GENETIC STUDIES OF THE OFFSPRING OF IDENTICAL TWINS
A Model for the Analysis of Quantitative Inheritance in Man

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In conjunction with full-sib and parental observations, half-sib analysis permits an estimation of the genetic and environmental variance as well as a partitioning of the genetic variance into its additive, dominance and epistatic components. The offspring of identical twins are a unique class of human half-sibs who provide an unusual opportunity to resolve and measure several additional potentially important sources of human variation including maternal effects, the influences of common environmental factors and assortative mating.

The genetic model thus developed for the analysis of quantitative inheritance in man has been applied to the analysis of total ridge count and birth weight, confirming the existence of a major additive genetic effect on ridge count and a significant maternal effect on birth weight.

INTRODUCTION

The analysis of data obtained from half-sibs has long been recognized as a powerful technique for the delineation of quantitative inheritance in lower organisms, but the method has seldom been applied to elucidate human inheritance. In conjunction with full-sib and parental observations, half-sib analysis permits an estimation of genetic and environmental variance and a partitioning of the genetic variance into its additive and dominance components, as well as the detection of epistatic interactions and maternal effects. The offspring of identical twins are related to each other in the same way as half-sibs, and the multiple unique relationships that exist within these kinships provide an unusual opportunity to resolve and measure potentially important sources of human variation. A model for the analysis of data from MZ twin " half-sibships " is developed here and its usefulness is explored. For previous descriptions and applications of the model see Bader et al. (1973), Bingle (1974) Kang et al. (1974), Nance et al. (1974), and Nance (1975).

DESCRIPTION OF THE MODEL

The structure of the data is shown in the Figure. The offspring of male and female identical twins provide two independent sets of data, and, as shown below, contrasts between them permit the detection of genetically determined maternal effects. Numerous additional relationships exist within the data which allow the joint estimation of several important genetic and environmental parameters.

Half-Sib Relationship

MZ twins possess identical sets of nuclear genes and consequently their offspring are related to each other in the same way as are half-sibs. The total variation of the offspring, including both genetic and environmental effects, may be partitioned by a nested analysis of variance into: among half-sibship, between sibship-within half-sibship, and within sibship mean squares as described by Snedecor (1961). The number of sibships within each half-sibship is fixed at two but the number of offspring within each sibship is variable. Consequently, numerical approximations for the coefficients (b_1, b_2, and a) of the between-within (σ^2_B) and the among (σ^2_A)

components of variation must be calculated from the observed distribution of family size as shown in Table 1. Once the coefficients have been determined, the variance components may be estimated from the mean squares. The genetic interpretation of the variance components of the half-sib analysis of variance is summarized in Table 2. For the most part the interpretation follows the conventional model for half-sib analysis that has been developed in lower organisms (Falconer 1961, Comstock 1955) with the important exception that the availability of both maternal and paternal half-sibships of equivalent size and number permits the inclusion of maternal effects in the model. Since the genetic expectations for the within sibship component of the analysis of variance for male and female MZ twin half-sibships are identical, these components are pooled, leading to a total of five distinct relationships from the two classes of kinships.
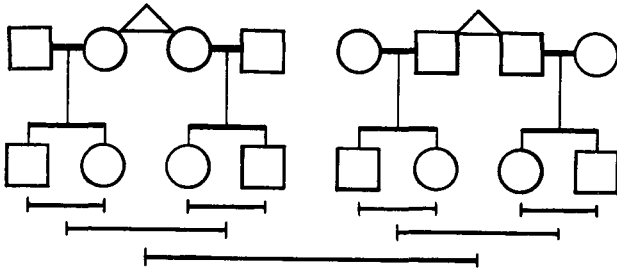

Figure. Structure of MZ twin half-sibship data, illustrating how total variation may be partitioned into within sibship, between sibship-within half-sibship and among half-sibship components.

