

**9th International Congress on Twin Studies**

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## 001

**THIRTEEN-YEAR FOLLOW-UP OF COGNITIVE DEVELOPMENT IN 32 TWIN PAIRS**

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This is a follow up study of twins including 32 families and their twins attending grade six within the Stockholm area. The twins have been followed from birth onwards. The main purpose with the study is to describe the cognitive development by using ability tests and relate these to the teachers ratings of the twins adaptation to the school situation. Another aim is to see if the twins who were prematurely born are predisposed to below-average mental growth at 13 years of age. As described in earlier reports, the twins are more susceptible to lower birth weight, shorter gestation period and birth complications.

The ability tests were opposites, metal folding, number series and a mathematical test as well as questions about interest, attitudes toward school, leisure activities and future educational plans.

There were no differences between boys and girls, but in every test the girls performed a little better than the boys. In comparing the ability for twins and singletons I have used a singleton sample from 1990. The twin group had somewhat lower scores than the singletons. At 13 years of age 21 of the 64 twins with physical and psychological disorders at four years of age had lower results at all the ability tests. Most of them were prematurely born or small for age.

## 003

**THE JAPANESE ASSOCIATION OF TWINS'MOTHERS  
YUKIKO AMAU**

(The Japanese Association of Twins'Mothers)

JATM was started in 1968 with only 23 mothers of twins. It is going to celebrated the 30th anniversary in November this year. It has become a nation-wide organization with the number of membership approaching 4000.

Activities in the last five years :

Opening of a new office

Up to March 1996, the office of JATM was located at private residence of Mrs'Amou (The founder). In April 1996, a new independent office was opened, equipped with computer systems to cope with increasing members.

Starting of "Twinline"

In April,1994, telephone consultation "Twin line" was started with the cooperation of 40 members. In Jan. 1997 "Twinline"was also set up at JATM office, with specialist members answering calls.

Promotion of regional activities

Recently, local Public Health Centers are showing more interest in supporting mothers of multiple birth children. We have regional meetings in cooperation with the Centers.

## 002

**DESIGN AND ANALYSIS OF TWIN AND SIBLING-BASED ASSOCIATION STUDIES**

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In recent years, several factors have renewed enthusiasm for use of association studies for quantitative trait loci (QTL) mapping. These include burgeoning advances in the ability to quickly and efficiently genotype bi-allelic markers at great density, the increased focus on populations that may exhibit greater genetic homogeneity and disequilibrium due to historical geographic or social factors, and advances in statistical techniques for such studies. This presentation will focus on the last of these three developments. In particular, I will focus on (1) the development of the transmission disequilibrium test (TDT), (2) its extension to quantitative traits, and, more recently, (3) its extension to designs that involve siblings but no parental information. This most recent development should be especially relevant to researchers with access to large twin samples. Using this sibling/twin-based TDT approach, methods to capitalize on and accommodate such factors as multivariate data, cost-considerations, and extreme sampling will be discussed. With respect to extreme selection, issues of power, cost, robustness, and distinctions between selectively sampling from "infinite" populations versus finite super-samples will be considered.

## 004

**KEIO TWIN PROJECT: A PRELIMINARY REPORT**

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This is a preliminary report of Keio Twin Project (KTP), the on-going psycho-biological research project which aims at the genetic and environmental etiology of psychological and psychiatric characteristics. Keio Twin Registry (KTR) has been constructed from the official residential registration lists since 1992. It currently contains the records of names, addresses, and birthdays of over 5000 twin pairs who live in and next to Tokyo. Among 2000 pairs of twins from 16 to 27 years old in KTR, about 300 pairs responded to our request for a four-hour research including several personality inventories, working memory tasks and cognitive ability tests, family environment questionnaire, and blood samples. Data of 218 twin pairs have been already provided by the end of March, 1998. The current sample consists of 42 MZm, 75 MZf, 18 DZm, 45 DZf, 5 UKm, 6 UKf, 27 OPS (zygosity by self-report).

## 005

## ANALYSIS OF PRENATAL TWIN BEHAVIOR

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**OBJECTIVE:** To describe developmental activities and inter-twin reactions in utero and to compare behavioral patterns within subgroups of different zygosity, chorionicity and sex.

**METHODS:** Up to now >100 mothers of twins/triplets have volunteered to take part in behavioral studies. From 8 to 12 weeks transvaginal and later transabdominal ultrasound examinations were performed at 1-week intervals. Twin activities, inter-twin contacts and hemodynamics were analyzed from video tapes separate for MC/DC, MZ/DZ groups and twin pairs of different gender. In addition, the influence of nicotine, caffeine and various diseases was evaluated. From 26 weeks onwards also FHR-tracings and reactions to stimulation were analyzed.

**RESULTS:** Video tapes will be demonstrated to illustrate characteristic patterns. By analyzing the development of activities, hemodynamics and reactions towards inter-human touch new phenomena and normal values in twin pregnancies were established. We found significant differences in behavior between subgroups of different sex, chorionicity and zygosity (uni- and multivariate analysis) even before 20 weeks. Finally we found, that parents enrolled in the study experienced their pregnancy as more positive than mothers with common controls.

**CONCLUSIONS:** Implications of the state of the art for future research implicate the definition of a life quality in utero, anthropological, medical aspects as well as the impact on early bonding between parents and their future multiple offspring.

## 007

## PREDICTION OF PREMATURITY IN TWIN PREGNANCY BY MULTIFACTORIAL ANALYSIS

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**OBJECTIVE:** To investigate the diagnostic value of longitudinal and cross-sectional transvaginal echography (TVE) of the cervix in comparison with clinical, bacterial and laboratory values including CRP/ fibronectine in multiple gestation.

**METHODS:** In 25 twin pregnancies delivering after 35 weeks longitudinal cervical examinations (TVE) were performed in a standing and recumbent position from 15 weeks onwards to term. In a cross-sectional study of 150 twin pregnancies measurements between 26 and 28 weeks were compared with clinical and laboratory examinations.

**RESULTS:** The mean cervical length decreased from 50 to 26mm in a recumbent and from 47 to 20mm in a standing position, the ratio recumbent/standing increased from 5 to 31%. Funnelling was observed from 20 weeks onwards in a standing, but only after 30 weeks in a recumbent position. Within the cross-sectional study the transvaginal length and structure had a higher diagnostic capability in twin pregnancies to predict premature delivery < 35 weeks than all clinical and laboratory values (ROC-analysis of continuous values/ sensitivity and specificity of qualitative data, regression analysis).

**CONCLUSIONS:** Our results support a policy aimed at the prevention of prematurity in twin pregnancies by restraining standing work. The impact on specific interventions dependent on the early individual TVE findings has still to be evaluated.

## 006

## DEVELOPMENT OF PERINATAL CARE IN EAST-/ WEST-BERLIN 1950-90: A PUBLIC HEALTH TWIN MODEL

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**OBJECTIVE:** To investigate the developmental quality of perinatal care within an unique epidemiological twin model, West-and East-Berlin, separated by different political and health care systems between 1950 and 1990.

**METHODS:** Number of deliveries, maternal and infant mortality, the introduction of new technologies and perinatal care were evaluated from government and 19 hospitals archives. 1291 questionnaires were evaluated within a representative group of mothers delivering their first child between 1950 and 1990.

**RESULTS:** Infant and maternal mortality decreased in East- and West Berlin by around 10. Expensive techniques such as ultrasound or CTG-monitoring were earlier introduced in West-, general measures such as screening for diabetes or transfer of risk patients were earlier introduced in East-Berlin. There were significant improvements by time such as the frequency of controls, quality of information and experience of pregnancy and delivery ( $p < 0.001$ ) and increasing differences between East-and West Berlin mothers such as the age of the first delivery, motivation for controls, support of family and social care during the first year after delivery (more positive in East-Berlin,  $p < 0.001$ ).

**CONCLUSIONS:** The results are a basis for hypotheses/further studies within epidemiological twin models with the same historical, cultural, environmental background but different health care systems.

## 008

## IRM IMAGES OF CEREBRAL CENTRAL SULCI: A MONOZYGOTIC TWINS' STUDY

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Central sulci, the sensorimotor cortex's seat, show variability in form, length and depth from brain to brain (and between the hemispheres of the same brain. In this work, for the first time, their lengths, at the surface and in the depth of the brain was measured on IRM images, using 3 D image software. The technique of measure developed, gives high interobservers correlation coefficients for the surface's lengths (0,96), less high for the depth's lengths. This technique of measure was applied to monozygotic twins and the Inter Class Correlation Coefficients between co-twins'homologue sulci, although weak, is significant. So, if there is a possible genetic influence on the central sulci's morphometry, the results show that the nongenetic factors are important in their development. Further, it was found that the monozygotic twins have the same probability as no twins pairs to be discordant for the asymmetry of this sulcus.

009

## DUTCH TWIN-FAMILY STUDY OF SMOKING BEHAVIOR

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We have collected longitudinal data by questionnaires in over 13,000 subjects from 3386 families. Subjects were asked about health-related behaviors (tobacco and alcohol use, physical exercise) and completed an extensive battery of personality inventories.

Names and addresses of adolescent twins were obtained from Dutch City Councils. Questionnaires were mailed to adolescent twin pairs and both their parents in 1991, 1993 and 1995. In 1995 one or two siblings of the twin pair were also included in the study. In 1997 the twins and all their siblings were asked to participate. A total of 534 families participated on all 4 occasions. The number of families that participated on three, two and one occasion equals 856, 834 and 1162, respectively.

Results for tobacco use (data from 1991 and 1993) show that smoking initiation in adolescents is to a large extent influenced by environmental factors common to siblings growing up in the same family. There is a smaller contribution of genetic factors. Genetic factors, however, explain the resemblance between parents and their offspring for smoking initiation. There is no evidence for cultural inheritance.

Multifactorial threshold models were applied to the data on smoking initiation and quantity smoked. The heritability of quantity smoked was high (86%). There was no evidence for sex differences in heritabilities for smoking initiation or quantity smoked.

011

## TWINNING IN FAMILIES WITH DOWN SYNDROME

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Among 866 liveborns with Down syndrome (DS) 3 monozygous sets concordant by trisomy 21 (MDS), and 6 children from dizygous sets discordant by trisomy 21 (DDS) were revealed, for a rate 1.04%, similar to population rate. Proportion of monozygous twins was 30%, not different from the proportion in healthy children. Mean maternal age at birth was 29.4 yr (30.1 in overall DS group). Gestational age was lowered compared to normal population: 258.5 and 251.0 days in MDS and in DDS, correspondingly. All pregnancies were complicated with early and late gestosis. In 5 out of 6 cases of DDS the affected newborns were delivered after normal children. Apgar score was 7 in all cases, average weight was 2400.0 g in MDS and 2357.0 g in DDS, lowered by 214.4 g compared to their normal sibs. There were no unlike-sexed twin sets. Sex ratio (proportion males to females) twins was 1.0 in DDS twins and 0.5 in MDS twins. All DDS children had cardiac defects of different gravity. One set of MDS was discordant by cardiac defect, the another one represented incomplete concordance. 4 out of 6 DDS died at first year, one girl died at 5 yr, one girl aged 4 yr is alive hitherto. Of 3 monozygous twins, one male set died at 1.5 months, in both female sets one girl died, the another one is alive (aged 5 and 10 yr).

Familial predisposition to twinning from paternal side was in question in two cases. In one family where mother was a carrier of Robertsonian translocation 13;14, the first pregnancy was resulted in male MDS twins with the same translocation, the next pregnancy was completed with healthy dizygous unlike-sexed twins discordant by translocation.

010

## SUPPORTING PROFESSIONALS SUPPORTING FAMILIES

Elizabeth Bryan. Multiple Births Foundation, Queen Charlotte's & Chelsea Hospital, Goldhawk Road, London W6 0XG, UK.

An increasing number of professionals are seeking information and advice from the MBF when they feel inadequately equipped to respond to the needs of the multiple birth families in their care.

Not only are the numbers of such families increasing but new dilemmas are arising for which, inevitably, few people have the necessary experience - pre treatment for infertility counselling, fetal reduction, pre-school behaviour problems and adolescent identity crises are examples.

The MBF's aim is for its teaching materials to become an integral part of the training programme of all the relevant professional groups from infertility specialists to teachers of adolescents. Meanwhile it provides a telephone advisory service, literature for parents and professionals (including Guidelines<sup>1</sup>), a dual purpose prenatal training pack<sup>2</sup> for training health carers and preparing parents, Twins Clinics (used also for teaching and as a model for others in the UK and overseas) and a Resource Centre.

Multiple birth families will only receive the vital information, advice and support they need when their special problems are recognised by all carers - whether in health, social or education services.

1. *The Impact of Multiple Births. Guidelines for Professionals.* MBF 1997
  - a) *Facts about Multiple Births*
  - b) *Multiple Pregnancy*
  - c) *Bereavement*
2. *Preparing for Multiples* - containing 2 videos, slides and literature. MBF

012

## THE BERLIN TWIN STUDY ON CARDIOVASCULAR PHENOTYPES: COMBINING TWIN METHODOLOGY AND MOLECULAR GENETIC TECHNIQUES

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Hypertension, left ventricular hypertrophy and lipid disturbances, all of which are influenced by genetic variance, are strong risk factors for cardiovascular disease. In an attempt to localize and characterize genes influencing these risk factors we selected 120 sets of MZ twins and 90 sets of DZ twins without known cardiovascular disease. In these subjects blood pressure at rest and during stress, cardiac function and morphology as well as lipid levels were measured. Heritability of these measures was estimated by conventional path analysis. Based on these results association and linkage analyses were carried out for a number of candidate genes.

The known association between angiotensin-converting enzyme gene polymorphism and ACE activity could be confirmed in our sample. In addition to this result it could be shown that the ACE gene is the only major gene influencing ACE activity by differentiation between MZ pairs and DZ pairs concordant or discordant for the polymorphism. In a sib-pair analysis (Haseman-Elston approach) we could show linkage between resting systolic blood pressure, cardiac wall thickness and the gene locus for Insulin-Like Growth Factor 1. Finding genes influencing cardiovascular phenotypes in the normal physiological range is an important step in the search for genetic polymorphisms involved in disease processes. Studies in DZ twins are a very efficient way to detect quantitative trait loci and thus they are of major importance for complex phenotypes and diseases.

## 013

## AN INVESTIGATION INTO THE EXPERIENCES AND NEEDS OF THE FATHERS OF MULTIPLES

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“No father should underrate his importance to his family” - Twins and the Family, Audrey Sandbank, 1988.

The objective of this study was to collect information regarding the experiences of fathers and learn how they perceive their needs during the various stages of multiple pregnancy: antenatally, during delivery; postnatally and in the early years. In the UK many writers have acknowledged the importance of the fathers' role without looking at their specific needs. A questionnaire was sent to fathers in a pilot study based in the Midlands and North West, UK. This addressed specific issues such as whether fathers were present at delivery because they wanted to be there or because they were expected to be there and their involvement in decision making.

“... the position and feelings of fathers of twins deserves more attention than they often receive...” - Nature and Nurture of Twins, Elizabeth M. Bryan, 1983.

## 015

## EFFECTS OF TWIN TYPE ON FETAL PARAMETERS

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**Objective:** To examine the relationship between twin types, divided by zygosity (DZ and MZ) chorionicity (MC and DC), and birthweight (BW) discordancy (more or less than 15% intertwin weight difference at delivery) on fetal biometric measurements, including biparietal diameter (BPD), abdominal diameter transverse (ADT), femur length (FL), and transverse cerebellar diameter (TCD) at 18, 23, 28 and 32 weeks of gestational age (GA).

**Study design:** More than 71% (n=94) of the fetuses studied were born at “ideal” term (between 35 to 38 weeks), and 29% (n = 38) were delivered at preterm (31 up to 34 weeks). We distinguished twins by zygosity, and chorionicity, and we divided them into two BW groups. We compared intrapair and intergroup twins for BPD, ADT (circumference [C] and area [A]), FL, and TCD parameters.

**Results:** For example, preliminary results indicate within-pair variance BPA and AA smaller in DC-MZ than MC-MZ and DZ. The most striking result concerns the AA in MC-MZ at 23 GA, the intraclass correlation (ICC) is significant close to 0.50, whereas it is not significant and close to 0.0 at 32 GA. However, MC-MZ BPA ICC are close at 23 and 32 GA to 0.50. The fetal parameters for each GA which can be linked to the BW discordancy are also analyzed.

**Conclusion:** For convenience, it is suggested to differentiate and compare MC-MZ, DC-MZ, and like-sex DZ of same birthweight in twin research. Few studies address the influence of twin types which provide unexpected and somewhat surprising results.

## 014

## THE NORTH AMERICAN TWIN STUDY 1989-91

Arturo Cervantes, Louis Keith, Grace Wyslak, John Kiely, Donald Keith, Emile Papiernik

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**Objective:** Examine 1989-1991 birth cohort of US by maternal race/ethnic characteristics.

**Materials and Methods:** 1989-91 linked birth/infant death data set used with 263,987 twins. LBW/VLBW, delivery <38 & 28 weeks and infant/neonatal/postneonatal mortality studied vs mothers age/marital status/edu./race/ethnicity /birth place (US/nonUS)/prenatal care/parity by uni/multivariate and X2 tests.

**Results:** Study group was non-Hispanic White[nHW] (65%), nonHispanic Black[nHB] (18%), Mexican[M] (7.1%), nonHispanic other[nHo] (3.6%), Asian[A] (2.4%), Central/South American [CSA] (1.6%), Puerto Rican[PR] (1.3%), other Hispanic(1.2%), Cuban[C] (0.2%). 13% mothers born outside US: CSA highest (96%), followed by C(81%), M(61%), PR(44%). Only 4% nHW and 7% nHB non-US born. Twins highest in nHB(2.7%), nHW (2.3%); less in M(1.8%)nHO(1.7%). 80% mothers received early care: M(61%), nHW(87%), C(88%)(Chi-square p<0.001). <28 week delivery 7.4% in nHB, 5.5% in PR, 2.8% in A, 3.4% in M, 3.8% in CSA(p<0.001). VLB and VLBW 14.8% and 6.4% in nHB, 11.9% and 4.4% in PR, 7.3% and 2.6% in A, 7.3% and 2.9% in M, and 7.5% and 2.9% in nHW infants(p<0.001). Neonatal/postneonatal death 3.3% and 1.4% in nHB, 2.7% and 1.1% in PR; 1.8% and 0.5% in C, 1.6% and 0.6% in A, 1.9% and 0.7% in M.

**Conclusion:** Mexicans and Asians have significantly lower rates of adverse birth outcomes than other race/ethnic groups in similar high-risk socio-economic circumstances. Data show nonUS status associated with reduced risk of adverse twin birth outcomes.

## 016

## MAXIMUM-LIKELIHOOD METHODS OF ASSOCIATION AND LINKAGE

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Powerful methods currently exist for detecting association in samples of individuals when parental genotypic data are available, allowing simultaneous control for such things as admixture and population stratification, which could otherwise yield false-positive results. However, there are no available methods for detecting allelic associations in unselected, population-based samples of sibships which allow for such statistical control. It is now widely accepted that variance components methods for mapping QTLs using sibships are optimally powerful. We propose an extension of the maximum-likelihood variance-components method of detecting linkage in siblings which incorporates a model on the phenotypic means in addition to the usual model of covariance structure conditional on allelic sharing. The method involves partitioning the mean effect of a locus into a between- and within-family component, thereby controlling for stratification and admixture, while simultaneously modelling linkage, resulting in a further increase in power in cases of weak association due to the trait locus not being in complete disequilibrium with the marker locus. Power is explored for the method under various conditions and the method is compared with a simple analysis-of-variance approach to association data. Support:NIDA Center Grant from NIH and a Programme Project grant from the Medical Research Council of Great Britain



## 017

ALCOHOL AND SMOKING EXPERIENCES OF THE UNITED STATES NATIONAL ACADEMY OF SCIENCES-NATIONAL RESEARCH COUNCIL (NAS-NRC) TWIN PANEL OF WORLD WAR II VETERAN TWINS Christian, J.C., & Reed, T. Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN 46202-5121 Fax: (317) 274-2387

In 1955, the NAS-NRC ascertained a panel of 15,924 white-male, veteran twin pairs born between 1917 and 1927. Currently, there are 10,000 surviving members of this panel, with about 4,500 complete pairs, at an average age of 76. Measures of smoking and drinking were obtained on participant twins on three occasions over 30 years time. Ongoing studies are documenting the effects of smoking and alcohol intake on aging and their interactions with the genetics of aging. Smoking frequency fell from a high of 80% to 52% in the 1960's and has drastically declined over the last decade. Smoking was found to be 60% heritable and a risk factor for general mortality, cancer, lung disease, heart disease and loss of bone mass. Drinking behavior was found to be stable over time, especially in non-smokers, and 50% familial. Medical records document a 3.9% frequency of alcoholism. In contrast to smoking, moderate alcohol intake was associated with lower mortality, but only in non-smokers. There are indications that smoking and alcohol consumption share genetic covariation.

## 019

RECURRENCE RISK ESTIMATION USING POPULATION REGISTRY DATA: PROSTATE CANCER AMONG SWEDISH AND FINNISH TWINS.

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Recurrence risk 'p' indicates the fraction of relatives of an index case who are susceptible for disease. Risch (Biometrics 1983) presented a likelihood-based method to estimate 'p' including information on the age distribution of onset. This approach cannot easily be applied to population registry data found in the Nordic countries: Using registry information it is ambiguous as to which relative is the proband in multiplex kindreds. Information is available from a certain date, not from birth, possibly leading to ascertainment biases related to selective survival.

Prostate cancer (PCA) recurrence risks were estimated for MZ and DZ twins in Finland and Sweden to exemplify modifications to Risch (1983) for population registry data, i.e.  $p_{MZ}$  and  $p_{DZ}$ . Twin and cancer registers had been linked to identify pairs with occurrences. The first-affected twin in each pair was considered the index case. The fraction of lifetime risk from diagnosis for the index case to diagnosis/end of follow up for the twin was used to estimate 'p', conditioned on surviving unaffected to the index age and using person-years of risk in the age interval to adjust for high risk and low survival at advanced ages. For each country about one-third of twins were susceptible for MZ pairs, less than half for DZ pairs. About 3% lifetime risk is found for men in these countries.

Country	Period	Pairs	$p_{MZ}$ (95% CI)	$p_{DZ}$ (95% CI)
Sweden	1976-95	356	0.39 (0.27-0.54)	0.14 (0.07-0.23)
Finland	1976-95	62	0.42 (0.12-0.84)	0.15 (0.03-0.42)

These preliminary estimates indicate substantial inherited susceptibility for PCA, higher than the several percent found using segregation analyses, and the potential value of the analytic approach.

