The Editors of the Proceedings of the Nutrition Society *accept no responsibility for the abstracts of papers read at the Society's meetings for original communications.*

PROCEEDINGS OF THE NUTRITION SOCIETY

ABSTRACTS OF COMMUNICATIONS

A meeting of the Nutrition Society (Clinical Metabolism and Nutritional Support Group) was held in Bodington Hall, University of Leeds on Thursday and Friday, 21/22 November 1991, when the following papers were presented.

https://doi.org/10.1079/PNS19920040 Published online by Cambridge University Press

Basal metabolic rate and fuel oxidation rates in chronic obstructive pulmonary disease. By J. H. GREEN, P. N. BRAMLEY and M. F. MUERS, *Department of Medicine, St James's University Hospital, Leeds LS9 7TF*

Patients with the emphysematous type of chronic obstructive pulmonary disease (COPD) are often hypermetabolic (Green & Muers, 1991) and, in the absence of a reduced energy intake compared with the recommended daily allowance (Hunter *et al.* 1981), this could explain why these individuals become thin and wasted as the disease progresses. The increased basal metabolic rates (BMRs) of these patients is commonly attributed to the increased work of breathing. Therefore, hypermetabolism may also be characteristic of other kinds of COPD, even though weight loss may not be a clinical feature.

We have now measured BMR in six further emphysematous COPD patients (pCO_2 <5·0kPa), nine other smoking-related COPD patients (pCO_2 >6·0kPa), eight chronic asthmatic patients and six healthy controls. There were no significant differences in the mean ages, weights or muscle mass derived from simple anthropometry (Heymsfield *et al.* 1982). All the volunteers gave informed consent to the procedures, which were approved by the Leeds Eastern Health Authority (Ethics) Committee. They attended the laboratory after an overnight fast and BMR and fuel oxidation rates were derived using a flow-through indirect calorimeter (Datex Deltatrac Metabolic Monitor) and measurements of urinary nitrogen excretion made using the Kjeldahl method. Routine lung function tests were carried out within 2 weeks of the metabolic study.

Measured BMRs were compared with values predicted for age, height, weight and sex using the Harris-Benedict equation. There was no difference between the mean (SE) measured and predicted BMR in the control (5541 (272) *v.* 5881 (245) kJ/24 h) or emphysematous COPD groups (5552 (370) *v.* 5069 (149) kJ/24 h). The hypercapnic COPD and asthmatic patients had BMRs higher than predicted (6126 (387) *v.* 5405 (250), $P<0·05$; 6293 (197) *v.* 5701 (245) kJ/24 h, $P<0·01$). All the controls had mean measured BMRs within 10% of predicted values, while only 4/6 emphysematous, 5/9 hypercapnic and 3/8 asthmatic patients were within this normal range, the rest differed by >10% from predicted values. The fasting fuel oxidation rates were similar between groups, with non-protein respiratory quotients of 0·86 (0·02) (emphysematous), 0·85 (0·01) (hypercapnic), 0·84 (0·02) (asthmatic) and 0·88 (0·22) (control).

Thus, some patients with asthma and both types of smoking-related COPD are hypermetabolic. The metabolic rate of individual patients could not be predicted from detailed static lung function tests, arterial blood gases, pharmacological therapy or simple anthropometric measurements. These data suggest that factors other than the increased work of breathing may be needed to explain the high incidence of hypermetabolism in COPD.

Green, J. H. & Muers, M. F. (1991). *European Respiratory Journal* **4,** 813–819.

Heymsfield, S. B., McManus, C., Smith, J., Steven, V. & Nixon, D. W. (1982). *American Journal of Clinical Nutrition* **36,** 680–690.

Hunter, A. M. B., Carey, M. A. & Larsh, H. W. (1981). *American Review of Respiratory Diseases* **124,** 376–381.

Nutrition team audit. By C. E. PLESTER, K. C. H. FEARON, R. RICHARDSON, P. ROGERS, C. SEDGWICK, J. MCWHIRTER, H. REDDY and O. J. GARDEN, *Hospital Nutrition Team, University Department of Surgery, Royal Infirmary, Lauriston Place, Edinburgh EH3 9YW*

Although it is recommended that nutritional support be monitored by a nutrition team (Payne-James & Silk, 1990), it is not clear what information needs to be collected and what can be regarded as a successful outcome. To audit the function of our hospital nutrition team we designed a patient nutritional care record which is updated weekly and the information entered on a computer database. This report is an analysis of the first 12 months' data.

To assess nutritional outcome, changes in weight, mid-arm muscle circumference (Harpenden calipers), body cell mass (RJL Systems Inc, BIA 101) and serum albumin concentration were extracted from the database. Patients were scored on their first and last assessments as 'improved', if three or more variables had increased, 'deteriorated' if three or more variables had decreased, and 'stable' for intermediate patterns. This system was chosen because these variables were the ones most frequently used by the nutrition team to assess individual patient's progress and avoid classifying patients who become clinically oedematous as 'improved'.

Of 121 patients assessed, 113 received nutritional support (twenty-three medical, forty-seven surgical, fifteen renal and twenty-six ITU). The catheter sepsis rate for TPN was 4·7/1000 d fed. Of those patients receiving nutritional support, 61/113 were not audited for nutritional outcome: 25/61 because they were assessed once only (died or fed <1 week) and 36/61 because insufficient information was available (e.g. 22/36 not weighed).

Nutritional support	Energy intake† (MJ/d)	Nitrogen intake (gN/d)	Days fed (d)	Days lost (d)	Nutritional outcome		
					Improved (%)	Stable (%)	Deteriorated (%)
TPN	9·8	12·5	20	1	37	48	15
SEM (*n* 27)	0·3	0·4	3	1			
ENT	5·7*	7·6*	14	3	28	36	36
SEM (*n* 14)	0·7	1·0	3	2			
Combined	10·3	10·9	44	5	9	45	45
SEM (*n* 11)	0·3	0·8	10	2			

† Excludes spontaneous oral intake which was estimated to be approximately 2·1 MJ/d in all three groups.
* ENT *v.* TPN or Combined (Student's *t* test) $P<0·0001$.

The results demonstrate the difficulty of providing an index of nutritional outcome for the majority of patients even with a highly motivated nutrition team (61/113 not available for audit). Patients fed enterally received significantly less energy and N than patients on TPN or combined feeding ($P<0·0001$). The worst outcome was observed in patients on combined support, possibly because these were the most severely ill group. Overall, our nutrition team achieved either an improvement or stabilization of nutritional status in over 70% of the patients audited.

This work was supported by Clintec Nutrition, Abbott Laboratories and Kabi-pharmacia Ltd.

Payne-James, J. & Silk, D. B. A. (1990). *British Medical Journal* **103**, 1–2.

Infection with human immunodeficiency virus does not prevent the acute anabolic response to nutrition. By D. C. MACALLAN[1], M. A. MCNURLAN[2], P. J. GARLICK[2] and G. E. GRIFFIN[2], [1]*St George's Hospital Medical School, London SW17* and [2]*The Rowett Research Institute, Bucksburn, Aberdeen AB2 9SB*

Weight loss is a common and important feature of infection with the Human Immunodeficiency Virus (HIV). It is multifactorial in origin; important contributors appear to be reduced food intake, gastrointestinal disease with malabsorption, and disturbed intermediary metabolism. Several studies have suggested that infective processes impair or block the normal anabolic response to nutrition. This study set out to clarify the disturbances of protein metabolism in HIV infection and quantify abnormalities in the acute response to nutrition.

Subjects recruited were either HIV-positive individuals with stage IV disease (AIDS; *n* 14) or controls (defined as 'low risk' of HIV infection; *n* 6). Subjects remained fasted for the first 4 h, they were then fed for 4 h using a parenteral nutrition regime at a rate equivalent to 155·5 kJ (37·2 kcal)/kg per d and 0·2 g nitrogen/kg per d via a peripheral intravenous infusion. (This was chosen to avoid the confounding effects of malabsorption associated with enteral nutrition.) Subjects received a primed constant infusion of [1-^{13}C]leucine over the whole 8 h study period. Leucine flux was estimated from the isotope enrichment of leucine in serum and rates of oxidation calculated from the enrichment of breath carbon dioxide and serum α-ketoisocaproic acid combined with respiratory gas analysis (Melville *et al.* 1989).

In this setting, normal individuals respond to nutrition by switching from net protein catabolism to net anabolism by both a reduction in whole-body protein degradation and an increase in synthesis. Results are expressed in μmol leucine/kg fat-free mass (derived from anthropometric indices; Durnin & Womersley, 1974) per h and are shown as mean (SD). In response to feeding, mean leucine flux increased from 93·7 (18·6) to 121·9 (28·7) μmol/kg per h ($P<0·01$), degradation decreased from 93·4 (19·2) to 77·7 (30·7) μmol/kg per h ($P=0·07$) and synthesis increased from 72·5 (20·8) to 99·7 (33·3) μmol/kg per h ($P<0·02$).

HIV infected individuals have a higher rate of whole-body protein turnover than controls in the fasted state. Leucine flux is elevated at 117·7 (19·6) *v.* 93·7 (18·6) μmol/kg per h ($P=0·02$) and this consists of an increased rate of protein synthesis, 99·0 (19·1) *v.* 72·5 (20·8), and increased rate of degradation, 117·4 (19·8) *v.* 93·4 (19·2) μmol/kg per h.

Individuals with HIV infection are still able to make a normal acute anabolic response to the provision of nutrition in terms of whole-body protein turnover. This is true even in individuals who were in a weight-losing phase of their illness. This change is similar in magnitude in HIV-infected individuals to that seen in control subjects; in HIV the net balance changes from −18·4 (4·5) fasted to +20·3 (7·6) μmol/kg per h fed, whereas in controls it changes from −20·9 (5·6) fasted to +22·0 (4·4) μmol/kg per h fed (not significantly different between HIV and control). In HIV infection, feeding is associated with increased flux, from 117·7 (19·6) to 138·2 (15·6) ($P<0·01$), reduced degradation, from 117·4 (19·8) to 95·0 (14·7) ($P=0·02$) and increased synthesis, from 99·0 (19·1) to 115·3 (13·1) ($P<0·01$) μmol/kg per h in the same way as is seen in controls.

These findings reveal increased protein turnover in stage IV HIV infection consistent with a hypermetabolic cachexic pattern. In addition, they demonstrate the ability of HIV-infected subjects to make an anabolic response given an adequate nutritive stimulus and thus emphasize the importance of a positive approach to nutrition in HIV infection.

Durnin, J. V. G. A. & Womersley, J. (1974). *British Journal of Nutrition* **32**, 77–97.

Melville, S., McNurlan, M. A., McHardy, K. C., Broom, J., Milne, E., Calder, A. G. & Garlick, P. J. (1989). *Metabolism* **38**, 248–255.

The independent metabolic effects of anaesthesia and surgery. By F. CARLI, J. WEBSTER and G. RONZONI, *Department of Anaesthesia, Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex HA1 3UJ* and K. KHAN and M. ELIA, *Dunn Clinical Nutrition Centre, 100 Tennis Court Road, Cambridge CB2 1QL*

We have previously studied the independent effects of enflurane anaesthesia and surgery (Carli & Elia, 1991). In the present study we have extended our investigations to the effects of isoflurane and halothane (1MAC) on the circulating concentration of metabolites and cortisol.

Two groups of women (isoflurane group (*n* 12); age 45 (SE 5) years, BMI 25 (SE 3·2) kg/m^2: halothane group (*n* 6); age 45 (SE 9) years, BMI 23·5 (SE 2·6) kg/m^2) scheduled for elective total abdominal hysterectomy were studied. All subjects gave informed consent, and ethical approval was obtained from the local Ethics Committee.

Central venous blood samples were taken before general anaesthesia, during 2 h of anaesthesia alone, during surgery with anaesthesia (1 h), and for 2 h post-operatively (recovery). The subjects were unpremedicated, well oxygenated (Hb saturation >98%), and actively maintained at normothermia (36–37°). All patients received 6 ml saline (9 g NaCl/l)/kg throughout the study and no blood products.

Plasma metabolite	Anaesthetic	Pre-anaesthesia		Anaesthesia		Surgery		Recovery	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Lactate	I	1·0	0·5	0·8	0·5	1·2**	0·7	1·4**	0·7
(mmol/l)	H	0·9	0·2	1·0	0·1	1·1*	0·5	1·0	0·3
Glucose	I	5·5	0·9	5·6	0·9	7·5**	1·2	7·9**	1·1
(mmol/l)	H	5·8	0·5	5·6	0·5	6·9*	1·1	6·6*	0·8
Alanine	I	256	118	287*	76	300*	115	286	109
(μmol/l)	H	249	101	329*	93	339*	78	248	87
Glutamine	I	395	109	451**	115	448*	106	323*	77
(μmol/l)	H	445	63	520	79	491	69	428	75
BCAA	I	331	197	402	139	427	134	360	101
(μmol/l)	H	293	53	333	40	392**	57	322	54
Cortisol	I	380	290	124*	64	598*	104	980**	165
(nmol/l)	H	382	90	187*	108	559	158	685	242
Albumin	I	36	5	31**	4	30**	3	31**	3
(g/l)	H	35	3	29**	3	30**	3	29**	3

I, isoflurane; H, halothane; BCAA, branched chain amino acids.
*P<0·05, **P<0·005 compared with pre-anaesthesia values (paired t test).

Plasma lactate and glucose concentrations in both groups were not affected by anaesthesia alone but increased during surgery and recovery. There were also some changes in the plasma amino acid concentrations both during and after administration of anaesthesia alone. No differences were observed between the two groups for any of the metabolites. Plasma cortisol concentrations fell progressively during anaesthesia (P<0·01) and increased sharply during surgery and recovery. In contrast, the plasma albumin concentration decreased during anaesthesia and remained depressed thereafter (P<0·001).

The clinical significance of some of these changes, especially the major reduction in plasma cortisol concentration produced by anaesthesia alone, is uncertain.

Carli, F. & Elia, M. (1991). *Acta Anaesthesiologica Scandinavica* **35**, 329–332.

Metabolic responses to interleukin-1 (IL-1) are attenuated by dietary eicosapentaenoic (20:5 *n*-3) and docosahexaenoic (22:6 *n*-3) fatty acids in the rat. By A. L. COOPER[1], K. WEDDELL[1], T. A. B. SANDERS[2] and N. J. ROTHWELL[1], [1]*Department of Physiological Sciences, The Medical School, University of Manchester, Oxford Road, Manchester M13 9PT* and [2]*Department of Nutrition and Dietetics, King's College London, Campden Hill Road, London W8 7AH*

The eicosanoids, in particular the prostaglandins (PG), mediate many of the actions of IL-1 including fever and the associated rise in energy expenditure (Rothwell, 1990). Endogenous PG production can be modified by dietary 20:5 *n*-3 and 22:6 *n*-3 fatty acids (Sanders *et al.* 1983). We have investigated the effect of *n*-3 fatty acids on the pyrogenic and thermogenic responses to IL-1 in the rat.

Male Sprague-Dawley rats (100 g body-weight) were fed over a period of 8–9 weeks; control or *n*-3-supplemented semi-synthetic diets which were identical except for the type of fat provided: linoleic in the control diet and 20:5 *n*-3 and 22:6 *n*-3 (25% of a micro-encapsulated fish oil formula, Dry Omega-3, Dancochem) in the experimental diet. In both cases fat provided 100 g/kg diet with the other major constituents being (g/kg diet): starch 500, casein 200, sucrose 100. Body-weight gain and food intake were similar in both groups. After 4 or 8 weeks, control and experimental groups were injected with either saline (9 g NaCl/l) or recombinant human IL-1 (1 μg/rat given intraperitoneally). Oxygen consumption ($\dot{V}_{O_2}$) was measured by indirect calorimetry for 2 h before and 2 h after the injection. Colonic temperature (T_c) was determined immediately after measurements of $\dot{V}_{O_2}$. The PGE_2 concentration in the cerebrospinal fluid (CSF) of animals studied 8–9 weeks after supplementation was assessed by radioimmunoassay. Results are expressed as mean (SEM) (*n* 8–11).

Administration of IL-1 into control animals caused a 1·1 (0·2)° fever and a 20 (6)% rise in $\dot{V}_{O_2}$. Supplementation with *n*-3 fatty acids significantly inhibited the rise in T_c (0·5 (0·1)°, $P<0·05$, ANOVA) and reduced the increase in $\dot{V}_{O_2}$ (9 (3)%). Responses to IL-1 were similarly attenuated in *n*-3 fed animals at 8–9 weeks. The rise in T_c was reduced by 0·8° ($P<0·001$, ANOVA) and $\dot{V}_{O_2}$ by 60% compared to control animals given IL-1.

