

## ABSTRACTS

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Monday 16 June

### 1A SYMPOSIUM: INCIDENCE AND FACTORS OF TWINNING

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#### THE PROBABLE EXPLANATION FOR THE FALLING TWINNING RATE IN SCOTLAND

Ian MacGillivray

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Over the past decade there has been a falling incidence of twinning in Scotland. This could possibly be accounted for by the falling age of child bearing, or the falling parity, as it is known that both age and parity influence the incidence of twinning. However, from a study of the Aberdeen data, falling parity does not appear to be the reason and, from a study of the whole Scottish data, age is also not the explanation. The fall in incidence has occurred in the age group over thirty. The probable explanation is that fertile women are more likely to have twin pregnancies and their fertility has been reduced by use of the contraceptive pill.

#### THE CHANGING INCIDENCE OF MULTIPLE BIRTHS: ONE CENTURY OF ITALIAN STATISTICS

Paolo Parisi, Giancarlo Caperna

The Mendel Institute, Rome

The incidence of multiple births in Italy has been assessed for a period of 110 consecutive years, 1868–1977, during which the general population increased from 25 to 57 million inhabitants and the birth rate decreased from 37 to 14 per mil, with an average number of total maternities of almost 1 million per year and an average number of multiple births of over 12,000 per year. Rates of twin, triplet, and quadruplet and quintuplet births have been assessed, and zygosity estimates have been derived. As a first step, the general variability in the incidence of opposite-sex twinning has been examined, with special respect to the decline found to characterize the last thirty years and to the influence of factors such as maternal age, parity, and birth control. It would appear that not only the reduction of maternal age and parity fails to account for the observed decline, but that the latter is also not easily explained in terms of contraception and decreasing birth rates.

**ANALYSIS OF TWINNING RATES IN JAPAN**

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Twinning rates in entire Japan in 1951–1968 and 1974 were analyzed using data in vital statistics of Japan and the ‘‘Survey on Socio-Economic Aspects of Vital Events-Plural Births in 1975’’. Twinning rates by zygosity were estimated using Weinberg’s method from 1955 to 1967 and 1974, where sex of the twins is given. Up to 1966 MZ twinning rate increased slightly, but decreased thereafter. DZ twinning rate declined in the entire period. Maternal age is given in the statistics from 1960 to 1967 and for 1974. In all years overall twinning rate increased with maternal age except in mothers over 40 years of age. DZ twinning rate increased up to the age group of 35–39 years and decreased thereafter. The same but less marked tendency that DZ twinning rate is seen in MZ twinning rate. The secular decline of DZ twinning rate is evident in mothers over 25 years of age, especially in the age group 35 years or more. MZ twinning rate remained most constant in the maternal age group of 20–24 years, and the increase up to 1966 becomes more evident as maternal age increases, while in the youngest maternal age group (<20 years) a slight decrease rather than increase was seen. Besides, analyses were made on the association of twinning rate with birth order, month of conception, latitude, proportion of parents whose relatives had plural births, and proportion of mothers treated with ovulation-inducing hormone.

**FACTORS INFLUENCING THE INCIDENCE OF TWINNING**

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In a study carried out in an African population in Western Nigeria and a Caucasian population in Aberdeen, Scotland, it was found that DZ twinning rates varied with maternal age and parity, the MZ twinning rate remaining fairly constant. However, women aged 30–34 were found to have the highest rate in Western Nigeria whereas the peak in Aberdeen population occurred in the older age group, 35–39 years. Other factors which influenced DZ twinning rates were maternal height, social class and ethnicity (in the Nigerian population), and illegitimacy (in the Aberdeen population). No significant association was found between twinning and maternal blood groups or season of the year in either of the two populations. An important factor which also influenced twinning in the two populations was the maternal serum FSH level. The levels were much higher in the Nigerian population than in the Aberdeen population. Furthermore, in the Aberdeen population, twin-prone and non-twin-prone women had similar serum FSH levels, whereas the levels were much higher in twin-prone women in the Nigerian population. This finding is consistent with the fact that the Nigerian population has a much higher twinning incidence (approx. 50 per 1000 maternities) than Aberdeen population (approx. 12 per 1000 maternities).

## 1B SYMPOSIUM: EMBRYOLOGY AND TERATOLOGY OF TWINNING

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### MALFORMATIONS UNIQUE TO THE TWINNING PROCESS

Walter E. Nance

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A group of rare malformations including acardia, fetus-in-fetu, fetus papyraceous, and Siamese twinning, occur exclusively in multiple births. Other defects involving midline structures, including symmelia, extrophy of the bladder, and possibly midline neurologic defects, may have an increased incidence in twin births but also occur in singletons. Known and postulated pathogenic mechanisms which can give rise to discordant malformations in twins include intrauterine crowding, competition resulting from variation in placental implantation site, antenatal vascular anastomoses, meiotic errors, and cytoplasmic abnormalities resulting in a blighted ovum. Examples of these malformations will be discussed in relation to the postulated pathogenic mechanisms.

### MONOZYGOTIC TWINNING AND STRUCTURAL DEFECTS

Albert Schinzel

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Structural defects are more common in MZ twins than in DZ twins or singletons. In a first category fall defects that are part of the MZ twinning, such as conjoined twins, or some early embryonic malformations, the reason for this presumably being the common etiology for both the MZ twinning and the early malformation problem. The other two categories are considered secondary to the MZ twinning process. Such are the vascular interchange between the MZ twins and the deformations due to crowding in utero during late gestation. The latter do not differ from those of DZ twins.

### THE LESSONS FROM MULTIPLE PREGNANCIES IN MAMMALS

Kurt Benirschke

San Diego Zoo, California

Several species of mammals have provided excellent models for an understanding of the biology of twins but they have not been fully exploited. A brief review of past achievements will be provided but primarily directions for future definitive research will be given. Several closely related species of armadillo (*Dasypos*) produce identical multiple offspring regularly. They have 2, 4 or 4-12 "identical" offspring regularly. The reasons for this polyembryony is not understood but could be studied by embryo transfer between these similar animals. Although monochoorial, the placentas share no vascular anastomoses and graft rejection between offspring has once been documented. These animals are also unique in that they possess a nonbicornuate uterus, rely on fetal adrenal progesterone for pregnancy maintenance and the various pregnancy complications of monozygotic twins in man do not exist.

Marmoset always produce fraternal twins, share placental blood vessels, are blood-chimeric for life but suffer none of the sterilizing consequences in male/female combinations as are typical of the artiodactyl freemartins. Before the circulating HY antigen can be held responsible for the latter phenomenon it is mandatory that the normal genital development of chimeric female marmoset be explained. A similar situation is true of human blood chimeras.

The twinning gene (DZ twins) exists in some species commonly, yet some related forms do not exhibit twinning. This is for instance true of some lemurs. How is this gene translated into multiple ovulation? Presumptively different quantities of pituitary (? hypothalamic) hormones are produced. With the use of bioactive hormone determinations it may be possible to define where the twinning gene acts biologically because of the temporally concise ovulatory events in these species.

Whole-body-chimeras are in fact most likely twins by conceptual standards. Because of the coat color markers of cats this relatively common phenomenon might best be studied in that species. Other animals (sheep) can serve as models for the understanding of the intrauterine life of twins that is so inaccessible in man. Pertinent examples will be given of these circumstances.

**MULTIPLE AND SINGLETON PREGNANCY: DIFFERENCES BETWEEN MOTHERS AS WELL AS OFFSPRING**

Gerald Corney

The Galton Laboratory, University College, London

It is widely recognised that twins differ from singletons in many ways, but not so generally known that mothers of twins may be demonstrably different from those of singletons. Some of these differences characterising both mothers and offspring will be discussed in relation to zygosity and also placentation.

## 1C WORKSHOP: TWIN DATA ANALYSIS

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### ARE DISTANCES BETWEEN DZ TWINS FOR POLYGENES AND MAJOR GENES CORRELATED?

E. Defrise-Gussenhoven, Y. Michotte, C. Susanne

Centre of Biomathematics, Free University of Brussels

It is reasonable to expect that multivariate distances between DZ twins for blood groups and for biometric data should be correlated. In other words, the more different blood groups DZ twins will have, the more they will differ physically. Indeed, two DZ twins with many common blood groups will have identical pieces of DNA coming from the same piece of DNA of one of the parents. These identical pieces will also carry other identical genes including possibly some polygenes coding for biometric characters. Many identical polygenes will result in measurements for DZ twins which differ only slightly from each other. The techniques of distances were often used successfully by the authors, as well for quantitative multivariate biometric data as for qualitative data such as blood groups. Since 24 blood groups and about 30 body measurements are determined, this study could provide some information about the localization of polygenes.

### GENERALIZED DISTANCE IN TWINS

Sylvia De Bie

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With the advent of electronic computers it became possible to analyse biometric differences between twins with multivariate statistical techniques, such as generalized distance (G.D.)

$$G.D. = \sum_{i=1}^p \sum_{j=1}^p \delta_i \delta_j \rho_{ij} \quad (i, j = 1, \dots, p)$$

in which  $\delta_i, \delta_j$  are the differences between the members of a twin pair and in which  $\rho_{ij}$  are the elements of the inverse of the correlation matrix of a reference population. Half the generalized distance (G.D./2) is distributed as a  $\chi^2$  distribution with  $p$  degrees of freedom. Our sample consists of 111 MZ (56 males and 55 females) and 120 DZ (53 males and 67 females) twin pairs and of 561 controls (280 males and 281 females). For all individuals, ab-ridge count, maximum atd angle, main line index, and pattern intensity were counted. Males and females were not pooled as the correlation matrix was different. Preliminary results indicate that the generalized distances are larger in DZ than in MZ twins in males as well as in females.

### DETECTION OF THE GENETIC EFFECTS OF MARKER LOCI BY PARTITIONED TWIN ANALYSIS

W.E. Nance, L.A. Corey, P.M. Winter, M. Mosteller

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Partitioned twin analysis provides a new method for detecting the phenotypic effects on quantitative traits of chromosomal regions containing specific marker loci. When parental typing data are available, DZ twins may be partitioned into subsets of pairs who share 0, 1 or 2 alleles at a polymorphic marker locus. An analysis of variance of the resulting subsets yields six mean squares whose expectations may be combined with those for the two mean squares derived from MZ twins to permit a clear resolution of the additive and dominance effects of the marker locus from the genetic effects of all other loci. We have applied the model to data on total ridge count and stature in a sample of 73 MZ and 75 DZ twins and their parents who were segregating for the ABO, MNS or Rh loci. No significant effects on total ridge count were detected for any of the loci studied. However, an analysis of age and sex adjusted stature scores in 70 MZ pairs and 71 DZ pairs who could unambiguously be assigned to one of the three subgroups suggested that a major component of the total genetic variance (40–60%) in stature appears to be attributable to genetic variation within the region on chromosome one that contains the Rh locus. Although the analysis in this small sample of twins cannot be considered definitive, it illustrates how partitioned twin analysis may be used to disclose unexpected sources of genetic variation in man.

### TESTS FOR GENETIC-ENVIRONMENTAL INTERACTION IN TWINS

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With quantitative traits, regression of within-pair variance on pair means for MZ twin pairs can provide evidence for genetic-environmental interaction. This approach is investigated by simulation studies.

### ZYGOSITY TEST ON THE BASIS OF GROWTH MEASURES: A BAYESIAN APPROACH

C. Rossi<sup>1</sup>, G. Brenci<sup>2</sup>, R. Ziparo<sup>3</sup>  
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A statistical index is proposed in order to determine zygosity on the basis of weight and height and a Bayesian test of hypotheses. Some Roman twin data are analyzed on the basis of the euclidean distance index, which appears to be the best for an easy calculation and for its genetic interpretation based on the formulation of genetic distance. An MZ twin pair has a genetic distance equal to zero and a statistical distance due to environment which may be relevant during fetal life but then decreases with time. In a DZ pair, the genetic distance is greater than zero, which adds to the environmental factors and produces a larger variability in growth measures. The proposed index will be applied to zygosity determination based on height and weight at birth.

### METHODOLOGICAL IMPLICATIONS OF ZYGOSITY DIFFERENCES IN DEVELOPMENTAL RELATIONSHIPS

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Using multivariate statistical methods, we are finding that we can identify twin zygosity with 97+% accuracy in either sex, on an individual basis, without reference to within-pair comparisons. The differences we see involve the multivariate group mean vectors, within-group covariance and correlation matrices, and measures of side-to-side and within-side developmental coherence based on generalized distance. Results indicate pervasive differences in developmental integration of growth in the head region, as a function of zygosity. Given such differences between zygosity groups, at least one of those groups is not representative of the general population. Other evidence suggests, in fact, that neither twin zygosity group is equivalent to singletons in these respects. Therefore, at least with particular reference to questions of intellectual and behavioral development, twin-study methods estimating genetic variance as a function of zygosity-group differences in distribution of within-pair similarities must be considered questionable. Methods for the separation and characterization of zygosity-dependent and -independent variation are under study.

### THE USE OF TWINS IN ANALYSING THE HUMAN MATING SYSTEM

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Several authors have recently introduced the term "asymmetric assortative mating" into the behavioural genetic literature but no consistent parsimonious model has been offered. Such a model is now presented which permits the problem to be specified with great generality. The issue is resolved by recognising that assortment is always symmetric for some aspect of the phenotype (e.g., "fitness"), and that asymmetry arises if sexes differ in their genetic basis of the trait on which assortment is based. The model confirms many of the intuitive notions already expressed and illustrates how data on the behaviour of twins and their spouses may resolve the genetic and cultural basis of the human mating system.

**RELEVANCE OF THE MARRIAGES OF TWINS TO THE CAUSAL ANALYSIS OF NONRANDOM MATING**

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Marital correlations can arise either from effects of common home environment or nonrandom mating. Although nonrandom mating has traditionally been viewed as a homogeneous reciprocal process, it seems clear that some genotype may mate assortatively and others at random or even disassortatively. Furthermore, the factors which influence nonrandom mating may differ by sex. Data on twins and their spouses permit the estimation of four distinct correlations: the marital correlation,  $r_{HW}$ , the correlation between a twin and the spouse of the cotwin,  $r_{TS}$ , the spousal correlation,  $r_{SS}$ , and the twin correlation,  $r_{TT}$ . An analysis of these correlations in male and female twins permits resolution of the potential genetic or environmental causes of marital correlation as well as detection of concordant assortation in the marriages of twins and sexual asymmetry in the process of mate selection. We have applied the model to the analysis of data on stature and the Verbal, Blocks and Information subtests of the Wechsler. For stature, a substantially higher correlation was observed among spouses of 50 male than 73 female MZ twin pairs giving evidence for asymmetry in the process of mate selection. For the Information and Vocabulary subtest scores, there was evidence for concordant assortation without asymmetry, while for the Blocks subtest there was no significant evidence for concordant assortation. An accurate treatment of the potential effects of assortative mating, concordant assortation, and sexual asymmetry in the mate selection process is essential for any rigorous genetic analysis that extends beyond the confines of the nuclear family unit.

## 1D CONCURRENT SESSION: TWIN RESEARCH IN CLINICAL STUDIES

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### GENETIC STUDY OF INFECTIOUS DISEASES OF CHILDHOOD IN A SAMPLE OF TWINS

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The Mendel Institute, Rome

A study of the infectious diseases of childhood has been carried out on a sample of 656 twin pairs. Whereas no role of genetic factors could be detected for whooping cough, scarlet fever, heritability estimates of 25% to 46% were found for measles, chickenpox, and rubella.

### MYOFACIAL PAIN DYSFUNCTION SYNDROME IN TWINS

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Institutes of <sup>1</sup>Medical Genetics, <sup>2</sup>Community Dentistry, and <sup>3</sup>Psychiatry, University of Oslo; and <sup>4</sup>Department of Human Genetics, Medical College of Virginia, Richmond

The Myofacial Pain Dysfunction Syndrome (MPD) was investigated in 94 (21 males and 73 females) pairs of twins. MPD is a syndrome of muscle tenderness, clicking or popping noise in the temporomandibular joint, and limitation of jaw function. No organic finding which may explain the symptoms is made by clinical or radiographic investigation. The syndrome is thought to be related to reactions to emotional or physical stress. The frequency of MPD symptoms (past or present) was found to be about 10% in male and 27% in female twins investigated by a questionnaire. These frequencies are similar to those obtained in a population survey. The amount of stress (burden) was not found to be increased among patients compared to a control group in a previous investigation. No difference was found in pairwise or casewise concordance rates between MZ and DZ twin pairs. The findings suggest that inherited personality characteristics do not form a predisposition to the syndrome. Rather, environmental influences give rise to this specific stress-reaction pattern.

### RESULTS OF A MONOZYGOTIC COTWIN CONTROL STUDY ON A TREATMENT FOR MYOPIA

J. Theodore Schwartz

Division of Hospitals and Clinics, Bureau of Medical Services, US Public Health Service

This is a report on the outcome of a myopia treatment study originally described at the First International Congress on Twin Studies as an example of an ongoing prospective investigation employing MZ cotwin controls. One cotwin received a standard spectacle correction for myopia as the control; the other was managed using a combined treatment comprising especially prepared bifocal spectacles and topical, shortacting, cycloplegic eye drops (tropicamide) at bed time. Upon completion of the 3½ year observation period, the control twins showed, on the average, a greater increase in myopia than their cotwins who received the study treatment. The difference in myopic progression between treated and control twins was not statistically significant. However, the author is reluctant to reject the hypothesis of a treatment effect on the basis of the present findings. Theoretical study design and observational considerations pertaining to this view will be discussed along with other twin study applications that could expand present understanding of the nature, progress, and management of myopia.

### DISCORDANCE FOR HYPODONTIA IN MONOZYGOTIC TRIPLETS

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Hypodontia is a well known familial trait, but the phenotypic expression of the trait may vary. Prenatal factors appear to interact with the genetic predisposition. Different teeth may be missing in different family members, in kindreds with familial hypodontia. However, absence of 2-2 has relatively rarely been reported. A set of triplets was subjected to extensive genetic marker studies in 21 systems and found to be MZ. The triplets and their parents were examined. Complete dental



records were available for the triplets from the age of 7 years. The mother lacked 2-2. Triplet A lacked -03 and -2. Triplet B lacked -03 and the eruption of 6+6 had been abnormal. In the same triplet, -2 had had inadequate space for development and this had motivated regulation, and removal of -4. Furthermore, 5+5 had been removed due to lack of space for normal development. Triplet C lacked -2. The birthweights of the triplets had been: A, 1250 g; B, 1800 g; and C, 2000 g. Since the triplets were MZ, the variation observed probably reflects the effects of environmental/nutritional factors or, more hypothetically, of cytoplasmic factors. Thus, the findings in this set of identical triplets illustrate some of the nongenetic phenotypic variation in hypodontia.

### CHROMOSOMAL STUDIES IN TWINS AND THEIR MOTHERS

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Cytogenetic studies were performed on 86 couples of twins and their mothers. The incidence of gonosomal and autosomal aneuploidy (mosaics or not) in the twins was compared to the incidence found in a large study of normal singleton newborns; also, the inheritance of heterochromatic chromosomal variants was studied. A significant increased incidence of variants of chromosomes 9 and 15 was found in the mothers, especially of DZ twins. A genetic tendency to DZ twinning is known. The possibility exists that the heterochromatic areas in chromosomes 9 or 15 play a role in hormone metabolism, as other personal studies on male hypogonadism and infertility suggest. Aneuploidy was found in three couples: in all of them a variant 15 was segregating and in one couple a variant 9 too.