## 018

BLOOD PRESSURE IN BIRTH WEIGHT DISCORDANT TWINS

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**Background:** A negative association between birth weight and later life blood pressure has been observed and interpreted as causal (the fetal-origin hypothesis). The association could, however, also be due to genetic or time-stable social factors affecting both birth weight and later life blood pressure. These confounders can to some extent be controlled for through studies of twins discordant for birth weight.

**Material:** By using automatic blood pressure meters, systolic blood pressure was measured three times on 311 MZ and 150 DZ twin pairs aged 11 and 318 MZ and 166 DZ twin pairs aged 17, who took part in The Minnesota Twin Family Study. Birth weights were obtained from birth records in nearly all cases.

**Results:** In accordance with previous reports we observed in this population a small but statistically significant negative correlation between birth weight and systolic blood pressure, when current weight was controlled for (partial  $r = -0.08$ ,  $p < 0.001$ ). However, no negative correlation was found between intrapair difference in birth weight and intrapair difference in systolic blood pressure, when difference in current weight was controlled for (partial  $r = 0.02$ ,  $p = 0.46$ ).

**Conclusion:** In this study the observed negative correlation between birth weight and systolic blood pressure disappeared when control for genetic and social factors was included.

## 020

GRADE-OF-MEMBERSHIP ANALYSIS OF COGNITIVE AND FUNCTIONAL STATUS IN DANISH TWINS AGED 75-79:

WHICH ASPECTS ARE INHERITED? Larry S. Corder, Marvin A. Mulder, Kaare Christensen, Elizabeth H Corder. Demographic Studies, Duke University. FAX: 919 684-3861 E-Mail: larry@eds.duke.edu

Grade of membership (GoM) analysis was used to construct phenotypes from cognitive/functional status information obtained from Danish twins aged 75 to 79 ( $n=418$  in intact pairs, 68% female). The data optimally defined seven pure types using Akaike's information criterion. Zygosity made only a minor contribution to forming the pure types. Activities of daily living (ADL) score, the need for a proxy informant (i.e. often found for demented subjects), and gender-specific information contributed strongly to forming the pure types. For example, pure type I was characterized by poor functional and cognitive status and by a history of stroke. Pure type VII was characterized by men with good function and poor cognition without a history of stroke. The GoM scores for each individual (i.e. the degree of relatedness of the person to each typology) were considered to be phenotypes. Heritability for each phenotype was investigated using an established approach for twins, namely Mx models. Results may better define which aspects of cognitive/functional status in late age are inherited.

021

FEBRILE SEIZURE AND EPILEPSY IN VIRGINIA-BORN TWINS

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Recent advances in the neurosciences, in seizure classification procedures and in genetic methodologies have provided important new tools for elucidating the factors important in determining risk for seizures. Twin studies provide an efficient means for assessing the relative importance of the contributions of genotype and environment to this risk.

Members of the Virginia Twin Registry were surveyed to identify those positive for a history of seizures of some type. Among 9,782 pairs where medical history information was available, a history of seizures was reported in one or both members of 709 twin pairs.

Using data based upon self or parental reports of seizure, probandwise concordance rates were 0.32 (MZ) and 0.05 (DZ) for epilepsy and 0.37 (MZ) and 0.08 (DZ) for febrile seizure. Using medical record and/or detailed family interview information, a history of epilepsy and/or febrile seizure could be validated in 221 individuals included in 195 twin pairs thus far. Probandwise concordance rates in the validated sample were 0.37 (MZ) and 0.06 (DZ) for epilepsy and 0.60 (MZ) and 0.15 (DZ) for febrile seizure.

The rates observed in both the self-reported and validated samples are consistent with the existence of a significant genetic contribution to risk for seizures. However, rates based upon self-reported information appear to more greatly under-estimate those observed for febrile seizure in validated pairs than those observed for epilepsy.

023

THE INFLUENCE OF GENES AND URBAN/RURAL ENVIRONMENT ON AGE AT MENARCHE IN FINNISH TWINS

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We report data on age at menarche (AAM) from FinnTwin16, a longitudinal population study of five consecutive birth cohorts of Finnish twins. The sample includes 1,902 sisters from same-sex female twin pairs; data on AAM was self-reported at age 16. Mean age at menarche was 13.28 years. The correlation for AAM for the full sample was 0.77 for the 509 pairs of MZs and 0.36 for the 437 pairs of DZs. To estimate genetic and environmental components of variance for AAM, Mx modeling was used. The best-fitting model was the AE model, with 78% of the variance in age at menarche attributed to genetic factors and 22% attributed to unique environment. The influence on AAM of urban/rural environment, dichotomously indexed from government statistics, was also assessed. Although the mean age at menarche did not differ among girls from urban and rural environments, results suggest the possibility of a gene by environment interaction. The intrapair difference for DZs was significantly greater for twin pairs living in an urban environment than pairs living in a rural environment ( $p = 0.024$ ). Accordingly, the intrapair correlation for AAM among DZs in urban settings ( $r = 0.31$ ) was smaller than that of DZs from rural environments ( $r = 0.44$ ). No significant differences were found among MZ twin pairs, for whom correlations were 0.76 in urban environments and 0.80 in rural settings. FinnTwin16 is supported by AA 08315.

022

THREE CASES OF MAJOR ANOMALIES ASSOCIATED WITH ICSI (INTRACYTOPLASMIC SPERM INJECTION). PRELIMINARY REPORT

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At the Infertility Centre of the University of Gent, multiple pregnancy occurred in 100 patients treated with ICSI. Fifty of these delivered in East-Flanders and are analysed in this presentation. The other 50 cases will be investigated in a second stage. As in other multiple births registered in the East Flanders Prospective Twin Survey (EFPTS), steps are taken to collect basic perinatal data, to analyse placental structure and to determine zygosity with as much accuracy as possible. The 3 cases with major anomalies are summarised in the Table.

Register N°	M o t h e r	Placenta	T W I N I	T W I N II
4696	Age 29 - gravida I, para I	di-chorial	Female - birthweight 645 g - mors in utero at 26 weeks - hydrops foetalis, supraventricular tachycardia	Female - birthweight 1870 g - live birth - no anomalies
4737	Age 28 - gravida I, para I	di-chorial	Male - birthweight 2990 g - live birth - no anomalies	Female - birthweight 1700 g - mors in utero at 34 weeks - agenesis of left kidney, anus imperforatus
4893	Age 27 - gravida I, para I	di-chorial	Female - birthweight 2700 g - live birth - agenesis of right kidney, malrotation of gastro-intestinal tract, anus imperforatus, hydronephrosis and hydrocolpos	Female - birthweight 2300 g - live birth

This report awaits the collection of additional data to allow for conclusions regarding a possible association between ICSI and major anomalies. As others, we think that one has to maintain surveillance on the short- and long-term consequences of artificial reproduction technologies and that anomalies in ART children should be rapidly reported.

024

GENETIC COVARIANCE STRUCTURE MODELING OF SIB-PAIR DATA: A SIMULATION STUDY OF THE PI-HAT AND IBD MIXTURE APPROACH TO MODELING A QUANTITATIVE TRAIT LOCUS FOLLOWING SELECTION

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Genetic covariance structure modeling of a quantitative trait locus (QTL) in sib-pair data requires both phenotypic data and DNA marker data of the sibs. The use of selective sampling procedures designed to identify the genetically most informative sibpairs will mean that in practice marker data will be available for only a small portion of the sibpairs. One way to analyze such incomplete data with Identity-by-descent (IBD) mapping is to use the population expectations for the IBD distribution of the markers and for pi-hat ( $\pi = IBD/2$ ) and to proceed with the analysis as if marker data were available for the entire sample. The aim of the present study is to investigate through simulation the effects of this procedure on chi-squared tests and parameter estimates. We investigate the effect on the power to detect a QTL of several selection strategies and the effects, if any, of selection on the accuracy of the parameter estimates. The latter concerns both the parameters' standard errors and the bias in estimates.

## 025

## FREQUENCIES OF ABO AND Rh ALLELOGENES AMONG TWINS IN BELGRADE SCHOOLS

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In a sample of 720 twins from Belgrade schools, significant differences between MZ and DZ pairs have been observed in ABO and Rh blood group occurrences. A and O blood groups are almost equally frequent in MZ and DZ male twins (about 40%) whereas in DZ females and female/male twins A group is twice as frequent (52:25%). AB genotype is even 3.5 times less present in MZ boys than in DZ girls as a consequence of significantly different frequencies of A, B and O alleles in these two samples ( $p < 0.001$ ). Rh<sup>-</sup> blood group is also more common in MZ girls (18%) as compared to MZ boys (12%). However, the total sample of 720 twin individuals did not show a significant difference in the frequency of the blood groups studied in respect to the control sample being about 170,000 of blood donors from Belgrade whereby the calculated alleles frequencies amounted to:  $pA=0.32$ ;  $qB=0.12$ ;  $rO=0.56$ ;  $pRh^+ = 0.63$ ;  $qRh^- = 0.37$ . In addition, 10 triplets and one quadruplet were analysed for ABO, Rh, Mn, Kell-Cellano, Duffy and Kidd system. The prevalence of O blood group was evident.

## 027

## TAMBA ADVOCATES

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In 1996 a grant was received from the UK Department of Health for the telephone helpline - TAMBA Twinline - for publicity and awareness raising. This was entitled "Spreading the Word" A number of regular mass mailings to TAMBA members, other similar child/parent related organisations, Social Services, Citizens Advice Bureaux, Health Clinics, GPs, and Maternity Hospitals resulted. Representatives attended conferences and seminars, and included promotional material into delegates packs.

A database was set up to maintain records and review publicity and public relations initiatives and their effectiveness. A major initiative was the setting up of a new pilot project - TAMBA Advocates - aimed at raising awareness amongst members and the public to the services of TAMBA and Twinline. This increased awareness, undertaken by trained parents advocates for other parents and families with twins, triplets and more.

Over the past 18 months five training days have been held across England giving over 70 parents of multiples an opportunity to learn more about TAMBA, and other related services. It included the needs of multiple births families in the early days, through to just after birth. Additional knowledge and skills can be provided at follow up training days

TAMBA advocates will be independent of TAMBA but aware of its specialist services and are able to provide independent support. They can help families who find it difficult to access information, support or advice on their special situation.

## 026

## INTRAPAIR TWINS' RELATIONS AS A FACTOR OF PSYCHOLOGICAL DEVELOPMENT

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The aim of the study, was to explore environmental variables (intra-pair relations), that may affect the development of children, and to assess, how they tell on differences and similarity of MZ and DZ twins. In Moscow longitudinal twin study age differences as well as changes in heritabilities are traced through 4 ages: 6 years (the last pre-school year), 7 years (the beginning of school education), 10 years (transition to middle school) and 13-14 years (the age of changes in heritabilities, that can be related to maturation rate). Experimental tasks refer to 4 psychological areas: temperament (questionnaires and interviews with teachers and parents), IQ (WISC), cognitive styles (EFT, MFFT) and creativity (TTCT). Environmental measures discussed here include intrapair twins' relations.

The results reveal, that intrapair relations affect: 1) the level of development (e.g. twins with apparent intrapair role distributions have higher level of intelligence and creativity), 2) the variation in measures of temperament, intelligence, and creativity, 3) the structures of the correlations, which differ in the groups of leaders and non-leaders like in the groups with different chronological ages, 4) intrapair similarity of MZ and DZ twins (the effect of intrapair relations is quite different in the pairs of MZ and DZ twins and changes with age; delayed effects of intrapair relations is more apparent in the pairs of DZ twins). The estimates of heritabilities vary in the groups with different intrapair relations (e.g. in 4 ages estimates of heritabilities of PIQ are 0,0, 0,43, 0,46 + 0,36 - in the groups with role distribution and 0,54, 0,45, 0,70, 0,48 - in the groups without role distribution).

## 028

## TAMBA TODAY - 21 YEARS: AN UPDATE

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A poster display to show areas where TAMBA is developing in its attempts to modernise its infrastructure through a new management structure, revised Vision and Values and image. The efforts in moving towards this new status, involve the appointment of its first paid part time Director and the first "suite" of two offices away from the dining room of the TAMBA Administrator. Hand in hand with this goes the ever increasing need to maintain and consolidate the funding base of an organisation like TAMBA. Externally, the work of the Health and Education group has increased. A new parent Survey to match experiences of multiple birth families against the national Audit Commission survey into maternity services by users, Parentcraft classes for multiple birth families are increasing, and the development of the Honorary Consultant service - relatively unique in the UK to TAMBA, have brought a positive benefit to our members. We plan to revise and update our image, especially through the leaflets and booklets we offer to all interested in multiple births. The launch of the Antenatal membership to cover a need that has grown as parents need for information early in pregnancy increases. The development of specialist support groups to cater for areas of unique need. 1999 will be TAMBA's 21st Birthday and we intend to raise our awareness through events and activities to involve our families, professionals and the public at large, with a side by side campaign to increase our membership to help us take our work forward. The proposed changes to our communications within and outside TAMBA and how we relate to our members, professionals and the Public will be the focus of our presentation. All this activity will be placed within the context of the needs of the multiple births family, how they have increased with the changes in medical and social attitudes and activity in the 1990s and the changing millennium.



## 029

REGIONAL AND TEMPORAL DIFFERENCES IN TWINNING RATES IN THE BALTIC SEA AREA. Aldur W. Eriksson, Kari Degerstedt and Johan Fellman. Folkhälsan Institute of Genetics, Population Genetics Unit, Helsinki, Finland. (E-mail: aldur.eriksson@folkhalsan.fi)

Populations in and around the Baltic Sea basin have among the highest reported twinning rates among Whites, e.g. in Sweden above 17/1000 at the end of the 18<sup>th</sup> century. In some insular isolates (Åland, Gotland) twinning rates between 20-25/1000 have been noted. Up to the 20<sup>th</sup> century the eastern parts of central Sweden, including Gotland, had considerable higher twinning rate than than the south-western regions of Sweden.

Not only Scandinavians (Danes, Swedes and Norwegians) but also Finns, Estonians and Latvians have relatively high twinning rates. During 1945-59 the twinning rate was particularly high in Finland, mainly caused by high rates in rural areas, particularly in the relatively isolated core area of the East-Finns, where the twinning rate in 1930-59 was extremely high, actually among the highest reported among Whites in the 20<sup>th</sup> century.

During the 20<sup>th</sup> century the rates of multiple maternities and particularly the dizygotic twinning rates have decreased astonishingly, particularly in Sweden where the twinning rate during the last part of the 18<sup>th</sup> century was almost twice as high as it was in the 1960's. The triplet and quadruplet rates were about 3 to 4 times as high. The regional and temporal variations in twinning rates seem to be only partly explained by changes in the maternal age and parity.

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## 031

DELAYED INTERVAL DELIVERY IN MULTIPLE PREGNANCY AFTER IMMATURE BIRTH OF THE FIRST MULTIPLET

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**OBJECTIVE:** To analyze multiple pregnancies after immature/premature delivery of the first multiplet when delayed interval delivery was attempted and to avoid selection biases of selected case reports by a series of 21 cases from one center.

**METHODS:** Within a period of 6 years delayed interval delivery was attempted in 16 twin and 5 triplet pregnancies after delivery of the first multiplet following a strict protocol of intake criteria and specific measures such as cord ligation, disinfection, antibiotic and tocolytic treatment, corticosteroids for lung maturity and surveillance of the ongoing pregnancy.

**RESULTS:** The mean gestational age at delivery of the first child was 24+4 (16-30) weeks, 6 of those 21 first multiplets survived. The mean interval between the delivery of the first and following multiplet was 19 (2-73) days. 13 of the 26 second respectively third multiplets survived. Ten of the 13 survivors developed without complications, in 3/13 there were sequelae of prematurity such as cerebral palsy, retinopathy and bronchopulmonary dysplasia. No maternal complications were observed.

**CONCLUSIONS:** Though the optimistic results from a selection of single case reports cannot be confirmed in this at present largest series, delayed interval delivery offers an alternative for the remaining multiplets after immature/early premature delivery of a first multiplet. Larger multicenter trials following strict intake criteria and protocols are demanded for an overall analysis of success rate and the long-term outcome of those high risk-multiplets.

## 030

RECURRENT TWINNING IN FAMILIES WITH HIGHER MULTIPLE BIRTHS. Aldur W. Eriksson<sup>1</sup>, D. Joop Kuik<sup>2</sup> and Johan Fellman<sup>1</sup>. <sup>1</sup>Folkhälsan Institute of Genetics, Population Genetics Unit, Helsinki, Finland; <sup>2</sup>Free University of Amsterdam, The Netherlands. (E-mail: aldur.eriksson@folkhalsan.fi)

Studies on twinning in families of higher multiple maternities are few and the results are controversial. In a pilot study on consecutive triplet sets on the Åland Islands (1740-1939) we noted a very high twinning rate (80 per 1000) in sibships of triplets, i.e. a good four times higher than in the general population. We have studied the incidence of repeated multiple maternities in a good 10,000 offspring of close relatives of 637 triplet sets born in Finland between 1905-59 according to the information we have got from the parish archives. Also stillborn and extramarital children have been included. So far also 44 families of quadruplets born 1760-1959 in Sweden and Finland have been studied. Among mothers of triplets the rate of recurrent multiple maternities was 41/1000. In the sibships of mothers of triplets the twinning rate was 25/1000 but in the sibships of fathers of triplets only 13/1000, i.e. even lower than in general population (14.7/1000). In the sibships of opposite-sexed triplets the twinning rate (50/1000) was considerable higher than in the sibships of same-sexed triplets (32/1000). In sibships of triplets, not only the dizygotic but also the monozygotic twinning rate (according to the Weinberg law) was more than twice as high as in general population. In sibships of the quadruplets the rate of twinning seems not to be as extremely high (83/1000) as was reported by Weinberg, 1909. The same seems to be the case in sibships of parents of quadruplets

Supported by grants from the foundations of Liv and Hälsa, Helsingfors, and the Signe and Ane Gyllenbergs Stiftelse, Helsingfors.

## 032

STATISTICAL ANALYSIS OF THE SEASONAL VARIATION OF TWINNING. Johan Fellman & Aldur W. Eriksson Folkhälsan Institute of Genetics, Population Genetics Unit, POB 211, FIN-00251 Helsinki, Finland. (E-mail fellman@shh.fi)

There have been few secular analyses of the seasonal variation of human twinning and the results are conflicting. One reason is that the seasonal pattern of twinning varies in different population and during different times. Another reason is the use of different statistical methods. The methods are applied on twinning data from different populations and for different periods.

The changing pattern of seasonal variation in twinning rates and total maternities in Denmark was traced for three periods (1855-69, 1870-94 and 1937-84). By the method of Walter and Elwood (1975) the seasonal distribution of twin maternities showed for the periods in the 19<sup>th</sup> century highly significant sinusoidal departures. Main peaks of both twin and general maternities can be seen in March to June and local peaks in September. During the spring-summer season the twinning rates were higher than the average indicating stronger seasonal variation for the twin maternities than for the general maternities. For 1937-84 there was a similar but less accentuated pattern. Studies of other populations are performed and compared with the Danish results.

The more accentuated seasonal variations of twinning in the past indicate that some factors in the past affected females during the summer-autumn and around the Christmas to be more fecund and particularly to be more polyovulation prone and/or be more able to complete a gestation with multiple embryos.

Supported by grant from the foundation of Liv and Hälsa, Helsingfors.

## 033

DEVELOPMENTAL VARIATION IN RELATION TO ENVIRONMENTAL STRUCTURE AND STIMULATION  
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In a previous longitudinal Swedish twin study we followed more than 300 twin and control pairs through the Swedish compulsory school. A difference between twin girls and their controls was found but not for the twin boys. Twin girls were physically smaller and had lower average results on both ability and achievement tests. One explanation for this could be a positive selection of the male sample.

In addition to a comparison of twins and controls we used the twin sample to investigate hereditary and environmental influences on physical and mental development during adolescence. For many variables environmental structure and stimulation was related to genetic variation so that a more restricted environment decreased genetic variation. These findings resulted in the development of an educational model that has been used in research in many different fields, such as cross-cultural studies, health care, special education, sports training etc.

The application of this model has resulted in a more elaborated understanding of structure and stimulation in educational settings. Some examples of this will be given.

## 035

TWIN NON-STRESS TESTING: A STUDY OF INTERTWIN PHYSIOLOGIC BEHAVIOR PATTERN  
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**OBJECTIVE:** To assess normal intertwin behavior pattern by acceleration of heart rate in response to movement by Nonstress Testing (NST). **STUDY DESIGN:** A longitudinal behavior study of 42 twin pairs included analysis of 506 tracings from 253 NSTs serially performed at in third trimester. Each twin was identified at each visit by its location established at initial and serial sonography. Number of accelerations/20mins, maximum magnitude and duration of accelerations for each twin were analysed. Synchronicity of acceleration was expressed as a percentage of greater number of accelerations in the more active twin. These characteristics were noted at <31, 32-34, 35-37, >37 gestational weeks (A, B, C, D). **RESULTS:** Average accelerations/ 20mins, maximum magnitude and duration of accelerations were, 6.02/20mins, 16.5 bpm, and 29.4 mins respectively. Synchronous accelerations occurred 56% of the time overall. As pregnancy progressed, one or the other twin was found to be more active than the other after 32 weeks. Mean number of concordant accelerations decreased as pregnancy advanced beyond 32 weeks. Incidences of concordant accelerations in groups A, B, C and D were 70%, 58%, 56%, and 46%. Concordant or discordant behavior was not related to concordant or discordant fetal growth. **CONCLUSION:** A large series of longitudinally observed NST tracings revealed a high degree of fetal activity concordance, being highest prior to 32 weeks. Thereafter, one or the other twin is more active through pregnancy. Concordancy was not related to fetal growth.

## 034

AGE AT MENARCHE IN 3,521 DANISH TWIN PAIRS AGED 18-41 YEARS

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An Australian twin study (Treolar & Martin, *Am J Hum Genet* 1990; 47: 137-48) found that total genotypic variance for age at menarche was approximately 65%. The greater part of the genetic variance was found to be non-additive, but with non-additivity decreasing for the later birth cohort in the study (1951-64). We studied 3521 Danish twin pairs born 1953-76 who in a questionnaire in 1994 reported age at menarche. The correlation for onset of menarche was 0.70 (SE: 0.01) for MZ and 0.34 (SE: 0.02) for DZ twins. Biometrical models revealed that for the overall sample an AE model provided the best fit with an estimated  $a^2=0.71$ . We divided the sample in four age groups of six birth cohorts. Biometrical analyses allowing for parameters to vary over the four age groups showed - in accordance with the Australian study - evidence of non-additivity in the oldest group. However, for the Danish twins born after 1958 (82% of the sample) we found no evidence of genetic non-additivity.