The CSF concentration of PGE_2 in control animals measured 2 h after IL-1 injection (8–9 weeks) was 220 (74) pg/ml (*n* 6) compared to 45 (10) pg/ml (*n* 4) in control animals injected with saline. Supplementation with *n*-3 fatty acids reduced the magnitude of this response by 47% (117 (40) pg/ml, *n* 7).

The inhibitory effect of *n*-3 fatty acids on the responses to IL-1 may be due to a reduction in the production of PG within the central nervous system. This effect may result from altered membrane phospholipid composition resulting from reduced availability of arachidonic acid, the precursor for eicosanoid synthesis.

A grant from MAFF is gratefully acknowledged.

Rothwell, N. J. (1990). *European Cytokine Network* **1**, 211–213.
Sanders, T. A. B., Chua, E. & Bolster, N. (1983). *Proceedings of the Nutrition Society* **42**, 99A.

Effect of Ibuprofen on the acute-phase response and whole-body protein turnover of weight-losing cancer patients. By T. PRESTON[1], K. C. H. FEARON[2], F. P. WINSTANLEY[3], C. SLATER[1], D. C. MCMILLAN[3], A. SHENKIN[4] and O. J. GARDEN[2], [1]*Department of Health Physics, SURRC, East Kilbride G75 0QU, Departments of Surgery, Royal Infirmary,* [2]*Edinburgh EH3 9YW,* [3]*Glasgow G31 2ER* and [4]*Department of Chemical Pathology, Royal Liverpool Hospital, Liverpool L69 3BX*

We have demonstrated previously that, in patients with cancer, an acute-phase protein response (APPR) is associated with elevated whole-body protein turnover (WBPT) and a shorter duration of survival (Fearon *et al.* 1990). The aim of the present study was to determine whether administration of the non-steroidal anti-inflammatory agent, Ibuprofen, might attenuate the APPR and reverse some of the associated changes in body protein metabolism.

Cancer patients with hepatic metastasis received either 3 d of Ibuprofen (1200 mg/d; *n* 7) or no treatment (*n* 6) prior to study. WBPT was measured immediately prior to surgery with a primed constant infusion of [^{15}N]glycine. Serum interleukin-6 (IL-6) and C-reactive protein (CRP, an index of the APPR) were measured in blood samples taken prior to and following treatment with Ibuprofen. The results are shown in the Table.

		WBPT (g protein/kg per d)		CRP (mg/l)		IL-6 (U/ml)	
Treatment	*n*	Median	Range	Median	Range	Median	Range
No Ibuprofen	6	5·6	4·93–7·45	80	34–116	107	59–210
Pre-Ibuprofen	7	—	—	39*	17–64	61*	23–88
Post-Ibuprofen	7	5·47*	3·92–5·70	24**	18–44	70	40–84

* Not significant *v.* untreated group (Mann-Whitney test).
** Significant *v.* pre-treatment (paired *t* test, $P<0·01$).

Although Ibuprofen treatment produced a significant reduction in the APPR (CRP concentration), this change was not associated with a fall in circulating IL-6 concentration. Furthermore, Ibuprofen failed to alter whole-body protein kinetics. Although these results bring into question the role of circulating IL-6 as the main signal for CRP production in patients with advanced cancer, they do not exclude modification of a second messenger system.

The authors acknowledge the Scottish Hospital Endowments Research Trust for financial support, and Professor D. C. Carter for clinical support.

Fearon, K. C. H., McMillan, D. C., Preston, T., Hansell, D. T., Shenkin, A. & Garden, O. J. (1990). *Clinical Nutrition* **9**, Special supplement, p. 21.

Lymphocyte protein synthesis: an in vivo measure of activation. By K. G. M. PARK[1,2], S. D. HEYS[1,2], O. EREMIN[1] and P. J. GARLICK[2], [1]*Department of Surgery, Aberdeen University, Foresterhill, Aberdeen AB9 2ZD* and [2]*Rowett Research Institute, Bucksburn, Aberdeen AB2 9SB*

Lymphocyte activation leads to an enhancement of cytotoxicity and the production of growth factors which have important actions on many organ systems. These changes are associated with a significantly increased metabolic activity in the lymphocytes. Conventional measurements of lymphocyte activation have relied on the uptake of tritiated thymidine of these cells in vitro. Thymidine uptake, however, is inhibited by certain lymphokines, which may in themselves be produced by activated lymphocytes and mononuclear cells, in particular by interferon. Protein synthesis has previously been used as a measure of in vitro lymphocyte activation (Kay *et al.* 1971), and in the present study we have determined the effects of lymphocyte activation on protein synthesis measured in vivo.

Rates of protein synthesis were determined by intravenous injection of 4 g L-[1-^{13}C]leucine (20 atoms % enrichment)/70 kg body-weight and measurement of the incorporation of label into protein peripheral blood lymphocytes (PBL) after a 60 min period. PBL were separated from whole blood on ficol hypaque gradients, during which time further incorporation of leucine was inhibited by cycloheximide. Using this technique PBL protein synthesis was measured in seven patients with metastatic colonic carcinoma prior to and after a 5 d infusion of the lymphokine interleukin 2 (IL-2). IL-2 was administered as part of a phase II trial for the treatment of metastatic cancer. In these patients in vitro thymidine uptake was also measured on lymphocytes isolated before and after IL-2 infusion.

The pre-IL-2 fractional rate of PBL protein synthesis ranged from 4·2–8·2%/d, mean 6·2 (SD 1·08)%/d. Following 5 d of IL-2 infusion the mean rate of PBL protein synthesis was 29·1 (SD 2·69)%/d. There was in addition a corresponding increase in thymidine uptake by the post-infusion PBL compared with the pre IL-2 values (mean increase 490 (SD 260)%).

These data demonstrate that the in vivo activation of lymphocytes results in a marked increase in their rate of protein synthesis, which is likely to have a significant influence on whole-body protein metabolism. In addition, measurements of lymphocyte protein synthesis may provide a dynamic method for the in vivo assessment of lymphocyte activation.

We are grateful to EuroCetus, Amsterdam, for the gift of human recombinant IL-2.

Kay, J. E., Ahern, T. & Atkins, M. (1971). *Biochimica et Biophysica Acta* **247**, 322–334.

Effects of surgical trauma on muscle protein synthesis at local and distant sites. By A. GHUSAIN-CHOUEIRI and P. W. EMERY, *Department of Nutrition and Dietetics, King's College, London W8 7AH*

Surgical trauma causes negative nitrogen balance which is believed to represent net loss of protein from muscle, but there is conflicting evidence as to the changes in rates of protein synthesis and degradation which may be responsible for this loss. We have previously reported that minor injury has different effects on protein synthesis in injured and uninjured muscles in the same animals (Ghusain-Choueiri & Emery, 1991), and have now extended these observations by studying the effects of more severe surgical trauma in mature female rats.

Surgery was performed under halothane anaesthesia, and consisted of a 5 cm mid-line incision into the peritoneum followed by mobilization of the intestine. The muscle was then sutured and the skin closed with stainless steel clips. The whole procedure lasted approximately 7 min. Control rats were anaesthetized but not injured. All animals were allowed free access to food and water throughout the study. Protein synthesis was measured 2, 24 or 48 h later using the large-dose phenylalanine method (Garlick *et al.* 1980) in a 1 cm-wide strip of the abdominal muscle including one side of the wound, and in one gastrocnemius muscle.

Time after injury (h)	*n*	Food intake (g/d)		Change in body-wt (g/d)		Fractional rate of protein synthesis (%/d)			
						Abdominal muscle		Gastrocnemius muscle	
		Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
2 (Injured)	5	16·7	0·8	4·1	0·9	10·5**	0·4	10·4	0·5
2 (Control)	6	16·9	1·0	4·7	0·5	12·7	0·5	10·6	0·6
24 (Injured)	5	9·7***	0·6	−6·1*	1·4	11·5	0·6	7·9	0·4
24 (Control)	5	15·3	0·9	−1·3	1·1	9·8	1·8	8·5	0·4
48 (Injured)	10	13·1***	0·4	0·0**	1·1	27·0***	2·0	12·0	1·4
48 (Control)	10	17·1	0·6	5·6	0·9	15·5	1·7	11·4	1·7

Significantly different from control: *$P<0·05$, **$P<0·01$, ***$P<0·001$.

Abdominal surgery caused a significant reduction in food intake, body-weight and N balance (58 (SEM 12) *v.* 143 (SEM 11) mg N/d at 48 h, $P<0·001$), but had no effect on protein synthesis in the leg muscle. This is particularly surprising in view of the known effect of decreased food intake in reducing muscle protein synthesis. In the abdominal muscle the rate of protein synthesis fell slightly immediately after injury but returned to normal by 24 h. However, there was a massive increase in abdominal muscle protein synthesis at 48 h, corresponding with the smaller local increase in protein synthesis which we have previously observed in response to minor injury in leg muscles (Ghusain-Choueiri & Emery, 1991). Protein synthetic activity may thus provide a sensitive index of the repair and regrowth of damaged tissue.

Financial support from the Wellcome Trust is gratefully acknowledged.

Garlick, P. J., McNurlan, M. A. & Preedy, V. R. (1980). *Biochemical Journal* **192**, 719–723.
Ghusain-Choueiri, A. & Emery, P. W. (1991). *Proceedings of the Nutrition Society* **50**, 166A.

The influence of respiratory quotient and serum lipid levels on thermic effect of continual enteral nutrition. By L. SOBOTKA, Z. ZADAK and J. CHALOUPKA, *Department of Metabolic Care and Gerontology, Charles University, Hradec Kralove, Czechoslovakia*

The increase in energy expenditure during feeding is known as the thermic effect of nutrition (TEN). It can lead to unwanted hypermetabolism which can be especially dangerous for critically ill patients. TEN is dependent on the quantity and composition of nutrients administered (Jequier, 1986). It can also be dependent on other factors like age, sex and body cell mass. It is also known that TEN is reduced in severely malnourished patients. The aim of the present study was to detect some metabolic parameters which can influence TEN during continual enteral feeding.

Nine subjects who were dependent on continual nasojejunal tube feeding (Hill *et al.* 1985) were studied. After an overnight fast, resting energy expenditure (REE) and basal respiratory quotient (B-RQ) were measured by indirect calorimetry (MMC-Horizon). Blood for measurement of serum lipid levels was withdrawn immediately thereafter. Then intrajejunal administration of a complete tube-feeding diet (Nutrodrip Standard, Sandoz Nutrition) containing 14% of total energy as protein, 52% as carbohydrate, and 34% as fat was initiated. The rate of delivery was 1·6 times higher than the basal REE. REE and TEN were evaluated 2, 5, 24 and 48 h after the onset of diet administration and these values were compared with B-RQ and basal serum lipid levels.

TEN rose during the study from 4·9 (SD 3·4)% at 2 h to 7·7 (SD 4·2)% at 24 h. A decrease to 6·2 (SD 4·2)% was observed at 48 h, but none of these changes was statistically significant. However, TEN was dependent on the fasting metabolic situation. This is apparent from the significant positive correlations found between TEN measured 2 and 5 h after the onset of continual nutrition administration and B-RQ. Also, TEN evaluated at 24 and 48 h correlated positively with basal serum levels of very low density lipoprotein (VLDL).

			Significance
2 h	TEN *v.* B-RQ	0·92	$P<0·001$
5 h	TEN *v.* B-RQ	0·88	$P<0·001$
24 h	TEN *v.* VLDL	0·80	$P<0·01$
48 h	TEN *v.* VLDL	0·74	$P<0·01$

We conclude that the thermic effect of continual enteral nutrition is dependent on the nutritional status of the patient as measured by fasting RQ and serum VLDL levels.

Hill, J. O., DiGirolamo, M. & Heymsfield, S. B. (1985). *American Journal of Clinical Nutrition* **42**, 1290–1298.

Jequier, E. (1986). *Clinical Nutrition* **5**, 181–186.

Plasma amino acids and peptiduria during intravenous infusion of a short-chain ovalbumin hydrolysate, or its equivalent amino acid (AA) mixture, in man. By G. K. GRIMBLE[1], P. C. AIMER[1], P. MORRIS[1], A. RAIMUNDO[1], B. WERYK[2] and D. B. A. SILK[1], [1]*Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London NW10 7NS* and [2]*Department of Physiology and Anatomy, The University of Dundee, Dundee DD1 4HN*

We have previously shown that purified protein hydrolysates (>67% di- and tripeptides, <10% AA; Grimble *et al.* 1987) are a well utilized iv. nitrogen source in man (Grimble *et al.* 1988; Grimble & Silk, 1989). Their attraction is as a low osmolality alternative to free amino acid solutions for peripheral parenteral nutrition. The present study investigated plasma amino acid profiles and peptiduria during continuous infusion of one such hydrolysate in man.

Seven healthy subjects (four male, three female, 25·8 (SE 1·1) years) were fasted from 18.00 h on the previous day and voided their bladder before the start of the study (baseline collection). Subjects were infused via the antecubital vein, on two separate occasions, for 6 h with a complete TPN formula (4·5 g N/l, 28 g fat/l, 105 g glucose/l) containing either an ovalbumin hydrolysate or an equivalent AA mixture at 13 g N, 7·95 MJ (1900 kcal)/24 h. Blood samples were taken at 0, 2, 4 and 7 hours and urine collected for 7 h. Plasma amino acids were measured by HPLC. Urinary peptides and pyroglutamic acid (pyGlu) were measured by high-performance capillary electrophoresis (HPCE) and ion-exclusion HPLC, respectively.

As expected, the plasma concentrations of several essential amino acids increased during infusion. However, differences between infusion periods in the concentration of individual amino acids at each time point failed to reach statistical significance for any amino acid (Student's paired *t* test). Excretion of pyGlu was 174 (SE 62) μmol and 79 (SE 13) μmol during hydrolysate and amino acid infusions, respectively ($P<0·05$, Student's paired *t* test). The mechanism of HPCE separation allowed tentative assignment of the following classes of peptides: basic, neutral and large neutral. Peptide electrophoretograms of infused material and baseline, hydrolysate and AA infusion urine differed markedly. Peptides could be detected in baseline urine samples and in collections made during either infusion period. Peptiduria was higher during hydrolysate infusion, but there was a relative enrichment in neutral and large neutral peptides, compared to infused material.

Increased loss of amino acids by urinary peptide excretion did not lead to imbalances in plasma amino acid profiles. The marked difference between infused and excreted peptide profiles suggests that utilization of peptides from the hydrolysate was sequence specific. Higher pyGlu excretion during hydrolysate infusion may reflect renal brush-border hydrolysis of pyGlu-peptides and low renal absorption of free pyGlu. This implies that pyGlu excretion depends not only on glycine status, as suggested earlier (Moran *et al.* 1989), but also the form and amount of pyGlu infused parenterally. We therefore conclude that highly-purified short-chain protein hydrolysates show promise as a suitable low osmolality alternative to free amino acids and synthetic dipeptides in peripheral parenteral nutrition.

Grimble, G. K., Raimundo, A. H., Rees, R. G., Hunjan, M. K. & Silk, D. B. A. (1988). *Journal of Parenteral and Enteral Nutrition* **12** (Supplement), 15S.

Grimble, G. K., Rees, R. G., Keohane, P. P., Carwright, T., Desreumaux, M. & Silk, D. B. A. (1987). *Gastroenterology* **92,** 136–142.

Grimble, G. K. & Silk, D. B. A. (1989). *Nutrition Research Reviews* **2,** 87–108.

Moran, B., Persaud, C. & Jackson, A. A. (1989). *Proceedings of the Nutrition Society* **48,** 75A.