### A STUDY OF MUTABILITY IN MZ TWINS

L. Gedda, A. Noto, C. Di Fusco, E. Roselli, G. Brenci

The Mendel Institute, Rome

The study of the frequency of chromatid exchanges in lymphocyte cultures of MZ twins treated with BUdr indicates that these exchanges are genetically influenced. It is confirmed that chromatid exchanges are a parameter of mutability.

### QUINACRINE MUSTARD (QM) and NUCLEOLAR ORGANIZER REGION (NOR) HETEROMORPHISMS IN TWINS

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Patterns of NOR activity in 640 metaphase spreads from 12 MZ and 8 DZ twin pairs were studied to evaluate the heritability of this chromosomal heteromorphism. NORs were stained by a modification of the Ag-AS technique and counterstained with quinacrine mustard dihydrochloride to facilitate chromosome identification. Additionally, QM heteromorphisms were scored in 305 metaphase spreads. Depending on the presence and intensity of staining, each acrocentric chromosome was assigned a score of 0-4 for the NOR and a score of 0-3 was designated for each chromosome with a QM heteromorphism. In this study, all karyotypes were read blind with respect to zygosity and pair membership. Since the members of a homologous pair could not always be individually identified, average total pair scores for NOR and QM heteromorphisms were calculated and employed in further analyses. A discriminant function analysis of pair score differences in MZ and DZ twins revealed that, in our sample, the probability of accurately determining zygosity with NOR scores was 0.93 and with QM scores was 0.99. We conclude that NOR and QM scores are highly heritable and of great value in zygosity determination. Data were collected from 687 metaphase spreads on the frequency with which an acrocentric chromosome was found in a satellite association. A significant correlation was found between this frequency and the degree of Ag-AS stain of the NOR. This study, therefore, confirms previous results showing that a high degree of NOR activity is found in those chromosomes most often involved in satellite associations.

### UNCOMMON BIRTH DEFECTS AND MULTIPLE PREGNANCIES

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Department of Pediatrics, University of Florence

**CYTOGENETIC AND ANTIGENIC STUDIES IN ONE PAIR OF TWINS, A NORMAL BOY AND A TRISOMIC 21 GIRL WITH CHIMERA**

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A pair of diamniotic monochorionic twins, a phenotypically normal boy and a mongoloid girl, was studied. Cytogenetic analysis demonstrated a mosaic pattern (46,XY and 47,XX,+21) in the lymphocyte cultures of both infants during the first week after birth, while immuno-hematological studies revealed total antigenic identity and an immunological tolerance. Although monozygosity could be assessed with a probability of 99.77% (14 blood systems), it was hypothesized that these twins were DZ, but possessed a blood chimera resulting from a hematopoietic graft in the early stages of embryonic development. A follow-up of the twins during their first year of life indicated that these were indeed DZ twins with an uncommon blood chimera. It was therefore concluded that the study of antigenic blood markers is insufficient for determining monozygosity in cases presenting chimera. Previous publications on discordant twins (normal and trisomic 21, normal and haplo-X, etc.) classified as MZ should be reviewed and corrected.

**SAMPLING SURVEY ON ATOMIC-BOMB-EXPOSED AND -NONEXPOSED TWIN PAIRS: PILOT CASE STUDY FROM A SOCIOHISTORICAL VIEWPOINT**

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A twin sampling was conducted on the following material: 1. Matsubayashi survey of atomic-bomb-exposed families in Hiroshima, undertaken in 1946; 2. Survey of atomic-bomb survivors, undertaken by the Japanese Welfare Ministry in 1965; 3. Atomic-bomb-exposed family survey, undertaken by the Hiroshima Prefecture and City Governments; 4. Investigations of atomic-bomb victims exposed in the proximal area from the hypocenter. Out of the 470 pairs selected, there were 220 exposed pairs, 172 of which of the same sex. Preliminary results of a pilot study based on depth interviews, sociohistorical researches, and psychological tests of two exposure-discordant twin pairs will be presented.

**SAMPLING SURVEY ON ATOMIC-BOMB-EXPOSED AND -NONEXPOSED TWIN PAIRS: PILOT CASE STUDY ON THE NATURAL HISTORY OF DISEASE**

Y. Satow, N. Okamoto, H. Okita

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A study of the natural history of disease as related to the effects of atomic-bomb exposure was conducted through a twin-control study based on a sample of exposure-discordant, mainly MZ twin pairs. The main physical examinations include zygoty determination, blood, urine, liver function, X-ray examination, and immunogenetic analyses. Preliminary results of a pilot study of two exposure-discordant twin pairs will be presented.

## 1E CONCURRENT SESSION: TWINS, PARENTS OF TWINS, AND RESEARCH

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### RESEARCH: COMMITMENT AND COMMUNICATION

Joyce Maxey

Vice President/Collective Members, International Society for Twin Studies (ISTS)

Research work is a tremendous responsibility that demands total commitment. Communication is the vital link that nurtures the growth of awareness and understanding between research groups. Commitment has its core: a concern for mankind, a strong belief in the work to be done, with vision for the future, a cooperative spirit in relationships, and a singleness of purpose to give the time and energy needed to meet the challenges of research.

### A RESEARCHER'S GENERAL REMARKS

Ronald S. Wilson

University of Louisville Medical School, Kentucky

### THE INTERNATIONAL TWINS ASSOCIATION (ITA): PAST, PRESENT, AND FUTURE

Elsbeth Corley, Beverly Simmons

International Twins Associations (ITA)

### THE TWINS CLUB ASSOCIATION OF GREAT BRITAIN

Judi Linney

Twins Club Association of Great Britain

### ROLE OF THE NATIONAL ORGANIZATION OF MOTHERS OF TWINS CLUBS, USA, (NOMOTC) IN TWIN RESEARCH

Marion P. Meyer

Executive Secretary, National Organization of Mothers of Twins Clubs, USA (NOMOTC)

NOMOTC has been functioning since 1960 as a clearing house for information on twins. In the absence of a national twin registry, NOMOTC is the central source of twin subjects in USA. It represents one third of the known MOTC and maintains an up to date listing of all known clubs. NOMOTC actively promotes research and encourages every mother of twins to participate. Results of interorganizational and professional research projects are published in a quarterly newsletter. NOMOTC is organized and available to serve as coordinator or liaison between scientists and local mothers of twins. It can assist researchers: 1. by distributing questionnaires on a nationwide level; 2. by releasing addresses of clubs to approved researchers; 3. by conducting projects at annual conventions.

### PARENTS OF TWINS AND THE NEED FOR RESEARCH INTO THE IMPACT OF A MULTIPLE BIRTH

Joan Craig, Sheryl McInnes, Brian McLean

Parents of Multiple Births Associations of Canada (POMBA)

The Parents of Multiple Births Associations of Canada was formed in 1979 to serve as a parent service organization for the Parents of Twins Club in Canada. Its service is threefold: research projects and reporting, publication and/or distribution of books and booklets, education programs for health personnel and hospital use. We knew in the beginning that in order to offer help to parents, we had to know how the circumstances of a multiple birth affected the family as a whole

and the impact on each member of the existing family. Literature searches turned up very little useable information on the subject, we therefore set up our own questionnaire and distributed this through our membership. The results of this questionnaire presented us with more questions than answers but it did determine that for many families the arrival of twins or triplets created a crisis situation. This helped us develop supportive literature and our Education Program. However, it did not tell us what the effect of this disruption of family life had on the development of the twins themselves. We, therefore, would like to appeal to the International Society for Twin Studies for the creation of a working group study on the impact of a multiple birth on the family and the consequences of this impact on the subsequent development: social, emotional, and intellectual of the twins.

#### **THE BENEFIT OF COOPERATIVE RESEARCH INTO MULTIPLE BIRTH AT PROFESSIONAL AND VOLUNTARY ORGANISATION LEVELS**

Patricia Stewart

Australian Multiple Birth Association (AMBA)

The paper will outline the need for information in Australia directed towards the social aspects of multiple birth as defined by parents at the First National Convention of the Australian Multiple Birth Association in 1973. It will define briefly how a research programme was initiated by AMBA to meet these needs, and will summarise evidence from several surveys conducted by the Association. This evidence, includes medical, management, and statistical information as well as resulting activities which have alleviated many of the problems associated with multiple birth children at both parent and health care personnel level. The paper will also outline several research studies conducted at a professional level, in which the members of AMBA have participated, or are participating, with emphasis on those studies which were initiated and/or promoted by AMBA. Attention will be drawn to the need for mutual cooperation between parents of twins, twins, and persons involved in research about twins, so that more information may become available at all levels of multiple birth interest. In particular, AMBA will outline the reasons and means whereby this cooperation has been initiated in Australia.

#### **OUTREACH PROGRAMS FOR MULTIPLE BIRTH ORGANIZATIONS**

Donald Keith, Louis Keith

Center for Study of Multiple Gestation, Chicago

The paper will discuss the real need for all organizations concerned with multiple births to conduct active outreach programs to contact the new parents. Each year another group of parents must struggle to find the same information that has already been disseminated.

#### **THE DERMATOGLYPHIC COLLABORATIVE STUDY: HAND FEATURES USABLE FOR TWIN ZYGOSITY ASSESSMENT**

Warner H. Klopfer<sup>1</sup>, Paolo Parisi<sup>2</sup>

<sup>1</sup>Department of Anatomy, Tulane University, New Orleans; and <sup>2</sup>The Mendel Institute, Rome

The results of a successful example of collaboration between scientists and Twins and Mothers of Twins Organizations will be discussed. The joint effort of the Mendel Institute in Rome and of tens of Clubs in the United States and other countries, coordinated by the Vice President/Collective Members of the International Society for Twin Studies, has resulted in the collection of finger, palm, and plant prints of now over 2,500 pairs. While the print collection is still progressing and a variety of studies are being planned, a preliminary application to twin zygosity assessment has been tried. About 100 dermatoglyphic and anthropometric features of the hand have been tested and the results will be discussed.

#### **THE DEVELOPMENT OF A POPULATION-BASED TWIN PANEL**

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Department of Human Genetics, Medical College of Virginia, Richmond

The Virginia Twin Registry is a population-based panel of twins born in Virginia since 1915, as ascertained from birth records maintained by the Virginia Health Department. With one-third of the birth record search completed, members of 8680 like-sexed and 4750 unlike-sexed pairs have been ascertained. It has been possible, thus far, to obtain current addresses for 4812 like-sexed pairs

born in the years searched subsequent to 1932, or an overall success rate of 52%. Several strategies have been employed in making initial contact with twin pair members. Of those initially contacted by mail and sent a one-page zygosity questionnaire, 47% of those with a valid mailing address completed and returned the questionnaire and agreed to participate in further studies. Of those initially contacted by telephone, 97% agreed to complete a series of zygosity, health history, and pregnancy history questionnaires. Questionnaires have been completed and returned by at least one pair member in 74% of the pairs who received them. Preliminary analyses of questionnaire responses has revealed a history of twinning in the families of 41% of the twin pairs returning questionnaires and in 18% of the families of their spouses. In three cases, both the individual ascertained from birth records and his or her spouse were twins. Population-based twin registries are of particular value for the ascertainment of twins with rare traits or for the analysis of traits which can be influenced by ascertainment bias. Our experience suggests that vital record searches provide a feasible mechanism for developing large population-based twin registries.

#### **THE MOTHERING OF TWINS, TRIPLETS, AND QUADRUPLETS**

Esther R. Goshen-Gottstein

School of Education, Bar Ilan University, Ramat Gan, Israel

This study examined mothers' attitudes and patterns of behavior with twins, triplets, and quadruplets. It was directed toward learning the nature of the basic issues confronting such mothers. During home-observations special attention was focused on: 1. mothers' ambivalence in such a situation and the differing forms in which this could be expressed; 2. mothers' coping strategies when faced with the unusual demands made on them; 3. the factors that encourage mothers to unitize or to individualize their children.

## 2A SYMPOSIUM: TWIN STUDY DESIGNS IN MEDICAL RESEARCH

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### **MATCHED-PAIR METHODS IN EPIDEMIOLOGY AS A PARADIGM FOR TWIN RESEARCH**

Colin White

Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut

Twins may be used for two different types of investigation in genetics and epidemiology. In one case, the unit of study is the twin pair: e.g., when the assessment of concordance for a particular disease is the issue of interest. In the second case, twin is being compared with twin: the unit of study is the individual and the twins are being used as subjects, because they provide well-matched pairs; we are interested in observing the outcome, e.g., when one smokes and the other does not.

### **METHODOLOGIC PROBLEMS IN MATCHED-PAIR STUDIES USING TWINS**

Zdenek Hrubec

Medical Follow-up Agency, National Academy of Sciences - National Research Council, Washington

Twin Studies either aim to estimate heritability, or they aim to rule it out in evaluations of relationships between other factors. Matched-pair designs using twins are especially useful for the latter purpose. When they use MZ twins, comparisons of trait-discordant twin pairs control all genetic effects including gene-gene interactions. When there are gene-environment interactions such comparisons are valid for the specific distribution of the genotypes included. Members of twin pairs are naturally age-matched, and they share many environmental exposures, especially during childhood. Effects of childhood factors generally cannot be controlled otherwise, especially if the endpoints studied only appear later in life. Random allocation of twin pair members to two different experimental treatment groups is exquisite methodology.

The success of observational studies depends on appropriate definitions of trait manifestation and of twin pair discordance for the trait as defined. Varying definitions involve varying loss from the critical study comparison of the twin pair defined as concordant. The extent of this loss depends on trait prevalence and on the within-pair association of the trait, and it may affect the efficiency of the study design. As in matched observational studies of individuals, twin pair matches may sometimes be inappropriate. The use of twins reduces but does not eliminate the possibility that an observed relationship is estimated incorrectly due to unsuspected biasing variables.

## SEQUENTIAL COLLECTION AND ANALYSIS OF DATA

Jacob E. Bearman

Center for Health Sciences, Ben-Gurion University of the Negev, Tel Aviv

Taking the matched-pair design as a model in twin research, the application of the methods of sequential analysis provides a means for using matched-pair data in a manner that is more efficient than with "classical", fixed sample-size methods, at least in some situation. When the pairs present themselves sequentially, and the response-variable on both members of each pair can be ascertained before the next pair is available and/or its pair of response-variable are determined, then sequential analysis leads (for the same, fixed, probability values) to sample sizes which (on the average) will be materially smaller (usually near 50%) than those needed with more commonly used methods; one type of question that can be answered by this method might be whether the proportion of the matched pairs (twins) in one category (for example, have had a particular experience) is larger (or smaller) than their pairs in the other category. Similar to the requirement for any matched-pair design, this method tacitly assumes that the members of each matched pair were randomly assigned to the two categories, an assumption frequently violated in twin studies. Emphasis will be placed on a heuristic explanation of what is involved in sequential analysis, and how this leads to the saving in sample size. An example will be presented of the application of the sequential method in a therapeutic trial using matched pairs.

## TWIN AZYGOTIC TEST: AN APPLICATION TO ITALIAN TWIN DATA

L. Gedda<sup>1</sup>, C. Rossi<sup>2</sup>, G. Brenci<sup>1</sup>, R. Ziparo<sup>3</sup>

<sup>1</sup>The Mendel Institute, Rome; <sup>2</sup>Department of Probability Calculus, and <sup>3</sup>Department of Physiology, University of Rome

A Bayesian model of qualitative analysis of twin population data independent of zygosity was developed that can be applied to any qualitative genetic trait in twin population data, provided no specific source of variation be introduced by the twin condition, and allows not only estimation of the frequencies of MZ and DZ twins as well as of gene frequencies, but also verification of the trait's mode of inheritance. This model allows the calculation of the posterior distribution of the unknown parameters  $p$ , which represents gene frequency, and  $m$ , which represents the probability for a twin to be MZ. Italian twin data were analyzed to get posterior estimations for  $p$  and  $m$  by means of mean and mode of the posterior distribution.

**A COMPARATIVE STUDY OF INDIVIDUAL DIFFERENCES IN PERSONALITY: AN ITALIAN TWIN STUDY**D. Fulker<sup>1</sup>, P. Parisi<sup>2</sup>, H.J. Eysenck<sup>1</sup>, L. Gedda<sup>2</sup><sup>1</sup>Institute of Psychiatry, University of London, and <sup>2</sup>The Mendel Institute, Rome

An Italian translation of the Eysenck Personality Questionnaire (EPQ) was sent to twins associated with the Mendel Institute in Rome. In all, 603 pairs of twins completed the questionnaire, falling fairly evenly in the five classes: MZ male and female; DZ male, female and opposite-sex pairs. Questionnaire responses were factor analyzed and the *extraversion*, *neuroticism* and *lie* factors emerged with very similar patterns of loadings to those typical of English-speaking subjects. The *psychoticism* factor was less satisfactory, particularly in the female twins. The data on twins were analyzed by the method of maximum likelihood. The neuroticism scale indicated additive genetic variation, and no effect of home environment, in agreement with findings from English-speaking twins. Extraversion, however, differed in the Italian sample in that a significant negative variance component for the effects of home environment was indicated. Further analysis suggested some compensatory effects of home environment and/or the effect of one twin on the other, although it was not possible to resolve the issue using just twins. The lie scale indicated additive genetic variance and a small but insignificant effect of home environment, a finding similar to that obtained with English-speaking twins. For psychoticism there was insufficient variance among females to result in any satisfactory analysis, but for males, some additive genetic variance was indicated. Since the scoring of the psychoticism factor differed considerably from that used with English-speaking subjects, national comparison was not possible.

**ARE PERSONALITY TRAITS STABLE?**

Lindon Eaves

Department of Experimental Psychology, University of Oxford

The examination of several large bodies of twin and family data relating to the principal dimensions of Eysenck's personality theory suggests that the social environment plays relatively little role in the determination of personality differences. Indeed, additive genetic factors and individual specific environmental experiences account for roughly equal proportions of the variance in personality measures. Closer study, however, reveals that the expression of genetic factors in personality changes significantly with age. In particular, inherited differences in juvenile personality do not persist entirely into adulthood and there are inherited differences in adult personality which are not apparent in juveniles. The higher order factors do not exhaust all the information about genetic differences which are reflected in the responses of subjects to items on different occasions. Thus, genetic factors are as highly specific in their effects as those of the environment, and contribute as much as environmental factors to the interaction of subjects and situations.

**PERSONALITY RESEMBLANCE AMONG ADOLESCENTS AND THEIR PARENTS IN BIOLOGICALLY-RELATED AND ADOPTIVE FAMILIES**S. Scarr<sup>1</sup>, P.L. Webber<sup>2</sup>, R.A. Weinberg<sup>2</sup>, M.A. Wittig<sup>3</sup><sup>1</sup>Psychology Department, Yale University, New Haven, Connecticut; <sup>2</sup>Department of Psychoeducational Studies, University of Minnesota; <sup>3</sup>Department of Psychology, California State University, Northridge

Studies of personality resemblance among adolescent and young adult twins are numerous and consistent in finding moderate similarity among MZ cotwins and greater MZ than DZ resemblance. From his review of dozens of personality scales administered to thousands of twin pairs, Nichols (1976) concluded that all dimensions of personality seem to be equally heritable, and about half of the differences in personality are due to genetic differences. There is no evidence for common family environment as a contributor to twin similarity (Loehlin 1979).



