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PREVALENCE OF CRANIAL SCAN ABNORMALITIES IN PRETERM TWINS IN RELATION TO CHORIONICITY AND DISCORDANT BIRTHWEIGHT

Session: Pediatric Aspects of Twinning

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Objective. The purpose of this study was to determine the incidence of ultrasonographically detected cerebral white matter lesions in preterm twins at birth, in relation to chorionicity, discordant weight and twin-twin transfusion syndrome (TTTS).

Methods. In this retrospective study, perinatal, neonatal, and cranial scan data of 78 monochorionic (MC) and 80 dichorionic (DC) pregnancies delivered between 24–34 weeks of gestation (341 infants) were collected. Data were analyzed according to discordant birthweight (> 20%), single intrauterine death and TTTS.

Results. The cerebral white matter lesion (WML) was seen in 14% of preterm twins and was higher in MC than in DC infants (25 vs. 4%; $p < .01$). Monochorionic twins with discordant birthweight (37%), TTTS (38%), single intrauterine death (67%), have higher incidence of cerebral WML than concordant birthweight infants (7%). Similarly, in DC twins WML incidence was higher in discordant than concordant birthweight infants (13% vs. 2%; $p < 0.05$). Univariate analysis suggests that WML was significantly associated with monochorionicity, discordant birthweight, TTTS and co-twin demise.

Conclusion. Cerebral white matter lesion was six-fold higher in the preterm MC than in DC infants. Discordant birthweight, TTTS and survivor of co-twin demise appear to be the most important risk factors for cerebral white matter lesion.

EDUCATION OF MULTIPLES

Session: Language Development

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Most twins do not have specific educational problems, but there is an increased risk of being delayed or having a functional impairment. This paper is based on longitudinal Swedish twin data and illuminates the importance of both variation in individual development and environmental influences. In most western societies today school has become more individualistic and pupils are expected to seek their own information in books or by computer. This will present problems for children that have reading and writing difficulties or have a growth deficit which means that they need concrete and structured direction at school. A restrictive and stimulating educational environment at the start of their schooling will be necessary for these children in order to develop to their full potential. They have a right to feel safe and self-confident at school, and gradually a more permissive approach can be introduced with project-based learning.

NEUROMATURATION OF PRETERM MULTIPLES

Session: Poster

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Objective. To compare preterm multiples with appropriate for gestational age (AGA) singleton controls with respect to degree and rate of neuromaturation using a clinical measure of neuromaturation that we developed.

Design/Methods. We have a total sample of 500 high risk preterm infants born 1995–2000 with birthweights < 500 gms or GA < 33 weeks who were serially examined in the Johns Hopkins NICU. The 106 multiples were matched for GA and postmenstrual age (PMA, GA + chronologic age) when first examined to AGA singleton controls. For each exam, we calculated a Maturity Score (MS) by summing exam items that emerge with age and its component Tone Subscore (TS) and Reflex Subscore (RS). For each infant, we plotted these scores against PMA at the time of the exam and drew a line of best fit. Groups were compared as to actual scores at the initial exam and 2 descriptors of the line of best fit (Individual Score Slope and a y–intercept, the Predicted Maturity Score at 34 weeks PMA). Significance was defined as $p < .1$.

Results. Mean GA was 28 weeks. Mean PMA at first exam was 30 weeks. Paired sample t test showed no differences in initial MS, Individual Maturity Slope, Predicted MS at 34 weeks PMA, all Tone (TS) variables and Predicted Reflex Subscore at 34 weeks PMA. Multiples had a lower mean Initial Reflex Subscore (23.9 vs. 25.5, $p = .05$) but higher mean Individual Reflex Slope (3.3 vs. 4.0, $p = .04$). In several linear regression models with Reflex Slope as the outcome, multiple gestation was significant ($p = .04$–$.08$). When intrauterine growth restriction (IUGR) was added to the model, IUGR was significant ($p = .08$) but the multiple variable was not ($p = .15$).

Conclusion. Shortly after every preterm birth, multiples are less mature than singletons in development of deep tendon and primitive reflexes. Their tone is not different. Preterm multiples mature more rapidly and catch up to singletons by 34 weeks PMA. Amiel-Tison et al. reported advanced maturation in preterm IUGR infants and in multiples born at 32–37 weeks gestation (Brain Dev (1991), 13–67, paper presented at European Congress of Perinatal Medicine, 1994). Obstetricians should not assume advanced neuromaturation in multiples delivered before 32–34 weeks gestation.

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HERITABILITY IN ADOLESCENT IDIOPATHIC SCOLIOSIS: A COHORT STUDY OF TWINS

Session: Pediatric Aspects of Twinning

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The genetics of adolescent idiopathic scoliosis (AIS) are obscure. Although most cases are sporadic, about 25% of the patients are reported to have a positive family history. The purpose of this study was to examine the contribution of genetic factors to the pathogenesis of AIS.

Materials and methods. The present cohort from the Danish Twin Register consists of Danish twin pairs born between 1931 and 1982. Establishment of zygosity throughout the period has been based on four questions of similarity with an accuracy of approximately 95%. All registered twins received a questionnaire in the spring of 2002. The total number of twins was 46,418. 34,944 (75.3%) answered the question "Have you been diagnosed with scoliosis?" The pair-wise concordance estimates the probability that both twins are affected in a pair in which at least one is affected, while the proband-wise rate estimates the probability that a twin will be affected given that the twin partner is. Concordance was compared using the Chi-square test.

All scientific-ethical committees in Denmark have approved the study.

Results. The sex distribution was 19,037 (54.5%) females and 15,907 (45.5%) males. The overall self reported prevalence of scoliosis was 1.36% (95% confidence limits (c.i.l.) 1.26–1.47). Stratified according to gender we found a male and a female prevalence of 0.96 (95% c.i.l.

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0.80–1.14) and 1.71% (95% c.i.l. 1.53–1.91) respectively, and this difference was statistically significant ($p < .001$). The prevalence of AIS was not significantly different between monozygotic (MZ) and dizygotic (DZ) twins and the figures were as would be expected from the literature.

Of 11,740 twin pairs who both answered the above question, 463 indicated that they had been diagnosed with scoliosis. The pair-wise concordance was 0.13 (95% c.i.l. 0.05–0.27) for MZ and zero (95% c.i.l. 0–0.03) for DZ twin pairs, while the proband-wise concordance was 0.25 (95% c.i.l. 0.17–0.37) for MZ and zero (95% c.i.l. 0–0.03) in DZ twin pairs. This difference was statistically significant ($p < .05$).

Conclusion. The higher incidence of AIS in MZ individuals than in DZ individuals may provide a clue to the etiology of AIS. The higher concordance rate of MZ pairs confirms the contribution of a major genetic component while indicating the need to identify possible environmental triggers. The risk of developing scoliosis in a twin whose twin partner has scoliosis is less than hitherto believed.

GENETIC AND ENVIRONMENTAL INFLUENCE ON MATHEMATICAL ACHIEVEMENT AND COGNITIVE ABILITIES IN JAPAN

Session: Language Development

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The genetic and environmental relationship between verbal/spatial cognitive abilities and mathematical performance was investigated in 79 pairs of Japanese twins (55 pairs of monozygotic (MZ) twins and 24 pairs of dizygotic (DZ) twins whose age range was from 12 to 15 years old). Verbal and spatial cognitive abilities were measured by the Kyodai Nx Intelligence Test and mathematical performance was assessed by a test battery that contained calculation, equation solving, and word problems. Univariate genetic analysis revealed that only additive genetic factor explains the twin similarity of verbal cognitive ability, and common environmental factor explains that of spatial cognitive ability. Mathematical performance is explained by both additive genetic and shared environmental factors. Multivariate genetic analysis showed that phenotypic correlation between cognitive abilities and mathematical performance is mediated only by shared environment.

HIGH BONE TURNOVER IN GROWTH RESTRICTED MONOCHORIONIC TWINS WITH DISCORDANT BIRTHWEIGHT

Session: Poster

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Objectives. Little is known about fetal bone metabolism in twins. Alteration in bone turnover in fetal life may result in diminished bone mass at birth with future osteoporotic risk in adult life. The aim of this study was to investigate fetal bone turnover in monochorionic pregnancies complicated with discordant growth.

Methods. Matched maternal and fetal cord blood samples were collected in 32 monochorionic twins with ($n = 16$) discordant birthweight of > 20% and 16 with concordant birthweight of < 20% ($n = 16$). The samples were assayed for cross linked carboxyl terminal telo-peptide of type I collagen (ICTP), a marker of bone resorption, and the carboxyl terminal propeptide of type I pro-collagen (PICP), a marker of bone formation, by radio-immunoassay.

Results. In discordant MC pregnancies, fetal ICTP levels were higher in the growth restricted (IUGR) twin than the larger (AGA) co-twin ($p < .001$) but PICP levels were similar in twin pairs. The ratio of PICP/ICTP in the growth restricted twins was lower than those of AGA co-twins ($p < 0.01$). In contrast, fetal ICTP and PICP levels, as well as ratios of PICP/ICTP, were similar in twins with concordant weight. The fetal PICP ($r = .69$; $p < .05$) and ICTP ($r = 0.66$; $p < .05$) concentration decreased with gestation. The maternal concentrations of ICTP and PICP were comparable in the two groups and were lower than those of the fetal levels.

Conclusions. These data indicate that growth restricted MC twins exposed to the same maternal environment have an abnormal bone metabolism with a high turnover bone disease which raises the possibility of bone loss in growth restricted infants in later life.

FROM INFERTILITY TO MULTIPLE PARENTHOOD: A DREAM COME TRUE?

Session: Poster

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The great majority of young adults assume that their life course will include bearing and raising children. Presuming fertility, they use contraceptive methods to prevent pregnancy until conditions in their lives are conductive to the achievement of this central goal. When pregnancy is attempted, however, some couples find that their goal of becoming a parent is beyond their control. Try as they might, an avenue they have expected to provide fulfillment in life remains out of reach.

There is no doubt that infertility is deeply distressing and individuals are responding with a range of responses. Reaction to infertility is expressed in emotional effects, loss of control, effects on self-esteem, identity, beliefs, and social effects.

Assisted Reproduction Technologies (ART) seem to be the ultimate salvation of the current infertile generation, as they provide a technical solution that bypasses the infertility problem, and helps them fulfill their goal of creating new life. However, ART are a mixed blessing. They are highly stressful and have the potential to lead to significant negative consequences, particularly when they fail. Moreover, multiple pregnancies are a prevalent outcome of ART — pregnancies that have been associated with relatively high rates of fetal loss, prematurity, low birthweight and perinatal complications. In light of the above, we may wonder "Are ART multiples a fulfillment of a parental dream?"

Prematurity is involved with a wide spectrum of malformations and medical complications. Parenting premature multiples causes the parents enormous stress, and demands great coping resources, which are probably depleted due to a prolonged process of infertility, fertility treatments, and a high risk pregnancy. Couples who are not able to achieve the goal of a healthy, full-term pregnancy "successfully" experience more stress and may question the blessings of ART.

PSYCHOSOCIAL RESOURCE DEPLETION IN PARENTS OF TWINS AFTER ASSISTED REPRODUCTION VERSUS SPONTANEOUS CONCEPTION

Session: Psychosocial Issues in Families with Multiple Births

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Objective. To examine the effect of mode of conception (spontaneous versus induced) on parenting stress, psychological well being and marital quality during the transition to parenthood among parents of twins.

Methods. The Parenting Stress Index was assessed in 37 parents of twins conceived by assisted reproduction and compared to that of 38 controls who conceived spontaneously.

Results. First time parents after assisted reproduction experienced a significantly higher level of parenting stress than parents who conceived spontaneously (89.3 vs. 72.8, $p < .01$). Primiparas following assisted reproduction score lower on psychological well being than controls ($p < .05$). The two study groups did not differ in their perception of marital quality. In addition, Assisted Reproduction Technologies (ART) primiparous mothers experience higher levels of parenting stress and lower level of psychological well being in comparison to primiparous mothers who conceived spontaneously.

Conclusions. The transition to parenthood following assisted reproduction is demanding for both parents of twins. In particular, first time mothers may require qualified emotional support to facilitate adjustment to twin parenthood.

STRESSORS EXPERIENCED BY PARENTS RAISING MULTIPLE BIRTH CHILDREN

Session: COMBO II

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From the shock, uncertainty, and anxiety that often accompany the diagnosis of multiple pregnancies, to the isolation, physical and mental exhaustion that can follow delivery, parents raising multiple birth children experience unique stressors. Although the psychological, social, and economic aspects of multiple pregnancies are of critical importance to parents, children and communities, these areas have not received the same amount of attention as medical aspects. The purpose of this study

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was to expand on the existing body of psychosocial knowledge by identifying the major causes of distress for parents of multiple birth children.

The study subjects were obtained with the assistance of five multiple birth support organizations in the northern New England region of the USA. Data were collected using the Life Distress Inventory (LDI) created by E. J. Thomas, M. R. Yoshioka, and R. D. Ager. This 18-item self-rating tool measures the current level of subjective distress experienced across various areas of life and function: social functioning, life satisfaction, finance and employment, and marital distress (Thomas, et al., 1992).

In addition, open-ended statements and questions were asked to help identify educational needs ("Parents expecting multiple birth children should know…"), areas of distress unique to multiple birth families ("What are the biggest challenges in raising your multiples?"), and positive aspects of parenting multiple birth children ("What are the best things about having multiples?")

Results from this study will benefit health care providers and multiple birth organizations supporting families expecting or raising twins, triplets, quadruplets, or more.

BEHAVIOR GENETIC AND MOLECULAR ANALYSES OF READING AND SPELLING

Session: Language Development

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The behavior genetic and molecular bases of the Dual-Route Cascaded (DRC) model of reading and spelling were examined in a large unselected adolescent twin sample. Data were in accord with the DRC model of reading as a quantitative normal trait, with no categorical genetic or environmental events grading some readers as dyslexic. DRC further predicts that there should be no genetic or environmental effects for regular word reading, over and above irregular and non-word performance. This prediction is tested using multivariate behavior genetic analyses. Over 70% of variance in measures of both lexical and sub lexical reading and spelling was genetic, with little evidence for shared environmental effects. Possible evidence for sex linkage is discussed. Multivariate modeling is used to examine the relationship of reading to spelling. Finally, linkage analyses on a 400 marker genome-wide scan are reported.

APOLIPOPROTEIN E–SURVIVAL AND COGNITIVE FUNCTIONING IN DIZYGOTIC TWINS DISCORDANT FOR THE EPSILON4 ALLELE

Session: Complex Disorders III

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Twin studies have shown that the variation in cognitive functioning can be attributed to both environmental and genetic factors, but that genetic factors become increasingly important with age. To investigate the influence of Apolipoprotein E (APOE) on survival and cognitive functioning among the oldest (age 71–93), we genotyped 2311 subjects from two population based studies (LSADT97 and the Danish 1905 cohort). In both studies cognitive tests were performed, including the Mini Mental State Examination (MMSE), and five brief cognitive tests selected to be sensitive to age-related memory and verbal fluency. DNA samples were only taken from subjects who were able to perform our interview without the help of a proxy, so this study does not include severely demented subjects. The results show a significant decrease in the epsilon4 allele frequency by age, but only a slight correlation between MMSE and APOE genotype tested with a linear regression (coeff: –.43; 95%CI: –.81 to –.06) and no correlation between the five brief cognitive tests and APOE genotype.

A total of 69 DZ twin pairs participated and to refine our study, we selected an additional 177 DZ pairs from LSADT99. In total, 76 of these pairs had discordant genotypes with regard to the epsilon4 allele — one twin had no epsilon4 alleles and the co-twin had 1 or 2 epsilon4 alleles. The survival probability were significantly different between those two groups (p = .01, logrank test), but there were no significant differences in cognitive functioning neither measured by MMSE (p = .52, one-way ANOVA) nor by the five brief cognitive tests (p = .43, one-way ANOVA).

PROGRESSIVE AGE RELATED INCREASE OF MULTIPLE FOLLICLE GROWTH IN NATURAL INTRA UTERINE INSEMINATION CYCLES

Session: Poster

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Introduction. One of the risk factors for multiple pregnancies is increasing age. These multiple pregnancies are mainly dizygotic, indicating that this could be related to natural multiple follicle growth. Until now, age related increase in natural multiple follicle growth has not been documented. In our infertility clinic, many patients are treated with intra uterine insemination (IUI) in a natural, monitored cycle. Data from these patients allow us to study natural multiple follicle growth in women of reproductive age.

Methods. A retrospective analysis of a database containing all patients who underwent IUI from 1995 to 2003 was carried out. In our centre, the standard procedure is three unstimulated cycles followed by 3 stimulated cycles irrespective of indication (male infertility, cervical hostility, unexplained infertility). For the current analysis, we selected all patients who had an ultrasound at day of hCG. Multiple follicle growth was defined as 2 or more follicles over 14 mm in diameter. We compared the proportion of patients with multiple follicle growth in one or more cycles over four age categories.

Results. From the 455 patients included in the study, 105 showed 2 or more follicles over 14 mm at time of hCG, while 350 never had multiple follicle growth. Occurrence of multiple follicle growth increased with age. For the age categories < 24 years, 24–29 years, 30–35 years and 36–41 years, the percentage of women with multiple follicles were 0%, 14.5%, 23.4% and 25.5% respectively (p < .05). Overall, the basal follicle stimulating hormone (FSH) levels were 7.65 ± 6.16 U/L (mean ± *SD*) in patients with monofollicular growth and 9.93 ± 8.34 U/L in those with multiple follicle growth (p < .02). In particular, in women older than 30 basal FSH levels were higher in patients with multiple follicle growth.

Conclusion. Natural multiple follicle growth increases with (female) age and is associated with a significant increase in basal FSH levels. These data support the hypothesis that the age related increased risk of natural multiple pregnancies is the result of multiple follicle growth and ovulation due to excessive endogenous FSH secretion, the result of increasing ovarian age and decreasing ovarian feedback.

MULTIVARIATE TWIN ANALYSIS USING MIXED LINEAR MODELS

Session: Poster

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Univariate and multivariate analyses of twin data are usually performed using purposely written maximum likelihood software that model the covariances between MZ and DZ twins. In this study, we can show that commonly used models (e.g. the ACE model) can be fitted using (standard) software that estimate variance components in mixed linear models. Applications of univariate and multivariate maximum likelihood analyses are given by analyzing quantitative traits associated with the metabolic syndrome. Up to 8 traits were analyzed simultaneously in multivariate analyses. In addition, we show, using both theory and numerical examples that the variance components for one trait phenotypically adjusted for another trait (e.g., Waist adjusted for BMI, by fitting BMI as a covariate) is a straightforward reparameterisation of the estimated covariance components from a bivariate analysis on the two traits.

For the ACE covariance model, an equivalent linear model is obtained by modeling (in addition to a residual effect) two random effects, one that estimates a between pair (either MZ or DZ) variance and one that estimates a variance between "genotypes", for which a DZ pair has two levels and an MZ pair only one level. The expected values of these components under the ACE model is $^1/_2$var(A) + var(C) and $^1/_2$var(A), respectively. Thus, any statistical package that can handle mixed linear models (e.g., SAS, SPSS, Genstat, Splus) can fit ACE models. For software that can handle pedigree data, the A, C and E effects can be modeled directly. We have used software written for mixed linear models and large pedigrees, ASREML, to perform univariate and multivariate analyses.

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The models described were applied to analyze the phenotypic data on metabolic syndrome related traits from 756 twin pairs (311 MZ and 445 DZ) of the Danish Twin Registry.

MULTIVARIATE GENETIC ANALYSIS OF OBESITY RELATED PHENOTYPES

Session: Complex Disorders I — Metabolic Syndrome, Obesity

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The cause of obesity has both a genetic and an environmental component as demonstrated in multiple family, twin and adoption studies. However, the obesity phenotype appears to be a complex and composite phenotype in which different compartments of adipose tissue exhibit different biology and hence may have different genetic and environmental determinants of their sizes. Particularly, the difference between the trunk, and especially abdominal fat mass, and the peripheral fat mass is important. On the other hand, there may well be common determinants of the total fat mass as well, and these may be reflected in the levels of leptin, which is secreted by the adipose tissue and is assumed to play a major role in providing a feedback signal important in central body weight regulation.

Isolated and shared genetic and environmental contributions to the following obesity-related phenotypes were investigated: body mass index (BMI); waist and hip circumferences; skin-fold thickness at the biceps, triceps, scapula, and crista sites; the sum of extremity skin-folds (biceps and triceps) and the sum of trunk skin-folds (scapula and crista); total sum of skin-folds; and fasting plasma leptin concentration. The phenotypic information was analyzed from 756 twin pairs (311 MZ and 445 DZ) of the Danish Twin Registry, using univariate and multivariate models. ACE and AE models were fitted with residual maximum likelihood (REML), using mixed linear models. To minimize the standard errors of estimated genetic correlations, all data were analyzed simultaneously, fitting sex and age as covariates.

From the univariate analyses, the heritability estimates of all body measures were in the range of .52 through .68 with standard errors ranging from .03 through .11, whereas leptin showed an estimated heritability of .30 with a standard error of .12. All body measures showed very small common environmental influences, and for leptin, this was estimated to .14 (standard error of .10).

Bivariate and multivariate analyses revealed large genetic correlations and also large environmental correlations (> .5) between the various body measures, but they were also clearly below 1.0. The genetic correlations between the leptin and the various body measures were large, whereas the environmental correlations were usually small.

MULTIVARIATE GENETIC ANALYSIS OF THE METABOLIC SYNDROME

Session: Complex Disorders I — Metabolic Syndrome, Obesity

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The metabolic syndrome, a group of symptoms related to insulin resistance, impaired glucose tolerance/diabetes, obesity, hypertension, and dyslipidaemia (raised triglycerides level and low high-density lipoprotein [HDL]) is becoming a major problem. Understanding the genetic basis of this syndrome is important in order to provide better diagnostics, treatments and counseling. Genetic and environmental contributions to the syndrome related traits were investigated by analyzing phenotypic information from 756 twin pairs (311 MZ and 445 DZ) of the Danish Twin Registry, using univariate and multivariate models. ACE and AE models were fitted with residual maximum likelihood (REML), using mixed linear models. To minimize the standard errors of estimated genetic correlations, all data were analyzed simultaneously, fitting sex and age as covariates.

From the univariate analyses, the heritability estimates of height, weight, BMI, waist circumference, cholesterol level, HDL, low-density lipoprotein (LDL), 30 minutes insulin, and systolic and diastolic blood pressure were all larger than 0.50. The heritability of very low density lipoprotein (VLDL), triglyceride, lipoprotein B, glucose 30 and 120 minutes, and fasting and 30 minutes insulin were between .30 and .50. Estimated heritability for lipoprotein A, fasting glucose, albumin, and creatinine were less than .3. For most traits, the estimates of a common environmental component were small, except for all lipoproteins (AI, B and E), where more than 30% of phenotypic variation was due to common shared environmental effects.

Multivariate analyses revealed large genetic correlations (> .5) between BMI and waist, triglyceride and VLDL, fasting insulin and waist, glucose 120 minutes and fasting insulin and insulin 120 minutes, fasting insulin and insulin 120 minutes. The estimated genetic correlations between BMI and either systolic or diastolic blood pressure, cholesterol level and VLDL and triglyceride were .28, .26, .39 and .39, respectively. For the remaining combinations of core phenotypes associated with the metabolic syndrome, estimated genetic correlations were close to zero.

A COMPARATIVE STUDY OF INTERPERSONAL PROBLEMS AMONG TWINS AND SINGLETONS

Session: Poster

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The purpose of this study was to compare interpersonal problems among high school and college student twins and singletons. The subjects were 40 twin pairs (n = 80) and 80 singletons. All subjects (n = 160) were asked to complete the Inventory of Interpersonal Problems (IIP). The results revealed that twins scored significantly lower than singletons on sociability and intimacy subscales. Twins also scored slightly lower than singletons on total IIP. No statistically significant difference was found in the mean scores for assertiveness, submissiveness, responsibility, and controllability subscales of IIP between the two groups. Results suggest that twins may have a lower rate of interpersonal problems than singletons.

MUNICIPAL SERVICES FOR FAMILIES WITH TWINS AND HIGHER ORDER OF MULTIPLE BIRTHS IN DENMARK

Session: COMBO II

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This survey is the largest ever conducted of municipal offerings for families with twins and higher order of multiple births in Denmark. The survey aims at uncovering the level of service that municipalities offer families from newborn until the children start primary school. The overall purpose is to put focus on the extremely different support and guidance of families that takes place. All municipalities in Denmark have received a questionnaire and 94.3 percent have answered.

The motivation for this survey is the dramatic increase in multiple births in the last ten years and legislation that specifies what level of service a municipality must offer multiple birth families.

The following four topics are covered:

- services offered during maternity leave
- services offered from municipal health care personnel
- day-care services offered when maternity leave ends
- start of primary school.

In 32.5 percent of the municipalities, twin families were offered some form of help in the home during the first 3–6 months, however only 1.48% of the municipalities offer practical assistance from a social worker. In 18.08%, twin mums are allowed the opportunity to become a day-care person for their own children, either unconditionally or depending on available jobs in the local municipality day-care sector. In 2.58% of the municipalities, it is recommended either splitting up or keeping twins together in school; the remaining have a flexible approach. In 34.7 % of the municipalities, there are extended services offered from health care personnel. Finally, a top-10 list of twin friendly municipalities in Denmark has been compiled based on the individual municipality combined services offered to families. This top-10 list will be correlated with the statistical density of multiple births in individual municipalities in order to identify the most important areas of improvement for twin families.

GENETICS OF SMOKING AND NICOTINE DEPENDENCE

Session: Genetics of Nicotine Dependence (Symposium)

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Despite substantial reductions in the prevalence of smoking in the past years, over one third of adults in the Netherlands continue to smoke.

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Nicotine is more addictive than most illicit drugs and a large proportion of cigarette smokers are nicotine dependent. Our longitudinal study of monozygotic (MZ) and dizygotic (DZ) twin pairs, their parents, siblings and spouses in the Netherlands shows that genetic factors contribute to variation in smoking initiation, in the liability to heavy use of tobacco, and in nicotine dependence. For smoking initiation (SI) a heritability of 36% was found and for number of cigarettes smoked (NC) 51%. Both SI and NC were also influenced by shared environmental factors. In contrast, nicotine dependence (ND) was only influenced by genetic (75%) and unique environmental factors.

With the rapidly advancing tools of statistical and molecular genetics, a new challenge in studying the genetics of human addiction is to move from latent variable modelling, which can demonstrate the existence of genetic susceptibility, but not identify the genes, to linkage and association tests which can localize and identify the susceptibility genes directly. In a subsample of families not selected for nicotine dependence, we carried out QTL linkage analyses using a 405 microsatellite marker set. Linkage analyses were performed on data of 536 DZ twins and siblings from 192 families, forming 592 sibling pairs. QTLs were found on chromosomes 6 (LOD = 3.05) and 14 (LOD = 1.66) for SI and on chromosome 3 (LOD = 1.98) for NC. Strikingly, on chromosome 10 a peak in the same region was seen for both SI (LOD = 1.92) and NC (LOD = 2.29) which may explain the overlapping etiological factors for SI and NC.

In addition, we collected 1009 DNA samples from family members (426 twins, 317 siblings and 266 parents) from 302 families specifically selected for the presence of concordant (n = 142) and discordant (n = 45) ND sibling pairs. These DNA samples will be used to test SNPs in candidate genes. We are currently performing a replication study of the EPAC (*e*xchange *p*rotein directly *a*ctivated by *c*AMP) gene which showed a modest association with nicotine dependence in a Caucasian sample collected in Virginia.

Supported by NWO (985-10-002 and 904-61-090) and ZonMW/NIDA (3100.0038), the Virginia Tobacco Settlement Foundation (Contract #8520012) and grants DA–11287 and MH–01458 from NIH (USA). Genotyping was carried out by the Center for Medical Genetics in Marshfield.

QUANTITATIVE GENETIC MODELLING OF VARIATION IN THE DYNAMICS OF HUMAN BRAIN MORPHOLOGY: A LONGITUDINAL STUDY IN MONOZYGOTIC AND DIZYGOTIC TWINS AND THEIR SIBLINGS

Session: Poster

Rachel G. H. Brans[1], Rene S. Kahn[1], Danielle Posthuma[2], Hugo G. Schnack[1], Dorret I. Boomsma[2], and Hilleke E. Hulshoff Pol[1]

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Background. Most of global brain volumes and certain focal brain areas are under significant genetic control (> 80%) and this finding can be generalized to the singleton population. Lateral ventricle volume is mostly determined by environmental factors. During aging, brain volumes change constantly. Gray matter decreases in adulthood, while white matter increases and eventually starts to decrease around the age of 45 years. However, to what extent genetic and environmental factors mediate the dynamics of the brain is still unknown.

Aim. The aim is to study to what extent (percentage) genetic and environmental factors influence changes in brain morphology during aging. We hypothesize that genetic factors have a large influence on the aging brain.

Methods. To estimate the genetic and environmental influences on brain volumes and focal brain density, we use an extended twin design. One hundred and twelve pairs of monozygotic and dizygotic twins and their siblings (n = 259) scanned at baseline with MRI1, are rescanned after five years. Diagnostic interviews and subtests of the WAIS are completed for medical, behavioral and neuropsychological assessment.

Mx software will be used for multivariate structural equation modeling to analyze the data.

Seventy-two percent of the subjects have agreed to participate in this longitudinal study. So far, 172 subjects have been scanned twice.

With this study we hope to get more knowledge about the development of the healthy brain and about the interaction between brain and genetics. It may contribute to the knowledge of genetic liability for diseases that affect the integrity of the brain, such as schizophrenia.

THE SIMILARITY OF SMOKING BEHAVIOR OF ADULT TWINS

Session: Genetics of Nicotine Dependence

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Both genetic and environmental factors have been found to affect smoking initiation and maintenance, but less is known about the genetic architecture of various other smoking-related behaviors.

The aim of this study is to examine the role of genetic and environmental factors in smoking behaviors in a large twin cohort. Questionnaires with an extensive smoking history section were mailed to adult twins of the Finnish twin cohort in 1975, 1981 and 1990. The data on like-sexed pairs that responded in 1981, and who were both ever smokers (current or former) in 1981, included 1140 monozygotic (MZ) and 2127 dizygotic (DZ) twin pairs who smoke aged 24 years and over (mean age 41) in 1981. Univariate genetic modeling was done by using the Mx-statistical package.

In general, the correlations for age at initiation, cigarettes smoked per day, and nicotine content per cigarette were greater for MZ pairs than DZ pairs. For all men the heritability estimates for age at initiation was .36 (95% CI .21–.51) and cigarettes smoked per day 0.49 (95% CI .44–.54), while for all women the corresponding heritability estimates were .67 (95% CI .60–.72) and 0.52(95% CI .46–.57), respectively. Among pairs in which both twins were current smokers, corresponding heritability estimates were for men 0.33(95% CI .24–.41) and 0.47(95%CI .39–.54) and for women .47(95% CI .36–.57) and .27(95% CI .00–.55), respectively. Common environmental effects were minor.

Both genetic and specific environmental factors are important in many aspects of smoking behavior.

Study is funded by NIH grant DA12854 and Doctoral Programs of Public Health, University of Helsinki.

SPECIAL PROBLEMS FACING FAMILIES WITH HANDICAPPED HIGHER–GRADE MULTIPLE BIRTH CHILDREN

Session: COMBO II

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The ABC-Club e.V. is the largest German organization of and for families with higher-grade multiple birth children (triplets and more).

Our experience has shown that families with one or more handicapped multiple birth children are often confronted with exceptional hardships. Based on this experience, we sent out a questionnaire to our 1500 member families.

The main issues we wanted to investigate were the type of handicap, surgery that was necessary, persisting handicaps and treatments thereof, support for the families and strategies for dealing with problems.

Our investigation revealed that the majority of multiple birth children, including those without persisting handicaps, were forced to have abdominal and thoracic surgery within the first three years. About 50% of the children needed special therapy such as physiotherapy, logopedic therapy, etc. before starting school. About 4% of the children were diagnosed to be severely handicapped under German law, which entitles them to receive state and local government support.

It became evident in our investigation that little was known about the dire situation of these families, and that as a result, little support was provided to them. Most families had to rely only on themselves.

What measures can be effective to ease the burden of these families?

The ABC-Club has been trying to find answers to this question and has since organized special support and recreational trips for affected families.

BUILDING A TWIN REGISTRY IN WASHINGTON STATE

Session: Twin Registers and Methodology

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Many twin registries in the USA are constructed by linking birth records to state drivers' license records. In Washington (WA) state we identified a way to build a state-wide, population-based twin registry directly from drivers' license records. This is possible because of a fortuitous quirk in the WA Department of Licensing (DOL) identification system. The license/identification number in WA is an encrypted version of the applicants' date of birth, and first and last name. However, because twins typically have the same last name, often highly similar first names and identical dates of birth, this method, when first implemented decades ago, resulted in the issuance of duplicate license numbers. To solve this problem the WA DOL soon began asking all applicants, "Are you a

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twin?" This is unique to Washington; this question is not used by any other state. Since obtaining approval from the WA Attorney General in 1999, computerized records of newly licensed twins have been transmitted to us on a weekly basis. We receive the names, addresses, telephone numbers, places of birth, and heights and weights for all twins. We continue to receive information from the WA DOL on ~100 new twins per week. The Registry is assembled by mailing each twin a letter, information sheet, brochure, and a brief survey on sociodemographics, habits, health conditions and service use, and the contact information for the co-twin. As of March 2004, we have enrolled ~2000 twin pairs (30% of index twins; 75% of co-twins), and are enrolling ~80–100 new pairs per month. Among all twins, 88% are white, 18% foreign born and 7% come from a Spanish-speaking country. The average age of the twins is 29; 47% are older than 30. We have also established a clinical protocol for the collection of additional data on all twins participating in research studies requiring an in-person visit. These pairs undergo a physical examination and tests for fitness and respiratory function, donate biological samples, and complete ancillary questionnaires. Three grants have been funded in the last year, and three more are under review. Plans for the further growth of the Registry are discussed.

TOTAL AND NATURAL TWINNING RATES IN THE GRAMPIAN REGION OF SCOTLAND 1976–2002

Session: Current Developments and Findings from Twin Studies

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Twinning rates throughout the world have been increasing lately and this has largely been attributed to increasing numbers of multiple pregnancies resulting from assisted reproduction.

In the Grampian region of Scotland, it is possible to extract from the Aberdeen Maternity and Neonatal Databank data relating to all twin pregnancies in the area. Linkage to the infertility registers enables identification of those multiple pregnancies resulting from the management of infertility, either as a result of ovulation induction or assisted reproduction techniques, for example, IVF. This allows us to examine the total twinning rate for the region and the natural twinning rate.

The time period under review is 1976 and 1992 with a total of 1941 twin pregnancies being identified.

The total twinning rate has increased as expected but surprisingly the spontaneous natural rates increased as well.

Factors known to contribute to such changes will be considered.

Age, parity, height and body stature have all altered over the same time period. Age, height and weight have increased in the population whereas parity has decreased. The interaction between these in the determination of twinning rates will be presented.

GENETIC AND ENVIRONMENTAL INFLUENCES ON INDIVIDUAL DIFFERENCES IN ACADEMIC ACHIEVEMENT IN ADOLESCENTS

Session: Poster

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The aim of this study is to analyze the impact of genetic and environmental factors on scholastic achievement in adolescents. The sample consisted of 175 pairs of MZ and same-sex DZ twins aged 12–14 years. We analyzed the intrapair similarity of MZ and DZ twins in measures of reading, literature, foreign language, mathematics, history, science and several other school subjects.

MZ twins were more similar than DZ twins in achievement in all the school subjects. Nevertheless, the heritability for measures of academic achievement varied widely in range (from .77 for Russian Language to .26 for Physics). Genetic influence on individual differences in achievement in humanitarian subjects was more than in the natural sciences.

We suppose that at least some of the genetic contribution to school achievement may reflect the genetic contribution to general cognitive functioning.

TWIN STUDIES ON AGING AND LONGEVITY (SYMPOSIUM)

Session: Aging and Longevity — Insight from Twin Studies

Kaare Christensen[1] (chair), James W. Vaupel[2], Matt McGue[3], Nancy Pedersen[4], and Stig Berg[5]
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James W. Vaupel: **The Remarkable Plasticity of Aging**

Within the last decades a new paradigm about aging processes has emerged. Previously aging was regarded as a very mechanistic process with little room for external factors to influence it. However, evidence ranging from population level to individuals to model organisms and genetic studies all suggest that the aging processes are plastic and modifiable.

Kaare Christensen: **Aging, Functioning, Survival and Perceived Age**

The Longitudinal Study of Aging Danish Twins comprises a multidimensional assessment of Danish twins aged 70+ every second year since 1995. Here results on physical functioning, rate-of-change and late life health are presented together with new findings on perceived age, which is shown to be highly heritable and associated with mortality after controlling for age.

Matt McGue: **Psychological Functioning in the Longitudinal Study of Aging Danish Twins (LSADT)**

LSADT is a cohort-sequential study of Danish twins aged 70 years and older. Participating twins are assessed every two years for up to five assessments and included in the assessment are measures of depression symptomatology and cognitive functioning. Findings from longitudinal analysis of the depression and cognitive data will be presented to illustrate the diverse nature of genetic and environmental influences on late-life psychological functioning.

Nancy Pedersen: **Swedish Twin Studies of Cognitive Abilities Late in Life**

There are three longitudinal twin studies of aging in Sweden, all of which include assessments of health, personality, and physical and cognitive functioning. The purpose of this presentation will be to summarize the findings concerning genetic variation for cognitive abilities late in life. For some abilities, performance is relatively stable until very old age, while for others, there is accelerating decline after age 65–70. Genetic variance may remain stable or decrease, depending on the measure.

Stig Berg: **Aging, Gender Differences and Survival in Swedish Twin Studies**

For a better understanding of health, social and psychological functioning in late life, it is of paramount interest in the analyses to include the effects of gender and survival. Although gender and distance to death are key elements in the comprehension of the aging process, these factors are often "forgotten" in both normative studies and in research concerning the influences contributing to change in individual differences. The effects of the gender and survival factors will be discussed based on data from the Swedish Twin Registry and Swedish gerontological twin projects.

RISK AND PROTECTIVE FACTORS IN AFFECTIVE DISORDER: A CROSS-SECTIONAL HIGH-RISK TWIN STUDY

Session: Poster

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Objective. To investigate whether it is possible to identify risk or protective factors for developing affective disorder by a high-risk design using a cohort of psychiatrically healthy twins who have a co-twin with depressive or bipolar disorder (a high-risk twin).

Method. A linkage between the Danish Twin Registry and The Danish Psychiatric Research Registry identified twin pairs in which at least one of the twins had been treated in a psychiatric hospital setting for an affective episode. The high-risk twins are compared to a control group: twins without a known history of affective disorder among their co-twin and their first degree relatives. The high-risk twins and control twins are matched on zygosity, age and gender. The first part of the study is a cross-sectional investigation, and afterwards participants are followed for five years.

Psychiatric Interview. Schedule for Clinical Assessment in Neuropsychiatry Interview SCAN 2.1; Hamilton Depression Scale; Cambridge Cognitive Examination; The Stroop Test; 15 Word-Pairs; learning and memory attention; Trail Making Test.

Biological Measures. Routine blood tests; stress-hormone by salivary cortisol; magnetic resonance imaging.

Self-Rating Measures. Eyesenck Personality Questionnaire; WHOQOL Quality of Life; Becks Depression Inventory; Coping Inventory for

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Stressfull Situations; Kendlers List of Life Events; Inventory of Interpersonal Problems.

Results. The linkage identified 245 twins who have a co-twin with a depressive or bipolar disorder. The study started to include participants by May 2003 and is still ongoing.

GENETIC FACTORS AND DEPRESSION — A DANISH TWIN STUDY

Session: Complex Disorders III

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The frequency of depression is high in the elderly and is often found associated with development of age-related diseases, cognitive decline, functional disability, and mortality.

If conceptualizing that major clinical depression is merely the extreme of a quantitatively measurable depression symptomatology, it can be argued that there is a genetic relationship between normal variation in mood and susceptibility to development of major depression.

In a recent study using longitudinal data from Danish twins it was shown that the variance of occasion specific depression, as measured on a depression symptom scale, was moderately heritable. However, when assessing the average level of mood at multiple occasions, at least 60% of the variation was determined by genetic factors.