The effect of alanyl-glutamine peptide supplementation on muscle protein synthesis in post-surgical patients receiving glutamine-free amino acids intravenously. By J. M. BARUA[1], E. WILSON[2], S. DOWNIE[1], B. WERYK[1], A. CUSCHIERI[1] and M. J. RENNIE[1], [1]*Department of Anatomy and Physiology, University of Dundee, Dundee DD1 4HN* and [2]*Department of Surgery and Anaesthetics, Ninewells Hospital and Medical School, Dundee DD1 9SY*

We investigated the effects on muscle protein synthesis of Ala-Gln peptide supplementation of a non-glutamine-containing parenteral amino acid solution in post-operative surgical patients. The studies were approved by the Tayside Health Board Ethical Committee. Each of the patients (four female, four male, 66–79 years, 44–85 kg), who had undergone curative resection for oesophageal carcinoma, were studied during routine post-operative admission to the Intensive Care Unit. Mean APACHE II score on admission to ICU was 9·13. From the second post-operative day, patients were provided with nutrition consisting of a conventional commercial amino acid solution (11·5 g N) plus 450 g glucose, 70 mmol Na^+ and 80 mmol K^+, all in 2·5 l water/24 h. On the third post-operative day, the patients were studied between 08.00 and 16.00 hours, when they also received a primed, constant infusion of 1-[^{13}C]leucine (1 mg/kg prime, 1 mg/kg per h). The protocol required measurements of the incorporation of 1-[^{13}C]leucine into muscle protein over two 4-h periods. In the first, the conventional solution was supplemented with alanine (4 mg/kg per h) and glycine (8 mg/kg per h) in amounts isonitrogenous with the Ala-Gln (11 mg/kg per h) given in the second 4-h period, when the alanine and glycine were discontinued. Biopsies were taken from the tibialis anterior at 4 and 8 h; muscle obtained at surgery provided the baseline. The [^{13}C]enrichment of blood and muscle-free leucine, blood ketoisocaproate (KIC), and muscle-protein leucine were analysed (Bennet *et al.* 1989).

	No Ala-Gln supplementation				Ala-Gln supplementation			
Muscle protein synthesis (%/h)	Blood KIC†		Muscle-free leu†		Blood KIC†		Muscle-free leu†	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
	0·025	0·004	0·043	0·004	0·039*	0·003	0·078*	0·008
95% Confidence interval	0·016–0·034		0·032–0·047		0·033–0·053		0·059–0·091	

* Significantly higher than no Ala-Gln supplementation, $P<0·05$.
† Precursor surrogate used to calculate protein synthesis.

The results provide evidence that the supplementation of a conventional amino acid solution with Ala-Gln results in an approximate doubling in the rate of muscle protein synthesis, from a value which is much lower than normally seen in healthy fed subjects. The effect was apparent no matter whether the mixed tissue-free pool or the blood KIC was used as a surrogate index of the true leucyl-tRNA labelling.

Supported by Baxter Healthcare, Clintec, Tayside Health Board, University of Dundee, The Wellcome Trust, Ajinomoto GmbH and Kabi-Pfrimmer.

Bennet, W. M., Connacher, A. A., Scrimgeour, C. M., Smith, K. & Rennie, M. J. (1989). *Clinical Science* **76**, 447–454.

Glutamine promotes interleukin-2 production by concanavalin A-stimulated lymphocytes.

By P. C. CALDER and E. A. NEWSHOLME, *Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU*

Glutamine plays an important role in the metabolic processes associated with recovery from illness or injury. For this reason there has been great interest in the provision of glutamine or glutamine precursors to such patients. Part of the rationale behind such therapy is the immunostimulatory action of glutamine. Specific immunomodulatory effects of glutamine are not well documented, although it has been shown that glutamine is required for in vitro mitogen-stimulated proliferation of rat (Szondy & Newsholme, 1989) and human (Parry-Billings *et al.* 1990) T-lymphocytes. Interleukin-2 (IL-2) is an immunoregulatory cytokine synthesized and secreted by activated T-lymphocytes. Since IL-2 plays a central role in the control of T-lymphocyte proliferation, it was of interest to investigate the effect of glutamine on IL-2 production by stimulated lymphocytes.

Rat lymphocytes were prepared and cultured (in the presence of concanavalin A; Calder *et al.* 1991) in a medium containing various concentrations of glutamine. After 24 or 48 h the culture medium was removed, serially diluted twofold and bioassayed for IL-2.

Glutamine concentration (mM)	[IL-2] (units/ml)			
	24 h		48 h	
	Mean	SEM	Mean	SEM
2·0	7·58	1·06	6·70	0·43
1·0	7·50	1·60	5·80	1·27
0·5	5·58	0·72	4·83	0·53
0·2	5·00	1·06	3·40	0·47
0·1	2·70	1·24	2·63	0·20
0·075	2·10	0·50	2·67	0·27
0·05	1·98	0·28	2·62	0·18
0·025	1·60	0·30	2·47	0·23
0·01	1·16	0·20	2·17	0·33
0	0·70	0·10	2·03	0·27

In the absence of glutamine, IL-2 concentration in the culture medium was low. As the concentration of glutamine was increased, the concentration of IL-2 in the medium increased. The effect of glutamine on IL-2 concentration was greater at 24 h than at 48 h. Since T-lymphocyte proliferation is dependent upon the production and secretion of IL-2, these observations suggest that glutamine may stimulate lymphocyte proliferation by promoting the production of IL-2. Whether this is a specific effect of glutamine upon the IL-2 synthetic pathway or a general effect upon protein synthesis is not known. To our knowledge, this is the first time that the production of an important immunoregulator has been shown to be dependent upon glutamine levels.

Calder, P. C., Bond, J. A., Bevan, S. J., Hunt, S. V. & Newsholme, E. A. (1991). *International Journal of Biochemistry* **23**, 579–588.

Parry-Billings, M., Evans, J., Calder, P. C. & Newsholme, E. A. (1990). *Lancet* **336**, 523–525.

Szondy, Z. & Newsholme, E. A. (1989). *Biochemical Journal* **261**, 979–983.

Glutamine increases protein synthesis in heart, skeletal muscle, liver and gut of dexamethasone-treated rats. By P. W. WATT, H. S. HUNDAL, S. DOWNIE and M. J. RENNIE, *Department of Anatomy and Physiology, University of Dundee, Dundee DD1 4HN*

We have previously reported an anabolic effect of glutamine on muscle protein synthesis in the rat (MacLennan *et al.* 1987). We have now extended the work to study the effects of glutamine (Gln) administration in circumstances in which tissue can be depleted of glutamine, i.e. dexamethasone treatment.

Female Wistar rats (200–250 g) were treated intraperitoneally for 8 d with dexamethasone (0·44 mg/kg) or saline (9 g sodium chloride/l; control). Animals were pair fed on standard rat pelleted diet. On day 9, all rats (*n* 20) were anaesthetized with sodium pentobarbitone (Sagatal, 50 mg/kg) and infused with 1-[^{13}C,^{15}N]leucine (both 99%) at 5 mg/kg per h after a bolus of 5 mg/kg. At the same time, six control and six dexamethasone-treated rats were injected with a solution containing 180 mM Gln and 60 mM NaCl at a dose of 20 ml/kg. The other six from each group were injected with the same volume of saline. After 1 h, blood and tissue samples were taken for analysis of amino acids in plasma and tissues and enrichment of plasma and tissue leucine. Four animals died under anaesthesia before tissue sampling (three control and one glutamine-injected).

	Glutamine concentration (mM)									
	Plasma		Heart		Muscle		Liver		Gut	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Control	0·69	0·06	9·10	1·30	8·14	0·22	7·90	0·45	0·81	0·07
Control + Gln	1·20*	0·05	15·50*	0·44	12·60*	0·51	13·30*	0·51	1·92*	0·15
Dexamethasone	0·64	0·05	13·60	1·40	2·40*	0·56	8·10	0·42	0·89	0·23
Dexamethasone + Gln	1·28*	0·11	14·81	0·91	11·20*	0·52	12·13*	0·55	2·03*	0·39
					Protein synthetic rate (%/h)					
Control			0·61	0·05	0·25	0·02	2·03	0·10	3·03	0·17
Control + Gln			0·67	0·05	0·22	0·13	2·85*	0·23	3·75*	0·25
Dexamethasone			0·62	0·04	0·19*	0·01	2·11	0·13	3·40	0·20
Dexamethasone + Gln			0·82*	0·05	0·23	0·01	2·88*	0·22	4·21*	0·25

Significantly different from control group (Student's *t* test): *$P<0·05$.

Whole-body leucine flux, assessed by ^{15}N and ^{13}C, was depressed by raised plasma Gln in control and corticosteroid-treated animals: ^{15}N from 2200 (SEM 180) to 1020 (SEM 55) μmol/kg per h; ^{13}C from (SEM 20) to 529 (SEM 14) μmol/kg per h.

The results demonstrate that:

(a) dexamethasone treatment decreases muscle water glutamine concentration, but has little effect on other tissues.

(b) Gln replacement elevates Gln in plasma and all tissues.

(c) dexamethasone decreases muscle protein synthesis but seems to raise it in all other tissues.

(d) Gln stimulated protein synthesis in most tissues studied, especially after treatment with dexamethasone.

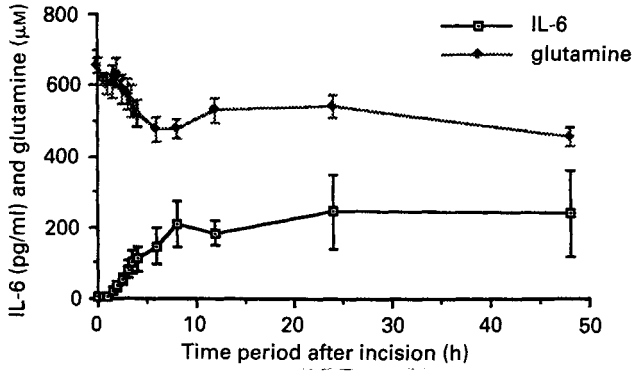
(e) raising plasma Gln concentration reduced leucine transamination and whole-body protein breakdown (leucine flux).

This work was supported by Action Research, Pfrimmer GmbH and the MRC. PWW is a Wellcome Trust Lecturer.

MacLennan, P. A., Brown, R. A. & Rennie, M. J. (1987). *FEBS Letters* **215**, 187–191.

Effects of major and minor surgery on plasma glutamine and cytokine concentrations. By M. PARRY-BILLINGS and E. A. NEWSHOLME, *Cellular Nutrition Research Group, Department of Biochemistry, University of Oxford OX1 3QU* and R. BAIGRIE, P. M. LAMONT and P. J. MORRIS, *Nuffield Department of Surgery, John Radcliffe Hospital, Oxford OX3 9DU*

Surgery is known to impair the immune response, resulting in an increased risk of sepsis (Lennard, 1985). The mechanisms underlying this impairment are not understood. Glutamine and the cytokines have been shown to be important in immune regulation. The present study aimed to elucidate further the mechanisms of post-operative immunosuppression by examining the relationship between glutamine metabolism and cytokine elaboration. The plasma levels of glutamine, alanine, glutamate, branched chain amino acids, interleukin (IL)-1, IL-6 and tumour necrosis factor (TNF) were measured frequently in patients before, during and after elective aortic aneurysm surgery (major surgery, nine patients) or inguinal hernia repair (minor surgery, five patients).



Mean plasma concentrations (with SEM) of glutamine and IL-6 following major surgery.

Following major surgery, the plasma concentration of glutamine was rapidly and markedly decreased in all patients: the concentration was decreased 2·5 h post-incision and remained so until the end of the study (168 h post-incision). The extent of this decrease varied between subjects, but in four patients was >40%. The plasma concentrations of other amino acids were also changed post-surgery, but in contrast to that of glutamine they returned to control, pre-surgery values by 168 h post-incision. In contrast to the marked effect of major surgery on plasma glutamine levels, minor surgery was without effect on these levels. There was a significant negative correlation between the plasma concentrations of IL-6 and glutamine following major surgery (0–8 h: r 0·95, $P<0·0001$). In contrast, no correlation was apparent between the plasma levels of glutamine and IL-1 or TNF (TNF was not detected).

Given the proposed role of glutamine for cells of the immune system and the experimental evidence which suggests that normal plasma levels of this amino acid are essential for a response of these cells to an immune challenge (Parry-Billings *et al.* 1990), it is suggested that this large and prolonged decrease in the plasma glutamine level may be one factor causing immunosuppression following major surgery. Furthermore, the correlation between changes in the plasma concentrations of glutamine and IL-6 is intriguing and warrants further investigation.

Lennard, T. W. J., Shenton, B. K., Borzotta, A., Donnelly, P. K., White, M., Gerrie, L. M., Proud, G. & Taylor, R. M. R. (1985). *British Journal of Surgery* **72,** 771–776.

Parry-Billings, M., Evans, J., Calder, P. C. & Newsholme, E. A. (1990). *Lancet* **336,** 523–525.

Evidence for tumour-induced changes in basal metabolic rate in patients with small cell lung cancer. By SUSAN A. JEBB[1], R. J. OSBORNE[2], A. K. DIXON[3] and M. ELIA[1], [1]*MRC Dunn Nutrition Unit, 100 Tennis Court Road, Cambridge CB2 1QL* and *Departments of* [2]*Clinical Oncology and Radiotherapy*, and [3]*Radiology, Addenbrooke's Hospital, Cambridge CB2 2QQ*

There have been many conflicting reports in the literature concerning changes in basal energy expenditure in patients with cancer. The interpretation of energy expenditure data may be complicated by concomitant changes in body composition, particularly proportional changes in organ size relative to total fat-free mass (FFM), since the energy expenditure of the liver, brain, spleen and kidneys account for over half of basal metabolic rate (BMR) (Elia, 1992). Changes in the mass of these organs have the potential to cause major changes in total energy expenditure which are independent of changes in the metabolic activity per unit weight of tissue.

The study group comprised seventeen patients with small cell lung cancer, eleven male and six female, age 62 (SD 12) years, height 1·67 (SD 0·09) m, weight 67·5 (SD 12·5) kg and body fat 26·4 (SD 10·8)%. Measurements were made at diagnosis and after about 12 weeks of treatment. Accordingly, patients acted as their own controls. Measurements included BMR (Deltatrac), fat and FFM by dual energy X-ray absorptiometry (Lunar) and organ volume (liver, kidney and spleen) from serial abdominal CT scans.

Following treatment, two groups of patients could be identified; those who responded to treatment, with substantial shrinkage of their tumour (responders) and those whose disease progressed despite treatment (non-responders) (see Table). In the responders there was a decrease in BMR with no significant changes in body-weight, FFM and organ size, indicating a decrease in the metabolic activity of tissues. In contrast, in the non-responders BMR was unchanged despite a decrease in weight, FFM and organ size, suggesting an increase in the metabolic activity per unit weight of tissue.

	Responders (*n* 10)		Non-responders (*n* 7)	
Change	Mean	SD	Mean	SD
Weight (kg)	+0·00	4·96	−4·93	5·78
FFM (kg)	+0·26	2·72	−2·40*	2·53
Organ volume† (cm^3)	−156	198	−453	347
BMR:				
MJ/d	−0·617**	0·412	−0·004	0·360
MJ/kg per d	−0·010***	0·004	+0·006*	0·005
MJ/kg FFM per d	−0·013***	0·008	+0·005*	0·005

Significantly different by paired *t* test: $*P<0·05$, $**P<0·01$, $***P<0·001$.

† Measured in seven responders and four non-responders with no organ metastasis and in whom changes in body-weight and BMR were not significantly different from the group as a whole.

These changes, standardized for changes in body composition and organ size, suggest a direct or systemic tumour-induced effect on energy expenditure in this group of patients.

Elia, M. (1992). In *Energy Metabolism: Tissue determinants and Cellular Corollaries* [J. Kinney, editor]. New York: Raven Press (In the Press).

A multi-tracer investigation of the effect of a flooding dose administered during the constant infusion of tracer amino acid on the rate of tracer incorporation into human muscle protein. By K. SMITH[1], P. ESSEN[2], M. A. MCNURLAN[3], M. J. RENNIE[1], P. J. GARLICK[3] and J. WERNERMAN[2], [1]*Department of Anatomy and Physiology, University of Dundee, Dundee DD1 4HN*, [2]*Departments of Anaesthesiology, Huddinge and St Göran's Hospitals, Stockholm, Sweden* and [3]*Rowett Research Institute, Bucksburn, Aberdeen AB2 9SD*

Rates of muscle protein synthesis measured by the constant infusion and the flooding-dose techniques differ by twofold. A recent study suggested that flooding dose of [^{13}C]leucine given during the constant infusion of [^{13}C]valine tracer increased the rate of tracer incorporation into muscle protein (Smith *et al.* 1991). We have now conducted further studies on six healthy subjects. Post-absorptive subjects received a primed, constant infusion of 1-[^{13}C]phenylalanine (99%, 0·75 mg/kg prime, 0·75 mg/kg per h) over 7·5 h. Three subjects received, in addition, a primed, constant infusion of 1-[^{13}C]valine (99%, 1·5 mg/kg prime, 1·5 mg/kg per h) over 7·5 h, but after 6 h a flooding dose of 1-[^{13}C]leucine (0·05 g/kg; 20 APE) was administered. In the other three subjects a primed, constant infusion of 1-[^{13}C]leucine (99%, 1 mg/kg prime, 1 mg/kg per h) was challenged with a flood of valine (75 mg/kg; 20 APE). Venous blood was taken before and during the investigation. Quadriceps muscle was biopsied at 30, 360 and 450 min. Analysis of plasma and muscle free amino acid was carried out by gas chromatography–mass spectrometry. Muscle protein amino acids were separated chromatographically and their isotope enrichments measured by IRMS.

