinical phenomenon of associated movements.

9-03-15 THE SYNDROME OF RECURRENT PURE SENSORY TIA'S: IN VIVO IMAGING OF ASSOCIATED THALAMIC INFARCTION.

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We present a case study and literature review to clarify the pathoanatomic substrate of recurrent pure sensory TIAs.

Ischemia related pure sensory symptoms present as one of two clinical syndromes: 1)Sudden onset of persistent unilateral face, arm, and/or leg hypoesthesia, preceded by no or few TIAs, or 2)Frequent episodes of transient unilateral hypoesthesia/paresthesia not progressing to permanent deficit. The first is widely recognized; recent CT/MR series have reported 90 cases associated with brainstem, thalamus, or thalamocortical projection sensory pathway infaction. Though equally common, the syndrome of recurrent transient hemihypoesthesia is underrecognized and has a less well described pathologic substrate. One previous case with postmortem documentation of a ventroposterolateral (VPL) thalamic infarct has been reported.

A 60 year old woman had over 50 transient episodes of left hemibody hypoesthesia over the previous 15 years. Interictal neurologic exam was normal. MRI showed a small infarct in the VPL nucleus of the right thalamus. Symptoms resolved with warfarin therapy.

We believe this is the first reported case of recurrent transient hemihypoesthesia associated with VPL thalamic infarction imaged in vivo.

9-03-16 EXTERNAL VALIDATION OF THE OXFORDSHIRE COMMUNITY STROKE PROJECT CLINICAL CLASSIFICATION OF CEREBRAL INFARCTION

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We have attempted to validate the OCSP classification in the Perth Community Stroke Study (PCSS).

The PCSS evaluated 536 cases of stroke, 331 had a first ever cerebral infarction and complete follow-up data. Of these 30% were classified as total anterior circulation infarcts (TACI's), 31% as parital anterior circulation ischemic infarcts (PACI's), 26% as lacunar infarcts (IACI') and 14% as posterior circulation infarcts (POCI's). Follow-up data showed that the percentage of patients who were dead or disabled at 12 months was 89% for patients with TACI's (96% in the OCSP), 58% for patients with PACI's (45% in the OCSP), 47% for patients with LACI's (39% in the OCSP) and 61% for patients with POCI's (38% in the OCSP). The rate of recurrence was greater for patients with PACI's and LACI's as was found in the OCSP.

The results of this study generally support the validity of the OCSP clinical classification of cerebral infarction and suggest that it may be generalized to the patient population.

9-03-17 ANTIPHOSPHOLIPID ANTIBODIES (apl) AND ISCHEMIC STROKE IN THE YOUNG

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In a study realized in our Service with 69 ischemic stroke patients aged between 14 and 44 years, a laboratory investigation found that anticardiolipin antibodies (acl) were present in 5 patients and lupus anticoagulant (la) in 8.

However, concordance between these 2 tests occurred only in 3 patients. None of them fulfilled criteria for SLE, 3 presented characteristics of Sneddon syndrome and 1 showed recurrent thrombosis; cardiovascular disfunction was diagnosed in 3 patients (mitral valvular lesions).

Cerebral infarcts occurred in carotid territory in 8 patients and in vertebro-basilar system in 2 patients.

Two patients received heparin followed by warfarin and 8 received aspirin.

Only one patient had recurrence of the neurological symptoms. The presence of apl should always be considered in the diagnosis of stroke in young patients.

9-03-18 PREDICTING THE PROGNOSIS OF CEREBRAL INFARCTION BY CLINICAL AND COMPUTED TOMOGRAPHIC FINDINGS

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The early diagnosis and prediction of prognosis of stroke have enormous management potential both for appropriate therapy and for evaluation of newer treatment modalities. In this regard beside the clinical assessment, neuroimaging techniques, especially computerized tomographic (CT), have a great value.

Among the stroke patients who were admitted to our department since January 1987, 622 consecutive patients with cerebral infarction who had a detailed clinical assessment, and cranial CT scans within the first week after onset of stroke, were included in our study. We investigated correlation of risk factors, clinical, and CT findings with short-term prognosis. All patients underwent cranial CT, and 28.7% of them had no lesions on initial CT scans. The overall case fatality rate was 21.7%. We concluded that age, depression of consciousness, conjugate eye deviation, large frontotemporal infarcts ($p < 0.001$), heart diseases ($p < 0.01$), and hyperglycemia ($p < 0.05$) were closesly related with mortality in acute phase of cerebral infarction.