The aim of this study was to investigate any possible association between the average level of depression symptomatology and polymorphisms in several genes of the serotonergic system, which has been suggested are implicated in susceptibility to major depression.

The study participants were drawn from the 1997 wave of the Longitudinal Study of Aging Danish Twins (LSADT), in which depression symptomatology scores have been assessed up to four times, each with two year intervals. Two different approaches are employed, one using the quantitative measure of depression symptoms in a sample of all dizygotic twins and one using a sample of dizygotic twins who are either extremely discordant or extremely concordant for a high depression score.

EPIGENETIC DISCORDANCE IN IDENTICAL TWINS

Session: Molecular Genetics and Twin Studies

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Identical twins form by the splitting of a single embryo and share identical DNA sequences. However, identical twins may be discordant for many traits, including most complex diseases. The reasons for this discordance are unknown and we propose that epigenetic features, and in particular DNA methylation, may contribute to the discordance between identical twins. We have chosen the "amplification of inter-methylated sites" (AIMS) technique to conduct a genome-wide scan to identify methylation differences between monozygotic twin pairs. In addition, we are examining insulin-like growth factor-2 (IGF-2) as a candidate gene for epigenetic discordance using a novel allele-specific expression assay. The function of IGF-2 is associated with height and other growth-related traits and aberrant IGF-2 expression in lymphocytes is associated with specific methylation changes that occur frequently in the normal population, increasing the odds of finding discordance at this locus. We report here on our findings to date and describe the allele-specific expression assay, which has further application to the study of imprinted genes.

"EVERYTHING CAME WITH A PRICE": WOMEN'S DECISION-MAKING REGARDING MULTIFETAL REDUCTION

Session: Psychosocial Issues in Families with Multiple Births

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This phenomenological study described women's experiences regarding their decisions to undergo or forgo multifetal reduction (MFR). The sample included eight women who had conceived higher-order multiple (HOM) pregnancies (triplets to nonuplets) following infertility treatment.

All of the women described the emotional, physical, and financial costs of infertility treatment. Although aware that it was possible to conceive multiple fetuses, the discovery of their HOM pregnancies left them shocked and utterly unprepared to face a new set of treatment decisions (i.e. MFR). Rather than choosing how many embryos to transfer, or whether to continue or cancel a treatment cycle, they were now choosing whether or not to undergo MFR. If they chose to reduce they were asked to decide how many of their fetuses to keep or to terminate. Decisions to reduce were made reluctantly, with the women's primary concern being the health of their multiples.

The costs of "success" were enduring for these women regardless of their choices. Women who declined MFR described the stressors and financial cost of raising HOMs. They were also acutely aware that one or more of their children would not be with them had they made a different decision. Women who chose MFR described delivering and raising their multiples as a bittersweet experience. They were very conscious of what they had lost. They felt isolated and uncomfortable seeking support from any multiple birth organizations. The hidden, lasting costs of infertility for these women pose new challenges for health professionals assisting them before, during and after their HOM pregnancies.

TH1 AND TH2 CYTOKINES AND IGE IN IDENTICAL TWINS WITH VARYING LEVELS OF CIGARETTE CONSUMPTION

Session: Complex Disorders II and Immunology

Wendy Cozen[1,2], David Diaz-Sanchez[3], W. James Gauderman[1], John Zadnick[1], Myles G. Cockburn[1], Ann S. Hamilton[1], Minna Jyrala[3], and Thomas M. Mack[1,2]
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Some suggest that tobacco smoke may skew the immune system toward a Th2 pattern. However, the effects of genetics, or childhood exposures could explain these results. We compared Th1 (INF-g) and Th2 (IL-4, IL-5 and IL-13) cytokine and IgE levels in members of 45 pairs of non-asthmatic monozygotic twins with varying levels of current cigarette consumption to determine if smoking was associated with Th1/Th2 function after accounting for genetic factors. Cytokines and IgE were measured from serum or PHA-stimulated PBMC supernatant using enzyme-linked immunosorbent assays (ELISA), and compared using analysis of covariance and Wilcoxon signed rank test for pairs. A statistically significant dose-response was observed between levels of smoking and IL-13 (p = .05). Mean IL-13 level among heavy smokers (20+ cigarettes/day) was 146% higher than that among non-smokers (+26.2 pg/ml; p = .04). When compared directly to each other, the IL-13 level was significantly higher in the smoker than in his or her non-smoking twin (p = .02). The mean IL-5 level among heavy smokers was 166% higher than that among light (< 20 cigarettes/day) smokers (+3.4 pg/ml; p = 0.03). No statistically significant differences in INF-g, IL-4 or IgE levels were observed. Smoking is associated with increased levels of IL-13, supporting the hypothesis that tobacco smoke promotes allergic airway disease.

CYTOKINE PATTERN IN UNAFFACTED MZ TWINS OF YOUNG ADULT HODGKIN LYMPHOMA PATIENTS SUGGESTS SUSCEPTIBILE IMMUNOPHENOTYPE

Session: Complex Disorders III

Wendy Cozen[1], Parkash S. Gill[1], Rizwan Masood[1], M. Towhid Salam[1], Sue Ann Ingles[1], Wei Wang[1], Alexandra Nieters[2], Myles Cockburn[1], W. James Gauderman[1], Malcolm C. Pike[1], and Thomas M. Mack[1]
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Previously we demonstrated that unaffected MZ twins of cases were 99 times more likely to develop young adult Hodgkin lymphoma (HL) than expected, based on population incidence rates (Mack, 1995), suggesting genetic factors are involved in etiology. We hypothesized that a genetically determined cytokine imbalance favoring humoral immunity, inflammation and B-cell growth over cell-mediated immunity, and innate immune surveillance might be responsible. Because the disease could affect cytokine measurement, we used 54 unaffected MZ twins of young adult HL cases as surrogate cases. Matched controls were spouses (61%) or friends (17%) within five years of the age of the twins. When no spouse or friend was available, USC employees matched on ethnicity and age were used as controls (22%). Cytokines were measured from PBMC supernatant using ELISA. The geometric mean difference and percent difference in cytokine levels between the surrogate cases and their matched controls were estimated in an ANCOVA model that included gender and age, modeled as a continuous variable.

IL-6 and IL-8 levels were 68.6% and 53.3% higher in surrogate cases compared to controls (p = .04 and .35, respectively). IL-2 and INF-g were each 7.8% lower, IL-10 was 18.6% lower, and IL-12 was 37.6% lower in surrogate cases compared to controls, although none of these differences were statistically significant. There were no significant differences in cytokine levels by age or gender. To date, we have genotyped the common polymorphisms of the IL-6 and IL-10 promoter. We have previously

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reported that an IL-6 genotype (–174G > C) associated with lower IL-6 levels was protective (OR for CC vs. GG = .29; 95% CI = .10–.87) (Cozen, in press, Blood). We also found that an IL-10 polymorphism associated with higher levels (–1082 A > G) was protective (OR for GG vs. AA = .54; p = .20).

Unaffected MZ twins of young adult HL cases have higher levels of inflammatory cytokines (IL-6, IL-8) and lower levels of anti-inflammatory (IL-10) and cell-mediated immune response cytokines (IL-2, IL-12, INF-g), compared to controls. So far, genotype results are consistent with the phenotype data. This cytokine pattern may represent a heritable immune phenotype associated with increased susceptibility to young adult HL.

VISUAL CHARACTERIZATION OF THE MYTHOLOGICAL HERO TWINS IN ANCIENT MAYA CERAMIC VASES

Session: Poster

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Objective. To describe the theme of twinship in ancient Maya pictorial ceramics using the Kerr Maya Vase Database, a quasi-representative sample of the staggering and as yet unquantifiable corpus of Mesoamerican art.

Background. The Maya Vase Database is an archive of peripheral or rollout photographs of more than 1700 ancient Maya vases created by Justin Kerr. Rollout photography allows photographing a vase continuously so that the entire image can be viewed at once in a two-dimensional manner.

Pre-Columbian ceramic vases illustrate scenes of the exploits of the Hero Twins described in the Popol Vuh or "Book of Counsel", the single most important document in Maya mythology. The pictorial imagery of these vases constitutes the oldest documented mythology of the New World.

Methodology. A computerized search of the Maya Vase Database using the key word "twins" found 211 vases, of which there are 128 Polychrome, 56 Codex style, 3 Black and White, 16 Carved, 8 Incised and 40 Molded.

Results. Classic Maya pictorial ceramics are replete with imagery of the Hero Twins, Hunahpu and Xbalanque. The Hero Twins have specific skin markings and distinctive costumes that identify them. Both wear an elaborate headband, which is probably the most important iconographic identification tool. Hunahpu has either a single black spot, or three dots on his cheek and large spots on his body. In contrast, Xbalanque has jaguar-like spots on his lower face and patches of jaguar pelt on his arms, legs and back. He usually wears a shell on his forehead.

The Hero Twins are depicted as hunters using blowguns, and as ball players wearing animal headdresses and yokes. It has been suggested that images of catfish and large sun-like disks found on some vases also symbolize the Hero Twins. In the Popol Vuh, the Hero Twins sacrificed themselves in a bonfire and then magically reappeared as catfish. At the end of the story, they rose up to the sky to become the Sun and the Moon.

Conclusions. Review of rollout photographs and related commentaries of the Maya Vase Database suggest that Hero Twins served many and varied roles within a complex mythological system. However, their physical depiction changed as the Maya civilization evolved over time and space within the geographic confines of Mesoamerica.

THE IMPORTANCE OF GENETIC FACTORS IN SCHEUERMANN'S DISEASE

Session: Pediatric Aspects of Twinning

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Although Scheuermann's disease is the most frequent cause of hyperkyphosis during adolescence, the mode of inheritance and the role of environmental factors are still unknown.

The purpose of this study was to examine whether genetic factors contribute to the pathogenesis of Scheuermann's disease.

Materials and methods. The present cohort from the Danish Twin Registry consists of all Danish twin pairs born between 1931 and 1982. Establishment of zygosity has been based throughout the period on four questions of similarity, with an accuracy of approximately 95%. All registered twins received a 17-page questionnaire in the spring of 2002. The total number of twins was 46,418. Seventy-five percent returned the questionnaire, and of these 97.3% answered the question "Have you been diagnosed with Scheuermann's disease?" The pair-wise concordance was compared using the Chi-square test.

All scientific-ethical committees in Denmark have approved the study.

Results. Of the 34,007 respondents, 943 reported having Scheuermann's disease, 380 females and 563 males. The overall self-reported prevalence of Scheuermann's disease was 2.8% (95% confidence limits c.i.l. 2.6–3.0). Stratified according to gender we found a male and female prevalence of 3.6% (95% c.i.l. 3.2–4.1) and 2.1% (95% c.i.l. 1.9–2.3) respectively, and this difference was strongly statistically significant (Chi-square test 67.8 (p < .0001)). The prevalence of Scheuermann's disease was not significantly different between the cohorts of monozygotic (MZ) and dizygotic (DZ) twins and the figures were as would be expected from the literature.

Of 11,436 twin pairs who both answered the above question, 645 indicated that they had been diagnosed with Scheuermann's disease. The pair-wise concordance was 0.19 (95% c.i.l. .13–.25) for MZ and .07 (95% c.i.l. .04–.11) for DZ twin pairs. This difference was statistically significant (Chi-square test 13.3 (p < .001)). The proband-wise concordance was .31 (95% c.i.l. .25–.37) for MZ and .13 (95% c.i.l. .09–.17) in DZ twin pairs.

Conclusion. We found an overall prevalence of Scheuermann's disease as expected from the literature (2.8%), with a significant male prevalence.

Both the pair-wise and the proband-wise concordance was larger in MZ than in DZ pairs. This higher concordance rate of MZ pairs confirms the contribution of a major genetic component, while indicating the need to identify possible environmental triggers.

NEGOTIATING CONFLICT IN A TWIN RELATIONSHIP

Session: Twin Family and Twin Relations

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There is compelling evidence that young children's friendships support long-term cognitive, social and identity development. However, there is little documentation of the social world of friendship for the twin outside of the family. This paper examines how children who are twins organize their everyday friendships, with particular focus given to how twin children negotiate aspects of conflict within friendships. Conflict as a type of social interaction has been identified for aligning and realigning the social worlds of children. The study drew on the accounts of 60 twin children (10 MZ, 10DZss, 10 DZos pairs) aged 6–10 years and their parents (n = 30). The children engaged in a sticker activity in which they represented their friendships. Using this as a resource, the children were asked about whom their friends were, the attributes of friendship, and examples of everyday friendship encounters. These conversations were audio-recorded and transcribed. The transcribed conversations were analyzed to examine, from the children's own perspective, how they constructed friendship with their twins and playmates. Further, mothers were asked to discuss their perspective of their children's friendship patterns. This paper focuses particularly on how one family negotiates aspects of twinship and friendship to show the complexities of dealing with conflict.

INSIGHTS INTO THE MOLECULAR MECHANISMS OF ABNORMAL AND NORMAL BEHAVIOR

Session: Poster

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Epigenetics refers to regulation of gene activity that is controlled by partially stable modifications of DNA and chromatin. Putative epigenetic dysregulation of normal genes may provide an explanation for a number of unclear issues in major psychosis and other behavioral disorders that cannot be explained by the traditional DNA sequence-based theories. Such issues include discordance of monozygotic twins, sexual dimorphism and parental origin effects, fluctuating course and sometimes recovery. In addition, numerous molecular aberrations identified in psychiatric diseases are consistent with putative epigenetic defects. For example, dopamine D2-like receptors and their genes have been subjected to detailed pharmacological, imaging, and genetic studies. However, it remains unclear what molecular mechanisms cause the changes in density of the D2 receptors. Such changes are consistent with inborn and/or acquired plus age-dependent changes in epigenetic regulation of the receptor genes. Apart from the molecular mechanisms of abnormal behavior, epigenetic strategies may shed a new light on the fundamental aspects of normal behavior such as gene–environment interactions, as well as an understanding of the true source of what traditionally has been called "non-shared environment".

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ACTING THE PART: IDENTITY POLITICS AND THE PERFORMANCE OF TWINSHIP AT TWIN FESTIVALS IN THE USA

Session: Twin Family and Twin Relations

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"Acting the Part" is a qualitative, dramaturgical study of twins at play, and describes the expressive styles of twinship as performed by identical twins participating in twin festivals. The study draws from and contributes to anthropological theories on the embodiment and performance of identity. Research methods include participant observation by a pair of identical twin anthropologists, and the analysis of narrative interview data collected during the summer of 2003 at the Twins Days Festival (Twinsburg, Ohio) and the Annual International Twins Convention (Atlanta, Georgia). Twenty-two sets of twins, ages 22–74, were interviewed. The study depicts how twins perform in the collective public settings of a festival, as well as and in face-to-face interactions. Analysis focuses on how festival twins create impressions and manipulate perceptions of twinship identity vis-à-vis other sets of twins and the general public. A range of overlapping expressive styles referred to in the performance literature as genres, scripts, and play frames are used to analyze the twins' enactment of twinship. Genres identified include: (1) parade and contest twins; (2) militant twins; (3) good and evil twins; (4) un- or anti-twins; (5) tactile twins; and (6) caretaker twins. Special attention is paid to styles of presentation of the twin dyad and self and other within the dyad. Conclusions show how performance styles both conform to and challenge modern American constructions of self and other. The study challenges twin researchers' stereotypes of anthropology and offers new insights to twins as a topic for cultural analysis.

ASSOCIATION BETWEEN APOE GENOTYPE AND DEMENTIA IN TWINS USING BIVARIATE LOGISTIC REGRESSION

Session: Statistical Issues in Twin Studies II

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Bivariate logistic regression (BLR) can be used for analyzing the effect of genotype on ordinal traits using twin data when both monozygotic (MZ) and dizygotic (DZ) twins have been genotyped. While information from MZ twins cannot be used in Generalized Estimating Equation (GEE), bivariate logistic regression can and allows for evaluating whether the twin similarity can be explained by the candidate gene. This study compares the results of the association of the APOE genotype and dementia using GEE and BLR using twin data.

All members of the Swedish Twin Registry aged 65 and older were screened for cognitive impairment, with suspected cases of dementia receiving complete clinical diagnostic evaluations. A total of 750 complete twin pairs (405 MZ and 345 DZ pairs) with APOE genotypes and a diagnosis for dementia was available for this study. GEE and bivariate logistic regression were carried out using STATA.

Initial GEE analysis of dementia in DZ twins shows a large significant effect of genotype, where the e4 allele conferred increased risk for dementia ($z = 6.32$, $p < .0001$). Bivariate logistic regression shows a similar substantial effect of APOE genotype for dementia. Although the within pair similarity adjusted for age and sex is not significantly different for MZ compared to DZ twins, a decrease in within pair similarity for MZ twins is observed when APOE genotype is taken into account. If the difference in within pair similarity for MZ and DZs would disappear completely, this would suggest that APOE genotype explains all the genetic risk for dementia.

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THE HUMAN FERTILIZATION AND EMBRYOLOGY AUTHORITY COMMITMENT TO REDUCING MULTIPLE BIRTHS FROM IVF: THE NEW GUIDANCE

Session: Controversies on Obstetric Issues

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The Human Fertilization & Embryology Authority (HFEA) was established in 1991 in the UK through the HFE Act. The role of the HFEA is to license and monitor clinics providing in vitro fertilization and infertility treatments using donated gametes, the storage of gametes and embryos, and any research using human embryos. The HFEA is required by law to produce a Code of Practice giving guidance about suitable practices to be followed in the licensed centers. Since its inception the HFEA has been concerned about the high multiple birth rates and the first Code of Practice published in 1991 limited the number of eggs or embryos to be transferred to three. All HFEA policies are kept under review. Based on more recent data and the recommendations of professional bodies, new guidance is given in the recently published 6th edition of the HFEA Code of Practice. In a single treatment cycle, a maximum of two eggs or embryos can be transferred to a woman of less than 40 years of age, with no exceptions. Women aged 40 and over may have a maximum of three eggs or embryos. The new policy will be monitored through the HFEA inspection process and through data collection from the clinics.

MATERNITY SERVICES FOR PARENTS OF TWINS AND TRIPLETS: A SURVEY OF THEIR EXPERIENCES

Session: Twin Family and Twin Relations

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The Multiple Births Foundation (MBF) supports multiple birth families by working with health care and other professionals to raise awareness and provide education about the special needs of the parents and children.

One of the main aims of the MBF is to improve the national standards and consistency of care by establishing a network of midwives with specialist expertise in multiple births. As part of the evidence gathering to identify the needs of parents, a questionnaire was sent to all those whose multiple birth infants were born between January 2002 and September 2003 (358) at Queen Charlotte's & Chelsea Hospital. The aim of the survey was to find out if parents received adequate information and support, from the diagnosis of the pregnancy through to discharge from the hospital. The response rate was 44% (149 twins, 7 triplets). Eighty percent of the deliveries were by caesarean section. Fifty-eight percent said that they were satisfied with the information they received about the pregnancy and the practical aspects of caring for more than one baby. Of the remaining 42%, many would have liked more written information and advice about how to cope. Thirty-four percent of the babies were breast fed and 50% by a combination of breast and bottle. Fifty-eight percent of those who breast fed said they had good help and support. The survey has identified areas where the care for mothers with multiple births can be improved. In particular, the MBF is working with Queen Charlotte's & Chelsea Hospital to develop specific information and guidance for mothers on feeding twins and more.

GENDER–MIX AND BIRTHWEIGHT–IQ ASSOCIATION

Session: Poster

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It is widely known that there is an association between birthweight and childhood IQ. To control for confounding by familial factors Matte et al., (2001), studied this relationship in sibships of the same sex and found an association only in boys. The impact of genetic factors on this association can also be determined through the investigation of birthweight and IQ in twins. If genetic factors influence the association, for DZ twins the association between intra-pair differences in birthweight and IQ is expected to be positive, while for MZ pairs no association is anticipated.

With the Wechsler Intelligence Scale for Children–Revised (WISC-R), IQ was measured in 596 twin pairs with different intra-pair birthweights. The twins (173 DZ same sex, 169 unlike sex, 254 MZ, aged 8–14 years) were selected at random from the East Flanders Prospective Twins Survey. Zygosity was determined by placental examination, blood groups and DNA fingerprinting. Birthweight was obtained from the obstetrical record.

Comparison in MZ and same-sexed DZ twin pairs between co-twins with lowest and highest birthweight showed no significant association between birthweight and IQ. In male DZ pairs the association was suggestive but not significant.

In contrast, the same comparison in opposite-sexed twin pairs resulted in a significant association ($p = .02$). The effect is more pronounced when the female co-twin is heavier than her twin brother: her mean IQ (105.1) is significantly higher than that of female co-twins with lowest birthweight (IQ 99.6) and significantly higher than the mean IQ of same-sexed female DZ co-twins, whether of highest (IQ 99.2) or lowest (IQ 100.1) birthweight.

These results are very suggestive for a gender-mix effect mediating the association between birthweight and IQ. As co-twins are the same age and share influences such as prenatal factors, parental age and smoking, socioeconomic status, parity and gestational age, the influence of these possible confounders is negligible.

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MODELLING HERITABILITY IN LONGITUDINAL TWIN STUDIES

Session: Statistical Issues in Twin Studies II

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Latent growth curve models have been suggested for the analyses of longitudinal twin data.

Here we study the process of cognitive decline late in life based on a sample of twins from the Swedish Adoption Twin Study of Aging (SATSA), and we relate growth curve models for multivariate normal traits to the larger framework of latent variable models.

We define new measures of heritability and discuss their invariance to the chosen time scale and to the scale of the fixed effect covariates. We proceed by presenting a model for the dropout process, distinguishing dropout due to death and due to reasons other than death. A marginal approach and a random effects approach are contrasted when jointly modeling the mean dropout for the individual twin and the within twin pair dependence in dropout. Both the mean and the dependence structure may depend on observed covariates, such as zygosity. We end by discussing effects of superimposing different dropout models on the longitudinal twin models

SCHOOL ACHIEVEMENT: TWINS AND SINGLETONS

Session: Poster

M. S. Egorova, J. D. Chertkova, O.V. Parshikova, S. D. Pyankova, and N. M. Zyrianova
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The study tested the hypothesis that twins are at relatively high risk for learning problems. School achievement data were obtained from twins (2200 pairs of MZ twins and same and opposite sex DZ twins) and about 4500 singletons from the same school classes. Age of the subjects was 7–17 years. The sample is representative of the Russian school-age population. The results suggest that the youngest group of twins (7–10 years) is at an increased risk for learning problems: the differences between twins and singletons are significant, or of borderline statistical significance. The risk for learning problems for the older group (11–17 years) depends on family SES, intra-pair relations of twins, and twin sex and zygosity.

THE STRUCTURE AND HERITABILITY OF AGGRESSIVENESS

Session: Poster

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The present study investigates: (1) the relation between multiple dimensions of aggressiveness and the nature of their variation; (2) the relationship between aggressiveness and personality variables; (3) parent–adolescent relations and their role in the development of aggressiveness. There were 818 adolescent participants (14 and 16 year olds, boys and girls, with normal and delinquent behavior) included in the study. To measure aggressiveness we used two questionnaires and two projective methods. Subjects also completed Adjective Check List, and the Russian versions of Eyesenck Personality Questionnaire and Big-5 Questionnaire.

An obliquely rotated principle component analysis of the dimensions of aggressiveness yielded a five factor solution showing mutual independence of five dimensions of aggressiveness. The same analysis of the dimensions of aggressiveness and personality characteristics was conducted. Different measures of direct aggressiveness loaded on a factor of Neuroticism. Indirect aggressiveness loaded (negatively) on factors of Openness to the new experience and Agreeableness. Reactions to frustration loaded on a factor of Extraversion. Factor analysis of the aggressiveness and personality measures in the normal and delinquent groups showed variations in the content of factors.

THE GENETIC FACTORS IN CONGENITAL CLUBFOOT

Session: Pediatric Aspects of Twinning

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Clubfoot is one of the most common congenital orthopedic disorders with a reported incidence varying from 0.64 to 6.8 per 1,000 live births. Its etiology remains speculative and involves both environmental and genetic factors.

The purpose of this study was to establish a congenital clubfoot twin cohort that enables us to provide estimates of concordance.

Methods. The Danish Twin Register comprises more than 65,000 Danish twin pairs born between 1870 and 2001. In the spring of 2002, a questionnaire was sent to 46,418 twins born between 1931 and 1982, and 75% returned the questionnaire.

Establishment of zygosity is based on four questions of similarity with a calculated accuracy of approximately 95%.

The question "Were you borne with a clubfoot?" was answered by 34,485 twins. The sex distribution in these was 54% females and 46% males.

All the scientific–ethical committees of Denmark have approved the study.

Results. Ninety-four answered "yes" to the above question giving an overall self-reported prevalence of congenital clubfoot of .27% (c.i.l. .22–.34%) with female and male prevalence of .25% (c.i.l. .18–.33%) and .31% (c.i.l. .22–.41%) respectively ($p = .29$).

Fifty-five complete twin pairs (both twins answered the question) were identified, representing 12 monozygotic (MZ), 22 dizygotic same sex (DZss), 18 dizygotic other sex (DZos), and 3 with unclassified zygosity. Of these, 4 pairs were concordant, 2 MZ and 2 DZss. The pair-wise concordance was 17% (c.i.l. 2%–48%) for MZ, 9% (c.i.l. 1%–32%) for DZss and 5% (c.i.l. 0.6%–18%) for all DZ (DZtot). The proband-wise concordance was 29% (c.i.l. 7%–51%) for MZ, 17% (c.i.l. 5%–29%) for DZss and 10% (c.i.l. 4%–16%) for DZtot.

Conclusion. We consider the self-reported prevalence of .27% in this big cohort to be a reliable figure since congenital clubfoot is a relatively specific disorder not easily overlooked or mistaken for other frequent disorders. The fact that we did not find any difference between the two sexes is surprising since a female to male ratio of 1:2 is generally reported.

Our findings indicate that 1 in 6 of MZ twin pairs, 1 in 11 of DZss twin pairs and 1 in 20 of DZtot twin pairs both are affected. Our findings confirm that the risk of a second MZ twin being born with clubfoot is 1 in 3. It seems that the more genetically alike, the greater the risk of congenital clubfoot given that one twin is affected. We have found no evidence for a purely genetic origin of clubfoot.

MULTIPLE MATERNITIES IN FAMILIES WITH TRIPLETS AND QUADRUPLETS

Session: Twin Registers and Methodology

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We have studied in church archives the rate of multiple maternities among relatives of triplets born in Finland (1905–59), and of quadruplets born in Sweden (1746–1956).

Of the 631 sibships of triplets so far traced in Finland, 96 (15.4%) had one or more (up to four) recurrent multiple maternities. In these sibships the rate of recurrent multiple maternities was around 41/1000. Not only the estimated dizygotic twinning rate, but also the monozygotic twinning rate, seems to be almost three times as high as expected. In the sibships of the parents of triplets, multiple maternities were found in 12.9% of the sibships on the maternal side but in only 7.5% on the paternal side. In the sibships of 587 mothers of triplets, the rate of multiple maternities was 25/1000, but in the sibships of 570 fathers of triplets there was a low rate of twinning, 13/1000, which is even lower than in the general population (14.5/1000) for the period 1875–1929. Among other relatives of triplets there also seems to be a higher rate of twinning on the maternal than on the paternal side.

In 59 sibships of quadruplets in Sweden (1746–1956) the twinning rate was 47/1000. The twinning rate in sibships of the same-sexed quadruplets was 43/1000 and in sibships of unlike-sexed quadruplets 48/1000.

In the sibships of mothers of quadruplets in Sweden the twinning rate was 17/1000, which is only a little higher than in the general population (14.5/1000) for the period 1749–1959. Among the offspring of 31 sibs of the mothers of quadruplets, the twinning rate was 39/1000. Among the offspring of sisters of quadruplets the twinning rate was higher (47/1000) than among the offspring of brothers (30/1000). The offspring of the 54 sibs of the quadruplets had 251 children among 245 maternities, including 5 multiple maternities (one set of triplets) and the rate of multiple maternities was 20/1000. In one sibship there were two sets of twins.

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Work on the Swedish triplet families and on the Finnish quadruplet families is in progress.

Our results so far indicate that the inheritance of twinning or higher multiple maternities may be confined only to the dizygotic component, i.e. that Weinberg's differential rule does not hold true in families with repeated multiple maternities.

TWIN CHILDREN'S FRIENDSHIPS AND EXPERIENCES OF TRANSITION FROM HOME TO PRE-SCHOOL EDUCATION

Session: Poster

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Children who have supportive friendships have been found to adjust more readily to life transitions than those who do not have such support. The twin situation presents a particularly significant context within which to observe social relationships in a transition context. On entering an educational context a twin child has the experience of a life-long relationship with a same aged child. Is this supportive in the transition context or not? In negotiating new friendships the presence of a sibling might make a difference. Does the presence of a co-twin facilitate or disrupt friendship formation? Is separation into different classes a good thing or bad? This poster presents data from the study of a two-classroom pre-school unit in which, during 2003, there were 6 sets of twins and 1 set of triplets. Of these multiple birth children, ten (five pairs) agreed to participate in the study. The children were interviewed about their relationship with their co-twin, their friendships, twin identity and experience of transition from home to the pre-school setting. The data indicate the individual and unique nature of the transition experience for each individual twin child.

A CROSS-SECTIONAL STUDY OF HEIGHT, WEIGHT AND BODY MASS INDEX IN YOUNG ADULT ITALIAN TWINS

Session: Poster

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Introduction. Height, weight, and body mass index (BMI) are multifactorial characteristics responding to both genetic and environmental influences. A few estimates of their heritability (i.e. the proportion of variance due to genetic factors) have been made, and most of these exclusively within a univariate approach.

Aims. The aims of this study were:
- To estimate the heritability of height, weight and BMI, testing for possible sex differences.
- To determine whether the covariance between height and weight has a genetic or environmental basis.

Methods. The twin method was used in this study. The data set was derived from the Italian Twin Registry, and consisted of about 1100 twin pairs, all born in 1983.

The effect of genetic and environmental factors was estimated via Structural Equation Modeling. An univariate model for BMI and a bivariate Cholesky decomposition for height and weight were considered.

Results. For BMI, the heritability estimates were 0.86 and 0.87 in males and females respectively. No evidence was found for either common environment (χ^2 = 1.75, df = 2, p = .42), or sex differences (Chi^2 = 1.71, df = 3, p = .63).

A bivariate AE Cholesky model provided heritability estimates of .93 (males) and .94 (females) for height, and of .88 (males) and .90 (females) for weight. It also indicated that genes and environment were simultaneously responsible for the covariance between height and weight, as shown by a substantial genetic (rg) and environmental (re) correlation in both sexes (males: rg = .46, re = .42; females: rg = .48, re = .24).

CHANGE IN GENETIC AND ENVIRONMENTAL FACTORS ON BODY HEIGHT FROM DEVELOPMENT TO MATURITY: A CROSS-SECTIONAL EXAMINATION OF TWO BIRTH COHORTS OF ITALIAN TWINS

Session: Poster

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Introduction. Although the genetics of body height have been investigated in the past, most studies have focused primarily on adult individuals, in order to avoid possible distortions due to a phenotypic expression not yet completed.

Aims. This study examined the change in genetic and environmental factors on body height from the age of development to maturity. Heritability was expected to increase as a result of an increasing gene expression during development and a declining effect of common environmental influences at older ages.

Methods. In 2003, around 630 twin pairs from Northern Italy, born between 1985 and 1994 (age 8–18 years), and around 1100 twin pairs from throughout Italy, born in 1983 (age 20 years), were enrolled by mailed questionnaire in the Italian Twin Registry.

After pooling the data of the 2 cohorts, heights were residualised for age and the residuals were used in genetic modeling. An univariate ACE model allowing for different parameters both between cohorts and between sexes was fitted.

Results. A significant heterogeneity of parameters between birth cohorts was detected (Chi^2 = 75.120, df = 6). The best model incorporated all three sources of variance (A, C, E) for the youngest cohort, and only additive genetic and unique environmental variance for the oldest one. Under this model, the heritability estimate increased from 64% to 93% in males, and from 37% to 94% in females. Within the youngest cohort, common environmental influences appeared to be more important among females than males.

Results were independent of the different geographic location of twins.

ASTHMA AND ALLERGIC RHINITIS IN ITALIAN YOUNG TWINS

Session: Poster

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The relationship between asthma and rhinitis seems to be central to the overall understanding of the pathogenic mechanism of respiratory allergy. A number of twin studies on asthma and allergic rhinitis co-morbidity carried out in high prevalence areas suggested the presence of genetic factors common to both diseases.

In 2003, around 1700 twin pairs born between 1983 and 1994 (age 8–20 years) were enrolled by mailed questionnaire through the Italian Twin Registry. The occurrence of respiratory allergies was evaluated using the ISAAC (International Studies on Asthma and Allergies in Childhood) Project questionnaire.

The heritability of asthma and allergic rhinitis, as well as the correlation in genetic liability to these respiratory diseases, will be estimated under the assumption of the classical twin model.

Preliminary results show a lifetime prevalence of asthma and of allergic rhinitis of 7.7% and 17.1% respectively, with small differences within gender. The pair-wise concordance for asthma is .60 in MZ and .23 in DZ. As regards allergic rhinitis, the same figure is .45 in MZ and .20 in DZ. Structural equation modeling indicates that in this initial data set (300 pairs) around 75% of the variation in liability to asthma and allergic rhinitis (separately) is due to genetic effect.

Final results will be compared with those of other countries in order to evaluate whether the mechanism of genetic influences on respiratory allergy varies among different geographical areas.

HERITABILITY OF NECK PAIN

Session: Poster

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Introduction. The etiology of non-specific neck pain is not known. One study has shown a genetic influence on cervical disc degeneration. However, the relative importance of genetic and environmental factors on non-specific neck pain has yet to be established.

Objective. To determine whether genetic factors may partly explain presence of non-specific neck pain.

Materials and methods. In April 2002 a questionnaire was sent out to all twins born between 1931 and 1982 who were registered with the Danish Twin Registry and who had agreed previously to participate in future studies. In total 34,352 twins participated (74%).

Proband-wise concordance rates with 95% confidence intervals were calculated. Tetrachoric correlation coefficients of the liability of neck pain were estimated and through biometrical modeling (path analysis) the relative variability of genetic and environmental components of liability of neck pain were calculated.

Results. The proband-wise concordance rates for MZ (0.59, 95% ci 0.57 to 0.61) and for DZ (0.53, 95% ci 0.51 to 0.54) were statistically significant different (χ^2 30.5, df 1, p < .0001). The tetrachoric correlation

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coefficients for MZ (rMZ 0.45) and DZ (rDZ 0.21) indicated an additive genetic component with an AE model as best model fit (0.44 a2, 0.55 e2).

Conclusion. These results indicate a genetic influence on the presence of non-specific neck pain. Further studies will show how the genetic and environmental factors may interact on this trait (i.e. age and gender).

Acknowledgment. This study was supported by the Foundation of Chiropractic Research and Post Graduate Education.

DISAPPEARING REGIONAL HETEROGENEITY IN THE TWINNING RATES IN SWEDEN, 1751–1960

Session: Poster

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Sweden has the oldest continuous population records for a whole nation, beginning in the 17th century and including information about twinning. The twinning rate has been among the highest known among Europeans and has shown strong temporal and regional fluctuations. After the 1920s, an accentuated decrease in the rates of multiple maternities took place in Sweden; the twinning rate was hardly 50% of what it had been 200 years earlier (Eriksson & Fellman, 1973). Maternal age and parity cannot satisfactorily explain the temporal and regional differences in the twinning rate. Recently, we analyzed the regional and temporal variations in the twinning rate in Sweden and, in the absence of parity data, considered the crude birth rate as a proxy variable. The study confirmed the main result, earlier stressed by us, that differences in the twinning rates cannot be satisfactorily explained by demographic data on a macrolevel (Fellman and Eriksson, 1987, 2003).

We studied the temporal and regional variations in the twinning rate in the 25 counties of Sweden from 1751 to 1960 and tested the hypothesis that the twinning rates for the counties converge towards a common low level by presenting a geometrical model for the trends of the regional twinning rates. We also considered the range of the regional twinning rates for the period 1751–1960. The regional heterogeneity was also measured with the coefficient of variation. All these methods support our hypothesis that the regional variation is gradually disappearing. This study supports our earlier findings that the regional heterogeneity cannot be explained by differences in the distribution of the maternal age. We suggest that the convergence may be caused by the increased migration of citizens, leading to breaking up of isolates, and by increased urbanization and industrialization (Eriksson & Fellman, 2004)

CORRELATION BETWEEN THE TWINNING AND THE TRIPLET RATES

Session: Poster

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It has been noted that for populations and periods with high twinning rates the rates of higher multiple maternities are also high (Eriksson, 1973; Eriksson & Fellman, 1973). We analyze the association between the rates of multiple maternities based on correlation coefficients, which are suitable if there are approximately linear relationships between the variables. Statistical analyses of the correlation coefficients are presented elsewhere (Fellman & Eriksson, 2004). In order to eliminate the effect of time-dependent factors, we also study the partial correlation coefficients when time is kept fixed and the correlation coefficients for cross-sectional data.

We considered the rates of multiple maternities in Sweden and in its 25 counties for the period 1751–1960. After the 1780s particularly, a decreasing tendency can be observed in Sweden and consequently, the effect of external variables can be assumed to be monotonic. After 1960, the rates of the multiple maternities show marked increases caused by the increased use of ovulation inducers and in vitro fertilization. These increases are more accentuated for the triplet and quadruplet rates than for the twinning rate. The temporal variations in the twinning, triplet and quadruplet rates are rather similar. However, the minimum quadruplet rate appears already in the period 1931–60. We also noted that the strong variations in the rates could not be satisfactorily explained by maternal age. The correlation coefficients between time, the twinning rate and the triplet rate showed strong regional variation. The same was observed when we eliminated the time and considered the partial correlation coefficients between the twinning and the triplet rates and when we considered the correlations obtained in the cross-sectional regional data. Our opinion is that the variations are caused by other influential, time-dependent factors and that the effects of these factors show strong regional variation. Our general conclusion is that, after elimination of exogenous factors, the correlation between twinning rate and triplet rate is moderate.

GIFTEDNESS AND TWINNING

Session: Poster

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Based on the findings that:

- an increased dosage of testosterone during the crucial period of prenatal development results in right brain hemisphere dominance;
- the dominant right hemisphere and particularly the frontal cortical area is supposed to be the physiological marker of a "gifted brain";
- there is a close link between Spearman's g and frontal lobe functions which are necessary for the realization of the creative process;
- patients with the left-sided variant of fronto-temporal dementia showed the emergence of visual and musical talents;
- the right frontal cortex of Einstein's brain possesses a significantly greater neuronal density when compared with a control group of autopsied men;
- the population of gifted individuals exhibits right hemisphere dominance;
- there is a large number of left-handers among subjects with high intelligence and among the twin population;
- in adults the average level of testosterone is significantly higher in blood plasma if they are left-handed, ambidextrous and right-handed with the family left-handedness;
- left-handed individuals have a more strongly developed corpus collosum, which compensates for the unusual dominance of the right hemisphere;
- MZ male twins have increased levels of testosterone, and the right frontal dominance in MZ male twins may be a result of the joint prenatal life of male twins;
- more complicated skin patterns in MZ twins are situated often on the left hand (which corresponds to the right hemisphere) when compared with the single-born population;

we hypothesize the following: male twins during prenatal development have an increased exposure to testosterone that leads to a more complicated development of the right hemisphere, which becomes dominant. These peculiarities of male twins' development result in a potential giftedness. However, male twins rarely realize this potential due to unfavorable socio-psychological conditions during postnatal development. Our hypothesis provides explanation for widely scattered findings in physiological and psychological literature about androgens, intelligence, handedness, hemisphere specialization and twins. For the details of this hypothesis see Fingelkurts and Fingelkurts (2003) Gifted brain and twinning: Integrative review of the recent literature. Chapter 1. In *Advances in Psychology Research*, Vol 20 (pp. 3–32). Nova Science Publishers, Inc. Url: http://www.bm-science.com/team/chapt2.pdf

TAMBA PARENTING FOCUS GROUPS

Session: Poster

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In the UK there is a growing national focus on supporting parents and offering training to enable them to carry out effective parenting at different stages of their children's development. This training is offered by a range of parenting organizations and through statutory channels.

It became evident that there was a need to develop a course specifically aimed at parents of multiples to complement the work of other providers and to meet the unique needs of multiple birth families. In addition, it is hoped that developing Tamba's services in this new direction will enable the organization to access new sources of funding in the UK.