Half-sibs share one-quarter of their genes, and, since all of their common genes are derived from a single parent, or in the present case, genetically identical parents, the among half-sibship component of variance, σ^2_A, which is equivalent to the covariance of half-sibs, provides an estimate of $1/4\ V_A$, the additive component of the total genetic variance. As shown by Comstock (1955), the half-sib covariance also includes the epistatic effects of additive genes. Finally, although it may be permissible to assume that there is no environmental variation among half-sibships in experimental animals (Mather and Jinks 1971), this would clearly be an oversimplification for many human traits. Consequently, an among half-sibship environmental component, V_{EH}, is included in the model.

The within sibship component, σ^2_W, is equivalent to the total phenotypic variance minus the covariance of full sibs. Therefore, it includes $1/2\ V_A$ and $3/4\ V_D$, as well as the epistatic interaction components shown in Table 3. The within sibship environmental component, V_{EW}, may be thought of as a source of environmental variation that affects all individuals irrespective of their genetic relationship.

The between sibship-within half-sibship component, σ^2_B, is equivalent to the full-sib covariance minus the half-sib covariance. Consequently, it includes $1/4\ V_A$ and $1/4\ V_D$ as well as the epistatic interaction components given in Table 2. As in the interpretation of the two previous components, a source of environmental variation, V_{ES}, is included to take into account possible environmental differences between sibships-within half-sibships.

Maternal Effects

As noted previously, maternal effects can be detected by contrasting the analysis of variance of MZ male twin half-sibships with that for MZ female twin half-sibships. To the extent that genetically determined pre- or postnatal maternal effects influence a trait, we would expect the offspring of MZ female twins to resemble one another more than the offspring of male MZ twins, resulting in an inflation of $\sigma^2_A\female$, the among half-sibship component for female twins. On the other hand, the offspring of male MZ twins are born to genetically unrelated mothers, and if there is a significant maternal effect, $\sigma^2_B\male$ will be increased in comparison with $\sigma^2_B\female$. Since all of the offspring within a sibship are born to the same mother, genetically determined maternal variation does not enter into the within sibship mean square, and, as noted previously, the data for male and female twin half-sibships may therefore be combined to obtain a pooled estimate of the within sibship mean square. Of course, if there were any reason to suspect that the V_{EW}'s for the two classes of twins are not equal, two separate equations could be used. In the present model, age, sex and parity effects are confounded with V_{EW}. However, the presence of these effects can be detected by performing the analysis with and without adjustment for these variables and noting the influence on the resulting estimates of V_{EW}.

Monozygotic Twin Relationship

The phenotypic similarity of MZ twins provides one of the most incisive measures of genetic determination that can be obtained in human genetics. If an analysis of variance is performed on data from MZ twins, the within pair component will estimate the within pair environmental variance while the among pair component

Table 1. *Analysis of variance of half-sib data*

Source of variation	DF	Mean square	Expected mean square
Among half-sibships	$N - 1$	MSA	$\sigma^2_W + b_2\,\sigma^2_B + a\sigma^2_A$
Between sibships-within half-sibships	N	MSB	$\sigma^2_W + b_1\sigma^2_B$
Within sibships	$\Sigma\,(n_{i1} + n_{i2}) - 2N$	MSW	σ^2_W
Total	$\Sigma\,(n_{i1} + n_{i2}) - 1$	MST	

$$b_1 = \frac{\Sigma\,(n_{i1} + n_{i2}) - \Sigma\,(n^2_{i1} + n^2_{i2})\,/\,(n_{i1} + n_{i2})}{N}$$

$$b_2 = \frac{\Sigma\,(n^2_{i1} + n^2_{i2})\,/\,(n_{i1} + n_{i2}) - \Sigma\,(n^2_{i1} + n^2_{i2})\,/\,\Sigma\,(n_{i1} + n_{i2})}{N - 1}$$

$$a = \frac{\Sigma\,(n_{i1} + n_{i2}) - \Sigma\,(n_{i1} + n_{i2})^2\,/\,\Sigma\,(n_{i1} + n_{i2})}{N - 1}$$