## 036

POLYHYDRAMNIOS CAN BENEFICIALLY AFFECT TWIN-TWIN TRANSFUSION SYNDROME PREGNANCIES  
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Increased amniotic pressure (polyhydramnios) is frequently associated with unexplained stillbirths. Most likely, the placenta is compressed reducing the intervillous space. By analogy with the heart's coronary circulation during the cardiac contraction phase we hypothesized that polyhydramnios affects the placental parenchymal microcirculation but not the large chorionic vessels.

We measured placental perfusion pressure-flow curves in three fresh healthy term singleton placentas, placed in a closed perfusion cabinet and submerged in perfusion liquid under standard physiologic conditions. Weights placed on the sliding piston lid of the cabinet raised the cabinet's inside pressure, mimicking ~25 mmHg polyhydramnios.

The results showed that polyhydramnios increases the parenchymal resistance, except at high perfusion flows. Consequently, compressed placentas could influence twin-twin transfusion syndrome (TTTS) pregnancies that include arteriovenous (AV) plus arterioarterial (AA) anastomoses. Without polyhydramnios, the two oppositely directed anastomotic blood flows (AV, AA) can be large but continuously strive toward minimal net fetofetal transfusion. Polyhydramnios, however, may strongly reduce AV but not AA transfusion, resulting in a net AA transfusion developing from recipient to donor twin.

Surprisingly, polyhydramnios may benefit ~50% of all TTTS pregnancies, namely those caused by AV and AA, because the AV component of fetofetal transfusion is selectively suppressed.

## 037

## IS THERE A RATIONALE FOR LASER OR AMNIOCENTESIS IN TWIN-TWIN TRANSFUSION SYNDROME PREGNANCIES?

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Therapy of twin-twin transfusion syndrome (TTTS) is surrounded by controversy. We propose a rationale for either laser or amniocentesis based on the underlying placental anastomotic pattern.

Assumptions: TTTS results with equal probability from five typical placental anastomotic patterns. Fetoscopy causes a 15% premature rupture of membranes (PROM), versus 1.5% for amniocentesis.

Laser coagulation of all chorionic vessels which cross the intertwin septum causes fetal death if the vascular equator is close to one of the cord insertions. Predicted and clinical [1] survival: 55%. Laser coagulation of all communications crossing the vascular equator causes fetal death if the placenta is unequally shared. Predicted and clinical [2] survival: 65%. Selective laser coagulation of AV anastomoses causes fetal death by PROM only. Predicted survival: 85% (no clinical data available). Assuming that amniocentesis mainly prevents PROM, so mild TTTS cases survive (no single AV's)[3], predicted survival is 60%, clinical survival is 60±22% (203/336 in 12 publications 3). Laser has significantly lower reported morbidity than amniocentesis (5% versus 19±5% 3).

We propose that amniocentesis or laser can be selected for TTTS therapy if the placental anastomoses are better known.

[1] Y Ville, J Hyett, K Hecher, K Nicolaidis. *N Engl J Med* 332:224-7, 1995. [2] JE De Lia (personal communication 1998). [3] MJC van Gemert, AL Major, SA Scherjon. *Eur J Obstet Gynaecol Repr Biol* 78(1),1998.

## 039

## PATERNAL GAMETIC GENES AND INFERTILITY-TWINNING PATERNALLY DEPENDENT FAMILIAL SYNDROME

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Many aspects of human reproduction biology are unclear. In the last 20 years a series of an important cytogenetic discoveries were made: finding that in triploids an additional genome in 75% cases has paternal origin due to dispermy; discovery of regular natural triploid and diploid androgeny resulting in hydatidiform moles; high primary frequency of twin conceptions on the level of 5-10%; postmeiotic gametic gene activation and genomic imprinting.

This background gives us possibility to explain some long known puzzling familial case of direct paternal influence on twinning (both in human and animals). I suggested the existence of definite paternal genes which being activated in male gametes in the process of fertilization may lead to dispermy, diplospermy (meiotic mutation) or heterochrony in male pronuclei mitotic division. This result in triploidy, androgenic moles and double fertilization of two meiotic products of oogenesis with possible appearance of twins. These twins will be exceptional: non mono-or dizygotic but intermediate ones, so called sesquizygotic. The primary chimeras among siblings of twins are also possible in such pedigrees. An exceptional twins (1-3%) were regularly described in the process of mass twin screenings. On the level of reproduction pattern the familial cases are expected which combine hereditary (recurrent) infertility (triploidy, moles, chimeras) and twinning tendency. The examples of such pedigrees are found. I suggest to title this phenomenon as an Infertility-Twinning Paternally Dependent familial syndrome (ITPD). The most ancient example of such ITPD syndrome is described in the Bible, in the Abraham pedigree.

## 038

GENDER DIFFERENCES IN COGNITIVE ABILITIES: A STUDY OF OLDER UNLIKE-SEX TWINS LIVING IN SWEDEN  
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Previous research has found that women, on average, perform better than men on reasoning and verbal cognitive tasks, and that men, on average, perform better than women on spatial cognitive tasks. Men have been found to do better on Block Design tests, and women excel on Digit Symbol tests. A population-based sample of unlike-sex twins aged 70-80 (N=249 pairs) in Sweden were assessed in their homes by registered nurses. This sample provides a unique opportunity to examine gender differences in an ideally matched group of males and females. Among the health-related variables assessed were tests of cognitive skills. Paired sample analyses were performed on seven of these tests. Results confirmed that brothers had significantly higher scores than their twin sisters on the figure rotation exercise ( $p < .001$ ); the brother-sister correlation  $r = .067$ . Sisters had significantly higher scores than their twin brothers on two memory tests: Thurstone picture test ( $p < .01$ ;  $r = .230$ ) and a Word Recall test ( $p < .001$ ;  $r = .226$ ). Sisters also out-performed their brothers in a test of perceptual speed ( $p < .01$ ;  $r = .096$ ) and a test of reasoning skills, a Number-Symbol test ( $p < .01$ ;  $r = .366$ ). Contrary to our expectations from the literature, there were no significant gender differences in the Synonyms test ( $r = .406$ ) or the Block Design test ( $r = .283$ ). Otherwise our findings support previous research indicating, on average, better spatial cognitive skills for men, and better reasoning skills for women. The sisters also excelled in memory and perceptual speed. Further work includes linkage of the cognitive data with health data, including such measures as blood pressure, respiratory volume, pulse rate, medication usage, and medical conditions.

## 040

## HOW DO GENETIC INFLUENCES CONTRIBUTE TO DIFFERENCES ALCOHOLISM RISK IN EUROPEANS?

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Although research has indicated that alcohol dependence is genetically influenced, less work has examined how genetic factors operate on dependence. One way in which genetic factors might influence dependence is through alcohol metabolism. The Australian alcohol challenge study provides an opportunity to examine this possibility. The present analyses were conducted on 159 pairs of twins (MZP=36, MZM=33, DZF=35, DZM=25, DZO=30; mean age = 23.1 years in 1979) who completed both the alcohol challenge protocol (obtained between 1979 and 1981) and a telephone interview survey (conducted in 1992-1993). In the alcohol challenge protocol, subjects' blood alcohol concentration levels were measured on six occasions (over a three hour period) following the administration of a standard weight-adjusted dose of alcohol. The telephone interview, adapted from the SSAGA [Bucholz, KK, Cadoret, R, Cloninger, CR, et al. A new, semi-structured psychiatric interview for use in genetic linkage studies: A report on the reliability of the SSAGA, *J Stud Alcohol* 1994; 55: 149-158], included assessments of parental and respondent alcohol dependence (DSM-IIIr criteria). Although both blood alcohol concentration levels and peak blood alcohol concentration showed genetic influence (assessed through quantitative genetic modeling), neither measure appeared to be related to either respondent or parental alcohol dependence. Supported by NIH Grants AA07535 and AA07728

## 041

## MULTIPLE BIRTH DATA BASE

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The National Organization of Mothers of Twins Clubs, Inc. (NOMOTC) has one of the largest data bases of multiples and their children in the United States and possibly the world. NOMOTC, founded in 1960, began this "Multiple Birth Data Base" over 10 years ago. Over 12,000 mothers of multiple birth children have completed a "Multiple Birth Data Form" (MBDF) to become part of this data base. This represents over 24,000 multiple birth children. The MBDF is a two-page questionnaire which asks questions about the parents, the multiple pregnancy and the multiples themselves. The data base is used by the Research Department of NOMOTC to find participants for professional research studies. It is also used to help casting agents find twins (usually identicals) for roles in movies or television shows. The first 1900 entries to this data base were studied recently and the results will be discussed.

## 043

## HOW SCHOOL CHILDREN PERCEIVE THEIR FAMILY ENVIRONMENT: COMPARING JERUSALEM WITH KIBBUTZ TWINS AND SINGLETONS

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The research reported here compares perceptions of their family environment by school age twins and singletons raised either in Jerusalem or in an Israeli kibbutz. It extends the traditional twin design, in which the resemblance of MZ twins is compared with that of DZ twins, by adding matched singleton pairs who have no biological relationship but share a major part of their environment.

The *Family Environment Scale (FES)*, was administered to 55 quartets of 3rd to 7th graders in Jerusalem and 60 quartets in 27 kibbutzim, each quartet consisting of a twin pair (MZ or DZ) and two matched singleton children in the same school class. The FES is a widely used self-report questionnaire that assesses various features of the family atmosphere. We selected 24 items from the original 90, based on a mapping sentence with three facets: A- the child's role in choosing, planning, doing, assessing; B- aspects of autonomy, order, organization; C- the family's aims, rules and duties. The true-false format of the FES items was altered to a six-point rating scale from 'completely true' to 'not at all true'.

A *Smallest Space Analysis (SSA)* gave identical intercorrelational structures for Jerusalem and kibbutz children, even though city and kibbutz pupils differed in their mean ratings of "Organization", "Rules", and "Aims". Intraclass correlations for MZ, DZ, and singleton pairs gave patterns indicating genetic influence for questions relating to "Aims", "Order", and "Organization", but not for "Autonomy" and "Rules".

## 042

## LONG TERM EFFECT OF PRENATAL HETEROGENEITY AMONG MZ TWINS: A FOLLOW-UP STUDY.

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Long term effects of differences in placentation in MZ twins are a controversial subject. An effect was clearly established for birth weight but data on psychological traits are inconclusive. We studied 20 pairs of monochorionic MZ (MC MZ) and 24 pairs of dichorionic MZ (DC MZ) twins (Spitz et al., *C P C*, 1996, 15, 283-308). A chorion effect was observed for the Block Design (WISC-R) confirming a previous report: MC MZ pairs were more similar than the DC MZ pairs. For anthropometrical measures an expected effect in the reverse direction was found. No chorion effect was significant for the other variables.

A follow up was undertaken 3 years later including cognitive, personality variables and national academic evaluations. The sample included 16 pairs of MC MZ and 22 pairs of DC MZ. A chorion effect was observed again on anthropometrical variables but the effect was not replicated for the Block Design. However the MC MZ were more similar than the DC MZ for two other cognitive variables: Perceptual organization in the WISC-R and global visualisation in a Belgian reasoning test. For personality variables very few effects were significant.

It is thus probable that, if chorion effects exist on psychological traits, it accounts for a small part of the phenotypic variance only.

## 044

## COGNITIVE ABILITIES ACROSS THE LIFE SPAN: RESULTS FROM A TWIN STUDY SPANNING 55 YEARS

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In the year 1937, 90 pairs of twins (49 MZ and 41 DZ pairs) at the age of around 11 were psychologically observed and tested during their stay at a six-week holiday camp. 30 years later in 1967, 28 EZ pairs, 16 DZ pairs, and 11 singletons whose partner had deceased could be tested again. Further 25 years later in 1992, 24 EZ pairs, 9 DZ pairs, and 22 surviving singletons were tested a third time. The subjects now were around 66 years old. This unique longitudinal design allowed for the study of developmental processes and of longitudinal changes of the genetic basis of personality.

In this paper, data on cognitive abilities are presented, particularly on the German WAIS which was used both in 1967 and 1992. Fluid and crystallized cognitive abilities show a very high stability over the adult age period. Persisting genetic factors form the basis for the stability of visual-fluid abilities whereas persisting factors of the shared environment stabilize the verbal-crystallized abilities. Differences between the families, in terms of varying educational levels of the twins' parents, can be identified as constituting the long-lasting influence on the twins' intelligence level.

Cognitive aging, that is the individual changes of the intelligence level from middle to late adulthood, is influenced by individual changes in cognitive speed. Since speed and fluid intelligence can be shown to have a common genetic basis, some conclusions about the genetic basis of cognitive aging can be drawn.



## 045

## THE HERITABILITY OF DEPRESSION - MULTIPLE INFORMANTS

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The aim of the present study was to estimate genetic and environmental influences on depression, and to evaluate effects of different informants on those estimates. In earlier studies, genetic influence has been estimated to account for 30 - 46%, and, in some studies, as much as 60 - 80% of the total variance. Past research has suggested that the source of informant may influence estimates of heritability, so we examine that issue here. This study is a part of an ongoing nation-wide twin-family study of behavioral development and health habits (Pulkkinen, Kaprio & Rose, 1998). Data were collected through the Multidimensional Peer Nomination Inventory (MPNI) and its parallel versions, Teacher and Parental Rating Forms. The twins (468 MZ and 487 DZ twin pairs) represented subsets of three 12-year-old twin birth cohorts (b. 1983 - 1985) in Finland. Heritability of depression was assessed by intraclass correlations and by model-fitting analyses, with Twinan90- and Mx-programs. DZ correlations were significant, but lower than MZ correlations, in patterns suggesting genetic influence. Model-fitting confirmed significant additive genetic influence for depression rated from all three sources. There was evidence of common environmental effects in all ratings, but these were significant only in the teacher rating data. Parameter estimates from teacher ratings and peer nominations were closer to each other than were either teacher ratings and parental ratings or peer nominations and parental ratings, suggesting that estimates of heritability and common environment vary with source of behavioral ratings.

## 047

## A FAMILY-FOCUSED APPROACH TO LANGUAGE INTERVENTION WITH MULTIPLES: WHO BENEFITS AND WHY?

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Early language delay is more common in twins than singletons and is associated with later reading and attentional problems. Yet there are few early intervention services specifically for multiples. The Ontario-based Hanen parent programme is attracting increasing attention as a cost-effective family-focused intervention that can be modified to suit the needs of specific groups. The WA Twin Child Health Study (WATCH) is monitoring language development at one and two years of age and here we describe our initial work in modifying the Hanen approach for multiples. Each Hanen programme takes up to 8 high-risk families and teaches them to interact positively with their children in ways that facilitate language development. Group sessions for parents are combined with home visits to customise the parent-administered intervention. The Hanen focus is on issues such as turn-taking and responsiveness, the variables often believed to be associated with twin language delays. Given the depression and isolation reported by many mothers of infant multiples, we predict the Hanen approach may benefit the mother as much as the children and thus gains may be more permanent than in predominantly child-centred approaches. Although each program involves 250 hours work by a trained speech pathologist, this represents a very economical approach to early language intervention with multiples. Funded by Healthway (WA)

## 046

## PREDICTORS OF CHANGE IN ADHD SYMPTOMATOLOGY IN TWINS AND THEIR SIBLINGS: PERSPECTIVES FROM THE AUSTRALIAN TWIN ADHD PROJECT

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Previously we have identified Attention Deficit Hyperactivity Disorder (ADHD) to be the one behavioural problem more common in twins than in their siblings and closely associated with speech and reading problems. Our ATAP study (the Australian Twin ADHD Project) has used our two waves of data four years apart on 1550 families to demonstrate that much of the consistency of the Inattentive and Hyperactive-Impulsive symptoms of ADHD during childhood and early adolescence is due to genetic influences. Growing-up together leads to twins becoming increasingly similar in the Hyperactive-Impulsive but not their Inattentive symptoms. Consistent with this difference between the two symptom groups, speech and reading problems were predictive of which twins did or did not improve in Inattention, while changes in Hyperactivity/Impulsivity were associated more with other behavioural problems such as Conduct Disorder and Oppositional defiant Disorder. Given the Inattentive subtype of ADHD is far the most common but is often overlooked, the possibility needs to be explored that speech problems may serve as an early marker for ADHD in twins and may even give a clue as to appropriate early intervention. Funded by NHMRC (Australia)

## 048

## IMPLICATIONS OF FINDINGS FROM TWIN STUDIES FOR PHARMACOGENETIC (INCLUDING GENE-MAPPING) STUDIES OF ALCOHOL AND NICOTINE DEPENDENCE AND OTHER SUBSTANCE USE DISORDERS.

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Twin and adoption studies provide strong evidence for an important genetic contribution to risk of alcohol dependence; and twin studies, at least, also suggest important genetic effects on smoking and illicit drug use, and nicotine and illicit drug dependence. Using data from telephone diagnostic interview surveys of the Australian 1981 cohort twin panel, we show that it is possible to distinguish between genetic effects on level of substance self-exposure, and genetic effects on dependence vulnerability (conditional upon level of exposure) - with the former more strongly associated with history of conduct problems or similar measures of behavioral undercontrol/impulsivity; and the latter with measures of negative affect/depression. Sampling designs for linkage studies that target heavily dependent individuals (e.g. affected sibships identified through treatment sources), though quite informative for mapping genes that affect exposure level, may be suboptimal for finding genes that lead to differences in vulnerability. Yet from such long-term perspectives as medications development, identifying 'vulnerability' genes may be much more informative than identifying 'exposure' genes. We discuss research strategies that may be more informative for finding genes that lead to differences in dependence vulnerability. (Support in part: NIH-AA07728, AA07535, AA10249, Aus.Nat.Health Med Res Cou)



## 049

CARDIOVASCULAR DEATHS IN DANISH TWINS 1943-1993.  
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Results from twin studies of diseases can only be meaningfully applied to the general population if twins and singletons have the same disease etiology. Barker has advanced the fetal origins hypothesis that retardation in intrauterine growth increases the risk for adult diseases such as cardiovascular diseases. Twins experience considerable retardation in intrauterine growth and MZ more than DZ twins. Phillips suggested that this hypothesis affects the validity of the classic twin method. All death certificates issued in Denmark since 1942 have been computerized including personal identification items and cause(s) of death according to international classification rules. All Danish like-sexed twins born 1870-1930 who were alive on January 1, 1943 (10,196 males and 11,457 females) have been linked to this nationwide register for the period 1943 through 1993. Comparison with the general population was made through the standardized mortality ratio. In all, cause of death were ascertained for 6,687 male twins and 6,631 female twins. Cardiovascular (CVD) disease was cause of death in 3,189 male twins (940 MZ, 1,882 DZ and 567 UZ) and 3,184 female twins (852 MZ, 1,546 DZ and 786 UZ) resulting in the following SMR's:

Males				Females			
MZ	DZ	UZ	All	MZ	DZ	UZ	All
0.87	0.91	1.08	0.93	0.90	0.94	1.23	0.98

Overall mortality SMRs are similar to these CVD SMRs. Therefore, we conclude that the intrauterine growth retardation in twins do not increase the risk of CVD mortality in either MZ or DZ twins and the classic twin method is still valid for these diseases.

## 051

SELF-REPORT OF INSUFFICIENT SLEEP IN ADULT TWINS  
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Sleeping less than desired (sleep deprivation) is an increasing problem. In 1990 a questionnaire yielded responses from 12,502 twin subjects (mean age 44, range 33-60 years, response rate 77%), including 1298 MZ and 2419 like-sexed DZ twin pairs. The respondents were asked to assess their usual need of nocturnal sleep to be fit next day, and how long usually sleep per 24 hours. A difference  $\geq 1$  hour was considered insufficient sleep (IS).

IS was less common in men (16.0%) than in women (23.6%). There was a significant age dependency. Among those <40 years 19.9% of men and 27.5% of women reported IS, and among those  $\geq 50$  years 12.9% and 19.2%, respectively. Reported sleep length, insomnia and daytime sleepiness significantly correlated with the frequency of IS. Among those sleeping <7 hours per night 31.6% of men and 48.4% of women had IS, whereas among those sleeping  $>8$  hours about 5% in both genders. 43.8% of men and 49.3% of women with insomnia  $\geq 3$  nights weekly had IS; the corresponding figures in those with insomnia less often than weekly were 12.9% and 20.2%. When daytime sleepiness occurred daily 37.5% of men and 43.9% of women had IS, but when it occurred less often than weekly IS was present in 9.7% of men and in 13.9% of women. IS also significantly increased in both genders with increasing levels of psychic stress and exhaustion.

IS is common in population, affecting about 1.5 times more often women than men. It is significantly associated to many sleep and health parameters. Pairwise analysis of the occurrence of IS and structural equation modelling to estimate genetic and environmental components of variance in the liability to IS will be computed.

## 050

ON WHY "COMMON ENVIRONMENTAL EFFECTS" ARE SO UNCOMMON IN THE LITERATURE

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In practice, standard application of the classic twin model, with its implicit assumption that the effect of environmental factors shared by twins are independent of zygosity, usually results in estimates of common environment effects that are not statistically significant. Consequently, the "parsimonious" model often attributes all within-pair aggregation in a trait to genetic factors, a state of affairs that seems incredulous to the non-genetic reader. The lack of evidence for common environmental effects often predicted by the textbook application of biometrical modelling may not be a proper interpretation of reality.

Some issues that need to be taken into consideration include; the implicit assumption above, lack of statistical power, the age group under consideration and the temporal nature of effects of cohabitation, the inbuilt bias in the currently popular biometric modelling approach which allows only a simplistic model for shared environmental effects, and the lack of suitable designs and data to critically address the confounding of shared genes and shared environments.

Several examples will be presented demonstrating plausible effects of shared environment on familial aggregation in bone mineral density, blood lead, disc degeneration, and risk factors for heart disease.

It is concluded that twin researchers should take a Popperian approach to modelling, seeking to falsify genetic hypotheses rather than trying to support them.

## 052

Trends of twinning and triplet rates in 17 countries during the period from 1972 to 1996

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Secular changes in twinning and triplet rates were analyzed using vital statistics in Austria, the Czech Republic, the Slovak Republic, England and Wales, Germany, the Netherlands, Switzerland, Denmark, Finland, Norway, Sweden, Canada, Australia, Hong Kong, Israel, Japan, and Singapore during the period from 1972 to 1996. Among 17 countries, these multiple birth rates in the Czech Republic and the Slovak Republic remained constant from 1972 to 1994, whereas twinning and triplet rates increased significantly year by year in the other 15 countries. During these periods, the twinning rate increased 2-fold in Denmark, 1.6-fold in Norway and Sweden, and 1.5-fold in Switzerland, Japan, Germany, and Hong Kong.

The triple rate increased 9-fold in Norway, 8-fold in Austria, and 7-fold in Switzerland and Germany. Among 17 countries, zygotic twinning rates were obtained in eight countries and zygotic triplet rates in six countries. The monozygotic twinning and triplet rates remained constant during the examined period in each country. On the other hand, the dizygotic twinning rate increased significantly year by year in six countries, the dizygotic and the trizygotic triplet rates increased significantly in England and Wales, Germany, Switzerland, Denmark, and Japan.