This presentation will discuss the pilot course run by Tamba in conjunction with Parentline Plus and the subsequent setting up in 2004 of focus groups to assist us in developing and refining the pilot sessions into a robust six-part course.

The course will offer parents opportunities to share experiences and explore solutions to their parenting situations in a supportive and non-judgmental environment.

We expect elements of the final course will include:

- sibling rivalry in a multiple birth family
- play with multiples
- being a parent of multiples
- parenting multiples after assisted conception
- parenting triplets and higher order multiples
- fathers of multiples.

The presentation will discuss lessons learned during the pilot course and focus group sessions. The parenting support needs identified in this recent work will be of interest to professionals and COMBO members.

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TAMBA STRATEGY IN ACTION

Session: COMBO I

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At ICTS 2001 Tamba presented work on strategic planning and development of the organization. The Twins & Multiple Births Association has since reached a milestone of 25 years of supporting families of twins, triplets and more in the UK. This presentation will demonstrate the organization's progress against these plans over the past three years and look at reasons for success and failure.

In particular the following strands will be discussed:

- infrastructure and membership development
- media and campaign work
- outreach project
- support services
- current challenges.

This overview of Tamba's work since the last ICTS will also touch on other areas of the organization's achievements which are being presented on more fully by other speakers at the Congress. It will also update participants on specific topics presented to COMBO in 2001, in particular progress on the campaign for more comprehensive financial support for multiple birth families in the UK.

THE ROLE OF GENES AND ENVIRONMENTS FOR ALZHEIMER'S DISEASE IN THE HARMONY STUDY: TESTING SEX-LIMITATION MODELS WITH AGE ADJUSTED THRESHOLDS

Session: Poster

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Background. Twin studies have shown high heritability for Alzheimer's disease (AD), yet have diverse limitations with respect to samples or methods.

Objectives. To evaluate heritability of AD in a total population of older twins, including like and unlike sexed pairs.

Methods. Cross-sectional design. All members of the Swedish Twin Registry aged 65 and older (N = 14,435) were screened for possible cognitive impairment, with suspected cases of dementia receiving complete clinical diagnostic evaluations. Relative importance of additive genetic, shared environmental, and non-shared environmental influences were estimated using Mx raw data option, applying a sex limitation model with ordinal data and with thresholds weighted by age.

Results. There were 392 pairs in which one or both members of the pair had AD. The best fitting model permitted equating parameters for men and women, and allowed for dropping shared environmental influences from the model without significant loss of fit. Heritability for AD was 79%, with 21% of the variation accounted for by non-shared environmental influences. The regression coefficient for age was –.07 for men and –.09 for women. For pairs concordant for AD, intrapair difference in age of onset was significantly greater in DZ than in MZ pairs, suggesting that there are also genetic influences for the timing of the disease.

Conclusions. In the largest twin study to date, we confirm that heritability for AD is substantial. Still, risk factors other than shared genes also play a significant role.

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INTRAUTERINE GROWTH CURVES IN TWIN PREGNANCIES: WHAT ARE THE DETERMINANTS?

Session: Current Developments and Findings from Twin Studies

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In the present study the influences of placental weight and cord insertion on intrauterine growth curves are shown. The analysis is based on data of twin pairs of the East Flanders Prospective Twin Survey (EFPTS) (Belgium), born between July 15, 1964 and June 5, 2003 (n = 6597 pairs). This population-based register accurately determines zygosity and chorionicity at birth on the basis of sex, placental structure and genetic markers, in combination with a questionnaire later in life. Pairs were excluded from analysis when one or both infants were stillborn, or when zygosity determination was less than .95 accurate.

Intrauterine growth curves were established by presenting cross-sectionaly birthweight and placental weight according to gestational age and location of cord insertion, taking sex, zygosity and chorionicity into account. The growth curves were compared by analysis of variance.

At birth male twins were heavier than female twins, DZ twins weighed more than MZ twins, and DC twins weighed more than MC twins. However, there were no differences in intrauterine placental growth for zygosity or chorionicity. Additionally, twins with a central cord insertion had higher intrauterine weights from week 32 onwards than twins with a peripheral cord insertion.

Conclusion. Location of cord insertion seems to be a more important marker for intrauterine growth than placental weight.

PREDICTORS OF REPRODUCTIVE FITNESS

Session: Behavioral Genetics

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Religion and education explain no more than 1% and 2% of variance respectively in reproductive fitness. Mortality and morbidity also make very little contribution, so it seems likely that behavioral factors account for much of the variation. Factors such as the increasing cost of living accompanied by a steady rise in the number of women who are better educated and in pursuit of careers are often cited when explaining the decline in fertility. Indeed, there are significant linear trends between fertility and education, SES, age at menarche, age at first reproduction, and age at menopause. However, none of these variables can explain more than 4% of the total variance. Likewise, measures of personality, psychological distress, family income, smoking, and political party affiliation have also failed to explain more than 2% in the variance fitness. We have developed a pilot questionnaire that measures personal, social and economic considerations relating to family planning and reproductive zeal. Our intention is to follow a younger cohort of Australian twins over time in order to identify which responses best predict reproductive fitness. To date, complete data are available from 586 subjects aged 17 to 25 years. An overview of the study design, work in progress, and summary statistics based on the available data will be presented. Included will be biometrical genetic model fitting results for several of the reproductive zeal measures.

ADULT RUSSIAN TWINS DURING THE TIME OF PERESTROIKA

Session: Poster

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This study has been performed in the context of the first Russian longitudinal adult twins' project, devoted to the analysis of genetic and environment influences on individual differences on psychological development during the transition from the early to middle adulthood. MZ and DZ twins were examined for first time at the age of 20–25 and for the second time at the age of 40–45 years. This period of twins' lives coincided with Perestroika in Russia. This poster presents data on life events and changes that occurred with the twins for the last 15 years, which were described and analyzed in the context of special conditions of this historical period, connected with cardinal transformations, reorganizations of social instability in structure of economic, social and psychological life conditions. The structural interview was developed and used in addition to the standardized methods. Life events and changes, taking place in spheres of twins' lives such as family and peer relation-

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ships, attitudes, work, socio-economic status, life style, and quality of life are described. Similarities and differences of the family structure in parental families and the twins' own families, twins' parenting styles, and within twin-pair relationships had been assessed. The emotional attitudes toward occurred events, the twins' satisfaction degree and degree of significance of these changes have been analyzed. The results show that twins went through a great number of life events and changes. Most of them were characterized as very stressful.

AN EXPLORATION OF PARENTS' EXPERIENCES OF SELECTIVE FETICIDE IN TWIN PREGNANCIES

Session: Psychosocial Issues in Families with Multiple Births

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Selective feticide is an option for parents following the prenatal diagnosis of an abnormality in one twin, or where the intra-uterine death of one or both babies appears imminent and one is sacrificed to give the other a chance of survival.

Parents with twins are more likely to be faced with this decision as congenital malformations are more common in multiple pregnancies. Until recently, selective feticide was contra-indicated in monochorionic twins because feticide of the affected twin would have resulted in the death of the healthy twin. However, new techniques have made this possible. Twin-to-twin transfusion syndrome (TTTS) occurs in approximately 10–15% of monochorionic twin pregnancies and is associated with an extremely high morbidity and mortality. The aim of this study was to learn more about parents' experiences of selective feticide, to explore the decision-making process, to investigate how parents cope with their experience, and to determine the appropriateness and level of support received by parents. Semi-structured interviews were carried out with five couples. Four of the couples were interviewed separately from their partners and a joint interview was carried out with one couple. The data analysis is ongoing and is being carried out according to the principles of Interpretive Phenomenological Analysis (IPA). The initial findings indicate a stark difference in the decision-making process between couples who terminate for a fetal abnormality and those who terminate for preterminal TTTS. The study explores how coping strategies tend to be linked to the meanings placed on the pregnancy, both by the parents themselves and by others, and the degree of isolation experienced by parents.

CEREBRAL PALSY AND INTRAUTERINE GROWTH IN TWINS: A EUROPEAN MULTI-CENTRE STUDY

Session: Health Prognosis and Twin Births

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Objective. To describe the relationship between birthweight for gestation and risk of cerebral palsy in twins.

Methods. Data from nine European cerebral palsy registers for the years 1976–1990 were harmonized and aggregated. Using both birthweight and fetal sex-specific growth standards for twins, a standard deviation score (Z-score) was derived for each case. Gestational age-specific cerebral palsy rates were calculated for each Z-score band, and rate ratios compared with the a priori Z-score reference band of 0.67 to <1.28 (equivalent to the 75th to <90th percentiles).

Results. The analysis included 373 cases of cerebral palsy in twins. For births at > = 32 weeks' gestation, the patterns of cerebral palsy rates were similar for both standards: the rates were higher for both light and heavy-for-gestation babies compared to the optimum weight for gestation in the reference Z-score band. The rate ratios were significantly higher for twins in Z-score band below –1.28 (<10th percentile) compared to the reference band.

However, for preterm births (<32 weeks), the significantly higher risk for cerebral palsy in light-for-gestation babies was only observed when using fetal growth standards.

Conclusions. An increased risk of cerebral palsy in twins is associated with deviations from optimal intrauterine growth for babies born at >= 32 weeks' gestation, as was earlier reported for singletons (Jarvis S., Glinianaia S.V. (2003) Lancet, 362, 1106–11). The pattern for twins born at lower gestational ages is not so consistent, but this may be partly an issue of identifying appropriate weight standards for preterm twins.

STATISTICAL METHODS FOR DRAWING CAUSAL EFFECTS FROM TWIN STUDIES

Session: Statistical Issues in Twin Studies II

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While the goal of many twin studies is to quantify the causal effect of an exposure on an outcome, most commonly used statistical methods provide measures of association, not of causal effect. Recent developments in statistical methodology have offered new insights on how causal effects can be inferred from observational data. In this talk, we investigate how these results can be extended and applied to draw causal inference from twin studies. We use the results to estimate the effects of assisted reproduction techniques (ART) on perinatal outcomes from 4,988 twins. All data were collected within the framework of the East Flanders Prospective Twin Survey (EFPTS) (Belgium), which prospectively collects information on all multiple pregnancies born in the province of East Flanders. These data are unique for estimating the causal effects of iatrogenic (multiple) pregnancy because they contain accurate information on zygosity and chorionicity by means of systematic placental morphology examination, determination of cord blood groups and DNA fingerprinting. Probabilistic causal networks, d-separation rules and potential outcome methods (Pearl, 2000) are used to reveal how causal effects can be inferred from the available data. Subsequently, appropriate generalized estimating equations are used to estimate those effects. Comparisons with the more conventional genetic structural equation models (Neale & Maes, 2002) will be made.

A TWIN STUDY OF GENETIC AND DIETARY INFLUENCES ON KIDNEY STONES

Session: Complex Disorders III

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To examine genetic and non-genetic factors associated with kidney stones, a twin study was conducted using the Vietnam Era Twin (VET) Registry. The VET Registry is a sample of 4774 male twin pairs born in the US between 1939 and 1955. In 1990 a mail/telephone health survey was administered to Registry twins; the survey included a question on the doctor diagnosis of kidney stones and a food frequency questionnaire. Twin concordance rates and correlations were used to estimate heritability. Odds ratios (OR) with 95% confidence intervals (CI) were obtained for dietary factors in twins discordant for stones. The response rate to the survey was 71% (3391 pairs). The proband concordance rate for kidney stones in MZ twins was significantly greater than in DZ twins (32% vs. 17%; $p < .001$). The tetrachoric twin correlations for kidney stones were 0.59 in MZ and 0.31 for DZ pairs; the heritability of kidney stones was 56%. In the analysis of diet, daily intake of milk (2+ vs. 0 cups, OR = 0.4, 95% CI 0.2, 0.9) and coffee (5+ vs. 0 cups, OR = 0.4, 95% CI 0.2, 0.9) were protective against kidney stones. Solid dairy products, fruits and vegetables, meat and fish, tea, and calcium supplements were not associated with kidney stones in a multivariate analysis. Our results suggest that the development of kidney stones is strongly influenced by genetic factors. The protective effects of milk and coffee consumption confirm the results from earlier cohort studies. Further research identifying the genetic basis of kidney stone formation and potential gene by environment interaction effects is warranted.

DELIVERY MODE IS THE MAJOR DETERMINANT OF STRESS URINARY INCONTINENCE IN PAROUS WOMEN: ANALYSIS OF 288 IDENTICAL TWINS

Session: Twin Registers and Methodology

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Objective. Identical twin studies are regarded as an ideal methodology for assessing environmental disease factors. We conducted a survey at the 2003 Twins Days Festival, to evaluate modifiable risk factors associated with stress urinary incontinence (SUI).

Methods. The 67-item survey was completed by 144 identical twin sister pairs ($n = 288$). To account for correlated data within pairs, we implemented logistic regression models for repeated binary measures. Medical,

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obstetrical and demographic factors underwent univariate analysis and entered multivariate regression based on $p < .25$. Three models were utilized: (A) all pairs including those with nulliparous women ($n = 288$), (B) pairs for which both sisters gave birth by either vaginal or cesarean delivery ($n = 196$), and (C) pairs for which both sisters had at least one prior vaginal birth ($n = 146$). This enabled evaluation of risk factors while maintaining statistically valid reference groups.

Results. Mean age was 47.5 (21–79), parity 1.8 (0–7), 45% menopausal, mean BMI 26.6, 90.3% Caucasian and 7.0% Black. SUI was reported by 53.9%. Among parous women, 83.8% had > 1 vaginal birth, and 65.5% of them reported SUI; among 16.2% who delivered by "cesarean only", 35.5% reported SUI. Regression Model A focused on non-obstetrical factors, confirming associations between SUI and age > 40 (OR 4.6, $p = .001$), menopause (OR 1.8, $p = .02$), parity ($p = .001$) and BMI > (OR 2.8, $p = .002$). The major study findings derive from Model B, assessing obstetrical risk factors in parous-parous twin pairs. This model revealed delivery mode as the only factor independently predictive of SUI — with delivery by "cesarean only" conferring a nearly three-fold reduction in risk relative to women with prior vaginal birth (OR 0.36, $p = .013$). Model C evaluated factors specific to vaginal birth. Neither forceps (OR 1.8, $p = .16$) nor episiotomy (OR 1.2, $p = .71$) were significant.

Conclusions. This is the first application of an identical twin research design to female incontinence. Among all modifiable factors, delivery mode was the most potent determinant of post-reproductive incontinence, with vaginal birth conferring a markedly higher risk of SUI (OR = 2.78, $p = .013$) than cesarean. These findings may provide new insight into the epidemiology of female incontinence, and the impact of obstetrical choices.

TWIN DELIVERY VS. SINGLETON DELIVERY: KEY DETERMINANTS OF INCONTINENCE RISK AFTERWARDS

Session: Controversies on Obstetric Issues

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Background. Debate on the obstetrical management of twin pregnancies has centered mostly on fetal outcomes, with scant attention devoted to maternal pelvic floor conditions that may adversely impact on quality of life. We compared rates of stress urinary incontinence (SUI) among "mothers of twins" and "mothers of singletons" of equal parity, and assessed potential risk factors.

Methods. Anonymous questionnaires were administered to "Mothers of Twins" attending the National Organization of Mothers of Twins Club's annual convention, and to "Mothers of Singletons" attending the 2003 Twins Days Festival. The sample consisted of 329 women, each reporting a total parity of two, including 78 mothers of two singletons, and 251 mothers of twins with no additional singleton births. Explanatory variables were chosen to enter multivariable models based on $p < .25$, and included gestational order (single vs. multiple), delivery mode, age, weight of largest baby and hysterectomy. Chi^2, *t*-tests and multiple logistic regression were performed using SAS.

Results. Within the study sample($n = 329$) the mean age (*SD*) was 38.5 (8.5) years; 35.0 for mothers of twins versus 45.1 for mothers of singletons ($p < .001$). Mothers of twins were 7.7 times more likely to have delivered by cesarean than mothers of singletons ($p < .001$), and reported lower rates of stress incontinence (34.3 vs. 55.1%, $p = .001$). Univariate analyses revealed the following to be associated with SUI: Multiple gestation, vaginal delivery mode, increasing age, and hysterectomy. According to the final regression model, SUI was associated negatively with "cesarean only" birth mode (OR 0.54, $p = .018$) and positively with age > 40 (OR 2.5, $p = .002$). Gestational "order" (twins vs. two singletons) did not remain significantly predictive of SUI ($p = .80$) after controlling for delivery mode and age.

Conclusion. Birth mode is a key determinant of post-reproductive urinary incontinence, with lower rates following cesarean delivery. Within this cohort, sharply higher rates of cesarean among mothers of twins appeared to underlie a decreased risk of subsequent incontinence. Conversely, among mothers of singletons a greater tendency towards vaginal birth mode was associated with increased risk of incontinence. As "optimal" obstetrical guidelines for twin delivery continue to undergo debate, implications of various strategies on the maternal pelvic floor should be considered.

THREE-GENERATION GENETIC AND EPIGENETIC PERSPECTIVE FOR BIODEMOGRAPHY AND TWINNING

Session: Pediatric Aspects of Twinning

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Unlike males, newborn girls have all their gametes ready. Oöcytes are the largest, most complex human cells, wherein development begins long before fertilization. A generation g(n) individual develops from g(n – 1) mother's egg cell, which became an oocyte under genetic, epigenetic and gestational influences from the g(n – 2) grandmother. Every oocyte physically, genetically and epigenetically links three generations. This understanding is fundamental for robust reproductive biodemography, including twinning. Three passages between primordial germ cells and primary oocytes in g(n – 2) gestation have fundamental implications for healthy development for at least two subsequent generations:

1. Meiosis-I, beginning in g(n – 2), finishing in g(n – 1) 10–50 years later is error-prone; 80–90% of all aneuploidies arise there (Science (2002), 296, 2181–3).
2. Several dozen parentally imprinted loci regulate critical aspects of reproduction and embryogenesis. Imprint resetting in oogenesis requires erasure, X-reactivation and epigenetic maternalization — all variable and fallible. Imprinting error may predispose a blastocyst to twinning and generate MZ discordance for disorders of imprinted genes (Lancet (2003), 361, 1975–7). Epigenetic dynamics of the primary oocyte in the g(n – 2) generation or its maturation in g(n – 1) may produce genotype/phenotype changes in g(n) cohorts.
3. The germ cell pathway is the most sensitive target for insertional mutagenesis via mobile elements, yielding clusters of similar mutations or developmental defects in successive generations. Such events common in viral epidemics need reanalysis from this three-generation perspective. Effects of the 1918 influenza pandemic on the genotype/phenotype pattern of individuals whose grandmothers were pregnant in 1918 must be compared with cohorts from grandmothers pregnant before and after. Similar genetic/demographic analyses must be applied to environmental catastrophes like Chernobyl. This approach is a logical cornerstone for biodemographic studies including temporal variation in rates of twinning and associated anomalies.

DISPERMY AND RESULTING TWIN/MOLE ODDITIES

Session: Poster

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A reasonable estimate suggests that about 7% of human oocytes are dispermic. At least four resulting abnormal scenarios are expected:

1. fusion of all pronuclei and occurrence of diandric triploidy and partial moles;
2. immediate depolarization of triploids;
3. developmental repression of female MII products, fusion of two male pronuclei and complete mole appearance;
4. equal oocyte division with extrusion of large second polar body and possible fertilization of two female MII products resulting in twins.

These twins will have two distinct paternal genomes but two similar maternal genomes, differing only due to female crossing-over in MI. Such twins were labeled as the Sesquizygotic or SZ twins, hardly differing from usual DZ. There is direct and indirect cytogenetic and molecular evidence that three reproductive oddities: dispermic triploidy, diploid androgenesis (complete moles) and SZ/DZ twinning exist as interconnected entities. They depend on paternally transmitted genes that express in the haploid male gametes.

The preferable choice of one dispermic scenario of fertilization decreases the others. This approach can explain the old ethnic twinning enigma: higher mole incidence and lower DZ twin rate in Japan and some other Asian populations. Postzygotic diploidization of androgenic diploids presents explanation for diverse unusual cases of twin/moles associations and mosaic/chimerism (Golubovsky, 2003).

INFANT FEEDING AND SLEEP IN TWINS AND SINGLETONS

Session: Poster

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Although the relationship between sleep behavior, and somatic, psychological, and relational factors has been studied, the factors influencing sleep in infancy are still not well understood. However, night waking in infants has been found to be associated with breastfeeding. In Norway, the rate of breastfeeding is very high, and often continued towards the

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child's first birthday, even though most women work outside the home. The rate of breastfeeding in Norwegian mothers has increased during the last thirty years compared to preceding decades. At the same time, there has been a large increase in women joining the workforce. Earlier data (1996) showed that twin mothers breastfeed at about the same rate and length of time as mothers of singletons. Thirty years ago, bottle feeding, especially in twins, was the recommended practice. The health policy of strongly advocating breastfeeding well into the child's first year, and the long maternity leave with full pay and time off to breastfeed, are likely to be contributing factors to this rather recent cultural change in feeding method. No large scale data on sleep practices and frequency of sleep problems in infants and small children are available from the same period.

In the present study four samples are studied: A cohort of twins (n = 103 pairs) born in 1970, almost all bottle fed, were studied at nine months, and mothers' reports on their children's sleep behavior, including night waking, were recorded. A similar twin sample born in 1995–96 (n = 92 pairs) were studied at the same age, along with a sample of singletons (n = 24) born at the same time. Almost all the twins and singletons were breastfed at the age of nine months. Their sleep behavior was recorded in the same manner as in the first twin sample.

A large national study is ongoing in Norway, where data are collected on singletons and twins. Their mothers are requited to the study in pregnancy, and followed through their child's first and second year. The fourth sample is from this large national sample (n = about 4000), studied at the same age as the other samples, on the same variables, to answer the research questions on the relationship between feeding method and sleep behavior, especially night waking, and the total amount of sleep, in twins, and in singletons. It is also of interest to study the rate, amount and length of breastfeeding in the large national sample to follow the cultural trend in preferred feeding practice for mothers of twins and singletons.

COMPLETE HYDATIDIFORM MOLE AND COEXISTING LIVE FETUS IN DICHORIONIC TWIN PREGNANCY: REPORT OF TWO CASES

Session: Poster

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Background. Multiple pregnancies consisting of a complete hydatidiform mole and coexisting live fetus are relatively rare, arising 1 in 20,000–100,000 pregnancies. Hydatidiform mole is a premalignant condition and early evacuation of the uterus is mandatory. The management of these pregnancies is difficult because they can be associated with complications such as fetal death, vaginal bleeding, pre-eclampsia, and an increased risk of persistent gestational trophoblastic pregnancies.

Cases. We report two cases of dichorionic (DC) twin pregnancies at 11 and 14 weeks of gestation consisting of coexisting live fetuses. Case 1 and Case 2 were 43 and 22-year-olds respectively. We offered prenatal management and pregnancy termination after both parents were informed about possible persistent gestational trophoblastic disease. The parents of both cases opted for pregnancy termination. The beta-hCG levels of Case 1 and Case 2 at diagnosis were 1,100,000 mIU/ml and 1,200,000 mIU/ml. The pregnancies were uneventfully terminated by suction curettage and pathologic examination confirmed the complete hydatidiform mole with coexisting normal DC twin pregnancies. The hCG levels declined appropriately on follow-ups.

Conclusion. The management of DC twin pregnancy, with pregnancy termination in the complete hydatidiform mole and coexisting live fetus is controversial, and the decision-making process is a dilemma for the physicians and parents. Large case series and randomized studies are needed to develop definitive protocols.

ACARDIUS ACEPHALUS PYGOPAGUS TETRAPUS PARASITIC TWIN

Session: Poster

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Background. Although conjoined twins are rare, there are now many reports of symmetric and asymmetric cases in the literature. We report a case of acardius acephalus pygopagus tetrapus parasitic twin.

Case. The case was a 30-year-old, gravida four woman referred to the maternal fetal unit due to polyhydramnios at 28 weeks of gestation. She had no history of medical illness and screening for gestational diabetes was negative. Detailed ultrasonographic scanning was done to look for fetal anomaly. Ultrasonographic examination revealed polyhydramnios with amniotic fluid index 30 cm and two rudimentary lower extremities joint at sacrum in addition to normal lower extremities. Scanning for cranio-spinal, thoraco-abdominal, gastrointestinal and genitourinary system was normal. The case was delivered by caesarean section at 38 weeks. The newborn was operated at the neonatal period after diagnostic investigation confirmed conjoined twin at sacrum but no relation with spinal canal. Rudimentary lower extremities were resected. The postoperative period was uneventful and the newborn was discharged as healthy. Post-natal follow-up was normal at one year of age.

Conclusion. Acardius acephalus pygopagus tetrapus parasitic twin is a rare conjoint twin with a favorable outcome.

A COMPARATIVE STUDY OF ATTACHMENT STYLES AMONG TWINS AND SINGLETONS

Session: Poster

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The infant–mother affectional bond influences the infant's attachment behavior. The mother–child relationship is considered as the main determinant of attachment style. The aim of this study was to examine the effect of co-twin presence on the development of attachment style. The participants were 30 twin pairs (n = 60) and 60 singletons. All participants (n = 120) were asked to complete the adult attachment inventory (AAI). Twins presented secure attachment style more than did singletons, and identical twins showed secure attachment style more than did fraternal twins; none of the results were statistically significant. However, the higher frequency of twins' secure attachment styles compared to the lower frequency of singletons` secure attachment styles could be explained by the proximity of a familiar person (the co-twin). This proximity expands the level of security through mechanisms of "relational system", "dependency" and "compensation" which in turn increases the frequency of twins' secure attachment styles. In the article results and implications are discussed.

DO COMMON GENES INFLUENCE MEASURES OF PELVIC ORGAN AND ELBOW MOBILITY?

Session: Poster

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Disorders such as pelvic organ prolapse and urinary incontinence have a considerable impact on women's health and have been associated with a lifetime risk of surgery of over 10%. Environmental influences have been widely studied, and a range of risk factors identified, with pregnancy and childbirth being the most influential. However, positive family histories and ethnic differences suggest that genetic factors are also influential. We examined measures of bladder neck and joint mobility (measures that have been associated with incontinence and prolapse in previous studies) and urethral rotation in a sample of 178 young, nulligravid, Caucasian female co-twins and their non-twin sisters to determine the heritability of these measures and the degree of genetic covariation between them. Genes appeared to influence about half of the variation in all measures. The pelvic organ measures were associated with elbow hyperextension at a phenotypic level (r = .19–.23) and these associations appeared to be almost entirely due to the influence of a common genetic factor (genetic r = .34–.56, unique environmental rs close to zero). Genes influencing elbow hyperextension accounted for 8% to 13% of the variation in the pelvic organ measures. We speculate that genes influencing connective tissue structure or metabolism may underlie this association.

A GENOME-WIDE STUDY FOR BITTER TASTE TO PROP IN THE BRISBANE ADOLESCENT TWIN SAMPLE

Session: Poster

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Since the 1930s it has been known that some individuals cannot taste phenylthiocarbamide (PTC) while others perceive it to be bitter. While this trait has been studied extensively, with 50% of individual variation attributed to genetic influences, it shows complex inheritance and the relevant genes have not been identified. We studied bitter-taste perception in a sub-sample of Brisbane adolescent and young adult twins (79 MZ & 157 DZ pairs, 96 non-twin siblings, aged 12–25 years). Participants rated the intensity of the bitterness of a saturated PROP (6-n-propylthiouracil) solution, which is chemically related to PTC, on a labeled-magnitude

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scale (i.e., continuous scale with seven descriptive words describing the intensity of the bitter taste). The mean intensity rating was 40.6 (28.8*SD*) units, corresponding to a rating of "strong". In concordance with previous work we found 58% of the variation in the perceived bitterness of PROP was due to additive genetic influences, and 42% to unique environmental factors and experimental error. A genome wide scan consisting of 753 markers, at an average spacing of approx. 5cM, was available for 346 participants from 154 families, mostly comprising a dizygotic twin pair and parents. Suggestive linkage to a region on chromosome 10 (lod 2.39 at marker D10S1426) and to a lesser degree on chromosome 13 (lod = 2.15 at marker D13S159) were indicated, but linkage to the previously reported regions on chromosomes 5, 7 and 12 was not supported. These analyses are currently being updated with a larger sample.

MAJOR GENETIC INFLUENCE ON THE REGULATION OF THE PITUITARY-THYROID AXIS: A STUDY OF HEALTHY DANISH TWINS

Session: Current Developments and Findings from Twin Studies

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Background. Intra-individual variation is smaller than the inter-individual variation in serum thyrotropin (TSH), free thyroxine (T4) and free triiodothyronine (T3) concentrations. This suggests that each individual may have a genetically determined thyroid function set-point.

Subjects and methods. A representative sample of self-reported healthy twin pairs was identified through the Danish Twin Registry. A total of 284 monozygotic (MZ), 286 dizygotic same sex (DZ), and 120 opposite sex (OS) twin pairs were investigated. A classical twin study was performed. After adjustment for age, sex and other covariates the intra-class correlations of serum TSH, free T4 and free T3 were calculated. To elucidate the relative importance of hereditary and environmental factors on the variation of these hormone levels, quantitative genetic modeling was used.

Findings. The intraclass correlations were consistently higher for MZ twin pairs than for DZ twin pairs. Regression analysis suggested that iodine intake played a small but significant role for the concentration of serum TSH and free T4, whereas cigarette smoking was without influence. In quantitative genetic modeling the heritability (with 95% confidence intervals) accounted for 64% (57% to 70%) of the variation in serum TSH concentration, and 65% (58% to 71%) and 64% (57% to 70%) for the concentrations of free T4 and free T3, respectively.

Interpretation. Genetic factors play a substantial role in controlling the pituitary-thyroid axis, indicating that each individual has a genetically determined thyroid function set-point. Whether this is of importance when treating individuals in whom pituitary-thyroid function has been disrupted by, for example, hypo- or hyper-thyroidism, remains to be clarified.

GENETIC AND ENVIRONMENTAL INFLUENCES ON BRONCHIAL RESPONSIVENESS AND EXHALED NITRIC OXIDE IN ADULT TWINS

Session: Poster

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Bronchial hyper-responsiveness (BHR) and levels of exhaled nitric oxide (NO) are intermediate phenotypes associated with, but not specific to, asthma. We explored genetic and environmental influences on BHR, NO, and the association between these measures.

Methods. The data were collected as a sub-study to the twin study at the Norwegian Institute of Public Health. Lung function was assessed by dynamic spirometry; bronchial responsiveness was assessed using a methacholine provocation test. BHR was recorded as the cumulative dose that caused a 20% fall in forced expiratory volume. Exhaled NO was measured by a chemiluminescence analyzer. The raw data were analyzed using structural equation modeling in Mx. to estimate the genetic and environmental influences on the phenotypic variances and the covariance between BHR and exhaled NO. Age, sex, smoking status and atopy were included in the models as covariates.

Results. A completely environmental model best explains variation in BHR, with shared environment accounting for 30 percent of the variation. Genetic effects explain approximately 57% of the variation in exhaled NO but there was no evidence of shared environment. The association between BHR and exhaled NO was small but significant (r = .14; p = .0056). The cross-twin cross trait correlations .23 (MZ) and .04 (DZ) suggest that genetic effects contribute to the association between these measures, and the most parsimonious model retained only the genetic correlation. In these data the small association between BHR and exhaled NO seems to be primarily explained by common genetic effects.

DOUBLE TROUBLES: EXAMPLES OF SPECIAL ETHICS ISSUES IN TWIN STUDIES

Session: Ethical Issues in Twin Studies

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Many of the ethics-related issues facing twin researchers are identical with those that characterize any study based on human participants. However, twin studies also raise some unique questions that could have implications for the development of research protocols, consent forms and ethics-related procedures of the particular study. This presentation will draw on experiences encountered by twin researchers in several European countries to illustrate some of these special issues. The perspective and personal story of a twin family member will also be presented.

GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO BACK AND NECK PAIN IN OLD AGE. A POPULATION BASED STUDY OF 2108 DANISH TWINS AGED 70 AND OLDER

Session: Aging and Longevity II

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Objectives. To determine the relative contribution of genetic and environmental factors in back and neck pain in old age.

Methods. Data on the one-month prevalence of back and neck pain from twin pairs participating in the population based Longitudinal Study of Aging Danish Twins formed the basis of this analysis. To assess twin similarity, proband-wise concordance rates, odds ratios and tetrachoric correlations were calculated and compared for monozygotic and dizygotic twins. Further, heritability estimates were calculated using bivariate probit estimation. Odds ratios for known environmental effects were estimated after controlling for age, sex and genetic effects.

Results. Modest or low and non-significant differences between monozygotic and dizygotic twin pairs were found for proband-wise concordance rates, odds ratios and tetrachoric correlations for both men and women. A current or previous diagnosis of osteoporosis, degenerative joint disease or lumbar disc prolapse was found to significantly affect the risk of back pain and rheumatoid arthritis, osteoarthritis, disc prolapse, and coronary heart disease significantly affected the risk for neck pan. Additive genetic effects explained approximately a quarter of the liability to report back pain in men and none of the occurrence in women. For neck pain no dominant genetic, additive genetic, or common environmental effects were found.

Conclusion. Additive genetic effects are modest contributors to BP in older men but not in women. Genetic factors play only a minor role in neck pain in old age.

CROUCHING TARGET, HIDDEN REGULATIONS

Session: Ethical Issues in Twin Studies

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"GenomEUtwin" is the moniker given to the multi-centre research project that uses twins to identify and study genes and environments that predispose to complex traits and diseases. The coordination and harmonization of ethics procedures in such multinational projects presents a host of challenges that are critical to the successful conduct of the research. October

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1 2002 was the official start date of the GenomEUtwin Study. Since then the Italian Data Protection Act has been updated (2003) and Biobank legislation has been introduced in Norway (2003) and Sweden (2002). These changes have had practical implications on the GenomEUtwin study, for instance, Sweden can include permission for future research studies in their participant consent letter whereas Norway cannot. Additionally, the participating Norwegian centre must now seek permission from the Ministry of Health in conjunction with the Regional Ethics Committee and Data Protection Agency in order to send its samples for gene analyses to Sweden and Finland as part of the GenomEUtwin study. The ramifications of recent changes on both the national research centre and potential twin cohort will be outlined. An update will be given of the legal framework of the individual partners and a brief description of proposed future legislation (and creation of new regulatory bodies) that may impact the study.

HOW CAN WE BEST ASSESS THE IMPACT OF A MULTIPLE PREGNANCY UPON THE FAMILY?

Session: Psychosocial Issues in Families with Multiple Births

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It is easy to list the things that may go wrong, medically or psychosocially, in a multiple pregnancy. It is much more difficult to identify why one family but not another may cope well with such issues. In the last few years we have been developing the widely-used ABCX model to identify A (stressors), B (support) and C (perceptions of stress and support) to quantify differences in coping style. This is illustrated with qualitative and quantitative data from the 200 families in our prospective study, which involved families from the time of diagnosis of multiples until the twins were six months old. Qualitative analysis of the interviews and diaries identified three key predictors: the relationship of mothers with their doctor and other health professionals, the perceived support from partner and family, and the quality of information (with much concern about the lack of local, recent, multiple-specific information). There was surprisingly little difference between those families who had used assisted reproduction, and those where the pregnancy was planned or unplanned.

Health professionals may want to think more about how their work is perceived by the multiple birth family and may also need to think more globally about how the pregnancy and birth are perceived by the family in the context of all the other possible stressors and supports in their lives. Not enough thought has been given to how a multiple birth impacts upon key aspects of the parenting role, both pre- and postnatally, for fathers as well as mothers.

THE "MULTIPLES IN SCHOOL" WEBSITE THREE YEARS ON

Session: COMBO II

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Our Multiples in School website — www.twinsandmultiples.org — was launched at the 2001 Congress. Since then there have been over 250,000 hits, it is listed extensively on search engines, and permission has been given to reproduce sections in many venues throughout the world and to translate parts into several languages. This presentation focuses on three issues:

What can be done to develop the site further?

While this is limited by our resources and the lack of evidence-based practice on multiples in school, two of the most frequently raised issues have been the management at home and school of very competitive multiples, and the provision of more information on multiples in secondary school. For technical reasons the Forum section was difficult to establish but is now functional — how best can it be used?

How can the website be more publicized and used more effectively?

Many families find the website too late, for example, after one twin has been awarded entry to a selective school, a point explicitly discussed in the website. Pat Preedy, Diane Galloway and Ann Thomas have developed a CD to help educate parents and teachers in the use of the website.

How best can we meet the needs of other countries?

In most First World countries the website has met with much acceptance despite differences in school systems. Many of the same issues arise in developing countries — what can be done by us and by COMBO to tailor the information appropriately?

SERUM FERRITIN AND FETAL GROWTH IN TWIN PREGNANCIES

Session: Poster

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Objective. To evaluate the relationship between serum ferritin levels and maternal weight gain, iron-deficiency anemia, and fetal growth in twin pregnancies.

Study Design. Serial measures of iron status, maternal nutritional status, and weight gain were collected on 105 mothers of twins.

Results. The mothers averaged 32.4 +/– 5.2 years, had body mass indices of 24.6 ± 5.8 kg/m2, were primarily white (86%) and primiparous (53%). Weight gain by 24 weeks (WG24) was 12.3 +/– 5.0 kg, and twin birthweight averaged 2497 +/– 459 g at 35.6 ± 2.0 weeks. Consistent with greater blood volume expansion, serum ferritin levels declined precipitously throughout pregnancy ($p < .01$). Adjusting for ethnicity, parity, and smoking (mean ± SE), ferritin levels were 63.4 +/– 4.4 microg/L first trimester, 35.7 +/– 3.1 microg/L second trimester, and 12.0 +/– 2.6 microg/L third trimester. Average third trimester levels were therefore at the usual cut-off for defining iron deficiency (12 +/– g/L). After length of gestation (177.1 +/– 13.2 g/week, $p < .001$), WG24 was the most significant predictor of twin birthweight (16.3 +/– 6.0 g/kg weight gain, $p < .008$). However, third trimester ferritin levels were actually lower with increased WG24 (–0.17 +/– 0.07 kg/mcg/L, $p = .01$). In the third trimester, ferritin levels averaged 16.8 +/– 1.8 microg/L and twin birthweights 2379 +/– 75 g for those with WG24 < 9.1 kg. In contrast, ferritin was 10.4 +/– 1.4 mcg/L and birthweights 2603 +/– 59 g for those with WG24 > 15.5 kg ($p < .05$). Levels of hemoglobin (g/dL) did not differ at varying levels of WG24.

Conclusions. These findings indicate that while most mothers of twins may have serum ferritin levels in the third trimester consistent with iron deficiency, unlike for singletons, this may actually be a clinical indicator of better fetal growth, as iron stores are utilized to support the growth of two fetuses.

MID-UPPER ARM CIRCUMFERENCE (MUAC) CHANGES IN LATE PREGNANCY PREDICT FETAL GROWTH IN TWINS

Session: Poster

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Objective. To test the hypothesis that changes in arm anthropometry can be used to determine risk of faltering growth in twin gestations.

Study Design. Serial data on mid-upper arm circumference (MUAC) and weight gain were collected on a sample of 50 mothers of twins receiving prenatal care through a special program for multiples. Changes in MUAC were monitored from 20–34 weeks, subsequent to the early weight gains associated with fetal growth in twins (0–20 weeks). Over this interval, MUAC should continue to increase, reflecting initially an increase in maternal fat and lean body mass (LBM), and later (28–34 weeks) increases in LBM alone. The concern is that mothers of twins may continue to evidence large weight gains, but may actually be losing LBM if unable to support fetal growth.

Results. The 50 mothers of twins were relatively older (age 32.4 ± 4.7 y), had above average body mass indices (BMI, 24.1 ± 5.5 kg/m2), and relatively high rates of weight gain (0.57 ± 0.21 kg/wk). The women were primarily white (90%), primiparous (50%), and 14% were obese (BMI > 29 kg/m2). Adjusting for gestation at delivery, black ethnicity, number of males, and pregravid BMI, a low rate of weight gain through 20 weeks (<0.40 kg/wk) was associated with a lower average twin birthweight (–173.8 ± 58.9 g, $p < .006$). From 20–34 weeks, there was no net change in MUAC (rate –0.01 +/– 0.17 cm/wk), but there was a highly significant correlation between weight gain at 20 weeks and subsequent change in MUAC ($r = 0.43$, $p < .002$). In models adjusting for gestation at delivery, black ethnicity, and number of males, both the rate of MUAC change and the percentage of MUAC change were significantly associated with average twin birthweight (340.3 +/– 166.0 g per cm/wk, $p < .05$; and 102.2 +/– 47.5 g per% change/wk, $p < .04$).