The purpose of our study is to determine whether the clinical assessment and CT findings are useful in predicting the clinical outcome after cerebral infarction.

9-03-19 DETECTION OF CEREBRAL EMBOLI DURING OPEN HEART SURGERY.

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Objective. The long-term aim of this study is to test the hypothesis that cerebral microemboli are an important etiological factor for neuropsychological deficit following open heart surgery. We are therefore monitoring the number of emboli entering the cerebral circulation during open heart surgery in an attempt to assess if their frequency may determine the degree of neuropsychological postoperative change.

Methods. Automatic transcranial Doppler monitoring (EME) of the right middle cerebral artery (MCA) is being continuously carried out for up to 6-7 hours. The recording starts before aorta cannulation and lasts until decannulation is carried out. The Doppler system automatically counts the number of emboli entering the MCA and may differentiate emboli from artefacts. In addition the Doppler findings are continuously recorded on a video tape for off-line analysis (audio and visual content).

Results. The results have to date shown that: 1. Automatic embolus detection may be carried out during open heart surgery. 2. Emboli may be differentiated from artefacts. 3. Solid emboli may be differentiated from gaseous bubbles. 4. The number of emboli entering the brain during open heart surgery may vary from a few up to several thousand. 5. The number of emboli depends on the type of surgery being carried out.

Conclusions. Cerebral emboli in varying numbers were detected in all patients studied.

9-03-20 WALLENBERG'S LATERAL MEDULLARY SYNDROME WITH LOSS OF PAIN AND TEMPERATURE SENSES ON CONTRALATERAL FACE: CLINICAL, MRI AND ELECTROPHYSIOLOGICAL STUDIES.

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Thirteen patients with Wallengerg's lateral medullary syndrome (WLMS) were studies. Clinical and magnetic imaging (MRI) evidence demonstrated infarction in the dorsolateral medulla which produced sensory loss of pain and temperature on one side of face ipsilateral to the lesion in 7 patients. However, in another 6 patients, infarction in a similar location produced loss of these senses on contralateral face. This is the first report of an analysis comparing these two conditions in WLMS patients, comfirmed by MRI. The finding of normal blink reflex (BR) and somatosensory evoked potentials (SEP) in the two groups of patients may indicate that impulses travel along central pathways of touch, vibration and joint position senses instead of pathways of pain and temperature senses, because patients present normal senses of touch, vibration and joint position. It is suggested that pathways of late blink reflex (R2) pass through medial lemniscus in ventromedial medulla instead of spinal trigeminal tract in dorsolateral medulla. Futher observation of the much longer latencies (about 29 msec) of normal R2 raises the possibility that impulses may travel along the longer pathways through medial lemniscus and up to thalamus or cortex.

9-03-21 CEREBRAL VASOREACTIVITY ASSESSED BY TRANSCRANIAL DOPPLER ULTRASOUND AND REGIONAL CEREBRAL BLOOD FLOW (rCBF) MEASUREMENTS.

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In 52 patients with unilateral carotid artery disease (31 with occlusion and 21 with tight stenosis) middle cerebral artery (MCA) blood flow velocities (V_{mca}) were compared with rCBF in the MCA perfusion territory ($rCBF_{mca}$). rCBF was measured by single photon emission computerized tomography and Xenon-133 inhalation. Measurements were performed under basal conditions and 20 mins. after i.v. administration of 1 g acetazolamide. Asymmetry in percentage V_{mca} increase (pathological side-normal side) was significantly larger ($p<0.01$) than the asymmetry in $rCBF_{mca}$ increase. A significant correlation ($r=0.63$, $p<0.01$) was found between asymmetry in V_{mca} and $rCBF_{mca}$ increase. The relationship between $rCBF_{mca}$ and V_{mca} was poor when each side was assessed separately. 6 subjects with normal CT scans and symmetric rCBF increases had an abnormal asymmetric increase in V_{mca}. This study shows a relatively good correlation between asymmetries in $rCBF_{mca}$ and V_{mca} increases when assessing vasoreactivity in patients with unilateral carotid disease. In some subjects a considerable collateral supply to the MCA perfusion territory was not detected when velocities were measured in the MCA alone.