## 053

## REPLICATING BEHAVIORAL ASSOCIATIONS USING DISCORDANT TWIN PAIRS

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Previous studies of singletons have shown that certain personality traits, including sensation seeking, are associated with alcohol consumption. Such associations are usually interpreted as evidence that the personality traits are individual risk factors for alcohol consumption or abuse. But singleton studies cannot rule out the possibility that such associations are due to factors arising between families rather than functional relationships between personality and alcohol use. We investigated the relationship between sensation seeking scores and drinking behavior in a sample of 4,125 Finnish twins (FinnTwin16 study). The first analysis compared drinking-related behaviors of all twins as individuals. Individuals above the 70th percentile for sensation seeking scores reported drinking alcohol more frequently and becoming intoxicated more frequently than individuals in the lower 30th percentile of the distribution. Family analyses were then conducted to attempt to replicate this relationship within DZ twin pairs. DZ pairs in which one member of the twin pair was in the upper 70th percentile of sensation seeking scores and the co-twin was in the lower 30th percentile were compared on alcohol related measures. Within discordant DZ twin pairs ( $n=95$  pairs), the high sensation seeking twins reported more frequent alcohol consumption and intoxication than the co-twins with low sensation seeking scores. MZ co-twins discordant for sensation seeking scores ( $n=16$  pairs) did not differ on these alcohol-related measures. Illustrations of how these types of simple twin comparisons can be used to explain the results of complex genetic modeling will be discussed. Support: AA-08315, AA-007611.

## 055

## HOSPITAL CARE IN TWINS DISCORDANT FOR SEDENTARINESS

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Many studies suggest that sedentary people have higher morbidity than those at least moderately active, but genetic selection has been claimed as an explanation.

We identified from the Finnish Twin Cohort 710 same-sex healthy twin pairs discordant for leisure-time sedentary lifestyle and 151 pairs discordant for total sedentariness at baseline in 1975, and enumerated from the beginning of 1977 their hospitalizations from non-psychiatric causes to the end of 1986, hospitalizations for ischemic heart disease to the end of 1992, and all-cause mortality to the end of 1994.

According to pairwise analyses the members of the twin pairs non-sedentary at leisure-time had less all-cause hospital admissions ( $P = 0.005$ ) and spent on average 43 percent fewer days in hospital ( $P = 0.001$ ) than their sedentary cotwins. Among twin pairs discordant for total sedentariness the non-sedentary twin spent on average 55 percent fewer days in hospital due to all-causes compared to the sedentary cotwin ( $P < 0.001$ ). The difference in use of hospital care for ischemic heart disease was greater among monozygotic ( $P = 0.023$  for number of admissions) than dizygotic twin pairs discordant for leisure sedentariness, whereas the all-cause mortality difference by sedentariness tended to be higher in dizygotic than monozygotic twins.

After accounting for genetic predisposition, physically active lifestyles are associated with reduced need of hospital treatments.

## 054

## THE DEVELOPMENT OF FINNISH TWINS IN VIEW OF TWO BIRTH COHORTS

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Twin pregnancies and deliveries have long been recognized as risk situations, the main risk factors for the infants being intrauterine growth retardation and prematurity, often followed by asphyxia, hypoglycaemia and hyperbilirubinaemia. Birth cohorts offer a good opportunity to study these risks and their impact on development of twins.

In the one year birth cohort for 1966 from the two Northernmost provinces of Finland, Oulu and Lapland, single births numbered 11,905 and twin births 163, and the corresponding figures for the 1985/86 one year birth cohort were 9362 and 115. The follow-up is going on in both cohorts.

Perinatal mortality and morbidity were higher for twins than singletons. Twins show some developmental delays when compared with all singletons or control singletons, matched by maternal factors, but the difference often vanishes when the comparison is made between the twins and their controls also matched by perinatal morbidity.

## 056

## PERINATAL COMPLICATIONS AND SCHIZOPHRENIA IN TWINS

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An association between perinatal complications and schizophrenia has been established, but it is not known whether this association is causal. Also an increased rate of schizophrenia in twins compared to the general population has been demonstrated.

The aim of this study was to evaluate if the increased rate of schizophrenia in twins could be explained by the increased occurrence of perinatal complications.

In 45 twin pairs with schizophrenia or schizophrenia-related disorders and 82 control twin pairs information about complications in the perinatal period was obtained from midwife reports. The individual complications as well as a sum score for complications using the McNeil-Sjöström scale were analysed using conditional logistic regression.

No significant association between a sum score for perinatal complications and schizophrenia was present. Two individual complications, the birth weight difference and the time between the delivery of the two twins in a pair, were associated with an increased risk of schizophrenia; and one complication, administration of chloroform to the mother, was associated with a decreased risk of schizophrenia. However these individual associations may have been caused by multiple testing.

The study does not support a causal association between a sum score of perinatal complications and schizophrenia.

## 057

## DIETING AS A PREDICTOR FOR MAJOR WEIGHT GAIN

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We studied prospectively, how dieting relates to the future risk of major weight gain (> 10 kg), and whether familial factors affect this relationship. Analyses were based on 7729 individuals (3536 men and 4193 women aged 18-54 years in 1975) from the Finnish Twin Cohort over two follow-up periods (6 & 15 years). For the study of familial factors, altogether 1705 pairs discordant for dieting from the same cohort were studied. The data on body weight, dieting, and potential confounders (smoking, coffee & alcohol consumption, energy expenditure at work and in leisure, marital status, educational level, social class) was obtained by mailed questionnaire in 1975. The follow-up data was obtained by questionnaires in 1981 and 1990.

There was a consistent trend for increased risk for major weight gain in dieting subjects. This trend was significant among young (18-29 yr) men (OR=2.01, CI95% 1.13-3.57 over 6 yrs and 1.74, 1.11-2.75 over 15 yrs) and older (30-54 yrs) women (2.43, 1.33-4.42 over 6yrs and 1.52, 1.06-2.22 over 15 yrs), and persisted after controlling for the confounders. Pairwise analyses suggested that genetic and familial influences may play a role in dieting behavior.

Baseline dieting is a risk factor for major weight gain, especially in women. The relationship between dieting and weight gain may indicate that there is a constant predisposition for weight gain in some individuals, as much as the results may indicate that the long-term effects of dieting are ineffective in maintaining weight loss.

## 059

## A TWIN STUDY OF PROBLEM BEHAVIOURS IN CHILDHOOD

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To investigate the importance of genetic factors on problem behaviours in childhood, we obtained ratings from teachers and parents of 131 monozygotic and 136 dizygotic twin pairs. The twins, aged between 7 and 11 years, were identified through schools in Southern England and therefore represent a general population sample. The results confirmed previous reports of high heritability for hyperactivity (e.g. Stevenson, 1992, *Behavior Genetics*, 22, 337-344): approximately 60% of the variance in both teachers' and parents' ratings were due to genetic factors. Previous research on the role of genetic factors on conduct problems (aggressive and antisocial behaviours) has produced mixed findings (see Plomin, DeFries, McClearn & Rutter, 1997, *Behavioral Genetics: A Primer*). The present results provide support for the view that such behaviours show high heritability in *pre-adolescent* children. Parents' and teachers' ratings on learning problems and inattentive-passive types of behaviour further emphasise the importance of genetic factors on children's behaviour.

## 058

## ATTACHMENT IN FINNISH TWINS AND SINGLETONS

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Introduction: The attachment of Finnish children is assessed taken notice to temperament of children and their parents, early separations, and parents' possible preference to nurse the baby.

Method: 58 twin families and 27 singleton families participated Strange Situation test when toddlers were 18 months of age, the attachment of children was assessed with both their parents.

Results: One third of children were securely attached (type B) with their parents, instead of two thirds, as reported about children in USA. Twins were more often securely attached when compared to singletons. The difference was most obvious when assessing attachment between children and their mothers.

Conclusions: Twinhood could be presumed to be a risk for secure attachment as parents sharing their time between two children have less resources to bond strongly to one child. In this study the effect of twinhood seem to be adverse, but more study has to be done to confirm this result.

## 060

## YOUNGER AGE AND LOWER GRAVIDITY IN TWIN PREGNANCIES IS ASSOCIATED WITH GREATER RISK OF PRETERM LABOR AND DELIVERY.

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OBJECTIVE: To study whether there exists an association of maternal age, gravidity (G), and parity (P) with preterm labor (PTL) and delivery.

STUDY DESIGN: A retrospective study of twin pregnancies was performed from 1987-95, including 48,195 deliveries, 535 of which were twins. The population was largely Hispanic (87.7%). Non-Hispanic patients (66), patients for whom there was inadequate information (7), and patients delivered prematurely for medical or obstetrical reasons without PTL (60), were eliminated from the study. The study was therefore controlled for race. The effect of maternal age, G, and P on PTL was studied using univariate analysis, with the Student's paired t-Test for age, and the Mann-Whitney test for G and P.

RESULTS: 217 twin pairs delivered at term (52.5%) and 196 preterm (47.5%). Of the latter, 37% had PPRM, and 63% had strictly PTL. For twins with PTL/delivery: mean age = 25.4 yrs, s.d. = 5.8; mean-G = 2.8, s.d. = 1.7; mean-P = 1.4, s.d. = 1.5. For twins delivered at term, mean age = 27.1 yrs, s.d. = 6.0; mean-G = 3.4, s.d. = 2.8; mean-P = 1.8, s.d. = 1.9. Younger maternal age ( $p < 0.005$ ), lower G ( $p < 0.02$ ), and lower P ( $p < 0.038$ ) were each significantly associated with PTL and delivery.

CONCLUSIONS: In a pure Hispanic population, younger maternal age, and lower G and P are each individually associated with a higher risk for premature labor and delivery.

## 061

## THE ENDOCRINOLOGY OF DIZYGOTIC TWINNING

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Dizygotic twinning is the result of multiple ovulation. This is turn associated with multiple follicle growth. Multiple follicle growth could be the result of higher serum levels of Follicle Stimulating Hormone (FSH). FSH is secreted episodically (pulses) about every 2 hours. In mothers of hereditary dizygotic twins indeed a clear increase in serum FSH is found. This isolated FSH increase is entirely related to an increase in number of FSH pulses. There are no differences in concentrations of ovarian feedback hormones such as oestradiol, inhibin A and inhibin B. This suggests that in hereditary twin mothers a separate FSH releasing mechanism is active. There are other situations with an increase in risk of dizygotic twinning without a hereditary trait. The most prominent non-hereditary situation with risk of dizygotic twinning is advanced maternal age. In premenopausal women a clear increase in serum FSH levels occurs with increasing age. It appears that this type of elevation of serum FSH is related to an increase of the pituitary responsiveness to the hypothalamic hormone Luteinizing Hormone Releasing Hormone (LHRH) responsible for both LH and FSH release by the pituitary. This increase in response results from a decline in ovarian feedback. In women with high FSH levels, lower concentrations of the ovarian hormone inhibin are found. This hormone is responsible for selective suppression of pituitary FSH secretion. Therefore, because of limitations in ovarian feedback in older women, some overshoot secretion of FSH cannot be prevented which thus may lead to multiple follicle growth and to an increase in risk of multiple pregnancy.

## 063

## NO PATERNAL EFFECT ON MONOZYGOTIC TWINNING.

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The etiology of monozygotic twinning is largely unknown. However, women that themselves are monozygotic twins have an increased - presumably genetic - probability of having monozygotic offspring. It is not known whether this effect is mediated through the fertilized egg or through the mother. In this study, 57,363 male twins in the Swedish Twin Registry born before 1972 were linked to the population registry and 3,500,000 deliveries during the period 1960-1996 were investigated. There was no increase in the probability for the male twins to have offspring that were twins (RR=0.93; 95% C.I. 0.84-1.04). This lack of association remained for both monozygotic and dizygotic fathers and was independent of the estimated zygosity of the offspring. The lack of increase in monozygotic offspring of male monozygotic twins and the increased risk of monozygotic twinning in female monozygotic twins suggest that the familiarity in monozygotic twinning is due to a genetic predisposition in the mother.

## 062

## COPING ABILITY AT MID-LIFE IN RELATION TO GENETIC AND FAMILY ENVIRONMENT INFLUENCES AT ADOLESCENCE. A FOLLOW-UP OF SWEDISH TWINS FROM ADOLESCENCE TO MID-LIFE

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**Abstract.** During the years 1964 to 1971 a group of twins and controls were followed from 10 to 16 years of age in the Swedish compulsory school. It was a nationally representative sample of 323 twin pairs, MZ and DZ, and 1193 controls attending the same classes as the twins. The main purpose was to study physical and mental growth during puberty as well as heredity-environment influences on these growth processes. Several kinds of information were collected.

After 20 years a follow-up has been made of this sample with the purpose of investigating heredity-environment influences on life situation, self reported health and coping ability in relation to information collected during adolescence. Present data are taken from 133 twin pairs as well as 322 controls.

The results showed higher mean value of coping ability at mid-life for male twins compared to female. Environmental influences on coping ability and perceived life situation at mid-life were analysed in relation to retrospective self ratings of family and school environment at adolescence. Results from regression analyses showed that social class affiliation and organization factors within the family were important for males but not for females concerning coping ability at mid-life. Cohesion and control within the family at adolescence influenced coping ability and perceived life situation at mid-life for both males and females.

Intraclass correlations were used for studying hereditary influences on coping ability. Genetic influences seem to be operating regarding the ability to cope with problems.

The participants of the study also gave their spontaneous opinion regarding upbringing of children. The correspondence of qualitative and quantitative measures on family and school environment indicated sufficient content validity.

## 064

## THE NORDIC CANCER IN TWINS PROJECT: THE IMPORTANCE OF GENES AND ENVIRONMENTS.

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Familial aggregation is evident for several cancer forms. However, few studies have been able to disentangle genetic from shared environmental effects. In this collaborative project, data from the Swedish, Finnish and Danish twin registries have been pooled. The database comprises 70,767 twin pairs. At least one of the twins had been diagnosed with cancer during the period 1943-1996 in 12,044 of those pairs. There was no evidence of major heterogeneity of twin resemblance for specific sites over countries. Familial aggregation was seen for stomach, colon, rectal, pancreas, larynx, lung, breast, cervix uteri, corpus uteri, ovary, prostate cancer and leukemia. Genetic factors seem to be the most important factor for familial aggregation for all of these cancers forms. For all countries combined, genetic factors accounted for approximately 25% of the variation for total cancer whereas there was little evidence for shared environmental effects. Nonshared environmental effects were most important and accounted for 75% of the variation. This study shows notable genetic effects for a number of cancers where previous twin studies have not had sufficient sample sizes. The familial aggregation is higher than suggested by segregation analyses, indicating that susceptibility for these cancer forms is inherited in a complex non-Mendelian fashion. This database will also be valuable also for exploring age differences in heritabilities as well as environmental risk factors for different cancer forms. The results will be of importance for guiding linkage and epidemiological studies investigating the etiology of cancer.



## 065

STRESS OF DAILY ACTIVITIES AND RISK OF BREAST CANCER: A PROSPECTIVE COHORT STUDY IN FEMALE TWINS IN FINLAND. Kirsi Lillberg\*, Pia K. Vrkasalo, Jaakko Kaprio, Lyly Teppo, Markku Koskenvuo\* \*Dept. of Public Health, Univ. of Turku, Lemminkäisenkatu 1, FIN-20520 Turku, Finland

The relationship between psychosocial stress and breast cancer risk has remained controversial partly due to the possibility of recall bias in a number of case-control studies. We investigated breast cancer risk in a prospective cohort study in adult female twins in Finland in 1976-96. The adult Finnish Twin Cohort was compiled from the Finnish Central Population Register in 1974 and comprises all like-sexed twin pairs born before 1958 with both cotwins alive and living in Finland on January 1, 1976. In 1975, the subjects were sent an extensive health questionnaire asking, eg, about one's experience of stress of daily activities (SDA), predicting in earlier studies incidence of mental problems as well as peptic ulcer. Altogether 10,519 female twins who answered this question constitute the present study cohort. Data on breast cancer were obtained by record linkage with the Finnish Cancer Registry for years 1976-96. Calculation of person-years at risk began on January 1, 1976, and ended at diagnosis of breast cancer, emigration, death or December 31, 1996, whichever came first. Age-adjusted hazard ratios were obtained from proportional hazard models. In all, 23% of the women had experienced no appreciable stressfulness, 68% had experienced some, and 9% severe stress. A total of 205 primary breast cancers were identified among them. The age-adjusted hazard ratios for breast cancer risk among these groups were 1.0, 1.1 and 0.84 by increasing level of stress (non-significant). Adjusting for smoking or body mass index did not materially change the results. Based on these preliminary results, we do not find evidence for an association between this indicator of psychosocial stress and breast cancer risk.

## 067

TAMBA'S HEALTH AND EDUCATION GROUP: TO DEVELOP PARENT/ PROFESSIONAL PARTNERSHIPS

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The group has grown from being a purely Medical group at its inauguration in 1978 to its current position as core support to all the work that goes on in the health and education field

It was early recognised that the educational needs of multiple birth children are also unique and sadly misunderstood by many professionals in that field. Today, much of the group's work is focussed upon the health emotional and educational needs of our special families. Regular study days, conferences, articles research and leaflets arise from the group's work.

The members remain largely parents who are professionals although TAMBA recognises the immense expertise built up over the years in this special field of its dedicated parents members, who are now considered the experts in the parenting of multiples world! Who really understands what it is like to be the parent of twins or more? Who has both experience and knowledge at their fingertips? An experienced TAMBA volunteer!

The Health and Education group is currently going from strength to strength in its work with Pat Preedy and her educational research. It is also busy collating data from a most successful survey into members about their childbirth experiences.

The Health and Education group is looking to work with other professional research organisations and, to identify other needs of the multiple birth family. This review will help us to prioritise and resource appropriate projects and services.

## 066

TAMBA TWINLINE: EVALUATING THE DIRECT SUPPORT TO FAMILIES AND PROFESSIONALS

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A presentation on the progress and a review the telephone helpline service set up in 1991 as a result of research into the needs of the multiple birth family and the services it required.

Emphasis will be placed on the development of the service, its daily operation and management, and the training and support needs of its volunteer Listeners, who are also parents of twins or more themselves.

The fact that this was originally a project, and thus easy to fund, but now a core service and thus more difficult to find regular sources of core funding, will be shown.

The findings on evaluating the call data, including types of call, and assessing the needs of families that arise from this data, will be highlighted. How TAMBA has attempted to offer services to help alleviate the difficulties parents raise through the provision of information and training at seminars and Study Days.

TAMBA Twinline has become part of TAMBA's main activities, perceived by members, and others, to be a vital service to the parents or soon to be parents of twins, triplets and more!

## 068

GENETIC AND ENVIRONMENTAL INFLUENCES ON TRANSITIONS IN DRUG USE

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Genetic and environmental factors influence drug abuse, but abuse represents the culmination of a sequence of events. Different levels of use may have different determinants. For example, genetic and environmental factors that influence whether an individual is exposed to a drug may be different from factors that determine whether a regular user becomes an abuser.

Approximately 8,000 twins from the Vietnam Era Twin Registry were interviewed by telephone. Members of the Registry are male-male twins who served in the military from 1965 to 1975. Data were obtained with regard to exposure to illicit drugs, initiation of use, continuation of use, regular use, and the diagnosis of drug abuse/dependence. Transitions are defined as moving from one stage (e.g., exposure) to the next stage (e.g., use).

Although marijuana had the highest prevalence of abuse, regular heroin users were more likely to become abusers of heroin than regular users of marijuana were to become abusers of marijuana. Subjects using heroin more than five times were more likely to become regular users of heroin than individuals who used other drugs. The first two levels of heroin use were about 50% heritable and there was not a detectable influence from the common environment. The most heritable transition for marijuana use was the transition from *Ever Use to Use More Than 5 Times*. Across drugs, the strongest influence of the common environment was on exposure. In general, genetic factors influence each transition, as well as exposure.



## 069

## THE CHANGING PATTERN OF MULTIPLE BIRTHS IN ABERDEEN FROM 1950-1995

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There was a fall in the multiple births rates in Aberdeen from 1950 to 1980 followed by a steep rise. This was due to changes in the DZ rates but the MZ rates remained constant. The initial fall was due to a decrease in parity and a decrease in maternal ages. The later rise was due to induced fertility.

## 071

## A COMPREHENSIVE MODEL FOR FAMILY RESEMBLANCE IN EXTENDED PEDIGREES

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A model for family resemblance in extended pedigrees was implemented in Mx. The ideal pedigree consists of a pair of monozygotic or dizygotic twins, their parents, siblings, spouses and children. Ninety one unique relationships between relatives can be derived. The full model allows testing for additive and dominant genetic effects, shared and unique environmental effects, special twin environment, special MZ twin environment (test of equal environment assumption), phenotypic assortative mating, vertical cultural transmission (from parental phenotype to children's environment), and genotype-environment correlation. Complete testing for sex differences (both in magnitude and effect) for either additive, dominance or shared environmental effects is available. The model can be fitted to correlation matrices or raw data. We illustrate the method with data from the Virginia 30,000.

## 070

## THE GENETICS OF SMOKING PERSISTENCE IN WOMEN: A CROSS-CULTURAL TWIN STUDY.

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The extent to which the same genetic and environmental factors influence the initiation of regular cigarette smoking and maintenance of the smoking habit, and whether there are differences by society and age cohort was examined using questionnaire survey data obtained from large samples of female like-sexed twins, 18-46 years of age, from three different countries: Australia (N=1,535 pairs), Sweden (N=5,916 pairs) and Finland (N=4,438 pairs). Each of these samples was subdivided into three age cohorts (AC), 18-25 years, 26-35 years, and 36-46 years of age. Consistent with most other studies, we found substantial additive genetic effects on the initiation of regular smoking. The magnitude of genetic influence for lifetime regular smoking was consistent across society for women (from youngest to oldest AC: 41%, 47%, and 56%), as were estimates of the relative contribution from environmental influences shared by twin and cotwin (from youngest to oldest AC: 45%, 24%, and 14%). For maintenance of smoking (i.e., still smoking at survey), our results indicated that up to 5% (95% Confidence Interval: 0-28%) of the variance in the youngest AC, and 24% (95% CI: 2-54%) and 15% (95% CI: 0-56%) in the two older ACs respectively could be attributed to the effects of genes independent from factors influencing smoking initiation. In contrast with smoking initiation, there was little evidence that environmental experiences shared by cotwins played an important role in the maintenance of cigarette use. Our results suggest that there are strong genetic influences on smoking behavior in women, and that genetic factors responsible for maintenance of the smoking habit may not be entirely explained by the same factors responsible for the onset of regular smoking (Support:NIH-DA00272, AA07535, AA07728, Australian NH&MRC).