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Conclusions. Changes in MUAC from 20–34 weeks are significantly associated with fetal growth in twin pregnancies. A positive change from 20–34 weeks probably indicates that the mother has adequate dietary intake or nutrient stores to continue to accrue LBM and support fetal growth, while a loss of MUAC indicates that intake or stores may be inadequate. This simple, relatively precise measure of change in maternal body composition during pregnancy may be useful in identifying fetuses at risk for faltering intrauterine growth.

PARENTHOOD AND EVERYDAY LIFE IN MULTIPLE FAMILIES

Session: Poster

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The research of children and young people, as well as the research of families, made from the nursing, scientific viewpoint, has increased in Finland, though the amount of research of multiple families has been rather small. Almost every multiple family uses the services offered by child and maternity clinics, which means that the nurses need a special kind of information when meeting with multiple families.

The aim of this research is to describe how the multiple families experience their parenthood and everyday life. The main issues of the research were:

1. What kind of experiences do the parents of multiple families have from their parenthood and the support they get?
2. How do the parents want the services for multiple families to be developed?

The data were collected with a thematic interview in the Eastern part of Finland. There were 14 parents of multiple families (n = 27) in the research, and they all had twins under four years of age. The material was analyzed with a qualitative method.

The results of the research showed that parenthood was considered as a productive matter and everyday life was seen as life full of activity. The parents wanted more support and information from the hospital staff. None of the parents had got special information about twins from the child and maternity clinics. They wish to have a group of their own as well as they are willing to have the change of using information technology. Besides, they hope for co-operation with associations for Multiple families. The report from the research is available in the Spring 2004.

It would be important in further research to find out how the co-operation between hospitals, clinics and the associations for Multiple families works. As well, the research should also cover support given by peer groups.

IS THE NATURAL TWINNING RATE STILL DECLINING?

Session: Poster

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Background. Twinning rates declined from the 1950s through the 1970s in many developed countries, even after controlling for maternal age and parity, but began to increase again in the 1980s. This increase is mainly attributed to infertility treatment, and it is unknown whether the "natural" twinning rate is still declining. A declining natural twinning rate can be seen as an indicator of declining fecundity of the population.

Aim. To investigate whether the natural twinning rate is still declining.

Material and methods. We used the Danish National Birth Registry to identify 62,122 singleton and twin births from the 24th gestational week occurring between 1998 and 2001 to women participating in the Danish National Birth Cohort, a nationwide study that enrolled women early in pregnancy. After excluding triplets, stillbirths, and abortions before week 24 (total 67 women) and women who reported infertility treatment (3908, 15.5% twin births), we calculated twinning rate among 58,165 women and compared these data to Statistic Denmark's data on twinning in Denmark 1940–2001.

Results. The overall twinning rate among live births in the cohort was 2.2%, which is similar to the contemporary national, level (2.0%). The "natural" twinning rate in the cohort was estimated to 1.3%, which is higher than the national low level of the 1970s (1.0%). Controlling for maternal age did not remove this tendency.

Conclusion. These results suggest that the decline in natural twinning has halted.

ROBUST MODELS FOR ANALYSIS OF QUANTITATIVE TWIN DATA

Session: Statistical Issues in Twin Studies II

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In my talk I will discuss two twin regression models that incorporate covariates in the variance structure of a continuous trait, in a manner that makes it possible to analyze gene-environment interactions also when the exposure variable is continuous.

The first model is sensitive to the specification of the underlying genetic model, since the impact of genetic versus environmental factors for example, depends on the genetic correlation between DZ twins. Here, an additive model corresponds to a genetic correlation of .5, whereas presence of dominance yields a correlation between .25 and .5.

I however show that the estimates describing the genetic component seem fairly robust, as long as the environmental component is modeled rather freely.

The second model is constructed so that the genetic effect can only express itself as a difference in covariance for MZ and DZ pairs. Thereby inference regarding the genetic component will always be robust against a wrong specification of the genetic correlation among DZ-twins.

The models will be illustrated by an analysis of the genetic component in body mass index. The available data are questionnaire data from the Danish Twin Registry.

GENETICS OF DIZYGOTIC TWINNING. DESIGN AND SAMPLE COLLECTION: A FEASABILITY STUDY

Session: Current Developments and Findings from Twin Studies

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Objectives. The aim of this study was to examine the feasibility, effectiveness and logistics of large-scale sample collection in families with sisters with natural dizygotic (DZ) twins. DNA, RNA, lymphocytes and plasma were collected in affected sister pairs (ASP) and their parents for a linkage study to identify genes that contribute to variation in natural DZ twinning.

Methods. Twenty-four ASPs were recruited from the Netherlands Twin Registry. Parents and/or additional siblings were recruited via the proband. Pedigree data about DZ twinning and fertility were obtained from telephone interviews. Blood and urine samples were collected after overnight fasting (between 7–10 am) on the 3rd day of the menstrual cycle at home or work. We collected DNA, lymphocytes, RNA (resting & after dexamethasone challenge), EDTA plasma, heparin plasma, citrate plasma and urine.

Results. Twenty-three ASPs were interviewed (one proband did not have a sister with twins) and visited for blood collection in two months. We collected blood on the 3rd day of the menstrual cycle in 11 of the 13 mothers. Ten mothers used oral contraceptives, and 23 were in menopause, used hormone UID or had had a hysterectomy. The quality of the samples after transport was good. RNA isolated from whole blood showed no degradation of transcripts and it should be feasible to perform gene expression profiling studies with these samples.

Conclusion. The study showed that it is feasible in the Netherlands to collect blood samples of high quality, when participants were fasting and on the 3rd day of menstrual cycle.

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A COMPARISION OF BODY COMPOSITION OF MOTHERS OF MONOZYGOTIC AND DIZYGOTIC TWINS

Session: Poster

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Objectives. Dizygotic (DZ) twinning runs in families and is suggested to be heritable. The factors influencing monozygotic (MZ) twinning remain illusive. One way to gain more insight into the mechanisms underlying MZ and DZ twinning is to compare characteristics between the mothers of MZ and DZ twins.

Methods. Information on height and weight was obtained from mothers of twins registered with the Netherlands Twin Register. Data were collected in mothers of newborn twins (2515 MZ and 4890 DZ twin mothers) and in mothers of adolescent and adult twins (1149 MZ and 1727 DZ twin mothers).

Results. Mothers of newborn DZ twins were significantly taller, heavier and had a higher BMI than mothers of newborn MZ twins. Similar significant differences in body composition were found in the mothers of older MZ and DZ twins. MZ twin mothers were younger than DZ twin mothers were at the time of birth of the twins. Correction for age of the mother did not alter the results for body composition.

Conclusions. MZ and DZ twin mothers differ in body composition. Body composition may be a causal factor that increases the risk of getting a DZ twin. On the other hand, it might as well be a marker of fertility.

Supported by NIH Grant R01 HD042157-01A1 and The Center for Neurogenomics and Cognition (VU)

WHAT IS THE IMPACT OF GENETIC FACTORS FOR FEV1 AND FVC?

Session: Poster

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Background. Previous research has shown that forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) are determined by genetics and the environment. FEV1 and FVC can be estimated from a formula containing height, age and gender. The purpose of this project was to determine whether genetic factors influence FEV1 and FVC, when adjusting for known variations caused by for example, height and age.

Subjects & methods. All participants filled out a questionnaire concerning previous and current lung diseases, other current diseases, allergies, smoking habits and use of medication. The participants also performed forced spirometry according to ATS criteria in Odense or Copenhagen, Denmark. In Odense a non-commercial pneumotach designed for this study was used and a Vitalograph dry-bellows spirometer was used in Copenhagen. Participants reporting respiratory diseases were excluded from the analysis.

A total of 1,190 twins representing 618 pairs were enrolled: 591 MZ (305 pairs) and 599 DZ (313 pairs).

Regression analyses were used to adjust FEV1 and FVC for height, age, gender, current smoking and place of spirometry. Weight and BMI were found to be not significant in these analyses and were therefore excluded. Then intraclass correlation was estimated on complete pairs using the loneway command in Stata 8.

Results. The intraclass correlation of FEV1 for MZ was .765 (95% CI: .716–.813), and .341 (.237–.446) for DZ. For FVC the intraclass correlation for MZ was .787 (.742–.832), and .386 (.286–.487) for DZ.

Conclusion: Since the intraclass correlations for MZ were significantly higher than those of DZ there are still genetic factors left to determine FEV1 and FVC when adjusted for height, age, gender, smoking habits and place of spirometry.

INCIDENCE OF CANCER IN DANISH TWINS BORN 1870–2001

Session: Poster

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The Danish Twin Registry was established in 1954, including information of all twins born in Denmark between 1870 and1910, and it was later expanded to include twins born 1911 through 2001. Zygosity diagnosis in same-sexed twin-pairs is based on information from mailed questionnaires to the twins, or to their closest relatives. The pairs are classified as monozygotic (MZ), dizygotic (DZ) or unknown zygosity (UZ) based on similarity questions. The Danish Cancer Registry contains information on all malignant diseases diagnosed in Denmark since 1943. All twins from same-sexed pairs and twins of opposite sex (OS) where both were alive on January 1 1943, or born after this date, have been linked to the Cancer Registry for the period 1943 through 2002.

A total of 124,795 twins (60,805 females and 63,990 males) from 62,409 pairs are included in this study. Based on calculation of standardized incidence rate ratio (SIR) it is shown that neither male nor female twins differ from the general population with respect to total cancer incidence. Results for specific cancer sites will be presented at the congress.

NEONATAL MORTALITY AND MORBIDITY OF TWINS ACCORDING TO THE MODE OF CONCEPTION AND CHORIONICITY

Session: Poster

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Objective. To determine whether there is a difference in neonatal mortality and morbidity of twins according to the mode of conception and chorionicity

Patients & method. Twins < 35 weeks who were admitted to NICU at Jichi Medical School Hospital (JMSH) from January 1997 through December 2002 were enrolled. The mode of conception was divided into assisted conception (AC: artificial reproductive technology and ovular induction) and natural conception (NC). Chorionicity was determined by pathological examination of placentas (monochorionic(MC) and dichorionic(DC)). Gestational age, birthweight, Apgar score at one and five minutes, neonatal death, need of mechanical ventilation (MV) and days on oxygen, ventilator, and of hospital stay were compared between two modes of conception or chorionicity. Student *t*-test and χ^2 test were used and $p < 0.05$ was considered significant.

Results. Two-hundred and fifty-three infants were admitted during the study period; 115 twins (54 pairs and seven neonates) from NC, and 138 (67 pairs and four) from AC. Mean gestational age, birthweight, Apgar score (1), need of MV, and neonatal death were not different between AC and NC, but Apgar score (5), was lower and days on oxygen and hospital stay were longer in NC group. Compared according to chorionicity, MC twins showed significantly lower gestation, Apgar score (1) and (5), and longer in oxygen administration, MV, hospital stay, but neonatal death was not different.

Conclusion. Neonatal mortality was the same irrespective of the mode of conception, or chorionicity, but neonatal morbidity was significantly higher in MC twins.

BIRTHWEIGHT AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDHOOD AND EARLY ADOLESCENCE: A PROSPECTIVE SWEDISH TWIN STUDY

Session: Language Development

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Background. Low birthweight has been suggested as a possible risk factor for attention-deficit hyperactivity disorder (ADHD).

Aims. To investigate whether there is a causal effect of birthweight on ADHD or if the association is mediated by shared environmental or genetic influences.

Method. ADHD was measured with the DSM-III-R criteria at age 8–9 and 13–14. We used both categorical and continuous approaches to investigate between and within twin pair effects. Sub-analyses on monozygotic (MZ) and dizygotic (DZ) twins were performed to control for genetic influence. A nation-wide population-based sample of 1,480 same-sex twin pairs born 1985–86 derived from the Swedish Twin Registry was used. Birthweight was collected prospectively through the Medical Birth Registry.

Results. A DSM-III-R diagnosis of ADHD was reached by 4.9% at 8–9 years age and 3.1% at age 13–14. The lightest twin in birthweight discordant pairs had on average 13% (age 8–9: mean difference 0.12; 95%CI 0.04–0.21; $p = .006$) and 12% (age 13–14: 0.11; 95%CI 0.02–0.21; $p = .018$) higher ADHD score compared with the heavier twin. Disadvantages were consistently in the lighter twin in sub-analyses of MZ and DZ twins. Mixed effects models showed birthweight as a contin-

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uous risk factor for ADHD symptom score (one extra kilogram reduced ADHD score 12%; 95%CI –19%, –5%; $p = .0011$ at age 8–9; age 13–14: $p = .078$).

Conclusions. Low birthweight appears to show an association with ADHD symptoms in childhood and early adolescence that is not due to genetic or shared environmental factors.

CHANGES IN TWINNING RATES IN SOUTH KOREA: 1981–2000

Session: Poster

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The present study is the first report of twinning rates in South Korea. Utilizing the birth record data from the Korean National Statistical Office, we analyzed the incidence of twin births in South Korea from 1981 to 2000. The proportion of MZ and DZ twins was estimated by the Weinberg method. The DZ twinning rate increased very sharply in recent years. We presume that this increase is a consequence of hormonal induction of ovulation and various other techniques of assisted reproduction. Seasonal variation of live births and stillbirths, birthweights, gestational age, and maternal and paternal ages of twins for the period 1981–2000 were also analyzed.

HERITABILITY ESTIMATES FOR THE CONSTITUTIONAL LEVELS OF MANNAN BINDING LECTIN (MBL) AND LUNG SURFACTANT PROTEIN D. A STUDY OF UNSELECTED LIKE-SEXED TWINS AT THE AGE OF 6–9 YEARS OF AGE

Session: Pediatric Aspects of Twinning

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Background. The collectins mannan-binding lectin (MBL) and lung surfactant protein D (SP-D) play a significant role in innate immunity. Structural as well as promotor variants are known for MBL, and different alleles correlate with low MBL concentrations in serum and predispose to infectious diseases in children. Structural variants are also known for SP-D and may be linked to disease states.

Aims. The aims of the present study were to provide heritability estimates for the constitutional levels in serum of MBL and SP-D in children.

Methods and results. ELISA-methods were used for the determination of MBL and SP-D in serum. A population of 26 monozygotic and 36 dizygotic like-sexed twin pairs aged 6–9 years was studied. Intraclass correlations were significantly higher in MZ than in DZ twins, indicating substantial genetic influence on both MBL and SP-D levels. Biometric model fitting showed that the estimated heritability was 0.96 (95% CI: 0.92–0.97) for MBL with the presence of non-additive genetic factors and non-shared environmental factors and 0.91 (95% CI: 0.83–0.95) for SP-D with additive genetic and non-shared environmental factors.

Conclusions. The data indicate very strong genetic dependence for the serum levels of both MBL and SP-D, factors of importance in innate immunity.

THE GENETIC BASIS OF T HELPER CELL POLARIZATION IN HUMANS

Session: Complex Disorders II and Immunology

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Background. T helper 1 (Th1) and T helper 2 (Th2) cytokines secreted by polarized effector T cells play a pivotal role in the development of autoimmune and allergic diseases. However, the genetic basis of cytokine production by T lymphocytes in humans is poorly understood.

Methods. To obtain insights into the genetic basis of T helper cell polarization, we investigated the genetic contribution to cytokine production and regulation of T cell specific transcription factors in a prospective twin study.

Findings. We found a substantial genetic contribution to the production of Th1 cytokines such as IFN-g and TNF-a with heritability of 0.85 (95% CI 0.74–0.95) and 0.72 (0.50–0.93), whereas no genetic influence on production of the Th2 signature cytokine IL-4 was observed. In contrast to GATA3, NFAT and NF-kB, intrapair variability of T-bet, the master transcription factor of Th1 cells, was very low among monozygotic and high among dizygotic twins, indicative of a strong genetic influence on T-bet (heritability 0.93, 95% CI, 0.84–1.0). Interpretation. Taken together, our data provide novel insights into the genetic regulation of human T helper cell polarization as a basis for the development of autoimmune and allergic diseases. These data suggest that signature cytokines and cytokine signaling events of Th1 rather than Th2 cells are genetically determined and implicate that Th2 associated diseases in humans might be due to genetic variations in Th1 cytokine regulation via T-bet. This concept is highlighted by the recent finding that inactivation of the T-bet gene in mice results in development of clinical hallmark features of asthma.

This study was supported by the DFG, SFB 490, A3.

THE EFFECT OF LOSING THE CO-TWIN ON THE CHANGES OF DEPRESSION SCORE

Session: Poster

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Several studies have explored the effect of losing a spouse on depression score, and some studies explored the impact of losing the co-twin on mortality. The aim of this work is to study the effect of losing the co-twin, for age 70 years or older, on the changes of depression score. The data from the Longitudinal Study of Aging Danish Twins included the information on depression symptoms and the Population Register of Denmark for period 1995 through 2003 will be used. Logistic regression analyses indicate that observed depression score is a strong predictor of future drop-out, suggesting the inappropriateness of the complete case analysis. The multiple imputation approach will be used to deal with this problem. The marginal generalized linear model, which related the mean change of depression score with zygosity, shows a significant effect. This means that monozygotic twins suffer more than dizygotic twins after losing the co-twin.

GENETIC ANALYSIS OF INCOMPLETE SURVIVAL DATA: AN APPROACH BASED ON PARAMETRIC SURVIVAL MODELS

Session: Statistical Issues in Twin Studies II

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Traditional parametric methods of genetic analysis of continuous phenotypes (e.g. heritability estimation) using twin data are well developed. These methods assume complete observation of the responses, such as height, weight or BMI. However, observations of survival outcomes such as age of onset or first diagnosis of a disease, longevity etc. are often incomplete because of censoring and are subject to selective sampling due to truncation. Typically both members of a twin pair had to be alive at a certain date in order to be included in the registry. Survival times of individuals who are still alive at the latest follow-up date are considered censored. These issues must be considered in a genetic analysis of survival data (e.g., heritability estimation) in order to avoid biased estimates of the genetic parameters. The problem might be aggravated when data from several twin registers with different inclusion criteria are analyzed together. Moreover, traditional methods of genetic analysis of continuous phenotypes are based on the bivariate normality assumption, which is not appropriate for the study of survival traits like longevity, when the phenotype distribution is skewed.

In this paper we consider the application of parametric bivariate survival models for dealing with these issues. These models allow for flexible specification of marginal survival time distributions (thereby dealing with non-normality of the outcomes) and at the same time provide the possibility for dealing with censoring and truncation within the maximum likelihood framework, making it feasible to jointly analyze data from different twin registers. Under the assumptions of independent censoring and truncation the parameters may be estimated by parametric maximum likelihood, yielding estimates with well-studied statistical properties. Such models may be developed using the idea of bivariate frailty or, more generally, using bivariate copula functions.

The main idea of the approach is to fit a model to incomplete survival data and then compute the predicted quantities of interest (e.g. correlation coefficients of the survival times) from the model using the estimated parameter values. Confidence intervals for the predicted quantities of interest (e.g., correlation coefficients) may be computed either using Monte Carlo method based on multivariate normality of the estimates, or via constrained maximum likelihood. The approach is illustrated using examples from twin survival data.

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EFFECTS OF BIVARIATE TRUNCATION ON HERITABILITY ESTIMATES IN SELECTED SAMPLES

Session: Aging and Longevity II

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Methods for estimation of heritability (i.e., proportion of variance of genetic factors relative to the total phenotypic variance) of continuous phenotypes are well developed and widely used. This methodology is based on polygenic models of quantitative genetics, where the additive effects of many independent genetic loci inherited in a mendelian fashion are combined with additive normally distributed effects of the environment, leading to a bivariate normal distribution of the twins' phenotypes. This theory permits to relate heritability with correlation coefficients of the trait for identical (MZ) and fraternal (DZ) twins, allowing for estimation of heritability based on MZ and DZ correlations.

In many applications the sample of MZ and DZ twins is subjected to selection. For example, in the analysis of twin survival data heritability of the residual lifespan of twins both survived until a certain age is considered. Here the aim is to study the age-dependence of genetic influence on human longevity by estimating heritability of residual lifespan. In other situations, the analysis is often restricted to twin pairs where both individuals are healthy, which may result in a selection of twin pairs, where both phenotypes should be above a specific cut-off point.

In this paper we study the effects of such truncation on heritability estimates using simulated data from a polygenic model. Traditional heritability estimates are obtained using the conditional correlation coefficients of MZ and DZ twins in the truncated sample and compared with "true" heritability values computed directly from variances of genetic and environmental components that are directly observable in the simulation. This analysis yields a number of seemingly unexpected findings.

In particular, correlation-based heritability estimates decline with increasing truncation, where as "true" heritability is increasing. Moreover, heritability defined as the proportion of genetic variance relative to the total phenotypic variance may exceed 100% in the truncated sample because of negative dependence between the genetic and environmental components which is induced by the selection process. Other findings include, that heritability in MZ twins is different from heritability in DZ twins and the marginal distribution of MZ twins is no longer the same as the distribution of the DZ twins. We discuss the implications of these results for genetic analysis of survival traits and other continuous phenotypes.

LOW BIRTHWEIGHT AND TYPE 2 DIABETES: A STUDY ON 11 162 SWEDISH TWINS

Session: Poster

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The aim of our study was to investigate the association between low birthweight and diabetes in a population-based Swedish twin sample.

A cohort of 11,162 same-sexed Swedish twins born between 1906 and 1958 was used in order to investigate the risk of developing Type 2 diabetes between and within twin pairs by utilizing random effects linear models.

Between pairs there was a significant increase in risk of developing Type 2 diabetes for a 1 kg increase in their mean birthweight (OR = 2.13; $p < .01$), adjusted for age, sex, BMI, and smoking status. The corresponding risk within pair was 2.03 ($p = .07$) for monozygotic twins and 1.15 ($p = .71$) for dizygotic twins.

The study suggests that reduced fetal growth increases the risk of Type 2 diabetes due to an in utero programming effect possibly caused by intrauterine malnutrition. However, it does not exclude the possibility of a common genetic mechanism.

HERITABILITY OF LIPIDS IN AFRICAN- AND EUROPEAN-AMERICAN YOUTH

Session: Poster

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Objectives. Twin studies of lipids have found heritability of 50–80% for total cholesterol, LDL, HDL and triglycerides, but have mostly involved Caucasian twins. Blacks are known to show a healthier lipid profile, but relatively little is known about ethnic differences in genetic and environmental influences on lipids.

Methods. We studied a sample of 106 black and 106 white twins (30 singletons and 91 complete pairs: 49 MZ, 21 DZ and 21 opposite sex) from the southeastern US (mean age 17.9 ± 3.2; 79% fasting). Lipids were assayed with the Cholestech LDX system and LDL calculated with the Friedewald formula. Prior to analyses, values were adjusted for fasting status. We used GEE to test for effects of sex and ethnicity on the means, controlling for the dependence within twin pairs. Structural equation modeling was used to estimate genetic and environmental effects on each lipid variable.

Results. Females showed higher HDL values than males ($p < .01$) and blacks showed higher HDL and lower triglyceride values than whites ($p < .01$). Parameter estimates for all lipids could be set equal across sex and ethnicity, with AE models showing the most parsimonious fit (based on hierarchic χ^2 tests and AIC). Heritability ranged from 56%–82%, with the remaining variation explained by non-shared environmental effects.

Conclusions. We confirm a healthier lipid profile in black youth. Although limited by modest sample size and power we find no evidence for ethnic differences in heritability estimates, which were consistent with previous research in Caucasian twins.

TRENDS IN TRIPLET STILLBIRTH RATES IN JAPAN, 1975–1998

Session: Poster

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Stillbirth rates of triplet births in the whole of Japan were analyzed using vital statistics from 1975 to 1998. Stillbirths were registered at 12 weeks of gestation or later. The stillbirth rate was significantly higher in like-sexed than in unlike-sexed triplets for the period 1975–1998. During the 23-year period the stillbirth rate decreased by 1/7 for like-sexed (from 342 to 49 per 1000 births) and by 1/4 for unlike-sexed triplets (from 195 to 54). The decrease in the stillbirth rate in the 23-year period was more drastic in triplets, for both like-sexed and unlike-sexed sets, than in singletons and twin births. Risk factors for the stillbirth rate in triplets were like-sexed sets, younger or older maternal age, shorter gestational age and lower birthweight. However, declining stillbirth rates may be attributed to improvements in medical care for triplet pregnancies.

Recommendation of an optimum day to give birth for triplet pregnancy is 34–35 weeks of gestation for Japanese women.

DIFFERENTIAL CONCORDANCE OF MULTIPLE SCLEROSIS AMONG MONOZYGOTIC TWINS ACCORDING TO LATITUDE OF BIRTH: ROLE OF GENETIC AND NON-GENETIC FACTORS

Session: Complex Disorders II and Immunology

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Background. The pair-wise concordance (PC) of multiple sclerosis (MS) among monozygotic (MZ) twins varies from 20–40% in high incidence populations. Reports of lower concordance (< 7%) have appeared from France and Italy. We set out to evaluate the PC of MS among MZ twins according to latitude of birth-place in North America and to determine the factors responsible for any observed difference.

Method: One thousand, two hundred and ninety-four North American twins with MS were ascertained from 1980–1991. The members of 844 pairs, including 299 MZ pairs, completed a questionnaire providing information on gender, perceived zygosity, date/place of birth, and details of diagnosis. Twins born in Canada and adjacent US states were considered to be of "northern" birth, and the remainder "other". Twins with one Celtic or Scandinavian grandparent were compared to those with other ancestry. Diagnoses made before age 29 were considered "early".

Result. The PC for MS among "northern" MZ pairs (17.5%) was 2.2 (95% CI 1.2–4.0) times greater than that for MZ twins from "other" places (8.7%). PC for twins of Celtic/Scandinavian ancestry was higher (24.4%)compared to others (11.7%), and that for MZ pairs with early diagnosis (18.2%) was higher than those diagnosed later (6.7%). The effects of ancestry and early diagnosis were independent of each other, and both contributed to the effects of latitude. Pair-wise concordance in DZ twin pairs did not differ by latitude, ancestry, or early diagnosis. The average age at diagnosis was significantly earlier by 2 years among MZ ($p = .02$) than DZ ($p = .01$) twin pairs. Age at diagnosis was unrelated to ancestry.

Conclusion. Concordance for MS among MZ twins varies by latitude, and both genetic and environmental factors appear responsible.

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LEPTIN AND POLYCYSTIC OVARY SYNDROME — A TWIN STUDY

Session: Poster

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Introduction. Polycystic ovary syndrome (PCOS) is a common endocrinopathy with symptoms such as obesity, insulin resistance and hyperandrogenemia. PCOS could be the result of a genetic disorder. Genetic discrepancy in the production of leptin, known also as a product of obesity gene, may lead to various endocrinopathies such as PCOS.

Objective. The objective of this study was 1) to find the incidence of PCOS using a golden standard; 2) to ascertain the genetic property of leptin; and 3) to find the association between leptin concentration and PCOS.

Method and Materials. One hundred and fifty four Teheran residents, female-female twins including 48 pairs of monozygotic (MZ) and 29 pairs of dizygotic (DZ) twins, aged 15–45, were studied. Clinical, ultrasound and biochemical findings were used to diagnose PCOS.

Result. The incidence of PCOS using biochemical and clinical features was 16.2%. Correlation coefficient between serum leptin levels of MZ twins was more than that of the DZ. The serum level of leptin was similar between subjects with or without PCOS irrespective of their zygosity.

Conclusion. It was concluded that: (1) the incidence of PCOS is high among twins; (2) Leptin is likely to be genetically determined, although the effect of environmental factors cannot be denied; (3) this study did not find any association between the diagnosis of PCOS and leptin level. However, the link between the two may lie with other entities such as eating disorders and/or obesity.

SUBCLINICAL EATING DISORDER, POLYCYSTIC OVARY SYNDROME: IS THERE ANY CONNECTION BETWEEN THESE TWO CONDITIONS THROUGH LEPTIN — A TWIN STUDY

Session: Complex Disorders I — Metabolic Syndrome, Obesity

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Introduction. The genetic property of subclinical eating disorder (SEB) and the link between SEB and polycystic ovary syndrome (PCOS) has been studied before but the role of leptin within this connection has never been investigated.

Objectives. The objective of this study was: (1) to study the genetic property of SEB; (2) to find a link between leptin, SEB and PCOS.

Method and material. One hundred and fifty-four (77 pairs) female-female Iranian twins including 96 MZ individuals (48 pairs) and 58 DZ individuals (29 pairs) participated in the study. Clinical, biochemical and ultrasound tools were used to diagnose polycystic ovary syndrome. A BITE questionnaire was filled out for subjects.

Result. Eight percent of subjects were diagnosed for subclinical eating disorder. No significant difference was found between intraclass correlation of MZ and DZ ($z = .57$, $p = .569$). Serum leptin level was correlated significantly with bulimia score ($p < .007$). The mean (+/– *SD*) value for bulimia score was found to be higher among PCOS+ subjects (3.27 ± 5.51) in comparison with PCOS– subjects (2.06 ± 4.48) ($p < .001$).

Conclusion. Genetic property of subclinical disorder was not confirmed as shared environment might have played a major role in likeliness of DZ twins as well as MZ. Leptin is linked with both subclinical eating disorder and PCOS.

REDUCTION IN FUNCTIONAL ABILITY AND QUALITY OF LIFE AS CONSEQUENCES OF PRE-TERM BIRTH

Session: Health Prognosis and Twin Births

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The number of prematurely born children increases every year. Some of the reasons are that more twins are born as a result of IVF, and that we have become better at saving the lives of those born very early.

Very prematurely born children begin their lives in a tough way, often by acute Caesarean section under dramatic circumstances after which they are immediately taken away from their mother, put into an incubator and taken to the NICU.

They go through a long period in an acute environment with intensive care. They receive respiratory support, sometimes from a respirator, sometimes from a C-PAP system. Daily, they are having blood drawn, a probe is put down through their gullet, and they have very little contact with their parents.

A rudimentary central nervous system makes the pain and the many negative sense impressions even harder for the small babies; it might also cause sense integration problems, hyperactivity and difficulties in concentrating and learning.

All these violent and unpleasant experiences in the early babyhood are very traumatic and will in most cases have psychological consequences.

When the children grow up, they are often afraid and insecure, lack self-confidence and are very vulnerable. In addition, many of them have difficulties with food, language, sleep and motor function.

We can, however, help these children achieve a higher functional level, similar to the way we can psychologically repair the consequences of adults' traumatic experiences.

When there is a balance in the motor function, in the ability of integrating the senses and in the psychological and emotional life, the children's sleeping and eating habits, language skills, learning ability and social relations will improve significantly.

USING CAUSAL MODELS TO INVESTIGATE GENETIC AND ENVIRONMENTAL CORRELATIONS AND INTERACTIONS UNDERLYING THE SES-HEALTH GRADIENT

Session: Behavioral Genetics

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Given the robust finding that people in higher SES groups tend to experience better physical health, several psychosocial variables, including perceived control, negative and positive affect, and social relations have been identified that appear to help explain the social class health gradient. All these variables show consistent genetic influence. They are also substantially intercorrelated at the genetic level, and there is evidence for interactive effects. Using a nationwide sample of twin pairs from the National Survey of Midlife Development in the United States (MIDUS), we fit structural equation models to genetic and environmental variance-covariance matrices in order to test causal hypotheses about the nature of the relationships among these variables.

GENETICS OF NICOTINE DEPENDENCE

Session: Genetics of Nicotine Dependence (Symposium)

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Despite the public health significance of cigarette smoking, and evidence from adult and adolescent twin studies for a strong genetic influence on smoking behavior (heritability estimates as high as 70%), there has been little research designed specifically to identify genes that contribute to risk of addiction to nicotine in humans. Progress in behavior genetics methodology has enabled the definition of better drug-related phenotypes, and combined with recent advances in molecular genetics, has increased the feasibility of identifying susceptibility genes of modest effect for complex diseases such as addiction to nicotine in large-scale data collection projects. The speakers at this symposium will be reporting the first results for large-scale gene mapping studies in Australia, Finland, the Netherlands and the UK set up to identify specific chromosomal locations or candidate genes that have at least a moderate effect on risk for persistent tobacco use.

Understanding factors that determine why some individuals make the transition from experimentation with cigarettes to persistent and dependent smoking is an important goal given the health consequences and economic costs of smoking. Identifying genes with at least a moderate influence on smoking behavior may have important long-term implications for improved treatments of smoking cessation. While no genes for nicotine dependence have yet been identified, the high heritability from twin studies indicates that possible genes may be found.

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GENETIC AND ENVIRONMENTAL FACTORS SHARED BETWEEN SELF-ESTEEM AND TEMPERAMENT DIMENSIONS

Session: Poster

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Previous twin studies reported that additive genetic and individual specific environmental effects were the best explanations of self-esteem. However, there have been few behavior genetic approaches to examine genetic and environmental traits of the vulnerability of self-esteem. The purpose of this study is to clarify temperament as an indicator of the vulnerability to self-esteem, using a Japanese twin sample. Participants were 252 pairs of twins, consisting of 162 pairs of monozygotic (MZ) twins and 90 pairs of dizygotic (DZ) twins in their adolescence. Temperament was assessed by Cloninger's Temperament and Character Inventory (TCI). Self-esteem was also assessed using Rosenberg's Self-Esteem Scale (RSES). Among temperament dimensions, novelty seeking (NS) and harm avoidance (HA) had a significant relationship with self-esteem. As a result of univariate twin analysis, NS, HA and self-esteem showed significant additive genetic contributions and individual specific environmental effects. By using trivariate twin modeling, we found that the covariation of NS and self-esteem was explained by environmental factors. On the other hand, results of our study suggest that the covariation of HA and self-esteem was due largely to genetic factors; 50% of the variance in the genetic factors of self-esteem can be explained by HA that have been reported to be heritable in previous twin studies. Although genes that relate to self-esteem have not been found, it is possible that genetic factors concerning HA that may be related to neurotransmitters (e.g., serotonin) indirectly contribute to self-esteem.

FREQUENCY AND COMPLICATIONS OF TWIN PREGNANCIES IN IRAN

Session: Poster

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Objective. To evaluate the frequency and complications of twin pregnancies in Iran.

Methods. An observational and cross sectional study was performed on all pregnant women who were admitted to Firoosabadi Hospital for delivery between March 1996–Feb 1998.

Results. From 11,965 deliveries, 130 cases were twins with a relative frequency of 1.08%. Complications were: abortion = 4.6%; IUFD (for the first fetus = 10%, for the second fetus = 17.8%,and for both = 11%); congenital malformations = 5.4%; preterm delivery = 63%; neonates RDS = 17.7%; neonates icterus = 21.6%; PROM = 20%; cord prolapse = 0.8%; pre-eclampsia = 17.1%; and weight discordance = 9%.

Conclusion. Preterm delivery was more than for the other sites and more than the world statistics for twin pregnancy.

This difference may be because of the socio-economic situation of our patients; this hospital is in downtown Teheran in a poor area, and improper nutrition, poor hygiene, younger-aged mothers, environmental stress and hard physical activity may have a role in it.

A CASE-CONTROL AND CO-TWIN CONTROL STUDY OF PERSONALITY AS RISK FOR CHRONIC FATIGUE AND CHRONIC WIDESPREAD PAIN IN THE SWEDISH TWIN REGISTRY

Session: Complex Disorders II and Immunology

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The importance of personality traits (Neuroticism and Extraversion) as risk factors for chronic fatigue syndrome (CFS) and its common co-morbidity, chronic widespread pain (CWP), was assessed in adults in a prospective study design. Participants were the members of the Swedish Twin Registry, born before 1958. Screening for CFS and CWP was performed between 1998 and 2002, based on CDC-94 criteria and American College of Rheumatology criteria respectively, without clinical evaluation. Neuroticism and Extraversion were measured by a mailed questionnaire in 1973. Of all the participants from like-sexed pairs (19,171 for CFS and 27,919 for CWP), 2,036 reported fatigue lasting more than 6 months, and 2,095 reported pain lasting more than 3 months. Cases and controls were matched for age and gender in matched case-control analyses, and twin pairs discordant for the case status were used in co-twin control analyses. Higher Neuroticism was associated with higher risk of both CFS and CWP. Higher Neuroticism was also associated with more severe forms of the illnesses. Neuroticism showed greater association with CFS than with CWP. Estimated risk was smaller in co-twin control analyses than in matched case-control analyses, and smallest when using monozygotic co-twins only, suggesting genetic and familial mechanisms confounding the association between Neuroticism and CFS/CWP. Higher Extraversion was associated with lower risk of CFS in matched case-control analyses. However, the relationship disappeared when adjusted for Neuroticism, suggesting that Neuroticism moderates this association. In conclusion, Neuroticism has long-term influences on the onset and severity of CFS/CWP, partly mediated by genetic and shared environmental factors.

OPTIMAL BIRTHWEIGHT AND GESTATIONAL AGES FOR TWIN AND TRIPLET NEONATES IN JAPAN

Session: Poster

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Objective. To determine the birthweight and gestational age associated with the lowest fetal mortality for Japanese twins and triplets.

Study design. A population-based analysis of all multiple births (203,288 live births and 17,137 fetal deaths) in Japan between 1995 and 1999. Perinatal mortality was compared by categories of birthweight and gestational age, for twins and triplets versus singletons, and within each plurality by the lowest rate compared to all other rates as relative risks ± 95% CIs.

Results. The overall versus lowest perinatal death rate per 1000 conception for singletons was 8.06 versus 1.4 at 3500–4000g and 40–41 weeks; for twins, 37.1 versus 4.2 at 2800–3100g and 36–37 weeks; and for triplets, 58.6 versus 1.2 at 1300–1600g and 34–35 weeks. Beyond these plurality-specific lowest ranges, the risk of fetal death increased, more for twins than singletons, and most for triplets.

Conclusion. Perinatal death rates can be reduced by more than 90% with attainment of birthweight and gestational age within a plurality-specific ideal range.

DISCORDANT BIRTHWEIGHT AND PERINATAL DEATH IN JAPANESE TWINS

Session: Poster

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Objectives. To determine the cut-off point for discordant twins, and to clarify whether perinatal deaths are caused by discordancy or low birthweight itself.

Methods. Using a population-based analysis of all twins born between 1995 and 1999 in Japan, discordancy was determined as (larger birthweight — smaller birthweight)/ (larger birthweight) × 100. Logistic regression analysis was undergone setting perinatal deaths as endpoint.

Results. Ninety percent of relative cumulative frequency corresponded to 25% of discordancy. Among twins with discordancy of more than 20%, perinatal mortality rate was higher than that among discordancy of less than 20%. Logistic regression analysis showed that both discordancy and low birthweight are significant factor for perinatal death.

Conclusion. Perinatal death of Japanese twins was significantly affected by both discordancy and low birthweight.

MONOZYGOTIC TWINS WITH TAR SYNDROME

Session: Poster

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TAR syndrome (TARS, MIM274000) is a rare autosomal recessive disorder. We propose a report on MZ brothers with TARS. The probands were born after the first pregnancy by cesarean section to a 24-year-old female and 22-year-old male. Their parents deny consanguinity. Twins birthweight were 3000g and 3100g. Their length was 50cm. Both babies had symmetric bilateral radial talipomanus, forehead nevus flammeus at birth. Anemia resistant to medicines Fe-contained, anisocytosis, poikilocythaemia decreased with advancing age. MZ twins aged 23 months had round flat face, down-slanting palpebral fissures, sparse and fair scalp hair, eyebrows and eyelashes, short nose, flat nasal bridge, symmetric shortness of forearm, bilateral radial aplasia and radial deviation of

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hands, hypoplastic thumbs with depressed thumb abduction, hypoplasia and clinodactyly of the 5th fingers of hands, delayed motor development and mild mental retardation. Laboratory investigations revealed the number of blood platelets to be at the low normal level (12-month-aged). X-ray study confirmed presence of bilateral radial aplasia

BEREAVEMENT SUPPORT WEBSITE

Session: COMBO II

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As multiple birth parents we are repeatedly faced with situations unique to having twins, triplets or more. We often find a frustration with the inability of society to appreciate the fact that having multiple birth children is not the same as having two closely spaced singletons.

This also applies to bereavement situations where one, more or all of a multiple birth set may have died. The journey through grief is unique for any parent, but can often be far more complex when it concerns multiple birth children, yet all too often bereaved multiple birth parents are expected to react in the same manner as parents who have lost a singleton child. We do not say the loss of a singleton child is any less tragic, we are just saying it is different.