Table 2. *Offspring data: Genetic interpretation of variance components*

Variance component	Covariance estimated	Genetic interpretation								
		V_A	V_D	V_{AA}	V_{AD}	V_{DD}	V_M	V_{EH}	V_{ES}	V_{EW}
(1) $\sigma^2_{A\male}$	covHS$\male$	1/4	0	1/16	0	0	0	1	0	0
(2) $\sigma^2_{B\male}$	covS$\male$-covHS$\male$	1/4	1/4	3/16	1/8	1/16	1	0	1	0
(3) σ^2_W	V_T-covS	1/2	3/4	3/4	7/8	15/16	0	0	0	1
(4) $\sigma^2_{B\female}$	covS$\female$-covHS$\female$	1/4	1/4	3/16	1/8	1/16	0	0	1	0
(5) $\sigma^2_{A\female}$	covHS$\female$	1/4	0	1/16	0	0	1	1	0	0

Table 3. *Parental data: Genetic interpretation of variance components*

Relationship	Parameter	Genetic interpretation								
		V_A	V_D	V_{AA}	V_{AD}	V_{DD}	V_M	V_{EH}	V_{ES}	V_{EW}
MZ Twins:										
(6) Among pairs	σ^2_{AT}	1	1	1	1	1	1	1	0	0
(7) Within pairs	σ^2_{BT}	0	0	0	0	0	0	0	1	1
Twin-Spouse Covariance:										
(8) Among twin sets	covTS$_A$	0	0	0	0	0	0	1	0	0
(9) Within twin sets	covTS$_W$	0	0	0	0	0	0	0	1	0
Spouses of Twins:										
(10) Among pairs	σ^2_{AS}	0	0	0	0	0	0	1	0	0
(11) Within pairs	σ^2_{WS}	1	1	1	1	1	1	0	1	1

will include all of the genetic variance as well as the variance attributable to environmental differences among pairs (Table 3: 6-7). In conventional twin studies, MZ twins are often compared with DZ twins, and the assumption is made that the environmental similarities and differences among DZ twins are equivalent to those of MZ twins. However, since MZ and DZ twins are almost never members of the same family, this assumption is demonstrably false in detail and implausible in the aggregate. In the present model, however, note that environmental effects on the parents, including those acting on the twin parents, may be partitioned into exactly the same three components as in the offspring analysis. This is possible because the parents and children generally live in the same home and many potentially important sources of environmental variation such as diet, socioeconomic status, geographic location, climate, religion, or exposure to culture, books, pollution or trace elements will tend to be distributed within and among the parents and their offspring in a similar manner. Thus a simultaneous estimate of the environmental effects across the parental and offspring data would seem to be a far more valid and appropriate approach than that of the conventional twin analysis. It should be noted that no provision is made in the present model for systematic environmental differences between generations, although this feature could also be incorporated if necessary.

Husband-Wife Relationship

The covariance between husband and wife has been used by some investigators to estimate the effects of living in a common environment, and by others as a measure of assortative mating. Resolution of these two effects may not be important for many traits, but for others, such as psychological variables, the distinction may be critical since assortative mating tends to inflate the additive component of the genetic variance in the offspring (Crow and Kimura 1970) while environmental covariance does not. In the present model, the husband-wife covariance may be partitioned into among and within twin set components (Table 3:8-9). If assortative mating is present, the genetically identical twin of an assortatively mated individual should show a similar tendency to mate assortatively. If a pooled estimate of the among half-sibship environmental variance, V_{EH}, is obtained, it may then be compared with the estimate derived from the among twin set component of the twin-spouse covariance; if the latter is larger, the excess will provide a measure of the effect of assortative mating. Similarly, disassortative mating would lead to a lowering of the estimate of V_{EH} obtained from the among twin set component of the husband-wife covariance in comparison with the pooled estimate.

Relationship Between Spouses

An analysis of variance between and among the genetically unrelated spouses of the MZ twins can provide yet another estimate of V_{EH} (Table 3:10-11). As in the case of the husband-wife covariance, assortative mating will, if present, inflate the among half-sibship variance component. However, in contrast to the husband-wife covariance, disassortative mating will also augment this component.