## 072

## THE TWIN SERVICE NETWORK - PROMOTING REGIONAL MULTIPLE BIRTH RESOURCES

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Multiple births currently affect 2.6% of U.S. infants and constitute an emerging public health issue. To improve the capabilities of health systems to document, assess and reduce the elevated health and psychosocial risks associated with multiple births, the Twin Service Network Project developed a methodology for enhancing service systems' capacity to deal appropriately with the needs of multiple birth families. A community-based advisory council assisted in developing a network of multiple birth resources and training in Alameda and Contra Costa Counties, CA to target the region's 6,000 multiple birth children and their families, 48% of whom are ethnic minorities and of whom 15% are living in extreme poverty. Replication of the model has been initiated in the six counties of the San Francisco Bay Area and in Los Angeles County, which regions together produce 7% of U.S. multiple births.

The overall significance of this project lies in a validated model for regional networks of multiple birth training services and community resources and an integrated package of workbooks and training and parenting education materials that are available to other states and regions for assessing the needs of multiple birth infants and children and networking provider training and resources to address them.

## 073

## LONGITUDINAL TWIN STUDY OF EXTRAVERSION AND NEUROTICISM: RUSSIAN SAMPLE

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The purpose of the study is to examine hereditary and environmental influences on extraversion and neuroticism during adolescence. The study is conducted in context of Moscow ongoing longitudinal study of psychological traits. The design is a longitudinal twin study with a sample of the same-sex twins. Extraversion and neuroticism were measured in two occasions: in 1994-1995, twins aged 13-14 (126 MZ and 84 DZ twin pairs), and in 1997-1998, twins aged 16-17 (32 and 28 pairs respectively). The Russian version of EPI (Eysenck & Eysenck, 1964) was chosen as a method. Model-fitting analyses was used for genetic analyses of observed data. We fitted four basic models (the 'environmental', the 'simple genetic', the 'genotype-cultural' and the 'dominance' model) to the mean squares for extraversion and neuroticism. At the 1st occasion in the case of neuroticism, the 'genotype-cultural' model fits very well ( $V_a=28,4\%$ ,  $E_b=19,34\%$ ,  $E_w=52,22\%$ , chi squares - 0,07). The variation of extraversion is best explained by a very simple genetic model ( $V_a=52,2\%$ ,  $E_w=47,8\%$ , chi squares - 1,005). The preliminary results of 2nd occasion are not complete because of longitude to be our current study, and number of subjects to increase. In case of neuroticism, 'dominance' model now fits well ( $V_a=23\%$ ,  $V_d=11,36\%$ ,  $E_w=65,61\%$ , chi squares - 0,086). Variation of extraversion is explained by the same simple genetic model ( $V_a=35,1\%$ ,  $E_w=64,9\%$ , chi squares - 2,166). Thus there is tendency for genetic influences on extraversion to decrease during adolescence. The nonshared environment begin to play the main role in forming individual differences. The factors of twins environment and its connection with differences in personality traits are investigated in our study as well.

## 075

## MOLINNESS, MELANOMA AND CDKN2: A TWIN PARADOX.

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The incidence of melanoma is rising rapidly throughout the western world, and nowhere more than in Queensland which has a particularly susceptible, largely Celtic population subject to very high UV exposure. Recently a major gene for familial melanoma (CDKN2, MTS1, MLM, p16) has been mapped to chromosome 9p. It is not yet clear what proportion of melanoma risk is attributable to it, but the overall heritability of melanoma appears to be low. We do know that having a high density of common moles (melanocytic nevi) confers a greatly increased risk of melanoma.

We have counted moles on the skin of 400 random twin pairs in SE Queensland at age 12 and have found  $r(mz) = 0.94$  and  $r(dz) = 0.50$ , consistent with almost totally genetic determination of mole count in this population. By typing D9S942, a dinucleotide repeat marker 5kb 5' of CDKN2, we can classify DZ twins by IBD status. Sib pair linkage analysis reveals that as much 20-40% of variance in mole counts may be due to variation at or near the 9p familial melanoma locus. Since the heritability of moliness is high, and of melanoma is low, yet CDKN2 has a major influence on both, the etiologic relationship of moliness and melanoma appears paradoxical. The possibility of finding further tumor suppressor genes by QTL linkage analysis of mole count will be discussed.

## 074

## SOME ANTHROPOLOGICAL CHARACTERISTICS OF SCHOOL-AGED TWINS FROM BELGRADE

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Studies were performed in 82 elementary school in Belgrade, containing 82,282 pupils. There has been found 525 pairs of twins between the ages of 7 and 15 years. Concordance in the colour of hair and eyes in monozygotic twins amounted to 100%, whereas that in twins of various sexes was only (0.48). Besides the concordance in the colour of eyes was low (0.63). The mean percentage divergence in height and body mass is considerably higher in dizygotic (DZ) than in monozygotic (MZ) twins ( $1.72 \pm 0.34 : 0.47 \pm 0.11$ ;  $6.43 \pm 1.34 : 2.28 \pm 0.64$ , respectively). No differences were observed in height in school-aged twins in respect to the order of birth either in MZ or DZ twins except at 9 years of age, being higher in DZ twins (131.7 : 137.1 cm). The differences in height between MZ and DZ twins were found only at 14 years of age being higher in MZ female twins (166.2 : 160.4 cm). No differences in body mass between male twins according to their zygosity were observed. In female twins according to zygosity there was established difference in body mass at 14 years of age being higher in MZ twins (57.1 : 51.3 kg). In the sample studied by 14 years of age female twins have menarche 100%. No significant differences were observed in the appearance of menarche between MZ and DZ twins, being 12.57 and 12.48 years respectively. Concordance for the appearance of menarche is greater in MZ (0.47) than in DZ (0.27) twins. As for school performance the concordance is higher in MZ (0.80) than in DZ (0.66). However, there is not a significant difference in school performance between school-aged twins and non-twins.

## 076

## GENETIC STUDIES OF MOTHERS OF SPONTANEOUS DIZYGOTIC TWINS (MODZT)

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DZ twinning is familial and this suggests there may be an inheritable abnormality of the control of ovulation that predisposes to double ovulation. In our previous studies of MODZT we found that they double ovulate in about 20-30% of cycles and that gonadotrophin levels were elevated both at mid-cycle and in the early follicular phase. We are now performing a linkage search for genes influencing DZ twinning using pairs of sisters who have both had spontaneous DZ twins and results of this will be reported.

## 077

## TWIN-PAIRS WITH PHENYLKETONURIA (PKU).

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In Russia the frequency of PKU ranges from 1 per 5600 to 1 per 10000 live births. The frequency of multiple pregnancies is at least 1 per 80 or 100. Expected probability of twins with PKU is 1 per 450000-1000000. It is very important to analyze and discuss so rare cases.

Six twin pairs, aged from 5 yr. to 28 yr. with PKU have been under our observation so far: three twin-pairs females concordant; one concordant and one discordant twin-pairs, male; one discordant sister-sick brother twins. Only two twin-pairs females were born in St. Petersburg and were revealed by neonatal screening programme. We used the earliest adequate diet and drug therapy that was very successful. The others were born out of St.Petersburg and did not have a chance to be examined by neonatal screening. In these cases PKU was revealed when these clients were 10-23 months old; diet and drug therapy were unfavourable. Molecular analysis was performed to diagnose four twin-pairs in the Laboratory for prenatal diagnosis of the Institute of obstetrics and gynaecology named after D.O.Ott. Two concordant female pairs and one male of sister-brother pair were homozygotic persons with R408W allele. One concordant twin-pair male was compound with R408W allele and IVS-10 allele.

## 079

## TWIN BIRTH, PREMATURITY AND BRAIN LESIONS OBSERVED IN THE NEONATAL PERIOD:

THEIR EFFECTS ON DEVELOPMENT AT SIX YEARS OF AGE  
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The study to be reported in this paper forms part of a prospective longitudinal study of 183 children born prematurely in London between 1984 and 1986. Our aims were: (1) to determine whether prematurely born twins differed from singletons in developmental outcome at 6 years of age; (2) to describe the sequelae for twins who were concordant and discordant on neonatal cranial ultrasound examination. The 14 twin pairs included in the cohort were individually matched with 28 singletons on gender, gestational age, birthweight and type of brain lesion recorded by ultrasonography during the neonatal period. The follow-up assessments conducted at 6 years included the Movement Assessment Battery for Children, the Developmental Test of Visual-Motor Integration, Touwen's Examination of the Child with Neurological Dysfunction, verbal IQ and reading subtests from the British Ability Scales, the Pictorial Scale of Perceived Competence and Social Acceptance for Young Children, and Rutter's Behaviour Questionnaire for Parents and Teachers.

When twins and singletons were compared on our measures of perceptual-motor competence, neurological functioning and verbal abilities, there were no significant group differences. However, twins rated themselves as being less competent in the cognitive domain than the singletons. In contrast, the parents of twins observed fewer behavioural problems than did the parents of singletons.

When both twins had brain lesions, outcome at 6 years was less favourable than when both twins showed no evidence of brain damage. In case of the 3 pairs of twins with discordant ultrasound findings, the ones with a lesion at birth obtained equal or slightly lower scores in the neuromotor and cognitive domains than the ones without a lesion. Such a tendency was not observed in 2 out of the 3 matched discordant singleton pairs on their verbal IQ scores. These results demonstrate the advantage of using twins in order to investigate the sequelae of neonatal brain lesions among prematurely born children.

## 078

## CHILDHOOD SEXUAL ABUSE AND PARENTAL REJECTION: PRELIMINARY RESULTS FROM A COTWIN-CONTROL STUDY.

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We have previously observed that twins reporting a history of childhood sexual abuse (CSA) were more likely to display lifetime psychopathology than were their non-abused cotwins and that, for women, shared environmental factors influenced the risk of reported CSA. The present study explored the relationship between CSA and perceived parental rejection in 3,762 Australian twins through the use of a 14-item version of the Parental Bonding Instrument [Parker G,Tupling H, Brown LB. A Parental Bonding Instrument. Brit J Med Psychol 1979;52:1-10]. Levels of parental rejection were assessed for (1)twins from pairs concordant for CSA, (2)twins from pairs in which only the respondent reported CSA, (3)twins from pairs in which the respondent did not report CSA but the cotwin did and (4)twins from pairs in which neither reported CSA. Results indicated that, for both males and females, twins for pairs concordant for CSA scored significantly higher on perceived parental rejection than twins from pairs in which neither reported CSA. The twins from CSA discordant pairs reported levels of parental rejection that were as high as those obtained from CSA-concordant pairs, regardless of the respondent's abuse status. These results suggest that CSA is associated with a rejecting family environment but that the relationship between these variables is not causal and may be mediated by other sources of family dysfunction.

## 080

MULTIPLE PREGNANCIES WITH UNFAVOURABLE OUTCOME AS A RESULT OF IN VITRO FERTILIZATION  
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In honour of Prof.Leonidas Z.Kaidanov

In vitro fertilization (IVF) is widely used as a modern, effective method for the solution of problem of infertility. It is very important to analyze and discuss any unsuccessful results of this method.

We report on results of two multiple pregnancies after IVF. Case report 1.Proband is a female gravida II, 41-year-old, after IVF. There were mastopathy, fibroadenomatosis and a pregnancy complicated in last medical history. This pregnancy ended in twin labor at 27 weeks' gestation. Birth weight of the first twin female was 970g; her birth length was 35cm; head circumference was 25cm. The second twin sister was born dead with multiple congenital anomalies ( birthweight was 900g).

Case report 2. Proband is primagravida, 35-year-old, after IVF. There were uterine endometriosis and myoma, ovary resection in last medical history. Outcome of this multiple pregnancy was triplets labor at 28-29 weeks' gestation. The first female had birthweight 1,25 kg, her birth length 39cm; Apgar scale was 5|7.The second male had birthweight 1,15 kg, his birth length 40cm; Apgar index was 5|6. The third male was born dead with fetal asphyxia. His birth weight was 1,45kg.

All three live children were admitted to our Psychoneurologic Children's Hospital with severe mental retardation, neurologic disturbances and multiple congenital anomalies. So far they have been under our observation.

## 081

## MUSIC THERAPY FOR TWIN PAIR WITH MENTAL RETARDATION.

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*Music expresses that which cannot be said and on which it is impossible to be silent.* Victor Hugo (1820-1885)

The main problem for children with mental retardation is the problem of adaptation, stimulation of their development and potential abilities. Music therapy (MT) as a method for rehabilitation and socialization of children with these disorders has not been in use long in St. Petersburg. Two 4-year-old twin boys from healthy nonconsanguineous parents, are under our observation. They were born at 38-39 weeks' gestation by Caesarean section to a 40 year old mother and a 42-year-old father in Turku (Finland). At birth, weight of twin A was 3,7kg ( 75th centile ), his length was 51cm (>25th & <75th centiles ): weight of Twin B was 3,6kg (>25th & < 75th centiles ), his length was 50cm (25th centile). Our twins have behavioral and communicative delays, speech disturbance like babbling. MT sessions last 30-35min once a week. The first set of studies included 24 sessions, now our twins have the second set. We work with each twin separately. The goals of MT sessions include eye-contact, attention span, on-task behavior, awareness of self and other, motor planning etc. Using various instruments we establish a music dialogue that allows these twins to express themselves. As the sessions progressed, our twins became able to focus their thoughts, behaviour and emotion without breaking apart. Among the benefits of MT there are improvement in behaviour outside the sessions, improved interpersonal skills, greater confidence in everyday life and positive progress in their speech abilities: now they have speech formed but with mild vocabulary and phonetics defects.

## 083

## X CHROMOSOME INACTIVATION PATTERNS IN MONOZYGOTIC TWIN GIRLS

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X chromosome inactivation patterns were investigated in the blood and buccal mucosa (BM) from 33 MZ and 5 DZ female twin pairs based on methylation of the X linked androgen receptor (AR) gene using a HPaII-PCR assay. The AR gene is methylated on the inactive X and undermethylated on the active X in normal females. The newborn twin girls come from the East Flanders Prospective Twin Survey and were characterised at birth with respect to their placentation -mono chorionic (MC) versus dichorionic (DC)- and their zygosity.

While X inactivation patterns in peripheral blood, which is from mesodermal origin, may differ among the members of an MZ twin pair, we reported that this is restricted to those twins that have a dichorionic (DC) anatomy. Mono chorionics (MC) do not differ substantially in their patterns of X inactivation. The generally accepted explanation for this finding is that MC twins share their placental blood supply during intrauterine life whereas DC MZ twins do not and therefore similar X inactivation patterns in this shared hemopoietic cell population would be expected in MC twin pairs. We have therefore investigated X inactivation patterns in the buccal mucosa of MZ twin girls, a tissue of ectodermal origin which is presumably not exchanged during intrauterine development. The intraclass correlation of X inactivation patterns between members of MZ twin pairs for buccal mucosa are 0.4 (p-value 0.064) for the DC MZ and 0.92 (p-value = 0.0001) for the MC MZ.

These data demonstrate that MC MZ twins have strikingly correlated X inactivation patterns in both ectodermal and mesodermal tissues, whereas DC MZ twins do not. MC MZ twins are thought to result from a later twinning event than DC MZ twins. Therefore, we propose that the timing of commitment to X inactivation occurs between the time of DC and MC MZ twinning, possibly around 4 days after conception. If this hypothesis is correct, the similarity in X inactivation of MC MZ pairs would be explained by the fact that splitting occurred after commitment to X inactivation, with both embryos deriving from a cell population in which X inactivation patterns were already established.

## 082

## ABNORMAL AND NORMAL DEVELOPMENT IN CHILDHOOD AND ADOLESCENCE

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University of Oulu, Finland

The development of twins is an inspiring topic of research, the focus of which is varying.

Twins' development can be studied from the genetic point of view, or in order to estimate environmental factors' impact on abnormal and normal development.

Twin pregnancy and delivery are risk situations. Thus the effect of perinatal morbidity on development is an important focus.

Early human relationships in twin families differ from those in other families, and connections between attachment and motor, cognitive and emotional development can be studied.

Inter-twin relationships can be characterized by co-twin dependence and dominance-submissiveness. Causes for these relationships and their consequences on development make up an inspiring field of research.

Practical point of view is also very important: how are the twins at school? How often do they need special support or special educational settings, and how could we detect early enough those twins who need support? What kind of support is indicated in each type of developmental delay or abnormality?

## 084

## THE INFLUENCE OF ENVIRONMENT AND HEREDITY ON INDIVIDUAL FEATURES OF SELF-REGULATION

Morosanova V., Konoz E., Malykh S. Psychological Institute, Moscow

Twin analyses were conducted to determine the relative influence of genetic and environmental factors on self-regulating in Russian twin sample. Sample included 24 pairs of monozygotic and 17 pairs of dizygotic twins aged 16 to 17. Differences in self-regulation (planning, modeling, programming, estimation of results, flexibility and independence) were studied on the base of the author's psychological questionnaires (V.I. Morosanova, 1988).

Self-regulation of human voluntary activity gathers such regulative processes as planning, modeling, programming, estimation of the results and regulative and personal traits (flexibility, independence). Behavior genetic techniques were used for genetic analyses of observed data. We fitted four basic models (the 'environmental model', the 'simple genetic model', the 'genotype-cultural' model, the 'dominance' model). In the case of planning, the 'simple genetic model' fits very well ( $V_a = 40,92\%$ ,  $E_w = 59,08\%$  and chi squares  $\hat{E} 1,888$ ). In the case of estimation of results, the 'environmental model' fits very well ( $E_b = 25,79\%$ ,  $E_w = 74,21\%$  and chi squares  $\hat{E} 1,117$ ). In the case of modeling, programming, flexibility, independence all models fit very poorly.

## 085

EDUCATION OF MULTIPLE BIRTH CHILDREN  
Rebecca E. Moskwiniski, Kelly Willenberg, J. Susan Griffith  
NOMOTC, P.O. Box 23188, Albuquerque, NM 87192

NOMOTC was founded in 1960 for the purpose of promoting the special aspects of child development which relate specifically to multiple birth children and their families. This presentation will emphasize the specific goal of guiding parents, teachers and other individuals having direct responsibility for the education of multiple birth children. It is intended as a set of general guidelines which will enable educators and school support staffs to become better acquainted with the special social and psychological considerations affecting multiple birth children and their families. A resource list will be included at the end of the presentation.

## 087

MULTIPLE INFORMANTS OF AGGRESSIVE BEHAVIOR:  
HERITABILITY OF AGGRESSION  
Elina Mäki-Korte, Lea Pulkkinen, Jaakko Kaprio, Richard J. Rose & Richard Viken  
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The aim of the present study was to estimate the genetic and environmental influences on rated aggression at age 12. Earlier studies suggest that genetic influences account for as much as 50% of the variance in aggression, but different informants produce different information in relation to children's behavior, so we explore effects of different informants on estimates of heritability. This study is a part of an ongoing nation-wide twin-family study of behavioral development and health habits (Pulkkinen, Kaprio & Rose, 1998). The data were collected with the Multidimensional Peer Nomination Inventory (MPNI) and its parallel teacher and parental rating forms. The twins (468 MZ and 487 DZ twin pairs) represent subsets of three 12-year-old twin cohorts (b. 1983-1985) from Finland. Heritability of aggression was assessed by examining patterns of intraclass correlations and by model-fitting analysis using Twinan90- and Mx. DZ correlations were significant, but lower than the MZ correlations, indicating genetic influences, and model-fitting confirmed significant additive genetic effects for all three measures of aggression. There was evidence for common environmental effects, significant for both teacher and parental ratings. Estimates of genetic and common environmental effects were more consistent for parents and peers than for parents and teachers or for peers and teachers, suggesting that estimates of heritability and common environment vary with source of the informant.

## 086

NATURE OR NURTURE  
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This Paper will discuss which factor is stonger in developing personality: nature or nurture? It is assumed that if nature is stronger, than there will be more similarities in personality between identical twins than between non-identical twins. If there is no significant differences between similarities among identical and non identical twins, it means that nature is not a significant factor in developing personality of the twins.

Two groups of twins, identical and non-identical, will be given EPPS (Edward Personal Preferences Scale) which consists of 15 needs. In both groups the EPPS scores will be correlated. Bigger scores of coefficient of correlation means more similarities. The significance of the differences between the two groups will be tested.

## 088

DIFFERENT ASPECTS OF TWINS FAMILY ENVIRONMENT  
AND SELF-PERCEPTION IN PRESCHOOL AGE  
Nadyseva V.V. Psychological Institute, Moscow

The aim of our study was to investigate specificity of parent-child relations and twins' self-perception. Battery of psychological methods was used: questionnaire for twins mothers, interview with mothers, drawing projective tests, scales of self-perception etc. Twin sample consists of 10 MZ pairs and 8 DZ pairs aged 6-7. Our hypothesis argues that differential parental (and other family members) treatment leads to the appearance of intrapair differences in twins' self-perception. The qualitative analyses of data permits to conclude that, first, patterns of parental behavior - more than zygosity or likeness of children - lead to differences in twins self-perception. Second, nonsimilarity in the level of self-perception depend not on differences in the parental treatment itself (presence/absence of differential behavior), but on the child expectations. Third, the self-concept of 'unhappy' member of twin pair (i.e. child, who doesn't content with distribution of adults' attention within the family) is more complex and contradictory compared with self-concept of co-twin.



## 089

## THE PHOG GENE ON Xpter-p22.32 APPEARS TO BE A QTL FOR STATURE IN ADOLESCENT TWINS.

Walter E. Nance, Arti Pandya, Hermine Maes, Jay W. Ellison, Susan H. Blanton, Richard M. Schieken, Department of Human Genetics, Virginia Commonwealth University, Richmond, Virginia, U.S.A.

In 1989, we showed how phenotypic and genetic marker data in twins can be used to measure the contribution of specific loci to variation in continuous traits. Although they are of no value for the mapping of QTLs, the inclusion of MZ pairs permits measurement of the relative contribution of the candidate gene to the overall genetic effect. Because the covariance of twins includes age related differences in gene expression, twins are more powerful than sib pairs for studies of QTLs. When parental data are available, our model also permits the detection of genomic imprinting, which is of particular importance for anthropometric variables (Nance, WE in AG Beam, Ed, *Genetics of Coronary Heart Disease*, Oslo 1992, pp 163). It has recently been shown that the PHOG gene in the pseudo autosomal region of Xp is responsible for the striking decrease in stature seen in Turner Syndrome (Ellison, JW et al, *Hum Mol Genet* 6:1341, 1997). The demonstration of haplo-insufficiency effects strongly suggests that individual differences in gene expression at this locus may contribute to normal variation in height. To test this hypothesis, we typed 140 DZ twin pairs for four polymorphic markers spanning a 7.1 interval cM in the subtelomeric region of Xp known to contain PHOG. Using Mapmaker Sibs, we found evidence for a QTL for stature in 14 ½ year old twins with a maximum lod score of 2.7 at the DXY233 locus. Since previous research has identified PHOG as a rational candidate locus for body stature, our findings provide strong support for the belief that polymorphic differences in PHOG contribute to normal variation in body size in addition to short stature seen in XOTurner Syndrome.