The Bereavement Support section of the AMBA Website is a work in progress. It is not only for the benefit of bereaved multiple birth parents, but also their families, friends, health care professionals and others wishing to assist them in their journey.

Too often, expertise in this area is lost or continued support is not able to be given, as bereaved parents either move on from their grief or find it is just too painful to continue with the support they were once able to give.

When fully operational it is hoped to provide a comprehensive support network for all multiple birth families who have experienced the loss of one, more, or all of their multiple birth children. Literature, links to other sites, forums for those wishing to contact others who have had a similar bereavement experience, and other support groups that might be of assistance are the basis of this ongoing support network.

GENETIC FACTORS IN SEIZURES: A POPULATION-BASED STUDY OF 47,626 US, NORWEGIAN AND DANISH TWIN PAIRS

Session: Poster

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Rationale. This study deals with the establishment of a sample of twins ascertained from population-based twin registries in three countries in order to study the importance of genetic factors for seizure liability.

Methods. Data on history of seizures were collected by questionnaire from twins ascertained from population-based twin registries in the U.S., Norway and Denmark. Concordance rates were calculated for all seizure categories within and across twin populations. Biometrical analyses were performed for epilepsy and febrile seizures in each twin population to estimate their heritability.

Results. A total of 6234 of 47,626 twin pairs screened reported a history of seizures. Concordance rates were significantly higher for the monozygotic (MZ) versus dizygotic (DZ) twins for all seizure categories within and across twin populations. Estimates of heritability based on model fitting procedures ranged from 70–74% for epilepsy and from 34–70% for febrile seizures.

Conclusions. The results of this study of the largest unselected, population-based sample of twins with seizures assembled to date confirm the importance of genetic factors in the occurrence of epilepsy, febrile seizures, other seizures and staring spells. All twins who reported a history of seizures are currently being clinically evaluated by neurologists, and seizures and epileptic syndromes are being classified. This sample is likely to provide an important resource for studying the genetics of epilepsy subtypes and febrile seizures. The study is supported in part by a NIH NINDS grant (NS-31564).

RELATIONSHIP IN RUSSIAN EARLY ADULT TWINS' FAMILIES

Session: Poster

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This study has been performed in the context of a Russian longitudinal adult twins' project aimed to analyze the genetic and environment influence on psychological traits during early adulthood. This poster presents data on twin family relationships: within pair relationships as well as child-parent relationships. Twins in the sample were 21–22 years old. Twins' family relationships were assessed using questionnaires and projective techniques. Special attention was paid to the analysis of differences and similarities in how twins of the same pair perceive themselves, their co-twins, and their relationships with co-twins and parents. Twins' perception of themselves, their co-twins and parents were compared on such traits as esteem, extraversion, and dominance. Significance of twins' relationships with different family members was assessed. The conflict resolution styles such as competition, avoidance, compromise, cooperation, accommodation, which twins use with their co-twins, were assessed. Zygosity and gender differences in family relationships are described.

GENETIC EFFECT ON X CHROMOSOME INACTIVATION: A STUDY OF YOUNG AND ELDERLY TWINS

Session: Molecular Genetics and Twin Studies

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Skewed X inactivation may be due to chance, to genetic factors, or to a selection against or in favor of cells with a specific genotype. Elderly females have a higher frequency of skewed X inactivation in blood cells than younger females. We have analyzed the X inactivation in 200 MZ and 258 DZ twin pairs. Two age groups were defined, young (< 55 years) and elderly (> 55 years), resulting in 118 young and 82 elderly MZ twin pairs and 146 young and 112 elderly DZ twin pairs. The frequency of skewed X inactivation (> 80:20) was similar (15%) in the young MZ and DZ twins, and also increased similarly (to 34%) in the elderly MZ and DZ twins. There was no parent-of-origin effect of the preferentially active X chromosome in DZ twins where the paternal X chromosome could be identified. We found a high intraclass correlation of the X inactivation pattern in both the young and the elderly MZ twins (.61 and .58) which was significantly higher than in the DZ twins (.08 and .09). Biometric analysis showed that dominant genetic effects accounted for about 60% of the variance in X inactivation pattern in both young and elderly twins. Shared intrauterine environment for monochorionic MZ twins may in part explain the high correlation for these. If the age-related skewing was a stochastic phenomenon, the correlation in MZ twin pairs would be expected to decrease with increasing age. This was not observed and our results thus indicate a genetic influence on the age-related skewing.

THE IMPACT OF POLYHYDRAMNIOS ON PREGNANCY OUTCOME IN TWIN GESTATIONS

Session: Poster

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Objective. To compare pregnancy outcome in twin pregnancies with and without polyhydramnios.

Study Design. A database of women receiving outpatient services was studied for the period 1988–2002. Included were women with twin gestations under 30 weeks gestation at start of outpatient services. We compared pregnancy outcomes for women with twin gestations having polyhydramnios (AFI 020) at admission (n = 201), to women with twin gestations that did not have polyhydramnios (AFI < 20) (n = 13,111).

Results. Obstetrical and perinatal outcomes in twin pregnancies were adversely affected by the presence of polyhydramnios. Mothers with versus without polyhydramnios had a tendency for vaginal bleeding (8.5% versus 5.1%, p = .051), placenta previa (4.5% versus 1.9%, p = .010), and delivery by Cesarean Section (71.1% versus 61.1%, p = .001). Delivery was shifted to earlier gestations in women with polyhydramnios (32.8 versus 35.1 weeks, p < .001), especially under 32 weeks (38.3% versus 12.7%). Fetal

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loss was notable; stillbirths (12.7% versus 1.1%, $p < .001$), and neonatal mortality (7.5% versus 1.1%, $p < .001$).

Conclusion. Polyhydramnios in twin gestations is associated with delivery at earlier gestations, and is more often by Cesarean Section. Perinatal mortality is significantly increased.

GESTATIONAL AGE AT ONSET OF UTERINE CONTRACTIONS AND PREGNANCY OUTCOME IN TWIN GESTATIONS

Session: Poster

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Objective. To identify the relationship between gestational age (GA) at onset of uterine activity (UA), and GA at delivery (GAD) in twin and singleton gestations.

Study Design. A database of women receiving outpatient preterm labor identification for the period 1988–2002 was analyzed, including 12,853 singleton and 4160 twin gestations enrolled at > 18 weeks' gestation that transmitted UA data for > 5 days. UA was monitored for a minimum of one hour, twice daily. Patients were grouped by gestation type and GA at first episode of UA > 6 contractions per hour; < 24 weeks, 24–28.9 weeks, 29–32.9 weeks, > 33 weeks. GAD was compared using independent samples *t*-test.

Results. 86.1% of twins vs. 74.5% of singleton gestations experienced UA > 6/hr ($p < .001$), with twins having an earlier GA at first UA elevation (25.9 ± 3.6 weeks vs. 27.8 ± 3.8 weeks, $p < .001$). Twins had an earlier GAD than singletons (34.9 ± 3.2 vs. 36.8 ± 3.2 weeks, $p < .001$). 26.3% of twins vs. 12.4% of singletons delivered at <34 weeks, $p < .001$. For both twins and singletons a consistent shift to an earlier GAD was noted for each onset of UA group compared to the successive onset of UA group, all $p < 0.001$. This was also true for each GA of onset of UA group comparing twins vs. singletons (earlier for twins).

Conclusion. For any given GA at onset of UA, twins are more likely to deliver earlier compared to singletons, and delivery is shifted to earlier GAs for those having threshold UA earlier.

HERITABILITY OF RECURRENT TONSILLITIS

Session: Poster

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Objective. The genetic contribution of tonsillitis may be a valuable step in the identification of genes contributing to the common liability for upper respiratory infections. The aim of the study was to estimate the heritability of recurrent tonsillitis in a cohort of twins from The Norwegian Institute of Public Health Twin Study born 1967 to 1979.

Methods. Self-report questionnaire data on recurrent tonsillitis from 9479 twins were analyzed. Under the assumption of a normally distributed underlying liability to recurrent tonsillitis, co-twin similarity for identical (MZ) and fraternal (DZ) twins was calculated using tetrachoric correlations. Structural equation modeling was used to test alternative models and to estimate the relative contribution of genetic and environmental effects to recurrent tonsillitis. Estimation of latent factors allows us to determine: (a) to what extent variation in recurrent tonsillitis is familial; and (b) the relative contribution of genetic and environmental effects to familial aggregation.

Results. The lifetime prevalence of self-reported recurrent tonsillitis was 11.7% (95%CI 11.0–12.3). Tetrachoric correlations were higher in MZ than in DZ twins in both males (.71 versus .12) and females (.60 versus .14). A model specifying additive and non-additive genetic effects and individual environmental effects yielded best fit. There is no evidence for sex differences in the genetic source. Difference in the magnitude of the genetic effects in males and females will be discussed.

Conclusions. A substantial genetic contribution to recurrent tonsillitis liability was found and the presence of sex differences in the heritability cannot be ruled out.

LAST DECADE'S INCREASE OF DUTCH MULTIPLE PREGNANCY BIRTHS IS PREDOMINANTLY THE RESULT OF NATURAL CONCEPTION

Session: Current Developments and Findings from Twin Studies

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Aim of the current study was to determine to what extent in vitro fertilization (IVF), ovulation induction(OI)/intra uterine insemination(IUI) and natural conception have contributed to changes in numbers of multiple births in the Netherlands from 1995 through 2002.

Data were used from the Netherlands Perinatal Registry (LVR-2), which contains the data of all Dutch hospital deliveries from 16 weeks of pregnancy duration including all multiples. From 1994 onwards, conception type is registered as either natural, IVF (ICSI) or OI/IUI. Over the period of 1995–2002 we extracted from the database for each type of conception the total number of boy-girl twin births to ensure dizygosity. We assumed that changes in trends in this twin birth type would be representative for the all DZ twins. We furthermore counted the number of high order multiple births. From 1995–2000 the number of DZ twin deliveries increased by 37%. The increase from IVF/ICSI was 64%, 27% from OI/IUI and 30% from natural conception. Natural conception accounted for 56% of the increase while IVF/ICSI and OI/IUI contributed 35% and 9% respectively. Maternal age did not change in the IVF/ICSI mothers (mean age 33.1 years), but it increased from 30.9 to 31.7 years in the OI/IUI twin mothers, and from 30.6 to 31.5 years in the natural conception group.

In 1995 and 1996 together a total of 57 high order multiples were born after IVF/ICS, 40 after OI/IUI and 47 after natural conception. In the years 2001 and 2002 together the number of large multiples after IVF/IUI declined to 18, and after OI/IUI to 34, but it increased to 66 after natural conception. In this latter group maternal age increased by about 0.25 yrs.

Parity had not changed while the total number of births per year had increased by 3%.

DZ twinning after IVF/ICSI and IO/IUI conception increased indeed but the largest contribution came from natural conception. For high order multiples a strong trend has been set towards lower rates after IVF/ICSI and to some extent also after OI/IUI, but there was a remarkable increase of high order multiple births after natural conception.

We postulate that increase of maternal age played a pivotal role in these demographic changes but in addition other changes in the environment are likely to be involved.

MONOZYGOTIC TWINS AND TRIPLETS AFTER ASSISTED CONCEPTION

Session: Controversies on Obstetric Issues

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High rates of multiple pregnancy occur after assisted conception, usually due to the transfer of more than one embryo or oocyte, resulting in dizygotic twins. Several studies have reported increased monozygotic twinning rates after ovulation induction or assisted reproduction.

Among 23,321 pregnancies notified to the register of assisted conception for Australia and New Zealand, there were 4343 (18.6%) twin pregnancies of at least 20 weeks' gestation and 559 (2.4%) triplet pregnancies.

For all types of assisted conception, the derived monozygotic twinning (MZT) rate was 4.5 (105/23,321) per 1000 confinements, similar to that in natural conceptions. After transfer of one, two, and three or more embryos, the derived MZT rates were 5.2 (7/1345), 5.5 (48/8677) and 3.3 (43/13,054) per 1000. Among 245 pregnancies for which the number of embryos transferred was not stated, the MZT rate was 28.6 (7/245) per 1000.

After conventional IVF, the derived MZT rate was 6.7 (88/13,175) per 1000. For IVF with fresh embryos, the MZT rate was 9.7 (92/9491) per 1000, but for thawed embryos, unlike-sex twins ($n = 233$) exceeded like-sex twins ($n = 229$).

After intracytoplasmic sperm injection (ICSI) with transfer of fresh embryos, unlike-sex twins ($n = 259$) exceeded like-sex twins ($n = 243$). For ICSI with thawed embryos, the MZT rate was 13.8 (13/941) per 1000.

After gamete intrafallopian transfer (GIFT), the MZT rate was 3.0 (20/6635) per 1000.

Among all triplet pregnancies, 26.4% (146/554) were like-sex.

These findings suggest that monozygotic twins and triplets occur in relatively few assisted conception pregnancies. Increasing the number of embryos transferred does not increase the monozygotic twinning rate.

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TWINNING RATES BY MATERNAL COUNTRY OF BIRTH IN AUSTRALIA

Session: Twin Registers and Methodology

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In countries with high levels of immigration over many decades, national twinning rates reflect the ethnic composition of the population, as well as maternal age and parity, and the use of fertility drugs and assisted conception. In Australia, mothers born in other countries account for more than 20% of all births.

Among more than 1.5 million births in a six-year period, the twinning rate was 13.1 per 1000 confinements. More than 5% were to mothers born in Asia. About 3% of all births were to Aboriginal or Torres Strait Islander mothers.

For mothers born in Australia, the age-standardized twinning rate was 13.7 per 1000 confinements. The rates for mothers born in selected other countries were as follows: New Zealand — 13.8; Greece — 13.8; Italy — 15.0; former Yugoslavia — 13.2; Lebanon — 13.6; Turkey — 10.0; Indonesia — 8.6; Malaysia — 12.2; Philippines — 8.3; Vietnam — 7.2; China — 7.3; India — 9.2; and Sri Lanka — 11.1 per 1000. For indigenous Australian mothers, the age-standardized twinning rate was 11.9 per 1000 compared with the actual rate of 9.5 per 1000. This difference reflects the much younger age of indigenous mothers.

Mothers born in Vietnam and China had the lowest twinning rates in Australia. The interpretation of ethnic variations in twinning has become increasingly complex because of the greater use of fertility drugs and assisted conception. More than 15% of twins in Australia are born after assisted conception. Analysis of twinning rates among indigenous Australians is often influenced by mixed ancestry.

GENETIC INFLUENCE ON PROLONGED GESTATION — A POPULATION BASED DANISH TWIN STUDY

Session: Poster

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Objective. The purpose of this study was to test a possible genetic component to prolonged gestation.

Study design. The gestational duration of single, first pregnancies by both female and male twins was obtained by linking the Danish Twin Registry, The Danish Civil Registration System and the Danish Medical Birth Register. A total of 2588 same-sexed twin pairs of whom both co-twins became parents during 1978–1996 were identified.

Results. The concordance rate for female twin pairs for a gestation of > = 41 weeks and > = 42 weeks, was higher for monozygotic twin pairs than for dizygotic twin pairs indicating genetic effects.

Biometrical modeling suggested that genetic factors account for 23% to 30% of the liability to prolonged gestation. The difference in concordance rate between monozygotic and dizygotic male twin pairs was small and the best fitting model indicated no genetic factors.

Conclusion. Maternal genes influence prolonged gestation. However, a substantial paternal genetic influence through the fetus was not found.

AN ANALYTIC STUDY OF THE IMPACT OF GENOTYPING ERROR IN MAPPING OF COMPLEX TRAITS USING SELECTED SIB PAIRS

Session: Statistical Issues in Twin Studies

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In the search for genetic determinants of complex traits, the use of selective designs appears to be the only way to gain sufficient power to detect typically small gene effects. A few authors have shown by simulation that the impact of genotyping error on evidence for linkage could be particularly severe in affected sib pairs designs, virtually masking most of the evidence for linkage. The impact on quantitative traits appears to be less dramatic in random samples; however it is unclear whether the same dramatic power losses hold in selected samples. A method of choice is now emerging for the analysis of quantitative traits arising from selected sib pairs — it boils down to a regression through the origin of excess IBD sharing on a function of the trait value, whose slope is an estimate of the linkage parameter. It was first proposed by Sham & Purcell (2001) and turns out to be equivalent to a score test. By use of a simple genotyping error model (at most one error at rate e in a sib pair genotype), we show analytically what effects such an error generating process induces when one marker with equally frequent alleles is used. It is shown that it results in a reduction of the slope estimate (i.e., of the estimated linkage parameter) by a factor 1–e/2 whether sib pairs are selected or not. In addition, the estimate of the regression slope can be further decreased or increased by a factor whose value depends on the selection of sib pairs and the genotyping error rate e. This simple result allows us to predict for example, that in affected sib pairs designs, the effect of genotyping error will be milder for rare traits than for highly prevalent traits. In extreme discordant designs, the effect can be either over-optimistic or pessimistic, depending on the definition of discordance, the genotyping error rate and the true linkage effect. It is argued that the simplistic error-generating model used is a good approximation of real-life situations. Our findings are backed up by simulations.

THE REPRESENTATION OF SIBLING RELATIONSHIP: A COMPARISON AMONG MZ AND DZ TWINS AND SINGLETONS

Session: Poster

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Background. Twins' relationship constitutes a peculiar relationship for both biological and psychological aspects. The present study investigated: (a) the representation of sibling relationships in twins and singletons; (b) the (in)congruence of children's ideas of their relationship in siblings' and twins' dyad.

Method. Sixty twins (30 dyads) and sixty siblings (30 dyads), with a maximum age gap of three years, were recruited. Of the twins, 32 were DZ and 28 MZ. Subjects were between six and 13 years of age; 31.3% were males and 68.8% females. Participants were administered the Assessment of Interpersonal Relations (Bracken, 1993) and the Thematic Drawing (Bombi and Pinto, 2000) in the context of the classroom. The TRI informs on the Intensity of relationship. Drawings were coded for the Similarity and Power Discrepancy scales.

Results. Analysis of Variance was performed on verbal and pictorial task. Results show that twins feels themselves to be more similar to their co-twin than siblings do, and that siblings underline hierarchy more than twins. Analysis of correlations revealed a significant intra-dyad on global Intensity for all the sample and on the Power Discrepancy for DZ twins and siblings. No incongruence in any of the sub-samples was found.

Conclusion. Findings are discussed considering the differences in the nature of sibling and twin relationships. Whereas siblings are conflictual partners with different status, members of twins' dyads have a special partner that is similar in age and sex, and share not only the family but also the external social world.

THE EFFECTS OF MULTIPLE BIRTHS ON MATERNAL ADJUSTMENT AND PREMATURE INFANTS' DEVELOPMENT

Session: Poster

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This longitudinal study was designed to explore the effects of multiple births (triplets and twins) on maternal behaviors and well-being, and on infant development.

The population included 60 mothers and their infants: 15 mothers of triplets; 15 mothers of twins; and 30 mothers of singletons. All infants were born prematurely. The three groups were matched for maternal age and education, family SES, infant gender and child order in the family. Mothers and infants were examined twice: during their stay in the Intensive Care Unit; and when the infants were 6-months old (corrected for age) at home. Data collection included information related to the medical status of the mother, especially during her pregnancy, maternal well-being, maternal attitudes towards the baby, maternal patterns of coping, marital relations, availability of social support, observations of infant-mother interactions (both in the ICU and at home), infant medical and neurological status, infant temperament, and infant development, as measured by the Bailey Developmental Scales. Three main questions investigated were as follows:

1. What are the effects of multiple births on mothers and infants;
2. Is it possible to predict infant development at 6 months of age from data collected in the ICU, and what are the most significant medical and psychosocial predictive variables;
3. What are the variables moderating the stress and negative effects of multiple births on mothers and infant development.

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TAMBA'S MATERNITY EXCELLENCE AWARD TO PROVIDE EFFECTIVE CARE TO TWIN FAMILIES
Session: COMBO I

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Tamba has developed and piloted a "Maternity Excellence Award" as part of its Partnership Project with parents and Maternity Units in West Surrey UK. The award aims to:

1. Highlight needs of families with multiples;
2. Encourage maternity units to provide an excellent quality of service to improve psycho social experience of the multiple birth;
3. Develop a sustainable partnership between health professionals and parent organizations;
4. Involve parents and carers in promoting and improving local services.

The Award is evidence-based and organized into 6 key areas:

- multiple birth guidelines;
- training & development of staff to support families;
- written information for families and professionals;
- parent support education to include psychosocial support;
- infant feeding support;
- support during hospital stay — physical, psychological and social and on discharge.

The criteria of assessment in each area are supported by reference to wide ranging, up-to-date resources produced by the voluntary sector, and health and social care professionals and organizations. Activities that can be used by maternity units to achieve each of criteria that supports families are also outlined.

Achievement is monitored by completion of a comprehensive checklist. This form of self-assessment encourages ownership and can also be used as part of an organization or individual's training program.

The award is designed to be realistic and has been developed from the parents' point of view. This award serves to highlight the needs of families, develop expertise and address clinical governance and raise the profile of maternity units. This initiative will ensure the physical, psychosocial and social support is available to multiple birth families.

GENOME WIDE SCAN AND CANDIDATE GENE ANALYSIS IN A FAMILY STUDY ON NICOTINE DEPENDENCE
Session: Genetics of Nicotine Dependence (Symposium)

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Smoking is of high importance for numerous public health problems and surprisingly little is known of the genetic elements contributing to nicotine addiction. An international consortium is performing a genome-wide scan for the identification of specific chromosomal loci behind addiction in a study sample of Finnish and Australian twins and their families. The family members (sibling pairs) have a history of heavy smoking. A diagnostic telephone interview is conducted and blood is drawn both from smokers and non-smokers. Nicotine dependence is being evaluated using DSM-IV criteria and the Fagerström score. Also other phenotypes describing smoking behaviour are used as quantitative and qualitative traits in statistical analyses. Our part of this international study is to perform a 10 cM genome-wide scan using Finnish families with at least one affected sibling pair. The ABI PRISM linkage mapping set (MD10) of 380 microsatellite markers is used for genotyping. Currently genome scan data exists for 76 families with 249 members (including 148 affected sib-pairs, ASPs). Initial linkage analyses suggest putative linked loci at 5q (ASP Z = 2.2) and 10q (ASP Z = 2.2), the 10q locus interestingly overlapping with a previously implied locus associated with nicotine addiction (Straub et al. (1999). *Mol Psychiatry*, 4, 129–144,). An additional 87 families with 273 members (including 122 ASPs) are currently being genotyped. Linkage analyses will be performed for the total study sample using various quantitative and qualitative traits. In addition to the genome-wide scan, a candidate gene approach is taken with six functional candidate genes, *CHRNA4, CHRNA5, CHRNA7, CHRNB1, CYP1A2,* and *CYP2A6*. Genotyping has been performed on 20 SNPs using Sequenom's MassARRAY system on 350 individuals from 121 Finnish families, and association analyses are ongoing.

Study is funded by NIH DA12854.

THE RELATIONSHIP EXPERIENCES OF ADULT OPPOSITE SEX TWINS: A PHENOMENOLOGICAL INVESTIGATION; A POSTER OF SOCIOGRAMS
Session: Poster

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This poster demonstrates data collection of sociograms, or relationship maps, part of the data collection from individual interviews carried out as part of the pilot study with one pair of adult opposite sex twins. The same data from interviews with two other pairs of twins is represented to compare and contrast the findings of the pilot, in preparation for the main project.

Each twin was asked to represent their world of relationships. Their reflections on their sociograms were recorded as part of the individual interviews, and then together in a group. The main themes the twins identified are represented.

The poster demonstrates some of the data collection processes being assembled for this research, which is conducted within the methodology of Transcendental Phenomenological philosophy (Moustakas,1994; Husserl,1967). A careful examination is made of different levels of external and internal communication, within and between the opposite sex twins and their others.

The structure of this methodology is employed to embrace and challenge validity of Psychodrama Psychotherapy theory and practice (Moreno, 1921).

Psychodrama is rooted in the philosophy of spontaneity and creativity; action and reflection mirror the relationship experiences of opposite sex twins.

This research is supported by Metanoia Institute, and the Dprof program, Middlesex University, London 2000–2007.

THE RELATIONSHIP EXPERIENCE OF ADULT OPPOSITE SEX TWINS: A PHENOMENOLOGICAL INVESTIGATION
Session: Twin Family and Twin Relations

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A phenomenological investigation is being carried out with three pairs of adult opposite sex twins.

In this presentation, the pilot study explores some of the data collection processes through the individual interviews with one pair of adult opposite sex twins.

The material from the individual interviews with the other two pairs of opposite sex twins will be shown to reflect on the similarities and differences of the findings in the pilot study. The reflections from these twins will be summarized.

This research is being conducted within the methodology of Transcendental Phenomenological philosophy (Moustakas, 1994; Husserl, 1967). It requires a careful examination of different levels of communication of external and internal processes, within and between the opposite sex twins and their other significant relationships, so the complex of evidence inform and cross reference each other. The structure of Transcendental Phenomenological methodology is employed to embrace and challenge validity in the complex process of Psychodrama Psychotherapy theory and practice (Moreno, 1921).

Psychodrama is rooted in the philosophy of spontaneity and creativity, therefore action as well as reflection creates a context in which the relationship experiences of opposite sex twins may be mirrored.

THE RELATIONSHIP EXPERIENCE OF OPPOSITE SEX TWINS. A PHENOMENOLOGICAL INVESTIGATION: TWELFTH NIGHT OR WHAT YOU WILL, BY WILLIAM SHAKESPEARE
Session: Poster

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As part of the investigations into the relationship experiences of opposite sex twins, the literature search has included many productions of *Twelfth Night*, and work with the twins in *Twelfth Night* by The Globe Theatre Company, 2002. This research activity has led to an unexpected interpretation.

It seems possible Shakespeare was commissioned to write a play for a festival at the Inns of Court, London. These Courts were a unique institution, full of students from Oxford and Cambridge learning common law. At this feast of liberty the law students elected a "Prince of Love" who presided over the unruly and rather rude celebrations in the "Kingdom of Love" held from Christmas until Candlemas (Arlidge, 2000). There are consequently many interesting socio-political interpretations of *Twelfth Night*.

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Shakespeare was the father of opposite sex twins. His twin son, Hamnet, died when he was 13. The age of the opposite sex twins in *Twelfth Night* would have been approximately the same age as Shakespeare's surviving twin daughter, Judith, who would have been about 17 when the first recorded performance of *Twelfth Night*, was held on Candlemas, February 2 1602.

A COMPARISON OF THE HERITABILITY OF PERCEPTUAL DISCRIMINATION SPEED AND IQ IN AUSTRALIAN AND DUTCH TWINS

Session: Behavioral Genetics

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Inspection time (IT) is a measure of perceptual discrimination speed that is shown to relate to complex cognitive indices such as IQ. In this study the effects of genes and environment on the inter-individual variation in IT between Australian (566 twin families including 129 siblings) and Dutch (317 families including 196 siblings) samples are compared. The IT task performed by both samples was the Pi-figure stimulus with a backward mask. Heritability estimates for IT (~0.36) were similar between Australian and Dutch cohorts. The Multidimensional Aptitude Battery measured IQ in the Australian sample, while the WAIS-3R was administered in Holland. A single trivariate model including IT, performance IQ and verbal IQ and specifying separate additive genetic, common environmental and unique environmental components of variance for each cohort was fitted to the data. Correlations between IT and IQ (performance and verbal) ranged –0.16 to –0.36. Assessment of the parameter estimates indicated that patterns of genetic and environmental variation and covariation were similar across countries, with genetic effects showing greater mediation of the IT–IQ relationship (bivariate heritability up to 0.36) than familial environmental effects. The similarity of IT heritability across country cohorts will allow samples to be pooled in forthcoming molecular genetic analyses of IT and IQ.

FETAL PHENOTYPES AND NEONATAL AND EARLY CHILDHOOD OUTCOMES IN TWINS

Session: Poster

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Objective. To evaluate factors associated with, and postnatal consequences of, altered patterns of fetal growth in twins.

Study Design. Fetal growth was measured at 28 weeks gestation on 218 twins, including head circumference, abdominal circumference, and femur length, and characterized as > or < = 10th percentile; children were followed through to age three. Logistic regression was used to generate odds ratios of perinatal factors associated with reduced fetal growth.

Results. Maternal height < 62 inches was associated with reductions in femur length (AOR 3.88, 95% CI, 1.42–10.57) and abdominal circumference (AOR 8.63, 95% CI, 2.41–30.94), while primiparity had a protective effect on both of these fetal measurements (AOR 0.28, 95% CI 0.13–0.64, and AOR 0.18, 95% CI, 0.06–0.60, respectively) as well as head circumference (AOR 0.32, 95% CI, 0.15–0.69). Smoking adversely affected femur and head growth (AOR 24.10, 95% CI, 3.69–157.57, and AOR 10.82, 95% CI, 1.73–67.79, respectively). Fetal reduction adversely affected femur and abdomen growth (AOR 5.85, 95% 1.52–22.51 and AOR 4.90, 95% CI 1.01–23.86, respectively), and monochorionicity and maternal weight gain < 0.65 lbs/week before 20 weeks adversely affected femur growth (AOR 5.47, 95% CI, 1.65–18.10, and AOR 3.39, 95% CI 1.34–8.59, respectively). At age three, all categories of twins with reduced growth by 28 weeks gestation were significantly shorter in height, and those with reduced abdominal circumference or head circumference at 28 weeks were also significantly lighter in weight compared to twins with adequate fetal growth by 28 weeks gestation.

Conclusions. These data identify short maternal height, smoking, monochorionicity, fetal reduction, and inadequate weight gain before 20 weeks as risk factors associated with reduced twin fetal growth by 28 weeks gestation, and significant residual reductions in height and weight through to three years of age.

RISK FACTORS FOR ADVERSE OUTCOMES IN SPONTANEOUS VERSUS ASSISTED CONCEPTION TWIN PREGNANCIES

Session: Poster

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Objective. To evaluate risk factors for adverse outcomes in spontaneous versus assisted-conception twin pregnancies.

Design. Historical cohort study.

Setting. Four academic tertiary medical centers.

Patients. Women pregnant with twins, including 2143 spontaneous and 424 assisted-conception; 2492 non-reduced and 75 reduced.

Interventions. None (observational).

Main Outcome Measures. Preeclampsia, preterm premature rupture of membranes (PPROM), birth < 32 weeks and < 30 weeks, low birthweight (LBW), very low birthweight (VLBW), and slowed mid-gestation fetal growth (< 10th percentile between 20–28 weeks).

Results. Among non-reduced pregnancies, assisted-conception was not significantly associated with any adverse outcomes; among nulliparas the risk for preeclampsia was increased regardless of method of conception; among spontaneous conceptions, the risks for PPROM, LBW, VLBW, and slowed mid-gestation fetal growth were increased. Among all pregnancies, fetal reduction increased risks for birth < 32 weeks and < 30 weeks, LBW, VLBW, and slowed mid-gestation fetal growth. Among nulliparas with assisted conceptions, fetal reduction increased the risks for birth < 30 weeks, VLBW, and slowed mid-gestation fetal growth.

Conclusions. These findings indicate that in twin pregnancies, assisted conception is not a risk factor for adverse outcomes, but rather specific factors that are more common among these pregnancies, such as nulliparity and fetal reduction, increase risks.

SPECIALIZED PRENATAL CARE AND MATERNAL AND INFANT OUTCOMES IN TWIN PREGNANCY

Session: Poster

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Objective. This study was undertaken to evaluate the effect of a prenatal nutrition and education program on twin pregnancy, neonatal, and early childhood outcomes.

Study Design. This prospective intervention study of women who participated in a specialized program (Program Pregnancies) versus non-participants included twice-monthly visits, dietary prescription of 3000–4000 kcal/day as a diabetic diet, pregravid BMI-specific weight gain guidelines for 20 weeks, 28 weeks, and after 28 weeks, multimineral supplementation, and patient education.

Results. Program participation was associated with improved pregnancy outcomes (preeclampsia, AOR 0.41, 95% CI 0.23–0.75; PPROM, AOR 0.35, 0.20–0.60; preterm labor, AOR 0.45, 0.30–0.68; delivery < 36 weeks, AOR 0.62, 0.43–0.89; delivery < 32 weeks, AOR 0.27, 0.15–0.51; LBW, AOR 0.42, 0.29–0.61; VLBW, AOR 0.30, 0.15–0.61), significantly longer gestations (+7.6 days), higher birthweights (+220g), lower neonatal morbidity (NICU Admission, AOR 0.48, 0.36–0.64; ROP, NEC, IVH, or ventilator support, AOR 0.44, 0.31–0.62), length of stay (–5.3 days) and cost per twin (–$14,023). Through to three years of age, Program children were significantly less likely to be rehospitalized (AOR 0.31, 0.10–0.91) or to be developmentally delayed (AOR 0.65, 0.44–0.96).

Conclusions. Program participation was associated with improved outcomes at birth and through to age three.

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THE RISE IN MULTIPLE BIRTHS IN THE UNITED STATES: WHO, WHAT, WHEN, WHERE, AND WHY

Session: Poster

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Who is having multiple births? Almost two-thirds of all twins born from 1996–2000 were born to non-Hispanic white mothers; they were also two to three times more likely to have a triplet birth than mothers of any other group.

What kinds of multiple births are on the rise? The steepest climb has been for triplets and quadruplets. Between 1989 and 2000, the number of births in triplet deliveries jumped 160% (from 2,529 to 6,742), and the number of quadruplet births by 120% (from 229 to 506). The number of quintuplet and other higher order multiples almost doubled (from 40 to 77), whereas twin deliveries increased a comparatively moderate 32% (from 90,118 to 118,916).

When have these trends occurred? The frequency of twin births has risen from 1:48 births in 1985 to 1:33 births in 2001. Triplet and higher-order births have risen dramatically, from 1:2,702 in 1980, to 1:539 in 2001.

Where are multiple births occurring? Massachusetts, Connecticut, and New Jersey reported the highest rates of twin and triplet and higher order births for 1996–2000. The Massachusetts twin birth rate of 37.1 per 1,000 was one-third higher than the national rate, and almost double the twinning rate for Hawaii (19.7). The highest triplet and higher-order birth rate was reported for New Jersey (368.44 per 100,000), twice that of the nation as a whole (177.1) and more than four times that of the lowest State-specific triplet and higher-order birth rate (67.1 for Wyoming).

Why have multiple births risen in the United States? Women are postponing child bearing because of career and educational opportunities, and multiple births occur at naturally higher rates among older mothers. Older maternal age alone, without the use of fertility-enhancing therapies, is believed to account for one-fourth to one-third of the rise. Another indirect factor may be the rise in divorce and subsequent remarriages, with many women starting second families at older ages. The single-most important factor, though, is fertility-enhancing therapies: fertility drugs, artificial insemination, and assisted reproductive technology (ART).

THE PSYCHOSOCIAL CONSEQUENCES OF MULTIPLE BIRTH CHILDREN FOR FAMILIES — DOES ASSISTED REPRODUCTIVE TECHNOLOGY MAKE A DIFFERENCE?

Session: Psychosocial Issues in Families with Multiple Births

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The twinning rate in England and Wales increased from just below 1% in 1980 to 1.47% in 2002. Most of this increase is attributed to the development and practice of assisted reproductive techniques, including ovulation induction, in vitro fertilization (IVF) and intra cytoplasmic sperm injection (ICSI), with some contribution from delayed maternal age at childbirth. Improvements in neonatal care mean that a higher proportion of pre-term and low birthweight babies, many of whom are twins or triplets, now survive.

Most studies of the impact of iatrogenic multiple births on psychosocial functioning in families have concentrated on whether IVF/ICSI per se affect children's development; at present there is little evidence of differences compared with spontaneously conceived children. Many studies exclude twins and higher multiples, in spite of their high prevalence among children conceived by IVF and ICSI (currently 27% in the UK).

This review presents mixed findings from the few small studies that compare parenting stress, child behavior and psychosocial wellbeing in families with twins conceived with and without medical assistance. A study of one-year-old twins indicated higher parental stress scores and lower psychosocial wellbeing among first time mothers of twins with a history of subfertility, than in mothers of twins conceived naturally or mothers who already had children. Two other small studies of twins at age five have shown few differences, in one an indication of greater parenting stress associated with parenting IVF twins. Strategies for further research on the psychosocial needs of twin families will be discussed.

ASCERTAINMENT OF OLDER TWINS IN THE MID-ATLANTIC TWIN REGISTRY

Session: Poster

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Published data from genetic epidemiological studies of cancer derive mostly from Scandinavian countries, which have access to large population-based registries of twins whose records are matched to publicly available medical databases and cancer registries. To the contrary, establishing a substantially large twin registry in the U.S. and collecting cancer-related information from a sufficiently large, genetically informative sample is both costly and time-consuming. Vu's Virginia Institute for Psychiatric and Behavioral Genetics (VIPBG) hosts the Mid-Atlantics Twin Registry (MATR), one of the largest population-based twin registries in the country, and has conducted large-scale surveys including potentially relevant risk factors for cancer.

The aim of this study is to test the feasibility of tracking older twins who have not been contacted for ten or more years and obtaining follow-up information by questionnaire.

The MATR includes twins born or living in Virginia, North Carolina and South Carolina. All adult (age 18 and above) twins and other multiples in the MATR have filled out one or more zygosity, health and/or lifestyle/personality questionnaires. Extensive data are available on demographics, health and disease, obesity, smoking, drinking, exercise, attitudes and quality of life. Of over 3000 MATR twins aged 60 and above, current addresses were obtained using the Internet services of Accurint for 2079 twins who are not deceased and have not refused to participate in research. The twins were sent a two-page follow-up questionnaire focused on updating demographic data and obtaining cancer-related information such as family history of cancer, cancer survival, and a range of risk factors. Response rates were 20% after one mailing and 28% after the rEmailing. Results from this pilot project are critical in evaluating the feasibility of extending this approach to tracking and follow-up of other older twins and relatives and in exploring other options of ascertaining a large genetically and cancer informative sample of older twins.

GENETIC AND ENVIRONMENTAL INFLUENCES ON TEMPERAMENT IN LATE ADOLESCENCE: RESULTS FROM A MOSCOW LONGITUDINAL TWIN PROJECT

Session: Poster

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This study was completed as part of a Moscow longitudinal twin project and aimed to explore genetic and environmental contributions to temperament in late adolescence. Fifty-three pairs of monozygotic (MZ) and 55 pairs of same-sex dizygotic (DZ) Russian twins aged 16–18 years (M = 16,41; SD = 0,37) completed the children's version of the Structure of Temperament Questionnaire (STQ; Rusalov, 1990), designed to measure eight dimensions of human temperament. STQ dimensions include four object and four subject related dimensions, which refer to the Anokhin four-stage structure of the functional system: the afferent synthesis is related to Ergonicity; the programming stage to Plasticity; the execution stage to Tempo; and feedback to the acceptor of the results of action to Emotionality. Significant genetic influences were revealed on all STQ dimensions. Model-fitting analyses showed that a simple genetic model, in which the additive genetic and non-shared environmental effects are included, and in which shared environmental coefficients are dropped from the model, provides the best fit to the data. Under this model, additive genetic influences accounted for a substantial amount of variance in Object-related Ergonicity (a^2 = 64%; χ^2 = 3.92; p = .42), Social Ergonicity (a^2 = 42%; χ^2 = 1.22; p = 0.88), Object-related Plasticity (a^2 = 27%; χ^2 = 1.98; p = .74), Social Plasticity (a^2 = 40%; χ^2 = 2.78; p = .60), Object-related Tempo (a^2 = 32%; χ^2 = 2.44; p = .66), Social Tempo (a^2 = 47%; χ^2 = 1.31; p = .86), Object-related Emotionality (a^2 = 43%; χ^2 = 0.82; p = .94) and Social Emotionality (a^2 = 37%; χ^2 = 1.92; p = .75). Non-shared environmental effects explained the rest of the total variance in these dimensions. These findings are consistent with the majority of twin studies of temperament that typically find moderate heritability estimates, with no evidence for shared environmental influence.