Parent-Offspring Relationships

As shown in Table 4, two conventional and three unique parent-offspring relationships exist within the data. For example, the phenotypic covariance between a child and the twin parent differs from that between the child and the twin aunt or uncle only because of the increased environmental similarity of the former; while the covariance between the offspring and the genetically unrelated aunt or uncle provides another estimate of V_{EH}, the among half-sibship environmental component.

DATA ANALYSIS

Each of sixteen relationships described in Tables 2-4 can be used to obtain an equation of estimation, and measurement of the genetic and environmental parameters of interest can then be achived by the simultaneous solution of appropriate sets of the foregoing equations by the least squares method. Two approaches are possible, a weighted and an unweighted analysis. For the latter, it is convenient to use variance components, and each component is assumed to be known with equal accuracy. For the former approach, mean squares must be employed, and are weighted by the reciprocal of their sampling variances. Thus, for the unweighted analysis, the equations of estimation can be represented by

$$MG = C \tag{1}$$

where M is an $m \times n$ matrix of variable coefficients for m equations in n unknowns, G is the $n \times 1$ column vector of genetic and environmental parameters whose estimates are desired; and C is the $m \times 1$ column vector of variances and covariances that are derived from the data. The least square estimate of G, i.e., $\hat{G}$, can be obtained first by premultiplying each side of equation (1) by the transpose of the M matrix, M', and then by the inverse of the product

$$\begin{aligned}
M'\,M\,G &= M'\,C \\
(M'\,M)^{-1}\,M'\,M\,G &= (M'\,M)^{-1}\,M'C \\
G &= (M'\,M)^{-1}\,M'C\,.
\end{aligned} \tag{2}$$

Table 4. *Genetic interpretation of parent-offspring covariances*

Relationship	Parameter	Genetic interpretation of covariance				
		V_A	V_{AA}	V_M	V_{EH}	V_{ES}
(12) Offspring-Mother	covOM	1/2	1/4	1	1	1
(13) Offspring-Father	covOF	1/2	1/4	0	1	1
(14) Offspring-Spouse	covOS	0	0	0	1	0
(15) Offspring-Twin Aunt	covOA	1/2	1/4	1	1	0
(16) Offspring-Twin Uncle	covOU	1/2	1/4	0	1	0

Table 5. *Analysis of total ridge count data from offspring of 23 male MZ twin pairs*

Source of variation	DF	Mean square	Expected mean square
Among half-sibships	22	4398.58	$\sigma^2_W + b_2\sigma^2_B + a\sigma^2_A$
Between sibships-within half-sibships	23	2068.96	$\sigma^2_W + b_1\sigma^2_B$
Within sibship	71	1331.93	σ^2_W
Total	116		

$$b_1 = 2.3981 \qquad b_2 = 2.6755 \qquad a = 5.0606$$
$$\hat{\sigma}^2_W = 1331.93 \qquad \hat{\sigma}^2_B = 307.34 \qquad \hat{\sigma}^2_A = 443.50$$

Table 6. *Analysis of total ridge count data from offspring of 28 female MZ twin pairs*

Source of variation	DF	Mean square	Expected mean square
Among half-sibships	27	4719.63	$\sigma^2_W + b_2\sigma^2_B + a\sigma^2_A$
Between sibships-within half-sibships	28	1795.69	$\sigma^2_W + b_1\sigma^2_B$
Within sibships	77	901.49	σ^2_W
Total	132		

$$b_1 = 2.2787 \qquad b_2 = 2.4478 \qquad a = 4.7062$$
$$\hat{\sigma}^2_W = 901.49 \qquad \hat{\sigma}^2_B = 392.42 \qquad \hat{\sigma}^2_A = 607.19$$