	Tracer incorporation (APE/h × 10^4)		Muscle free enrichment (APE)	
Leucine flood . . .	Phe	Val	Phe	Val
Pre flood	26 (4)	48 (8)	6·08 (0·09)	8·64 (1·05)
Post flood	83 (5)	136 (8)	6·72 (0·65)	9·59 (1·05)
Valine flood . . .	Phe	Leu	Phe	Leu
Pre flood	29 (3)	23 (2)	6·72 (0·16)	4·72 (0·30)
Post flood	58 (5)	42 (8)	6·95 (0·23)	5·27 (0·40)

Values are means with their standard errors in parentheses (*n* 3).

In all subjects the flooding dose caused a marked increase in the rate of incorporation of ^{13}C tracer supplied by constant infusion (Table), but the increase depended on the amino acid infused as tracer and that given as the flood. The constantly-infused tracer increased its muscle free labelling by less than 15% by the end of the flooding period. Muscle protein synthesis rate calculated using the tissue free amino acid as precursor and based upon the constant infusion of phenylalanine, valine or leucine tracer were 0·042, 0·062, and 0·051%/h respectively. During the flooding period rates from the tracer infusion were similar to those obtained from the flooding amino acids, but stimulation by the leucine flood was greater than by the valine flood, although rates from the flooding amino acids were similar (valine 0·088%/h, leucine 0·085%/h). Interpretation is difficult because of the lack of information concerning the dynamics of aminoacyl-tRNA labelling during the 90 min flooding period. It is possible that flooding with either leucine or valine stimulates muscle protein synthesis; alternatively, increased incorporation could be due to increased labelling of the aminoacyl-tRNA during the flood because of interactions in membrane carriers shared by the three amino acids.

Smith, K., Barua, J. M., Watt, P. W., Scrimgeour, C. M., Rickhuss, P. K. & Rennie, M. J. (1991). *Clinical Nutrition* **10**, O21, 7.

Correlation of albumin synthesis rates with the Child–Turcotte score (CTS) in patients with cirrhosis of the liver. By P. E. BALLMER[1], D. WALSHE[1], M. A. MCNURLAN[1], P. W. BRUNT[2] and P. J. GARLICK[1], [1]*Rowett Research Institute, Aberdeen AB2 9SB* and [2]*Department of Internal Medicine, University of Bern, Inselspital, CH-3010 Bern, Switzerland*

Albumin synthesis rates (ASR) were measured in patients with cirrhosis of the liver using a newly-developed method with [^{13}C]leucine (Ballmer *et al.* 1990) and compared with values in healthy controls in order to investigate the usefulness of ASR as a potential liver function test.

All subjects were on a standard diet (Ballmer *et al.* 1992; 1 g protein/kg body-weight (BW)) 3 d prior to the study. After an overnight fast they were injected with L-[1-^{13}C]leucine (57 mg/kg BW, 20 atoms %) and blood samples were drawn at intervals up to 90 min. Serum albumin was isolated and leucine separated. The ^{13}C-enrichment of the serum free leucine and of the [^{13}C]leucine in albumin was measured by mass spectrometry. ASR were calculated as fractional synthesis rates (FSR, in %/d), where FSR is the percentage of the intravascular albumin mass (IAM) synthesized per day. FSR multiplied by IAM gives values for the rate of absolute albumin synthesis (ASR, in mg/kg per d).

Serum albumin concentration was slightly decreased in cirrhotics (37 (SEM 3) g/l; n 9) compared with controls (44 (SEM 1) g/l; n 8; $P = 0{\cdot}03$). FSR was identical in the two groups (7·9 (SEM 0·3) %/d controls, 7·9 (SEM 1·1) cirrhotics) and ASR showed a trend towards a decrease in cirrhotic subjects, 119 (SEM 17) mg/kg per d compared with 146 (SEM 8) in controls ($P>0{\cdot}05$). However, there was a significant correlation between ASR and the CTS (r −0·7347, $P = 0{\cdot}024$): the higher the CTS (reflecting a poorer clinical condition) the lower was the ASR.

These results indicate that ASR might be a quantitative reflection of liver function in patients with cirrhosis of the liver.

Ballmer, P. E., McNurlan, M. A., Milne, E., Heys, S. D., Buchan, V., Calder, A. G. & Garlick, P. J. (1990). *American Journal of Physiology* **259**, E797–E803.

Ballmer, P. E., Weber, B. K., Roy-Chaudhoury, P., McNurlan, M. A., Watson, H., Power, D. A. & Garlick, P. J. (1992). *Kidney International* (In the Press).

Insulin reduces leucine oxidation and improves nitrogen balance in the parenterally-fed state. By B. C. N. ANG[1], D. HALLIDAY[2], A. J. WADE[3] and J. POWELL-TUCK[1], *Departments of* [1]*Human Nutrition* and [3]*Sports Medicine, The Royal London Hospital, Whitechapel, London E1 2AD* and [2]*Nutrition Research Group, Clinical Research Centre, Watford Road, Harrow HA1 3UJ*

Five healthy volunteers were fed parenterally over a total period of about 20 h with a balanced feed providing approximately 1·3 times resting energy expenditure and 12·4 g nitrogen as L-amino acids/24 h. The non-protein energy content of the feed was provided as 900–1000 ml 10% Intralipid (49·3 (SD 2·4)% total energy) with the remainder supplied in the form of glucose (34·5 (SD 3)% total energy). During the TPN they were allowed only water by mouth. After a mean (range) run-in period of 11 (6–15) h, whole-body leucine turnover was measured over two periods of 2 h using as tracer a constant infusion of 1 mg [^{13}C]leucine/kg per h. Both leucine and bicarbonate pools were primed (Matthews *et al.* 1980). In randomized order, turnover was measured on and off a euglycaemic clamp employing an infusion of 40 mU actrapid insulin/m^2 body surface area per min, and a variable intravenous infusion of potato starch glucose in order to establish hyperinsulinaemia with stable blood glucose. Collections of breath and plasma ketoisocaproate (KIC) were started 2 h after the onset of the prime. Arterialized plasma sampling was carried out through an indwelling catheter placed retrogradely in a warmed hand. Carbon dioxide expiration rate was calculated using a computerized system of ventilated hood, flow meters and CO_2 analyser. Whether clamped or unclamped studies were performed first, a period of 120–150 min was used to establish new isotope and metabolic steady states for the second component of the study. The mean and standard deviation of the rates of leucine flux calculated from plasma [^{13}C]ketoisocaproate (Q_{KIC}), *oxidation* of leucine (Oxidn), synthesis (S) of leucine into protein and leucine appearance (B) are expressed as μmol/kg per h and are shown in the Table.

		Plasma insulin	Q_{KIC}	Oxidn*	S	B	S–B*
Clamp	Mean	83·8	141	22	119	112	7
	SD	27·5	20	5	18	17	4
No clamp	Mean	18	151	26	125	122	3
	SD	18	16	4	16	14	5

Significantly different by paired *t* test: *$P<0·05$.

Infusion of supraphysiological doses of insulin resulted in decreased oxidation of leucine and increased net leucine retention in the parenterally-fed state.

Matthews, D. E., Motil, K. J., Rohrbaugh, D. K., Burke, J. F., Young, V. R. & Bier, D. M. (1980). *American Journal of Physiology* **238,** E473–E479.

Growth, nitrogen retention and peptiduria in TPN-fed rats receiving short-chain protein hydrolysates. By G. K. GRIMBLE[1], A. K. WENNBERG[2], L. MAGNUSSON[2], P. C. AIMER[1], P. MORRIS[1] and D. B. A. SILK[1], [1]*Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London NW10 7NS* and [2]*Research and Development, Kabi Pharmacia Parenterals, Stockholm S-112 87, Sweden*

High osmolality of peripheral nutrition solutions, which contributes to infusion phlebitis, may be reduced by substituting free amino acids (AA) with well-utilized synthetic dipeptides (Furst, 1991). Short-chain protein hydrolysates (di- and tripeptides >67%) offer similar possibilities (Grimble *et al.* 1987, 1988; Grimble & Silk, 1989) and were examined in this study of TPN-fed rats.

Forty male Sprague-Dawley rats (160–180 g), on TPN (1·25 MJ (300 kcal)/kg, 32% energy as lipid, 0·9 gN/kg) received either an ovalbumin hydrolysate (Group A), an equivalent AA control (Group B), a casein hydrolysate (Group C), an equivalent AA control (Group D), or a commercial AA preparation (Group E) as sole N source for 7 d. At sacrifice, organ weights were measured. Urine collections (24 h) were analysed for urea, NH_3, total N, peptides (by high-performance capillary electrophoresis) and pyroglutamic acid (pyGlu).

	Group A		Group B		Group C		Group D		Group E	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
					Wt gain (g/d)					
Days 2–4	−0·08	0·24	0·25	0·27	−0·29	0·35	0·80	0·34	0·78	0·32
Days 5–7	2·1	0·3	3·8	1·7	4·2	1·1	2·4	0·5	3·8	0·7
					Relative organ wt (g/kg)					
Liver	43·8	2·6	36·7	1·0	50·7[ab]	1·1	34·2	0·5	35·8	0·7
Kidney	9·1[a]	0·2	7·6	0·2	8·9[a]	0·1	7·6	0·1	8·0	0·1
Muscle (EDL)	0·45	0·03	0·47	0·04	0·47	0·04	0·46	0·02	0·47	0·01

[a]$P<0·05$ *v.* equivalent AA control; [b]$P<0·05$ *v.* Group E (Student's paired *t* test).

After starting TPN, growth onset was delayed in groups A and C whilst liver (C) and kidney (A and C), but not EDL, weights were higher. All animals were in positive N-balance from day 2, the casein hydrolysate promoting significantly lower N retention. Peptiduria was higher in hydrolysate-infused animals (A and C) than in AA controls (B and D), there being a marked enrichment in larger, neutral peptides in urine. pyGlu excretion fell in the AA control and casein hydrolysate-infused groups (B 144·7 (15·8) *v.* 22·5 (2·9), C 187·4 (30·7) *v.* 85·1 (12·5), D 236·0 (13·6) *v.* 145·0 (18·4), E 128·1 (18·6) *v.* 33·0 (7·5) μmol/d, mean (SEM) day 1+2 *v.* day 6+7 $P<0·05$) but not in group A (171·6 (6·5) *v.* 159·1 (15·1) NS).

We conclude that the growth of liver and kidney during hydrolysate infusion reflects adaptation of these organs of peptide disposal. Lack of congruence between infused and excreted material confirms that intravenous metabolism of small peptides depends on their sequence. pyGlu excretion may be influenced by the form (free or peptide-bound) and amount of pyGlu infused, as much as by glycine sufficiency (Moran *et al.* 1989). Since >90% of hydrolysate amino acids were peptide-bound, yet were well utilized, short-chain protein hydrolysates show considerably more promise as a low osmolality N source for peripheral TPN.

Furst, P. (1991). *Clinical Nutrition* **10,** Suppl., 19–24.
Grimble, G. K., Raimundo, A. H., Rees, R. G., Hunjan, M. K. & Silk, D. B. A. (1988). *Journal of Parenteral and Enteral Nutrition* **12,** Suppl., 15S.
Grimble, G. K., Rees, R. G., Keohane, P. P., Cartwright, T., Desreumaux, M. & Silk, D. B. A. (1987). *Gastroenterology* **92,** 136–142.
Grimble, G. K. & Silk, D. B. A. (1989). *Nutrition Research Reviews* **2,** 87–108.
Moran, B., Persaud, C. & Jackson, A. A. (1989). *Proceedings of the Nutrition Society* **48,** 75A.

The cytokine response to abdominal sepsis. By D. J. LEINHARDT[1], G. L. CARLSON[1], W. R. LAMB[2], P. E. C. BRENCHLEY[2], R. A. KAY[2], K. A. SHIPLEY[1] and M. MUGHAL[1], [1]*Department of Surgery and North Western Injury Research Centre, University of Manchester, Hope Hospital, Salford M6 8HD* and [2]*Regional Immunology Service, St Mary's Hospital, Manchester*

The grading of sepsis by the scoring system of Elebute & Stoner (1983) allows an objective assessment of a patient's septic state but fails to take into account the recently-described cytokine response to infection which is thought to play an important role in the pathophysiology of sepsis (Hack *et al.* 1989).

We have investigated the relationship between the cytokine response and the sepsis score by measuring serum levels of interleukin-6 (IL-6) and tumour necrosis factor (TNF), and plasma levels of the complement complex Cls-Cl esterase inhibitor (an index of classical pathway complement activation) in fifteen patients with intra-abdominal sepsis.

A total of twenty-seven measurements were made, with multiple (between two and five) measurements in nine of the patients, at sepsis scores ranging from 0 to 29.

	TNF		IL-6		Cls-Cl		Sepsis score	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*
TNF	1·000	0·000	0·774	0·000	0·183	0·360	0·271	0·172
IL-6	0·774	0·000	1·000	0·000	0·236	0·236	0·581	0·001
Cls-Cl	0·183	0·360	0·236	0·236	1·000	0·000	0·432	0·024

Serum levels of IL-6 correlated strongly with sepsis score ($P<0·004$, Spearman rank test).

Although Cls-Cl esterase inhibitor levels also correlated with sepsis scores ($P<0·05$, Spearman), there was no correlation between TNF concentrations and sepsis scores ($P>0·2$, Spearman).

The role of cytokine in the pathogenesis of sepsis is poorly understood and further investigation is required. Further refinements of sepsis scoring and perhaps even treatment may involve the routine measurement of cytokine concentrations.

Elebute, E. A. & Stoner, H. B. (1983). *British Journal of Surgery* **70**, 29–31.

Hack, C. E., DeGroot, E. R., Felt-Bersma, R. J. F., Nuijens, J. H., Strack van Schijndel, R. J. M., Eerenberg-Belmer, A. J. M., Thijs, L. G. & Aarden, L. A. (1989). *Blood* **74**, 1704–1710.

Changes in tissue protein distribution in the rat after sequential injections of turpentine.

By MONICA WUSTEMAN and MARINOS ELIA, *Dunn Nutrition Unit, Milton Road, Cambridge CB4 1XJ*

In this study we have investigated the changes in the distribution of tissue protein that are produced using the turpentine model of clinical injury (Wusteman *et al.* 1990) and have evaluated whether or not serial injections of turpentine have any advantage over the single injection model of injury (Jennings & Elia, 1990; Wusteman *et al.* 1990*a*,*b*).

Three separate subcutaneous injections of turpentine were given at days 0, 2 and 4 (each 2 ml/kg body-weight) to groups of six to eight rats (age 36–40 d). All rats were killed 48 h after the last injection. Saline (9 g sodium chloride/l)-injected and pair-fed control groups were included in the study.

The Table (mean (range) values) shows that repeated injections of turpentine produced a sustained elevation in plasma α2 macroglobulin (α2M), persistent hypoalbuminaemia and a persistent reduction in muscle glutamine (Gln) concentration associated with a reduction in plasma Gln concentration. None of these effects were observed in the pair-fed controls.

	Saline-injected control	1 injection (+2 d)	2 injections (+4 d)	3 injections (+6 d)
Plasma α2M (mg/l)	<50	2968*** (1125–4863)	2992*** (1263–5575)	1996*** (850–3500)
Plasma albumin (g/l)	30·8 (28·0–32·3)	24·1*** (21·4–27·8)	17·43*** (14·7–20·0)	17·26*** (15·5–20·2)
Muscle Gln (mmol/kg wet wt)	6·25 (5·38–7·02)	4·96* (4·02–5·47)	4·05*** (3·16–5·38)	4·93* (2·58–5·26)
Plasma Gln (mmol/l)	0·795 (0·731–0·894)	0·784 (0·687–0·880)	0·670** (0·557–0·726)	0·587** (0·505–0·65)

Significantly different from control: *$P<0·05$, **$P<0·01$, ***$P<0·001$.

