Acta Genet Med Gemellol 28:41–50 (1979)
The Mendel Institute / Alan R. Liss, Inc.

Received 11 September 1978
Final 15 December 1978

Effects of Type of Placentation on Birthweight and its Variability in Monozygotic and Dizygotic Twins

L.A. Corey[1], W.E. Nance[1], K.W. Kang[2], J.C. Christian[2]

[1] *Department of Human Genetics, Medical College of Virginia, Richmond;* [2] *Department of Medical Genetics, Indiana University School of Medicine, Indianapolis*

Birthweight was measured on 188 monochorionic monozygotic, 54 dichorionic monozygotic, 102 like-sexed dizygotic, and 94 unlike-sexed dizygotic liveborn twin pairs. Overall, males were found to be significantly heavier than females. These differences were not significant, however, when birthweights were compared within zygosity/chorion-type categories. Males were also characterized by a slightly greater overall total variance. Comparisons of intrapair variation of monochorionic and dichorionic monozygotic twins revealed significant differences between monochorionic pairs and dichorionic separate pairs and no significant differences between monochorionic pairs and dichorionic fused pairs. The results of this study suggest that placental proximity may have as important an influence on variation in birthweight as does the presence or absence of vascular anastomoses.

Key words: Birthweight, Twin pregnancy, Placental effects, Length of gestation, Sex effects, Fetal hormones

Variation in human birthweight is known to be influenced by such factors as length of gestation [3, 6], race [1], sex [17], parity [9] and maternal smoking history [11]. In addition, "maternal factors" are recognized to have powerful and possibly overriding effects on the expression of this trait [10, 13], but the relative importance of fetal geno-

This is paper No. 80 of the Department of Human Genetics, Medical College of Virginia, and was funded in part by the Medical College of Virginia Twin Panel grant P01 HD10291-02 and in part by the Genetic Center grant (Indiana University Human Genetics Center grant, PHS P50 GM 21054) and a postdoctoral training grant PHS DE 00007.

type versus maternal factors, and the nature of the maternal factors or effects involved, are unresolved issues. Maternal influences can be subdivided into three general categories: (1) Those conditioned by cytoplasmic genes, (2) those which arise from effects of the maternal genotype on the pre- or postnatal environment of the fetus and (3) those representing exogenous intrauterine environmental influences such as alcohol intake or maternal diet. Nance et al [15] reported that approximately 40% of the variation observed in birthweights of singleton offspring of identical twins could be accounted for by maternal factors, but were unable to infer the nature of those factors.

Through twin studies of prenatal factors, Naeye et al [14] and Gedda and Poggi [5] found that, in addition to effects of sex difference, type of chorionic development appears to account for a large portion of the variation in intrapair difference observed in birthweights of twins. In extreme cases the fetal transfusion syndrome can lead to marked differences in body size at birth which may persist into adult life [19]. The present study was designed to assess the effects of sex, zygosity and chorion type on birthweight and its variability in monozygotic (MZ) and dizygotic (DZ) twins in order to characterize the genetic, maternal and environmental factors influencing this trait.

MATERIALS AND METHODS

Birthweights were measured on 118 monochorionic and 54 dichorionic MZ, and 102 like-sexed and 94 unlike-sexed DZ liveborn twin pairs as part of a study of consecutive twin deliveries at the hospitals affiliated with the Indiana University School of Medicine and with the Medical College of Virginia. The number of chorions was established by gross and microscopic examination of fetal membranes. Zygosity was confirmed by typing for nine polymorphic blood group systems. Length of gestation to the nearest week was determined by history. The individuals included in the study were characterized by gestational ages ranging between 28 and 44 weeks. Information was also obtained on race, parity and maternal age. The monochorionic class was not further subdivided by amnion type because of the small number within the monoamniotic subgroup. Within each zygosity type, however, the dichorionic class was subdivided into "fused" and "separate" categories according to pathology. In the sample of twins studied, female pairs slightly outnumbered male pairs in all categories.

Statistical Methods

In all statistical analyses performed, birthweights were expressed in grams. The distribution of raw data was tested for departures from normality using chi-square Goodness-of-Fit tests [18]. In preliminary analyses, regression techniques were used to determine if effects of race, gestational age, parity, or maternal age accounted for any significant proportion of the observed variation in raw birthweights. Raw data were adjusted for those effects which were found to be significant, and the distributions of adjusted birthweight values within sex/zygosity classifications were tested for departures from normality before further analysis was undertaken.

Variation among and within pairs within zygosity/sex/chorion-type classification was examined by analyses of variance for paired data under an extension of the classical twin model which includes type of chorionic development [2]. Under this model, variation resulting from genotype by environment interaction is not partitioned from total environmental variation. For this reason, the environmental components specified should best be thought of as containing variation attributable to genotype by environment interaction as well as that attributable to other environmental sources.

RESULTS

Unadjusted birthweight values from each sex/zygosity/chorion-type category were examined for departures from normality. While there was, in general, no evidence of significant skewness, several sex/zygosity categories were characterized by significant kurtosis. Multiple regression analyses of birthweight data with length of gestation, race, parity and maternal age serving as covariates revealed that race and length of gestation accounted for a significant proportion of the variation observed in raw birthweights. The nonsignificance of effects of parity and maternal age on birthweight in this study population may be a result of an association between these effects and length of gestation. Because the intent of this study was to examine effects of sex and chorion type on birthweight, raw birthweight values were adjusted for race and gestational age before further analyses were undertaken.

Following adjustment of raw birthweight values, observations on twin pairs within each sex/zygosity/chorion-type category were reexamined for departures from normality. The results obtained provided no evidence of significant skewness or kurtosis in any of the categories. The use of standard statistical test procedures would, therefore, seem appropriate to compare means and variances between categories.