The expected values of the statistics are then found by

$$E(C) = M\hat{G} \tag{3}$$

To perform the weighted analyses it is necessary to replace the variance components in C with their mean squares, resulting in the column vector $\mathfrak{S}$. A new matrix, $\mathfrak{M}$, must also be calculated, composed of the coefficients appropriate to the mean squares. The elements of this matrix are calculated by summing the products of the coefficients for each variable in the component model (Table 2:5) times the appropriate b or a coefficients in the expected mean square of the analysis of variance shown in Table 2 or comparable coefficients for the parental data. Algebraically, the procedure may be represented by

$$\mathfrak{M} = AM, \tag{4}$$

where

$$A = \begin{pmatrix} A_1 & 0 & 0 \\ 0 & A_2 & 0 \\ 0 & 0 & I_5 \end{pmatrix}, \qquad A_1 = \begin{pmatrix} a & b_2\male & 1 & 0 & 0 \\ 0 & b_1\male & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & b_1\female & 0 \\ 0 & 0 & 1 & b_2\female & a\female \end{pmatrix} \text{ and } A_2 = \begin{pmatrix} 2 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 2 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 2 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

for the sixteen equations given in Tables 2-4. Next, each side of the matrix equations is weighted by $\mathfrak{B}^{-1}$, the inverse of the variance matrix of $\mathfrak{S}$, and the equations are solved for $\mathfrak{S}^*$ as described previously:

$$\mathfrak{B}^{-1}\,\mathfrak{M}\mathfrak{G} = \mathfrak{B}^{-1}\mathfrak{S} \tag{5}$$
$$\mathfrak{M}'\,\mathfrak{B}^{-1}\,\mathfrak{M}\mathfrak{G} = \mathfrak{M}'\,\mathfrak{B}^{-1}\mathfrak{S}$$
$$(\mathfrak{M}'\,\mathfrak{B}^{-1}\,\mathfrak{M})^{-1}\,\mathfrak{M}'\,\mathfrak{B}^{-1}\,\mathfrak{M}\mathfrak{G} = (\mathfrak{M}'\,\mathfrak{B}^{-1}\mathfrak{M})^{-1}\,\mathfrak{M}'\,\mathfrak{B}^{-1}\mathfrak{S}$$
$$\mathfrak{S}^* = (\mathfrak{M}'\,\mathfrak{B}^{-1}\mathfrak{M})^{-1}\,\mathfrak{M}'\mathfrak{B}^{-1}\mathfrak{S} .$$

The $\mathfrak{B}$ matrix is an $m \times m$ diagonal matrix whose non-zero elements are the sampling variances of $\mathfrak{S}$. The variances are calculated from the formulae

$$v_{ii} = 2\,c^2{}_i/(N_i + 2) \tag{6}$$

or

$$v_{ii} = (w^2{}_i + c_j c_k)/(N_i + 2), \tag{7}$$

and where c_i is the mean square whose variance v_{ii} is to be estimated, and c_j and c_k are the variances of two variables whose covariance is w_i, and N_i is the degrees of freedom (Mather and Jinks 1971). Although the variance component analysis described previously or the mean squares from an analysis of variance are equally suitable for the unweighted analysis, formulae (6) and (7) can be applied only to mean squares with their associated degrees of freedom. The advantage of the unweighted analysis is that a single coefficient matrix, M, may be applied to all analyses using the same genetic model while in the weighted analysis a specific $\mathfrak{M}$ matrix must be determined for each data set. The diagonal elements of the $\mathfrak{B}$ matrix should be calculated not from the observed values of $\mathfrak{S}$ but from their expected values based on the weighted estimates of $\mathfrak{S}^*$ (Hayman 1960). Consequently, the estimates of $\mathfrak{S}^*$ must be calculated by an iterative procedure: based on the unweighted estimate of $\mathfrak{B}$, $\mathfrak{S}^*$ and new estimates of $\mathfrak{S}$ are calculated. These in turn provide a second estimate of $\mathfrak{B}$ from which $\mathfrak{S}^*$ and $\mathfrak{S}$ are recalculated. At the conclusion of the iteration, the variance-covariance matrix of $\mathfrak{S}^*$ may be calculated from the relationship

$$\text{Var } \mathfrak{S}^* = (\mathfrak{M}'\mathfrak{B}^{-1}\mathfrak{M})^{-1} . \tag{8}$$

The diagonal elements of this matrix are the variances of the parameters estimated by $\mathfrak{S}$, based on large sample theory and the assumption that the original variables are normally distributed, and may be used to establish approximate confidence intervals for the estimated parameters. Additional details concerning least square estimation of genetic parameters are provided by Mather and Jinks (1971) and by Jinks and Fulker (1970).