## 091

## GRANDPARENTING MULTIPLES / YOUR MULTIPLES' GRANDPARENT

National Organization of Mothers of Twins Clubs, Inc.  
P.O. Box 23188, Albuquerque, NM 87192

These two surveys were sent to the membership of NOMOTC from October 1994-March 1995. "Grandparenting Multiples" was completed by 504 grandparents of multiples and "Your Multiples' Grandparent" was completed by 506 parents of multiples. Results of these two surveys and our conclusions will be presented.

## 090

## PROFESSIONAL RESEARCH PROJECTS

National Organization of Mothers of Twins Clubs, Inc.  
P.O. Box 23188, Albuquerque, NM 87192

Since 1985, NOMOTC has worked with physicians, psychologists, sociologists and other researchers to help them find participants for their research projects. This poster presentation will highlight results from many of these studies. Some of the subjects researched include: Tourette's syndrome, Experiences of Twin Loss, Atopic Illnesses, Partial Perinatal Loss in Multiple Births, Breastfeeding Multiple Birth Infants, and Gender-Based Differences in the Language Socialization of Young Children. This poster will also highlight currently active studies.

## 092

## BEING A MULTIPLE / BEING A SIBLING TO MULTIPLES

National Organization of Mothers of Twins Clubs, Inc.  
P.O. Box 23188, Albuquerque, NM 87192

These two surveys were sent to multiple birth families of NOMOTC from March-September 1996. "Being a Multiple" was completed by 194 multiple birth children, and "Being a Sibling to Multiples" was completed by 192 singleton siblings of multiples. Results of these two surveys and our conclusions will be presented.

## 093

SOCIAL SKILLS OF MULTIPLES / COMPETITIVENESS  
AMONG MULTIPLES

National Organization of Mothers of Twins Clubs, Inc.  
P.O. Box 23188, Albuquerque, NM 87192

These two surveys were sent to the membership of NOMOTC from October 1993-March 1994. "Social Skills of Multiples" was completed by 280 mothers of multiples, and "Competitiveness among Multiples" was completed by 299 mothers of multiples. The purpose of these studies was to examine the social development and competitiveness of multiples. Results of these two surveys and our conclusions will be presented.

## 095

TESTING OF HUMAN HOMOLOGUES OF MURINE  
OBESITY GENES AS CANDIDATE REGIONS IN FINNISH  
OBESE SIBPAIRS

Miina Öhman, Laura Oksanen, Katariina Kainulainen, Olli A. Jänne, Jaakko Kaprio, Markku Koskenvuo, Pertti Mustajoki, Kimmo Kontula, Leena Peltonen  
National Public Health Institute, Department of Human Molecular Genetics, Helsinki, Finland

Obesity increases the risk of cardiovascular disease, non-insulin dependent diabetes mellitus and osteoarthritis. The human homologues of recently discovered murine obesity genes provide relevant candidates to study the genetic component of obesity in humans. We analyzed the human counterparts to murine obesity genes *ob*, *db*, *agouti*, *tub*, *melanocortin 4-receptor (MC4-R)* and mitochondrial uncoupling proteins 2 and 3 (*UCP2* and *UCP3*). We found no significant evidence for linkage to any analyzed loci in our total study material of 105 obese ( $BMI \geq 32 \text{ kg/m}^2$ ) sibpairs including 46 were dizygotic twin pairs. However, several markers on 6 cM chromosomal region flanking the *MC4-R* gene showed sharing of alleles identical-by-descent (IBD) more frequently than expected. A selected subset of non-diabetic obese sibpairs showed sharing at the *p*-value of 0.003 with these markers. We therefore screened seven obese subjects included in our sibpair material for sequence variations in their *MC4-R* gene, but no mutations of apparent causal relationship were found. In conclusion, we found no evidence for significant contribution of the chromosomal loci corresponding to the murine single-gene obesity genes for human morbid obesity. However, further studies are still needed to clarify whether DNA alterations within or adjacent to the *MC4-R* gene could influence this phenotype.

## 094

SOFTWARE TOOLS FOR STATISTICAL ANALYSIS OF TWIN  
DATA, INCLUDING DATA FROM TWIN PEDIGREES AND  
GENOMIC SCANS

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Much formal analysis of twin data is best carried out within the framework of structural equation modeling. Path diagrams may be drawn and models fitted directly from the diagram within the Mx program, which also displays parameter estimates and model fitting statistics on the diagram. The use of special definition variables allows a host of alternative models to be specified, including those in which e.g. heritability changes as a continuous function of age, or sibling interaction as a function of contact. In addition, models that make use of genetic marker information can be specified in this manner, as each sibling pair has different probabilities of sharing 0, 1 or 2 alleles identical by descent at a locus. A further elaboration of these models deals with the idea that the population contains a mixture of distributions, such that some cases conform to one type of model while others belong to another class (e.g. high vs. low heritability). Such mixture distributions offer another way to view sibling resemblance at a particular quantitative trait locus. Extensions to multivariate analyses, latent variable models, non-random sampling, and multilocus models involving epistasis are easily achieved.

## 096

GENETIC ANALYSIS OF MOTOR DEVELOPMENT,  
LANGUAGE DEVELOPMENT AND SOME BEHAVIOR  
CHARACTERISTICS IN TWIN INFANCY.

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Tamaho, Yamanashi, Japan 409-3898.

As was already pointed out many behavior characteristics are genetically controlled. Genetic analysis was made as to this point in more detail. Subjects were 831 twin pairs, consisting of 609 MZ, 120 same-sexed DZ and 102 opposite-sexed DZ pairs, who were the applicants at the Junior High School affiliated with Tokyo University, Japan. Their motor and language development and some behavior characteristics were analyzed.

The results were as follows: (1) As to motor development, intraclass correlation coefficient of the beginning age of 5 items of MZ pairs were all higher than those of DZ pairs. Moreover, 64% of MZ pairs started at the same month as for all 5 items, while 21% of the same-sexed DZ pairs. (2) As to language development, MZ and the same-sexed DZ pairs showed nearly the same correlation concerning the month of "have 1 to 2 words" and that this correlation was higher than that of the opposite-sexed pairs..

(3) As to behavior characteristics, significant difference between MZ and the same-sexed DZ pairs in concordance rate were observed concerning sleeptalking and nail-biting. Moreover, sex difference in concordance rate was observed in nail-biting.

It was suggested that motor and language development and some behavior characteristics in infancy were genetically controlled and that sex difference was important in some of them.

097

**THE EFFECTS OF PARENTAL SMOKING AND HEREDITY ON THE ETIOLOGY OF CHILDHOOD STRABISMUS: A TWIN STUDY.** J. F. Orlebeke<sup>1</sup>, D. L. Knol<sup>1</sup> & F. D. Koole<sup>2</sup>, Dept. Biological psychology<sup>1</sup> and Dept. Ophthalmology<sup>2</sup>, Vrije Universiteit, De Boelelaan 1111, 1081 HV Amsterdam, The Netherlands. Fax: +31 20 4448832. Email: JF.Orlebeke@psy.vu.nl

Strabismus (squint), parental smoking, birth weight and zygosity were assessed by questionnaire - filled out by the parents - in 3078 six year old twin pairs. Strabismus was measured by answering the question: "Have the children ever been treated for strabismus (squint) by a doctor?" (yes/no) and parental smoking with the question: "Do you smoke at present?" (no, pipe/cigars, less than 10 cigarettes per day, more than 10 cigarettes per day). Data were complete for 2606 pairs of twins.

Prevalence of strabismus was 6.4%. Having one affected proband-twin, the probability of finding an affected co-twin is thus 6.4% in case of random pairings of individuals. The actual pairwise concordances are 52% for MZ twins and 14% and 11.6% for DZ same sex and DZ opposite sex twins respectively. This suggests a strong genetic influence where both additive genetic factors and epistasis seem to play a part. Maternal and not paternal smoking increases the probability of squint in second borns only. Strabismus decreases from about 13% in children weighing less than 1500 grams to about 3% in children weighing more than 3250 grams. The maternal smoking-strabismus association was reduced but still significant after correction for the association between maternal smoking and birth weight. **In conclusion**, one may say that there is a very strong genetic influence on childhood strabismus. Low birth weight and maternal smoking enhance the risk for strabismus, very likely partly because of the birth weight reducing influence of maternal smoking and partly because of a different, as yet unknown, mechanism.

099

**IQ LEVEL AND SELF- AND OTHER-PERCEPTION.**  
Parshikova O.V. Psychological Institute, Moscow

The aim of this study is to analyze the variations in self- and other-perception as a result of IQ level. The sample includes 38 DZ and 55 MZ pairs of twins, aged 16-17.

The methods were WAIS and semantic differential (self-perception and perception of co-twin). Semantic differential included 9 scales: active, delicate, patient, selfish, purposeful, sensitive, masterful, distrustful and disappointed.

The results of correlation analyses show the relation between Vocabulary and 3 measures of self-perception - unmasterful, trustful, optimistic and between Picture Completion and perception of oneself as unmasterful. High scores in Vocabulary are also related to evaluation of co-twin as active, trustful and optimistic.

During the group analyses all twins were divided into 3 groups according to the level of their IQ (high, medium, low). Significant differences were found between high- and low-IQ groups in following measures of self- and other-perception: active, selfish, masterful, distrustful and disappointed. Obtained results are interpreted in the context of the interrelations between intelligence and personality during development. Genetic analyses allows to estimate the role of heredity in this interrelation.

098

**GENETIC INFLUENCES ON OSTEOARTHRITIS OF THE HIP: A STUDY OF WORLD WAR II VETERAN TWINS**

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The prevalence of osteoarthritis of the hip varies dramatically by racial group, suggesting that genetics may play a part in this disease. In addition, a recent study of osteoarthritis of the hand and of the knee among women showed a significant genetic influence.

The prevalence of hip pain due to arthritis and of hip replacement surgery were ascertained by telephone survey among twins in the NAS-NRC Twin Registry, who were all white males born in the years 1917-1927.

Using a liberal definition of concordance for hip surgery in which concordant pairs now include twins pairs in which one twin had surgery and the non-operated twin has experienced hip pain, additive genetics is estimated to account for 41% of the variance in liability for hip surgery, common environment for 54%, and unique environment for only 5%; i.e., the trait is roughly 95% familiarly determined. In a further analysis in which hip pain and hip surgery are measured on a single three-category scale (no hip pain; pain, but no surgery; and hip surgery), additive genetics accounts for 31% of the variability in liability for this "progression to hip surgery" and unique environment accounts for the remaining 69%.

These data show that there are significant genetic and common environment effects on the liability for self-reported hip pain and hip surgery. They also suggest that there is a natural biological progression from hip pain to hip surgery that is significantly influenced by genetics.

100

**A CANDIDATE GENE AND GENOME SCAN STUDY OF HYPERTENSION IN FINNISH TWINS: EVIDENCE FOR LINKAGE**

Markus Perola, Katariina Kainulainen, Päivi Pajukanta, Joseph Terwilliger, Jaakko Kaprio, Markku Koskenvuo, Ann-Christine Syvänen, Erkki Vartiainen, Leena Peltonen, Kimmo Kontula  
Correspondence: National Public Health Institute, Dept of Human Molecular Genetics, Mannerheimintie 166 00300 Helsinki, Finland

We carried out a genetic linkage candidate gene study in Finnish hypertensive dizygotic twins and their affected sibs (329 hypertensive individuals of 142 families). Of the several loci studied, two intragenic markers for the angiotensin II receptor type-1 ( $AT_1$ ) showed some evidence for linkage. A closer examination of this gene locus was carried out using subsets of non-obese sib pairs with early onset of hypertension and uniform geographical origin. Upon these stratifications, we obtained suggestive evidence for linkage of hypertension to the area containing the  $AT_1$  gene with a multipoint lod score of 2.7. A genetic association study showed an increase in the frequency of the A1166->C allele of the  $AT_1$  gene in the hypertensive individuals. Sequence analyses of the coding region and 848 bp of promoter region in the DNA sample on eight index samples revealed a novel polymorphism of the  $AT_1$  promoter region which also associated with hypertension. In a novel variant of model-free multipoint linkage analysis allowing linkage disequilibrium in the calculations a lod score of 5.13 was obtained. We proceeded to a genome scan in 47 hypertensive twin sibpairs with similar strict phenotype as described above, scanning the genome with 10 cM map of highly polymorphic markers. The results of the genome scan are currently under analyses.

## 101

## TWIN PAIR CONCORDANT FOR DOWN'S SYNDROME (DS)

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In honor of Prof.Marguerite M. Tichomirova.

In St.Petersburg the frequency of DS is 14 per 10000 live births. The frequency of multiple pregnancies is at least 1 per 90 or 1 per 100. Expected probability of twins with DS is at least 14 per 1,000,000 live births. During 1985-1995 there were 79 children with DS in our PCH. In this group only one twin pair from nonconsanguineous parents was born to a 19-year-old mother (Rh-) and a 19-year-old father (Rh+); (mother's fourth pregnancy and the first delivery). The pregnancy was uncomplicated and delivery was normal and spontaneous at 39 week's gestation. At birth weight of the first girl was 2,73kg (>10th and < 25th centiles), her length was 46cm (<3d centile );weight of the second girl was 2,5kg (>3d and <10th centiles), her length was 45cm (<3d centile ). Apgar index for both sisters was 8/8 Their blood groups were the same O(I)Rh(+). DS of the twins was noted neonatally.

They were admitted to our PCH at 11 days of age.Classic cytogenetic culture of peripheral lymphocytes of the twins revealed identical karyotypes 47,XX+21. At 3 months of age the first girl suffered from acute bronchopneumonia. At 14 months of age she was taken away by her mother.

The second girl suffered from acute pneumonia at 27 days of age and died at 3,5 months of age. An autopsy showed confluent pneumonia, ventricular septum defect in the child with DS. There were some similarities between the clinical features in our MZ twins.

## 103

## A NATIONAL SURVEY OF MULTIPLES IN SCHOOLS IN ENGLAND

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Pat Preedy is Head Teacher of Knowle Primary School. In 1992 nine sets of twins started school prompting Pat to consider the educational needs of multiples and their families. With the support of TAMBA she began a major study for her Ph.D at the University of Birmingham.

A major part of the study was designing a questionnaire suitable for schools. Nearly 3 000 schools took part in the survey producing data from 11 878 twin children, 351 triplet children and 5 sets of quads.

The survey particularly investigates the reasons why educators separate multiples or keep them together and the particular issues that they think are important when educating multiples.

Many schools adopt rigid strategies with regard to multiples whilst failing to consider the issues within the school's aims, objectives and policies. This led to the development of a framework policy that can be adapted for school use.

## 102

## POSTNATAL DEPRESSION AND TWIN BIRTH

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The authors have noted that the existence of a postnatal depression after a twin birth has not been extensively studied. Cox's self-questionnaire (1994) was never used for this detection in the case of twin birth. The hypothesis of the authors is that the difficulty for the mother to differentiate the twins represents a sign of depressive suffering. The population is composed of 300 new mothers of healthy children. Three groups: mothers of singletons, mothers of dizygotic twins and finally, mothers of monozygotic twins. Two self-questionnaires are sent to the mothers of twins, three months after birth: 1) The zygosity questionnaire (differentiating the twins) (Charlemaine, 1997). 2) The "EPDS" (Edinburgh Postnatal Depression Scale) (Cox, 1994). The mothers of singletons receive only the "EPDS". Not only does the study show a correlation between postnatal depression and the difficulty of differentiating twins, but also that postnatal depression is more prevalent when twin births occur.

## 104

## DO MULTIPLES START SCHOOL AT A LOWER POINT THAN SINGLETONS? DO THEY MAKE LESS PROGRESS?

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This paper considers cognitive differences between twins and other higher multiple births (TAMBs) when they start school and their progress in reading and mathematics.

The data is from the Performance Indicators in Primary Schools (PIPS) project which has developed an on-entry assessment designed to provide a solid base against which the relative progress (Value-added) of pupils can be measured.

Teachers were also asked to assess pupils on the Attention Deficit Hyperactivity Disorder (ADHD) scale at the end of the first year in school. This information was used to check out an earlier finding that twins were more prone to score highly on this scale.

The PIPs project collects data on multiples every year. Not only are new cases being added to the database but it is intended to follow these pupils for several years providing unique and exciting data about the progress of TAMBs in school.



## 105

## EMPLOYMENT &amp; LIFESTYLE WITHIN FORMER EAST/WEST-GERMAN PREGNANCIES: AN EPIDEMIOLOGICAL TWIN MODEL

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**OBJECTIVE:** To examine the impact of lifestyle, work conditions and employment within former East- (GDR) and West-(FRG) Germany before the reunification between 1987 and 1990.

**METHODS:** Out of 4043 (GDR) and 3946 (FRG) pregnant women 3070, resp. 3374 data sets were analyzed after exclusion of cases with missing values, twins or stillbirths. Odds Ratios (OR, 95%-Confidence Interval, 95% CI) of multiple parameters were evaluated.

**RESULTS:** East-German mothers were younger than West-German mothers (mean: 23 vs. 27 years). In West- compared to East-Germany there was a higher percentage of smoking mothers (21% vs. 12%), and an overall lower percentage of working mothers (58% vs. 87%), though the differences within nulliparous pregnant women were small (82% vs. 89%). In East-Germany the differences between working mothers with different parity was relatively small (85% for primi- and 78% for multiparous women), whereas in West-Germany the proportions were significantly smaller: 38% resp. 26%. All differences described above reached statistical significance (chi-square-Test). In West-Germany there was a 1.4 higher risk for working mothers to deliver a small-for-gestational-age infant (OR = 1.4; 95%-CI: 1.1-1.7), no significant association was found for East Germany. After adjusting for smoking, parity and age using multiple logistic regression the association was also not longer found for West German women.

**CONCLUSIONS:** The major differences between the East- and West-German mothers reflect the somehow controversial social and health care policies of the former GDR and FRG. The impact on outcome parameters is further analyzed and will be discussed.

## 107

## HAY FEVER AND ASTHMA IN ADOLESCENT FINNISH TWINS: GENETIC LIABILITY AND PERINATAL FACTORS

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FinnTwin16 is a longitudinal study of five consecutive birth cohorts of Finnish twins, their siblings and parents. During 1991-1994, 2483 families with 16-year-old twins (opposite-sex pairs included) were mailed questionnaires about health and habits of the twins and their parents including questions on the birth of the twins, and doctor-diagnosed hay fever and asthma (response-rate 81%).

Hay fever was more often reported in boys (14.1 %) compared to girls (10.0 %) but there was no difference between zygosity groups. MZ twin pairs (probandwise concordance rate 60%) were more concordant for hay fever than DZ twin pairs (32 %), whereas there was no difference between opposite-sex (30%) and like-sexed (34%) DZ twins. Corresponding data for asthma is reported by Laitinen T. & al. in *Am Rev Respir Crit Care Med* 1998; 157(4).

In twins with at least one parent with hay fever, heritability for hay fever was 77 %, whereas in twins with unaffected parents, it was 67 %. The variation in shared family environment accounted for at most a modest part of the variability in liability to hay fever (0-13%). However, large number (3 or more) of older siblings protected against development of hay fever but not against asthma.

In twin pairs discordant for asthma (135 pairs), there was no intrapair difference in either birth weight or length. Gestation, Apgar score or hospitalisation due to neonatal pulmonary disease did not predict, either, an increased risk of asthma or hay fever.

Our data show high heritability of both asthma and hay fever with little influence of perinatal factors on the occurrence of these traits at adolescence.

## 106

## SPECIFICITY OF MZ AND DZ TWINS' DEVELOPMENT: CURRENT RESULTS FROM A LONGITUDINAL STUDY

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The longitudinal study of infant twins is conducted using the Bayley Scales of Infant Development (BSID-II) with the aim to reveal biological and psychological determinants of early development. Twins are tested at the ages of 4, 8 mo, 1, 2, and 3 years. We analyze the data of mental and psychomotor scales of the BSID in details by grouping them in subscales. The results confirm that twins are a group of biological and psychological risk. The mean MDI and PDI of our twins sample are about 85-90 approaching the age norms only by 3 years. The compensation of biological risk happens also at the age of 3 years. There is a specific dynamics of the compensation which is different in MZ and DZ twins: correlation of birthweight (especially) and gestational age on one hand and MDI on the other hand in MZ twins remains significant from 4 mo to 2 years, while in DZ twins we observe the only significant correlation at 4 mo, then the correlations become insignificant. Factor analysis of subscales indexes also shows that there are different factor structures in MZ and DZ twins samples which implies some differences in "traces" of their development through the studied ages. It also supports the compensation of biological risk by 3 years (biological variables become isolated factor). At the age of 3-3.5 years we nevertheless observe selective delays in development of higher functions such as classification, self-identification, intersensory integration.

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## FLUCTUATING ASYMMETRY AND BEHAVIORAL RESEMBLANCE BETWEEN MZ CO-TWINS AND THEIR OFFSPRING

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In a previous report (Rose, et al, *Behavior Genetics*, 1987) and replication (Bogle et al, *Behavior Genetics*, 1994), MZ cotwins asymmetric for a palmar dermatoglyphic measure were less alike than concordantly symmetric pairs for personality scales. Recently, Furlow et al (*Proc. R. Soc. Lond*, 1997) reported that an index of fluctuating asymmetry (FA), assessed with anthropometric measures, correlated with IQ test scores. Does FA index genotypes susceptible to random environmental influences on personality and IQ? We sought an answer in re-analyses of data previously collected, on kinships of MZ twin parents. The data set includes >50 pairs of MZ twins, their spouses, and >250 of their offspring, forming sibships and genetic half-sibships, with results for cognitive tests (e.g., WAIS/WISC Subtests, ETS tests of perceptual speed and spatial ability) and 12 bilateral anthropometric measures (e.g., length of arm, foot, hand, and mid-finger, etc). First results yield no evidence that FA is heritable (non-significant correlations for FA in MZ twins), nor do we obtain significant correlations between FA and IQ test scores across individuals (no confirmation of Furlow, et al). Average FA of twin and sibling pairs correlated with their absolute intra-pair differences for one IQ subtest, but that association was not found for other subtests, and additional analyses are planned.

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## IS NORMAL ADOLESCENCE IN TWINS THE SAME AS THAT OF SINGLETONS?

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It has been shown (Sandbank 1988) that twins differ from singletons in the way that they relate to their parents. Given their unique relationship from conception it is not to be expected that the process of separation would mirror that of singletons or even that the process would always run smoothly.

The author looks at some of the more tragic twin cases that have been reported in the British press in order to look at how and why the journey through adolescence can go so badly wrong.