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THE US MATCHED MULTIPLE BIRTH FILE, 1995–2000

Session: Poster

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This report describes the world's largest and most comprehensive research data set on multiple births. The Matched Multiple Birth File, 1995–2000 includes records for all births, fetal deaths and infant deaths reported in twin, triplet, and quadruplet deliveries in the United States over the 6-year period. Included are individual records of births and deaths in multiple deliveries, and also matched sets of records of multiple births. The vast majority of records, 96%–99% depending on plurality, are matched to the corresponding set mate. This large data set is comprised of more than 320,000 sets of twins, 12,000 sets of triplets, and 700 sets of quadruplets. The file allows for research on multiple deliveries by an broad range of characteristics, for example, maternal age, parity, education, race and ethnicity, prenatal care utilization, medical risk factors, and tobacco use. Some infant characteristics available in the data set are sex, set order, gestational age, birthweight, and cause of death. Examples of selected research results such as mortality risk by plurality and gender-type of set will also be presented.

PANEL DISCUSSION OF THE EDUCATIONAL ISSUES AFFECTING MULTIPLES

Session: Poster

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This will be an open panel discussion of the educational issues affecting multiples as learners. The presenter will begin by reporting on some of the themes from his research on how multiples learn including: (1) role of expectations peers and adults have in academic environments; (2) how male and female same-age siblings react to competitive and cooperative learning situations; and (3) an assessment of teachers' and administrators' knowledge of multiples as learners.

After a brief introduction of these themes, attendees will be encouraged to discuss and plan appropriate strategies for addressing issues affecting multiples as learners.

DIVERSE LEARNING CHARACTERISTICS OF MZ/DZ TWINS AND THE RESPONSE OF THE EDUCATIONAL SYSTEM TO THOSE UNIQUE NEEDS

Session: Psychosocial Issues in Families with Multiple Births

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The collaboration of researchers studying the education of multiple birth children and parents of multiples groups, such as the National Organization of Mothers of Twins Clubs, Inc., can result in a positive change in the educational environment.

This presentation will review findings from Dr. Mascazine's studies into learning styles of twins, including his most recent study into "How identical and fraternal twins learn: Styles and Issues." Examples will be provided to illustrate how this research translates into educational practice.

Additional psychosocial considerations affecting the education of multiple birth children will also be addressed through a review of NOMOTC's seven-part "Guidelines for the Education of Multiple Birth Children." These guidelines were developed following a review of several studies on the topic representing different types of research (e.g. descriptive-interpretative, correlational). Data from NOMOTC's most recent studies with educators and parents on this topic will be included, as well as data collected by Dr. Mascazine on the impact of the use of NOMOTC's education-related materials with preservice and inservice teachers.

RELIABILITY OF ULTRASOUND ASSESSMENT OF CHORIONICITY IN TWIN PREGNANCY

Session: Controversies on Obstetric Issues

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The aim of our study was to determine the reliability of ultrasound assessment of chorionicity in twin pregnancy in comparison with postpartum placental assessment.

Our study was conducted at the Aberdeen Maternity Hospital, Aberdeen, UK. We studied 167 sets of twins delivered between March 2001 and March 2004.

Chorionicity was determined using high resolution ultrasound on the first visit scan. Scans were performed by trained ultrasonographers in a routine clinic. During the first trimester chorionicity can be assessed as early as five weeks post-conception. Determination of chorionicity in late second and third trimesters is a challenge and consideration has to be given to fetal gender, placental location and number, as well as characteristics of the dividing membrane.

Antenatal diagnosis of chorionicity was compared with postpartum determination of chorionicity by detailed examination of the placenta and membranes by specifically trained laboratory staff or, if possible, by histological examination of the dividing membrane.

The implications for management of twin pregnancy antenatally will be considered in the context of our findings.

MIRROR IMAGED HANDEDNESS: A FINITE MIXTURE DISTRIBUTION APPROACH

Session: Behavioral Genetics

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The theory of mirror imaged handedness proposes a mechanism which acts to increase the rate of discordance within MZ twin pairs and increase the rate of left-handedness across MZ twins. The effects are hypothesized to occur more frequently in later-splitting monochorionic (MC) MZ twins than in their earlier splitting dichorionic (DC) counterparts, as it is more likely that lateralization will have been established in the blastocyst prior to twinning. One approach to detecting mirror imaging is to compare the rates of discordance in MC and DC MZ twins. However, recent reports have suggested that retrospective reports of chorionicity are frequently inaccurate. We have used a mixture distribution approach, which takes into account the unreliability of chorionicity using estimates of diagnostic accuracy to weight the likelihood of the data according to the probability that any given pair is either MC or DC. This method was applied to data from Australian (711 MC MZ, 2611 DC MZ, 3821 DZ) and Dutch (754 MC MZ, 2158 DC MZ, 5302 DZ) twin pairs. Even allowing for up to 50% inaccuracy in reported chorionicity, we found no difference in the covariance of MC and DC twins, and MZ twins were no more likely to be left-handed than DZ twins in either the Australian or the Dutch samples. These findings suggest no systematic effects of mirror imaging.

HERITABILITY OF SERUM LEPTIN LEVELS: A TWIN STUDY

Session: Poster

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Objective. *To study the contribution of genetic factors to the variation of serum leptin concentration in healthy, normotensive twins.*

Methods. A total of 57 pairs of twins was investigated: 28 female and 19 male pairs of monozygotic (MZ) twins; and six female and four male pairs of dizygotic(DZ) twins. The zygosity of twins was determined by comparing the concordance of the genotype of nine fluorescence-labeled microsatellite markers; the genetic analysis using analysis of variance-based method. Serum leptin levels were determined in duplicate by a radioimmunoassay Kit (Linco Research, Inc., St. Charles, Missouri) as previously described.

Results. The test of genetic variance revealed a significantly larger within-pair variance of serum leptin in the DZ twins, in comparison with the MZ twins.

The corresponding heritability estimate was 0.11 for serum leptin, yet after adjusting for BMI, gender, and uric acid (UA), heritability was decreased to 0.015.

Log serum leptin was correlated significantly with blood pressure (SBP $r = .355$ $p < .001$; DBP $r = .339$; $p < .001$). Stepwise multiple linear regression analysis revealed that only BMI, gender and uric acid (UA) were linked independently to serum leptin ($R^2 = .788$, $p < .001$). Heritability was estimated at 31.5% for BMI, 23.1% for SBP and 48.4% for DBP.

Conclusion. Our data indicate that environment rather than genetic factors are important determinants of leptinemia. Both environmental and genetic factors contributed to the variation of blood pressure and BMI.

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EFFECT OF EARLY MATERNAL WEIGHT GAIN ON TWIN FETAL GROWTH AND BIRTH OUTCOMES: A THEORETICAL FOUNDATION

Session: Poster

S. Min, B. Luke, B. Gillespie, L. Min, R. B. Misiunas, V. H. Gonzalez-Quintero, C. Nugent, F. R. Witter, R. B. Newman, G. D.V. Hankins, D.A. Grainger and G.A. Macones??
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Objective. To construct a theoretical framework that characterizes twin fetal growth and determines twin birthweight and length of gestation, and to examine the effect of early maternal weight gain.

Study Design. This retrospective study was based on live born twins of at least 28 weeks' gestation from Ann Arbor, Michigan; Miami, Florida; Baltimore, Maryland; Charleston, South Carolina; Galveston, Texas; Wichita, Kansas; and Philadelphia, Pennsylvania. A nonlinear mixed model of fetal growth was specified by Gompertz (and spline) function of gestational age with multiplicative and additive covariate effects. A nonlinear model of birthweight was expressed as a function of length of gestation, augmented by a linear model for length of gestation. Covariates considered were maternal weight gains in three periods (conception–20 weeks, 20–28 weeks, 28–36 weeks), race, mother's height and pregravid weight, multiparity, smoking, pre-eclampsia, and male gender.

Results. Only multiplicative effects were significant in the fetal growth model with Gompertz function. The growths in periods two and three occurred in the ratio of roughly 2:3. Growth prior to week 12 was not significant in the multiplicative effects spline model. Both early and mid maternal weight gains were highly significant ($p < .0001$) in the reduced fetal growth models and the spline birthweight model. Early maternal weight gain was the only significant factor (negatively) in the length of gestation model.

Conclusion. Early maternal weight gain is a significant factor in improving twin fetal growth and birthweight in a framework of proportional growths and a recursive system of length of gestation and birthweight.

BIRTHWEIGHT REFERENCES FOR TRIPLETS

Session: Poster

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Objective. To formulate growth references that reflect triplet fetal and neonatal populations at each gestational age by combining serial ultrasonographic estimates of fetal weights and measured birthweights.

Study Design. This historical cohort study was based on 188 pregnancies of live born triplets of at least 23 weeks gestation from Ann Arbor, Michigan; Miami, Florida; Springfield, Illinois; Baltimore, Maryland; and Charleston, South Carolina. Intrauterine growth, based on ultrasonographic fetal weight measures, was modeled as a function of gestational age for each infant to estimate fetal growth at regular intervals. Linear regression models with quadratic terms and no intercept (to constrain the size to be zero at conception) fit the growth pattern well. Ultrasonographic fetal weight estimates near birth suggested a bias (usually upward and differing by site) in comparison with actual birthweights. The bias (assumed proportional over the gestational period) was estimated for each triplet as the ratio of predicted fetal weight at birth (on the basis of ultrasonographic measurements) to actual birthweight and corrected. Weight percentiles were generated.

Results. Well-grown triplets did not fall substantially below singletons until 30 weeks and twins until after 34 weeks. Trichorionic vs. mono- or dichorionic placentation resulted in 27% higher growth at the 10th percentile, 5% higher growth at the 50th percentile, and 4% higher growth at the 90th percentile by 34 weeks.

Conclusions. The overall pattern of fetal growth for well-grown triplets does not differ from that of singletons and twins until late gestation, confirming that well-grown fetuses have similar growth potentials, regardless of plurality.

MY OWN REGISTER "TWINS, TRIPLETS AND MORE" ("TTAMOM")

Session: Poster

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In memoriam Professor E. I. Schwarz.

During the last decade the author has been setting up her own register of twins, triplets and more, their families and families with multiple pregnancies and labors in their family history. The register includes two subgroups: Twins and triplets with congenital malformations and inherited diseases; and random families with multiple pregnancy and labor. The first cohort includes about 49 pairs of twins and one set of triplets from a family that has many children with congenital disturbances. The second cohort includes 216 families with twins. Author is a medical geneticist certificated and experienced. All these families are under her professional patronage. For our contact and connection we use phone, Email, different forms and questionnaires etc. Our discussions of the problems of family health are free of charge. As predictive genetic counseling the insertion (I)/deletion (D) polymorphism of ACE gene among ten twin sisters was studied. The most frequent question for genetic counseling is prognosis of complex and oncological diseases.

DRINKING HABITS IN TWINS AND SINGLETONS

Session: Poster

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Objective. To study whether twinship contributes to risky drinking of alcohol, by comparing alcohol use by twin and singleton males and females.

Subjects and methods. The Northern Finland Birth Cohort 1966 (NFBC-66) includes 198 twins and 8569 singletons with expected date of delivery in the year 1966, who responded to the follow-up questionnaire at the age of 31.

Alcohol use and socio-demographic factors were inquired by questionnaire, and maternal age and parity were taken from delivery records.

Results. There was no difference between twins and singletons in abstinence. However, twin males drank less often and smaller amounts of alcohol at one time compared to singleton males. Logistic regression showed that male twins' risk for hazardous alcohol use, compared to singleton men, still decreased when the socio-demographic background factors were taken into account. The alcohol consumption by females did not differ significantly between twins and singletons.

Conclusions. Twins have their co-twin for support both when facing problems and practicing social skills. This positive context of twinship can be seen as a protective factor against heavy use of alcohol.

THE ROLE OF INTRA-OVARIAN GROWTH FACTORS IN DIZYGOTIC TWINNING

Session: Current Developments and Findings from Twin Studies

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Natural pregnancy in women leading to dizygotic twins, clusters in families and is under genetic control. The aim of our studies is to understand molecular mechanisms that influence DZ twinning and fertility using a combination of genome wide and candidate gene approaches. One critical pathway controlling fertility and infertility is growth factor signaling between different cell types in ovarian follicles. The growth factors BMP15 and GDF9 are expressed in the oocyte and play key roles in follicle development and twinning frequency. We sequenced GDF9 in probands from twenty DZ twinning families. We identified a four base pair deletion in exon 1 of GDF9 in two sisters with DZ twins. The deletion introduces a premature stop codon resulting in a truncated protein. It was not observed in individuals from 429 other families included in our study. We genotyped eight single nucleotide polymorphisms (SNPs) across the GDF9 locus in 379 families with two sisters who have both given birth to spontaneous DZ twins (1527 individuals) and 226 triad families with mothers of twins and parents (723 individuals). There was no evidence for association between common variants in GDF9 and twinning in our families. We conclude that rare mutations in GDF9 may influence twinning, but twinning frequency is not associated with

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common variation in GDF9. To search for other mechanisms that play a role in human DZ twinning, we are collecting 1000 sister pair families from Australia and the Netherlands. We will complete a genome screen in these families to find genes associated with twinning and human fertility.

HLA HAPLOTYPE SHARING IN DIZYGOTIC TWINS

Session: Molecular Genetics and Twin Studies

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Jawaheer and others (1996) reported increased sharing of HLA haplotypes in 93 dizygotic (DZ) twin pairs. There was no evidence of increased sharing in 128 sib-pairs suggesting DZ twins are genetically more similar at the HLA complex than sibs from separate pregnancies (Jawaheer et al., 1996). A second study of 114 twin pairs from the Danish Twin Registry failed to replicate this result and found twins were not more similar at the HLA locus (Titlestad et al., 2002). We recruited a population based sample of 419 families of adolescent DZ twins from schools in the Brisbane and surrounding areas of south eastern Queensland. Samples were collected from twins, sibs and their parents. We recently completed genome scans in these DZ twin pairs including markers close to the HLA locus. Marker information is also available from both parents for 85% of these twin families. Results of identity-by-decent sharing around the HLA locus in these families will be reported.

PHYSICAL GROWTH CURVES IN JAPAN AND TWINS' GROWTH DATA

Session: Poster

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When a parent registers a pregnancy with a municipal city office, physical growth curves are widely distributed through the mother-child booklet. These curves are regarded as the standard for Japanese physical growth from birth to six years old. These are the time series data of the height, the weight, the girth of the head, and the obesity index against the birth age. A baby is investigated under the normal physical growth when baby's data are within the range 3%–97%. The situation is more crucial in the case of multiple births. Multiple births are only 1% of all birth cases in Japan, and the average gestational age is 36–37 weeks. Even for the average multiple birth case, the physical growth curve is outside the range 3%–97%, which makes it difficult to predict and diagnose the really problematic cases. This also becomes one of the stresses for parents early in the nursing. There are some symptomatic treatments, for instance the corrected month age. However, they do not bring a true solution.

Weight is an especially important index compared with other growth data. We focus on the time series data of weight and discuss the problem and subject of the future by investigating the possibility of improved methods using some twins' growth data.

GENETIC INFLUENCES ON SMOKING BEHAVIOR

Session: Genetics of Nicotine Dependence (Symposium)

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Adult and adolescent twin studies have demonstrated that many aspects of smoking behaviour, such as smoking initiation and smoking cessation, are strongly influenced by genetic makeup. Heritability estimates for these traits range from 50–70%, and candidate genes for smoking-related traits are beginning to be identified through linkage and association studies. We report the results of twin and linkage analyses of smoking behavior in a large sample of Australian twins. Information regarding alcohol and drug use has been collected from these twins through a number of questionnaires and interviews, providing a range of measures of smoking behavior. A subset of these twins has also been genotyped for the purpose of linkage analysis. The results of these analyses may provide insight into why some individuals are more likely to progress from experimental to dependent cigarette use, and the factors that influence smokers' ability to successfully stop smoking tobacco.

ERYTHROPOIETIN IN CORD BLOOD OF TWINS: ASSOCIATION WITH SIZE AT BIRTH

Session: Poster

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We recruited women with twin pregnancies in Melbourne and Adelaide and collected cord blood to measure erythropoietin (EPO) as an indicator of oxygen supply to each fetus and a possible marker of placental sufficiency. Birthweight standard deviation score (SDS) was calculated. We used generalized estimating equations (GEE) for analyses treating twins as individuals and because EPO values were skewed we used log EPO in analyses.

Cord blood was collected from both infants of 145/200 (73%) pairs. Geometric mean EPO was higher in boys and with increasing gestation, but did not differ significantly between monochorionic versus dichorionic twins.

Log EPO was negatively related to birthweight SDS (dependent variable). This association appeared stronger in children delivered by elective Caesarean (ECS) versus other delivery modes (beta –1.26 vs. –0.36 respectively; $p = .045$ for interaction), and in males versus females (beta –1.79 vs. –0.18; $p = .02$ for interaction). There was no evidence of interaction with chorionicity ($p = .3$) or gestation length ($p = .8$).

Within twin pairs the log EPO — birthweight SDS relationship remained, and was stronger in pairs delivered by ECS versus others (beta –1.83 vs. –0.81; $p = .01$ for interaction).

Since the association was seen and was stronger in infants delivered by ECS, we suggest cord blood EPO was influenced by factors operating during gestation, but there was an additional influence of factors during labor and delivery.

A correlation between EPO and gestation length has been observed in singleton pregnancies and may reflect increasing placental insufficiency with longer gestation.

MORBIDITY AND MORTALITY IN TWINS: A PROSPECTIVE TWO YEARS STUDY IN KASHAN, IRAN

Session: Poster

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Introduction. Twin pregnancies have been considered as high risk because of the associated complications and unfavorable outcomes. To determine the incidence, morbidity and mortality of twin pregnancies, this study was carried out in Kashan, Iran.

Material & Methods. In this prospective study all the twins who were delivered between 2000 and 2002 were investigated. Details of gestational age, mode of delivery, maternal age, sex, birthweight, season of birth, cause of admission, mortality, and use of ovarian stimulating drugs were recorded and analyzed.

Results. During the study period there were 10,011 deliveries of which 142 were twins, giving an incidence rate of 14.1/1000 deliveries.

In total 38% of newborns were delivered vaginally and 62% by cesarean section.

The age range of the twins' mothers was 18–37 years. Eighty-one percent were preterm whereas 19% were term at delivery. Fifty-eight of the twins (40.8%) required admission.

Neonatal complications include prematurity, hyperbilirubinemia, hyaline membrane disease, hypoglycemia, septicemia, hypocalcemia, perinatal asphyxia, intraventricular hemorrhage, necrotizing enterocolitis and congenital malformations.

The most seasonal prevalence of twin pregnancy was in winter. Twenty-six percent of mothers had a history of ovarian stimulating drugs consumption.

The incidence of low birthweight(LBW), very low birthweight (VLBW) and normal weight among the twins was 9%, 55% and 36% respectively. The highest mortality rate was among the VLBW groups and was directly related to prematurity.

Conclusion. Since the outcome is dependent on gestational age and birthweight, the closer the gestational age is to term, and birthweight is to normal, the better is the outcome.

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POSTPARTUM DEPRESSION: RESULTS OF A STUDY OF 1345 MOTHERS OF MULTIPLES

Session: Poster

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Postpartum depression (PPD) is a common and prevalent psychiatric disorder that affects women when they are undergoing many physical and emotional changes. During the first year after childbirth, 10–15% of women develop postpartum depression. Psychosocial factors, such as stressful life events and poor social support contribute to PPD. Mothers of multiples tend to have higher than normal stress associated with their pregnancies. This study was performed to find out if births of twins or higher order multiples were associated with higher than normal levels of PPD. The participants were obtained from the National Organization of Mothers of Twins Clubs, Inc. (NOMOTC) and Mothers of Supertwins (MOST). One thousand, three hundred and forty-five mothers of multiples responded. Results showed that a higher percentage of mothers of multiples reported experiencing depression than mothers of singletons in previous reports. Data also indicated several individual stressors on the risk of PPD following a multiple birth. This presentation will review these findings and show similarities and differences in data between mothers of higher order multiples and those with twins.

MONOZYGOTIC TWIN CASES OF THE AGENESIS OF THE CORPUS CALLOSUM WITH SCHIZOPHRENIC DISORDER

Session: Poster

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We report here the identical monozygotic twin cases of the agenesis of the corpus callosum that demonstrated schizophrenic disorder. Patients were 26-year-old twin brothers and both cases were diagnosed as having schizophrenic disorder by DSM-III-R's diagnostic criteria. On magnetic resonance imaging both cases demonstrated the total agenesis of corpus callosum and the anterior commissure was hypertrophic. We speculate that the developmental disturbance of the corpus callosum might be related to the cause of the psychiatric disorders in the present cases.

DISCORDANT MZ TWINS WITH CLEFT LIP AND PALATE: A MODEL FOR IDENTIFYING GENES IN COMPLEX TRAITS

Session: Molecular Genetics and Twin Studies

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Monozygotic (MZ) twins are commonly discordant in birth defects with a complex gene/environment etiology. Explanations for these differences include differential environmental exposure in utero, variability in imprinting or X inactivation (in female pairs) or stochastic effects. Occasionally MZ twins are discordant for chromosomal and single gene disorders. In a handful of these unusual cases, somatic mosaicism has been identified as the mechanism. For complex traits, such as cleft lip and palate, discordant MZ twins offer the possibility for identifying somatic mutations in candidate genes in affected twins which can provide strong confirmatory evidence that a particular gene is involved in the disorder. MZ twins have an advantage over other paired comparisons, in that DNA sequencing of candidate genes should only identify those rare etiologic mutational events responsible for the discordances, as single nucleotide polymorphisms (SNPs) should be completely identical in MZ twin pairs. In this report we describe our preliminary experience with a collection of MZ and DZ twins with cleft lip and palate including extensive DNA sequencing performed on a collection of 13-candidate genes in fourteen discordant pairs. We have failed to identify any somatic differences in more than 11,000 base pairs of DNA sequenced in fourteen MZ pairs for a total of approximately 250,000 base pairs of sequence comparisons, supporting the hypothesis that non-etiologic post-twinning mutations are rare. This project outlines a method for using a similar approach in other complex traits. Sequence comparisons of discordant MZ twins can identify etiologic mutations in a cost-effective manner and take advantage of the frequent occurrence of discordant MZ pairs available.

GENERALIZED MARGINAL MAXIMUM LIKELIHOOD APPROACHES TO THE ESTIMATION OF ITEM RESPONSE AND FACTOR ANALYTIC MODELS TO DATA FROM TWINS

Session: Statistical Issues in Twin Studies II

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Takane & DeLeeuw (1987, *Psychometrika* 52, 393–408) showed that confirmatory factor analysis and normal ogive item response theory models are equivalent. In the context of a twin study, therefore, the multivariate model known as the latent phenotype, common pathway, or psychometric factors model is essentially a direct extension of this model to data collected from twins. The significant complication of this approach is that the residual, item-specific variances may correlate in twin pairs, which implies a form of lack of conditional independence of the items, and which is difficult to overcome with traditional IRT software. To alleviate this problem, modifications were made to the Mx software that permit the efficient fitting of latent phenotype models to large numbers of items by generalized marginal maximum likelihood. Thus analyses involving 25+ binary or ordinal items measured on each twin are rapidly accomplished. Illustrations and limitations of the method are discussed.

LOW BIRTHWEIGHT AND SCHIZOPHRENIA — A SWEDISH TWIN STUDY

Session: Poster

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Background. Epidemiological studies have shown that low birthweight is associated with increased risk of schizophrenia. However, the association might be confounded by common shared environmental effect (e.g., intrauterine malnutrition), or due to the fact that the genetic vulnerability for schizophrenia is mediated by pre- and perinatal stress.

Aim. To investigate the association between low birthweight and schizophrenia in a population-based Swedish twin sample.

Methods. We linked the Swedish twin register and the nation-wide hospital discharge register to identify twins with schizophrenia and their co-twin, and retrieved birth records from hospital archives from 172 twins. As controls we used: (1) unaffected unrelated twins matched for age and sex; and (2) unaffected co-twins.

Results. In analysis with unrelated twins, individuals with low birthweight had an increased risk of schizophrenia. No such associations were found when the co-twins were used as controls. Further, there was no difference in birthweight between the twins with schizophrenia and the unaffected co-twins.

Conclusion. Previous reported association between low birthweight and risk of schizophrenia might not be causal. Rather, the association might have been confounded by genetic and/or shared environmental influences.

CONCORDANCE, DISEASE PROGRESSION AND HERITABILITY OF CELIAC DISEASE IN ITALIAN TWINS

Session: Poster

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Twin approach was adopted to estimate the contribution of genetic factors to celiac disease (CD).

Seven thousand records of the Italian Celiac Disease Association were matched with the Italian Twin Registry, which includes approximately 650,000 potential twin pairs born before 31 December 1995. Eighty-one twin pairs were identified (2.3 twins/100 individuals) and 73 entered the study. Twenty-three pairs were monozygotic (MZ, 6 male-male) and 50 were dizygotic (DZ, 12 male-male, 15 female-female and 23 opposite sex).

Overall, 17/23 MZ and 5/50 DZ twin pairs were CD concordant; proband-wise and pair-wise concordances were 85% and 73.9% in MZ and 18.2% and 10.0% in DZ twins. Proband-wise concordances in pairs with HLA genotypes coding for DQ2 or DQ8 susceptibility molecules and identical HLA chromosomes were 83% and 31% in MZ and DZ twins, respectively.

In 11 concordant pairs (9 MZ, 2 DZ) symptoms appeared almost simultaneously in both twins, thus discordance time was short (< = 2 years). In 8/10 (6 MZ, 2 DZ) concordant pairs with symptom-less co-twins, the discordance time was within one year, and in 2/10 (1 MZ and 1 DZ) 10 and 37 years. One-year cumulative probabilities of remaining

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disease-free were 43% and 92% for MZ and DZ co-twins, respectively. After 5 years, the probability was 29% for MZ and unchanged for DZ co-twins.

Using structural equation modeling with incomplete ascertainment, estimated heritability of liability to CD will be presented considering different scenarios of population prevalency.

FETAL SURVEILLANCE AND THE NOCEBO EFFECT: RECOMMENDATIONS FOR A NORMAL PREGNANCY, VAGINAL BIRTH AND OPTIMAL OUTCOME

Session: Controversies on Obstetric Issues

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Despite increasing screening, monitoring, and surgical delivery of twin pregnancies, the incidence of preterm births and low birthweight infants has steadily increased in the past three decades. Evidence has shown that bed rest is not only useless, it is harmful. Neither tocolytics nor ultrasound has improved outcome. This session will explore what we learn from mothers who carry normal birthweight babies to term, birth them naturally, and breastfeed.

GENETIC AND ENVIRONMENTAL INFLUENCES ON DSM-IV ANXIETY DISORDERS: DIMENSIONS IN ITALIAN TWINS AGED 8–17

Session: Poster

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The preliminary results of an ongoing study of behavioral assessment among twins aged 8–17, resident in the Provinces of Milan and Lecco and enrolled through the Italian Twin Registry are presented. Out of 2, 015 families contacted by mail, 973 agreed to participate on the survey. These data are based on the first 228 twin pairs who agreed to participate: 75 pairs were classified as MZ (42 male, 35 female) and 151 pairs as DZ (30 male, 49 female, 72 opposite sex) by questionnaires. Parents filled in the CBCL6-18 scale and twins filled in the Italian version of the SCARED (Screen for Children Anxiety Related and Emotional Disorders) scale, a self-assessment instrument for screening DSM-IV anxiety disorders in children and adolescents. Psychometric properties of the SCARED scale were evaluated (Chronbach alphas > .85) and structural equation modeling was applied using Mx (Neale, 2003) to the five factors — Panic Disorder (PD), Separation Anxiety Disorder (SA), Generalized Anxiety Disorder (GAD), Social Phobia (SP) and School Phobia (SchPh) — originally identified by Birmaher et al.,1997.

For SA, SP, PD SchPh and PD the best fitting model was an AE model, with heritability estimates of .61 for SA, .55 for SP, .52 for SchPh, and .43 for PD. Significant shared environmental influences were found only for GAD (χ^2 = .29, with heritability of .18).

HIGH RISK OF CONGENITAL HYPOTHYROIDISM IN MULTIPLE DELIVERIES

Session: Poster

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Newborn twins have increased chance of prematurity. This can affect thyroid function and consequently it could to be a risk factor for transient or permanent congenital hypothyroidism (CH). According to the nationwide CH neonatal screening programme a biochemical assessment of thyroxine (T4) and/or thyroid stimulating hormone (TSH) is performed within a few days from birth. Positive results of screening tests are confirmed by definitive tests of thyroid function on serum. It has been recently reported that fetal blood mixing between a hypothyroid and an euthyroid twin can cause a lowering of TSH at screening in the hypothyroid baby and may result in a delayed or missed CH diagnoses.

We investigated the Italian population of CH infants recorded in the Italian National Register for CH from 1989 to 2000. During that period 2,159 CH babies were diagnosed in Italy by neonatal screening. Among them 80 were twins and only four couples and one triplet were concordant for CH. A significantly higher risk of CH (RR:2.1, C.I.95% 1.34–3.25) was found in multiple deliveries when compared to single deliveries. Moreover, although we could not separate monochorionic twins from the others, after adjustment by multivariate analysis significantly lower TSH values at screening were observed in twins than in singletons, and the mean percentage increase in TSH between screening and recall was higher in the twin CH newborns (307.9%) as compared to singletons (129.5%).

In conclusion, these results suggest that a greater attention should be paid to multiple deliveries and special guidelines for CH screening procedure in twins are needed.

GENETIC AND ENVIRONMENTAL INFLUENCES ON SOCIO-POLITICAL ATTITUDES

Session: Poster

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The goal of the research was to assess the relative contribution of genetic and environmental factors to the phenotypic variability of socio-political attitudes in a Polish sample. The attitudes considered were described on two dimensions: Moral conservatism–liberalism (MC–L) and Free market economy–government intervention (FME–GI). The study was conducted on 119 pairs of monozygotic (MZ) and 123 pairs of dizygotic (DZ) same-sex twins, aged from 18 to 25. The zygosity of twin pairs was assessed by means of the self-reported Questionnaire of Twins Physical Resemblance. The data from the study was analyzed by model fitting using the method of maximum likelihood carried out by LISREL8 program. Only the MC–L scale demonstrated significant additive genetic influence (0.28). Additionally, it was found that the variance of two attitudes dimensions considered was in the most part explained by shared environment. This factor accounted 37 and 53 percent of the scales variability (MC–L and FME–GI, respectively). The non-shared environment explained 35 (MC–L) and 47 (FME–GI) percent of the attitudes variability.

ZYGOSITY DIAGNOSIS AND MISCLASSIFICATION IN YOUNG TWINS ASSESSED BY QUESTIONNAIRE FOR TWINS' MOTHERS IN JAPAN

Session: Poster

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The first part of the present study deals with the determination of zygosity in twins of childhood age by simple questionnaire. The subjects were 224 twin pairs and their mothers, consisting of 159 monozygotic (MZ) and 65 same-sex dizygotic (DZ) pairs, identified by genetic markers including DNA samples. Mothers of twins responded to 19 questionnaire items dealing with twin similarity in 16 items about physical features and three items about the degree of similarity and frequency of being mistaken (confusion of identity) when twins were about one year of age. The results of stepwise logistic regression analysis were as follows: the total accuracy of the mothers' questionnaire was 91.5% when using only the items dealing with confusion of identity. The total accuracy of mothers' questionnaire responses rose to 95.1% when we used all 19 items. In addition to "the frequency of being mistaken", two physical features, namely "shape of fingers" and "shape of eyebrow", were very informative. In conclusion, twin zygosity can be estimated by the use of the mothers' simple questionnaire with sufficient accuracy even in very young twins about one year of age. We also studied the problem of zygosity misclassification at birth, which has been paid little attention in Japan, using information on zygosity obtained from four independent samples, by means of a questionnaire, which included questions that assist in zygosity determination mentioned above. We found that even now many MZ twins in Japan may be misclassified as DZ at birth based solely on the number of placenta.

CONSTRUCTION OF A JAPANESE DATABASE ON INFANT TWINS AND THEIR FAMILIES: THE CHARACTERISTICS OF BASIC OBSTETRICAL AND PHYSICAL GROWTH DATA

Session: Poster

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We have been constructing the continuous database system of Japanese twins and their families, mainly to the purpose of contributing to maternal and child health care and to genetic epidemiologic twin family studies. Two large subgroups of different methods of data collection were compared with each other, and with twins' birthweight data based on vital statistics. The purpose of the present study is to estimate the selection biases of our database. Twins of first subjects were school applicants,

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consisting of 1092 twin pairs, and second subjects were children of members of several maternal associations, consisting of 937 pairs. Data on perinatal obstetrical findings of mothers and twins' growth and development after birth recorded in the Maternal and Child Health Handbook, which was offered to every Japanese pregnant woman, were gathered by means of questionnaire. Body size parameters at birth were slightly smaller in the maternal associations group. Nevertheless, not only birthweight itself, but relative birthweight difference in percentage were nearly the same compared with twins' birthweight norms obtained from vital statistics. In addition, body weight and height after birth through six years of age of both groups were nearly the same. These findings supported the representativeness of our database at least for physical development. It was concluded that the present methods of data collection are one of the best possible way in Japan.

INCIDENCE OF FALLS AMONG OLDER FEMALE TWIN PAIRS

Session: Aging and Longevity II

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Objective. To examine environmental and genetic effects on risk of falls among older community dwelling female twins.

Methods. Data on falls was obtained from 97 monozygotic (MZ) and 116 dizygotic (DZ) female twin pairs aged 63 to 76 years. They filled in daily a fall calendar for an average 349 (SD 42) days. Those reporting a fall were phoned monthly to collect more detailed information about the fall and possible injuries. The relative importance of genetic and environmental factors for fall risk was studied by comparing proband-wise concordance and tetrachoric correlations in MZ and DZ twins.

Results. No significant differences in age, body height and mass, and number of chronic conditions were observed between MZ and DZ co-twins. The total number of falls was 433. At least one fall was experienced by 99 MZ twins of whom 44 suffered at least one injurious fall. The corresponding figures were 101 and 44 in DZ twins. Pair-wise concordance for any fall was .46 (95% CI 0.33–0.58) for MZ and 0.33 (95%CI 0.21–0.45) for DZ twins; tetrachoric correlations were 0.392 among MZ and 0.167 among DZ twins. For falls with injuries, the pair-wise concordance was 0.27 (95% CI 0.14–0.41) for MZ and 0.21 (95% CI 0.09–0.34) for DZ twins; corresponding correlations were 0.241 and 0.246 for MZ and DZ twins.

Conclusion. The present study indicates that among community dwelling older women genetic factors are moderately related to likelihood of falling. However, the risk of injurious falls is mostly associated with other than familial factors.

DEPRESSION, COGNITIVE FUNCTION AND PHYSICAL PERFORMANCE IN ELDERLY ITALIAN TWINS

Session: Poster

F. Pannozzo, C. Lo Noce, R. Cotichini, C. Fagnani, V. Patriarca, L. Nisticò, C. D'Ippolito, P. De Sanctis Caiola, R. Cirrincione, S. Pulciani, S. Giampaoli, and M. A. Stazi.

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Within a longitudinal study on cardiovascular risk factors carried out by the Istituto Superiore di Sanità, and conducted in Central Italy, 150 twin pairs aged 65 to 75 years were enrolled and examined to evaluate depression, cognitive function and physical performance.

Depression was evaluated with the Depression Scale of the Center for Epidemiologic Studies (CES-D Scale). Global cognitive function was tested with the Mini Mental State Examination (MMSE), the stroop test, the word recall and animal word fluency test. Physical performance was evaluated with the ADL, I-ADL, and the Short Battery of tests for Lower Extremity Physical Performance. All the tests were administered by a trained interviewer.

Fasting blood samples were obtained and total cholesterol, HDL and glucose tests performed on each study participant. Blood pressure and anthropometric measurement were also collected.

The contribution of genetic and environmental factors to the covariation of liability to depressive symptoms, cognitive function and physical performance will be evaluated by twin structural equation modeling and presented.

SEX DIFFERENCES IN THE STRUCTURE OF THE PHENOTYPIC VARIANCE (DATA OF MOSCOW TWINS 16–17 YEARS OLD)

Session: Poster

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The study of adolescent twins (78 pairs of MZ twins and 70 pairs of DZ twins) included WAIS and eight personality questionnaires. The results revealed:

1. no significant sex differences in intelligence and personality characteristics;
2. higher similarity of DZ boys as compared with DZ girls;
3. lower similarity of MZ boys as compared with MZ-girls.

Sex differences in intrapair correlation bring to the differences in the structure of phenotypic variance of boys and girls: lower heritability and higher shared environment in the sample of the girls. The possible reasons for these results — gender differences in intrapair twin relations, the different psychological age of adolescent boys and girls, the role of genetic factors, are discussed.

TWO DANISH NATIONAL TWIN STUDIES ON ANKYLOSING SPONDYLITIS

Session: Poster

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Objective. To estimate the influence of genetic factors in the etiopathogenesis of ankylosing spondylitis (AS).

Methods. The study comprises three Danish nationwide twin cohorts. In 1994 37,388 Danish twin individuals born 1920–1941 and 1953–1982 were asked by questionnaire if they had AS. The cohort born 1953–1982 plus twins born 1931–1952, a total of 46,331, received the same questionnaire in 2002. The twins responding AS were subsequently invited to participate in a clinical study. Main outcome measures were the proband-wise concordance rate of AS in monozygotic (MZ) and dizygotic (DZ) twins.

Results. In 2002, 58 twins reported AS in addition to 28 in 1994. Sixty-eight (79%) responded to an invitation regarding a clinical examination, of which 45 agreed to participate. Based on a clinical examination and scrutinizing of medical records, 31 probands were diagnosed with AS. Four of their co-twins were either dead or had emigrated, and four did not respond to the invitation to participate in the study, resulting in 23 complete pairs. One DZ co-twin was identified as a secondary AS case. A total of 0/3 MZ pairs and 1/20 DZ pairs were concordant for AS, rendering a non-significant difference in proportions at 5% (95% CI = –5% to 15%).

Conclusion. These results cannot substantiate the anticipation that genes play a key role in the ethiopathogenesis of AS.

CO-TWIN DEPENDENCE AND TWINS' PSYCHO-EMOTIONAL WELL-BEING AND HEALTH FROM ADOLESCENCE TO EARLY ADULTHOOD — A LONGITUDINAL STUDY OF DEVELOPMENT AND HEALTH OF FIVE CONSECUTIVE BIRTH COHORTS OF FINNISH TWINS

Session: Twin Family and Twin Relations

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Objective. Relatively few studies have concentrated on the qualities and implications of the relationship between twin and co-twin. The objective of this study was to investigate the contribution of twin relationship and co-twin dependence to twins' psycho-emotional well-being and health from adolescence to early adulthood.

Subjects and methods. The study population is from the FinnTwin16 study, which consists of five consecutive birth cohorts of twins born in 1975–1979 (n = 5747) and their families. Baseline assessments were collected through mailed questionnaires sent to twins when they were 16 years old. Follow-up questionnaires were completed by twins at ages 17, 18 and as young adults aged 22–27.

Results. At the age of 16, over one third of MZ twins and one fifth of DZ twins had reported dependence on their co-twin. When the association between co-twin dependence and twins' psycho-emotional well-being

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was studied, the results indicate that co-twin dependent twins were likely to report more somatic and psycho-emotional symptoms in adolescence. At the last follow-up as young adults, twins who had reported dependence did not differ in general in their life satisfaction or psycho-emotional well-being compared to independent twins. However, among MZ and same-sex DZ twins, the dependent co-twins were likely to report more somatic symptoms and problems with self-reliance even as young adults.

Conclusions. Twin relationship and co-twin dependence may influence twins' psycho-emotional wellbeing and experienced health. However, long-term outcomes suggest that these influences are likely to be transitory and diminish with increasing age.

GENETIC MODELING OF BRAIN MATURATION IN PUBERTY: A LONGITUDINAL STUDY IN HEALTHY TWINS

Session: Poster

Jiska S. Peper[1], Marcel P. Zwiers[1], Marieke E. van Leeuwen[2], Stéphanie M. van den Berg[2], Dorret I. Boomsma[2], René S. Kahn[1], and Hilleke E. Hulshoff Pol[1].

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Puberty is a critical period in human development. Physical growth takes place, large amounts of gonadal hormones are secreted and children show changes in behavior and cognition. Moreover, it is also a period which is probably very significant for brain maturation. Recent findings have shown that during puberty, gray matter volume in the brain starts to decrease whereas up to that period it has constantly been increasing in volume. White matter continues to increase until adulthood. It is hypothesized that this alteration in brain composition is necessary for optimal adult functioning.