Both turpentine injections and pair feeding reduced weight gain to 30% of that in control animals fed *ad lib*. At the end of the study the abscessed rats showed a 19% higher protein content in the liver ($P<0·01$) compared with the pair-fed group, a similar content in the small intestine ($P>0·05$) and a 20% lower protein content in the gastrocnemius muscle ($P<0·01$). There was also loss of protein from the skin which was caused by a reduction of skin thickness (Mean (range) values; control: 0·807 mm (0·650–0·836); abscessed: 0·560 mm (0·530–0·580); pair-fed: 0·841 mm (0·810–0·890)).

The data suggest that the use of repeated doses of turpentine has advantages over the use of a single dose. It produces a more prolonged metabolic response and a low plasma glutamine concentration (commonly seen after human injury) which is not observed after a single injection. The study also demonstrates the complex changes in the distribution of protein between various tissues following injury. The loss of N from the skin could make an important contribution to the overall N balance of the body and have important functional consequences.

Jennings, G. J. & Elia, M. (1990). *Nutrition* (In the Press).
Wusteman, M., Wight, D. G. D. & Elia, M. (1990*a*). *Clinical Nutrition* **9** (special supplement) p. 75.
Wusteman, M., Wight, D. G. D. & Elia, M. (1990*b*). *American Journal of Physiology* **259**, E763–E769.

Absence of hypermetabolism following operation in the newborn infant. By L. K. R. SHANBHOUGE and D. A. LLOYD, *Department of Child Health, University of Liverpool* and *The Royal Liverpool Children's Hospital, Alder Hey, Liverpool L12 2AP*

It is well established that resting energy expenditure (REE) is increased significantly by multiple trauma, and to a lesser extent by surgical trauma. Studies in adults assessing the effect of an elective operation on REE have yielded conflicting results, and for newborn infants there is little information available. In a previous study of newborn infants it was found that, 3 d after surgery, REE was no different from predicted REE levels (Talbot, 1982; Shanbhouge *et al.* 1991). The purpose of the present study was to measure REE in neonates before and at different intervals after an uncomplicated major abdominal or thoracic operation.

REE was measured using a validated open circuit indirect calorimeter. During the study infants remained at rest in their incubator in a thermoneutral environment. They did not receive parenteral or enteral nutrition prior to or during the study.

In thirteen neonates who had an uncomplicated abdominal or thoracic operation, REE was measured preoperatively and on post-operative day 3. A further fourteen neonates had REE measured on the 1st or 2nd post-operative days. There was no significant difference in the mean gestational age or birth weight between the groups of patients.

	Preoperative (*n* 13)		Post-operative					
			24 h (*n* 7)		48 h (*n* 7)		72 h (*n* 13)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
V_{O_2} (ml/kg per min)	6·22	1·15	6·06	0·98	5·92	1·14	5·92	1·14
V_{CO_2} (ml/kg per min)	5·19	1·12	5·72	0·93	5·87	0·75	5·31	1·09
RQ	0·83	0·1	0·94	0·05	0·99	0·12	0·89	0·09
REE kJ (kcal/kg per d)	180·71 (43·19)	33·26 (7·95)	180·41 (43·12)	28·95 (6·92)	177·44 (42·41)	31·71 (7·58)	174·47 (41·70)	33·22 (7·94)

There was no significant difference in oxygen consumption, carbon dioxide production, respiratory quotient or REE between the preoperative and post-operative groups. We conclude that an uncomplicated major operation does not increase REE in the newborn infant.

Shanbhouge, L. K. R., Jackson, M. & Lloyd, D. A. (1991). *Journal of Paediatric Surgery* **26,** 578–580.
Talbot, F. B. (1982). *American Journal of Diseases of Children* **55,** 455–456.

The effect of *n*-3 and *n*-6 polyunsaturated fatty acids on the T-cell function of healthy controls and weight-losing pancreatic cancer patients. By J. S. FALCONER, K. C. H. FEARON and J. A. ROSS, *University Department of Surgery, Royal Infirmary of Edinburgh, Edinburgh EH3 9YW*

Patients with advanced cancer (particularly those with marked weight loss) may become immunosuppressed and this is thought to be associated with disease progression and a propensity to infection. There is increasing evidence that polyunsaturated fatty acids of the *n*-3 and *n*-6 families can modulate the immune response in both rodents and humans. Different investigators have, however, reported both stimulatory (Kelly & Parker, 1979) and suppressive (Calder *et al.* 1991) effects upon the immune system. We have investigated whether the *n*-3 fatty acid eicosapentaenoic acid (EPA) or the *n*-6 fatty acid linoleic acid (LA), either individually or in combination, have any demonstrable effect on the in vitro activation of human T-lymphocytes.

Five healthy volunteers and eight weight-losing patients with pancreatic cancer were studied. Following isolation, lymphocytes were incubated for 72 h in medium containing fatty acid complexed to bovine serum albumin (BSA) (1:1) in the absence or presence of the mitogenic lectin phytohaemagglutinin (PHA). The fatty acid supplementation consisted of either 30 μM-EPA, 30 μM-LA or a mix (1:1) of EPA and LA at a final concentration of 30 μM. BSA alone was used as the control. Lymphocyte activation was assessed in vitro using the reduction of the tetrazolium dye 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT) to a purple formazan product as a measure of metabolic activity (Mosmann, 1983). The ratio of MTT activity between the PHA-stimulated and unstimulated lymphocytes allowed calculation of an activation index (AI).

	Activation index			
	Control group (*n* 5)		Pancreatic cancer group (*n* 8)	
Fatty acid	Mean	SE	Mean	SE
BSA alone	2·434	0·26	1·569	0·12
EPA	2·446	0·26	1·573	0·10
LA	2·804	0·37	1·605	0·14
EPA:LA mix	2·878*	0·28	1·725*	0·16

* Significantly different from BSA control: $P<0·05$ (Student's *t* test).

The pancreatic cancer patients had a significantly reduced activation index compared with the healthy controls ($P<0·01$ Student's *t* test). Fatty acid supplementation with either EPA or LA alone had no significant immunomodulatory effect. However, a combination of EPA and LA led to a significant increase in the AI in both the healthy control group (18% increase, $P<0·05$) and in the pancreatic cancer group (10% increase, $P<0·05$).

These findings suggest that attempts to improve the T-lymphocyte function of patients with advanced cancer may require a mixture of *n*-3 and *n*-6 fatty acids rather than either class alone.

This work was supported by the Cancer Research Campaign and the Melville Trust for the Care and Cure of Cancer.

Calder, P. C., Bond, J. A., Bevan, S. J., Hunt, S. V. & Newsholme, E. A. (1991). *International Journal of Biochemistry* **23**, 579–588.

Kelly, J. P. & Parker, C. W. (1979). *Journal of Immunology* **122**, 1556–1562.

Mosmann, T. (1983). *Journal of Immunological Methods* **65**, 55–63.

Measurement of whole-body protein turnover using [^{15}N]-glycine as tracer fails to demonstrate changes in response to hyperinsulinaemia in post-absorptive man. By B. C. N. ANG[1], A. J. WADE[2], D. HALLIDAY[3] and J. POWELL-TUCK[1], *Departments of [1]Human Nutrition* and *[2]Sports Medicine, The Royal London Hospital, Whitechapel, London E1 2AD* and *[3]Nutrition Research Group, Clinical Research Centre, Watford Road, Harrow HA1 3UJ*

Our previous studies, using [^{15}N]-glycine as tracer, showed no effect on whole-body protein turnover (WBPT) and urea production rate during insulin infusion in patients undergoing total parenteral nutrition, in contrast with published studies using [^{13}C]-leucine and euglycaemic clamping in post-absorptive man. To test the methodology we have, therefore, used [^{15}N]-glycine to assess turnover in post-absorptive subjects, on and off a euglycaemic, hyperinsulinaemic clamp. WBPT was measured in nine healthy, overnight-fasted, supine volunteers, mean (range) age 33 (25–39) years, on two separate days, in randomized order, using a single intravenous dose of 200 mg [^{15}N]-glycine tracer with calculations based on both urinary ammonia and urea end products. Corrections were made for accumulation of ^{15}N in the unexcreted urea pool by blood sampling before and after the 9 h studies. Isotope ratio mass spectrometry was employed for all ^{15}N analyses. On one occasion (clamp) the subject received intravenously 40 mU insulin/m^2 surface area per min while plasma glucose was maintained at baseline levels with a variable intravenous infusion of glucose. On the other occasion the subject was studied unclamped. Because there was no nutrient intake (water only) during the study, breakdown of protein to amino acids is equal to flux (Q). Protein synthesis rates (S) were calculated by subtracting the total urinary N, corrected for retention of N in the unexcreted urea pool (N excr), from the flux. Results are expressed in mgN/kg body-weight per 9 h, and we include results employing both the arithmetic (ar) and harmonic (hm) means (Fern *et al.* 1985) as well as the data using only urea or ammonia as end products. Mean plasma insulin concentrations (Ins) are expressed as μunits/ml.

		Ins	Q_{NH_3}	Q_{urea}	Q_{hm}	Q_{ar}	S_{NH_3}	S_{urea}	S_{hm}	S_{ar}	Nexcr
Clamped	Mean	78*	220	185	167	203	198*	163	145	181	22*
	SD	11	56	163	83	80	57	153	75	70	13
Unclamped	Mean	9	170	271	191	210	124	225	145	165	45
	SD	4	55	89	61	62	62	82	63	59	12

* Significantly different from unclamped values: $P<0{\cdot}05$.

The study had 95% power to detect a 25% difference in protein turnover (alpha = 0·05), assuming a within-person coefficient of variation (pessimistically (Fern *et al.* 1984) of 15%. We observed reductions in N excretion (and urea production) on the clamp, but were unable to demonstrate the underlying changes in WBPT using this tracer.

Fern, E. B., Garlick, P. J., Sheppard, H. G. & Fern, M. (1984). *Human Nutrition: Clinical Nutrition* **38C**, 63–73.

Fern, E. B., Garlick, P. J. & Waterlow, J. S. (1985). *Human Nutrition: Clinical Nutrition* **39C**, 63–73.

Bed rest decreases whole-body protein turnover in the post-absorptive state. By B. C. N. ANG[1], D. HALLIDAY[2], S. GEORGIANNOS[3] and J. POWELL-TUCK[1], *Departments of [1]Human Nutrition* and *[3]Surgery, The Royal London Hospital, Whitechapel, London E1 2AD* and *[2]Nutrition Research Group, Clinical Research Centre, Watford Road, Harrow HA1 3UJ*

Whole-body protein turnover was measured in five healthy, overnight-fasted, male volunteers, mean (range) age 32 (25–39) years, on two occasions separated by more than one month, using a single intravenous dose of 200 mg [^{15}N]-glycine tracer with calculations based on both urinary ammonia and urea end products (Fern *et al.* 1985). Corrections were made for accumulation of ^{15}N in the unexcreted urea pool by blood sampling before and after the 9 h studies. Isotope ratio mass spectrometry was employed for all ^{15}N analyses. On one occasion (resting) the subject lay supine on a couch for the duration of the study; on the other (ambulatory) he was allowed to carry out his usual day-to-day activities which did not include sport. Because there was no nutrient intake (water only) for the duration of the study, breakdown of protein to amino acids is equal to flux (Q). Protein synthesis rates (S) were calculated by subtracting the total urinary N, corrected for retention of N in the unexcreted urea pool (N excr), from the flux. Results are expressed in mgN/kg body-weight per 9 h, and we include calculated results employing both the arithmetic (ar) and harmonic (hm) means as well as the data using only urea or ammonia as end products.

		Q_{NH_3}	Q_{urea}	Q_{hm}	Q_{ar}	S_{NH_3}	S_{urea}	S_{hm}	S_{ar}	Nexcr
Resting	Mean	162*	264	185*	213	114*	215	136*	164	49
	SD	72	111	66	65	82	98	69	60	17
Ambulatory	Mean	232	354	254	293	183	304	205	244	50
	SD	115	94	49	37	112	92	47	31	11

* Significantly different from ambulatory values: $P<0{\cdot}05$.

We conclude that, within the limitations of this methodology, flux, breakdown and synthesis are reduced by rest, so that there is no change in N excretion or balance.

Fern, E. B., Garlick, P. J. & Waterlow, J. S. (1985). *Human Nutrition: Clinical Nutrition* **39C**, 63–73.

Augmentation of plasma arginine and glutamine by ornithine α-ketoglutarate in healthy, enterally-fed volunteers. By G. K. GRIMBLE[1], C. COUDRAY-LUCAS[2], J. J. PAYNE-JAMES[1], L. CYNOBER[2], F. ZIEGLER[2] and D. B. A. SILK[1], [1]*Department of Gastroenterology and Nutrition, Central Middlesex Hospital, London NW10 7NS* and [2]*Laboratoire de Biochimie, University of Paris XI, 92292 Chatenay-Malabry, France*

Ornithine α-ketoglutarate (OKG) moderates the catabolic response by reducing losses of both urinary nitrogen (Wernerman *et al.* 1987), and functioning polyribosomes and intracellular free glutamine from skeletal muscle (Wernerman *et al.* 1987, 1990) which characteristically occur after surgery. Whilst in these studies OKG was administered with total parenteral nutrition, little is known about its effects in enterally-fed patients. Oral administration studies in fasted subjects have suggested several modes of action (Cynober, 1991), including stimulation of human growth hormone (hGH) and insulin secretion and effects on intermediary metabolites, in meal-fed subjects (Cynober *et al.* 1984). In order to differentiate the action of OKG from that of continuous feeding, the present study examined changes in plasma amino acid kinetics following ingestion of OKG during nasogastric feeding.

In four separate experiments, 1 litre of enteral diet (Fortison, Nutricia) was administered nasogastrically for 12 h to six healthy, fasted volunteers (three male, three female, 19–25 years, 54–70 kg). In Expt 1, diet alone was infused, whilst in Expts 2, 3 and 4, respectively, OKG was administered with the diet (10 g), or as a 10 g or 20 g bolus, 30 min after the start of the diet infusion. Blood samples were taken at 30 min intervals to 3 h and hourly thereafter for plasma amino acid measurement. ANOVA and method of contrasts were used for statistical analysis and, unless otherwise stated, all values are given as the least squares mean for the entire diet infusion period.

Diet infusion alone significantly increased concentrations of Val, Ile, Leu, Met, Phe, Tyr, Ser and Cit ($P<0{\cdot}02$). OKG promoted additional increases in amino acid levels compared with Expt 1: Val, Leu, Ile, Met, Phe and Lys (Expt 2, $P<0{\cdot}02$); Leu, Ile, Tyr, Gly, His and Tau (Expt 3, $P<0{\cdot}01$).

	Plasma concentration of OKG-related metabolites (μmol/l)				
	Orn	Arg	Cit	Glu+Gln	Pro
Expt 1	65·2	89·4	35·0	619·3	257·0
Expt 2	154·9[a]	94·2	30·8[a]	659·7[a]	310·4[a]
Expt 3	167·2[a]	105·6[a]	32·3[a]	653·2[a]	305·0[a]
Expt 4	192·4[a]	86·2	27·9[a]	619·5	305·7[a]

[a] $P<0{\cdot}01$ compared with Expt 1.

These changes are similar to those observed following oral administration of OKG to fasted subjects (Cynober *et al.* 1984). In particular OKG profoundly affects levels of its own metabolites as well as those of apparently unrelated amino acids. This is dependent on dose and mode of delivery, in particular a bolus markedly increased levels of amino acids (Arg, Orn, Glu+Gln) with proposed anticatabolic properties.

Cynober, L. (1991). *Nutrition* (In the Press).

Cynober, L., Vaubourdolle, M., Dore, A. & Giboudeau, G. (1984). *American Journal of Clinical Nutrition* **39,** 514–519.

Wernerman, J., Hammarqvist, F. & Vinnars, E. (1990). *Lancet* **335,** 701–703.

Wernerman, J., Hammarqvist, F., von der Decken, A. & Vinnars, E. (1987). *Annals of Surgery* **206,** 120–124.