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## TWIN-MALE WITH de GROUCHY'S SYNDROME

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We report on a twin-male with severe developmental delay and karyotype 46,XYdel(18)(p11). Twin-brothers were born after 4-th pregnancy from nonconsanguineous parents. Both parents suffer from chronic alcoholism; mother is registered in a psychoneurologic dispensary.

The proband was referred to us from a psycho-neurologic children's hospital in connection with adoption of the twins. At a clinical examination at 37 months of age his height was 74 cm (<3d centile), his weight was 8,3kg (<3d centile). Our proband had multiple dysmorphic features: asthenic constitution, long face, short neck, epicanthic folds, flat broad nasal bridge, macrotia, ears de-formed and sticking out, microretrogenia, high-arched intact palate, chest deformed with short sternum, hypertelorism of nipples, upper brachymelia, brachydactylia, clinodactyly Y, nails'dysplasia, talipes valgus bilateral, wide separation between the 1st and 2nd toes, bila-teral cryptorchism, severe mental retardation and speech disturbance like babbling.

Classic cytogenetic culture of peripheral lymphocytes revealed a 46,XYdel(18)(p11). Clinical symptoms and laboratory investigation were in agreement with de Grouchy's syndrome.

At the same age his twin-brother had only mild mental retardation without multiple dysmorphic features. Discordance of twin-brothers at 5,5 years of age was more manifest and obvious.

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## PSYCHOTHERAPEUTIC REHABILITATION OF MZ TWIN A VICTIM OF SEXUAL ABUSE.

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In honour of Gregory I. Korchanov.

We report on MZ twin-female, 16-year-old, who took medical advice on her own after episode of sexual abuse. At the first doctor's advice she was emotionally depressed. She was apprehensive but cooperative. Patient's complaints were insomnia, apathy and indifference, indolence, tearfulness. From time to time she had suicidal reflection and thoughts.

Her mother and her MZ twin-sister showed highly correlated indices of personal-psychologic characters. These facts were used for *intrafamily* psychotherapy and MZ sister of our client played the role like a psychotherapist. We used psychotherapy referred to this person and mild drug therapy with great success. In 8 months our client did not have any negative symptoms.

Resume. 1. MZ twins have maximum solidarity of psychomotional experience.

2. Psychological tests show that MZ twins are highly concordant in their personal characters.

3. *Intrafamily* form of psychotherapy may be used for psychic treatment of one of the MZ twins with positive results.

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## DECREASE IN GRIEF FOR DECEASED TWIN AND NON-TWIN RELATIVES: AN EVOLUTIONARY VIEW

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Based on evolutionary reasoning we hypothesized that:

1) Fraternal twins would show greater reduction in grief intensity than monozygotic (MZ) twins for their deceased co-twins, 2) female twins would show less reduction in grief intensity than male twins for their deceased co-twins, and 3) twins would show less reduction in grief intensity for deceased co-twins than for other deceased relatives. Using a 7-point scale, 175 bereaved twins assessed their grief intensities as recalled 1-2 months after the loss and currently. Decrease in grief intensity was significantly greater for DZ twins than for MZ twins, as expected, although significant gender differences were not found. Participants also evidenced significantly less decrease in grief for deceased co-twins than for other deceased relatives. The implications of these findings for an evolutionary theory of bereavement are discussed.

Specifically, smaller change in grief for MZ than DZ twins, and for twins than nontwins, is consistent with the view that genetic commonality contributes to close social relations between relatives.

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## MOSCOW LONGITUDINAL TWIN INFANT STUDY

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We carry out the longitudinal study of infant twins from 3 to 42 months of age (22 DZ - 11 female and 11 male pairs and 16 MZ - 7 female and 9 male pairs) from 1994. The tests were made in the following age intervals: 3-5, 7-8, 11-12, 18, 24, 30, 36 and 42 months. In present time we have done 141 tests of twin pairs (282 tests of infants). The aim of this study were to evaluate the mental, motor, behaviour development, to assess the temperament and family attitude. We use the Bayley Scale of Infant Development (the second edition) and Ballerger Test of Infant Temperament "Baby Day". Data showed, that  $h^2$  of MDI was 0.13 in 1 year, 0.62 - in 2 years and 0.09 - in 3 years. Relatively  $c^2$  - 0.77 in 1 year; 0.27 - in 2 years and 0.84 - in 3 years. Twins have the peculiarities of the mental development, that could be expressed by asymmetry of the mental developmental dynamic. MZ twins demonstrated more dependence and the duration of mental development from biological factors. Twins had the poor control their inner tense and behaviour, because they had overflow of high tense. MZ were more desadaptive than DZ. We found unstable infant temperament in all ages.

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## GENETIC AND ENVIRONMENTAL INFLUENCE ON ALLERGIC VERSUS NON-ALLERGIC ASTHMA AMONG DANISH TWINS.

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The aim of this study was to compare the relative influence of genetic and environmental factors in the aetiology of allergic versus non-allergic asthma.

The classic twin study design was used to analyse data on self-reported asthma obtained by means of a mailed questionnaire to 34,076 individuals from the 1953-82 cohort of the nationwide Danish Twin Register. Asthmatic subjects were classified as allergic or non-allergic phenotypes due to the presence respective absence of concomitant hayfever and/or atopic dermatitis.

The cumulative incidence of allergic asthma (3.3%) was significantly higher than non-allergic asthma (2.6%) among 8,351 monozygotic (MZ) and 10,356 like-sex dizygotic (DZ) twin individuals. Only allergic asthma showed a significant trend across the cohort being more common in the younger age groups. The probandwise concordance rates and tetrachoric correlations for both allergic and non-allergic asthma were substantially higher in MZ compared to DZ twins ( $p < 0.001$ ). Biometrical modelling showed that a model including additive genetic and non-shared environmental effects provided the best overall fit to the data for both phenotypes. The estimated heritability in liability for allergic and non-allergic asthma was 0.77 ( $CI_{95\%}$ : 0.47-0.83) and 0.68 ( $CI_{95\%}$ : 0.42-0.76) respectively.

The results emphasize a major influence of genetic factors in the aetiology of both allergic and non-allergic asthma. Still, a substantial part of the total variation in liability to both phenotypes is due to non-shared environmental influence.

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## MATERNAL CHARACTERISTICS OF WOMEN DELIVERING NATURALLY CONCEIVED TWINS IN SOUZHOU, CHINA: PRELIMINARY OBSERVATIONS

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**Objectives:** To study maternal demographic characteristics of women delivering naturally conceived twins in Souzhou, China.

**Materials and Methods:** Data obtained by a single physician from original patient records at Souzhou Medical College, #1 Hospital was recorded onto a form in Mandarin for transliteration into English. Quantitative assessments and correlations were made.

**Results:** 58 records were reviewed. Mean maternal age was 25.2 yrs (range 21-29) for all but 2 cases. More mothers were 25-29 yrs (53.6%) than 21-24 (46.4%). Most resided in rural (46.4%) or urban (44.6%) areas; only 8.9% in suburbs. Of 27 reporting data, there were 4 viable births, 3 miscarriages, 2 premature births and 27 abortions. The pregnancy rank order was 1 (48.3%), 2 (34.5%), 3 (15.5%) and 4 (1.7%). 95.9% of mothers were gainfully employed: factory workers 35.4%, agriculture workers 33.3%, office workers 14.6% and service sector 12.5%. Prenatal visits varied from none in 32 women to 8 or more in 8 women. 25 urban mothers had 80, 5 suburban mothers had 12 and 26 rural mothers had 17 visits. Menarche was similar in urban, suburban and rural (14.5-15 yrs).

**Limitations:** Information regarding the infants was not transmitted with maternal data for reasons that are under investigation.

**Comments:** These data represent preliminary observations in an ongoing study of the natural twinning process in Chinese women of Han nationality residing in the coastal plain. Little information exists in the Chinese medical literature available to researchers using standard computerized bibliographical search engines.

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## TESTING SCHOOL EFFECTS USING A CLASSICAL TWIN MODEL EXTENDED TO INCLUDE CONTROL PAIRS

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The aim of this study is to apply a classical twin model to data collected for MZ and DZ twin pairs and control pairs in the same classes in the Swedish compulsory school. By doing this we are able to decompose the shared environmental variance into home and school variance. Our sample is taken from the fourth, fifth and sixth grades and on average the pupils are 12 years old. The number of MZ pairs is 29 and the number of DZ pairs is 35 with an equal number of controls for both groups. The instruments used are the Raven Progressive Matrices, a vocabulary test, a reading comprehension test and an arithmetic test. A comparison can be made of school and home environmental influences for twins separately and for twins and controls. In addition this can be done for the four different tests, which have different profiles concerning the importance of genetic, home and school influences. The school effects are moderate. Preliminary results indicate that they do not give a significant model improvement in most cases, if the genetic, home and non-shared environment effects are already in the model. The reason for lacking significance may very well be that our sample is quite small. However we think it is possible to do a preliminary investigation of some genetic models for twin-control data using this dataset.

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ESTABLISHING A POPULATION-BASED REGISTER OF MIDDLE-AGED TWINS IN DENMARK.

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The Danish Twin Register was established in the middle of the 1950's and initially it covered the period 1870-1930. During the last decade birth cohorts from 1953-94 have been included. Here we present the ascertainment of twins from the intermediate birth cohorts, 1931-1952, hereby bringing the Danish Twin Register to comprise more than a century of twin births.

The new twin cohorts were identified by use of the Danish Civil Registration System (CPR) and the Death Register at DIKE. Identification of twins was based on the fact that almost all twins are: a) born on the same date, b) born in the same parish, and c) given the same surname at birth. A search in CPR extracted all persons, who fulfilled those conditions. For persons who died before introduction of the CPR System (1 April 1968) information from the Death Register was used.

Confirmation of the twin status was obtained by a mailed one-page questionnaire which also included questions on birth weight, parents' age and vital status, and for twins questions on similarity in order to determine the zygosity of the twin pair. Approximately 11,000 twin pairs have been identified so far, with more than 6,000 intact pairs, where both twins have accepted to participate in further studies.

Hereby the Danish Twin Register covers all birth cohorts from 1870 to 1994 with more than 100,000 twins are included. From childhood to the oldest-old the register constitutes an exceptional valuable source for twin studies.

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THE GENETIC INFLUENCE ON THE AUGMENTATION OF THE AORTIC PRESSURE WAVE IS INDEPENDENT FROM THE EFFECTS OF AGING, BLOOD PRESSURE AND BODY HEIGHT.

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The augmentation index (AI), defined as the ratio of augmented systolic pressure to the pulse pressure, is an index of pulsatile load on the heart and has been shown to be an independent determinant of left ventricular hypertrophy. This elevation of central systolic pressure as indexed by the AI has been attributed to peripheral wave reflection. Important determinants include age, height and mean arterial blood pressure (MAP). We investigated whether AI is influenced by genetic factors and to what extent this influence was dependent on the effects of age, height and MAP.

AI and (central) MAP were based on the central aortic pressure wave derived from the radial waveform as measured by applanation tonometry. The subjects were 145 monozygotic and 332 dizygotic female twin pairs aged 18-73 years. A multivariate path model (Cholesky decomposition) including height, MAP, AI and age was used to analyse the data. Intraclass correlations for AI were 0.65 in MZ and 0.39 in DZ twin pairs, indicating a substantial genetic influence. As expected taller women had a lower AI ( $r = -0.26$ ), whereas the AI was positively correlated with age ( $r = 0.50$ ) and MAP ( $r = 0.36$ ). In the best fitting multivariate model 35% of the variance in AI was determined by genetic factors (of which 7% was due to genes in common with MAP and 1% to genes in common with height), 40% was due to unique environmental variation (of which 1% was due to environmental influences in common with MAP and 2% to environmental influences in common with height). The rest of the variation in AI (25%) could be attributed to the effect of age. The heritability of AI adjusted for age, height and MAP was 0.43.

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THE SOCIAL ANALYSIS OF TWINS

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The principal argument of this presentation is that twinship is an irreducibly – although not exclusively – social phenomenon. The author applies various social analyses to illuminate twinship as a social phenomenon. Variables such as gender, age, birth order and socio-economic status are considered, along with the role of different patterns of socialisation as these affect twinship. The role of the twin as distinct from the role of the non-twin is examined: to a very large extent, from conception, through gestation, childbirth and subsequently childhood and adolescence, the social processing and regulation of social members take place in unitary terms. Twins (and higher multiples) are an anomaly to such processes. Cultural expectations of twinship in terms of similarity of identity and similarity of behaviour are measured according to cultural archetypes of twins. How twins react to stigma, stereotyping and labelling are explored as an integral aspect of the social structuring of twinship. The structure of the 'self' and the subsequent or concurrent process of differentiation between twins are also examined. The argument concludes with suggestions for further areas of investigation.

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IS ORAL CONTRACEPTION (OC) AN AETIOLOGICAL FACTOR FOR TWINNING

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The decline in the twinning rates over the past forty years have been attributed to a decrease in maternal age and parity and the use of OC. To investigate use of OC in relation to twinning we studied a well defined population of Danish twin mothers with twin zygosity determined from blood samples and data on use of OC collected prospectively.

Design: Retrospective case-control study of women giving birth in 1980-1989 in a well defined geographical area.

Subjects: 399 twin mothers and 780 singleton mothers.

Main outcome measures: Odds ratio (OR) for twinning with 95% confidence interval (CI).

Results: ORs for twinning after use of OC.

Zygosity	OR	95% CI
All twins	0,86	(0,67-1,10)
DZ twins	0,79	(0,58-1,09)
MZ twins	1,03	(0,72-1,48)

None of the ORs are significant. Adjustments for confounders (age, parity, height and weight) by multiple logistic regression did not change the overall results.

Conclusions: The present study indicates that use of OC does not influence on twinning.



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## THE RELATIVE IMPORTANCE OF GENETIC AND ENVIRONMENTAL INFLUENCES ON AGE AT MENOPAUSE.

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Knowledge of the factors that influence the timing of menopause has important clinical implications. Early menopause is associated with an increased risk of cardiovascular disease, osteoporosis and ovarian cancer, whereas delayed menopause is associated with a higher risk of endometrial and breast cancer. Environmental factors, except for tobacco smoking, have failed to show independent influence on the age at natural menopause. Family history has been implicated as a predictor of early menopause. The aim is to 1) quantify the relative importance of genetic and environmental influences on age at menopause, 2) explore the association between age at menopause and lifestyle factors. The data are from a study of twins reared apart and together from the Swedish Adoption/Twin Study of Aging (SATSA) and a pilot study of complex diseases, both based on the Swedish Twin Registry. The results show both genetic and rearing environmental effects as sources of familial similarity for age at menopause. Environmental factors appear to be of greater importance than genetic influences for variation in age at menopause. There were significant differences in menopause dependent on smoking status: onset of menopause was delayed for current smokers. There is a need to explore further the implications of environmental factors on age at menopause.

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## ESTABLISHING A TWIN REGISTER IN SRI LANKA

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Background: Nearly all Twin Registers are based in developed countries and there is no Twin Register in the developing world. Objectives: To initiate the process of establishing a nation-wide Twin Register in Sri Lanka by starting a volunteer register first and working towards a population based register. Methods: Regular news paper advertisements, feature articles, radio talks, and television programs were used to publicise a competition for twins, their parents/relatives and friends requesting them to participate by sending in details of twins. Competition took place from 28/3/97 for a period of 3 months. It offered prizes for 3 winners selected by drawing lots. Advertisements highlighted the objective of the competition as establishing a twin register for future research and emphasised that informed consent would be obtained for individual research projects. Although others have previously used media publicity to enroll twins in twin registers, to the best of our knowledge this is the first time that a competition was used. Results: 4374 Twin Pairs (Same Sex: Male 1327, Female 1610. Different Sex 1118, Sex to be verified 321); 80 Triplets (Same Sex: Male 16, Female 24. Different Sex 39, Sex to be verified 1) and 2 Quadruplets (Different Sex) have registered. The oldest Twins, Triplets, Quadruplets are 80, 46, and 5 years old respectively. 75% of Twins, 85% of Triplets, and all quadruplets are less than 25 years old. Zygosity determination will be done shortly using the questionnaire method. This will be followed by several projects. Conclusions: Establishing a Twin Register for research purposes is possible in a developing country.

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## PSYCHO-SOCIAL ISSUES OF ASSISTED MULTIPLE BIRTH CONCEPTION

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The study was confined to social problems arising from the conception of twins or higher order multiples following assisted conception treatments. A review of the literature revealed that multiple pregnancy was frequently described as a "side-effect" of these treatments which contributed significantly to the professional and social evaluation of the programs. The problems described were categorised to determine those which could be addressed within the confines of a voluntary organisation.

The material recommended by the Australian Fertility Society for inclusion in packages available to parents considering assisted conception treatments was reviewed to determine the nature of that specifically directed to multiple birth. This was considered to be inadequate in regard to disclosure of the frequency of conception, risk factors of pregnancy and birth and the impact of a multiple birth on the family. Women participating in IVF and GIFT programs were interviewed to determine the influence of the multiple birth information over their decision to participate in the treatment. This was found to be minimal.

To compare Australian material with that available from other countries a search of the literature for information about selective reduction of multiple foetus' was undertaken, focusing on that available to couples to assist them in their decision making. The paucity of information available initiated a survey among couples who had faced this decision to determine the degree of disadvantage this lack incurred. The outcome of the survey precipitated interviews with medical and paramedical personnel and mothers who had chosen either to reduce or not to reduce the multiple pregnancy. These interviews resulted in the production of literature for the use of both Fertility Clinics and inquiries directed to the Australian Multiple Birth Association for information about the psycho-social aspects of assisted conception treatment and those of selective reduction.

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## AGE AND GENDER DIFFERENCES IN GENETIC AND ENVIRONMENTAL FACTORS FOR SELF-RATED HEALTH

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The more Self-Rated Health (SRH) is proved to be a predictor for future health status and mortality the more important it is to understand what constitutes SRH. The aim of this study was to evaluate the factors of importance for SRH in a sample of 554 pairs of twins, monozygotic, dizygotic, like- and unlike sexed. Specific research questions are: 1) What are the sources of individual differences in SRH? 2) Are there gender and age differences in genetic and environmental influences on SRH? The inclusion of opposite sexed twins facilitates distinguishing between differential heritability in males and females versus gender-specific genetic and environmental effects.

Older participants tend to rate their health less positively than those below 55 years of age and there is an increase in total variance with age. Most of the variation in the younger cohort (17-54 years) is attributable to the influence of non-shared environments. Genetic variance was substantially greater in the older cohort (55-82) for both men and women, however, the increase in total variance for women also reflected an increase of non-shared environment. No significant gender differences were found. Common findings of mean differences between gender do not seem to reflect gender differences in variance. These findings, based on cross-sectional data, suggest that SRH must be considered in the context of an individual's age.

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RECURRENT HEADACHES AMONG YOUNG TWINS Dan A Svensson\*, Bo Larsson, Bo Bille and Paul Lichtenstein. \*Division of Genetic Epidemiology, Institute of Environmental Medicine, The Karolinska Institute, Box 210, 171 77 Stockholm, Sweden. Fax. +46 8304571. E-mail: dan.svensson@imm.ki.se

Non-symptomatic headache is a common health problem. Prevalence is highly dependent on age and gender, with an increase in magnitude from childhood to middle age especially among females, and familiarity appears to be a risk factor. Data from adult twin samples relate self-reported migraine to roughly equal parts of genetic variation and non-shared environmental effects.

We have analysed environmental and genetic influences on recurrent headaches in a Swedish twin cohort of children 8 to 9 years old based on parent reports from a mailed questionnaire (N=1023 pairs). Diagnosis of migraine and tension headache was based on items covering most of the IHS criteria. A total of 265 twins screened positive for recurrent headache (39 concordant and 187 discordant pairs) and no apparent sex difference in prevalence was observed. The results of model fitting analyses showed that approximately two thirds of the liability for recurrent headache could be explained by genetic variation and about one third by non-shared environmental influences. A general sex-limitation model showed a significant better fit than a common effects sex-limitation model, suggesting that a different set of genes are involved in the etiology of recurrent headaches in the two sexes. When migraine and tension headaches were analyzed separately a genetic effect was seen in both subtypes. In addition, evidence was found for a shared environmental effect in girls. We conclude that genetic variation is important for recurrent headaches also in children and that there might be different etiologies for boys and girls.

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THE CHANGES OF INTRAPAIR SIMILARITY IN IQ DURING PUBERTY \*

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The aim of this study was to analyze the connection of the pubertal changes and the heritability of IQ. The sample consisted of 84 pairs of monozygotic (MZ) and 64 pairs of dizygotic (DZ) twins, aged 13-14 and their mothers. Twins performed WISC, aimed to test their IQ, while their mothers answered the questionnaire, devoted to the revealing of maturational rate (pubertal changes) of their children.

All twins pairs were divided into 3 groups according to the maturational rate 1) children in pre-puberty; 2) children at the beginning of pubertal changes and 3) adolescents with apparent pubertal changes. While MZ twins, as it was expected, reached the same maturational rate simultaneously, the age of pubertal changes of the members of DZ pairs often distinguished. So, the fourth group was defined (DZ twins, having some differences in the maturational rate). The intrapair correlation in IQ was 0.77 for MZ (rMZ) and 0.62 for DZ (rDZ) twins, measured for all the sample. For the first group rMZ= 0.664, rDZ=0.567; for the second rMZ= 0.682, rDZ=0.672; and for the third rMZ= 0.833, rDZ=0.698.

Therefore one can see that: 1. the level of intrapair similarity in IQ grow up almost linear both in MZ and DZ pairs as twins pass through puberty; 2. the minimum value of intrapair similarity were obtained among DZ twins with nonsimultaneous pubertal changes (about 0.5); 3. the second group MZ and DZ twins had no significant differences in intrapair similarity. Obtained data are interpreted basing both on social and biological hypotheses (similarity of social or biological changes gave more similarity in IQ).

\* Data of the Moscow Longitudinal Twin Study

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A MULTIVARIATE ANALYSIS OF WELL-BEING AND SYMPTOMS OF ANXIETY AND DEPRESSION AMONG TWINS  
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Data from 2 486 pairs of MZ and DZ twins on eleven questionnaire items pertaining to anxiety (Fearful, Tense and keyed up, and Nervous, Sleeping problems), depression (Hopelessness, Feeling blue, Worried), or well-being (Overall life satisfaction, Feeling weak or strong, Feeling sad or happy, and Loneliness) were entered in a multivariate analysis. Preliminary results showed that a common genetic factor explained 25 to 50 per cent of the variance for each item with the exception of sleeping problems (16 per cent). A common factor for environment shared by cotwins contributed to the variance for the anxiety items and some of the well-being items (typically between 10 and 20 per cent). Two common factors were specified for nonshared environment. The depression and well-being items loaded highest on one of these factors, and the anxiety items loaded on the other. Genetic effects specific for each item varied between zero and 17 per cent of the variance for all items except for sleeping problems (25%). Estimates of nonshared environmental factors specific for each single item, which to a large extent reflect measurement errors, typically ranged from 20 to 45 per cent of the variance.