NUMERICAL EXAMPLES

Total Ridge Count

The dermal ridge patterns of the fingertips are laid down during the first trimester of fetal life and remain largely unchanged thereafter. The total ridge count is a statistic obtained by summing over all ten fingers the numbers of dermal ridges traversed by lines drawn from the triradius of each digit to the nearest pattern core. If a finger pattern has two ridge counts, as in the case of whorls, only the larger is used to obtain the total ridge count (Holt 1968). Total ridge counts are approximately normally distributed in the general population and range in values from zero to about 300. As a group, males are consistently found to have somewhat higher ridge counts than females, although considerable variation in mean values is observed among different population groups. In the present study, total ridge counts were obtained from individuals in the families of 51 pairs of MZ twins. Zygosity was confirmed by extensive genotyping, and only those pairs in which both twins had at least one child were included in the study. Several families were incomplete, however, and could not be used for all of the comparisons. The sample comprised 28 female twin pairs, 23 male pairs and 78 spouses of these subjects. The female twins had a total of 133 offspring who were studied while the male twins had 117. The average total ridge count for males was 141.8 while for females it was 128.5,

in close agreement with previous observations in other populations of Western European extraction (Holt 1968). Prior to the analysis, the ridge counts were adjusted for sex to remove the effect of variation among families in the sex ratio of the offspring.

A nested analysis of variance was performed on the offspring data, and the results are shown in Tables 5 and 6. Although the within sibship mean square for male twins was greater than that for female twins, the ratio fell short of significance at the 5% level, using a two-tailed test ($F = 1.4774$ DF 71,77), and the estimates were pooled in the subsequent analysis. Four equations were selected in addition to the five derived from the offspring data. They were the within and among twin pair equations (6 and 7) and two of the parent-offspring equations (12, 13). A total of 39 twin pairs were used for the former, whereas 45 mother-child and 43 father-child combinations were used for the latter comparisons. In families with more than one child, the mean values of the offspring were used to estimate the parent-offspring covariances. The nine equations were solved for four unknowns, V_A, V_D, V_M, and V_{EW}, as shown below.

$$
\mathfrak{M} \qquad\qquad \mathfrak{G} \qquad\qquad \mathfrak{C}
$$

$$
\begin{bmatrix}
2.4340 & 1.4189 & 2.6755 & 1 \\
1.0995 & 1.3495 & 2.3981 & 1 \\
0.5 & 0.75 & 0 & 1 \\
1.0697 & 1.3197 & 0 & 1 \\
2.2885 & 1.3620 & 4.7062 & 1 \\
2 & 2 & 2 & 1 \\
0 & 0 & 0 & 1 \\
0.5 & 0 & 1 & 0 \\
0.5 & 0 & 0 & 0
\end{bmatrix}
\begin{bmatrix}
V_A \\
V_D \\
V_M \\
V_{EW}
\end{bmatrix}
=
\begin{bmatrix}
4398.58 \\
2068.96 \\
1107.98 \\
1795.69 \\
4719.63 \\
3749.82 \\
142.50 \\
953.06 \\
756.06
\end{bmatrix}
$$

The results of the analysis are shown in Table 7. Less than 9% of the total variation appeared to be determined by environmental factors, while nearly 80% was attributable to additive genetic factors, and the estimated value of V_A was more than two times its standard error. Positive values were also obtained for V_D and V_M but the estimates were not significant in this small body of data.

Birth Weight

Anamnestic procedures were used to collect data on birth weight and gestational age in the families of 46 MZ twins. The sample included the families of 20 MZ male pairs, with a total of 112 offspring and 26 female pairs with 142 offspring. Prior to the analysis, the birth weights were adjusted for gestational age and sex using the normative data of Lubchenco et al. (1963). Fewer data were available on the parental birth weights, and consequently only two additional equations resulting from the analysis of variance of the birth weights of the 46 twin pairs were included in the analysis, and the equations were solved for four genetic and environmental variance components as shown below.