If one accepts the twin results as representative of the U.S. and U.K. populations, then one would expect that biological siblings would have the same level of correlation as fraternal twins, and adopted, unrelated siblings should not resemble each other in personality at all. Similarly, parents and their offspring should have coefficients of similar magnitude to those of the DZ twins and ordinary siblings, unless nonadditive genetic effects are important sources of variance. Adoptive parents should not resemble their adopted children in personality at all.

In a study of adolescents and young adults, many of whom were adopted in early infancy, the biological sibling resemblance in personality exceeded that of adopted siblings, but the resulting heritability estimate was only half of that obtained from twin studies. Parent-child resemblance among biological or adoptive parent-child pairs was consistently lower than sibling resemblance, but the heritability estimates were similar to the 0.25 from sibling comparisons. The possible biases in twin study estimates of genetic differences in personality will be discussed.

#### **BLOOD GROUPS, PHYSICAL TRAITS, AND PERSONALITY SIMILARITY IN ADULT DIZYGOTIC TWINS**

J.M. Horn, R. Rosenman, K. Mathews

Department of Psychology, University of Texas, Austin

Similarity in Value Orientation, a major personality factor from the California Personality Inventory, is correlated with similarity in physical traits such as height and baldness, but is uncorrelated with degree of blood group similarity. However, similarity in Person Orientation, the second major personality factor from the CPI, is related to blood group similarity and may be related to physical similarity as well.

**2C WORKSHOP: MULTIPLE PREGNANCY**

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**TWIN PREGNANCIES FOLLOWING CONCEPTIONS ON DIFFERENT DAYS OF THE MENSTRUAL CYCLE**

Susan Harlap

Department of Medical Ecology, The Hebrew University, Jerusalem

The frequency of multiple deliveries was studied among 7456 births to Jewish women who observed the orthodox ritual of sexual separation each month. The day of resuming intercourse, relative to ovulation, was estimated from the characteristics of each woman's cycle and the number of days of sexual abstinence observed after the last menstruation. Ovulation was estimated to have occurred on or around the 14th day prior to the expected day of the next period. Multiple deliveries were least common, ranging from 10.3 to 10.8/1000, in women who resumed intercourse 4, 3 and 2 days prior to ovulation. They were increased, ranging from 21.1 to 36.4 in those who resumed intercourse on days 0, 1, 2 or 3+ following the estimated day of ovulation. These differences were observed for unlike-sexed sets and were not explained by any confounding effects of maternal age or other variables. Although these findings must be qualified by the inexactitude of our method of estimating the day of ovulation, they suggest that ovarian overripeness may be a major associate of polyzygosity.

**SEX RATIO OF TWINS ACCORDING TO ZYGOSITY AND PLACENTAL STRUCTURE**R. Derom<sup>1</sup>, M. Thiery<sup>1</sup>, R. Vlietinck<sup>2</sup><sup>1</sup>Department of Obstetrics, State University of Ghent; and <sup>2</sup>Division of Human Genetics, University of Louvain, Belgium

Because the sex ratio is markedly modified in monoamniotic twins (more than two thirds are female), such ratio might also be modified in MZ twins with other placental structure. Data are presented on a consecutive series of 1800 twin births. Accurate determination of zygosity in like-sexed twins at the time of birth is based on: 1. structure of fetal membranes; 2. typing of cord blood (ABO, Rh, MNS); 3. zymogram of placental tissue. MZ twins are separated in three groups according to the time of splitting of the zygote: 1. early (dichorionic placenta); 2. intermediate (monochorionic-diamniotic placenta); and 3. late (monochorionic-monoamniotic placenta). The sex ratio is compared in the three groups. The various hypotheses to explain the observed differences in sex ratio are reviewed and discussed.

**FURTHER COMMENTS ON THE REPRODUCTIVE PERFORMANCE OF TWIN SISTERS OF KNOWN ZYGOSITY**B. Thompson<sup>1</sup>, I. MacGillivray<sup>1</sup>, A. Sutherland<sup>2</sup><sup>1</sup>MRC Medical Sociology Unit and Department of Obstetrics and Gynaecology, University of Aberdeen; and <sup>2</sup>Institute of Animal Genetics, University of Edinburgh

In an attempt to study genetic components in reproductive performance, twin sisters have been identified, retrospectively, in the records of the Aberdeen Maternity Hospital (A.M.H.) from 1954. Eighty-one pairs have been located and zygosity determined from blood samples. In 46 cases (22 MZ, 24 DZ) both twins had their first baby in A.M.H. In 1979 a similar series of 34 twin pairs (18 MZ, 16 DZ) of primiparae were identified in Edinburgh hospital records and zygosity determined. Independently each series shows that MZ twins are significantly more alike in height and time of menarche than DZ twins. Combined the series give 40 MZ and 40 DZ pairs of primiparae and these will be used to consider certain aspects of reproduction, e.g., preeclampsia, weight gain and pattern of weight gain, birth weight allowing for sex, gestation, and smoking.

**PRECONCEPTIONAL PREDICTION OF TWIN PREGNANCIES**

Ph. Lazar, C. Berger, D. Hemon

Unit of Epidemiology and Statistics, INSERM, Villejuif, France

Prediction of twin pregnancies should help a better management of these high risk pregnancies. Recent progress in the use of ultrasonography has opened the possibility of an early and efficient detection of twin pregnancies. Such an advanced technology, however, cannot reasonably be used on a very large scale in a number of countries with a wide range of economic constraints. For this

reason, the preconceptional prediction of twin pregnancies should help at defining a more limited number of pregnancies which could then be screened for twinning using advanced technology. The results of a case control survey where more than 600 twin pregnancies had been compared to 600 singleton pregnancies are used to propose a method for preconceptional prediction of twinning and to evaluate its efficiency. This method is based upon the simultaneous consideration of the maternal characteristics associated with twinning, namely: age, parity, familial occurrence of twin births, weight, regularity of the menstrual cycles, blood group, previous use of oral contraceptives and/or of fertility drugs.

### ECOGRAPHIC IMAGERY OF AMNIOTIC MEMBRANES IN TWIN PREGNANCIES

R. Bessis, E. Papiernik  
Hôpital A. Béclière, Clamart, France

Early imaging of the septum is a necessary technique to identify each fetus and to make an individual growth survey. A particular echographic aspect of the membranes seems to be specific of dichorionic placentation.

### MEASUREMENTS OF BLOOD FLOW IN THE FETAL AORTA OF TWINS

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Differences between the first and the second twin and between MZ and DZ twins have been reported previously, e.g., in cord blood cortisol values, LS ratio of tracheal fluid, and in fetal breathing movements. Furthermore, the first twin has a larger BPD value throughout pregnancy in 80% of the cases, including MZ twins, although birthweight differences generally are small. Intrapair differences between MZ twins can at least partly be explained by placental transfusion. This phenomenon is difficult to study in utero. For noninvasive measurements of blood flow in the human fetal aorta and umbilical vein, a method has been developed which combines real-time B-mode ultrasonography and pulsed Doppler ultrasound. We applied this method to measure blood flow in the descending part of the fetal aorta in 9 twin pairs in the 32nd and 34th gestational week. The calculations of blood flow were based on estimation of peak blood velocity, a procedure which will lead to a slight overestimation of absolute flow but which permitted studying of relative differences. For normal singleton fetuses in the last trimester, blood flow in the descending part of the aorta has been shown to be closely correlated to fetal weight and estimated to be of 191 ml/min/kg. Fetal weight of the twins was estimated by means of ultrasonic measurements of the BPD and abdominal diameters.

This study did not reveal any differences in aortic blood flow between the smaller and the heavier of DZ twins (20 measurements in 5 twin pairs):  $180 \pm 29$  ml/min/kg and  $179 \pm 27$  ml/min/kg, respectively. In MZ twin pairs ( $n = 4$ ) the mean blood flow of the heavier twin was  $163 \pm 33$  ml/min/kg and in the lighter twin  $213 \pm 61$  ml/min/kg ( $p < 0.01$  paired *t* test). The mean intrapair difference in birthweight was 100 g in DZ and 262 g in MZ twins.

Thus, in MZ twin pregnancies the blood flow in the descending aorta of the smaller twin was significantly greater than of the heavier twin. This suggests that differences exist in the cardiac output of MZ twins. The present study is preliminary, but it demonstrates the feasibility of a new ultrasonic method for studying circulation in twin pregnancy.

### STEROID AND METABOLIC CHANGES IN TWIN PREGNANCY

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Although steroid hormones have been studied in singleton births, there have been no studies in multiple pregnancy in which preterm birth is a major problem. Plasma estradiol  $17\beta$  ( $E_2$ ), plasma estriol ( $E_3$ ), and plasma progesterone were measured serially by radioimmunoassay in uncomplicated twin pregnancies from 28 to 39 weeks of gestation. Plasma estradiol rose from 19.3 ( $\pm 0.9$  ng/ml) to 39.21 ( $\pm 10.59$  ng/ml) and plasma estriol from 155 ( $\pm 26.7$  ng/ml) to 336 ( $\pm 31.6$  ng/ml). The rise in plasma estrogens may have been due to 4 fetal adrenal glands producing an

excess of precursor substrate dehydroepiandrosterone sulphate. Plasma progesterone levels rose from 203 ( $\pm 16.5$  ng/ml) to 387 ( $\pm 95.4$  ng/ml). In triplet pregnancies, progesterone levels were above 500 ng/ml and estriol levels above 300 ng/ml; estradiol levels, however, were similar to twins. In an attempt to prolong pregnancy, oral salbutamol was administered which kept the maternal pulse above 100 bpm to a separate group of 50 twin pregnancies in whom plasma steroids were serially monitored. The perinatal and endocrine outcome was compared with 50 patients treated with traditional bed rest. The gestation of the salbutamol group were significantly prolonged, 271 vs. 258 days ( $p < 0.001$ ), with significantly increased mean birthweight, 2729 vs. 2326 g ( $p < 0.001$ ).  $E_2$  and  $E_3$  levels in the salbutamol group were lower than in the control study. Progesterone levels showed much fluctuation. In six triplet pregnancies there was only one perinatal death. The significance of these endocrine changes will be discussed in relation to parturition, hemodynamic and metabolic effects of sympathomimetic amines on the fetoplacental unit.

#### URINARY TRACT INFECTION IN TWIN PREGNANCIES

Dilip Ray

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Increased incidence of urinary tract infection (UTI) during pregnancy is thought to be due to ureteric dilation as a result of 1. compression by the enlarging gravid uterus at the level of the pelvic brim; 2. compression by the engorged ovarian veins; and 3. relaxation of its smooth muscle due to increased progesterone level in the circulation during pregnancy. All these factors cause stasis of urine, a predisposing factor for UTI, and it is likely that their effect will be more marked in multiple pregnancy. In order to test this hypothesis, all the cases of twin pregnancies delivered in 1974–1979 at the Baltimore City Hospital were studied retrospectively. Out of a total of 81 cases delivered between 23 and 41 weeks of gestation, 16 (18%) patients had UTIs and 3 of the 16 had clinical pyelonephritis. In a control study consisting of 1-3 matched singleton pregnancies for each twin pregnancy, the incidence of UTI was noted to be 7%, the difference being statistically significant ( $p < 0.01$ ). Therefore, the author suggests that mothers with twin pregnancies should be screened more carefully for detection of UTI.

#### TWIN DELIVERY: SPONTANEOUS LABOR OR INDUCTION?

G. Heluin, F. Lavigne, E. Papiernik

Hôpital Bécélère, Clamart, France

Three possibilities in twin delivery are compared: spontaneous delivery, induced delivery with oxytocyn, and without epidural analgesia. The results show the superiority of induction with epidural.

#### THE OUTCOME OF TWIN PREGNANCIES IN ABERDEEN

Ian MacGillivray

Department of Obstetrics and Gynaecology, University of Aberdeen, U.K.

An analysis has been carried out of the perinatal deaths and Apgar scores of the twins according to the presentations and types of deliveries. Factors such as the age of mother, complications of pregnancy and gestation have been taken into account in assessing the results, and tentative conclusions are reached regarding the most suitable form of delivery according to the circumstances.

#### DIAGNOSIS, TREATMENT, PERINATAL MORTALITY, AND OUTCOME IN TWIN PREGNANCY

Björn Westin

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Using 1973 as a starting point there was a marked decrease in perinatal mortality in twin than in singleton pregnancy. The main reason for this improvement was prolonged duration of pregnancy. Differences in Caesarean section rate had no correlation to perinatal outcome. During the course of

pregnancy the symphysis-fundus (SF) distance was measured about 15 times. The values obtained were plotted on a graph with reference values for singleton pregnancy (part of a gravidogram). SF values above mean + 2 SD for singleton pregnancy was regarded as suspicion of twinning. This suspicion was raised in 99% of cases and on average at the 24th  $\pm$  4 (1 SD) week of pregnancy. An acute increase of the SF curve during the last two months of pregnancy usually depends on hydramnios predominantly by MZ twins and implies an increased risk for impaired placental perfusion. Ultrasound screening in the second trimester was not accompanied by a higher detection rate of twin pregnancy than SF tape measurements. However, a diagnosis was made at an earlier stage of gestation. Strict bedrest significantly prolonged pregnancy, lowered the incidence of preterm births and of fetal growth retardation as well as the occurrence CNS damages.

### THE NORTHWESTERN UNIVERSITY MULTIHOSPITAL TWIN STUDY: III. CLINICAL CORRELATES

G.S. Berger<sup>1,2</sup>, R.F. Ellis<sup>3</sup>, L. Keith<sup>3</sup>, R. Depp<sup>3</sup>

With the Technical Collaboration of: R. Taylor<sup>2</sup>, and D.M. Keith<sup>4</sup>

Departments of <sup>1</sup>Obstetrics and Gynecology and of <sup>2</sup>Maternal and Child Health, University of North Carolina School of Medicine, Chapel Hill; <sup>3</sup>Department of Obstetrics and Gynecology, Northwestern University Medical School and The Prentice Women's Hospital and Maternity Center, Chicago; <sup>4</sup>Center for Study of Multiple Gestation, Chicago, and Calculon Corporation, Arlington, Virginia

The Northwestern University Multihospital Twin Study had developed a data base of 588 mothers and their 1126 twin concepti from a group of 13 hospitals in the Chicago metropolitan area. The deliveries under study took place between 1970 and 1975. Prior data analyses have characterized the maternal and infant populations as well as differences in mortality between the first- and second-born twin. The present paper is an attempt to delineate those obstetric parameters that significantly affect pregnancy outcome in twin gestation. Three major outcome variables (birthweight, Apgar score, and survival at birth) were correlated with antepartum and intrapartum factors which include: (1) Patient demographic characteristics; (2) Prenatal variables such as time of diagnosis of multiple gestation and pregnancy-induced hypertension; (3) Intrapartum factors including fetal presentation, mode of delivery, time-interval delay and anesthesia. The purpose of this paper is to complete the establishment of the data base for future comparisons of outcome variables in the five-year period between 1976 and 1980 during which time regionalized perinatal care centers were organized.

### THE EUROPEAN TWIN REGISTRY

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<sup>1</sup>Department of Obstetrics, State University of Ghent; and <sup>2</sup>Division of Human Genetics, University of Louvain, Belgium

Accurate recording of the zygosity of twins at birth, on a scale large enough to study the rate of concordance and discordance of the most common congenital malformations, is the first aim for which the registry is created. Approximately 40 teaching hospitals from EEC are collaborating. The minimal requirements for participating are: (1) registering of all multiple births; (2) recording of the type of placentation; (3) typing of cord blood (ABO, Rh, MNS) in like-sexed dichorial twins; (4) sampling and deep-freezing of placental tissue corresponding to each infant; (5) careful recording of congenital abnormalities; (6) autopsy on all perinatal deaths in twins; and (7) possibility to trace the twins for follow-up. All data are centralised. The twins are classified in three groups: MZ, probably MZ, and DZ. Type of incidence of malformations are compared in the three groups. The registry will also be used for other twin-related studies and for monitoring the quality of perinatal care. The incidence of preterm birth and the perinatal mortality rate are greatly increased in twin pregnancies. The fetal outcome in such pregnancies, therefore, is a sensitive measurement of the adequacy of obstetrical care.

## 2D CONCURRENT SESSION: TWIN RESEARCH IN PHYSIOLOGY AND ANTHROPOLOGY

### BLOOD PRESSURE IN TWINS

A. Heiberg<sup>1</sup>, P. Magnus<sup>1</sup>, K. Berg<sup>1</sup>, W.E. Nance<sup>2</sup>

<sup>1</sup>Institute of Medical Genetics, University of Oslo; and <sup>2</sup>Department of Human Genetics, Medical College of Virginia, Richmond

Blood pressures were recorded in two series of twins, one consisting of 200 pairs (Series A) and the other of 36 pairs (Series B). The twins in Series A were drawn from a population-based twin registry and were either 59 or 35 years of age with approximately equal representation of both sexes and zygosity categories within each age group. Series B consisted of 30 MZ and 6 DZ pairs, who were members of a twin club (14 to 71 years of age). Age and sex-adjusted blood pressure was normally distributed and the mean values were not significantly different between the MZ and the DZ twin group. The F ratios between the total variances were, however, of borderline significance between all MZ and DZ twins for diastolic pressure. The other groups showed no association between twin type and total variance. The following intraclass correlation coefficients and heritability estimates were obtained for adjusted blood pressures:

Twin Group	Systolic Pressure			Diastolic Pressure		
	$r_{MZ}$	$r_{DZ}$	$h^2$	$r_{MZ}$	$r_{DZ}$	$h^2$
All males	0.51	0.31	0.41	0.39	0.32	0.13
All females	0.63	0.30	0.49	0.69	0.18	1.03
TOTAL	0.60	0.32	0.56	0.59	0.24	0.71

It is concluded that a genetic contribution to the variation in normal blood pressure is found in most age and sex groups for both systolic and diastolic blood pressures, although marked heterogeneity is evident in the series examined.

### THE ATRIOVENTRICULAR CONDUCTION TIME: A HERITABLE TRAIT?

P. Møller, A. Heiberg, K. Berg

Institute of Medical Genetics, University of Oslo

The atrioventricular conduction time (the P-R interval) is a frequently measured ECG parameter. Race, sex, and heart rate are known to influence the P-R interval, but the within-subject variation has been shown to be very small. The inter- and intraobserver differences have been studied and found to be small. Clustering of persons with short P-R intervals was observed in a sibship. This initiated further family studies. Strong evidence for a familial influence on the P-R interval was obtained in 35 adult relatives of 6 and 9 probands with short and long P-R intervals, respectively. The P-R interval was measured in 33 twin pairs. The intraclass coefficient was 0.66 in MZ twins and 0.36 in DZ twins. These findings appear to confirm that there is a significant genetic influence on the P-R interval. The existence of genes with a major effect cannot be excluded.