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ATTACHMENT QUALITY, MENTAL HEALTH AND DEVELOPMENT OF FINNISH TWINS

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In this longitudinal study the toddlers' attachment quality was analyzed to both parents. Altogether 85 children (58 twins and 27 singletons) participated the Strange Situation Test (SST, Ainsworth) at the age of 18 months. The attachment quality was assessed by the method for preschoolers (PAA, Crittenden) and was classified to four patterns: A (avoidant), B (secure), C (coercive) and D (disorganized).

At the age of 36 months the toddlers' IQ was tested by the Stanford-Binet-test, and at 48 months the Children's Behavior Check List (CBCL, Achenbach) was filled in by both mothers and fathers separately.

The connections between attachment, development and mental health will be presented.

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**SLEEP APNEA (SA): AN INHERITED SYNDROME?**

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We review the evidence for inherited determinants of SA, a common chronic syndrome of major socioeconomic import. As expected, research was initiated by reports of families rife with SA that was often independent of obesity. The concordance/aggregation of symptoms of SA (e.g., snoring) has been demonstrated in Finnish MZ twins, in adult male participants in a prospective cardiovascular study and their family members, and in families with a proband with proven SA. Monitoring for increased apnea-hypopnea index (AHI) has provided quantitative corroboration. In the Cleveland Family Study, for example, odds ratios (ORs) for liability for SA in 1<sup>st</sup> relatives of probands was 2-5 relative to control families. ORs remained significantly >1 after adjusting the data for age, sex, race and body mass index, and varied directly with the number of affected family members. Parent-offspring and sib-sib correlations for AHI, adjusted in the same manner, were significant (0.17-0.18), yielding an  $h^2 = .42$ . The identifiable intermediate phenotypes in familial SA include age, race, sex, body habitus/obesity (some 7 candidate gene loci have been identified), craniofacial and upper airway morphology (genetic basis highly likely), control of ventilatory responses (especially to eucapnic hypoxia), presence of certain inherited syndromes (e.g., Prader-Willi, idiopathic congenital central hypoventilation), and anomalies of nerve/muscle/connective tissue function (e.g., Marfan syndrome). Twin studies have aided in determining the role of inheritance of many of these. We believe that the endogenous factors governing SA include genes controlling some of these intermediate phenotypes, and also other genes influencing respiration more directly. A number of candidate genes of the latter type can be identified, some (e.g., endothelin-3, brain-derived neurotrophic factor, RET proto-oncogene) already associated with abnormal respiratory control. Current efforts are directed toward genome mapping, with special emphasis on associations with candidate genes. Genes that are found to underlie SA may also be important in sudden infant death syndrome, which may be aggregated with SA.

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**'TWINS PARADOX': TOWARDS THE PROBLEM OF MUSICAL EDUCATION**

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The problem of "twins-situation" is an old enigma in paedagogics and psychology. The twin-situation reproduces principal regularities of human thinking development with its paradoxes and contradictions. The author has revealed some regularities in the development of twin children 5-14 years old at music school, showing that a twin pair is some kind of compressed spring of contradictions requiring to be studied together and not in separation. Twins, strange as it may seem, have quite different sets of emotional and psychological features. When nursed together (common case of family nursing), they display unpredictable (creative) characters of their nature and so make think them not identical indeed. Their emotional life is especially different, as revealed from their aesthetic tastes and preferences. In paedagogical practice, both family and institutional, a first difficulty is our inconspicuous identification of the twins under education. This mistake is very common and has many variants. The twins begin to protest against the identification very soon, and the situation risks to lead to unpredictable, even pre-stress behaviour. It is important that the twins under teaching may not be ranked in any way. Twins-situation clearly demonstrates that "every child is gifted" indeed. To create imaginary oppositions in living young people is a fatal kind of mistake. Unfortunately we know well that the mistake is quite common in education as such, not only music teaching, and is generally harder in earlier education, when erroneous ranking of children as more and less talented comes commonly from only adults' interests and is not based on children's real capabilities. How many artistic talents were killed in those passion motions, so far standing from real interests of children.

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**GENETIC INFLUENCES ON ENDOMETRIOSIS IN AN AUSTRALIAN TWIN SAMPLE**Susan A. Treloar and Nicholas G. Martin  
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Endometriosis is a gynaecological condition associated with marked morbidity from pelvic pain, menstrual disturbance and possible fertility problems. Increased prevalence in first degree relatives of sufferers of endometriosis has been reported by a number of studies, suggesting a familial predisposition.

Questionnaires were sent to 1,570 female twin pairs and 156 individual female twins (3,300 individuals) from a cohort of 1,979 female pairs obtained originally in 1980-82 from the Australian Twin Register. Validation of endometriosis self-report was sought where possible from a nominated specialist involved, a GP involved in treating their endometriosis, or from hospital or pathology record.

We obtained a 90% pairwise response, and a total of 3,096 individuals including incomplete pairs. 215 twins reported endometriosis, a self-reported prevalence rate of 0.07 amongst question respondents. Comparison of twin and medical reports indicated few false positive self-reports.

The ratio of MZ ( $r = 0.46 \pm 0.09$ ) to DZ ( $r = 0.28 \pm 0.13$ ) tetrachoric twin pair correlations for self-reported endometriosis suggested the contribution of additive genetic influences to risk of endometriosis in twins aged 31 and over in this sample.

Concordances for validated endometriosis supported this finding.

The project has led to a current linkage study of endometriosis by an Australian Collaborative Research Centre for Discovery of Genes for Common Human Diseases, of which we are part.

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**THE TWINS WITH TRISOMY X.**Vassilkova I.V., Pantova I.G., Shandlorenko S.K.  
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Two girls-twins are ten years old. The parents are apparently healthy. The mother was 36 years old and the father was 40 years old when the twins were born. The present gravidity was the fifth in that family. It passed with toxemia of pregnancy. The parturition began in time and finished with burning of the probands. One of them weighted 3100 g and was 49 cm long; another one weighted 2700 g and was 48 cm long. The physical and psychomotor development was adequate. The twins resemble each other. They have hyperstenic build, deformed skull, short neck (one of the twins has a small webbed neck), deformed chest, hypermobility of arm arthrooses, adenoidism, high palate, epicanthus, deformed ears, hyperthelorum of theles, and hair on nape below of normal line.

X-chromoplasm:

I-st twin — 34% "+" (10% double)

II-st twin — 40% "+" (12% double)

Both of the girls have the caryotype 47,XXX.

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## SEX CHROMOSOME ANOMALIES IN TWINS

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Among 610 Turner syndrome (TS) patients one monozygous twin set concordant by X chromosome monosomy (45X) and two sets discordant by X monosomy (45,X and 46,XX) were revealed (0.49%). Among 468 patients with Klinefelter syndrome (KS) there were two monozygous sets concordant by 47,XXY karyotype (0.43%). Thus, the twinning frequency was about two time lesser comparing to population value.

All newborns from twin sets were underweight. The TS monozygous twins were similar by clinical features and their expressions and had practically the same developmental rate with growth and bone age retardation, sexual infantilism. KS patients had significant differences in physical status within the pairs. In one set the second born child had hypospadias, cryptorchism and more prominent growth retardation. In another set one boy was retarded in thrive with delay in growth up to 11 cm and weight up to 12 kg compared with his brother at 18 yr.

These discrepancies within twins might be due to gestational conditions.

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## DYNAMICS OF INFANT TWINS CHARACTER'S DEVELOPMENT.

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As a part of longitudinal study of twins development we consider infant twins' character. There are 15 MZ pairs (116 measures) and 17 DZ pairs (78 measures). We use the test "Baby's day" by G.Balleiguer, which describes type of child's character (temperament + attitudes to parents).

Approximately one half twins have desadaptive character: difficult or passive. This character prevails in MZs in all ages. DZs after 2 years more often have easy character and in 3 years all have this one.

Factor analysis has revealed difficult structure and dynamics of developing self-regulation in MZ and DZ twins. DZs up to 1 year use parents' help and to 3 years may control self without external support. MZ twins, in opposite, in early ages use their inner regulative abilities and only to 3 years grow up to using external tools.

So the dynamics of MZ and DZ twins regulation development is different and in MZ twins is more inadequate.

Work is supported by the grant N 96-06-04228 of RHSF

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## LONGITUDINAL CHANGE IN THE DETERMINANTS OF FREQUENCY OF DRINKING AND FREQUENCY OF INTOXICATION IN ADOLESCENT TWINS.

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Middle adolescence is a time of rapid change in adolescent drinking. Between ages 16 and 18, abstinence decreases, and both frequency of drinking and drinking to intoxication increase. We investigated changes in the mean levels, and in the genetic and environmental determinants, of drinking and drinking to intoxication from age 16 to age 17. The sample comprised 958 pairs of same-sex twins from the FinnTwin16 study. Significant decreases in abstinence, and increases in frequency of drinking and drinking to intoxication were obtained. Significant genetic and shared environmental effects were present for both measures, at both ages, in both males and females, although shared environmental effects were smaller at age 17. For males, there was evidence of new genetic variation emerging at age 17 for both measures. For females, there were indications that new shared environmental variance was influencing both drinking and drinking to intoxication at age 17. Unshared environmental effects at ages 16 and 17 were largely independent. Further analyses investigated alcohol attitudes and personality as respective markers of the stable component of shared environmental and genetic influences on drinking during adolescence.

FinnTwin16 is supported by AA-08315.

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## Genetics Of Spontaneous And Induced DZ Twinning

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*Aim* of this study was to determine whether DZ twinning was genetically determined and if so what genes were responsible for it. A fixed-sized pedigree was taken of 2073 DZ twins from the East Flanders Prospective Twin Study. It included all the relatives up to the 3th degree (cousins, great-uncles and -aunts). All family members were verified in the civil registries. This allowed the inclusion of all abortions, stillbirths, liveborns and illegitimate children. The DNA of all informative relatives was examined. *Segregation analysis* of the spontaneous DZ families significantly excluded an X-linked, autosomal and simple additive multifactorial inheritance. It showed that spontaneous DZ twinning was inherited by an autosomal dominant gene with a gene frequency of 3.5% and a carrier frequency in the population of 7%. Its expression was sex-limited to women, and the penetrance in females was 10%. No phenocopies could be demonstrated. *Segregation analysis* of DZ twins induced after ovulation showed that this was also a genetic trait with the same gene frequency and carrier frequency and penetrance as the spontaneous DZ twins. There was no genetic heterogeneity between the spontaneous and the induced twins. *Gene Localization*: Five candidate DNA regions were examined. In 95 Fragile-X families with 486 mothers, 173 fathers and 2138 children, 28% of the families had twins. Of the 39 twins, 38 (97.4%) were DZ. The DZ twinning rate was significantly increased if the mother had more than 200 repeats or when she had more than 60 repeats, which she inherited from her father but not when she inherited them from her mother. We found no association nor linkage with the z-allele of  $\alpha_1$ -antitrypsin, which has been found to be increased in mothers of DZ twins. Five families informative for the receptor of the Gonadotropin Releasing Hormone (4q), suggested linkage (lod=1.33) at 1-3 cMorgan. The human equivalent (4q3) of the region, which causes DZ twinning in Boroola sheep, showed no linkage, nor did a region translocated to 4p13. Of the 14 families in which an undisclosed receptor was examined, 6 showed linkage (lod=2.48) at 0.1 cMorgan, and in 5 families linkage could be excluded (lod=-2.83). Of the 14 families where both the GnRH receptor and the new receptor were examined, all except one were discordant, suggesting that the genetic cause of DZ twinning may be heterogeneous. *Conclusions*: The causes of both spontaneous and induced DZ twinning are genetic. They are caused by a frequent (7%) dominant gene with sex limited expression. There is evidence for genetic heterogeneity: several genes could be responsible: paternally transmitted repeats of Fragile-X, GnRH-receptor and a new undisclosed receptor.



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PREVENTING ACCIDENTS IN MULTIPLE BIRTH FAMILIES.  
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In the UK, accidents are the leading cause of death in children. 31% of boys and 22% of girls require medical attention for accidents each year. In the under-5s, most injuries occur at home and are due to environmental hazards and dangerous behaviour.

In 1995, TAMBA (Twins and Multiple Births Association) conducted a postal survey of members with twins or triplets aged under 5 years. We collected information on all accidents that had required medical attention or advice at a doctor's surgery or hospital. We heard from 136 families, with a total of 266 different incidents, the peak age being 1-2 years. Boys had more serious injuries than girls. Factors felt to increase the risk of accidents included:

- parent's attention is frequently divided (eg. at nappy changing);
- the ominous silence that usually serves as a warning signal may be blotted out by the noise from a co-twin;
- twins compete with and try to copy one another, even though their own physical capabilities may differ;
- they collude together to shift objects that one alone could not;
- they fight and bite one another - with different age children, parents can reason with the older child. Toys become weapons;
- two playing with doors increases the risk of squashed fingers;
- bath time is more dangerous with two in the bath together.

Many accidents can be anticipated and so prevented. Most families used standard safety equipment. Other recommendations from our respondents were to use robust stairgates at the top and bottom of stairs, use door wedges, avoid toys with strings, avoid curtain cords, keep all fingernails short, have two adults to supervise in swing parks.

We discuss the possible association between accident-proneness and left-handedness in twins.

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MATERNAL WEIGHT GAIN AND BIRTHWEIGHT OF TWINS AND TRIPLETS

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This study investigated the relationship between maternal weight gain at delivery and birthweight of twins or triplets. The subjects were 1538 mothers of twins and 247 mothers of triplets. The following results were obtained;

- 1) In twin pregnancies, there was a significant difference in maternal weight gain at delivery among 5 groups classified from mother's prepregnant weight (Table1). Moreover, there was a significant difference in mean birthweight of twins among 5 groups.
- 2) In triplet pregnancies, maternal weight gain at delivery did not significantly differ by mother's prepregnant weight levels. There was a significant difference in mean birthweight of triplets among 5 groups classified from mother's prepregnant weight. The mean birthweight of triplets in mothers whose prepregnant weight was under 45 kg was significantly lower than those in other groups.

Table 1. Maternal pregnancy weight gain at delivery and mean birthweight of twins by mother's prepregnant weight

Mother's prepregnant weight (kg)	Maternal pregnancy weight gain at delivery (kg)	Mean birthweight of twins (g)
a < 45	13.31 ± 4.02 ***	2329.2 ± 408.7 ***
45 ≤ a < 50	12.67 ± 4.16	2261.6 ± 449.2
50 ≤ a < 55	12.51 ± 4.18	2384.6 ± 420.3
55 ≤ a < 60	11.94 ± 4.41	2403.6 ± 463.1
60 ≤ a	10.17 ± 5.65	2496.6 ± 386.6

Significant differences among all 5 groups (mother's prepregnant weight), by ANOVA, \*\*\* P<0.001

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GENETIC AND ENVIRONMENTAL INFLUENCES ON ADOLESCENT DRUG AND ALCOHOL USE IN THE COLORADO ADOLESCENT TWIN STUDY.

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It is well known that lifestyle choices such as use of alcohol, tobacco, or illicit drugs can have major effects on the health of individuals. Further, experimentation and decisions to use such substances are often initiated in adolescence. The present report investigates patterns of use of various substances, individually and jointly, in MZ and DZ adolescent twins. The Colorado Adolescent Twin Study is a longitudinal investigation which is seeking to explore the initiation of use as well as transition to regular or problem use of alcohol, tobacco, marijuana, and other illicit drugs in adolescent twins between the ages of 11 and 18. Presently, data have been collected for 1104 twins. The mean age of our sample is 14.4 years (sd=1.8). Looking at the sample by reported substance use: Alcohol: 426 respondents reported having ever consumed alcohol (more than just a taste of someone else's drink), while 314 reported having consumed alcohol in the past month; mean age of this 'ever' group was 15.5 years (sd=1.6), and mean number of drinks consumed at a time was in the 4 drinks. Tobacco: 334 subjects reported having used tobacco; the mean age of these subjects was 15.3 (sd=1.6), and the mean number of cigarettes smoked on an average day was 6. Marijuana: 224 Ss reported ever having tried marijuana, and all of these reported that they had used marijuana within the past month; the mean age of this group was 15.7 years (sd=1.5); the mean number of times that these individuals reported having smoked marijuana in the past month was 1 to 2 times. Genetic and environmental influences on the use of these substances individually and jointly will be presented. This research supported in part by grants from the Veterans Administration (V554-3828/3829) and NIDA (DA11015).

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HERITABILITY IN INDIVIDUAL FRAILITY: COMPARATIVE ANALYSIS OF SURVIVAL DATA FROM SCANDINAVIAN TWIN REGISTERS

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The survival data for MZ and DZ twins taken from Danish, Swedish and Finnish twin registers are analysed using correlated gamma-frailty model of bivariate survival. Despite the fact that survival data on Danish, Swedish and Finnish twins have different structure the results of analysis of all three data sets are similar. In all three cases frailty model with additive genetic and non-shared environmental components gives the best fit to the data. The estimates of narrow-sense heritability in gamma-frailty are about 50%. The underlying hazards corresponding to individual risks of death increase faster than the Gompertz hazard.

In all three cases the analysis of male data confirms our expectations about similarity of the marginal hazards and variances of frailty distribution and about dissimilarity of correlation coefficients for MZ and DZ twins. The results of analysis of female data are also very similar: the marginal life span distributions for MZ and DZ twins are the same. Surprising result is observed in the estimates of standard deviations and correlation coefficients of frailty distributions for female MZ and DZ twins: in accordance with the likelihood ratio test these standard deviations are different for twins in all three data sets, but the correlation coefficients of frailty are the same. Possible interpretations of such a result and further directions of research are discussed.

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## WEIGHT GAIN AND MATERNAL HEALTH CONDITIONS IN TWIN AND TRIPLET PREGNANCIES

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This study investigated the relationship between maternal weight gain in twin and triplet pregnancies and those health conditions. The subjects were 1538 mothers of twins and 247 mothers of triplets. The following results were obtained;

- 1) In twin pregnancies, the weight gain of mothers who did not suffer from toxemia of pregnancy was significantly lower than those who suffered from it. The mean weight gain of mothers who did not suffer from toxemia of pregnancy was 9.91 kg at 32 weeks, 11.90 kg at 36 weeks, and 12.75 kg at 38 weeks. Moreover, the weight gain of mothers who did not have edema during pregnancy was significantly lower than those who had it (2 or more times). The mean weight gain of mothers who did not have edema during pregnancy was 9.72 kg at 32 weeks, 11.96 kg at 36 weeks, and 12.83 kg at 38 weeks.
- 2) In triplet pregnancies, the weight gain of mothers who did not suffer from toxemia of pregnancy was significantly lower than those who suffered from it. The mean weight gain of mothers who did not suffer from toxemia of pregnancy was 8.10 kg at 28 weeks, 9.39 kg at 32 weeks, and 11.35 kg at 34 weeks. Moreover, the weight gain of mothers who did not have edema during pregnancy was significantly lower than those who had it (2 or more times). The mean weight gain of mothers who did not have edema during pregnancy was 7.83 kg at 28 weeks.

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## IS PRENATAL PREDICTION OF ANASTOMOTIC PATTERNS IN MONOCHORIONIC TWIN PLACENTAS FEASIBLE?

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The incompletely understood relationship between underlying placental anatomy, clinical outcome, and prognosis of severity in twin-twin transfusion syndrome (TTTS) hampers development of improved and consented clinical management. Our purpose is to show that placental anastomotic patterns may be predicted prenatally by combining longitudinally measured ultrasound data.

First, we recognize that fetal growth, expressed as difference between the two Estimated Fetal Weights divided by their average values, differs for the three pathophysiologic categories: [1] (1) unidirectional arteriovenous, (2) arteriovenous plus compensating, and (3) compensating superficial anastomoses plus unequal placental sharing. Second, we combine fetal growth with: (a) pulsatility indices of the umbilical arteries for assessment of placental sharing, (b) bladder filling of donor twins, possibly indicating compensating anastomoses, and (c) recipient's cardiac hypertrophy, most likely indicating an AV anastomosis. Third, we analyse the placenta following delivery.

Thus far, in our preliminary series of 10 monochorionic twins, we predicted the placental anastomotic patterns correctly in 9 cases.

Early assessment of the placental anatomy in monochorionic twins may improve clinical management of TTTS pregnancies.

[1] MJC van Gemert, HJCM Sterenborg. *Placenta* 19:195-208, 1998.

## 142

## ABSENCE OF ONE UMBILICAL ARTERY IN TWINS

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One umbilical artery in single pregnancies is found to be absent in 0.2% - 1.1% and the incidence of associated and varied malformations of the corresponding fetus is appreciably higher than for infants with 2 arteries.

It has been mentioned previously that in the umbilical cord of acardiac fetuses one of the two umbilical arteries is frequently missing. Single umbilical artery and abnormality of the associated fetus are found much more commonly in twin than singleton pregnancies.

Of the 474 fetuses in 237 consecutive twin pregnancies, there were 14 who lacked one umbilical artery (3.0%). Of 14 fetuses, 11 were suffering from varied malformations, such as acardiac monster, heart anomaly, anencephaly and so on. On the other hand, single umbilical artery in singletons was found to be only 72 (0.52%) of 13,879 fetuses.

There is considerable debate as to whether one umbilical artery is due to a primary aplasia or to a secondary atrophy of the missing vessel. Altshuler et al investigated this point and found that in a series of 48 cases there appeared to be an aplasia in 29 and an atrophy in 19. In fact, it is almost certain that both of the mechanisms can be invoked.

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## GENOTYPE AND ENVIRONMENT IN INDIVIDUAL VARIABILITY OF PARAMETERS OF NOVELTY IN CHILDREN FROM 6 TO 10 YEARS

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The impact of genetic and environmental factors on parameters of novelty was studied in a sample of twins aged 6, 7 and 10 years.

Subjects were 94 pairs of MZ and DZ twins of 6 years old, 79 pairs of MZ and DZ twins of 7 years old, 51 pairs of MZ and DZ twins of 10 years old. Instruments: Embedded Figures Test for children (time and number of training tasks), Classification of pictures (time of training tasks) and WISC (adopted for Russian population by A. Panasuk).

Results indicated that the parameters of novelty and IQ appear to increase in heritability from 6 to 10 years. Correlation analysis and ANOVA (analysis of variation) shows that IQ is connected with the parameters of novelty in 6 years, but the correlations are low and differ in samples of MZ and DZ twins. Age-to-age genetic correlations between IQ and all parameters of novelty appear to be nonlinear, demonstrate different mechanisms of regulation of characteristics of time and number of tasks.