Using Magnetic Resonance Imaging (MRI), research from our laboratory has shown that in adults, total brain volume, gray matter volume and white matter volume are for 90%, 82% and 88% respectively, genetically determined. This finding can be generalized to the singleton population[4], and is related to general intelligence. However, the role of the genetic, hormonal, and environmental factors mediating the developmental changes during puberty is poorly understood.

In this multicenter study we aim to elucidate the regulatory mechanisms and interactions by an extensive quantification of the developmental changes in early adolescence. For this purpose, 100 twin pairs with an additional sibling will be included at the age of nine years. Follow-up takes place two years later at age 11. Measurements consist of Magnetic Resonance Imaging–sMRI and DTI–to quantify brain volumes, density patterns and white matter tracks. Findings are compared to hormonal and cognitive assessments in the same subjects. For statistical analysis, structural equation modeling is done using Mx software.

COMBINED ANALYSIS OF GENOME SCANS FROM FOUR TWIN COHORTS TO LOCATE QUANTITATIVE TRAIT LOCI FOR BODY MASS INDEX AND STATURE IN THE GENOMEUTWIN PROJECT

Session: Molecular Genetics and Twin Studies

Markus Perola[1], Kismat Sood[1], Tero Hiekkalinna[1], Elisabeth Widen[1], Aarno Palotie[1], Dorret Boomsma[2], Jaakko Kaprio[1], Nick Martin[3], Toby Andrew[4], Tim Spector[4], and Leena Peltonen[1]

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Excessive amount of phenotype information is collected for study samples of common (and rare) diseases. With proper informed consent this data could be used to map QTL or other common phenotype loci using existing phenotypes. We performed QTL analysis of body-mass index (BMI) and stature (body height) using genotypic data from five genome-wide scans performed on the GenomEUtwin participating countries (www.genomeutwin.org). The study material consisted of a total of 5756 individuals from four different countries: Australia (n = 1749), Finland (n = 879), the Netherlands (n = 878) and United Kingdom (n = 2250). The genetic marker maps were integrated using our web-based tool Cartographer (www.bioinfo.helsinki.fi/cartographer), which orders heterogeneous marker maps using physical location information and interpolates the genetic distances from the DeCode genetic map, using its markers as an anchoring set. The raw marker data was pooled by a program developed by us, MERGESCAN. This program uses the information from Cartographer to produce common data files for genome-wide analyses. The markers and alleles can be either 1. pooled using allele frequency information, or 2. renamed so that the same markers across genome scans are analyzed separately but located at the same genetic location. Here, option 2 was used. We used the program Merlin for variance components analysis of the data set. Age and sex were used as covariates in the analyses. The covariate adjusted heritability of BMI was found to be 62% and of stature 86% in the pooled data set. We found evidence for a QTL on chromosomes 11q (lod = 2.04) and 20q (lod = 4.06) determining human BMI and a suggestive locus on chromosome 6 for stature, lod = 2.58. We plan to integrate more data in these analyses from GenomEUtwin participants in the near future.

SOME FEATURES OF SELF-CONSCIOUSNESS OF TWINS

Session: Poster

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In the majority of genetic studies there are applied the methods based on a self-estimation of the subjects. It is probable that the greater self-estimation similarity of MZ twins, in comparison with DZ, can cause exaggeration of the role of heritability. The goal was to study the relations between the partners and their influence on the psychological similarity of twins.

Methods. (1) Eyesenck Personality Inventory — EPI; (2) list of adjectives for the definition of the degree of identification with co-twin. EPI was given twice: the second time one group of twins saw the answers of the co-twin, and so the answers varied as a function of self-estimation of the co-twin. The other (control) group didn't see the answers of the co-twin.

Results. (1) changes in the answers of the first group were significantly larger than those of the control group (8.57 vs. 3.5); (2) knowledge of the answers of the co-twin essentially changed the answers, especially the level of extraversion-introversion; 3) the similarity of MZ twins increases more than the similarity of DZ twins in the first group (when the twin knew the answers of the co-twin).

Conclusions. Features of the relations in twin pairs (degree of identification, the tendency to be similar with co-twin, or to differ from him/her) can influence measurement of the psychological feature by a method based on a self-estimation and change the estimation of heritability.

NEUROLOGICAL SEQUELAE IN 3393 IVF/ICSI TWINS: A CONTROLLED NATIONAL COHORT STUDY

Session: Health Prognosis and Twin Births

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Background. In most European countries approximately 40% of children born after assisted reproduction are twins. The existing literature about neurological sequelae in these twins is limited. The first aim was to compare neurological sequelae in assisted reproductive twins with assisted reproductive singletons and naturally conceived twins. The second aim was to evaluate the role of intracytoplasmic sperm injection (ICSI) in the development of these sequelae.

Methods. Controlled national register based cohort study on neurological and psychiatric diagnoses. All assisted reproductive twins (n = 3,393) and singletons (n = 5,130) plus all naturally conceived twins (n = 10,239) born in Denmark between 1995 and 2000 were included. Children were identified by cross-linkage of the National Medical Birth Registry and the National IVF Registry. Neurological and psychiatric diagnoses were retrieved from the National Patient Registry and the Danish Psychiatric Central Registry.

Results. The crude prevalence of neurological sequelae (defined as cerebral palsy, mental retardation, infantile autism, Aspergers syndrome and retarded psychomotor development) was 8.8, 8.2 and 9.6 per 1000, respectively in twins and singletons after assisted conception, and naturally conceived twins, and of the specific diagnosis, cerebral palsy 3.2, 2.5 and 4.0 per 1000.

Odds ratio of neurological sequelae and cerebral palsy adjusted for child sex and year of birth in assisted reproductive twins vs.. control twins was OR 0.9 (95% CI 0.6–1.4) and OR 0.8 (95% CI 0.4–1.6), respectively. The corresponding risks for assisted reproductive twins versus singletons were for neurological sequelae OR 1.1 (95% CI 0.7–1.7) and for cerebral palsy OR 1.3 (95% CI 0.6–2.9). The risk of neurological sequelae was similar in ICSI vs. IVF children OR 0.9 (95% CI 0.5–1.7).

Conclusions. Surprisingly, twins from assisted reproduction have a similar risk of neurological sequelae as their naturally conceived peers and assisted reproductive singletons. Children born after intracytoplasmic sperm injection have the same risk of neurological sequelae as children born after in vitro fertilization.

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5-HT2A RECEPTOR DENSITY IS GENETICALLY DETERMINED

Session: Complex Disorders III

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Background. Measures of receptor density have been shown to show extremely high inter-individual variability. In particular, this applies for the 5HT2A receptor system where differences between individuals may differ with a factor of up to five. The aim of the present study was to address the possible role of genetic factors influencing the age independent inter-subject variation in 5HT2A receptor density measured by PET-[18F] altanserin.

Material and Methods. Twenty-four healthy male volunteers, 6 monozygotic (MZ) and 6 dizygotic (DZ) twin pairs with a mean age of 35 yrs (27–47 years) were recruited from the Danish Twin Registry. Each subject received a MRI scan and a PET scan. In all subjects the promoter –1438A/G and 452C/T polymorphisms were detected by a Taqman based allelic discrimination assay using the ABI 7700. Correlations of twins were estimated assuming equal variance and mean of MZ and DZ pairs. Inference was based upon assuming bivariate normality distribution of the phenotype.

Results. Our data demonstrate that genetically identical individuals have a much smaller variability in their 5HT2A receptor binding, in the order of 1/3 of unrelated individuals' variability. Intraclass correlation was .90 (.56–.97) in MZ twins compared to .51 (–.20–.85) in DZ twins. Additive genetic effects were estimated to 0.79. The *p*-value for the hypothesis of equal correlation for MZ and DZ twins was .06. In only two DZ twin pairs the genotypes for the –1438A/G and the 452C/T polymorphisms differed.

Discussion. The data indicates genetic influence on 5HT2A receptor density. However, data this sparse may have serious limitations or show artifacts. The -1438A/G and 452C/T polymorphisms are not major factors affecting the 5-HT2A expression. It now remains to be clarified which additional factors are of importance in the set-off of individual 5HT2A receptor density.

INFANT MORTALITY AND MODE OF DELIVERY AMONG DANISH TWINS 1978–2001

Session: Poster

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The number of multiple births in Denmark has increased sharply since the middle of the 1980s as a result of increased use of fertility treatment. Multiple births are associated with increased risk of complications during pregnancy and delivery, and increased perinatal and infant mortality. Throughout the period an increasing number of multiples has been delivered by means of caesarean section. Here we report on the development of infant mortality in relation to the mode of delivery of multiples in the period 1978–2001 in Denmark.

This study is based on all multiple births in Denmark in the period 1978–2001, including more than 42,300 children from 20,929 pregnancies. Data are collected from the Danish Medical Birth Registry, including obstetric information about mode of delivery, whether caesarean section was elective or acute, procedures during birth, and other information about the mother and the pregnancy. Data about the child include among other birth order, birthweight, gestational age, whether the child was stillborn or live born, and age at death if dead within the first year of life.

The infant mortality among multiples is in general four times the infant mortality among all births, and the proportion of stillbirths is twice the general proportion of stillbirths. The proportion of deliveries by means of caesarean section has increased from less than 25 percent in the late 1970s to more than 50 percent in the last years. Implication of the increased use of elective section will be discussed.

NEW TECHNOLOGICAL PERSPECTIVES ON TWIN STUDIES

Session: Poster

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In the recent past the assessment of the concordance for disease in monozygotic (MZ) versus dizygotic (DZ) twins represented the cornerstone of studies in genetics. Today, even though the formal genetics and epidemiology still give a valid contribution toward the identification of the genetic predisposition to illnesses, the molecular approach is taking over. The innovations introduced in biotechnology and the completion of the Human Genome Project are changing how to investigate genetics.

Here, we offer the perspective of molecular genetic studies performed on populations of MZ twins applying the new technologies. The theoretical identity at the DNA level of two twins and their discordance for disease represent the ideal setting to look for those subtle variations that account for their phenotypic differences. A genomic approach that would allow interrogating their entire genomes all at once is now made possible by a series of new micro-technologies.

We will focus on "microarrays", which consist of large numbers of probes immobilized on a solid substrate, and allow the testing thousand of specimens in each single experiment. The microarrays technologies can examine in depth both the genetic backgrounds and their products, and matched with bioinformatics they might define the regulation mechanisms of gene expression, and how these are related to the phenotypic differences in twins. The acquired data would, at the end, explain and/or predict changes in gene expression and proteins levels related to genetic and/or environment influences on normal and diseased phenotypes.

Their diagnostic, preventive, social and ethical implications must be carefully evaluated.

METHODS FOR SELECTION AND ANALYSIS OF MOST-INFORMATIVE SIB-PAIRS IN LINKAGE STUDIES

Session: Statistical Issues in Twin Studies

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No abstract supplied.

GENETIC AND ENVIRONMENTAL INFLUENCES ON EATING BEHAVIOR — THE SWEDISH YOUNG MALE TWINS STUDY

Session: Complex Disorders I — Metabolic Syndrome, Obesity

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Aims. Disturbed eating behavior is a major public health problem, which might be related to the increasing prevalence of overweightness and obesity. The aim of the present study is to attempt to disentangle genetic and environmental influences on eating behavior in a population-based cohort of young adult male twins.

Methods. The present study comprises 320 dizygotic (DZ) and 452 monozygotic (MZ) male twin pairs aged 24–30 years from all parts of Sweden. The "Three-Factor Eating Questionnaire Revised 21-item version" (TFEQ-R21) was used for assessment of eating behavior. This validated instrument consists of three dimensions: cognitive restraint; emotional eating; and uncontrolled eating. Structural equation modeling was used for estimating the heritability of eating behavior.

Results. The mean of BMI was 23.62 kg/m2 for MZ twins and 23.95 kg/m2 for DZ twins. Among MZ twins the within-pair correlations were .53, .36 and .43 (all *p*-values < .0001) for cognitive restraint, emotional eating, and uncontrolled eating. Among the DZ twins the corresponding within-pair correlations were .14, .11 and .10 (all *p*-values > .01). The best fitting models showed heritability of 45–60% for the different dimensions of the TFEQ-R21.

Conclusions. Genetic factors are of major importance for eating behavior in an unselected group of young adult twins. Non-shared environmental factors are also important, while environmental factors shared by twin brothers do not seem to contribute to eating behavior.

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LOSING THE CO-TWIN IN LATER LIFE: THE RELATION WITH THE MORTALITY RISK BY ZYGOSITY. AN ANALYSIS ON DANISH TWINS 75 YEARS OLD AND OVER

Session: Poster

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The heritability of life span (McGue et al., 1993) and the effect of the relationship between monozygotic twins on mortality risk (Rasulo et al., 2004) appear to suggest that in later life the co-twin loss should be related to mortality risk especially for monozygotic twins. In line with these hypotheses, we aim to verify if there is a mortality disadvantage after the monozygotic co-twin's death and if there is a significant time lag between loss and mortality risk. Our study extends a previous study on Danish twins aged 50–70 years (Tomassini et al., 2002) which has found an increased risk of dying in the second year after the loss, regardless of the zygosity.

The study is based on the Longitudinal Study on Aging Danish Twins from 1995 to 2001. We have assessed the role of the co-twin loss on a sample composed of 681 twins. Firstly, we have applied a Gompertz model to assess the effect of co-twin loss during the study time, independently from the time bereaved. Secondly, we have assessed the risk of dying at different time intervals after the loss. The time since bereavement has been divided into two time-dependent variables (until 3 years, more than 3 years) to minimize the loss of information. In accordance with our hypothesis, the estimates have shown that the co-twins' death is associated with an increasing risk of dying. Additionally, we have observed a significant increase in the monozygotic twins' risk of dying in the first three years after the loss.

In conclusion, these research findings appear to suggest that the relation between co-twin loss and mortality risk changes in later life, when identical twins have shorter survival times after losing the co-twin.

RISK OF DYING BY SHORT-TERM AND LONG-TERM WIDOWHOOD. AN ANSWER FROM THE CO-TWIN CONTROL METHOD

Session: Aging and Longevity II

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Previous studies have found that bereaved partners have an increasing risk of dying in the short-term after the loss and that this effect is stronger for men. However, one difficult issue in this kind of design is to find the appropriate control group. In fact, assessing the effect of widowhood on mortality requires one to compare the transition to death in the bereaved group to that in a very similar control group. In this way it becomes possible to disentangle the effect of bereavement by controlling confounding factors.

The difficulties in finding an adequate control group can be solved with a co-twin control design (Kaprio, 1994), in which the bereaved twins are compared to their still married co-twins.

Through the co-twin control method we assess the causal effect of widowhood by time spent in bereavement among old Danish twins. Data are provided by the Longitudinal Study of Aging Danish Twins from 1995 to 2001. We have distinguished the short-term from the long-term bereaved. The long-term bereaved were already widowed when the follow-up started, the short-term bereaved became widowed during the follow-up.

The hazard estimates show that the short-term widowed have a risk of dying significantly higher than their still married co-twins. On the other hand, results for the long-term widowed suggest that if the bereaved twins survived after becoming widowed, their risk of dying is actually lower than the risk for the still married co-twins.

With respect to gender differences, the coefficients for the time since bereavement are significant only for men.

In conclusion, our research findings confirm the hypothesis that widowhood increases the mortality risk especially in the short-term and that this effect is very strong for men.

HEPATITIS B SURFACE ANTIGEN AND HEPATITIS A VIRUS IMMUNE RESPONSE AFTER VACCINATION IS DETERMINED BY A FUNCTIONAL POLYMORPHISM IN THE INTERLEUKIN-10 PROMOTER REGION

Session: Complex Disorders II and Immunology

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Aims. IL-10 is a central immuno-regulatory cytokine. We have studied the influence of IL-10 promoter polymorphisms on the immune response to HBsAg and hepatitis A vaccination.

Methods. Ninety-six monozygotic (MZ) and 95 dizygotic (DZ) twin pairs were immunized with a HAV/HBsAg vaccine (Twinrix, GlaxoSmithKline). Anti-HBs and anti-HAV were measured four weeks after the last vaccination. We studied the distribution of IL-10 promoter polymorphisms (SNPs) (–1082, –819 and –592) and their influence on IL-10 promoter in reporter gene — and electrophoretic mobility shift assays.

Results. In the multiple regression analysis accounting for smoking, gender, body mass index and age the ACC haplotype (–1082, –819 and –592) had a strong influence on anti-HBs production. Individuals carrying the ACC haplotype (geometric mean titer (GMT) 5541 U/L, 95% reference range (RR) 4050–7621 U/L) had anti-HBs titres almost twice as high as individuals without this haplotype (GMT 2911 U/l, 95% RR 2221–3816 U/L, $p < 0.003$) Anti-HAV production was suppressed by the presence of the –1082A allele (GMT 6394 U/l, 95% RR 5343–7651 U/L) in comparison with individuals homozygous for the –1082G allele (GMT 10907 U/L, 95% RR 8189–14528 U/L, $p < 0.012$). The –1082A IL-10 promoter had a significantly decreased transcriptional activity, explained by a higher affinity of the –1082A allele to the suppressive transcription factor PU.1.

Conclusions. These results establish IL-10 promotor polymorphisms as important modulators of the immune response against hepatitis virus proteins. Our findings show a genetic determination of IL-10 secretion and a suppressive effect of the –1082A polymorphism on the promoter activity.

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HAIR LOSS AMONG ELDERLY MEN: ETIOLOGY AND IMPACT ON PERCEIVED AGE

Session: Poster

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Background. Androgenetic alopecia (AGA) is the most common type of hair loss in men, but little is known about the etiology of AGA in elderly men and its impact on perceived age.

Here we used a population-based twin study of men aged 70+ to assess the magnitude of the genetic component affecting hair loss and to examine the association between baldness and perceived age.

Methods. In the fourth wave of The Longitudinal Study of Aging Danish Twins we obtained digital photos of the face and vertex area of 739 elderly male twins, including 148 intact twin pairs. The degree of baldness and perceived age was assessed in each twin by five, respectively nine, nurses. The heritability of balding was estimated using structural-equation analysis, and it was tested whether baldness was associated with estimations of age.

Results. The intrapair correlation of degree of balding was consistently higher for monozygotic than for dizygotic twin pairs regardless of the baldness categorization used, and structural-equation analysis revealed a heritability of 79% (95% CI: 0.40–0.85) for the mean baldness index. The remaining variation could be attributed to non-shared environmental effects. There was only a very weak and statistically non-significant association between baldness index and overestimation of age.

Conclusions. The majority of the variation in baldness in elderly men can be explained by genetic factors, and hair quantity has little impact on perceived age in elderly men.

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THE ASSOCIATION OF A HTR2A POLYMORPHISM AND LONGITUDINAL CHANGE IN MEMORY PERFORMANCE IN THE SECOND HALF OF THE LIFE-SPAN

Session: Aging and Longevity II

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Background. Prior research suggests moderate genetic influences on memory traits in adulthood, yet relatively little is known about specific genes involved in memory performance in non-demented aging populations. A recent report of association of a HTR2A variant (H452Y) with episodic memory in young adults suggests serotonin may be important in the formation of memories.

Objectives. To consider the association of a nearby HTR2A polymorphism (–1438 G/A) and longitudinal memory performance in twins from the Swedish Adoption Twin Study of Aging (SATSA).

Methods. Memory performance scores were obtained from 798 non-demented twins across four in-person testing sessions spanning 13 years in total. Memory tasks tapped working memory (Digit Span), immediate and delayed recall (Names and Faces), and delayed figural recognition (Thurstone's Picture Memory). Five hundred and thirty-nine participants at the third in-person testing were sequenced for the HTR2A promoter polymorphism, –1438 G/A [dbSNP: rs6311]. A total of 498 individuals, including 219 twin pairs, had both genotyping and memory scores.

Results. Delayed figural recognition performance at age 65 as well as acceleration in change over age were associated with the HTR2A polymorphism. Specifically, those with the more common allele demonstrated higher memory performance on the Thurstone's Picture Memory task across all ages than those with the rarer allele. Heterozygotes showed the steepest decline over age compared to homozygotes.

Conclusions. The current findings imply a role for serotonin on longitudinal figural memory performance in the second half of the life-span.

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HOW DO THEY DO IT? COPING OF TWIN PARENTS

Session: Poster

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The present study examined coping opportunities utilized by parents of twins. This study was conducted as part of a larger ongoing research project on multiple birth children (data sets on twins and data sets on triplets and more) conducted by this author. The present study utilized data from 302 twin families from across the United States. Families responded to one-page survey sheets (front and back), and participation was solicited from subscribers to *Twins Magazine*.

Mothers and fathers separately rated their use of seven events that support coping. *T*-tests for paired samples were conducted on these measures to evaluate differences. Fathers reported receiving more support from family and close friends, having more time for pleasurable/recreational activities, and more time for rest or time alone. Parents did not differ on perceived support from their church, support from child care providers, perceived help with household tasks (washing, feeding, etc), or opportunities for fun with their children.

These findings suggest that fathers of twins receive more family support, have more time for fun, and more opportunities for rest to facilitate their coping. Interestingly, these findings differ from ratings of these measures of coping in a sample of parents of higher order multiples (Rhue, 2002). In that study, mothers reported greater support from family and friends, greater child care support and more time for fun with their children. It may be that higher order multiples still command more attention and outside support for mothers than do twins. Across both studies, fathers got more rest.

ENVIRONMENTAL INFLUENCES ON NEWBORN TWIN BEHAVIOR: IMPACT OF MATERNAL VARIABLES

Session: Current Developments and Findings from Twin Studies

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Predictive relations between maternal variables and newborn behavior were evaluated for 268 twins. The maternal variables included pregravid weight, weight at end of pregnancy, weight gain, age, parity, height, years of education, and body mass index. A comprehensive, four-hour assessment of each twin was completed in the nursery. The newborn assessment focused on behavioral aggregates that previously had differentiated between high- and low-risk infants, including irritability, soothability, activity while awake, activity during sleep, reactivity, and reinforcement value. Patterns of significant relations differentiated the twins based on sex and relative size of co-twins. For females, increased maternal weight gain was related to more mature patterns of irritability and soothability, and higher education was related to the reinforcement value of the newborn's behavior. For males, increased maternal weight gain was related to higher reactivity, whereas higher weight before pregnancy was related to lower newborn reactivity. There were no significant relations for larger twins. For smaller twins, increased maternal weight gain was related to more mature patterns of irritability, and increased age was related to less mature patterns of soothability and higher activity level. Previous research indicated that there were environmental influences on these newborn behaviors. These results suggest not only that maternal variables, particularly nutrition, contribute to that environmental influence, but that the influence is differentiated by relative risk of the co-twins.

A NATIONWIDE STUDY OF MULTIPLE SCLEROSIS IN ITALIAN TWINS

Session: Complex Disorders II and Immunology

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Introduction. Multiple sclerosis (MS) is a major cause of disability in young adults. There is indirect evidence of an etiologic heterogeneity of the disease, linked to the different clinical or pathological manifestations. Twin studies conducted in Northern Europe and North America have consistently demonstrated a higher disease concordance in MZ twins, highlighting the importance of genetic factors.

Objective. To investigate the genetic and environmental components of MS in continental Italy (a medium-prevalence area) and in Sardinia (a high-prevalence area).

Study population. The databases of 73 MS Clinics (33,589 patients) were matched with the Italian Twin Registry in order to identify twins among MS patients. Twin patients were contacted directly by their neurologist, who confirmed the diagnosis (according to the Poser criteria) and visited their co-twins. Zygosity was mainly assessed by questions regarding similarity.

Results. Two hundred and sixteen twin pairs were identified (198 from continental Italy and 18 from Sardinia). In continental Italy, proband-wise concordance was 14.5% for MZ twins and 4.0% for DZ twins, while in Sardinia it was 22.2% in MZ and none in DZ twins. The twinning rate in the MS population was lower than expected for the general population. The heritability estimated in continental Italy was 48%, whereas the shared and unique environmental contributions were 29% and 23%, respectively.

Conclusions. Twin rate and disease concordance are lower in Italy than in Northern Europe and North America. The under-representation of MS among Italian twins draws attention to possible protective factors, shared by co-twins, which might influence susceptibility to MS in Mediterranean areas.

TAMBA PARTNERSHIP PROJECT

Session: COMBO I

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In March 2001 Tamba received funding from three Primary Care Trusts in West Surrey to develop and share good practice. This is a partnership between Tamba, parents and local health professionals. This presentation will outline the achievements of the three year project including:

- the production of a new video "Expecting more than one", involving couples and maternity units from the project area and collaboration with the "Newcastle Twin Study";

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- development of a Parent Education Pack for those leading antenatal classes — a complete pack including guidelines on running classes, and Tamba booklets and leaflets
- bringing parents and professionals together in a conference and study day — an opportunity for sharing good practice, updating knowledge and establishing the real needs of parents
- the development and piloting of an evidence-based "Maternity Excellence Award".

This award serves to highlight the needs of families, develop expertise and address clinical governance, and raise the profile of maternity units.

This presentation will discuss partnership working, encourage ideas, and provide a model that could be followed by other COMBO members wishing to develop similar sustainable partnerships in their own countries

COMMUNICATING WITH PARENTS AND PROFESSIONALS

Session: Poster

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This will display the full range of leaflets, booklets, magazines, posters, cards, videos and packs that Tamba produces.

Tamba has developed a strong identity over the last three years and our publications reflect that. Our close communication with parents through Twins Clubs, Twinline, our website and national office means that our publications reflect the real needs and concerns of parents. Finding out the information they need has never been easier for the parents of multiples.

Tamba's contact with health professionals and teachers has also developed in strength. This has led to the addition of a Parent Education Pack, Research Review and Teacher Training materials to our range of materials for professionals.

Finally, we have also been able to produce a new "Expecting more than one" video aimed at both those involved in Parent Education and the parents themselves.

All our publications are continually evaluated and regularly updated.

BIVARIATE TWIN STUDY OF HEIGHT AND WEIGHT

Session: Poster

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Estimates of heritability of height and weight have been presented from numerous twin and other sibling and family studies. Many of these studies focus on overweight, and normally analyze body mass index (BMI) to look at relative weight (adjusted for height). Others are concerned with body size or composition, but analyze height and weight separately. However, relatively little is published regarding the bivariate relationship between height and weight. A key question asks how the genetic and environmental variance structures compare between analyses of BMI versus analyses of weight in a bivariate model with height. We address this question here, and also investigate genetic mediation of the relationship between height and weight and explore sex differences.

Population-based twin data (n = 9479) are analyzed from Norwegian cohorts born 1967 to 1979 who completed questionnaires in 1992 and/or 1998. The analyses are based on data from n = 3430 pairs who provided information on both height and weight for the same questionnaire, either in 1992, 1998 or both. The male cross-twin cross trait correlations (MZm 0.51, DZm 0.29) are substantially higher than the female correlations (MZf 0.30, DZf 0.19), and the DZu group (0.15) yields the lowest correlation. Preliminary analyses, using Cholesky decompositions, revealed significant sex differences in the magnitude of effects and in the factors explaining the relationship between height and weight.

PATHOGENESIS OF POLYCYSTIC OVARY SYNDROME DUE TO GENETIC FACTORS: A TWIN STUDY

Session: Poster

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Introduction. Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age. PCOS is diagnosed when two out of the three following symptoms are present: oligomenorrhea, hyperandrogenism and/or polycystic ovaries on ultrasound. Although familial clustering suggest a genetic predisposition, up to now the genetic influence on the pathogenesis of PCOS (heritability) has not been quantified. Twin sisters and their singleton sisters provide a unique opportunity to estimate heritability. The aim of this study is to estimate the heritability of PCOS.

Material & Methods: Twins registered with the volunteer based Netherlands Twin Register (NTR) receive mailed surveys every 2–3 years. The year 2000 survey contained items on a number of natural menstrual cycles in a year, hirsutism and acne. PCOS was defined as less than 10 menstrual cycles a year with hirsutism and/or acne. Data on PCOS were available for 1679 MZ female twins, 842 DZ female twins, 594 females of opposite sex (DOS) twin pairs and 1146 singleton sisters of twins.

The genetic factors (A), common environmental influences (C), and unique environmental influences (E) on the pathogenesis of PCOS were estimated using model-fitting techniques.

Results. The estimated polychoric correlations for PCOS were .71 for MZ twins and .36 for DZ twins, suggesting a large genetic influence. In the full model, genetic factors account for 58%, common environment factors for 12% and unique environmental factors account for 29% of the variances in the pathogenesis of PCOS. The full model could be reduced to a model including genetic factors (A = 71%) and unique environmental factors (E = 29%). However, the power of our analysis did not allow distinguishing between the later model and a model only accounting for common (C = 57%) and unique environmental (E = 43%) factors.

Conclusion. Our study may point to a strong contribution of genetic factors to the pathogenesis of PCOS.

A.M.B.A. NATIONAL POSTCARD QUILT

Session: Poster

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Life with twins, triplets and more can, on one hand, be double the trouble but on the other hand, be double the delight or triplet the treat!

Members of multiple birth families were invited to send a postcard that expressed their thoughts and feelings about being a member of that family. The postcards are made of fabric and this project is a way of not only communicating aspects of the lives of multiple birth families, but also to treasure those images and stories as a permanent record and a part of Australia's history.

The medium of fabric was chosen as most people find it difficult to express themselves through the mediums of drawing or painting, but are able to build an image which expresses a multitude of ideas with the use of fabric, needle and thread.

The original idea of creating a national quilt made up of images sent from all over Australia (postcards) was first introduced at the National Convention for the Multiple Birth Association held in Perth in 1999. There appeared to be much enthusiasm and out of the 150 packs that were sent out, by the end of 2002, 73 images from all over our vast country were turned into 14 individual quilts or hangings and contain a vast and intricate description of life with twins, triplets and more.

The postcards collectively have been lovingly nurtured into a traveling exhibition and like all babies, it began its journey into the world in Sydney during Multiple Birth Awareness Week, March 7–14 2004, and will now travel to all communities Australia-wide as a postcard to all Australians.

The Postcard Quilt Project also aims to promote awareness and will inspire all those who attend this traveling exhibition. These quilts were inspired by a dream to bring parents of twins or more together to share in a common activity without having to be together physically. It has been a way of including families from isolated, rural and metropolitan areas in a united endeavor with equal opportunity to be involved. A common thread connecting all the writings is the gratitude each has for having been involved in the Multiple Birth Association and for the support they have received from their local multiple birth clubs.

FATNESS AND FITNESS: THE IMPACT OF FITNESS ON THE GENETIC VARIATION OF TOTAL AND ABDOMINAL FAT

Session: Poster

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Background and Aims. High measures of total and central abdominal fat and low level of physical fitness are predictive of the development of type 2 diabetes. The aims of this study are: (1) to elucidate the relative importance of genetic and environmental factors on variation in total and abdominal fat; and (2) to assess the effect of adjusting for fitness on the total and the additive genetic variation of these two fat measures.

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Materials and Methods. One hundred and fifty-two female (79 MZ, 73 DZ) and 103 male (58 MZ, 45 DZ) twin pairs aged 18–57 years underwent anthropometric measuring and a fitness test. Total fat in percent (fat%BMI) was assessed by BMI, weight and age. Waist circumference was used as a measure of abdominal fat.

Results. Multivariate analysis methods were applied to these two measures of fat, adjusting for age and fitness. Waist circumference was also adjusted for total fat% BMI to investigate abdominal fatness independently of overall fatness. Adjusting for age, the heritability of fat%BMI was about 70% in both genders. Adjusting for age and overall fatness, the heritability of waist circumference was about 50% in both genders. Adjusting for fitness reduced the total variance of fat%BMI by one third, and most of this reduction was in the additive genetic component. However, the fraction of the total variation due to the genetic variation (the heritability) changed very little. The total variation of waist, adjusted for overall fatness, was not reduced after adjusting for fitness, in both genders.

Conclusions. A large proportion of the high heritability of total body fat (%) is due to genes implicated in fitness. There is little or no association between abdominal fatness and fitness.

VIRTUAL TWINS: UPDATED ANALYSES OF WITHIN-FAMILY ENVIRONMENTAL INFLUENCES ION INTELLIGENCE — AND A NEW ONGOING STUDY

Session: Behavioral Genetics

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Virtual twins (VTs) are same-age, unrelated siblings reared together from infancy. These pairs form a twin-like relationship, but without genetic relatedness. They can also be thought of as complementary to monozygotic twins reared apart. The last report from this ongoing study (Segal, 2000) yielded an IQ intraclass correlation of .26 ($p < .01$, $n = 90$) and a IQ subtest profile correlation of .08 ($n = 88$). New data, based on a larger sample confirms these findings ($n = 111$). Comparisons between adopted-biological and adopted-adopted pairs are also presented. These findings are considered in light of available twin and adoption data. Methods and goals of a new, ongoing study of twins, virtual twins and best friends will be discussed.

AN ANTENATAL SUPPORT INTERVENTION FOR PARENTS EXPECTING UNCOMPLICATED TWIN INFANTS IMPROVED PARENTAL COHESION DURING THE FIRST YEAR AFTER BIRTH BUT DID NOT CHANGE PERCEPTION OF PARENTING DIFFICULTY

Session: Poster

D. M. Sen
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Background. Mothers of twin infants report more emotional distress and feel ill-prepared for their unique parenting experience compared to mothers of singleton infants. In an attempt to reduce postnatal maternal psychological distress and improve father support, an RCT incorporating a midwife-led antenatal support intervention including "preparation for parenting of twins" sessions was introduced.

Design. Mothers who delivered within the first 24 months of the study were invited to participate in a face-to-face semi-structured interview. Eighty-four percent (75/89) mothers of twin infants and 87% (34/39) mothers of singleton infants agreed to participate. Mothers were prospectively followed from 20 weeks gestation to one year post delivery. Thirty-seven parents expecting "uncomplicated" twin infants (TI group) received the antenatal intervention support package, which encouraged "realistic" preparation for birth and parenting, relationship cohesion, and development of coping strategies. Thirty-four mothers with twin infants (TC group) and 39 (SC group) with singleton infants received standard care and advice. This abstract reports data from the one-year post delivery semi-structured interviews.

Results. TI mothers reported more father involvement ($p = <.05$), more partner support ($p = <.05$) and more positive statements about their relationship ($p = <.05$) compared to TC mothers. Mothers of twins identified the importance of routine ($p < .000$) and needed to make more SOS help calls ($p = <.05$) compared to mothers of singleton infants. However, there was no different in the mean score of perceived parenting difficulty between all three groups.

Conclusion. An antenatal intervention improved parental relationship and father support but did not change perception of parenting difficulty.

AN ANTENATAL MODEL OF CARE IMPROVES PREPAREDNESS FOR MOTHERHOOD OF TWIN INFANTS BUT DID NOT REDUCE MATERNAL POSTNATAL EMOTIONAL DISTRESS — AN RCT IN THE NORTH-EAST OF ENGLAND

Session: Poster

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Background. Mothers of twin infants have a two-fold increased risk of postnatal depression and anxiety and report feeling ill prepared for their unique experience. We hypothesized that an antenatal midwifery-led support package incorporating (1) twin antenatal clinic, (2) allocation to a specialist midwife, (3) invitation to antenatal preparation for parenting sessions and (4) additional home visits, would reduce the incidence of postnatal depression.

Design. One hundred and sixty-two mothers expecting uncomplicated twins were randomized to twin intervention (TI) or twin control (TC). Each TC case was matched with a singleton control (SC). A postal questionnaire, incorporating Edinburgh Postnatal Depression Scale, Hospital Anxiety Subscale, Maternal Emotional Wellbeing Scale (EWBS), Happy/Unhappy Face Visual Analogue Scale (FVAS) and assessment of maternal-infant attachment was sent at 24 weeks gestation, and at six and 12 weeks postnatal.

Results. Response rates were > = 77%. There were no differences at any time point in mean rank scores between TI versus TC. Mean FVAS scores were higher in TC versus SC at six weeks ($p < .05$), but not at 12 weeks postnatal. Caesarean section rate was higher in TI versus TC (68% vs. 49%, $p < .05$). TI mothers reported being "very satisfied" with antenatal care and felt more prepared for child care ($p < .01$) compared to mothers in the TC group.

Conclusion. An antenatal midwifery led model of twin care improved maternal satisfaction and preparedness for motherhood but did not improve maternal psychological wellbeing at six and twelve weeks postnatal.

THE USE OF TWINS FOR QTL MAPPING

Session: Statistical Issues in Twin Studies

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No abstract supplied.

GENETIC EPIDEMIOLOGY OF EPILEPSY: TWINNING, PTC LOCUS AND SUSCEPTIBILITY TO DISEASE

Session: Complex Disorders III

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The study explored the genetic susceptibility and prevalence of epilepsy in twins. The data on epilepsy were retrieved from the health records of 199 pairs of twins. Proband concordance rate in monozygotic (MZ) twins was 4 times than that in dizygotic (DZ) twins (0.67 vs. 0.17). Three of 15 (20%) affected twin kinships had epileptic first degree relatives. These findings indicated significant underlying genetic susceptibility to epilepsy with the Holzinger's heritability estimate being 0.45. The prevalence of epilepsy was similar in MZ (45.45) and DZ (45.11) twins and their non-twin siblings (47.60). In the general population from various nationalities, the mean prevalence rate of epilepsy varied from 5 to 17 per 1000. The appreciably higher prevalence rate in twin kinships could be attributed to peculiar development factors associated with the twinning process, or the intrauterine environment of mothers having tendencies to bear twins.

Of the genetic markers, PTC locus seemed to be associated with the susceptibility of epilepsy. The allele frequency of non-taster gene (t) seemed greater in epileptic twin kinships (0.71) than that in the general population (0.526). The frequency of non-tasters was similar in MZ and DZ twins and singletons: 27.3%, 26.7%, 27.7%, respectively. The PTC data in the general population was based on a sample of 278 individuals.

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EVALUATING WHOLE GENOME AMPLIFICATION VIA MULTIPLY-PRIMED ROLLING CIRCLE AMPLIFICATION FOR SNP GENOTYPING OF SAMPLES WITH LOW DNA YIELD

Session: Poster

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The amount of available DNA is often a limiting factor in pursuing genetic analyses of large scale population cohorts or epidemiological study samples. Further, association between higher DNA yield and several phenotypes, including diabetes mellitus, has recently been shown. This suggests that exclusion of samples with very low DNA yield may lead to biased results. Whole genome amplification (WGA) could present a solution to these problems. The multiply-primed rolling circle amplification (MPRCA) method is non-PCR based; it uses Phi29 DNA polymerase and random hexamer primers, resulting in products > 10 kb. We aimed to thoroughly assess the use of MPRCA for SNP genotyping of samples with low DNA yield. Among 800 samples obtained for the MORGAM study, which is part of the GenomEUtwin project, we identified 59 samples that had DNA yield < 7.5 µg. We compared the genotypes obtained for two replicate WGA samples to the genotypes obtained from the original genomic DNA by typing 16 SNPs using MassARRAY and 8 SNPs using allele-specific primer extension on microarrays. As a comparison, we studied 36 good quality and high yield DNA samples. No genotype discrepancies were identified among the WGA replicates and genomic DNA of the high yield DNA samples. In contrast, multiple genotype discrepancies were identified for 13 of the 59 low yield DNA samples. The highest portion of discrepancies was due to allele dropout in heterozygous genotypes in WGA samples. Thus, WGA is applicable for low DNA yield samples, but a higher rate of genotyping errors requires that increased attention be paid to genotyping quality control issues. We are currently testing whether pooling 2–3 WGA replicates for each sample prior to genotyping improves genotyping accuracy, and what guidelines should be followed to keep the rate of genotyping errors acceptable.

HERITABILITY OF BODY HEIGHT AND EDUCATIONAL ATTAINMENT IN INTERNATIONAL CONTEXT: A COMPARISON OF ADULT TWINS IN MINNESOTA AND FINLAND

Session: Behavioral Genetics

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We studied the effect of genetic and environmental factors on the association between self-reported height and education in Minnesota and Finland. Our data included 1598 twin pairs in Minnesota and 6269 twin pairs in Finland born between 1936–1955. Correlations between education and height were found in Minnesota (r = .07 in men and .12 in women) and in Finland (r = .16 and .13, respectively). This phenotypic correlation was mainly because of the correlation between shared environmental factors in Minnesota (rC = .38 and .36, respectively) and in Finland (rC = .74 and .37, respectively). An unshared environmental correlation was found only in Finland (rE = .13 and .06, respectively). The results are probably associated with averagely higher education in Minnesota, which decreases the effect of childhood environment on education seen as weaker correlation between height and education. Non-familial factors affecting education are probably different in Minnesota than in Finland, since in Finland they are partly associated with the factors affecting height.