### POSSIBLE RESTRICTIVE EFFECT OF NORMAL GENETIC MARKERS ON THE VARIATION IN SERUM CHOLESTEROL WITHIN MONOZYGOTIC TWIN PAIRS

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Several normal genetic markers are known to influence lipid levels in man. Thus, Sing and Orr showed that variation in four marker systems (ABO, haptoglobin, Gm, and Secretor) may influence serum total cholesterol level. If (part of) the effect of genetic markers is a stabilizing effect on the level of serum cholesterol, then MZ pairs who carry certain marker genes may show less within-pair variation than those who lack these genes. This possibility was examined, with respect to

serum cholesterol and ten genetic marker systems: ABO, Rh, MNSs, Lewis, P, Duffy, Kidd, Kell, C3, and Hp, in a sample of 97 MZ pairs. For each marker system the pairs of twins were grouped in two or more classes according to their genotype. The mean of the absolute intrapair differences in serum cholesterol was used as a measure of within-pair variation, and means were compared between groups of twin pairs with different marker types. Two of the ten F-tests gave significant ( $p < 0.05$ ) results, namely, the tests for the MNSs and the Kidd systems. No clear trend was found for the ABO and the Hp systems. It is concluded that a possible restriction on environmentally caused variability in serum cholesterol level is imposed by the genotype in two of the ten marker systems studied.

#### GENETIC CONTROL OF CELL MEMBRANE LOW-DENSITY LIPOPROTEIN (LDL) RECEPTOR ACTIVITY IN THE ABSENCE OF FAMILIAL HYPERCHOLESTEROLEMIA

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Cell surface receptors with high affinity for low-density lipoprotein (LDL) have been found in cultured cells from persons who are not homozygous for familial hypercholesterolemia (FH). Cells from FH heterozygotes have about half normal level of LDL receptor activity. Considerable variation in LDL receptor activity was observed in fibroblasts cultured from normal persons as well as from FH heterozygotes. The problem was approached by studying LDL receptor activity in cultured fibroblasts from 14 MZ and 21 like-sexed DZ, normolipidemic twin pairs of similar age. Cell association and degradation of 125I-LDL were assayed. For the two LDL receptor assays the intrapair differences were consistently smaller in MZ than in DZ twin pairs ( $p < 0.03$  and  $p < 0.04$ , respectively). These findings suggested a significant genetic influence on the variation in LDL receptor activity. However, the existence of more than one normal allele at the receptor locus has as yet not been proved. It may be speculated that part of the population variation in susceptibility to atherosclerosis may be caused by genetic variation in LDL receptor activity among individuals with normal plasma LDL-cholesterol values. Two MZ pairs were discordant for psoriasis. In both cases, the psoriatic twin had much lower LDL receptor activity than the cotwin. All 4 twins had normal serum lipid values. This observation may suggest that psoriasis can interfere with LDL receptor activity without causing gross changes in lipid levels.

#### DIETARY INTAKE IN MONOZYGOTIC TWINS

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As part of a study of dietary habits of MZ twins, complete three-day dietary intake logs were maintained by 15 male and 13 female pairs of identical Caucasian twins ranging from 25 to 61 years of age. Raw stature and weight scores were standardized to remove effects of age and sex using age and sex-banded U.S. population norms. The male twins included in the study were slightly taller and heavier than average, while the female twins were shorter and lighter than average. The mean caloric intake of males ( $2756 \pm 143$ ) was significantly greater than females ( $2074 \pm 98$ ). Male twins also tended to be more similar in mean caloric intake, with an intraclass correlation of  $0.72 \pm 0.13$ , than female twins ( $0.46 \pm 0.23$ ). Male cotwins were slightly more similar for the percentage of carbohydrates, proteins, fats, sodium, potassium, iron, and phosphorus in their diets than were female cotwins, while female twins were characterized by a greater similarity in calcium intake. There were no significant differences in mean intake of carbohydrates, fats, proteins, iron, phosphorus between males and females. However, mean sodium intake of males was significantly greater than that of females, while mean potassium and calcium intake of females was greater than that of males.

**THE INHERITANCE OF PLASMA AND RED BLOOD CELL MAGNESIUM, ZINC, AND COPPER LEVELS STUDIED BY TWIN AND FAMILY DATA**P. Darlu<sup>1</sup>, Y. Michotte<sup>2</sup>, E. Defrise-Gussenhoven<sup>3</sup>, J.G. Henrotte<sup>1</sup><sup>1</sup>Human Biometry Unit, National Research Council, Paris; <sup>2</sup>Pharmaceutical Institute and <sup>3</sup>Center of Biomathematics, Free University of Brussels

The variability of Mg, Zn, and Cu concentrations in plasma and/or erythrocytes was investigated by twin and family studies. Twins were sampled in two distinct ways and in two different West-European regions. In one of the samples they were divided in twins living together and separately. Two series of families were studied, one in a homogeneous environment, the other in a more diverse environment. Samples were compared by univariate and multivariate analysis. The following conclusions can be drawn: (1) There is a significant genetic variability of R.B.C. Mg and Zn and of plasma Mg but not of plasma Zn and Cu; (2) there is an influence of the common environment on the extent of resemblance between twins and between siblings for R.B.C. Zn and plasma Mg; (3) there is an interaction between the genetic and environmental resemblance for R.B.C. Zn. Furthermore, the analysis of covariance suggests that the genetic regulation systems of Mg and R.B.C. Zn are different. A biological interpretation is given.

**A GENETIC ANALYSIS OF TASTE THRESHOLD FOR PTC**

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Taste threshold for phenylthiocarbamide (PTC) was measured in 393 offspring from the families of 85 MZ twin pairs. The sample included data from 32 male half-sibships with 147 children and 53 female half-sibships with 246 children. PTC scores were bimodally distributed with modes at 1 and 8 and the antimode at 5. Nested analyses of variance were performed on the PTC scores of children contained in male and female twin kinships, respectively, yielding estimates for among, between and within components of variance. Solutions for the genetic expectation of the variance components under several models for which the assumption of no epistasis was made, were obtained utilizing generalized inverse techniques. Because of the non-normality of the distribution, a jackknife procedure was used to obtain 95% confidence intervals for the estimates of the genetic parameters. Analysis revealed that 37.9% of the observed variation of PTC threshold was due to additive genetic effects, 16.6% was due to dominance effects, 14.2% was due to maternal effects, 13.7% was due to a common sibship environment, and 17.6% was due to random environmental effects. This yields a broad-sense heritability estimate of 55% for threshold ability to taste PTC.

**STRUCTURE AND COLOUR OF THE IRIS IN TWINS**

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In 48 MZ and 15 DZ twins the micromorphological details of the iris were evaluated. Diagnosis of zygosity was based on 20 serological markers and physical similarity. Three concentric zones (inner, outer and marginal) of the iris were distinguished and judged according to colour and structure. The determination of pigmentation was made with help of the Martin-Schultz table. DZ twins differed markedly in the pigmentation of the inner and outer zone, to a less degree in that of the marginal zone. The structure showed a low degree of intrapair variability in both types of twins. One MZ twin pair was seen, in which only one twin showed partial heterochromia. The differentiation of the iris in zones and the separate evaluation of pigmentation and iris pattern can be regarded superior to merely considered "iris colour".

**VARIATIONS OF HERITABILITY AS A FUNCTION OF PARENTAL AGE**F. Lints<sup>1</sup>, P. Parisi<sup>2</sup><sup>1</sup>Genetics Laboratory, Catholic University of Louvain, Belgium; and <sup>2</sup>The Mendel Institute, Rome

The analysis of finger ridge counts of 530 twin pairs, classified by sex, zygosity, and parental age, has confirmed previous indications of a parental-age effect on the heritability of quantitative traits. The various estimates appear to increase with the parents' age at conception, the effect being much more evident and consistent in the case of maternal age.



**DETERMINANTS OF RIDGE COUNTS IN MONOZYGOTIC TWIN KINSHIPS**

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The inheritance of total ridge count (TRC) was studied in 967 individuals from the families of 111 pairs of MZ twins. The sample included data on 47 male half-sibships with 224 offspring and 64 female half-sibships with 299 offspring. The males in this sample had a mean ridge count of  $135 \pm 2$  and the females a mean ridge count of  $124 \pm 2$ . The distribution of scores for females showed evidence for significant skewness. For this reason, prior to the analysis, the data were corrected for sex and adjusted to normality using a power transformation. Nested analyses of variance were performed on the ridge counts from male and female half-sibships separately to derive estimates of among, between, and within variance components. These estimates were then used in a nonlinear least squares program to estimate genetic and environmental parameters and to determine the goodness of fit of various models. A model which included additive genetic and dominance effects could not be rejected ( $p = 0.67$ ) but did not fit the data as well as a simple additive genetic-random environmental model ( $p = 0.81$ ). The addition of maternal effects to the latter model also provided a satisfactory fit ( $p = 0.68$ ). However, there was no improvement in the goodness of fit over the simple model, and the estimated magnitude of the maternal effect was not significantly different from zero.

**GENETICS OF QUANTITATIVE VARIATION OF HUMAN SCALP HAIR DIAMETER**

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To understand the genetic basis of quantitative histological characteristics of the diameter of human scalp hair, 9600 strands from 48 pairs of zygosity-determined German twins were utilized. Data collected on diameter of scalp hair were statistically treated with analysis of variance model. The results of analysis of variance and heritability estimate indicate the presence of a measurable genetic component of variability in the diameter of human scalp hair. Besides variation of diameter between hair strands from two different individuals, the components of variations, such as (1) within strand variation, and (2) within individual between strands variation, are estimated.

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**2E CONCURRENT SESSION: TWIN RESEARCH IN BEHAVIOR GENETICS**


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**TWINSHIP AS HANDICAP: FACT OR FICTION?—A LONGITUDINAL STUDY**

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As part of a follow-up investigation, the general ability, learning competencies, moral development and social adjustment of a group of twins and singletons were assessed and compared. In the original investigation, the family interaction and social development of 46 pairs of 2½ year-old male twins and 44 male singletons of a similar age were studied. The results indicated that twins spoke less and were also spoken to less often by their parents than were singletons. The twins received fewer directions and verbal justifications of rules, less praise and approval and fewer overt expressions of affection. They expressed more attachment to their parents than did singletons. Subjects for the present investigation were 38 of the original twin pairs, now between 8 and 10 years of age, and a new group of 38 male singletons. Each of the 114 children were assessed at school. Measures included the Crichton Vocabulary Scale, the Raven's Progressive Matrices, the Peabody Individual Achievement Test, and two tests of moral reasoning, the Guilt Index and the Moral Advice Test. Classroom teachers rated the children for academic competence, dependence, independence, compliance, internalized standards, speech, peer relations, and social adjustment. Height and weight measures were taken for all children. Based on the results of the earlier investigation, as well as a number of other studies of twin development, it is hypothesized that differences will exist in the ability, achievement and social development of twins and singletons, although these differences may have diminished with age.

**PHENOMENOLOGY OF THE SELF IN THE STUDY OF TWINS**

Luigi Gedda, Silvia Borella  
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A study of 28 MZ and 20 DZ twin pairs fails to support the view that the twin condition be a specific source of conflicts or frustration. However, the self of the individual MZ twin appears to be particularly characterized by common instinctual and psychological motions leading to a tendency towards self-assertive attitudes.

**FACTORS IN DIFFERENTIAL DEVELOPMENT: A LONGITUDINAL STUDY OF MONOZYGOTIC TWINS**

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What are the biological and environmental determinants of continuity and discontinuities in development? Eight sets of MZ twins have been studied from gestation through preadolescence. Data on prenatal experience, family characteristics, early psychobiological endowment, preschool development, unusual experiences, and social and cognitive functioning have been used to understand similarities in development within and between twinships. At the twins' preadolescence, parents completed a scale which assesses 12 areas of adjustment. Children were interviewed about interests, peer and parental relationships, school and fantasies; parents were interviewed about children's health, social relationships, character, and cognitive competence. Teachers and pediatricians completed a Behavioral Report and provided records. Data was related to measurements obtained since gestation, including prenatal variables, the assessment of psychobiological competence at age one week, and IQ at preschool.

Children in six pairs were within a few points of each other on the newborn endowment scale (FES) and preschool IQ scores. In these sets, similar problems were manifested at age 5 years. In spite of similarities, parents finely discriminated between children, and there was no lack of individuation. Four of six pairs were rated very much alike in preadolescence in interest, school performance, temperament, strides toward independence, and heterosexual interest. Two other sets with similar early development had marked dissimilarities during later childhood. In one set, one child was hyperactive and required psychoactive medication; in the other set, one child was emotionally upset following a hernia operation and a loss of a testicle. In two sets, children were dissimilar as newborns (intrapair differences in FES of 9 and 11 points). Later differences could be traced to endowment. In one pair, Twin B's health problems were outgrown, but Twin A developed Crohn's disease at age 9. In the other, one twin was anxious, sad and easily intimidated, and had dermatitis; his cotwin was enuretic and moody. For this cohort of intensively studied MZ twins, personality development at preadolescence could be seen to reflect interactions between genetics, family life, and accidents of experience. Continuities could be discerned across behavioral stages.

**FINNISH TWINS REARED APART: PRELIMINARY CHARACTERIZATION OF REARING ENVIRONMENT AND PERSONALITY**

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A pilot study of like-sexed twins reared apart was carried in the Finnish Twin Registry to describe and compile data on the rearing environment. The survey also included a self-rating personality inventory using semantic differentials. So far, 286 twin pairs separated at age 10 or less have been characterized. Of these, 53 pairs were separated under age one, 66 at 1–2, 67 at 3–5, and 100 at 6–10 years of age. The most common reasons for separation were economic (34%), maternal death (19%), the mother being the sole family supporter (13%), paternal death (12%), and adoption by relatives (8%). The reason was unknown in 6%. After separation, 10% lived together two or more times and 20% one time. After separation, daily or almost daily contact between twins occurred in 28%, contact about once a month in 12%, every six months or less frequently in 51% and never in 9%. One half lived in the same community after separation and 37% went to the same school. After separation, 30% of twins were reared by their own mother, 26% by their own father, 25% by a foster mother, who was a relative, 10% by a foster father, who was a relative, 29% by a non-relative foster mother, and 21% by a non-relative foster father. 23% of twins were reared in other conditions. The relationship of rearing environment to personality factors will be presented and discussed.

**TWIN RESEMBLANCES IN PERSONALITY**

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Psychological tests and scales previously validated as measures of personality and creativity were administered to three samples of twins, one American and two Italian. Sixty pairs of like-sexed twins in late adolescence, evenly divided as to sex and zygosity, comprised each sample. This paper focuses on data from the most recently tested sample, the interpretation being supported by analyses conducted on the earlier samples. In the third sample, 32 pairs of the twins were instructed to fill out the Gough Adjective Check List, a set of 300 personally descriptive terms, so as to describe self. A comparison was then made between MZ and DZ pairs both for agreement on each of the 300 items separately and for the entire set. In general, for the set qua set there is no significant difference between MZ and DZ pairs, whether male or female, in the correlation of Twin A's self-description with Twin B's self-description. Nonetheless, there is an interesting group of adjectives in which there is a strong degree of concordance for MZ pairs and significantly less for DZ. These adjectives cluster around the key adjective "artistic", and the findings on nonverbal measures of creativity in all three samples support the adjective results. Further analysis by scales, including the recently published Gough ACL creativity scale and the Welsh Intellectence and Origence scales is under way.

**RORSCHACH TEST AND MYOKINETIC PSYCHODIAGNOSIS OF MIRA Y LOPEZ IN MZ AND DZ TWINS**

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This study aims at assessing the role of genetic vs. environmental factors in the determination of personality components, as well as the chronological fluctuations of their interactions. Two projective techniques, one verbal (Rorschach test) and one kinesigraphic (Mira y Lopez PMK test), were used, along with an intelligence test (Raven Progressive Matrices), in a sample of 28 MZ and 27 DZ pairs of twins of both sexes and two age groups, 14–20 and 25–65 years. The results are discussed in the light of the view that in the critical period of adolescence the twin bond may come to represent a powerful force leading to differentiation between twin partners.

**HEREDITY AND PERSONALIZATION IN VISUAL PERCEPTION**

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The administration of Zulliger's tables and some gestaltic pictures to a sample of 30 MZ and 25 DZ twin pairs has allowed to identify different degrees of "heredity" and "personalization" in visual perception. Hereditary factors are found to play a relevant role at the first level of perceptual organization, the formal-sensorial level, a minor role at the second, the objective-intellectual level, and practically no role at the affective-perceptual level, where personalizing effects are particularly evident.

**ENVIRONMENTAL CHILDHOOD SIMILARITY AND SIMILARITY IN ADULT PERSONALITY AND NEUROTIC DEVELOPMENT IN TWIN PAIRS**

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Originally the classical twin method assumed that the environment is no more similar for MZ than for DZ twin pairs. This assumption is now repudiated in several twin studies. The present paper deals with the consequences of more similar childhood environment of MZ twin pairs for the interpretation of the results of twin studies dealing with the importance of genetic factors in the development of personality and neuroses.

In a study of 299 like-sexed twin pairs where at least one of the twin partners had been admitted to any of the psychiatric institutions in Norway for milder psychiatric disturbances, it was shown that the intra-pair similarity in childhood environment was of no importance for intra-pair differences in oral, obsessive, and hysterical personality traits. Irrespective of childhood environmental similarity, MZ twins were more similar than DZ twins. As for concordance in neuroses, however, it was shown that the difference in concordance between MZ and DZ pairs disappeared when the childhood environment was very dissimilar. The results are interpreted as a support for a hypothesis about the development of neuroses as an interaction between heredity and environment. It is maintained that the classical twin method can give no universal estimate about the relative importance of hereditary and environmental factors in the development of neuroses. Any estimate is influenced by the environmental intra-pair variation in the twin sample.

#### THE MULTIPLE THRESHOLD MODEL OF DISEASE TRANSMISSION: APPLICATION TO TWIN DATA ON AFFECTIVE DISORDERS

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Concordance rates for bipolar and unipolar affective disorders in MZ twins are predicted in two-threshold models of inheritance where the two illness types are represented on a continuum of genetic-environmental liability.

#### A TWIN STUDY OF OBSESSIONALITY

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The Leyton Obsessional Inventory is a reliable measure of obsessionality which distinguishes satisfactorily between normal subjects and obsessive-compulsive neurotics, and provides scores on obsessional trait, symptom and resistance scales. The 42-item questionnaire version was completed by 450 twin pairs. Multivariate biometric analysis was carried out on the responses. Common environmental factors had virtually no influence on overall obsessionality, which had a heritability value of 0.48. The genetic correlation between symptom and trait scores was 0.63 suggesting that these scales measure variables less distinct than their names imply. Four principal components can be derived from the Inventory of which the "clean and tidy" factor had the highest (0.42) and the "incompleteness" factor the lowest (0.30) heritability. The resistance scores were examined using the threshold approach with cuts at 50 and 75% of the population; additive genetic variance was 0.41. Subjects also completed the Eysenck Personality Questionnaire. There was a weak negative relationship between obsessionality and both extraversion and psychoticism, but obsessional symptoms to a high degree and obsessional traits to a considerable degree were genetically correlated with neuroticism. This raises the question of how much of the undoubted genetic contribution to obsessionality in normal subjects is mediated through the transmission of a general tendency to neuroticism.