$$
\mathfrak{M} \qquad\qquad \mathfrak{G} \qquad\qquad \mathfrak{C}
$$

$$
\begin{bmatrix}
1.6476 & 2.9311 & 2.9311 & 1 \\
1.2473 & 2.6520 & 2.6520 & 1 \\
0.75 & 0 & 0 & 1 \\
1.2281 & 0 & 2.5499 & 1 \\
1.6194 & 5.3725 & 2.8460 & 1 \\
2 & 2 & 1 & 1 \\
0 & 0 & 1 & 1
\end{bmatrix}
\begin{bmatrix}
V_{AA} \\
V_M \\
V_{ES} \\
V_{EW}
\end{bmatrix}
=
\begin{bmatrix}
0.3869 \\
0.6205 \\
0.1222 \\
0.6015 \\
0.3012 \\
0.0741
\end{bmatrix}
$$

The results of the analysis are shown in Table 8. In the best fitting model, four genetic and environmental variance components had positive estimates. Approximately one-third of the total variation

could be attributed to genetically determined maternal effects. Two sources of environmental variation were detected, and the estimates of V_{EW} and the V_{ES} were both more than twice their standard errors. A small epistatic variance component was also detected, but its magnitude was less than the standard error of the estimate.

Table 7. *Total ridge count: Least square estimates of genetic and environmental variance components*

Component	ᴓ*	Proportion of total variance	Variance-covariance matrix of ᴓ*			
			V_A	V_D	V_M	V_{EW}
V_A	1525 ± 520	0.793	270692			
V_D	68 ± 375	0.035	$--180255$	140280		
V_M	165 ± 225	0.086	-84882.4	48863.1	50816	
V_{EW}	164 ± 37	0.086	3.40495	-1616.98	287.096	1346.14

Note: Symmetric elements of covariance matrix omitted.

Table 8. *Birth weight: Least squares estimates of genetic and environmental variance components*

Component	ᴓ*	Proportion of total variance	Variance-covariance matrix of ᴓ*			
			V_{AA}	V_M	V_{ES}	V_{EW}
V_{AA}	0.0142 ± 0.0367	0.064	0.001347			
V_M	0.0751 ± 0.0296	0.341	-0.000691	0.000877		
V_{ES}	0.0490 ± 0.0205	0.222	0.000286	$--0.000359$	0.000420	
V_{EW}	0.0819 ± 0.0281	0.373	-0.000962	0.000500	-0.000269	0.000790

Note: Symmetric elements of covariance matrix omitted.

Table 9. *Total ridge count: Comparison of observed correlations*

Relationship	Parameter	Estimated correlation	
		Holt (1968)	Present study
Parent-offspring	r_{PO}	0.40	0.44
Mother-child	r_{MC}	0.48	0.48
Father-child	r_{FC}	0.49	0.40
MZ twins	r_{MZ}	0.95	0.91
Husband-wife	r_{HW}	0.05	0.09
Full-sib	r_{FS}	0.50	0.49
Half-sib	r_{HS}	—	0.24

DISCUSSION

Conventional half-sib studies in man are subject to many potential biases which may be difficult, if not impossible, to control. Reciprocal matings are seldom available in equal numbers. The sibships are often small and unequal in size. Systematic age and parity differences are usually present. For half-sibs resulting from illegitimacy, death of the husband or wife, or divorce, all of the relevant parents are seldom available for analysis. Finally, unless the half-sibs are raised in different homes, genetic and environmental effects remain confounded.

In striking contrast, the offspring of identical twins are a unique class of human half-sibs in whom most of these methodologic difficulties can be circumvented. Since they are ascertained through parents of the same age and sex, the families of identical twins have the same expected size and mean age. MZ twins occur with equal frequency in all racial groups and the two sex types provide maternal and paternal half-sibships in approximately equal numbers. In general, the offspring of identical twins are reared in a home environment which is no different from the families of singletons. However, the fact that the sibships within each half-sibship usually live in different households permits a clear separation of genetic and environmental effects which does not depend upon the abnormal separation of children from their biologic parents. Finally, in contrast to conventional half-sibs, all of the relevant parents are usually available and eager to cooperate.