In vivo and in vitro assimilation of orally-administered dextran 40KDa in man. By G. K. GRIMBLE, S. C. COLLINS and D. B. A. SILK, *Department of Gastroenterology and Nutrition, Central Middlesex Hospital, Acton Lane, London NW10 7NS*

Short-chain fatty acids, derived from colonic fermentation of fibre, exert trophic effects on the ileo–colonic epithelia. This has prompted a search for soluble, non-viscous and well-fermented fibres for inclusion in enteral diets. The predominantly α-1,6 linked dextrans, resistant to hydrolysis by a mixture of glucosidases which converted maltodextrin to glucose within 5 min (G. K. Grimble, unpublished results), seemed to us and others (Edwards *et al.* 1991) to satisfy these criteria, especially since human jejunal perfusion studies have shown that α-1,6 glucosyl bonds were relatively resistant (compared with α-1,4 bonds) to brush-border hydrolysis (Jones *et al.* 1983). The present study investigated small bowel assimilation and in vitro colonic fermentation of dextran 40KDa. On two occasions, six fasted subjects (three male, three female, 20–36 years) consumed 20 g of lactitol (Grimble *et al.* 1988) or dextran 40KDa in 200 ml of water at 08.50 hours followed by 250 ml of diet (Ensure; Abbott Laboratories Ltd., Kent ME11 5EL) at 09.00, 12.00 and 15.00 hours. Baseline and hourly breath H_2 measurements were made. All subjects scored their gastrointestinal symptoms (Patil *et al.* 1987).

	Breath H_2 (mean (SE) ppm)										Symptom score	
Time . . .	Baseline		2 h		4 h		6 h		8 h			
Lactitol	25·3	(10·9)	48·0	(17·1)	98·5[a]	(26·1)	74·2[a]	(16·1)	54·5[a]	(18·7)	1·63[b]	(0·21)
Dextran	16·7	(7·5)	12·5	(3·5)	13·8	(9·2)	10·2	(5·9)	4·7	(4·3)	0·50	(0·19)

[a] $P<0·02$, paired Student's t test; [b] $P<0·05$ Wilcoxon matched pairs test).

Compared with lactitol, dextran 40KDa did not increase H_2 production and evoked a lower symptom score. Glycaemia after ingestion of 80 g glucose or dextran 40KDa was measured in one fasted subject. The area under the plasma glucose curve (mmol/l per min, 0–180 min) was: glucose 112·5, dextran 40KDa 81, both peaks occurring at 30 min. In vitro fermentation of 20 g glucose, maltodextrin (Caloreen) and two dextrans (40KDa, 5–40MDa) by stool samples from one subject (Patil *et al.* 1987) was performed. Initial fermentation rates (0–2 h, Meq H^+/h) were 8·6, 7·1, 2·2 and 2·9 respectively, the final value at 24 h (Meq H^+) being 152·4, 188·0, 152·3 and 140·6. Production (% total organic acid) of acetate, propionate and butyrate was: maltodextrin, 48·3, 0·6, 0·01; dextran 40KDa, 32·2, 7·1, 14·3; dextran 5–40MDa, 39·5, 10·2, 15·0, respectively.

High molecular weight did not limit rapid in vitro fermentation of dextran but little, if any, dextran 40KDa escaped small intestinal assimilation in vivo. The total capacity of brush-border glucosidases to hydrolyse significant amounts (20 g) of this α-1,6 linked polymer, in the presence of α-1,4 linked polymers (34·3 g/250 ml Ensure), is therefore large. In man, but not the rat (Edwards *et al.* 1991), dextran 40KDa does not behave as a non-absorbed polysaccharide. Higher molecular weight forms (>500 KDa) may, however, fulfil this role (Alsop & Milner, 1990).

Alsop, R. M. & Milner, J. (1990). European Patent EP 0 153 013 Bl.
Edwards, C. A., Bruce, M. & Ferguson, A. (1991). *Proceedings of the Nutrition Society* (In the Press).
Grimble, G. K., Patil, D. H. & Silk, D. B. A. (1988). *Gut* **29,** 1666–1671.
Jones, B. J. M., Brown, B. E., Loran, J. S., Edgerton, D., Kennedy, J. F., Stead, J. A. & Silk, D. B. A. (1983). *Gut* **24,** 1152–1160.
Patil, D. H., Grimble, G. K. & Silk, D. B. A. (1987). *British Journal of Nutrition* **57,** 195–199.

Ileal starch output in two groups of differing colonic cancer risk. By D. M. BRADBURN[1], J. C. MATHERS[2], A. GUNN[3], J. BURN[4] and I. D. A. JOHNSTON[1], *Departments of* [1]*Surgery,* [2]*Biological and Nutritional Sciences* and [4]*Human Genetics, The University, Newcastle upon Tyne NE1 7RU* and [3]*Ashington Hospital, Northumberland NE63 0SA*

Unabsorbed dietary starch provides a significant amount of fermentable substrate to the colon but the factors influencing starch absorption are poorly understood. Some consider unabsorbed starch to be protective against colonic cancer (CC) development (Bingham, 1990) whilst others have reported 'super efficient' starch absorption in recurrent polyp formers (Thornton *et al.* 1987).

To test the hypothesis that 'super efficient' starch absorption predisposes to CC risk, two groups of patients of differing CC risk were investigated. Seven ileostomists with a diagnosis of ulcerative colitis (UC, low CC risk) and six with familial adenomatous polyposis (FAP, high CC risk) were admitted to a metabolic unit after an overnight fast. A baseline polysaccharide-free diet was fed for 25 h (09.00–10.00 hours), and supplemented with a known starch load (mean 107 g, range 72–123 g) provided as conventional foods for 6 h (12.00–18.00 hours). Ileostomy effluent was collected 2-hourly and frozen immediately.

	Ileostomy output			Starch		
Group	Wet wt (g)	Dry wt (g)	Water (%)	Eaten (g)	Recovered (g)	Recovered (% intake)
UC	298	40	87	88	2·92	3·31
UC	429	61	86	113	4·88	4·34
UC	1320	103	92	113	10·03	8·92
UC	600	49	92	65	4·99	7·72
UC	440	46	90	60	2·10	3·50
UC	338	40	88	117	2·90	2·49
UC	348	44	87	117	3·50	3·13
FAP	686	64	91	108	6·85	6·33
FAP	608	64	90	115	4·59	3·98
FAP	299	28	91	84	1·58	1·89
FAP	309	36	89	112	2·43	2·17
FAP	396	48	88	108	4·21	3·91
FAP	415	59	86	105	3·78	3·61

In all cases <0·2 g starch was collected in the 2 h periods at the start and finish of the study. Ileal recovery ranged from 1·57–10·05 g (1·8–8·33% of intake) with no significant differences between patient groups. Both the absolute amount of starch and the proportion of intake recovered in ileal effluent were positively and significantly correlated ($P<0·001$) with ileal output of digesta wet and dry weights, but were independent of starch intake. The increased starch recovery was markedly less than the associated increase in ileostomy weight suggesting that other non-absorbed dietary components influence starch digestion.

DMB is funded by the Northern Regional Health Authority Locally Organised Research Fund.

Bingham, S. A. (1990). *Proceedings of the Nutrition Society* **49,** 153–171.
Thornton, J. R., Dryden, A., Kelleher, J. & Losowsky, M. S. (1987). *Digestive Diseases and Sciences* **32,** 1088–1091.

Changes in feeding behaviour in cachectic tumour-bearing rats during the period of tumour growth. By O. A. OBEID and P. W. EMERY, *Department of Nutrition and Dietetics, King's College, London W8 7AH*

Decreased food intake is a primary factor in the development of cancer cachexia, but there is conflicting evidence about the relative importance of decreased meal size (premature satiety) and decreased meal frequency (reduced perception of hunger) in the causation of this anorexia. This may be partly due to differences in the timing of the observations in relation to the progression of the disease. We have, therefore, made longitudinal measurements of meal size and meal frequency in tumour-bearing (TB) rats throughout the period of tumour growth.

Male Fischer 344 rats were housed individually in Skinner boxes and trained for 4 d to obtain food pellets by pressing a lever connected to a recording device. A suspension of Leydig cell tumour cells was then injected subcutaneously into the flanks of eight rats, and six controls were injected with cell culture medium only. Feeding behaviour was then monitored for 21 d, by which time the tumours had reached 8% of body-weight, total food intake had fallen by 50% and body-weight showed a deficit of 15%.

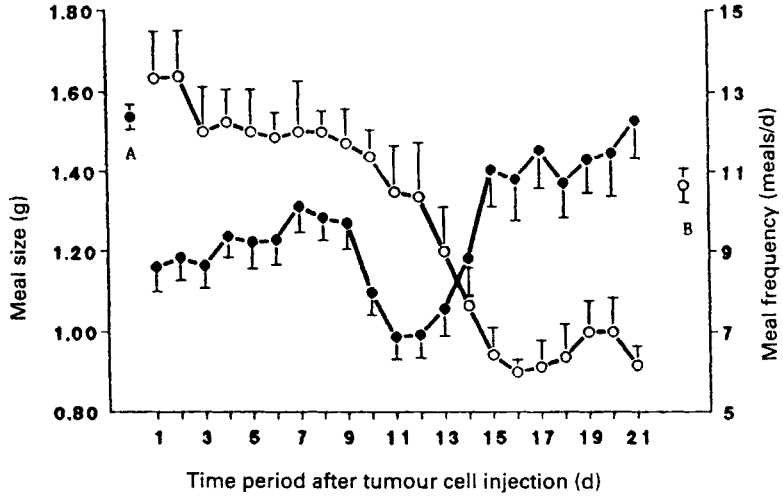


Fig. Meal size (●) and meal frequency (○) of TB rats, and meal size (A) and meal frequency (B) of control rats (mean values with standard errors).

Values for control rats did not differ significantly from day to day, and are shown as single points. In contrast, the feeding pattern of TB rats was clearly divided into three phases. For the first 9 d total food intake of TB rats was not significantly different from that of controls because meal frequency increased to compensate for a small decrease in meal size. Over the next 5 d food intake decreased sharply as a result of a further decrease in meal size and a decrease in meal frequency. The tumours became palpable during this period (on day 11). For the final 7 d food intake remained low because of markedly reduced meal frequency, although meal size increased to a level not significantly different from that of the controls. We have previously found that the period of hepatic glycogenesis following a meal is significantly extended in TB rats at this stage of tumour growth (Obeid & Emery, 1991), and this may delay the initiation of the next meal, causing the observed decrease in meal frequency.

Obeid, O. A. & Emery, P. W. (1991). *Proceedings of the Nutrition Society* **50**, 141A.

The effect of chronic dietary restriction on post-prandial glycogen and lipid synthesis in the rat. By T. T. A. CARPENTER, O. A. OBEID and P. W. EMERY, *Department of Nutrition and Dietetics, King's College, London W8 7AH*

We have recently observed that the rate of hepatic glycogen synthesis following a standard meal was almost twice as great in tumour-bearing (TB) rats as in *ad lib.*-fed controls (Obeid & Emery, 1991). However, food intake in the TB rats is known to be 40% lower than normal. We have, therefore, measured the rate of post-prandial glycogen synthesis in normal Sprague-Dawley rats whose food intake had been reduced by 40% for 9 d, using identical methods to those we used previously. Control rats were fed *ad lib.* There were six rats in each group.

Time after meal . . .	0		1		2		3	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Hepatic glycogenesis†:								
Restricted	0·54	0·11	1·58**	0·47	1·14	0·19	0·61*	0·14
Control	0·68	0·19	50·70	8·10	25·00	11·00	2·06	0·52
Hepatic glycogen content (mg/g):								
Restricted	30·52**	3·30	44·40*	6·90	40·39*	2·80	38·90	5·50
Control	6·82	1·00	22·94	0·81	29·32	2·00	32·42	3·80
Hepatic lipogenesis‡:								
Restricted	11·94	1·80	31·23**	3·60	21·30	1·50	13·82*	1·30
Control	14·02	2·40	12·66	1·20	17·22	2·87	9·75	0·88
Adipose tissue lipogenesis‡:								
Restricted	7·26	0·68	9·53**	0·88	9·18	1·10	11·66	1·20
Control	6·10	0·27	5·22	0·50	6·77	0·60	7·82	0·42

Significantly different from control group (by *t* test): $*P<0·05$, $**P<0·01$.
† μmol of ^3H_2O incorporated into glycogen/g tissue per h.
‡ μmol of ^3H_2O incorporated into saponifiable lipid/g tissue per h.

The rate of ^3H incorporation into glycogen was reduced almost to zero throughout the 3 h post-prandial period in the restricted rats. Part of this difference might be due to a reduction in the number of ^3H atoms incorporated per glucose unit, suggesting a switch to the more energetically efficient direct pathway of glycogen synthesis from glucose. However, this could not account for more than a fivefold reduction in incorporation, so there must also have been a reduction in the absolute rate of glycogen synthesis. The glycogen content of the livers of the restricted rats was much higher than that of the controls, both in the fasting state and throughout the post-prandial period, suggesting that food restriction suppressed the normal cycle of glycogen deposition and mobilization. On the other hand, there was a greater increase in lipogenesis in both liver and adipose tissue in the restricted rats, particularly 1 h after the meal, suggesting that the substrates which were not being used for glycogen synthesis were being used for fat synthesis instead. The changes caused by chronic food restriction were, thus, completely opposite to those observed in TB rats, emphasizing that the presence of a tumour interferes with the normal adaptive responses to a reduction in food intake.

Obeid, O. A. & Emery, P. W. (1991). *Proceedings of the Nutrition Society* **50**, 141A.

Can energy expenditure be measured in critical illness using [^{13}C]-labelled bicarbonate?

By J. C. DEVLIN, LYNN NEWMAN, S. T. BROOKES, THERESE A. SAMUELS, CERI J. GREEN and I. T. CAMPBELL, *Intensive Therapy Unit, Royal Liverpool Hospital, Liverpool L7 8XP* and *Europa Scientific, Crewe CW1 1ZA*

The standard method of measuring energy expenditure (EE) is by indirect calorimetry. This is cumbersome and there are problems with high inspired oxygen concentrations. There are other simpler possibilities. With a pulmonary artery catheter in place, O_2 consumption can be calculated from cardiac output measurements and the O_2 content of arterial and mixed venous blood (the reverse Fick principle; Scheeweiss *et al.* 1989). Also the use of a [^{13}C]sodium bicarbonate infusion to measure carbon dioxide production (V_{CO_2}) involves only an intravenous infusion and collection of expired air at the bedside (Elia *et al.* 1988). Problems in accuracy could arise, however, due to metabolic disturbances.

CO_2 production has been measured in nine critically-ill ventilated patients on ten occasions using a [^{13}C]-labelled infusion of $NaHCO_3$ and V_{O_2} measured on a separate group of nine critically-ill patients using the reverse Fick technique on two to eight (median four) occasions. EE was calculated assuming a respiratory quotient of 0·8. The results have been compared with EE measured at the same time using the Engstrom Metabolic Computer (EMC) (Regan *et al.* 1990). [^{13}C]$NaHCO_3$ was infused intravenously at 5 μmol/min for 8 h. Expired air was collected from the exhaust port of the ventilator (Engstrom Erica) prior to infusion and hourly throughout. Expired CO_2 concentrations were analysed during a continuous-flow isotope ratio mass spectrometer (Europa Scientific Tracermass). In all cases $^{13}CO_2$ concentrations had reached a plateau by 6 h. Median recovery of $^{13}CO_2$ at 6–8 h was 62·2 (range 51·7–69·3%, mean 61·6%). The mean recovery was used to calculate V_{CO_2}. O_2 consumption estimated from the bicarbonate infusion differed from the EMC value by −2·6 (SD 7·7)% and estimates of EE by −2·6 (SD 6·8)% of the EMC figure. O_2 consumption measured using the reverse Fick method differed from the EMC value by 2·4 (SD 15·9) and EE estimates by 1·97 (SD 15·7)% of the EMC figure. The SD of the % difference for the Fick estimate of EE was significantly greater than the bicarbonate estimate ($P<0·01$). It is concluded that the use of labelled bicarbonate produces a more precise indication of EE than using the reverse Fick technique, but more work is required to determine CO_2 retention in a wider range of critically-ill patients before it could be used with confidence clinically.

Elia, M., Fuller, N. & Murgatroyd, P. (1988). *Proceedings of the Nutrition Society* **47**, 247–258.

Scheeweiss, B., Druml, W., Graninger, W., Grimm, G., Kleinberger, G., Lenz, K. & Laggner, A. (1989). *Clinical Nutrition* **8**, 89–93.