#### TWIN-FAMILY STUDIES OF COMMON FEARS AND PHOBIAS

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Human fears can be categorized into two broad classes: those with a social or cultural basis (e.g., fear of god) and those that are, or once were of adaptive importance (e.g., fear of snakes). To evaluate genetic variance in adaptive fears, we administered a 51-item fear survey schedule to (1) MZ and DZ twins and their parents, (2) kinships of MZ parents, and (3) nuclear families. Subjects rated their fearfulness of each event or object on a seven-point scale. The total sample includes > 2000 individuals ranging in age from 10 to 70. Age and sex effects are removed by Z-transformation. Previous factor analysis of the fear survey identified four orthogonal factors

composed of fears that are highly prevalent in contemporary populations and that were of adaptive significance to early man. Results for our twin-family studies reveal evidence of significant genetic influences on both individual items and factor scores which measure such fears. Falconer heritability estimates range from 0.24 to 0.78 and midparent-offspring regression range from 0.18 to 0.50. These results are consistent with the suggestion, proposed by Darwin in 1877, that common contemporary fears represent genetic consequences of ancient dangers.

#### **TWINS REARED APART: PRELIMINARY FINDINGS OF PSYCHIATRIC DISTURBANCES AND TRAITS**

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In 14 MZ twin pairs reared apart since early life by nonbiologically related adoptive parents, psychiatric disturbances and general personality traits were assessed during a week of intensive psychological and medical work-up using personal interviews and a variety of psychometric assessments. Although there are some qualitative and some quantitative differences in the strength of expression of traits of psychiatric interest which presumably are due to environmental differences, there is no discordance in presence or absence of the following traits: phobias, nightmares, stuttering and other speech impediments, hyperactivity, similar abuse of alcohol and other medications, similar responses to stress, and similar personality patterns including emotional lability, tendencies to anxiety and depression, similar responses to bereavement, and temper tantrums.

#### **THE MAUDSLEY TWINS: SURVIVAL OF THE COTWIN AND FUNCTIONAL PSYCHOSIS**

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It has been suggested that obstetric complications may be associated with certain psychiatric diagnoses, particularly schizophrenia. However, despite higher stillbirth and infant mortality rates in twins than in singletons, the incidence of functional psychoses in twins is the same as for those of single birth.

All patients attending the Maudsley Hospital have routinely been asked about twinship since 1948. Those with a cotwin surviving childhood are incorporated into the twin register, and used for many genetic studies. However, a number of patients born twins are lost to this register because of death of the cotwin in childhood, so the original hospital records were examined for differences in those included and excluded from the register. Surprising numerical differences emerged. 408 twin pairs were identified from hospital records during the periods 1967–1969 and 1973–1978: in 140 of these (34%), the cotwin did not survive childhood. This figure is substantially higher than the 20% estimated from a general inner city sample of twins. Most interestingly, the rate of illness from functional psychosis was almost twice as high among those whose cotwin did not survive, compared to those pairs with double survival (9.3% and 17.1%, respectively,  $p < 0.02$ ). Looked at the other way, 50% of those suffering from manic-depressive psychosis and schizophrenia had a nonsurviving cotwin compared to 30% for character disorders and neurosis. Differences between the groups were looked for in age, social class, maternal age, and family history.

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### 3A SYMPOSIUM: TWIN RESEARCH IN DEVELOPMENTAL STUDIES

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#### SYNCHRONIZED DEVELOPMENTAL PATHWAYS FOR INFANT TWINS

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Developmental processes in infant twins are considered from the standpoint of how closely synchronized the twins are for growth spurts and lags, and whether the course of mental development follows the same trajectory as physical growth. The episodes of acceleration and lag may be independent for the two domains, so that an infant who is precocious in physical growth may not necessarily be advanced in mental development. The phasing of maturational episodes appears to depend upon timed gene-action systems which unfold in sequential order, and which promote new behavioral capabilities as well as physical growth. Data are reported from a large sample of MZ twins that were followed from 3 to 24 months of age, with measures made of height and mental development. The measures were analyzed separately for the degree of twin concordance over ages, as an indicator of how closely the twins' growth spurts were synchronized. Then the measures were correlated to determine whether the episodes of acceleration and lag occurred at the same time for height and mental development, or were out of phase. The results showed only a low-order correlation among measures, indicating that the episodes of rapid growth and lag were essentially independent for the two domains. By contrast, the twin concordance was very high for each measure separately. The results are interpreted in the broader context of timed gene-action systems of extraordinary precision which initiate and regulate the episodes of growth. Some recent results from developmental genetics and neurobiology are reviewed for their relevance to developmental studies of twins, especially in the area of behavior.

#### HEREDITY-ENVIRONMENT INFLUENCES ON GROWTH AND DEVELOPMENT DURING ADOLESCENCE

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Data concerning physical growth, mental ability and school achievement test results have been collected in Sweden for MZ and DZ twin pairs and a group of controls from 10 to 18 years of age. There are no separated twins included in this study so all twin pairs have been raised in the same homes and often also attended the same classes at school. A model for interpreting heredity-environment contribution on the basis of longitudinal twin data is presented. Interactional and correlational effects are hypothesized to vary depending upon type of characteristic studied and the permissiveness-restrictedness of environmental factors. For height growth and inductive ability a parallel trend is found for intrapair similarity in MZ and DZ twins over a time period. This would imply that these characteristics tend to be primarily controlled by genetic factors under the

circumstances prevalent for the twin group studied. Weight growth, especially for girls, verbal ability and school achievement test results, on the other hand, seem to be more susceptible to interactional and correlational influences, indicating that different genotypes will be affected and react differently to a similar environmental impact. This is reflected in a divergent trend for intrapair similarity in MZ and DZ twins. Earlier twin studies have generally interpreted interactional and correlational effects as genetic variance and therefore tended to overestimate such influences. The results of this study seem to imply that the relative contribution of different sources of variation depends upon type of characteristic studied but also the environmental room available for the expression of genetic factors.

#### **DEVELOPMENTAL PATTERNS IN MONOZYGOTIC TWINS REARED APART**

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MZ twins reared apart provide a powerful design for the detection of genetic influence on developmental phenomena. The demonstration of concordance for striking developmental changes in MZ twins and discordance in DZ twins is powerful, but not conclusive proof that genes are involved in the unfolding of the relevant processes. The demonstration of similar patterns of development in MZ twins reared apart would strongly bolster the within-family data.

We have gathered detailed life histories from 11 pairs of adult MZ twins reared apart from early in life. In some cases, we have also been able to retrieve school grades, medical records and a photographic history of morphological development. Using these records, it has been possible to demonstrate some remarkable similarities in the time of onset (and, in some cases, course of development) of: deterioration of school performance, development and maintenance of occupational interests, increases and decreases in weight, and development of psychiatric problems.

#### **THE INTERACTION OF FAMILY ATTITUDES AND COGNITIVE ABILITIES IN THE LA TROBE TWIN STUDY OF BEHAVIOURAL AND BIOLOGICAL DEVELOPMENT**

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The La Trobe Twin Study is a longitudinal investigation of more than 1000 children, comprising twins, their siblings and cousins, most being followed from birth but including older children for an analysis of cohort effects. In the general context of studying genetic and environmental influences on the course of development, the main emphases are on: (1) The growth of thought processes in the child; some of the problems and criteria are discussed for developing a test battery which focuses on current areas of controversy over children's thinking, rather than relying on standard cognitive tests. (2) The social impact of twins on the family situation and the long-term consequences for all children in the family. Apart from work on parental attitudes to twin similarity in relation to test performance, the stresses the twins impose on the parents, singleton sibs, and on the twins themselves have rarely been considered in genetic analyses. In cooperation with the Australian Multiple Birth Association, the major problem areas have been identified and a wider survey of the 10,000 sets of twins in the Australian National Twin Registry is being planned.

Combining longitudinal behavioural and biological data with detailed family, medical and social histories and annual attitude surveys involving parents, twins and siblings plus teachers' ratings, provides an opportunity for understanding far more about the course of development than conventional genetic analyses permit. Some specific hypotheses are discussed, especially the problem arising in any longitudinal study from feedback to the parents, children and teachers about the relative abilities of the twins and the consequences this may have for performance in subsequent years.

## 3B SYMPOSIUM: TWIN RESEARCH IN CHRONOGENETICS, AGING, AND CANCER

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### TWIN RESEARCH AND CHRONOGENETICS

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The study of MZ twins is the best test of the temporal dimension of the gene, i.e., of chronogenetics. As biochemical findings indicate, the lifespan of the gene's information (or chronon) depends on its stability (or ergon). The temporal dimension of the specific genotypes is reflected in the phenomenon of mirror imaging, in the parallel times of ontogenesis and senescence, as well as in the times of onset and evolution of hereditary pathology in twins (twins' synchronism). The similarity in the times of onset of both normal and pathologic genetically conditioned phenomena in relatives (family isochronism) can also be interpreted on the same basis. As a possible application, chronogenetics may be used for the identification of the most favorable individual environment, as well as for planning an individualized preventive medicine.

### AGING IN TWINS: FROM THE SEVENTH TO THE TENTH DECADE OF LIFE

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### THE AGE-DEPENDENCE OF DISORDERS OF AGEING: IMPLICATIONS FOR STUDIES OF TWINS

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Definitions of "ageing" are reviewed. The frequent identification of ageing with life-shortening and death is criticized. Such definitions exclude conspicuous conditions such as arcus senilis, and the loss and greying of hair which, of themselves, are not known to increase the risk of death. Another fairly common idea, that the term "ageing" should refer only to those conditions to which all aged persons are susceptible, would, if adopted, greatly restrict the scope for studies of twins in gerontology.

The autoaggressive theory of ageing is outlined and its scope with respect to fatal and nonfatal disorders is indicated briefly. Emphasis is given to its application to ischaemic heart disease (IHD), the most important single cause of death in many countries. Predisposition to IHD is genetically determined. The main form of the disease (8th ICD 410 and 412 in part) is initiated in predisposed persons by six somatic mutations in a single stem cell of the central system of growth control. Following the last random initiating somatic mutation a *latent period* elapses before death occurs. In England and Wales the average duration of this latent period is about 13 years in men and 26 years in women. The duration is largely genetically determined with wide variations from one subgroup to another. This additional role of inheritance introduces previously unrecognized complications for the study of concordance in twin pairs, some examples of which are described.

### RESULTS OF THE FORTY-YEAR LONGITUDINAL STUDY OF THE BERLIN TWIN SERIES

Gerhard Koch

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A follow-up of the Berlin twin series, originally studied in the forties, has been carried out. The study embraces 450 twin pairs (235 MZ and 215 DZ, including cases of multiple births). Most of the twins still live in Berlin and are 50–60 years of age, the age range being, however, 42–87. Degenerative diseases of the skeletal system were found most commonly, as well as cardiovascular diseases and diabetes, quite apart from benign and malignant tumors. With respect to the latter, the data thus far obtained from this study support the theory that genetic factors do not generally play a major role. However, high-risk families appear to exist. Stronger genetic effects appear to be at work in the case of benign tumors.



## 3C WORKSHOP: INTELLIGENCE—TWIN AND ADOPTION STUDIES

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### IN SEARCH OF THE MISSING, ENVIRONMENTAL VARIANCE IN COGNITIVE ABILITY

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After reviewing causes of inequality, Jencks has called attention to the fact that a large proportion of the total variance in cognitive ability has not been accounted for. He attributes this to "luck" and random factors. Some of the missing variance is probably systematic but of a more subtle nature than socioeconomic status and other gross demographic characteristics. Childrearing attitudes and other parental personality variables have been suggested. A search for the missing variance seems especially necessary now, because recent estimates of the genetic variance in ability are considerably lower than the 50% to 80% previously reported. This is particularly true for studies of infants, but it is also true for studies of older persons. For infants, it may be that the course of development in infancy is uneven and so rapid that measures at one particular time cannot meaningfully characterize the infant's status. For older persons, recent results have generally been corrected for the effects of age, which inflated resemblance in the older studies. We shall summarize several efforts to locate the elusive variance. Analyses will include results of the *Hawaii Family Study of Cognition*, the *Colorado Family Study*, the *Colorado Adoption Project*, and a study of students in which biographical data were correlated with ability test scores. In general, we found that the "environmental" variables in our studies accounted for about 10% of the total variance. Although these variables contribute to the child's environment, we suspect that they represent in part the genetic attributes of the parents.

### COMMENTS ON THE STUDY OF INTELLIGENCE USING TWIN AND ADOPTION STUDIES

Thomas J. Bouchard

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Behavior genetic studies of intelligence with twins and adopted children and/or adopted twins are experiments of nature. Unfortunately, nature does not conduct clean experiments. As a result, the problem of demonstrating hereditary influence on intelligence is a problem in construct validation and the only workable approach is methodological and measurement triangulation. Just as we argue that data from a variety of familial relationships should go into an overall estimate of heritability, we should argue in favor of multiple ways of carrying out studies within a degree of familial relationship. For example, most twin studies recruit via mother of twins clubs. The possible bias in favor of DZ twins of greater than average similarity in behavioral traits is very great. Epidemiologists learned the importance of comprehensive enumeration many years ago. The traditional twin design assumes that DZ twins have half their genes in common. The validity of this assumption should be tested in every study. Evidence is developing that in some large samples of twins, the DZ's are, in fact, more similar genetically than the expected 0.50. The construct "DZ twins have half their genes in common" has, in fact, never been validated. The data on total fingerprint ridge count suggests a DZ correlation of 0.54 and a full sib correlation of 0.50. Most twin and adoption studies recruit via families. Parents with serious child rearing problems and whose SES has dropped a great deal, are much less likely to participate in such studies than parents without these problems. It seems to me that we need studies that recruit via the twins and the adoptees themselves. It is necessary to avoid bias in selection with this design also, but in our own work, we have found that adoptees who were not well treated by their rearing parents are concerned with the issue and are very likely to participate. This approach also allows us to study mature adults as opposed to children and adolescents.

I find behavior genetic researchers have far too much faith in single measures of particular traits. Single measures always contain a great deal of specific variance and are very susceptible to distortion due to various specific and momentary factors. Any given construct should be measured with more than one instrument. The format of the instruments should be different if possible.

### **GENERALIZABILITY OF HERITABILITY ESTIMATES FOR INTELLIGENCE FROM THE TEXAS ADOPTION PROJECT**

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Various characteristics of adoptive families, adopted children, biological parents, and type of intellectual assessment may moderate estimates of genetic and environmental influences on intellectual development. Subsamples from the 300 families in the Texas Adoption Project were created by dividing the appropriate groups according to age, sex, or birth order of the child, socioeconomic status of adoptive home, I.Q. of biological or adoptive parents, or if individuals were tested by the same examiner. Estimates of genetic and environmental influences for these subsamples are compared.

### **PRELIMINARY FINDINGS FROM A STUDY OF THE FAMILIAL TRANSMISSION OF INTELLIGENCE USING JUVENILE TWINS AND THEIR PARENTS**

A.C. Heath<sup>1</sup>, L.J. Eaves<sup>1</sup>, P.O. White<sup>2</sup>, K.A. Last<sup>3</sup>, and others

<sup>1</sup>Department of Experimental Psychology, University of Oxford; <sup>2</sup>Institute of Psychiatry, University of London; and <sup>3</sup>Department of Genetics, University of Birmingham

Some 200 MZ and 260 DZ juvenile twin pairs, and the parents of 320 of these pairs, were tested individually using a modified form of Raven's Progressive Matrices, and another British nonverbal intelligence test. Merging the family study and twin designs combines their advantages, and enables the investigation of some biologically important issues which these designs separately cannot resolve. Data on twins and their parents enable the importance of assortative mating and either dominance or genotype-environmental covariance caused by the environmental effects of parents on their children, to be examined. Preliminary analysis of raw total scores on each test reveals that a substantial proportion of the variation therein (at least 50%) is attributable to additive gene action. The shared environment of children within a family has a smaller but significant effect. Assortative mating, giving rise to a correlation between the genotype of spouses, is also present, so that any analysis based on twin data alone would underestimate heritability. There is no evidence of dominance, perhaps because of the low power of such tests for genetical nonadditivity in humans. The hypothesis that there is no genotype-environmental covariance cannot be rejected, but for a more powerful and more complete analysis of the non-independence of genes and environment, data should be collected on MZ and DZ twins, their spouses, and their offspring.

### **ANALYSIS OF PERCEPTUAL SPEED ABILITY IN YOUNG ADULT TWINS AND IN KINSHIPS OF IDENTICAL TWIN PARENTS**

Richard J. Rose  
Department of Psychology, Indiana University, Bloomington

The multiple relationships within kinships of identical twin parents provide resolution of several sources of environmental effects, a unique evaluation of maternal influences, and a direct assessment of assortative mating. Offspring of identical twins are half-siblings reared in separate environments. These maternal and paternal half-siblings, combined with age-matched identical and fraternal twins, provide a data-set of unusual power to estimate genetic and environmental parameters of behavioral variation. The approach will be illustrated with representative results from perceptual speed tests administered to kinships of identical twin parents and to independent samples of young adult twins. Results from the two data-sets are in good agreement. Maximum likelihood estimation of genetic and environmental parameters was made from the mean squares of the twin and half-sibling data; results suggest that a simple model of additive genetic variance combined with effects of idiosyncratic environment provide an adequate fit to the data. Assortative mating is negligible, there are no significant effects attributable to shared experience, nor is there evidence of systematic maternal influences.

**TWINS AND SINGLETONS IN THE KIBBUTZ ENVIRONMENT**Michael Nathan<sup>1,2</sup>, Ruth Guttman<sup>1</sup><sup>1</sup>Department of Psychology, The Hebrew University, Jerusalem; and <sup>2</sup>Institute of Research on Kibbutz Education, Oranim, Israel

A variety of cognitive tests were administered to children from different kibbutzim. Each experimental unit consisted of a twin pair (MZ or DZ) and two children of equal sex and age taken from the same educational group and living unit. The purpose of the analysis was to compare levels of resemblances within MZ's or DZ's with controls from the same environment. The addition of a control group of nontwins from equal environments constitutes a logical addition to the common twin method. The hypothesis tested was that resemblance between the two controls would be positive but less than resemblance between the DZ's which would be less than between the MZ's. Such a finding would be a necessary condition for a hypothesis of genetic determination. Data are presented that show that considerable resemblances are often found on scores of single-born controls on various WISC subtests. These raise questions with regard to the heritability estimates obtained by comparing MZ with DZ correlations.

**AN ADOPTION STUDY OF ONE-YEAR-OLDS**

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Twin and adoption data agree that adolescent and adult intelligence is substantially influenced by heredity and common family environment; however, these two major behavior genetic strategies appear to yield conflicting results for infant "intelligence". Twin studies of one-year-olds suggest negligible genetic variance and very substantial between-family (common or shared) environmental influence. For example, the Louisville Twin Study reported twin correlations for one-year-olds of 0.67 and 0.63 for identical and fraternal twins, respectively. Although parent-offspring adoption studies involving one-year-olds also find little evidence for hereditary influence, these studies find no evidence for the influence of familial environment shared by parents and offspring. We shall present preliminary results for one-year-olds from the Colorado Adoption Project (a prospective, longitudinal study of adopted children), for their biological and adoptive parents, and for matched "control" (nonadoptive) families. We correlated Bayley mental scores of over 100 adopted one-year-old infants with general cognitive ability and specific cognitive abilities of their biological and adoptive parents and compared these results to data on 75 control children and their parents. In general, these preliminary parent-offspring adoption data suggest that hereditary and shared family environment have very little impact on one-year-old Bayley mental scores. Direct assessments of the environment of the adoptive homes also bore little relationship to the infants' mental scores. However, there is some suggestion in the data that parents' general cognitive ability is marginally related (via both heredity and common environment) to infant intelligence.