9-03-22 SHOULD HYPERTENSION BE TREATED AFTER ACUTE STROKE? – A RANDOMIZED CONTROLLED TRIAL USING SPECT

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Design: Randomized double blind placebo controlled trial.

Patients: Sixteen consecutive hypertensive patients, mean age 66 years (range 46 - 83), 4 men and 12 women, with middle cerebral artery infarction within 72 hours of onset, and blood pressure between 170 - 220 mmHg systolic, and 95 - 120 mmHg diastolic.

Intervention: Placebo (n = 6), nicardipine 20 mg (n = 5), captopril 12.5 mg (n = 3), or clonidine 0.1 mg (n = 2) given every 8 hours for 3 days.

Main Outcome Measures: Decline in blood pressure, change in cerebral blood flow as measured by single photon emission computerized tomography, and clinical change as determined by the NIH stroke scale.

Results: Blood pressure fell significantly in both the treated group as a whole, and those patients receiving placebo ($p < 0.001$). There was no difference in blood pressure levels between these two groups throughout the study period. Patients receiving nicardipine had a consistently lower pressure than the other groups. A significant negative relationship was noted between the maximum blood pressure fall and improvement in cerebral blood flow. There were 4 patients who dropped their blood pressure by more than 16% of baseline value on any 24 hours in the first 3 days. All either failed to increase or actually decreased their cerebral blood flow to the affected area. Three of these patients were treated with nicardipine. There was no significant difference in clinical course between the placebo group and treated group as a whole.

Conclusions: Hypertensive ischemic stroke patients with moderate elevations of blood pressure in the first few days do not require anti-hypertensive therapy.

9-03-23 EFFICACY OF NEFIRACETAM IN PATIENTS WITH CEREBRAL THROMBOSIS
: A STUDY USING EVENT-RELATED POTENTIAL TOPOGRAPHY

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In order to evaluate the efficacy of cerebral metabolic enhancer for patients with cerebral thombosis, electrical field distribution of event-related potentials(ERP's) was analyzed in terms of time and space. The study was carried out on 14 normal individuals, 14 chronic patients with cerebral thrombosis. For the ERP's components N1 and P3, reference-indipendent measures (latency, global field power, global dissimilarity, location of maximal or minimal potential, location of centroid) were determined.

The patients showed an abnormal P3 in latency, amplitude and electrical field on the scalp. In addition to that, N1 electrical field abnormalities were also seen.

These abnormal ERP improved after administration of cerebral metabolic enhancer(Nefiracetam: DM-9384). The improvement of ERP was more sensitive than that of various mental function scale.

These data suggest that time-course analysis of spatial distribution of ERP might be useful for evaluating the efficacy of cerebral metabolic enhancer.

9-03-24 PATTERNS OF VASCULAR INVOLVEMENT IN PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM

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Primary Angiitis of the Central Nervous System (PACNS) is a rare inflammatory disease of brain parenchymal and leptomeningeal blood vessels. It is often described as affecting mainly arteries 200 to 500 micrometers in diameter but exact rates of involvement of various vessels have not been determined. This study attempts to define these patterns of involvement. Six new histologically verified cases conforming to proposed diagnostic criteria for PACNS are reported, including an unusual case with biopsy evidence of involvement limited to veins and venules. The literature on PACNS since 1959 is reviewed to define the size and type of vessel affected, from histologic and angiographic data. Histologic involvement was found to be similar to that previously reported but angiographic involvement of large, named arteries may be more common than previously appreciated. A diagnostic algorithm incorporating noninvasive magnetic resonance angiography in certain cases of suspect PACNS is proposed.

9-03-25 NEUROPSYCHOLOGICAL VARIATIONS FOLLOWING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS

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Cardiac surgery with cardiopulmonary bypass (CPB) may cause cerebral damage by hemodynamic or embolic mechanisms.

We used an extensive test battery (Mini Mental State Examination (MMSE); Randt memory test; Token test; Zahlen-Verbindungs Test-G; Naming, Abstract Thinking, and Constructional Praxis evaluated according to Bisiach et al.) to study neuropsychological variations in 53 non-selected patients (M/F = 2.8; mean age 61.74 10.6) 2 days before and 5 days after the bypass surgery. Thirty-three of the 53 patients were re-evaluated after 2 months.