Anthropometric indices of lean body mass using ultrasound. By TRACEY WATT[1], D. WITHERS[2], D. MARTIN[2] and I. T. CAMPBELL[1], [1]*Intensive Care Unit, University Department of Anaesthesia* and [2]*Department of Radiology, Withington Hospital, Manchester M20 8LR*

The methods used to assess lean body mass (fat-free mass) are normally limited to simple anthropometric measurements: fat-free mass from body-weight and skinfold thickness, mid-arm circumference, and arm muscle area and arm muscle circumference. In critical illness these measurements are confounded by fluid retention as well as practical problems of weighing bed-bound patients. A method is needed to assess lean body mass non-invasively in patients with fluid retention. If fluid is retained in subcutaneous and visceral tissue and not in the body of muscle, ultrasound measurements of skeletal muscle thickness could be related to lean body mass in these patients, but any such relationship would first have to be established in normal subjects.

Fat-free mass was measured in thirty-one healthy volunteers (thirteen male, eighteen female; aged 19–86 (median 30) years) with Harpenden skinfold calipers using the methods of Durnin & Womersley (1974). Muscle thickness was measured, in the non-dominant limb at the mid-arm level over biceps, lateral head of triceps, mid-forearm anteriorly, mid-thigh anteriorly, mid-calf posteriorly and rectus abdominis muscle at the level of the umbilicus, using an ALOKA SSD 500 portable ultrasound machine with a 3·5 MHz linear array probe. Mid–upper arm circumference (MAC) was measured and arm muscle area (AMA) and arm muscle circumference (AMC) calculated (Gurney & Jelliffe, 1973). Correlation coefficients with fat-free mass were calculated for total muscle thickness measured at all six sites, (total muscle thickness)^2 × height, AMA, AMC and MAC. Correlation coefficient values were: total muscle thickness 0·959, (total muscle thickness)^2 × height 0·958, AMA 0·850, AMC 0·841 and MAC 0·789.

In normal volunteers ultrasound muscle thickness measurements are as good an indicator of lean body mass as the more established anthropometric ones of MAC, AMC and AMA. Whether they are of value in critical illness awaits further evaluation.

Durnin, J. V. G. A. & Womersley, J. (1974). *British Journal of Nutrition* **32,** 77–97.
Gurney, J. M. & Jelliffe, D. B. (1973). *American Journal of Clinical Nutrition* **26,** 912–915.

Daily body-weight changes in critical illness. By IRENE HALL, B. J. POLLARD and I. T. CAMPBELL, *Intensive Therapy Unit, Manchester Royal Infirmary, Manchester M13 9WL* and *Department of Anaesthesia, University of Manchester, Withington Hospital, Manchester M20 8LR*

Fluid retention occurs in acute illness, and in multiple organ failure peripheral and pulmonary oedema are both problems. Apart from a few anecdotal reports (e.g. Streat *et al.* 1987), there are no data on the patterns of fluid retention and weight change in these patients.

Daily weight records have been studied from an intensive care unit (ICU) where patients are weighed daily as part of fluid balance management. Records of 121 patients (sixty-eight male, fifty-three female) aged 12–93 (median 56) years were analysed. Most patients at some stage were ventilator-dependent. Forty-six died and seventy-five transferred to the ordinary ward. They were on the ICU for 3–55 (median 9) d. Mean weight for the period of admission was calculated from daily weights and ranged from 28·0 to 147·7 (median 66·9) kg.

If weight on discharge or death was in the lowest quartile of the total weight range the patient was classified as 'weight-losing', and if in the upper quartile as 'weight-gaining', and as 'weight-stable' if the discharge weight was in the middle half. Of the patients who died, five were weight-stable, eighteen weight-losing and twenty-three weight-gaining. Of those transferred six were weight-stable, eight weight-gaining and fifty-six weight-losing. This difference was significant, ($P<0·005$). Weight change in the patients ultimately transferred ranged from −16·7 to 2·6 (median −3·8) kg, with an interquartile range (IQR) of −6·4 to −1·5 kg, (− or + denoting direction of weight change at discharge or death). In patients who died the figures were −18·0 to 16·4 (median 3·7), IQR −6·0 to 6·5 kg. Expressed as a percentage of the patient's mean body-weight the figures are: transferred, −21·7 to 24·7 (median −5·0)%, IQR −10·35 to −1·73%; died, −19·5 to 27·2 (median 5·1)%, IQR −8·9 to 10·6%. The difference between those who survived and those who died was significant ($P=0·003$).

Median daily weight change for all patient days for those transferred was 0·1 (range −10·9 to 7·4, IQR −1·1 to 0·7) kg and for those who died 0 (−10·9 to 9·6, IQR −0·9 to 1·0) kg. The corresponding figures as a percentage of mean body-weight are 0·2 (range −13·4 to 18·2, IQR −1·6 to 1·0)% for those transferred and 0 (range −16·1 to 18·4, IQR −1·3 to 1·5)% for those who died.

In critical illness body-weight varies by up to 20–25%. Daily weight changes can be up to 15–20% but are usually in the 0–2 kg range. Not surprisingly, recovery is associated with loss of body-weight but no consistent pattern of weight change occurred in those patients who died. The range of weight changes may, of course, be different in a unit where patients are not weighed daily.

Streat, S. J., Beddoe, A. H. & Hill, G. L. (1987). *Journal of Trauma* **27**, 262–266.

The use of a four-component model for evaluation of the density and the hydration fraction of fat-free mass, and for validation of bedside prediction methods of body composition. By N. J. FULLER[1], S. A. JEBB[1], M. A. LASKEY[2], W. A. COWARD[1] and M. ELIA[1], [1]*MRC Dunn Clinical Nutrition Centre, 100 Tennis Court Road, Cambridge CB2 1QL* and [2]*Department of Nuclear Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ*

A four-component model of body composition (water, protein, mineral, and fat) was formulated from body-weight (BW) and body volume (BV; densitometry), total body water (TBW; deuterium dilution space) and bone mineral ash (A; dual-energy X-ray absorptiometry: fat (kg) = 2·747BV − 0·710TBW + 1·460A − 2·050BW. The model was applied to twelve female and sixteen male healthy adults, with body mass index (BMI) in the range 17–25 kg/m^2 and 20–28 kg/m^2, and fat as % BW in the range 20–38% and 12–25%, respectively. The bedside prediction methods (BMI equation, skinfold thickness (SFT), whole body resistance (WBR) by the Valhalla method (all described by Fuller & Elia, 1989), and near infra-red interactance (NIRI) by Futrex (Elia *et al.* 1990)) were compared to results obtained using this model. Density and hydration fraction of the fat-free mass (FFM) were calculated from the four-component model, to establish whether current values in classical densitometry (density FFM, 1·1 kg/l) and water dilution techniques (hydration fraction, 0·7194 or 0·732, for example) are appropriate. Evaluation was made of errors (SD) associated with the individual techniques, and of the propagation of these to estimation of body fat using the four-component model (assuming measurement precisions; density 0·0025 kg/l, TBW 0·45 kg, A 0·003 kg).

The agreement between the four-component model and bedside prediction methods is shown in the Table. The mean hydration fraction and density of FFM were found to be 0·7382 (SD 0·0213, range 0·6941–0·7837) and 1·1015 (SD 0·0073, range 1·0795–1·1110) kg/l, respectively, with no significant difference between males and females for either. The measurement error (SD) for body fat (four-component model) was 0·54 kg, compared to 0·78 kg for densitometry and 0·62 kg for TBW and for density and hydration fraction of FFM was 0·0020 kg/l and 0·0066.

Bias and 95% (2 SD) limits of agreement between the four-component model and bedside prediction methods of body composition (four-component model minus bedside method)

	Fat (% body-wt)			Fat-free mass (kg)		
Method	Female	Male	All subjects	Female	Male	All subjects
BMI	1·8 (7·7)	−0·1 (8·5)	0·7 (8·2)	−1·1 (4·6)	−0·1 (7·4)	−0·5 (6·3)
SFT	−0·2 (6·4)	0·3 (4·7)	0·1 (5·4)	0·1 (3·5)	−0·5 (4·2)	−0·2 (3·9)
WBR	3·0 (6·4)	3·7 (8·1)	3·4 (7·3)	−1·8 (4·1)	2·9 (7·1)	−2·4 (6·0)
NIRI	−2·0 (6·0)	2·2 (7·0)	0·4 (7·8)	1·0 (3·5)	−2·0 (6·0)	−0·7 (5·8)

The results suggest that the theoretically-improved four-component model is not compromised by propogation of errors. Although there may be substantial inter-individual variation in the density and hydration fraction of FFM, mean values currently applied in classical densitometry and water dilution techniques, are close to being appropriate for groups of healthy subjects such as those studied here. Finally, body composition obtained by the four-component model was better predicted by the use of SFT than by the other simple bedside techniques.

Elia, M., Parkinson, S. A. & Diaz, E. (1990). *European Journal of Clinical Nutrition* **44,** 113–121.
Fuller, N. J. & Elia, M. (1989). *European Journal of Clinical Nutrition* **43,** 779–791.

Low incremental workload cycle ergometry during in-patient nutritional treatment of patients with anorexia nervosa. By R. DAS GUPTA[1], J. POWELL-TUCK[2], A. J. WADE[3], J. TREASURE[4] and A. W. GOODE[1], *Departments of* [1]*Surgery,* [2]*Human Nutrition* and [3]*Sports Medicine, The London Hospital Medical College, London E1* and [4]*The Institute of Psychiatry, The Maudsley Hospital, London SE5 8AF*

Eleven patients fulfilling the criteria of the American Psychiatric Society for the diagnosis of anorexia nervosa were studied at the beginning and end of in-patient nutritional treatment during which they received hospital food providing about 40–50 g protein and 6·28 MJ (1500 kcal)/d in the first week, and double these subsequently, over a mean (range) period of 48 (27–87) d. Changes in body composition over the admission were assessed by body-weight and whole body potassium counting which was carried out at the Hammersmith Hospital using a ten-sensor ^{40}K detector. Body-weight increased from mean (range) 38·5 (32·6–44·5) to 49·3 (43·8–55·8) kg. Total body K (mmol) increased from mean (range) 1949 (1563–2349) to 2292 (2037–2882). At the beginning and end of treatment respiratory gas analysis was performed during cycle ergometry in which workload was increased in a standard protocol from 0–60 w in 20 w increments. Data for exercise ergometry are available for ten of the patients. Soon after admission two of the patients could not complete the low workload protocol, dropping out subjectively exhausted after 40 w, but all could complete the protocol by the end of treatment. Mean (SD) values for respiratory exchange ratio (RER) pedalling at 0 w were 0·92 (0·17) before and 0·78 (0·08) after treatment, at 20 w they were 1·01 (0·18) before and 0·85 (0·15) after treatment, and at 40 w were 1·11 (0·16) and 0·92 (0·12) before and after treatment respectively. These reductions in mean RER at workloads of 0, 20 and 40 w were all significant ($P<0·05$; paired t test). RER at low workloads is a *useful* objective index of weakness, is increased by undernutrition and can be reduced with treatment.

https://doi.org/10.1079/PNS19920040 Published online by Cambridge University Press

Biochemical indices of malnutrition in middle-aged onset patients with Parkinson's disease. By R. A. ABBOTT[1], H. MARKUS[2], M. COX[1] and A. TOMKINS[1], [1]*Nutrition Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1* and [2]*Department of Neurology, Middlesex Hospital, London W1*

Parkinson's disease (PD) is a common cause of chronic neurologic disability, resulting from degeneration of the basal ganglia in the brain. It has been postulated that impairment of antioxidant mechanisms may contribute to the emergence and progression of the disease (Parkinson Study Group, 1989). Also patients with PD have been noted to be thin and some are subject to considerable weight loss (Levi *et al.* 1990; Abbott *et al.* 1991), but little attention has been paid to serum protein and micronutrient status. In order to assess (i) protein and micronutrient status and (ii) nutrients associated with antioxidant function, blood samples were taken from forty-one patients with PD and forty-one age-matched, sex-matched controls.

	Controls (*n* 41)		PD patients (*n* 41)	
	Mean	95% CI	Mean	95% CI
Iron (μmol/l)	18·3	16·6–20·1	15·3*	13·6–17·0
TIBC (μmol/l)	55·1	52·6–57·6	56·4	53·9–58·9
Ferritin (μg/l)	94·2	74·1–114·3	86·2	65·9–106·4
Albumin (g/l)	45·7	44·8–46·7	44·2*	43·2–45·2
Vitamin A (μmol/l)	2·94	2·79–3·10	2·61**	2·46–2·77
Vitamin E (μmol/l)	32·0	29·7–34·2	22·00***	19·7–24·2
Vitamin E/chol (μmol/μmol)	4·61	4·33–4·90	3·29***	3·00–3·58
Zinc (μmol/l)	18·7	17·9–19·5	14·2**	13·4–14·9
Copper (μmol/l)	18·2	17·1–19·2	16·9	15·8–18·0

Significantly different from controls: *$P<0·05$, **$P<0·01$, ***$P<0·001$.
TIBC, total iron binding capacity; chol, cholesterol.

Patients with PD had significantly lower levels of serum iron, albumin and vitamin A than the control group, but no significant changes were seen in levels of ferritin or TIBC. This suggests that nutritional status is lower in PD compared with healthy controls. Highly significant decreases were found in the levels of vitamin E and zinc in the patients with PD when compared to control levels. Copper levels were lower, but this difference was not significant.

The lower levels of antioxidant-related micronutrients may contribute to the progression of PD, however, the levels in PD are not vastly different from other population studies. The biological significance of the differences in micronutrient between PD and controls is unknown but could be established if supplementation trials were developed.

We acknowledge the support of the Parkinson's Disease Society and the assistance of Drs Lees and Stern at the Neurology Department of the Middlesex Hospital.

Abbott, R. A., Markus, H., Cox, M., Hodkinson, M. & Tomkins, A. (1991). *Proceedings of the Nutrition Society* (In the Press).

Levi, S., Cox, M., Lugon, M., Hodkinson, M. & Tomkins, A. (1990). *British Medical Journal* **301,** 1026–1031.

Parkinson Study Group (1989). *Archives of Neurology* **46,** 1052–1060.

Admission characteristics of elderly orthopaedic surgical patients categorized into high and low nutritional risk groups by objective tests of nutritional status. By C. M. WILLIAMS[1], M. LUMBERS[2], L. DRIVER[1] and R. J. HOWLAND[1], [1]*The Nutritional Metabolism Research Group, University of Surrey, Guildford GU2 5XH* and [2]*NESCOT, Ewell, Surrey*

The aim of the present study was to determine whether in elderly orthopaedic surgical patients (total hip replacement and fractured neck of femur) there are specific social and medical factors which might contribute to poor nutritional status on admission to hospital, knowledge of which could be used in developing an admission nutrition-screening procedure for the elderly. Patients were categorized into high and low nutritional risk groups according to whether they had three or more of the following objective measurements below the fifth percentile on admission to hospital: body-weight, tricep skinfold thickness, mid-upper arm muscle circumference, serum albumin and haemoglobin (Morgan *et al.* 1986).

A detailed history of social and medical factors was taken on admission and measurements of mental function, hand grip strength and retinol-binding protein were made at the same time. Data have been analysed for all patients (high risk (HRA) and low risk (LRA)) and for patients admitted for emergency surgery only (high risk (HRE) and low risk (LRE)).

	HRA (*n* 14)	LRA (*n* 46)	HRE (*n* 13)	LRE (*n* 19)
Admission data	Median (25th; 75th percentile)	Median (25th; 75th percentile)	Median (25th; 75th percentile)	Median (25th; 75th percentile)
Age (years)	84·5 (79·2; 90·2)	77·0** (70·0; 82·0)	86·0 (81·5; 90·5)	80·0††(75·0; 85·0)
Mental function score	21·0 (19·0; 23·0)	23·0** (22·0; 23·0)	20·0 (19·0; 22·8)	23·0 (20·0; 23·0)
Handgrip strength (mm Hg)	2·0 (0·9; 3·6)	4·5* (2·0; 6·0)	1·5 (0·75; 3·75)	3·0 (0·5; 5·0)
Retinol binding protein (mg/l)	46·0 (34·8; 57·0)	47·0 (35·5; 57·0)	46·0 (34·7; 57.0)	39·0 (31·0; 44·0)
Patients living alone (%)	57	37	61	26
Patients recently bereaved (%)	29	6·5[a]	30	10·8
Needing assistance with food preparation (%)	57	32	61	21†
History frequent falls (%)	85	3·3***	85	5·3†††
Depression/apathy (%)	50	26	54	16[b]

*$P<0·05$, **$P<0·01$, ***$P<0·001$ compared with HRA; †$P<0·05$; ††$P<0·01$; †††$P<0·001$ compared with HRE.