**INTELLIGENCE TEST RESULTS IN OPPOSITE-SEX TWINS**

Siv Fischbein

Department of Educational Research, Stockholm Institute of Education

A short overview of sex differences in intelligence test results found in different studies is given and possible hereditary and/or environmental influences contributing to these differences are discussed. To study such influences a comparison of scores on a verbal, inductive and clerical speed test for opposite-sex twin pairs (OZ) and boy-girl controls (CO) matched for age are presented. These data have been collected in a Swedish longitudinal twin study called the SLU-project. The opposite-sex twin group tends to have somewhat lower average scores than the controls on all three tests, but the difference is only significant for the verbal test. Within pair correlations are of approximately the same magnitude for the opposite-sex twins and their controls ( $R_{OZ} = 0.32$  and  $R_{CO} = 0.19$ ). The largest difference between the two groups, however, is for the clerical speed test ( $R_{OZ} = 0.33$  and  $R_{CO} = 0.01$ ). This is also the only test showing a significant sex difference in favour of the girls for the total control group included in the SLU material ( $N = 569$ ). A combination of heredity-environment influences existing for the twins but not for the controls therefore seems to contribute to this difference.

**DEVELOPMENT OF PIAGETIAN LOGICO-MATHEMATICAL CONCEPTS AND OTHER SPECIFIC COGNITIVE ABILITIES**

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The Piagetian Mathematical Concepts Battery (PMCB), the Raven Coloured Progressive Matrices (PM), the Peabody Picture Vocabulary Test (PPVT), and a Visual Memory (VM) test were administered to 137 MZ and 72 DZ Caucasian, same-sexed, 4- to 8-year-old twin pairs. Parents completed the Moos Family Environment Scale and the Attitudes Toward Education Questionnaire. Sex and age were relatively equally distributed, while the distribution for socioeconomic status (SES) was skewed, with higher SES more prevalent. There were no sex differences for any of the tests or environmental variables. Because age correlated highly with test performance, all subsequent analyses were based on age-corrected scores. PM and PPVT performances were relatively independent, while VM ability was independent of the other three abilities. PMCB performance correlated 0.31 with PM and 0.36 with PPVT performance. After correction for test reliability, significant heritability was found for scores on the PMCB and the PPVT, and was indicated for VM performance. A new reliability estimate for the PM will be used to examine heritability for PM performance. There were no significant changes in any intraclass correlations across age. The results of step-wise multiple regression analyses performed to investigate environmental effects on test performance will be presented.

### 3D CONCURRENT SESSION: BIOLOGY OF TWINNING-I

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#### SECULAR VARIATIONS IN THE DIZYGOTIC RATE IN FRANCE, 1901–1968

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The secular variations in the DZ twinning rate in France are described for the period of time covered by the 11 population censuses between 1901 and 1968. It is shown that the DZ twinning rate declined over this period of time as it did in many other developed countries. The secular decline is then analyzed using population characteristics such as: fecundity, maternal age distribution, variations across the 90 French departments, population density, level of urbanisation, and migration. The results obtained are discussed in the frame of three possible explanations of the secular decline observed: genetic variations, environmental factors, and demographic trends.

#### EPIDEMIOLOGY OF TWINNING IN VIRGINIA

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Using annually published state vital statistics, we have documented twinning rates for the state of Virginia for 60 consecutive years, beginning with 1918. These data provide an unusual opportunity to compare secular trends in the rates among two racial groups, Whites and non-Whites (predominantly Black), living in the same geographical areas. In agreement with other studies, the overall twinning rates are higher among non-Whites than among Whites. When averaged over the entire time, non-White rates exceed White rates by a factor of 1.25. Twinning frequencies have declined among both races. The average rate for 1973–1977 declined from the average rate for 1918–1922, by 30% among Whites and non-Whites. As a rule, twinning rates in the two races rise and fall concomitantly from year to year, suggesting that environmental factors common to both races are the predominating influences affecting the frequencies in those years. However, there are some periods during which the twinning rates diverge significantly, suggesting the existence of race-specific factors as well. Birth records for every resident live birth are available for the period 1960–1974. MZ and DZ twinning rates were estimated for this period by the Weinberg method, and the effects of maternal age, parity, legitimacy, parents' educations, and urban-rural status on DZ twinning were investigated. A simple model is proposed to summarize how these factors influence the frequency of DZ twinning.

#### TWINNING IN AUSTRALIA: AN UNCONTROLLED SURVEY OF 1000 MULTIPLE BIRTHS

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<sup>1</sup>Department of Obstetrics and Gynecology, University of New South Wales and St. George Hospital, Kogarah, NSW, Australia, and <sup>2</sup>Australian Multiple Birth Association

The National statistics of multiple birth in Australia were surveyed in five yearly intervals from 1950 to 1977. The maternal age and parity in relationship to multiple birth in each five-year interval was compared, and alteration over the last 27 years will be discussed. The National statistics of the age of the mother in regard to all births from 1950 to 1977, in five yearly intervals, were studied, and changes in age of conception in this period were compared. The change in variation of multiple birth in various age groups over this period was assessed in association with the alteration in the age of women having multiple births. Those mothers who were ex-nuptial at the time of the birth were also surveyed and compared.

The Australian Multiple Birth Association National Twin Register of 1000 multiple births was reviewed. The ratio of male to female and MZ to DZ were surveyed and compared to the expected ratio according to Weinberg's formula. Furthermore, the ratio of time of cessation of oral contraceptive usage and the ratio of MZ and DZ twins was studied and compared with the expected ratios and the ratios seen in nonpill users. The incidence of congenital abnormalities in the AMBA Register sample was examined and comparison was made between oral contraceptive users and nonusers. Further comparison was made between the timing of cessation of oral contraceptive use and the time of conception. Some bias could be demonstrated in participants in the Register compared to the National Statistics, and although these will be discussed they were found to be nonsignificant in the findings.

**USES OF WEINBERG'S DIFFERENCE METHOD**

Gordon Allen

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Weinberg's difference rule states that the number of pairs of identical twins in an unselected series of twins is approximately equal to the difference between the numbers of same-sex and opposite-sex pairs. Its simplicity has sometimes been overlooked, partly because Weinberg's German term was incorrectly translated into English as "differential method". W.H. James has shown that the method may overestimate the number of MZ pairs by about 20%. Unless this can be disproved, appropriate adjustment should be made in estimating the DZ twinning rate in populations. When measurements or frequencies of a trait are available for a representative series of twins undiagnosed by zygosity, the difference method is useful not in significance tests, but to estimate the difference in mean or frequency between the zygosity types. One may also use the suspected proportion of MZ pairs among same-sex sets in an algebraic calculation of the difference. An extension of Weinberg's difference method permits estimation of the proportion of MZ triplets or quadruplets in large populations, but this is very sensitive to any error in the difference method.

**INCIDENCE AND FAMILIAL CLUSTERING OF TWINS IN THE MORMON GENEALOGY**

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The incidence of twinning in 1840–1940 as related to total fertility and mean age of mother is discussed. A number of large pedigrees with multiple sets of twins was identified and analyzed.

**FAMILIAL INCIDENCE OF TWINNING: PRELIMINARY RESULTS FROM THE ANALYSIS OF 719 TWIN PEDIGREES**

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The Mendel Institute, Rome

A total of 719 pedigrees have been collected through direct interview of parents of 520 DZ and 199 MZ twin pairs. Ascertainment was considered to be complete for (1) the twins' sibship, (2) the mothers' siblings and all of their offspring, and (3) the fathers' siblings and all of their offspring, resulting in a study population of 14,725 maternities out of the over 20,000 identified and excluding the 719 twin maternities used as *propositi*. Preliminary results show the total frequency of twinning to be increased in the families of twins. Although, as expected, the increase is highly significant among the maternal relatives of DZ twins, a significant increase is also found among the maternal relatives of MZ twins. The increase was not significant among paternal relatives; however, the possibility of some paternal influence may not yet be ruled completely out.

**THE AGE DISTRIBUTION OF DIZYGOTIC TWINNING IN CATTLE AND HUMANS: ETIOLOGIC IMPLICATIONS**

P.R.J. Burch

Department of Medical Physics, University of Leeds, UK

In an earlier publication I showed that the age dependence of DZ twinning in five human populations followed a common pattern. Up to  $t=39$  yr, the probability,  $P_t$ , of DZ twinning could be represented by:  $P_t = S \{1 - \exp(-kt^2)\}$ , where  $t$  is maternal age minus 2.5 yr;  $S$  is related to the proportion of the surveyed female population at risk to DZ twinning; and  $k$  is a kinetic constant, approx. equal to  $5.2 \times 10^{-4} \text{yr}^{-2}$ , in each population. Beyond  $t = 39$  yr,  $P_t$  falls rapidly. I suggested that the fall could be explained if women susceptible to DZ twinning tend also to be prone to an early menopause. Recent studies corroborate this suggestion. Further examples of the age patterns of DZ twinning in human populations are shown. These are compared with the dependence of the frequency of DZ twinning on parity (closely proportional to age), in various breeds of cattle. Remarkably, the parity-dependence of DZ twinning follows the above equation (putting parity proportional to  $t$ ), throughout the breeding life of the animals. This suggests that the biological

mechanism responsible for DZ twinning is probably similar in both species; I had proposed that this mechanism is "autoaggressive" in character. Many autoaggressive processes are precipitated and exacerbated by infectious and allergic agents. If DZ twinning falls into this category, then the seasonal fluctuations and secular changes in DZ twinning in human populations can be readily explained.

### **REPRODUCTIVE AND MENSTRUAL CHARACTERISTICS OF MOTHERS OF MULTIPLE BIRTHS AND MOTHERS OF SINGLETONS ONLY: A DISCRIMINANT ANALYSIS**

Grace Wyshak

Department of Preventive and Social Medicine, Harvard Medical School, Boston

The purpose of this study is to determine if women who have borne multiple births can be distinguished from women who have borne only singletons on the basis of their reproductive and menstrual characteristics. A discriminant analysis of the data, obtained from 4,762 mothers of multiple births (mostly twins) and 4,091 mothers of singletons only, revealed significant differences between these groups. The women were also divided into five subgroups: mothers of higher-order multiple births, two or more sets of twins, DZ (unlike-sexed) twins, like-sexed twins, and singletons only. This division led to a discriminant function with a predictive ability significantly better than chance—29% of the women could be correctly classified as compared with chance expectation of 20%. The most important discriminating characteristics are: ratio of present weight to height, length of average menstrual cycle, age at first live birth, and age at menarche. Other significant variables are: ratio of pregnancies to maternities resulting in live births, number of marriages, interval between first marriage and first live birth, and months until periods became regular around the time of menarche. These findings have implications for epidemiologists, geneticists, and reproductive biologists.

### **PARENTAL AGE, SIBSHIP'S SIZE, AND SIBSHIP'S SEX RATIO IN A TWIN SAMPLE**

L. Gedda, M.T. Lun, R. Carrega, E. Roselli

The Mendel Institute, Rome

The study of 613 twin pairs of both zygosity has shown (1) that increased paternal and maternal age plays a role in DZ twinning; (2) that the increase in age difference between the parents influences both MZ and DZ twinning; (3) that the sibship's size is 3.4 for DZ and 3.3 for MZ twins; (4) that the cotwins' sex correlates with a higher frequency of same-sex siblings.

### **HEREDITY, ENVIRONMENT, AND SPONTANEOUS ABORTIONS AMONG TWINS**

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During the fall of 1979, about 6,000 unselected female twin pairs aged 21–40 have reported in mailed questionnaires on the outcome of their pregnancies. The response rates were 89% and 83% for individuals and pairs, respectively. The aim of the study was to examine possible influences of heredity and environment on spontaneous abortions, and also to investigate whether changes in abortion rates could be used as an "alarm clock" at environmental incidents. The questionnaire contained information about pregnancies, spontaneous abortions, perinatal deaths and malformations, as well as place of residence during the first trimester. These data have been matched with the twin registry which contains information about, e.g., smoking, drinking, drug consumption, and personality items. Among 12,000 women with together about 15,000 pregnancies the rate of spontaneous abortions was 11% per pregnancy. Among 13,400 children the rate of perinatal death was 1.6%. Data will be reported with respect to the relationship between spontaneous abortions and genetic factors as well as personality items like stress, instability, and use of tobacco, alcohol, and certain drugs.

**THE ANALYSIS OF SPONTANEOUS ABORTION USING A NEW HALF-SIB MODEL FOR QUALITATIVE TRAITS**

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Analysis of the half-sib offspring of identical twins is a powerful method of estimating genetic, environmental, and maternal components of quantitative traits. We have extended the model to permit the analysis of qualitative traits and have obtained data on the reproductive histories of 248 MZ twin pairs from the Norwegian Twin Registry in order to search for evidence of a maternal effect on early fetal loss. The model uses a maximum likelihood method, assuming each parent in the half-sibship, with probability  $p$ , to be genetically at high risk for producing an "affected" offspring, thus resulting in eight possible mating types. Four additional parameters are estimated:  $a$ , the risk to the offspring if the mother is at high risk;  $b$ , the risk to the offspring if the father is at high risk;  $c$ , the risk if both parents are at high risk, and  $w$ , the sporadic risk. Analyses using the number of abortions and the number of full-term pregnancies in the half-sib design show that the risk if the mother is high risk (0.13940) is considerably higher than the paternal risk ( $\sim$  zero), indicating a maternal effect. The estimated frequency of high-risk parents was found to be approximately 0.50, reflecting the widespread incidence of individuals in the population who appear to be at a high risk for early fetal loss. Other factors of relevance to spontaneous abortion or reduced fertility will be discussed.



## 3E CONCURRENT SESSION: TWIN RESEARCH IN SMOKING, DRINKING, AND SUBSTANCE EXPOSURE

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### CHARACTERISTICS OF SMOKING-DISCORDANT MONOZYGOTIC TWINS

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Doubts that cigarette smoking is a causal factor for coronary heart disease (CHD) have been raised by studies of cigarette-smoking-discordant (SD) MZ twins. Among 451 adult female MZ pairs who completed questionnaires we identified 33 confirmed SD pairs. The SD smokers tended to smoke fewer cigarettes with lower tar content for a shorter duration, but with no less inhalation or use of unfiltered cigarettes, than all the MZ smokers. The median age of starting smoking was two years greater for SD smokers than for all MZ smokers and a larger proportion of the former had tried to stop (86% vs. 76%). Within the SD pairs, a greater proportion of the smokers than the nonsmokers reported alcohol, coffee, marijuana and hormone use, no college education, left-handedness, and lack of exercise or concern for physical fitness; the smokers were also thinner, on the average. Although many of these differences were not statistically significant, the data suggest that although smokers and nonsmokers within SD MZ twins are genetically the same, they are not matched for a number of other characteristics relevant to CHD. The differences resemble those between smokers and nonsmokers in the general population and, therefore, may not explain a greater similarity in CHD occurrence between smokers and nonsmokers within SD MZ twins than between smokers and nonsmokers in the general population. However, a greater similarity in CHD occurrence between smokers and nonsmokers in SD MZ twins may be partly explained by the relatively low intensity of smoking by smokers in SD MZ pairs.

### PULMONARY FUNCTION IN MONOZYGOTIC TWINS RAISED APART

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In order to assess the relative importance of heredity vs. environment in determining lung function, we measured pulmonary function (lung volumes, mechanics, gas exchange, and distribution of ventilation) in 11 pairs of adult MZ twins raised apart since infancy (as part of Minnesota Study of Twins Raised Apart). Five pairs were discordant and one pair was concordant for cigarette smoking. Four pairs were nonsmokers and had no history of lung disease. One additional nonsmoking pair was discordant for asthma. Similarity in pulmonary function was determined by correlating all tests between each pair after normalizing the value for size. Three of the four pairs of nonsmokers with no lung disease had similar pulmonary function. One twin of the remaining pair in this group worked as an arc welder and had worse pulmonary function than his brother. The nonsmoking pair discordant for asthma was also discordant for pulmonary function. Only one of the pairs discordant for smoking demonstrated a significant correlation between their pulmonary function tests. With the exception of one coal miner, the smoking twin had worse pulmonary function than the nonsmoker. The one pair in which both twins smoked had no correlation between their pulmonary function tests. We conclude that cigarette smoking, significant occupational exposure, or pulmonary disease can overcome hereditary influences on pulmonary function. A lack of correlation for pulmonary function between twins could always be explained by one of these factors. When these factors were absent, hereditary influences predominated in spite of the widely differing environmental background of each twin pair.

**STRUCTURAL ANALYSIS OF SMOKING, ALCOHOL USE, AND PERSONALITY FACTORS IN MZ AND DZ TWIN-PAIR RELATIONSHIPS USING THE LISREL MODEL**

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When studying the intrapair relationships in MZ and DZ twin pairs, it is necessary to assess whether the relationship between study variables in individuals is the same for twins of both types. The comparability of MZ and DZ twin populations should be known before comparing, eg, intraclass correlations or other measures of intrapair dependence. This comparison can be extended to include singletons when generalization to the whole population is going to be made. LISREL IV is a general method for estimating the unknown coefficients in a set of linear structural equations, including those containing measurement errors and assuming reciprocal causation between unmeasured variables. The method can be used for the statistical description and testing of covariance structures in several populations. Also a pooled covariance matrix can be estimated and the difference between two or more observed covariance matrices can be tested.

The influence of structural differences in behavioral models of MZ and DZ pairs on the intraclass correlations was investigated, using data from 20–29 year-old male twin pairs (N = 1989) in the Finnish Twin Registry. The variables in the model are defined as direct observed variables and unmeasured latent variables. The model consisted of some personality traits and tobacco use as independent observed variables and alcohol use as observed dependent variables. The analysis showed differences in the structural models of MZ and DZ pairs. After constraining the relations between smoking and personality to alcohol use to the same level in individuals of both groups, changes in the intraclass correlations were observed. Extension to discordant-pair analyses is discussed.

**A TWIN STUDY OF ALCOHOL USE**

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Institute of Psychiatry and the Maudsley Hospital, London

That alcoholism is a familial disorder is fairly well established, but whether this familial pattern is due to genetic or family environment factors is less clear. Partanen's 1966 twin study of 902 male pairs found a high heritability for the total amount drunk, in males; although obviously had no information on females. The current study used the Institute of Psychiatry twin register, a volunteer register comprising about 600 pairs, MZ and DZ and also both sexes. The study used an extremely detailed questionnaire which dealt with matters such as: alcohol consumption per week; general drinking trends over the past 12 months, and the psychological and physiological effects of alcohol upon the subjects. The preliminary results, on examination of the total consumption per week figures, as in Partanen (1966), seem very interesting. All male subjects had a very much higher consumption of alcohol than females, the males being in the "normal" range and the females tending to be very light drinkers and in many cases total abstainers. With respect to genetic factors, male subjects showed very little evidence of this, the correlations for MZ and DZ pairs being virtually identical. The females also followed a similar pattern with genetic factors being of very little importance. Indeed, there seems to be a wide variety of influences ranging from the complete absence of heritable factors to the presence of strongly heritable factors.