One of the major virtues of the present model is its flexibility. Although a very large sample size would doubtless be required to detect significant epistatic interactions, the model at least has the potential of measuring these effects if they are present. The model also permits resolution of the additive and dominance genetic effects from observations on individuals who are members of the same generation, which may be of particular importance for variables in which a constant environment cannot be assumed from one generation to the next. In contrast to the classical twin model, DZ twins are not utilized and no assumptions are made about the comparability of the environmental variation among and within these biologically and epidemiologically unrelated phenomena. Indeed, for variables thought to be unduly influenced by the unique prenatal relationship of MZ twins (Price 1960) or by the postnatal " twin situation " (Zazzo 1974), the two equations arising from analysis of the twins themselves could be omitted from the analysis. In this way, it would be possible to exploit the unique genetic relationship of identical twins, through the analysis of their offspring, without incurring the liabilities introduced by their unique environmental relationships.

The present model may be particularly relevant to the analyses of psychological traits. Previous studies of the genetic determination of normal psychological traits have been characterized by an almost obsessional concern with abnormal human relationships such as identical twins reared apart, and foster or adoptive children, in the mistaken belief that only through an analysis of these pathologic relationships can genetic and environmental effects be resolved. However, the present model clearly shows how a comparable resolution can be achieved from an analysis of normal subjects living in their own homes, who would appear to differ in no important way from the general population about which we wish to draw inferences. The ability to detect maternal effects is another important feature of the model. Documentation of a significant maternal effect on psychological traits such as intelligence test scores could serve to redirect efforts to improve the educational performance of children. Finally, the ability of the model to partition and identify nongenetic sources of variation may also prove to be of great importance. For example, it seems likely that environmental effects attributable to differences in diet would be distributed over all three environmental components while effects resulting from socioeconomic differences may be confined to a large extent to V_{EH} and V_{ES}.

Many previous studies have documented the important role that genetic factors play in the determination of the dermal patterns of the hands and feet. Holt (1968) has shown that the total ridge count is a continuously distributed metric trait which shows a high degree of genetic determination. The patterns of correlations she observed in relatives of various degree were consistent with the assumption that the total ridge count is a multifactorial phenotype that is largely determined by additive genetic factors. The correlations derived from the present study are compared with those of Holt

in Table 9. In the overall analysis shown in Table 7, genetic factors were found to be the major determinants of the total ridge count and in agreement with previous results, the genetic effects were largely additive in nature.

Several lines of evidence suggest that maternal factors have a major influence on birth weights. In experimental animals, reciprocal crosses between subspecies that differ markedly in body size yield offspring that tend to resemble the female parent. Although the weight differences are most striking at birth, they may persist throughout life (Walton and Hammond 1938). In her classical study of the genetic control of human birth weight Robson (1955) demonstrated the existence of a maternal effect on birth weight by showing that there is a greater correlation in the birth weights of matrilineal cousins than in cousins related through at least one male parent. It is of interest that in her thesis, Robson (1954) comments on the possible value that observations of the birth weights of the offspring of MZ and DZ twins might have in distinguishing uterine effects from genetically determined maternal effects, but it is not clear that she fully appreciated the unique genetic relationship of the offspring of identical twins. In a multivariate analysis, Morton (1955) showed that both maternal effects and parity effects made a major contribution to the observed variation in birth weights. Morton's sample of more than 15,000 sib-pairs included 30 pairs of maternal half-sibs and, although the data were not adjusted for gestational age, the observed correlation in the small sample of maternal half-sibs was actually greater than the estimated correlations between full-sib pairs. These observations and others led Ounsted (1972) to propose that fetal growth is regulated by the interaction of genetic factors in the fetus and the mother. In some women, small-for-dates infants appear to result from a genetically determined maternal factor which constrains fetal growth. Accelerated fetal growth, on the other hand, appears to be determined to a greater extent by additive genetic factors in the fetus. The present analysis confirms the existence of a major maternal effect on birth weight. The nature of the two significant environmental components is uncertain, but the V_{EW} component could, at least in part, result from parity effects while V_{ES} could result from dietary or other environmental differences between sibships.

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