GENETIC INFLUENCES ON COGNITIVE FUNCTION USING A COMPUTERISED NEUROPSYCHOLOGICAL ASSESSMENT OF PROCESSING SPEED, WORKING MEMORY, VISUAL MEMORY, AND EXECUTIVE CONTROL IN FEMALE TWINS

Session: Poster

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The current study is the first to use CANTAB (The Cambridge Neuropsychological Test Automated Battery), a battery of computerized cognitive tests, for the purpose of genetic analysis. A sample of 278 female-female Caucasian twin pairs from the UK (aged 18–76) performed such tests to establish the importance of genetic factors on four composite cognitive measures: visual memory, working memory, executive function and psychomotor speed. Estimates of heritability (additive genetic variance) were found to be 40% (95% CI 28–51), 34% (23– 45), 28% (14–40) and 23% (8–38), respectively. Age accounted for 5–23% of the variance. A general factor, accounting for 55% of the variance of the data, was found to correlate moderately and positively (r = .19) with a measure of general intelligence, NART (National Adult Reading Test) which itself had high heritability (74% (95% CI 65–81)).

USING SCHOOL CURRICULUM TO POPULARISE TWIN RESEARCH

Session: COMBO II

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University admission in Sri Lanka is based on an exam known as "A Level". It has three subjects and involves 2 years of studies and is considered the major filtering point for higher education. In 1997 new revised curriculum was introduced which includes two projects that every student has to complete and submit a report on; it is mandatory for all students irrespective of whether they do science, humanities or commerce. Although seen as an encouraging development, criticism was leveled against it as there was no adequate teacher training and a lack of guidance on how to do projects.

The Sri Lankan Twin Registry (SLTR) has been popularizing twin research through twin newsletters, electronic and print media. During the past 5 years we have been providing materials and guidance to "A Level" students to do projects regarding twins. Some academicians from the SLTR with others formed Forum for Research & Development (FRD–www.forumforresearch.org) to develop a research culture in Sri Lanka. As a part of this initiative a magazine called *Explore* was published in all three main languages: Sinhala, Tamil and English. It's aim is to provide a platform for "A Level" students to publish their projects, and to guide them and their teachers on methodological issues with the help of expatriate and local professionals. A summary of students' projects are published with an expert commentary by a professional to guide readers on how to do it better methodologically. The first issue of *Explore* is in circulation and carries a twin project done by a student.

ENVIRONMENTAL EXPOSURE AND ATOPIC STATUS IN MONOZYGOTIC TWINS DISCORDANT FOR ASTHMA

Session: Poster

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Aim. A monozygotic (MZ) twin-control study was performed to examine risk factors for the development of bronchial asthma. Fifty-five MZ twin pairs discordant for asthma were examined. The protocol included questionnaires, interviews and clinical physiological examinations with measurements of bronchial responsiveness, skin prick test, and total and specific serum immunoglobulin E. The diagnosis asthma versus not asthma in discordant pairs followed international guidelines.

Results. Sensitization to allergens such as house dust mite (Derm. pter.) and animal hair/dander were statistically discriminating factors occurring more frequently in the asthmatic subjects than in their non-asthmatic twin, when adjusted for other allergens by conditional logistic regression. No other determinants provided evidence that suggested an influence on the development of asthma, neither regarding birthweight or infection in childhood, nor housing conditions, occupation or smoking habits

Conclusion. Although there is a considerable genetic component in the etiology of asthma, these data suggest that sensitization towards house dust mite and animal hair/dander allergens are environmental risk factors for the development of bronchial asthma.

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SCHIZOPHRENIA AND GENOMIC INSTABILITY IN TWINS
Session: Molecular Genetics and Twin Studies

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Schizophrenia is a multifactorial disease caused by both genetic and environmental factors occurring early in development, although 50% of monozygotic (MZ) twin-pairs affected by schizophrenia are discordant for the disease. In the 1980s, an elevated (10%) probability of the disease was uncovered in all progeny of Danish MZ discordant for schizophrenia. Further, other research points to the importance of de novo mutations in this disease and genetic studies have uncovered linkage with multiple genes spread throughout the genome. These, and other results obtained by us, suggest there are environmental factors that prevent and/or minimize schizophrenia and that these factors may impact on a predisposition to genomic instability.

Our research compared the genomes of MZ twins discordant for schizophrenia to identify DNA changes that might be related to disease discordance. A genome scanning method called targeted genomic differential display (TGDD) was developed to analyze DNA around (CAG)n and other sequences implicated in neurological disease and/or known to be unstable. The results show that twins discordant for schizophrenia have a higher than expected number of mutations around multiple (CAG)n sites (χ^2, $p = .005$) and that an increasing number of genes linked to this disease have (CAG)n sites within their coding regions. Additional studies by us have linked chromosomal abnormalities and genes linked to schizophrenia to regions of the genome prone to mutation ($p = .01$). Hence, the results of disparate biological phenomenon implicate genomic instability and schizophrenia and hint at possible causes of this disease and possible preventive measures.

DOES MULTIVARIATE ANALYSIS OPTIMIZE THE HERITABILITY OF CARDIOVASCULAR REACTIVITY CHANGE SCORES TO STRESS?
Session: Complex Disorders III

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Objective. Cardiovascular reactivity (CVR) to stress has been implicated in the development of essential hypertension and twin studies indicate moderate heritability. However, findings have been inconsistent, potentially related to measurement characteristics of CVR change scores (stress minus rest) as opposed to levels. Here we test whether using all available information in a multivariate analysis of the hemodynamic change scores to stress optimizes heritability estimates for gene finding purposes.

Methods. We studied CVR to two different behavioral stressors in 308 white and 223 black twin pairs from the southeastern US including monozygotic and dizygotic twins of same- as well as opposite-sex (mean age: 14.7 ± 3.1; range: 10.0–25.9). Subjects were exposed to a virtual reality car driving simulation (5 min) and a social stressor interview (10 min). Hemodynamic variables included systolic and diastolic blood pressure measured by Dinamap, heart rate by EKG, and stroke volume and total peripheral resistance by impedance cardiography. A multivariate Cholesky decomposition model including all 5 CVR change scores was used. Models were fitted to raw data using Mx software and were replicated across stressors and ethnic groups.

Results. Significant familial influences were found that were best explained by shared environment (χ^2) rather than genetic factors in all four ethnicity-by-stressor groups (CE models). Except for car driving in whites (no sex differences; χ^2 range: 23–34%), parameter estimates were significantly different between the sexes with higher χ^2 estimates in males (range: 22–65%) than females (range: 8–27%).

Conclusions. Familial influences on the cardiovascular change scores to stress can be attributed to shared environment rather than genes. These results cast serious doubts on the usefulness of CVR change scores for gene finding studies. Focus on levels of CV measures during rest and stress is likely to offer much better prospects.

OBESITY REVEALS AN ASSOCIATION BETWEEN BLOOD PRESSURE AND THE G-PROTEIN B3-SUBUNIT GENE: HAPLOTYPE AND SIB-TDT ANALYSES IN FEMALE DIZYGOTIC TWINS
Session: Complex Disorders I — Metabolic Syndrome, Obesity

Harold Snieder[1,2] Haidong Zhu[1,3], Xiaoling Wang[1], Tim D. Spector[2], and Yanbin Dong[1,3]
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Objectives. The C825T polymorphism of the G-protein beta3-subunit gene (GNB3) has been associated with hypertension, although results are not entirely consistent. In a large sample ($n = 282$) of female Caucasian dizygotic twins aged 21–80 years, we aimed to investigate the association between blood pressure (BP) and the GNB3 gene as well as interactions with age and adiposity.

Methods. Five GNB3 polymorphisms (A-350G, A657T, G814A, C825T, C1429T) were genotyped by PCR-restriction enzyme assays.

Results. Regular association tests did not show a significant effect on BP for any of the 5 SNPs. However, strongly significant interactions between the A–350G, C825T and C1429T loci and adiposity (both body mass index and waist circumference) were observed for systolic BP ($ps < .01$) as well as diastolic BP ($ps < .05$), suggesting increases in adiposity amplify the effects of the SNPs on BP. Haplotype trend regressions of inferred haplotypes (PHASE 2.0) confirmed the effects of the GNB3 gene–obesity interaction on hypertension risk. Additionally, sib-transmission disequilibrium tests (sib-TDTs) showed significant associations with BP for the C825T and C1429T loci.

Conclusions. The presence of obesity reveals an association between BP and the GNB3 gene in white females. Our data point to adiposity as a final pathway through which gene–lifestyle interactions may exert their effects on the development of hypertension. Our results from the combined SNP, haplotype and sib-TDT analyses also support the hypothesis that the C825T is a susceptibility locus for hypertension, whereas effects of other loci on BP may result from their strong linkage disequilibrium with the C825T locus.

TWINSUK–BIOBANK STUDY
Session: Poster

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Starting in 2004, the TwinsUK biobank study will be collecting DNA, serum, and urine samples from approximately 10,000 UK twins aged 18–85 (50% monozygotic, 50% dizygotic). This will build upon St Thomas' current database, which is one of the most comprehensive collections of genotype and phenotype information on twins worldwide. TwinsUK will be used for heritability analysis, novel gene discovery, gene expression studies, and exploring environmental interactions. Over the course of three years, blood (70ml) and urine samples will be collected at St Thomas' Twin Research Unit in London as well as seven satellite centers. Fasting bloods will be used primarily for DNA extraction (150–200microg/ml) and Whole Genome Amplification to provide a further 100mg of DNA. Peripheral blood lymphocytes will also be stored to provide a perpetual source of DNA and some RNA. The urine samples and remaining blood will be used for metabolic turnover markers. Meanwhile, baseline health, drug history, and lifestyle questionnaires will be obtained for all participating twins to complement St Thomas' existing phenotypic databases. This data will be integrated with the new biobank resources to provide a unique resource for genomic and phenotypic information. A library of phenotypes and genes will be accessible via website to institutions worldwide, promoting future genetic studies as well as increased collaboration among database users. This project is being undertaken in collaboration with The London "IDEAS" Genetics Knowledge Park and is funded by the Wellcome Trust.

SOCIAL CONSEQUENCES OF BIRTH ORDER
Session: Twin Family and Twin Relations

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While birth order is important for managing the pregnancy and the delivery of twins, one of the areas least covered or even considered in the study of the social processing of twins is that of the question of birth

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order. The first question usually asked of the parent(s) of twins is, "Are they identical?" The question(s) which follow on from this are, "Which one is the older twin?" or "Who was born first?" The answers to these questions indeed have consequences, consequences which vary in different cultures with respect to, for example, inheritance and status differences. While the usual processing of members in Western societies takes place in unitary or individual terms, the negotiation of twinship may be colored by processes external to the twin unit which reinforce a presumed lack of individuality and the lack of autonomy. Therefore birth order — and its subsequent perception(s) — may lead us to pose alternative questions about identity formation in twins. Variations in assumed roles within the family on account of birth order and the behaviors which follow on from this may be very significant. Equally important is the empirical question of when the twins are actually told of their birth order and what, if any, consequences follow on from this. Thus birth order may be one more key to confronting aspects of identity formation in twinship.

A STUDY TO ASSESS THE KNOWLEDGE ON ANTENATAL CARE AND TWIN PREGNANCIES AMONG THE PREGNANT MOTHERS IN RURAL VILLAGES OF INDIA

Session: Poster

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In India women of child bearing age (15–44 years) contribute 19%, and children under 15 years of age about 40% of the total population; together they constitute nearly 59% of the total population. In India knowledge of antenatal care is very poor. Most mothers live in rural areas, so that there are a lot of problems in implementing antenatal care and a lot of wrong beliefs and myths on twin pregnancy among the mothers and also prevalent in society.

Objectives.
1. To assess the knowledge of antenatal care and twin pregnancies;
2. To identify the welfare intervention for pregnant women;
3. To identify the wrong beliefs related to pregnancy and child care.

Subjects And Methods. To conclude and achieve the objectives a descriptive design was used. The study was done among the pregnant women living in ten villages. In each village the study identified five pregnant women. All information was collected in their mother language, Tamil. The information was collected confidentially by the investigator in Tamil language. The clients are Tamil speaking rural mothers and most of them studied only up to primary level.

Eighty-two percent of the respondents did not know about high risk pregnancies; the remaining 18% of respondents knew about the risks of high risk pregnancy status. Ninety-two percent of the respondents said that twin pregnancy was God's work, while the remaining 8% said that it was due to natural causes. Sixty-five percent said that twin children are trouble makers in the family, the remaining 35% said that twin children double the joy in the family. Seventy-three percent said that lack of nutritional food intake during pregnancy leads to anemia, and the remaining 27% said that more intake of food leads to complications during delivery. Sixty-five percent said that visiting a primary health center regularly is good for the health of women and children, and the remaining 35% said that there is no need to seek medical help during pregnancy unless there is a problem. Eighty-five percent of the respondents believed that immunization during pregnancy saves mothers and children from various diseases, and the remaining 15% believed that immunization will not have any positive effects in life.

Conclusion. Educational intervention is necessary to improve the general knowledge of pregnant mothers regarding antenatal care and twin children. Early identification of a risk pregnancy and regular visits to a primary health center after the 7th month of pregnancy is essential among the pregnant mothers; knowledge of regular follow-ups during the pregnancy is very important. The importance of iron rich food is essential during pregnancy. Awareness about multiple pregnancies, abortion, twin pregnancy, malformation and risk mothers identification are very important to pregnant mothers.

INTENSIVE COURSE ON BIOETHICS: AN EVALUATION

Session: Ethical Issues in Twin Studies

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Objectives. To promote higher ethical standards in research through increasing awareness and training critical mass. This was a collaboration with the Forum for Research & Development, and the Institute of Psychiatry, UK, the WHO non-communicable disease initiative, the Centre for the Study of Human Rights, Colombo and the Sri Lankan Twin Registry.

Methods. The course duration was 40 hours. A compilation of literature was provided. Lectures were followed by question and answer sessions. Group work, journal clubs, task-based learning and open discussions were used. Special sections on assisted reproduction techniques and genethics were incorporated into the curriculum. Evaluation was based on structured feedback.

Results. Fifty (22 females) were selected from 135 applicants. There were members of ethical review bodies, universities and community-based organizations. Others were nurses, lawyers, and journalists. Forty-three participants (94%) completed the course by attending over 70% of training. Drop out was from media. Nine resource persons were endorsed by 75%–96% and another eight resource persons by 60% to 74% as very good or good. Only two were endorsed by less than 50% of the participants. Ninety percent reported "definitely acquiring new knowledge"; 70% reported definitely acquiring new attitudes; 90% reported that the course material was "good" or "excellent"; and 92% reported that the intensive course was up to their expectations. A web site, www.forumforresearch.org, was developed and teaching materials were posted. An Email discussion board (bioethicsforum@yahoogroups.com) was formed to continue to discuss ethical issues.

Discussion. There was an overwhelmingly positive response to the course. It revealed that there was a need for such a course. The need to continue with capacity building in ethics remains.

USE OF KEY INFORMANTS AND A COMMUNITY SURVEY TO COMPILE A POPULATION BASED TWIN REGISTER

Session: Twin Registers and Methodology

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Objective. Piloting of two methods to identify twins within two defined catchments: (a) using key informants and (b) using a door-to-door survey.

Design. A community survey — first, census officers obtained information from pre-defined key informants, then census officers visited the twins. Finally, all households in the GN division were surveyed to find if there were additional twins.

Setting. Two GN divisions from urban Kolonnawa and rural Kaduwela.

Results. Twenty of 31 twin pairs (65%) were detected through key informants in Kolonnawa and 13 of 27 (48%) twin pairs were detected through them in Kaduwela. The prevalence of twin pairs detected in Kolonnawa was 9.6 pairs and in Kaduwela 9.9 pairs per 1000 population. A further 65 twins were identified who lived outside Kolonnawa, and 14 identified who lived outside Kaduwela. The majority of twin pairs (33, 57%) detected were alive and residing within the Colombo district. Of these, 64% were identified by key informants. In 17% of pairs, one twin had died.

Discussion. Key informants detected the majority of unbroken twin pairs. The key informants who provided most information were the Grama Niladari and census officers. They are the key players, who carried out fieldwork in island-wide government census in 2001, and can be used to trace adult twin pairs with a fair degree of completeness.

AGE AND SEX DIFFERENCES IN HERITABILITY FOR IRRITABLE BOWEL SYNDROME

Session: Poster

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Little is known about the etiology of Irritable Bowel Syndrome. Even less is known about the relative importance of genetic and environmental influences on this disorder. Thus, we sought to evaluate further the importance of genes and environment for Irritable Bowel Syndrome with a classical twin design. Like- and opposite-sexed twins aged 40 years and older from the population based Swedish Twin Registry were contacted for a computer assisted telephone interview. A total of 45,750 (72.5%) individuals (16,572 complete pairs) participated. Through a diagnostic algorithm, 3,241 cases of Irritable Bowel Syndrome (Prevalence 7.17%) were identified. Proband-wise concordance rates were calculated stratified by zygosity, sex and age group. For the age group 40 to 54 years, concordances were 18% for monozygotic twins (13.7% for men and 20.3% for women), 12.9% for dizygotic twins (12.1% for men and 13.3%

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for women) and 10% for opposite-sexed twins. For the age group 55 to 64 years, concordances were 16.5% for monozygotic twins (9% for men and 19.5% for women), 14.5% for dizygotic twins (3.8% for men and 19% for women) and 8.5% for opposite-sexed twins. Among twins 65 years or older concordances were 14.5% for monozygotic twins (12.5% for men and 15.6% for women), 10.6% for dizygotic twins (10.5% for men and 11.8% for women) and 3.8% for opposite-sexed twins. Monozygotic concordances were slightly greater than dizygotic, suggesting genetic influences for Irritable Bowel Syndrome. The pattern of concordances suggests some sex differences in genetic risk.

MENTAL HEALTH AS A FUNCTION OF INTERNAL AND EXTERNAL RESOURCES AMONG MOTHERS OF TWINS AND SINGLETONS

Session: Poster

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The birth, pregnancy and care of twins are mostly portrayed as more stressful than those experienced by mothers of single children, focusing on the likelihood of mothers of twins experiencing depression and physical illness.

The aim of the present study was to examine the contribution of the infants' characteristics, mothers' internal (attachment style), and external (marital relationship) resources to the mental health of mothers of twins and singletons.

In the current study, 200 mothers of twins and singletons were approached during the first month following delivery. They were asked to complete the Mental Health Inventory (Veit & Ware, 1983), the Evaluating and Nurturing Relationship Issues, Communications and Happiness Scale (Fowers & Olson, 1989), the Close Relationship Questionnaire (Brannen et al., 1998), which assesses attachment style, the Infant Characteristics Questionnaire (Bates et al., 1979), the Family Inventory of Life Events and Changes – FILE: (McCubbin & Thompson, 1987), and socio-demographic and basic medical data regarding mothers and infants.

Our findings indicate a positive contribution of marital relationship, and negative contributions of infant's characteristics and mothers' attachment anxiety to the mothers' mental health, in both groups. These findings point to the fact that the birth of twins and the birth of a single child are normative life events that have more in common than previously acknowledged. It seems that mothers' mental health is more associated with her internal and external resources and her baby's temperament than to her being a mother of a single newborn or twins.

LANGUAGE DEVELOPMENT IN TWO DANISH TWIN PAIRS

Session: Language Development

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No abstract supplied.

INCIDENT ASTHMA AMONG YOUNG ADULT TWINS

Session: Poster

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Background. Longitudinal data on adult asthma are sparse. The objective of this study was to determine the incidence of asthma, and establish risk factors for the development of asthma in 12–41-year-olds during an 8-year period.

Methods. Of a population comprising 34,076 individuals born 1953–82, ascertained from The Danish Twin Registry, 19,349 with no history of asthma answered a questionnaire in 1994, and at follow-up in 2002. Subjects were regarded incident asthma cases when answering "yes" to the question "Do you have, or have you ever had asthma?" in 2002 and "no" to the same question in 1994.

Results. Incidence rates of asthma were 6.4/1000 and 4.5/1000 person-years among females and males, respectively. For all ages, the probability of adult-onset asthma was greater for females (OR 1.49, $p < .001$), and for both sexes there was a slow decline in probability with increasing age. There was a positive association between increasing BMI and risk of adult-onset asthma for both sexes (OR 1.05 per unit, $p < .001$). We found positive associations between a history of hay fever (OR 4.2 and 3.7, $p < .001$), eczema (OR 3.5 and 2.0, $p < .001$) and both (OR 6.9 and 8.0, $p < .001$) and incident asthma, for males and females, respectively.

Conclusions. There is a continuing high incidence of asthma past childhood, most pronounced among females. Increasing levels of BMI are associated with a greater likelihood of developing asthma for both sexes. A substantial proportion of adult asthma is preceded by upper airway allergic symptoms, thus pointing to a shared pathogenesis.

THE SOCIAL WORLD OF TWINS: IS BEING A TWIN A SOCIAL DISADVANTAGE?

Session: Psychosocial Issues in Families with Multiple Births

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Twinning is associated with multiple adversities which may impact upon the child's social world. Firstly twins have higher rates of disability which may affect social interaction. Secondly, the twin situation alters social interaction and may diminish the quality and quantity of family interaction. Thirdly, language delay, which occurs more frequently in twins, may impair social interaction. This presentation will examine the effects of the twin situation by presenting data concerning patterns of social interaction both within and outside the family.

The majority of research studies are focused on social experiences of young twins within the family. The most typical design compares mother–singleton dyads with mother–twin triads. Not surprisingly, these studies indicate considerable differences in social interaction but they do not distinguish the effects of two children from the effects of twinning. Evidence will be presented of family interactions in which this problem is overcome by using close spaced singletons as the comparison group where mother–child triadic interactions are compared.

Our knowledge of the effects of twinning on social interactions outside the home is limited and yet the body of evidence on friendship indicates that these are critical for social development and long-term well-being. Twin children, negotiate their friendships in the presence of a sibling. Their degree of physical similarity and the nature of the relationship with their co-twin may affect formation and maintenance of friendship. Do twin children have more or less friends? Are friendships qualitatively different from those of singletons? Data will be presented from studies of twin children's friendships.

SHARED GENETIC EFFECT ON STRENGTH AND WALKING SPEED IN OLDER FEMALE TWINS

Session: Aging and Longevity II

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Background and purpose. In old age, strength impairment and walking limitation often coexist and consequently the same genes may underlie both conditions. The purpose of the present study was to examine whether maximal isometric knee extension strength (IKES) and maximal walking speed (MWS) share a genetic component.

Methods. IKES and MWS over 10 meters were measured as part of the Finnish Twin Study on Aging among 101 monozygotic (MZ) and 116 dizygotic (DZ) female twin pairs aged 63–76 years. Quantitative genetic models for twin data were constructed using the Mx-program.

Results. No differences in age, body height or weight, IKES and MWS were observed between MZ and DZ twin individuals. The pair-wise correlations among MZ and DZ twins were 0.50 and 0.33 for IKES, and 0.61 and 0.48 for MWS, respectively. The bivariate genetic modeling showed that IKES and MWS shared a genetic component in common, which accounted for 50% (95% CI 36–61%) of the total variance in IKES and 29% (95% CI 18–43%) in MWS. In addition, IKES and MWS had their own specific non-shared environmental effects explaining 50% (95% CI 39–64%) of the variance in IKES and 41% (95% CI 32–52%) in MWS. Remaining variance for MWS was explained by specific shared environmental effect.

Conclusion. The same genes were underlying the individual differences in IKES and MWS, suggesting that some people may be more prone to old age functional limitation due to their genetic disposition. However, environmental effects also have a significant role in explaining the variability in both traits.

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HEALTH AND MORTALITY FOR MOTHERS OF TWINS: ANALYSIS FROM ENGLAND, WALES AND DENMARK

Session: Poster

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This study aims to determine whether mothers of twins have negative health outcomes and higher mortality compared to mothers of singletons, using data from England and Wales and Denmark.

The fertility context where a multiple birth occurs is now completely different from the past. More recent cohorts of mothers of twins probably include a proportion that have impaired fecundity as well as a proportion with above average fecundity, as this is associated with "natural" twinning. Having a multiple birth could be more associated with negative health outcomes for mothers that had twins after 1975, and less for the previous cohorts. Some studies also suggest a relation between the exceptional stress that twins induce and their mother's emotional and physical wellbeing. Mothers of twins are generally more fertile than mothers of singletons and previous findings on historical populations have reported links between high parity and later life mortality. These findings suggest that mothers of twins should have higher mortality compared to mothers of singletons.

For England and Wales we used the ONS Longitudinal Study, a record linkage of approximately 1% of the population of the 1971 Census of England and Wales. We considered cohorts born from 1915 to 1955. In addition to mortality, we used the presence of limiting long-standing illness present in the 1991 Census. The sample include 2250 mothers of twins and around 100,000 mothers of singletons.

For Denmark we used the linkage between the Danish Twins register and the Danish Civil Registration System. We included the mothers of twins born in 1953 and 1982.

A preliminary analysis of mortality compared the expected and the observed numbers of survivors for mothers of twins using the cohort mortality rates for the total population. The numbers of survivors among mothers of twins in England and Wales is lower for the oldest cohorts, but not significantly different for the younger cohorts. Additional survival analysis models are used to determine the possible disadvantage of having a multiple birth in terms of health (just for England) and mortality, controlling for several socio-economic factors included in the Census. Results for England show a significant effect of having twins on mortality after age 50 for cohorts born before 1925, while no significant effects on mortality have been found for the more recent cohorts. Furthermore, having twins has no significant effect on the presence of long term illnesses.

PREVENTION OF BIRTH OF DZ TWINS WITH MULTIPLE CONGENITAL MALFORMATIONS

Session: Poster

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Our client was a primigravida 20-year-old with 18–19 weeks of gestation. There was cervical erosion in her case report. Advancement of this pregnancy was complicated by threatened abortion at 16–17 weeks of gestation. The primigravida complained of nothing. Laboratory investigations showed the following: couple blood group was 0(1)Rh(+); aFP — 66.6E/ml(1,4MoM), estriol — 4,3ng/ml(1,5MoM) at 16 weeks of gestation. At 13.5 weeks of gestation ultrasound investigation revealed signs of the monochorion biamnion twin fetuses. At 23 weeks of gestation there were bichorion biamnion fetuses. Their parameters conformed to the gestation term. The first fetus had some features of congenital malformations (anomaly of CNS and urogenital system, increased density of intestine, mild shortness of tubular bones). Severe oligohydramnion was found too. The following features were found for the second fetus with ultrasound investigation: suspended particles in amniotic fluid, anomaly of CNS with increased density of the left cerebral ventricle. After genetic counseling the couple decided on interrupting this pregnancy. Diagnosis of multiple congenital malformations was confirmed by autopsy of the both fetuses.

GENETIC AND ENVIRONMENTAL SOURCES OF CONTINUITY AND CHANGE IN TEACHER-RATED AGGRESSION DURING EARLY ADOLESCENCE

Session: Poster

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Genetic and environmental sources of continuity and change in aggression were studied in a sample of 1041 twin pairs (364 monozygotic or MZ; 348 same-sex dizygotic, SSDZ; and 329 opposite-sex dizygotic, OSDZ) as part of an ongoing, population-based Finnish twin-family study. At ages 12 and 14, the twins' aggression was assessed by their classroom teachers, using a rating form of the Multidimensional Peer Nomination Inventory. Genetic and environmental sources of continuity and change were studied by fitting a longitudinal bivariate Cholesky decomposition model. Results emphasized differences in cross-sectional patterns of genetic and environmental factors at the two time points and across sexes. Significant genetic and environmental effects were found at both ages and for both sexes, but the importance of the genetic factors for boys, and of environmental factors for girls, increased during development. Longitudinal model fitting analyses revealed both genetic and environmental sources of continuity in aggression during years 12 and 14, but the results differed markedly by sex. Genes and common environmental factors rather equally explained continuity in aggression in boys, whereas environmental factors, primarily those arising from the common environments, explained continuity in girls. In addition to continuity in genetic and environmental factors, significant age-specific genetic and unique environmental factors were found for both sexes.

GENETIC VARIATION AND COVARIATION IN THE MMPI CLINICAL SCALES

Session: Poster

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The Minnesota Multiphasic Personality Inventory (MMPI) is one of the most widely used, and widely researched, measures of psychopathology. Given the ubiquity of the MMPI and recent strong interest in genetic influences on psychopathology, it is surprising that there has been so little research on genetic variation in the MMPI clinical scales. We report on genetic and environmental sources of variation in the MMPI clinical scales, based on a sample of 492 twin pairs who completed the MMPI. In line with recent interest in psychiatric co-morbidity, we also evaluate the sources of covariation among scales that assess different psychiatric symptom patterns. We found significant genetic influences on every clinical scale except MF (Masculinity–Femininity). Significant shared environmental effects were present only for MF. For all of the scales, the best fitting model was one in which heritability was set equal for males and females. Supplementary analyses revealed variability in the genetic effects for the subtle versus the obvious items in some scales. Both genetic and unshared environmental influences were significant sources of covariation among the clinical scales.

TWINNING RATES IN SINGAPORE FROM 1986 to 2002

Session: Twin Registers and Methodology

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Objective. To describe the number of twin births among different ethnic populations in Singapore.

Method. Using the Singapore National Registry of Births and Deaths from 1 January 1986 to 31 December 2002, the number of twin births was analyzed according to the three main ethnic groups in Singapore (i.e. Chinese, Malay and Indians). Further, the Weinberg's differential rule was used to estimate the DZ/ MZ ratio.

Results. Twin birth rates have increased steadily across all ethnic groups (from 6 to 10/ 1000 maternities). The largest increase in multiple births was among Indian fathers (from 6.9 to 9.9/1000 maternities) and Malay mothers (5.9 to 9.8/ 1000 maternities). Indians had the highest DZ/MZ ratio (1.03 for mothers and .91 for fathers), followed by the Chinese then Malays.

Discussion. Although increasing, Singapore's twining rate is still lower than in European countries. Similar to other Asian countries, Singapore's DZ/MZ ratio tends to be less than 1. However, in European countries, the DZ/MZ ratio tends to be greater than 1. Additional data for year 2003 will be presented at the conference. The establishment of a national twin register would enable more detailed analysis of genetic and environmental

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effects in multiple births and future plans to set up such a registry in Singapore will be discussed.

QUALITY CONTROL MANAGEMENT OF MICROSATELLITE GENOTYPING IN THE GENOMEUTWIN PROJECT

Session: Poster

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The GenomEUtwin project, encompassing six twin cohorts with over 0.6 million twin pairs, provides a unique opportunity to verify genetic variants behind common diseases. During the first 4 years, 2,000 twin pairs will be genotyped for 400 multi-allelic markers in two genotyping laboratories. Since commercially available genotyping software is only semi-automatic, requiring a substantial amount of manual data editing, proper quality control is imperative to ensure good quality data. The most stringent way to control for genotyping errors is to check for violation of Mendelian inheritance in extended pedigrees. In twin samples only sibling pairs are genotyped, and segregation check becomes impossible.

To detect sample mix-ups, plate mix-ups, technical problems related to PCR and electrophoresis, allele calling errors, marker mutations and null alleles, each laboratory will implement a local quality control procedure including manual rescoring of electrophoresis runs, plate control and duplicate samples in asymmetric shifting positions on each plate, evaluation of the proportion of alleles shared between siblings (GRR) and mutation and error detection through multipoint mapping (SIBMED).

Based on data from 52 monozygotic twin pairs (39,500 genotypes) the allele calling inconsistency was 0.5 discrepancies/1,000 genotypes. In a data-set of 654 clinically diagnosed dizygotic twin pairs genotyped for 230 markers, 9 pairs (1.4%) had identical genotypes. Using GRR, seven pairs (1.1%) showed allele sharing proportions consistent with sample mix-up. Overall, almost all detected genotyping errors were picked up by manual rescoring of electrophoresis runs. Since genotyping was done at 10 cM resolution, genotyping errors were not detected through multipoint mapping.

A COMMON GENETIC FACTOR UNDERLIES HYPERTENSION, RAYNAUD'S PHENOMENON, MIGRAINE AND CORONARY ARTERY DISEASE

Session: Poster

Frances M. K. Williams[1], Lynn F. Cherkas[1], Carol M. Black[2], Tim D. Spector[1], and Alex J. MacGregor[1]
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A common vasospastic mechanism has been proposed to account for the epidemiological association between a number of conditions with vascular etiology including hypertension, Raynaud's phenomenon, migraine and coronary artery disease. The underlying nature of the association, however, remains speculative. Here we investigate the genetic and environmental relationship between these conditions in a classical twin study conducted using questionnaire data from 525 monozygotic and 577 dizygotic female twin pairs recruited to the St Thomas' UK Adult Twin Registry.

Individually, all four traits had a significant genetic basis with heritability of 0.64 for hypertension, 0.46 for Raynaud's, 0.43 for migraine and 0.34 for coronary artery disease. Multivariate model-fitting explored the associations between the four variables simultaneously and demonstrated that a single common genetic factor underlies the four conditions, suggesting there is a considerable genetic basis for the vasospastic phenotype. Shared environmental factors such as diet and lifestyle do not appear to contribute to a predisposition to vasospasm.

A CO-TWIN ANALYSIS OF THE EFFECT OF MODERATE ALCOHOL CONSUMPTION ON BONE MINERAL DENSITY IN WOMEN

Session: Poster

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Background. Osteoporosis and fracture are associated with considerable morbidity and mortality in women. Risk factors need to be quantified precisely to allow accurate public health messages. The effect of moderate alcohol consumption on bone mineral density (BMD) and fracture risk remains unclear, despite a number of epidemiological studies. Discrepant study results may arise from differences in age, sex and smoking habits of subjects and lack of alcohol-specific designs. The unique matching of monozygotic (MZ) twin pairs for age, sex and genetic factors, all of which influence both BMD and the propensity to drink alcohol, allows a powerful study to be conducted with a relatively small sample size. The study of discordant MZ twin pairs in which one consumes alcohol and the other does not reveals the effect of alcohol on BMD while controlling for confounding variables.

Methods. Questionnaires were sent to 1358 female MZ twin pairs registered with the St Thomas' UK Adult Twin Registry. Demographic data, and health and lifestyle details were collected, specifically alcohol intake over the last 12 months and past/present smoking. Pairs discordant for alcohol consumption were invited to attend the unit, unaware of the hypothesis under investigation. BMD was determined at hip and lumbar spine. Evidence of altered bone metabolism was sought using fasting morning serum and urine bone turnover markers.

Results. Forty-six twin pairs were discordant for alcohol consumption with a "minimal drinker" twin consuming < = 1U/week. The "drinkers" of each twin pair consumed mean 8 U/week (standard deviation 7.8, range 2–28 U/week). Their mean age was 52, standard deviation 9.4, range 32–73 years. Associations between the intrapair differences in variables (BMD, alcohol consumption, bone markers) were examined using regression analysis (STATA software). Alcohol consumption was found to be associated with significantly greater BMD at sites in the lumbar spine and hip. There was no association between any bone marker and BMD or alcohol consumption.

Conclusion. Using unique exposure–discordant identical twins we have performed a study specifically to look at the effects of alcohol on bone. A positive association between moderate alcohol and BMD was found, in contrast to the well-documented deleterious effect of smoking, which was also confirmed. Alcohol consumption within recommended UK limits appears safe for bone.

PALATABLE DIFFERENCES: AN EXPLORATION OF THE DEVELOPMENT OF ANOREXIA NERVOSA WITHIN THE CONTEXT OF THE TWIN RELATIONSHIP EXPERIENCE

Session: Complex Disorders I — Metabolic Syndrome, Obesity

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The study explores the experience of female monozygotic twins and how these experiences may be related to the development of anorexia nervosa.

Results.

- Comparison seems to most often be about looks, and often minor physical differences will be emphasized to create a way of recognition.
- Understanding the twin relationship is not something that twins necessarily think about unless there is a problem.
- All the twins in this study described difficulties in being away from their twin.
- The relationship between the twins either enabled them to develop resilience and form a secure attachment for each other or an insecure attachment and little resilience to the pressures of the world.
- Jealousy and competitiveness seem to be more destructive when they originate from within the twinship. All of the twins described having feelings of jealousy and competitiveness.
- The contrast between CS1, CS2, and CS3 and CS4 seems to be about whether being a twin was who you are or what you are, that is, being a twin was the only way of defining their identity.

This study has highlighted some areas for further research:

- Further exploration of the process by which mothers resist their own ideas about child rearing in favor of someone else's ideas;
- Further exploration of the different areas of comparison, and enforced separation or togetherness, and the impact of these on twins' behavior;
- Further exploration of the meaning of being a twin as well as the meaning of having twins.

GENETIC LINKAGE IN TWIN STUDIES OF AGING AND LONGEVITY

Session: Statistical Issues in Twin Studies

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In this paper we combine methods developed for bivariate survival analysis with approaches to study genetic linkage. Our earlier studies show that bivariate survival models that take into account the influence of separate genes on life span or age at onset of disease may be successfully used in the analysis of twin survival data. In this paper we show that this approach can be extended to perform linkage studies, if, in addition to survival data for related individuals, the genetic markers data are available. We show that location of the gene at the chromosome can be identified using a two-step procedure. At the first step the parameters of bivariate survival functions must be estimated from bivariate survival data for twins without markers. The second step is focused on determining the position of longevity gene

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between respective markers. To calculate joint distribution of inheritance vector and genetic markers we extended the hidden Markov chain technique. We illustrate this approach with a simulation examples.

WHAT IS THE IMPACT OF SOME RISK FACTORS ON GENETIC INFLUENCES FOR DEATH FROM CORONARY HEART DISEASE?

Session: Twin Registers and Methodology

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The importance of the influence of some recognized risk factors on genetic influences for coronary heart disease (CHD) needs further clarification. We have, therefore, studied the impact of known risk factors such as hypertension, diabetes, body mass index, smoking, marital status, and socioeconomic status as measured by level of education on genetic influences for CHD-death. Both correlated gamma-frailty model, and univariate models such as Cox's model and gamma-frailty model respectively were utilized. We also compared these models regarding their suitability in genetic studies. The study was based on Swedish twins born between 1886 and 1925. By comparing univariate models we noted that risk factor estimates were in general lower obtained by the Cox's model compared with the estimates obtained by the univariate gamma-frailty model. When these two models were compared with the correlated gamma-frailty model it was found that risk factor estimates were larger for the later model. Our findings indicated that genetic influences are important for CHD-death. The heritability estimate obtained in the crude analysis by the correlated gamma-frailty model was .40 (.26–.54) among females and .59 (.41–.76) among males. Inclusion of risk factors in the correlated gamma-frailty model increased heritability estimates, primarily due to a substantial reduction in non-shared environmental variances. The genetic influences for CHD-death were only marginally mediated through the risk factors among males, but more so among females. Furthermore, correlated gamma-frailty model seems to be more appropriate for analyzing time-to-event data of relatives than the univariate models for studying genetic influences including observed risk factors.

GENETIC AND ENVIRONMENTAL INFLUENCES IN COGNITIVE ABILITIES OF 6- AND 7-YEAR-OLD TWINS

Session: Poster

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The present study is a part of Moscow longitudinal investigation of twins. The aim of this study was to compare the relative influence of genetic and environmental factors in the cognitive abilities of 6- and 7-year-old children. This period is critical in the development of children as they start school education, therefore we can expect changes in genetic and environmental determination of cognitive characteristics.

The sample was comprised of 94 pairs of 6-year-old monozygotic (MZ) and dizygotic (DZ) twins, and 79 pairs of 7-year-old MZ and DZ twins. We used nine different tests of cognitive abilities for children. ANOVA (analysis of variation) shows that IQ is connected with cognitive abilities: there are significant differences in the characteristics of cognitive abilities among children with high and low PIQ and IQ. From age 6 to 7, the number of cognitive characteristics connected with PIQ and IQ double. Analysis has revealed both quantitative and qualitative changes in connection between IQ and cognitive abilities from age 6 to 7.

Then we conducted psychogenetic analysis of cognitive characteristics that were connected with IQ. We have found for the most part that these characteristics are under genetic influences. The estimates of heritability for these characteristics are significantly higher than average for the full sample (h2 for 53% of them is higher then 0.30 in comparison with 20% of characteristics with such h2 for full sample).

Possible interpretations of these results are discussed.

observed when APOE genotype is taken into account. If the difference in within pair similarity for MZ and DZs would disappear completely, this would suggest that APOE genotype explains all the genetic risk for dementia.

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