**PSYCHOLOGICAL DEFICIT, BRAIN DAMAGE, AND THE GENETIC PREDISPOSITION TO ALCOHOLISM: A TWIN STUDY**

H.M.D. Gurling, R.M. Murray, C.A. Clifford

Institute of Psychiatry and the Maudsley Hospital, London

Out of 70 alcoholic twin probands attending the Maudsley Hospital since 1948, 61 have been investigated. Preliminary results show pairwise concordance rates for the establishment of the Alcohol Dependency Syndrome (WHO definition) as 24% for 33 MZ and 25% for 28 DZ pairs. A higher concordance is found for diagnoses other than alcoholism in the MZ twins. A cotwin control study of 10 pairs of MZ twins discordant for alcoholism, but concordant for educational attainment,

was conducted. Computerised brain tomography and psychological testing produced highly significant findings. Morphological changes similar to cerebral atrophy were found in the alcoholic probands compared to their cotwins in twin pairs aged from 32 to 67 years. A factor termed the "Atrophy Score", determined from sulcal width, Sylvian fissure, and interhemispheric fissure size combined with the ventricular-area/brain-area ratio gave a total atrophy score of 270 for the alcoholic probands compared to 90 for the cotwin control group. Psychological tests showed a marked deficit particularly of parietal and frontal lobe function in the alcoholics.

#### EXPERIMENTAL PAIN AND MORPHINE IN MONOZYGOTIC TWINS

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#### OLFACTORY SENSITIVITY IN TWINS

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An opportunity to investigate the genetic variability of olfactory sensitivity arose as part of the NHLBI Twin Study. Participants in this multicenter study were male veteran twins, aged 42–56, who were ascertained from the NAS-NRC Twin Registry and who volunteered to undergo a physical examination at the invitation of the NHLBI. Tests of olfactory sensitivity were successfully administered to 51 MZ and 46 DZ twin pairs who were examined at the facility in Framingham, Massachusetts. An individual's sensitivity was determined by exposure to serial dilutions of three chemical compounds thought to represent different "primary" odors. The compounds used were acetic acid, isobutyric acid, and 2-sec-butyl-cyclohexanone, belonging to the odor classes of "pungent", "sweaty", and "camphoraceous", respectively. Results of the twin analyses did not yield evidence for genetic variability of responses to any of the three odors tested. However, factors which were significantly associated ( $p < 0.05$ ) with odor perception included cigar, pipe and cigarette smoking, body fatness, alcohol consumption, and diabetes mellitus.

Thursday 19 June

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#### 4A SYMPOSIUM: TWIN RESEARCH IN TEMPERAMENT

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##### **THE SOCIAL DEVELOPMENT OF TWINS IN LONGITUDINAL PERSPECTIVE: HOW STABLE IS GENETIC DETERMINATION FROM AGE 2 TO 9?**

Hugh Lytton, Denise Watts

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This paper arises from a major investigation into the relation of the social characteristics (compliance, attachment, independence, activity level, speech) of young boys to parent-child interaction and genetic factors. The original investigation was conducted with a sample of 46 male sets of twins and 44 male singletons, 2–3 years old, and the twins of the sample are being followed up at home and at school, now that they are 8–10 years old. The primary method of investigation at the younger age was direct observation of the interactions of the twins with their parents in an unstructured situation in the home. The behavior of children and parents was recorded and coded, and summed behavior counts served as indices of the child social characteristics under study. We also used interviews and ratings, and an experimental situation, to obtain assessment of the same behavior tendencies via different methods. The use of these methods with twins will be discussed.

Thirty seven pairs of twins and their parents are cooperating in the present follow-up study. Mothers and fathers are being given interviews very similar to earlier interviews and the interviewer is allotting ratings for child characteristics, parallel to the ratings that were given at age 2, plus social maladjustment. The families are also being observed in structured interaction tasks and rated on various characteristics. The children are being given standardized achievement and intelligence tests, and measures of internalized moral orientation.

The genetic analysis of the 9-year data will be reported and discussed in relation to the earlier genetic results which were presented at the Twin Congress in Washington, 1977.

##### **GENETIC ASPECTS OF TEMPERAMENTAL DEVELOPMENT: A FOLLOW-UP STUDY OF TWINS FROM INFANCY TO 6 YEARS OF AGE**

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The assumption that genetic factors play an important role in the development of temperamental characteristics has been supported in a follow-up study of 53 pairs of same-sexed twins from infancy to 6 years of age. When the twins were 2 months, 9 months, and 6 years, nine temperamental traits were studied by interviews of the mothers. These traits were: activity, regularity, approach/withdrawal, adaptability, intensity, threshold, mood, distractibility, and attention-span/persistence. The definition of the temperamental traits and the method used for measuring the traits are mainly the same as in The New York Longitudinal Study, conducted by Alexander Thomas and Stella Chess and coworkers.

The MZ twins were more similar than the DZ twins for all the temperamental traits at all ages. The differences between MZ and DZ pairs changed, however, from infancy to 6 years in a way that made it possible to interpret these findings within an interactionistic framework. When more conservative estimates of heritability were applied to the data, the statistical significance of genetical aspects lost its importance for some of the temperamental categories. It appeared that the same temperamental categories which now were lowest in heritability were among the same categories which from other studies have been reported to correlate with behavioral problems in children. It is claimed that the greater similarity in MZ than DZ twin pairs may be interpreted as a consequence of more similar environment for MZ than DZ twin pairs, and not as a consequence of the genetic identity in MZ twin pairs.

## **TWIN STUDIES USING OBJECTIVE OBSERVATIONS OF TEMPERAMENT AND PERSONALITY**

Robert Plomin

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Early twin studies of temperament relied on parental ratings or interviews. Results of such studies support Loehlin and Nichol's two major conclusions concerning self-report twin studies of personality in adolescents and adults: (1) that all personality traits are influenced by heredity to the same moderate extent (twin correlations of 0.05 and 0.03, respectively, for identical and fraternal twins); and (2) that environmental influences salient to personality development are quite different from those widely presumed to be important. The source of environmental variance lies "within" rather than "between" families. Before the two conclusions are widely accepted for the domain of personality, one major limitation should be noted: These conclusions are based solely on data from self-report and rating questionnaires. Although few twin studies have employed objective observations of personality, such studies suggest more varied results.

The present investigation examined objective measures of activity, fidgeting, sustained attention, selective attention, and aggression, for a sample of 87 twin pairs from 5 to 11 years of age. Data included videotaped observations in standardized situations, objective test scores, and mechanical measures. Test-retest reliability was obtained for all measures. Contrary to the usual results for questionnaire studies, little evidence was found for genetic influence on reliable and objective behavioral assessments. Also in disagreement with the questionnaire studies, between-family environment appeared to be more important than within-family factors.

## **ASSESSMENT OF TEMPERAMENT IN TWIN CHILDREN: A RECONCILIATION BETWEEN STRUCTURED AND NATURALISTIC OBSERVATIONS**

Adam P. Matheny

University of Louisville School of Medicine, Kentucky

The Louisville Twin Study is conducting a large scale investigation of the emergence and persistence of characteristics of temperament as determined for twin infants and preschoolers. The methods of investigation include assessment of temperament by the following: neonatal evaluations, interviews with the parents, temperament questionnaires, behavioral ratings during mental testing, and direct observations. Direct observations, recorded by videotape, are made during a 3-hour visit during which structured, age-specific reference tasks - called vignettes - are used to evoke reliable individual variations of temperament. The vignettes are designed to be naturalistic and take into account the expanding competencies of the child. Behavioral ratings, pertaining to emotionality, activity, selective attentiveness, aspects of sociability, and interest in toys/play, are based on episodes when twins are together and separated, with and without parent. Comparisons of twins therefore can be made in terms of the individual child, the twin dyad and the triad of twins and parent for specific ages spanning the first years of life, and the comparisons point to the prospect of seeing the emergent features of temperament and how those features are shared by genetically-related children. Illustrations of characteristics of temperament will be shown in the context of the developing twins, and preliminary analyses will be discussed.

## 4B SYMPOSIUM: TWIN RESEARCH IN CORONARY HEART DISEASE

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### TWIN RESEARCH IN CORONARY HEART DISEASE

Kåre Berg

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Several published twin studies have revealed a higher concordance rate in MZ than DZ twins with respect to ischemic heart disease. These studies form part of the steadily accumulating evidence for a strong genetic influence on susceptibility to coronary heart disease (CHD). Also, several twin studies and other family studies have indicated a significant contribution of genes to the variation in total serum cholesterol level. This parameter has been clearly shown to be associated with risk for CHD. In recent years, it has become clear that not only the level of low density lipoprotein (LDL), the main carrier of cholesterol in serum, but also the level of high density lipoprotein (HDL) is of importance with respect to the propensity to develop CHD.

Within an extensive study of twins ascertained from the Norwegian population-based twin registry, the traditional serum lipid parameters as well as the HDL apoprotein levels have been examined. In a previously reported, preliminary study, heritability estimates of 0.55 and 0.38 were obtained for apo A-I and apo A-II, respectively. Recently completed studies on a new and much larger series of twins indicate that the genetic influence on the levels of these HDL apoproteins may be considerably stronger. Since several environmental factors that influence HDL levels have also been identified, one may hope that the relative strength of specific environmental influences and genes on the CHD-protective HDL will become measurable in the foreseeable future. The present data are in agreement with other information suggesting a substantial effect of genes on HDL quantity and quality.

### HUMORAL AND RENAL RESPONSE TO SODIUM LOADING AND DEPLETION DEMONSTRATE GENETIC VARIANCE IN NORMOTENSIVE MAN

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University of Indiana Medical School, Indianapolis

Twins provide an efficient method to investigate possible genetic and environmental influences on quantitative traits. Blood pressure (BP), plasma renin activity (PRA), aldosterone (PA), norepinephrine (PNE), urinary norepinephrine excretion (UNE) and sodium ( $\text{Na}^+$ ) excretion (UNA) were studied in response to  $\text{Na}^+$  loading and depletion in 37 monozygotic and 21 dizygotic twin pairs (age 16–27). The analyses performed incorporated tests of the basic assumptions of the classical twin model. On an ad lib  $\text{Na}^+$  intake there was no evidence for genetic control of PRA, PA, PNE, UNE or UNA. However, after  $\text{Na}^+$  loading (2 L normal saline over 4 hours) there was strong genetic influence on PA, PNE ( $p < 0.01$ ), UNA and UNE ( $p < 0.05$ ). The fractional excretion of  $\text{Na}^+$  showed genetic variance and was inversely related to BP. The mornings after  $\text{Na}^+$  loading and  $\text{Na}^+$  depletion both PRA and PA demonstrated a highly significant genetic influence ( $p < 0.005$ ) and were positively correlated with BP. No genetic effects on PNE or UNE were demonstrated and these variables did not correlate with blood pressure. It is concluded that these genetic influences brought out by  $\text{Na}^+$  loading and depletion are, on a day-to-day basis, overridden by environmental factors - most likely sodium intake. These data suggest: (1) UNE and PNE appear to be under environmental control and therefore not related to the heritability of blood pressure; (2) The heritability of BP may be related to the heritability of the renin system and the kidney's ability to excrete  $\text{Na}^+$ .

**COMPARISONS OF CORONARY HEART DISEASE RISK FACTORS IN MONOZYGOTIC AND DIZYGOTIC TWINS BY CHORION TYPE**

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**WEIGHT CHANGES IN ADULT TWINS**

R. Fabsitz<sup>1</sup>, M. Feinleib<sup>1</sup>, Z. Hrubec<sup>2</sup>

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## 4C WORKSHOP: PSYCHOSOCIAL FACTORS IN CARDIOVASCULAR DISEASE

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### STRESS AND CORONARY HEART DISEASE

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Names of 10,000 patients in the age group 40–69 who were admitted to larger medical wards of Norwegian general hospitals with coronary heart disease during the years 1971–75 have been checked against the national twin register. After exclusion of twins one of whom had died before age 40, a sample of 78 MZ and DZ pairs remained. In this report, the findings concerning the 32 same-sexed twin pairs where both twins were alive when the clinical interview took place in 1976 will be presented. Concordance figures for coronary heart disease was 38% in MZ and 17% in DZ (proband method), or 33% vs. 13% (pairwise method). In discordantly affected pairs a “stressing work situation” is the outstanding discriminating factor. In both MZ and DZ discordant pairs, the twin with coronary heart disease had, in the majority of cases, experienced the most pressing work situation prior to disease.

### CORONARY-PRONE BEHAVIOR IN ADULT LIKE-SEXED TWINS: AN EPIDEMIOLOGICAL STUDY

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Coronary-prone behavior was studied in the Finnish Twin Registry using questionnaire responses from 11,364 adult twin pairs (5,419 male pairs and 5,945 female pairs). A short rating scale developed by Bortner was used. The distribution of the study population on the A-B axis was unimodal with no distinctive grouping into A and B types. Mean A-type scores were highest in 30–40 year olds. The highest and lowest deciles were designated to represent type A and type B respectively. In this cross-sectional study, A-type men reported more often a history of coronary heart disease than B-type men, but the difference was not statistically significant. The association of A-type behavior and CHD-symptoms, however, will be clarified further in prospective studies. The characteristics of A-type fitted the Rosenman-Friedman typology: A-type men were more often self-employed or in white collar work and had larger incomes and more changes of residence. A-type persons experienced their daily activities to be more tiring but their work less monotonous. They were more extroverted and their life satisfaction was greater. A-type persons used spirits a little more often and spent less time on leisure-time physical activity than B-types. The intraclass correlations in MZ and DZ pairs differed significantly (male-MZ = 0.251, male-DZ = 0.052; female-MZ = 0.357, female-DZ = 0.117). Concordant and discordant pairs with respect to A-B axis were identified. The psychosocial correlates in these groups will be presented and discussed.



## 4D CONCURRENT SESSION: BIOLOGY OF TWINNING-II

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### ZYGOSITY-RELATED DIFFERENCES IN INTEGRITY OF DEVELOPMENTAL RELATIONSHIPS

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We have been performing multivariate statistical analyses of relationships among tooth diameter measurements of secondary dentition in twins. This system meets our present purposes by virtue of a reasonably tractable but interesting level of complexity, the proximity of its cellular origins to embryonic brain, and especially by sharing with the brain the requirement for developmental integration both within and between left and right halves. Our findings include: sex-by-zygosity interaction remaining at the multivariate level even after multiple-univariate gender transformations; inequality of zygosity group mean vectors in both sexes; and inequality of zygosity group covariance matrices in both sexes. Major contributions to the group differences arise from generalized weakness of developmental relationships among MZ's relative to DZ's, both within and between left and right halves. On the basis of these differences, we have been able to identify zygosity with very high accuracy without reference to within-pair comparisons. We consider these results to strengthen our working hypotheses: (1) that few if any sources of developmental variation affect single traits in isolation; (2) that integration of development among body systems represents sources of variance of basic interest, which integration may itself be subject to variable genetic control; and (3) that the most fundamental assumptions of twin study methods are subject to serious question especially in behavioral applications.

### PLACENTATION EFFECTS ON COGNITIVE AND PERSONALITY RESEMBLANCE OF ADULT MONOZYGOTES

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Twins differ not only in zygosity, but in placentation as well, and evaluation of intrapair variance among MZ cotwins of known placental type provides a research tool of considerable promise. We have assessed cognitive abilities and personality traits among adult twins drawn from the McMaster Twin Registry. In every case, zygosity and placentation are documented. Interim results for the Vocabulary and Block Design Scales of the WAIS are available for 32 MZ and 28 DZ pairs. The MZs are subdivided by placental type into 17 monochorionic (MC-MZ) and 15 dichorionic (DC-MZ) pairs. For the Vocabulary Scale, we find the expected difference associated with zygosity but no effect of placental differences within MZs. For the Block Design Subtest, by contrast, DC-MZs are no more alike than are DZs and exhibit significantly greater intrapair variation than do the MC-MZ pairs. Similar results have been found for the social introversion scale of the MMPI. These differences may reflect developmental consequences of variation in vascular communication in utero; alternatively, they may arise as a consequence of the differential timing of the embryological division. In our preliminary data, placental differences are associated with dermatoglyphic variation, but are not a function of differences in birthweight or handedness.

### MATERNAL EFFECTS ON BIRTHWEIGHT IN CHILDREN OF MONOZYGOTIC TWINS

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Department of Human Genetics, Medical College of Virginia, Richmond

Birthweight was measured on 592 children contained in 49 male and 71 female MZ twin kinships. Length of gestation by dates, sex, mother's stature, and father's stature were also recorded for individuals included in the study. The raw birthweights were normally distributed with a mean of  $3361 \pm 21$  g, and remained gaussian following adjustment for variation arising from gestational age and sex using U.S. population norms. To examine the degree to which maternal and paternal heights influenced variation in birthweight of offspring, birthweight data were further adjusted for maternal and/or paternal stature. Nested analyses of variance were conducted on the raw and

adjusted birthweights as well as the adjusted scores following removal of the effect of mother's stature, father's stature, and midparent stature by linear regression analysis. In all of the resulting data sets, the observed patterns of mean squares strongly suggested the existence of a major maternal effect. In all cases, the half-sib correlation for children of female twins was substantially larger than the correlation observed among the offspring of male twins. Adjustment for gestational age and mother's stature resulted in a 16% reduction of the total variance and an increase in the proportion of the total variance attributable to maternal effects. Regression for paternal stature further reduced the total variance. However, the proportion of the variance attributable to maternal effects only increased from 30% to 31% following adjustment for maternal stature, but rose to 42% following adjustment for paternal stature. These findings suggest that some of the genes which influence maternal stature must also contribute to the observed maternal effect on birthweight.

### BODY SIZE IN MONOZYGOTIC TWIN KINSHIPS

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Body weight and stature were measured in 1064 individuals in 51 male and 75 female MZ twin kinships. Prior to data analysis, raw height and weight measurements were converted to standard scores using age and sex banded U.S. population norms in order to remove effects of these characteristics on variation in height and weight. After appropriate measures had been taken to achieve heights and weights which were normally distributed, regression analyses were conducted to determine if stature accounted for a significant proportion of the variation observed in weight. As expected, a significant proportion of the observed variation in weight (17% in adults and 38% in children) could be accounted for by variation in height. Further, the relationship between stature and weight in adults and children, respectively, appeared to be qualitatively different, as reflected by the significant differences in the slopes of the two regression lines for these groups. The effect of stature on variation in weight was removed by regression techniques to focus attention on the nature of factors which influence residual variation in weight unaccounted for by age, sex, or height. Correlations between the various classes of relative contained in MZ twin kinships were then calculated for stature, raw weight, and weight adjusted for stature, respectively. Stature and, to a lesser extent, raw weight were found to be strongly influenced by genetic factors; while adjusted weight appeared to be largely environmentally determined, with members of male kinships more closely resembling each other than members of female kinships.

### A STUDY OF MIRROR IMAGING IN TWINS

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A study of lateral asymmetries has been conducted on a sample of 199 MZ and 353 DZ pairs. Mirror imaging appears to be significantly more frequent in MZ than DZ twins, a finding attributed to late embryonic division.