[a]$P<0·06$ compared with HRA; [b]$P<0·07$ compared with HRE.

High-risk patients (HRA and HRE) were significantly older than their low-risk counterparts ($P<0·01$) and both groups had a markedly higher history of frequent falls prior to the present admission ($P<0·001$). A greater percentage of patients in the HRE group reported needing assistance with food preparation ($P<0·05$) compared with LRE.

It is concluded that a screening questionnaire which derives information on patients' social and medical history may provide a useful admission procedure which could become part of the routine nutritional assessment of the elderly on admission to hospital.

Morgan, D. B., Newton, H. M. V., Jewitt, M. A., Hancock, M. R., Hullin, R. P. & Schorah, C. (1986). *Age and Ageing* **15**, 65–76.

Long-term follow-up of elderly orthopaedic surgical patients nutritionally assessed on admission to hospital. By M. LUMBERS[1], L. DRIVER[2], R. J. HOWLAND[2] and C. M. WILLIAMS[2], [1]*NESCOT, Ewell, Surrey* and [2]*The Nutritional Metabolism Research Group, University of Surrey, Guildford GU2 5XH*

Most studies which have analysed nutritional status on admission in relation to subsequent outcome have concentrated on the assessment of short-term outcome only. The present study has measured nutritional status on admission, of sixty elderly orthopaedic patients admitted for elective (total hip replacement) and emergency (fractured neck of femur) hip surgery. Nutritional and clinical indices of outcome were monitored during hospitalization and at 4, 8 and 24 weeks after discharge. Patients were categorized into the high nutritional risk groups if they had three or more values below the fifth percentile for body-weight, tricep skinfold thickness, mid-upper arm circumference, serum albumin and haemoglobin. Values for the fifth percentile were those derived from the healthy elderly population of Morgan *et al.* (1986), except for haemoglobin where the fifth percentile for the healthy adult population was used.

Comparison of some of the clinical outcome measurements determined at 24 weeks are presented for high- and low-risk groups obtained by this categorization. Data have been analysed for all patients (high risk (HRA) and low risk (LRA)), and for patients admitted for emergency surgery only (high risk (HRE) and low risk (LRE)).

	HRA (*n* 14)	LRA (*n* 46)	HRE (*n* 13)	LRE (*n* 19)
Clinical outcome at 24 weeks	Median (25th; 75th percentile)	Median (25th; 75th percentile)	Median (25th; 75th percentile)	Median (25th; 75th percentile)
Stay in acute hospital (days)	15 (12; 26)	15 (12; 26·3)	16 (12·5; 26)	16 (12; 27)
Stay in convalescence (days)	27·5 (5·3; 40)	0·0** (0·0; 10·3)	28 (10·5; 43)	0·0† (0·0; 22)
△ in ADL score (4–24 weeks)	−0·75 (−1·4; 0·0)	−1·5* (−2·0; −1·0)	−0·75 (−1·4; 0·0)	−1·0 (−1·6; −0·4)
Mortality (%)	28	9	23	16
Patients still on frames (%)	45	10·5*	50	33
Patients returned home (%)	29	72*	23	47

*$P<0·02$, **$P<0·0009$ compared with HRA; †$P<0·0009$ compared with HRE; ADL, Activities of daily living.

Duration of stay in the acute hospital was not significantly different between any of the groups, but duration of stay in the convalescent hospital was significantly longer in the HRE and HRA groups than in their corresponding low-risk groups ($P<0·01$).

Some of the other differences in clinical outcome found between HRA and LRA groups only probably reflect differences in proportions of elective and emergency admissions in these groups (HRA 1/14; LRA 27/46). However, differences in convalescence time between HRE and LRE groups are likely to reflect the different nutritional status of these patients on admission to the acute hospital. It is concluded that a simple nutritional risk assessment procedure which uses parameters easily measurable in most hospital wards is able to identify patients in whom there is a poorer clinical outcome. It is also concluded that assessment of clinical outcome in the immediate recovery period only is insufficient to demonstrate differences between high and low nutritional risk groups.

Morgan, D. B., Newton, H. M. V., Jewitt, M. A., Hancock, M. R., Hullin, R. P. & Schorah, C. (1986). *Age and Ageing* **15**, 65–76.

Nutritional influences on recovery and length of hospital stay in elderly women following femoral fracture. By KATRINA M. BROWN and NICHOLA A. SEABROOK, *Department of Nutrition and Dietetics, The Ipswich Hospital, Heath Road, Ipswich IP4 5PD*

Elderly people are often nutritionally compromised and specific nutritional needs are not routinely assessed in hospitals despite the importance of good nutrition in ensuring a favourable clinical outcome. The present study was designed to assess the influence of nutritional state (defined by nutrient intake and anthropometric variables) on rehabilitation and length of hospital stay in elderly women with fractured neck of femur (*n* 23).

Patients were classified as being either of normal weight (*n* 13; mean (SD) BMI 22 (2)) or thin (*n* 10; mean (SD) BMI 17 (1)) using expected weight for height, triceps skinfold thickness (TSF) and mid-arm circumference (MAC) measured by a single observer. Thin women were randomly assigned to receive a nutritional supplement or not (*n* 5 in each group). The controls received the normal hospital diet alone. Patients ate according to their own choice with intake recorded at each meal and between meals. Within 24 h of admission samples of venous blood were taken for routine analysis, including measurement of serum albumin, prealbumin, magnesium and zinc. Analyses were repeated weekly.

Blood chemistry was similar in all subjects and within normal reference ranges apart from serum albumin, prealbumin, and zinc. These were low in most patients, but had risen to within the low reference range by the time of discharge. Energy intake was greater (30%) in thin patients receiving Fresubin supplements, as was protein intake, but in all three groups both fell short of estimated requirements. Intakes below the recommended daily allowance for a number of vitamins and minerals were common, particularly vitamin C, iron, folic acid, and calcium. Vitamin C intakes of less than 40 mg/d were associated with formation of pressure lesions ($P<0{\cdot}02$). Every patient's diet was deficient in vitamin D.

Mean body-weight and upper-arm anthropometry decreased in all groups, the greatest losses occurring among normals and thin controls. Thin patients receiving the supplement and patients of normal weight with an adequate diet, recovered more quickly, and their stay in hospital was shorter, than thin patients who did not receive the supplement and patients of normal weight who received an inadequate diet ($P<0{\cdot}01$; mean (SD) stay in hospital 21 (6) and 47 (26)d) respectively. Undernutrition and duration of stay were associated with greater weight loss and reduction in MAC. A highly significant exponential relationship was found between percentage weight loss, MAC loss and duration of hospital stay ($P<0{\cdot}001$).

We suggest that weight loss and reduction in MAC may be useful objective measurements for identifying patients whose recovery may be delayed if they do not have nutritional support.

A comparison of the efficacy of polyurethane and silastic fine bore catheters for the peripheral venous delivery of intravenous nutrition. By N. J. EVERITT, M. MADAN, D. J. ALEXANDER and M. J. MCMAHON, *The General Infirmary at Leeds, Leeds LS1 3EX*

Silicone rubber and hydrophilic polyurethane fine bore catheters were compared for the delivery of intravenous nutrition via a peripheral vein in a randomized prospective study of fifty patients. Full intravenous nutrition (2·5 litres, 13 g nitrogen, 7·52 MJ (1800 kcal)) was administered daily for a median duration of 9 d. Heparin (1500 u) and hydrocortisone (15 mg) were added to each feed. A glyceryl trinitrate patch (5 mg) was used over the infusion site and changed daily. Twenty-five patients received thirty-two silastic catheters and twenty-five patients required twenty-seven polyurethane catheters.

Type of catheter . . .	Silastic	Polyurethane
Number of patients	25	25
Duration of feeding (d): Mean	9	9
Range	2–21	4–43
Episodes of:		
Thrombophlebitis (total)	4	4
Thrombophlebitis (/patient per d)	0·018	0·015
Occlusion without inflammation	2	9

The incidence of thrombophlebitis was similar in each group (four episodes in each), however, silastic catheters were more prone to occlude without the development of inflammation (nine episodes compared with two). There was no significant difference in the median lifespan of catheters which failed (silastic 118 h (*n* 16) *v.* polyurethane 166 h (*n* 7)). Eleven (44%) of the twenty-five patients receiving silastic catheters completed intravenous feeding without a line complication compared to twenty (80%) of the twenty-five patients in the polyurethane group (P=0·016; two-tailed Fisher Exact).

The value of fine bore catheters for the delivery of full intravenous nutrition via a peripheral vein is confirmed. We believe that this technique offers a safe and practical alternative to the routine use of central venous catheters for the delivery of parenteral feeding. Significantly more patients completed their period of feeding without catheter complications when the polyurethane catheter was used.

A randomized comparison between peripheral ultra-fine bore silicone catheters and central silicone catheters for the delivery of high osmolality intravenous nutrition.

By M. MADAN, D. J. ALEXANDER and M. J. MCMAHON, *University Department of Surgery, General Infirmary, Leeds LS1 3EX*

Fine bore silicone and polyurethane catheters have been shown in previous studies to be associated with a low incidence of thrombophlebitis in the provision of peripheral intravenous nutrition (IVN). To investigate which patients should be selected for peripheral intravenous nutrition we undertook a randomized comparison between fine bore silicone peripheral catheters and central silicone catheters for the administration of IVN with an osmolality of 1250 mosmol/kg. The feed provided 13 g nitrogen, 200 g glucose (3·34 MJ, 800 kcal) and lipid emulsion (4·18 MJ, 1000 kcal) daily.

Twenty-six patients were randomized to receive IVN through a peripheral fine bore silicone catheter (22G) and twenty-nine to receive IVN through a central silicone catheter (16G). The median duration of feeding was similar in both groups, 10·5 and 13·5 d. The incidence of thrombophlebitis was 0·023 episodes per patient/d and 58% (15/26) patients required only one catheter for the desired duration of peripheral IVN. Positive bacterial cultures were found in 9% of peripheral catheters, two patients had a pyrexia which settled on the removal of the catheter.

In the central IVN group the complications were: pneumothorax, 1; catheter malposition, 1; five patients developed a pyrexia requiring removal of the line but only one positive catheter tip culture was found (3%). A total of 73% of patients required only one catheter for the duration of feeding. The median catheter life span of central catheters was significantly longer than that of peripheral catheters, 308 *v.* 179 h ($P<0·001$).

These results suggest that a low incidence of thrombophlebitis can be achieved by the use of fine bore silicone catheters to provide high osmolality IVN for about 10 d. Catheter-related sepsis is not avoided by the use of the peripheral route. However, the insertion of a peripheral catheter is a quick, safe and repeatable technique which in addition avoids exposure to radiation.

A comparison of performance of five fine-bore naso-gastric feeding tubes. By G. FROST, U. HASAN, P. GOSH*, K. MASTERS, C. KING, M. KELLY, J. STANFORD, R. JONES, A. LOFTHOUSE and C. MACQUEEN, *Department of Nutrition and Dietetics, Hammersmith Hospital* and **Department of Gastroenterology, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS*

Enteral nutrition supplied via a fine-bore naso-gastric tube has become an accepted form of nutritional support. The use of polyurethane has increased the length of time that the tube can remain *in situ*. There is a wide range of polyurethane tubes on the market at a wide range of prices, but there is very little clinical data to back up their performance.

Forty patients requiring naso-gastric feeding were intubated on fifty occasions with one of five different feeding tubes: Flocare 110 cm, unweighted; Corsafe 110 cm, bullet tip, weighted; Corsafe 110 cm, bullet tip, unweighted; Swallow 110 cm, weighted; Swallow 110 cm, unweighted. All but six tubes were introduced by the same experienced physician (PG).

Data recorded at intubation included: time of intubation, number of attempts at passing the tube (clinically important for patient comfort), aspiration (reducing the need for chest X-ray) and length of time tube remained *in situ*.

Summary of results (median values with range in parentheses)

	n	Time of intubation (sec)	No. of attempts	Aspiration possible (%)	Days of intubation
Flocare unweighted	10	60 (60–120)	1 (1–2)	80	8 (1–27)
Corsafe unweighted	10	90 (60–300)	1 (1)	50	2 (1–10)
Corsafe weighted	10	120 (60–900)	1 (1–6)	60	4 (1–12)
Swallow unweighted	10	60 (60–300)	1 (1–7)	50	6 (1–33)
Swallow weighted	10	90 (60–430)	1 (1–3)	60	6 (1–14)

Analysis of co-variants showed no significant differences between any of the tubes for any variable. Failure analysis on days of intubation showed no significant difference between any tube. Approximately 60% of all tubes, regardless of make, were removed inadvertently and only 22% of these tubes were repassed.

From the criteria used in the present study, no one tube appeared to have any advantage over the others regardless of make or whether the tube was weighted or unweighted. These observations are similar to those reported by Silk *et al.* (1986). Tube failure may be improved by education of staff.

Our thanks to Cow & Gate, Merck and Viomedex for their support, and Miss Marion Power for her secretarial support.

Silk, D. B. A., Rees, R. G., Keohane, P. P. & Attrill, H. (1986). *Journal of Parenteral and Enteral Nutrition* **11**, 378–383.

Formulation of a glutamine-containing total parenteral nutrition mixture for clinical use.

By G. HARDY[1], D. WIGGINS[1], B. MCELROY[2] and G. R. THOMPSON[2], [1]*Oxford Nutrition, Metabolic Research Laboratory, Oxford OX4 3UH* and [2]*Royal Shrewsbury Hospital, Shrewsbury SY3 8XF*

Glutamine (Gln) may be a conditionally essential amino acid in trauma and stress. However, Gln supplementation of TPN has mostly involved use of a di-peptide because Gln itself is reportedly too unstable (Stehle *et al.* 1989). Gln is certainly unstable to heat sterilization but we have demonstrated that at 4° Gln degradation in various TPN mixtures can be less than 0·1%/d (Khan *et al.* 1991).

We have now established that a sterile 25 g Gln/l solution prepared aseptically in the hospital pharmacy can be stored for up to 30 d at 4° with loss of Gln less than 0·05%/d. There is no conversion to glutamic acid (Glu); conversion to pyroglutamate (Py-Glu) is 0·02%/d and ammonia formation is less than 0·4 mmol/l (Hardy *et al.* 1991). Compounding this stock Gln solution with Elamin (15% amino acids), Elolipid (20% fat emulsion), Elotrace B (Leopold Pharma), Glucose 50% and MVC 9+3 (Lyphomed) in 3 litre Ultrastab bags (Miramed), we have formulated a complete TPN regimen containing: 93 g amino acids (18 g as Gln) providing 15 g N, 8·36 MJ (2000 kcal), (50:50, glucose:fat), Na 80, K 80, Ca 5, Mg 7, P 30 mmol, trace elements and vitamins in 2500 ml.

Stability of this admixture and a Gln-free control has been evaluated following storage at 4° for 30 d. Samples were analysed at intervals for pH and by standard enzymic methods for Gln, Glu and NH_3. Particle size distribution (PSD) was determined using a Coulter Counter TAII.

Gln content decreased by 2·8% (<0·1%/d) while Glu was essentially unchanged and NH_3 increased from 0·106 to 2·53 mmol/l in the Gln mixture compared to 0·18 mmol/l in the control. The total NH_3 that could be infused from a single bag is less than 6 mmol (100 mg)/d which is well within the levels handled by mammalian tissues. pH was virtually unchanged (6·28 to 6·30) compared to the control (6·41 to 6·38). PSD (% < 2 μm) changed slightly more than the control but remained greater than 90%. The homogeneous mixture showed no evidence of emulsion breakdown.

We therefore conclude that this TPN admixture exhibits little loss of Gln during refrigerated storage over 30 d and that the preparation is pharmaceutically acceptable for clinical investigation. Preliminary results using this regimen in polytrauma patients suggest that improvements in N balance may be achieved with no observable adverse effects.

Hardy, G., Wiggins, D., Aimer, P., Grimble, G. & McElroy, B. (1991). *Clinical Nutrition*, Special Supplement **2**, 36.

Khan, K., Hardy, G., McElroy, B. & Elia, M. (1991). *Clinical Nutrition* **10**, 193–198.

Stehle, P., Mertes, N., Puchstein, Ch., Zander, J., Albers, S., Lawin, P. & Furst, P. (1989). *Lancet* **i**, 231–233.