After 5 days, independently from age and sex, the neuropsychological performance proved to be significantly worsened on 3 of the 7 tests administered: 3 words recall, speech and total score on MMSE; 5 items, paired words, repeating numbers, picture recognition on Randt memory test; verbal comprehension on Token test. The 33 patients examined 2 months after the intervention still showed disturbed memory and attention. CPB may cause protacted neuropsychological deficits.

9-03-26 WHOLE BODY MOTORICS GROUPS AND SCALE IN MEASUREMENT AND PROGNOSIS OF ACUTE ISCHEMIC STROKE

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An orginal, clinical method based on whole body motorics/WBM/ is demonstrated.It enables monitoring extensiveness and depth of brain ischemia during the acute ischemic stroke /AIS/. WBM scale is designed to the neurological deficits evaluation. WBM groups help to evaluate extensiveness of brain ischemia. We studied 334 patients suffered from AIS.Three WBM groups were created:

I group: patients without disturbances of body axis.
II group: patients with disturbances of body axis.
III group: patients with disturbances of body axis and consciousness.

Results are shown in the table:

WBM Group	Total	Improvement	Lack of Improvement	Death
I	186	13/71%/	51/27,9%/	2/1,1%
II	100	58/58%/	32/32%/	10/10%/
III	48	16/33,3%/	12/25%	20/41,7%/
TOTAL	334	207/62,1%	95/28,4%	32/9,5%/

WBM groups and scale are useful, non-invasive and repeatable method of stroke patients evaluation.

9-03-28 THE STUDY OF MECHANISM OF VASCULAR THROMBO-EMBOLITIC DISEASES TREATED WITH ENZYMATIC PREPARATION OF THREE SNAKE VENOMS IN CHINA

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36 rabbits were divided into 4 groups. Each rabbit had experimental embolism in the carotid artery. DFA, svate, purified svate, and saline treatment were given for 3 days. In the DFA group the occluded vessel opened. All preperations decreased the blood viscosity. There was no change in the saline treated group.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press

9-03-30 CIMETIDINE PARENTERAL FOR PREVENTION OF ACUTE UPPER GASTROINTESTINAL BLEEDING IN ACUTE STROKE PATIENTS

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The efficacy of Cimetidine parenteral in the prevention of acute upper gastrointestinal bleeding was evaluated in a prospective, randomized, placebo-controlled study in 67 acute stroke patients who had Glasgow Coma Scale 10 or less and score for bleeding.

The patients were randomized in two groups. In the first group consisted of 33 patients who received 200 mg every six hours regarded as treatment group and the second group 34 patients received placebo as control group.

Bleeding was defined as macroscopically visible bleeding.

The treatment group was significantly more effective than control group ($p < 0.001$), 6.1% of 33 patients compared with 64.7% of 34 patients who bled, respectively.

The mortality rate of treatment group (48.5%) also significantly fewer than control group (73.5%) ($p < 0.05$).

Cimetidine parenteral is effective.

9-03-31 **TRANSCRANIAL DOPPLER FINDINGS IN ACUTE ISCHEMIC STROKE.**

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We studied with Transcranial Doppler (TCD) 53 consecutive patients within 48 hours of their first ischemic stroke. TCD examination was repeated daily for the first week. The patients were subdivided into 4 groups, according to their presumed pathogenesis: cardioembolic (n.18); lacunar (n.16); atherotrombotic (n.9); undetermined (n.10). Seven patients (13.2%) had MCA occlusion on admission: neurologic deficit at entry and residual disability at 1 month were more severe (respectively, $p < 0.0001$ and $p < 0.002$) in these patients. TCD demonstrated MCA recanalization within the first week in 5 cases; 3 of them developed hemorrhagic infarction, as opposed to only 1 of the 46 patients without MCA occlusion ($p < 0.001$). The ratio of symptomatic to asymptomatic MCA mean velocities was inversely correlated to the severity of the neurologic deficit on admission in our 53 patients: this correlation remained significant in all subgroups except for lacunar strokes, which are attributed to small vessel occlusion. This ratio was inversely correlated also to residual disability at 1 month ($p < 0.001$). TCD is a useful tool for the diagnosis and monitoring of MCA occlusion. Its findings bear prognostic value in ischemic stroke.

https://doi.org/10.1017/S0317167100020783 Published online by Cambridge University Press