### EXCESS LEFTHANDEDNESS IN TWINS AND PARENTS OF TWINS

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Students of the genetics of lefthandedness consistently find that twins give them more problems than solutions. Both MZ and DZ twins are lefthanded 1.5 to 2 times as frequently as singletons. With large samples, a small MZ excess over DZ becomes significant. This is often ascribed to obstetrical difficulties of twinship, in spite of the fact that zygosity differences in frequency and severity of birth difficulties are much larger than the frequency difference in lefthandedness. In spite of evidence for a genetic basis from results other than twin studies, handedness of a given twin provides no information about the likely handedness of the cotwin: the distribution of handedness over twin pairs is almost perfectly binomial, in both zygositys. In large samples, MZ's show a small deficit of RH-LH pairs, in favor of concordance. What I have to offer is further

complication. In questionnaire data from 400 twin families of each zygosity, collected from the U.S. National Organization of Mothers of Twins Clubs, the parents of twins have the same excess frequency of lefthandedness as the twins themselves, in both zygosity groups, to the same extent among mothers and fathers of twins, with maternal aunts and paternal uncles as control groups. The sibs-of-twin-parents and the sibs-of-twins control groups show no significant differences from other comparable singleton samples. This suggests anomalous relationships between symmetry development and twinning of both zygositys, suggests that classic twin studies may not be appropriate to questions of behavioral development dependent on brain function asymmetry development, and suggests that the different twinning mechanisms may have more in common than previously recognized.

#### ON THE TIMING OF MONOZYGOTIC TWINNING EVENTS

Charles E. Boklage

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It is possible to make a reasonably exact estimate of the probability distribution of viable MZ twinning events over time. Such an estimate can be useful in speculation about the developmental origins and effects of twinning. My estimate depends on two assumptions: (1) MZ twinning events cannot occur before fertilization; (2) twin pairs sharing a particular structure achieved their cellular commitment to twinning after the differentiation of the shared structure was committed. A review of the literature totalling 1,670 MZ pairs shows that 68.9% of those pairs shared chorions. Among 7,687 pairs (of which 30.4% or 2,337 pairs should be MZ) 80 pairs, or 3.34% of the MZ pairs, shared amnions as well. Therefore, 65.6% of MZ twinning events occur between choriogenesis, on the fourth day of gestation, and amniogenesis, on the seventh. The distribution appears to be normal with mean 4.66 days and standard deviation 1.29 days. The peak (and 30% of total) probability occurs in the first of three days during which the inner cell mass is rearranged to become the bilaminar disc stage. Viable MZ events after amniogenesis are rare, involving a high proportion of anomalous development, including conjoinment. Since MZ twinning occurs most frequently during establishment of embryogenic bilateral symmetry, and conjoinment is always by way of corresponding parts of the anatomy—indicating incomplete formation of separate body symmetries rather than subsequent joining, this suggests that MZ twinning results from the establishment of two symmetry-organizing schemata at the cellular level.

#### CONJOINED TWINS: A CASE STUDY

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Conjoined female twins with different hand malformations joined in the thoraco-abdominal area with common heart small intestines and fusion of livers are described. The twins were born after 32 weeks of a pregnancy that was complicated by polyhydramnios. One of the thoracopagus twins was born dead while the second died after a few respiratory gasping movements. The combined weight of the twins was 2800 g and the common placenta 750 g. Two umbilical cords left the placenta united to one cord and split again before reaching the twins. One of the twins had a malformed thumb on the left hand loosely connected by a skin stalk. The other twin had a deformed incurved left hand with absent thumb and partial syndactyly of fingers II and III.

## 4E CONCURRENT SESSION: TWIN RESEARCH IN AGING AND CANCER

### A LONGEVITY STUDY OF TWINS IN THE MORMON GENEALOGY

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An analysis of twin longevity (2271 sets of twins) extracted from the Mormon Genealogy Data Base, born between 1800–1899, was undertaken to demonstrate the concordance in mean intrapair life span, by sex in same-sex and opposite-sex twin pairs. The data was collapsed in symmetric contingency tables defined by intervals of death for the corresponding twin set. Infant mortality was analyzed separately. A battery of various statistical measures of associations including measures of predictability and patterns of symmetry were discerned. The total life experience of male, female and opposite-sex sets of twins that survived infancy was described utilizing the standard cohort life table method. The similarities observed in overall life expectancy and survivorship curves for same-sex twins was fine-tuned and the conditional survivorship curves of one of the twin pair given that the other twin died in a young, middle, or old-age category. The results suggest significant genetic components in the life span of this cohort that need further examination utilizing the unique resource of the Mormon Genealogy Data Base.

### FAMILIAL FACTORS IN DEATHS BEFORE AGE 62: 30 YEARS OF FOLLOW-UP AMONG TWINS AGED 51 TO 61 YEARS IN 1978

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Subjects in the National Academy of Sciences-National Research Council Twin Registry of 31,848 male twin veterans were followed for mortality from 1 January 1946, or from the date of entry into military service if that was later, to 31 December 1978. During this time 3,571 deaths occurred among them, 835 due to trauma and 2,712 due to disease, according to preliminary counts. Mortality rates from all causes for the entire follow-up period were 10.2% among 11,348 MZ and 11.4% among 14,448 DZ twins. Among U.S. white males of the same ages as the two respective zygosity groups, a mortality of 13.6% would be expected in the MZ group and 13.7% in the DZ group. Observed mortality from trauma was 2.3% for MZ and 2.5% for DZ twins, with 3.0% expected in either group. Observed mortality from all disease was 7.9% for MZ and 8.8% for DZ twins, with 10.6% expected in the MZ and 10.7% in the DZ group. The casewise twin concordance rates, based on individuals, for total mortality were 28.3% for MZ and 17.6% for DZ twins. For trauma, respectively by zygosity, these concordance rates were 7.0% and 3.9%. For all disease they were 30.2% and 17.6%. Estimating heritability of liability to death from disease, as proposed by Edwards, provides values of  $h^2 = r = 0.52$  for MZ twins,  $h^2 = 2r = 0.49$  for DZ twins, and  $h^2 = 2(r_{MZ} - r_{DZ}) = 0.55$  using data for the two zygosity groups combined.

### INCIDENCE OF CHILDHOOD CANCER IN TWINS

Merton S. Honeyman

Connecticut Twin Registry, Connecticut State Department of Health Services

The incidence of congenital malformations and the rate of infant mortality is higher among the products of a plural birth than among singletons. Do the environmental hazards of a plural pregnancy increase the risk of childhood cancer among the individuals resulting from such a pregnancy? The Connecticut Twin Registry and the Connecticut Tumor Registry have been used to compare the observed and expected incidence of childhood cancer (0–14 years of age at diagnosis). The Connecticut Twin Registry contains a listing of all multiple births occurring in the State of Connecticut since 1897. The Connecticut Tumor Registry contains information on all cancers diagnosed in Connecticut residents since 1935. These registries were matched to identify twins born between 1935 and 1969 who had been diagnosed with cancer. All twins who died prior to one year of age were excluded from the study. The age specific incidence rates for cancer for the forty year period, 1935–1974, were used as a control to obtain the expected number of cancers. No increased incidence of cancer was observed in the twin population.

**CANCER IN ADULT LIKE-SEXED TWINS**

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Department of Public Health Science, University of Helsinki, and Finnish Cancer Registry

The Finnish Twin Registry contains information on all same-sexed twins that were born before 1958 and belonged to unbroken (living) pairs on 1 January 1967 in Finland. The Twin Registry was created by extracting from the Central Population Registry all pairs of individuals that had the same date and place of birth, and the same surname at birth. During further analysis these provisional pairs were divided into twins (17,357 pairs) and nontwins (3,666 pairs). Information on zygosity could not be obtained if both partners had died before 1974, and therefore was not used. The observed numbers of cancer cases among twins in 1967–1974 were obtained through computer-assisted record linkage between the Finnish Twin Registry and the Finnish Cancer Registry by making use of the personal identification numbers. The calculation of the expected numbers of cases was based on the person-years at risk, and the national annual age-specific incidence were observed, and by the Center Registry. In males, 172 cancers were observed, vs. 249.4 expected (relative risk 0.69). In females, 116 cases were observed, vs. 204.7 expected (RR 0.57). The relative risks of the most common types of cancer were between 0.43 and 0.75. Low risk ratios were observed especially in age groups over 60. The lower than expected risk of cancer among the twin population studied is possibly due to the conditions given for the formation of the cohort. Among the nontwin controls 71 cases were observed in males, 45 in females. The expected numbers were 71.7 and 60.3, respectively (RR 0.99 and 0.75). The subsequent risk of cancer among cotwins of cancer proband was also assessed. The observed number was 3 in males and 1 in females vs. 5.3 and 1.7 expected (RR 0.57 for both sexes). Only one fully concordant pair was found (prostate - prostate). Though follow-up time will have to be increased and information of zygosity taken into account, it can be concluded that genetic factors probably have little influence on overall cancer morbidity.

**CANCER STUDIES IN THE DANISH TWIN POPULATION**

Niels V. Holm

University Institute of Clinical Genetics, and the Danish Twin Register, Odense University

It is primarily intended to discuss the results obtained by the classical twin method and the cotwin control method in their relation to various procedures of sampling and analysis. A material of breast cancer (BC) cases observed in the Danish twin population, is used as a basis. This study material derives from the Danish Twin Register which comprises the total population of same-sexed twin pairs born in Denmark from 1870 through 1930, includes 45 MZ and 77 DZ female twin pairs in which at least one twin had BC and in which both partners were alive at the time of the first BC diagnosis. The information of BC was obtained through mailed questionnaires and death certificates, and in 98% of the cases verified through hospital records. Empirical data for the discussion is, i.e., being obtained by record linkage between the Danish Twin Register and the Danish National Cancer Register.

**CANCER INCIDENCE IN MOTHERS OF DIZYGOTIC TWINS**

Grace Wyshak

Department of Preventive and Social Medicine, Harvard Medical School, Boston

The purpose of this study is to determine whether mothers of twins, who have a higher level of gonadotropins than other mothers, have cancer incidence or cancer mortality rates different from those of controls. The study will be based on a follow-up of the experience of a study group of 3982 mothers who had male-female twins or other polyzygous births in Connecticut during the years 1925–1959; a control group of 3982 women matched pairwise on year of childbirth, age, number of previous children, race, and national origin; and a second control group of 3982 women randomly selected from mothers of singletons. In addition, the Connecticut Twin Registry will be searched for male-female twins and other polyzygous births occurring during 1960–1974; we expect to identify mothers of 2500–3000 male-female twins from this search. The Vital Statistics Records will be searched for controls chosen in the ratio of 4:1, and matched on age, race, and index year of birth. These women will be added to the study and control groups recorded for, since 1966, for cancers of all sites. The observed incidence of site-specific cancer will be compared with that expected among Connecticut residents of the same age and sex.

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Friday 20 June

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## 5A SYMPOSIUM: TWIN RESEARCH IN SMOKING, DRINKING, AND SUBSTANCE ABUSE

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### AN OVERVIEW OF TWIN STUDIES: THE ROAD TO PROSPECTIVE INVESTIGATIONS

Marc A. Schuckit

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This presentation will encompass a brief review of the type of investigations leading up to twin studies (i.e., family, genetic marker, and animal work). The twin investigations themselves breakdown into those dealing with drinking practices in nonalcoholic twins (e.g., Partanen, et al) and those comparing the concordance for alcoholism in MZ vs. DZ twin pairs (e.g., Kaij, et al). Both types of investigations taken together indicate probable heritable factors of importance in choosing to drink, drinking to the point of getting into trouble, and alcoholism - but do not establish whether the same factors are involved in each step of the process. While of great importance, the limitations inherent in twin work raise the need for other types of investigations including adoption studies (with their own assets and liabilities) and prospective studies utilizing young men at elevated risk for the future development of alcoholism. In the prospective arena we are presently utilizing men aged 21–25 with family histories of alcoholism and comparing their acute reactions to alcohol and metabolism of this drug to controls matched on demography and drinking history. The studies to date indicate that men with family histories of alcoholism develop higher levels of acetaldehyde while showing less subjective response to the acute effects of the drug. Thus, twin studies form part of a spectrum of alcohol-related genetic research.

### ADOPTION STUDIES OF ALCOHOLISM

Donald W. Goodwin

Department of Psychiatry, University of Kansas Medical Center, Kansas City

There have been four adoption studies of alcoholism. The first, conducted in the United States in the early 1940's, found no difference between adopted offspring of alcoholics and adopted offspring of nonalcoholics; neither group drank very much. More recently, a Danish study found that sons of alcoholics were four times more likely to be alcoholic than sons of nonalcoholics, whether raised by their alcoholic biological parents or by nonalcoholic adoptive parents. Moreover, they were likely to be alcoholic at an early age and have a form of alcoholism serious enough for treatment. Having a biological parent who was alcoholic did not increase their risk of developing psychiatric disorders other than alcoholism and did not predispose to heavy drinking in the absence of alcoholism. The familial predisposition to alcoholism in this group was specific for alcoholism and not on a continuum with heavy drinking. Two recent adoption studies tend to confirm these findings. A study of 2000 adoptees in Sweden found a significant correlation between abuse of alcohol among biological parents and their adopted-out sons. An Iowa study of 84 adult adoptees found that alcoholism occurred more frequently in adoptees whose biological background included an individual with alcoholism than in adoptees without this biological background. Alcoholism did not correlate with other biological-parental diagnoses. In conclusion, recent evidence from adoption studies indicate a genetic factor in at least some instances of alcoholism.

**GENETICS OF PSYCHOMOTOR PERFORMANCE UNDER ALCOHOL**

Nicholas G. Martin

Department of Population Biology, Australian National University, Canberra

It is everyday comment that some people are greatly affected by alcohol while others seem relatively tolerant. How much is this variation in susceptibility to intoxication genetically determined? We are training 18–35-year-old twins on a number of psychomotor tasks related to driving skills including motor coordination, body sway, hand steadiness, reaction time, and cognitive impairment. After training to plateau, twins are given a dose of alcohol (related to body weight) and performance is then measured on the same tasks at hourly intervals. Preliminary results on 80 pairs of twins will be presented. Thirty pairs of twins have been tested on two occasions, so repeatability data are available for all measures.

**BEHAVIORAL AND BIOLOGICAL PHARMACOGENETICS OF D-AMPHETAMINE**

Elliot S. Gershon

Biological Psychiatry Branch, NIMH, Bethesda, Maryland

D-amphetamine (IV 0.3 mg/kg) and placebo were administered on separate days in randomized order to 12 MZ healthy twin pairs. Double blind behavioral ratings were performed on videotapes of the first hour, and factor analysis was performed. Behavioral excitation and elation during the second 30 minutes after infusion were highly correlated within pairs and reproducible within individuals on repeat infusion. Early depression was found to be significantly correlated within twin pairs but not reproducible within individuals. Motor activity measurements over 24 hours showed that during the early morning hours some twin pairs had no quiescent periods and others did, implying correlated variation in amphetamine produced sleeplessness. Plasma amphetamine was correlated only with elation, and over the 24-hour period was not correlated within pairs. Behavioral excitation was highly correlated with resting methoxyhydroxy-phenylglycol (MOPEG) and with growth hormone elicited by amphetamine. A factor containing these three items was found to be highly correlated within members of the twin pairs. This implies that a norepinephrine-mediated response to amphetamine shows familial variation, presumably due to genetic variation in norepinephrine reactivity.

**FAMILIAL RESEMBLANCE FOR USAGE OF COMMON DRUGS**

Nancy L. Pedersen

Institute for Behavioral Genetics, University of Colorado, Boulder

In a Swedish study of families of twins, 75 MZ pairs, 62 DZ pairs, and their spouses and adult children answered an extensive battery of questionnaires concerning drug use, personality, health and environment. Twin intraclass correlations and intrafamily correlations and regression were calculated to estimate heritability for four types of alcohol use (beer, wine and spirits consumption, plus a measure of excessive drinking), coffee/tea, tranquilizer and sleeping pill use, and smoking status. Heritability estimates from the twin data were 0.28, 0.78, 0.18, and 0.84 for spirits use, coffee/tea use, tranquilizer use, and smoking status, respectively. DZ intraclass correlations for use of beer and wine were paradoxically greater than MZ correlations. For heavy drinking, the MZ correlation was 0.68 and the DZ correlation was 0.06. After dichotomization of all the items except coffee/tea use, which was normally distributed, MZ twins were somewhat more concordant than DZ twins for spirits consumption, heavy drinking, tranquilizer use, sleeping pill use, and smoking status. Family data estimates of  $h^2$  were as follows: beer consumption, 0.13; wine consumption, 0.32; spirits consumption, 0.17; heavy drinking, 0.41; coffee/tea consumption, 0.42; tranquilizer use, 0.24; sleeping pill use, 0.05; and smoking status, 0.32. Genetic and environmental correlations were computed from the family data to determine the extent to which pairs of measures share the same "genetic" factors (between family) and "environmental" factors (within family). Measures of alcohol consumption and smoking status generally have significantly greater genetic correlations than environmental correlations. Similarly, the genetic correlation between coffee/tea consumption and smoking status is greater than the environmental correlation.

**CIGARETTE SMOKING, USE OF ALCOHOL, AND LEISURE-TIME PHYSICAL ACTIVITY IN ADULT LIKE-SEXED MALE TWIN PAIRS**

J. Kaprio, M. Koskenvuo, S. Sarna

Department of Public Health Science, University of Helsinki

Cigarette smoking history, use of alcohol, and leisure-time physical activity were surveyed in the 1975 questionnaire study of the Finnish Twin Registry. In individuals, cigarette smoking and alcohol use were positively correlated ( $r = 0.32$ ), while a slight negative correlation of both variables to physical activity was found. In MZ pairs ( $N = 1537$ ) the intraclass correlations for cigarette smoking, alcohol use, and physical activity were 0.64, 0.54, and 0.57, respectively, and for DZ pairs ( $N = 3507$ ), 0.42, 0.28, and 0.26, correspondingly. Factor analysis followed by cluster analysis of the 15 study variables indicated that 8 distinct groupings of individuals could be formed. The distribution of MZ and DZ twins in the clusters was investigated. Both members of a MZ pair were found in the same cluster 3.1-fold compared to expectation, while DZ pair members were in the same cluster 2.5 times more often than expected.

**THE INFLUENCE OF PSYCHOSOCIAL STATUS ON THE RELATIONSHIP BETWEEN SMOKING AND DISEASE**

Birgitta Floderus-Myrhed, Rune Cederlöf

Department of Environmental Hygiene, Karolinska Institute, Stockholm

Previous investigations have clearly pointed to a competing influence on health of smoking and smoking-related factors. Still the interactions between smoking, psychosocial factors, genetics, and the occurrence of disease, are sometimes disregarded in contemporary studies. The present study aims at elucidating the importance of smoking and psychosocial status (instability) for disease when occurring separately and jointly. The study is based on the new Swedish twin registry (twins born in 1926–58), comprising 13,865 pairs where both members have answered a questionnaire including the variables studied. The issue was analyzed by comparing the disease experience within pairs with different patterns of discordance for smoking and instability. When occurring jointly, smoking and instability show a strong association with disease symptoms such as recurrent chest pain, severe chest pain > 30 minutes, and respiratory symptoms. When occurring alone, instability exerts a more pronounced influence on chest pain than does smoking alone. Smoking occurring alone exerts on the other hand a more clear influence on the conventional smoking-related respiratory symptoms, cough and chronic bronchitis, than does instability. The present findings show that psychosocial status adds significant information for the analysis of the relationship between smoking and health.