Adjusted mean birthweights for monochorionic MZ, dichorionic MZ (pooled over fused and separate chorion types), and DZ pairs within sex classifications are given in Table 1. While males were significantly heavier than females overall (3,019 ± 27 vs 2,892 ± 21), sex differences were not significant when birthweights were compared within zygosity/chorion-type categories. In all cases, however, members of like-sexed male pairs were slightly heavier, on the average, than members of like-sexed female pairs within the same chorion-type category. As shown in Table 1, dichorionic MZ pairs, on the whole, tended to be somewhat heavier than like-sexed dichorionic DZ pairs. Members of male MZ dichorionic pairs were slightly heavier than members of any other type of twin pair examined in this study.

Table 2 shows the mean birthweights of dichorionic fused and dichorionic separate twins within each sex/zygosity classification. MZ twins were classified by sex, and within each sex, monochorionic (MC), dichorionic fused (DCF), and dichorionic separate (DCS) placental types were distinguished, while DZ twins were divided into those showing completely separate (DCS) or fused (DCF) placentas, respectively. As reflected in Table 2, males outweighed females in corresponding categories, with one exception, that being

TABLE 1. Adjusted Mean Birthweights (g) of Twin Pairs by Placentation, Zygosity, and Sex Combination[a]

Sex	Monochorionic		Dichorionic[b]			
	n	$\bar{x}$	n	$\bar{x}$	b_1	b_2
				Monozygotic pairs		
FF	73	2,827 ± 41	30	2,899 ± 47	0.01	−0.35
MM	45	2,919 ± 73	24	3,074 ± 90	−0.41	0.65
				Dizygotic pairs		
FF			59	2,935 ± 49	0.22	0.18
MM			43	2,976 ± 69	−0.12	0.38
MF			45	3,065 ± 58	0.08	−0.23
FM			49	3,015 ± 55	0.43	−0.25

[a]Standard errors were calculated using the among-pair variances. b_1 and b_2 represent values of skewness and kurtosis, respectively.
[b]Pooled over fused and separate categories.

TABLE 2. Mean Adjusted Birthweights (g) of Dichorionic Twin Infants by Sex and Zygosity[a]

	Male twins		Female twins	
Pair type	n	x	n	x
		Dichorionic fused		
MZ	30	3,110 ± 119	32	2,860 ± 57
Like-sexed DZ	46	2,965 ± 83	60	2,972 ± 65
Male-female	21	3,079 ± 120	21	2,870 ± 81
Female-male	17	3,023 ± 99	17	2,935 ± 105
		Dichorionic separate		
MZ	18	3,015 ± 134	28	2,944 ± 78
Like-sexed DZ	40	2,990 ± 113	58	2,897 ± 75
Male-female	24	3,207 ± 80	24	3,080 ± 84
Female-male	32	3,151 ± 79	32	2,917 ± 60

[a]The variance used in calculation of standard errors for mean birthweights of like-sexed pairs is that associated with the among-pair partition of variation. The total variance of males or females was used in calculating standard errors for unlike-sexed pairs.

the DCF like-sexed DZ class. The average birthweights of male and female members of DCS unlike-sexed pairs with first-born males were slightly greater than those of corresponding male or female members of unlike-sexed pairs with first-born females or like-sexed MZ or DZ pairs. The mean birthweights of male and female members of DCF DZ pairs and of females of unlike-sexed DCS pairs with first-born females were intermediate between those of like-sexed MZ and DZ female pairs. The results presented in Table 2 suggest that there is no detectable birthweight advantage associated with unlike-sexed pairs in the DCF category.

Results from analyses of variance of birthweight data within sex/zygosity/chorion-type classifications are presented in Tables 3 and 4 for twin pairs of like and unlike sex, respectively. There are n−1 degrees of freedom associated with the among-pair partition of variance for all groups, and n degrees of freedom associated with the within-pair partition of variance for like-sexed categories. One degree of freedom, which is associated with sex, is partitioned from the degrees of freedom associated with the variation within unlike-sexed DZ twins. As shown in Table 3, significant heterogeneity was found in the total variance and in the variation among pairs in comparisons of MZ males and females in both the MC and DCF classes. No significant heterogeneity in intrapair variation which could be attributed to sex effects was found for like-sex pairs in any other zygosity/chorion-type category. Sex effects on intrapair variation, in this situation, are different from those associated with unlike-sexed pairs, in that they would not reflect differences related to an advantage held by one sex over the other with respect to competition between pair members for the same nutrient supply. The among, within and total variances of male MZ twins were, in all cases, slightly greater than those of their female counterparts. Male-DZ twins showed more variation among, but not within, pairs than did their female counterparts.

With the exception of the comparison between male DCF MZ and DZ twins, the variation among pairs was greater for DZ than for MZ twins in the same sex/chorion-type

TABLE 3. Analyses of Variance for Like-Sexed Within Sex/Zygosity/Chorion-Type Categories[a]

	Male pairs		Female pairs				
	df	MS	df	MS	F_A	F_W	F_{A+W}
Monochorionic							
A	44	479,927	72	247,414	1.9*	1.1	1.7**
W	45	86,223	73	78,827			
Dichorionic fused MZ							
A	14	422,878	15	103,296	4.1**	1.4	3.2**
W	15	70,257	16	50,683			
Dichorionic separate MZ							
A	8	324,490	13	168,745	1.9	1.7	1.9
W	9	49,626	14	29,731			
Dichorionic fused DZ							
A	22	318,604	29	254,970	1.2	1.0	1.2
W	23	94,214	30	96,763			
Dichorionic separate DZ							
A	19	515,200	28	328,761	1.6	1.4	1.3
W	20	84,270	29	119,024			

[a]MS = mean squares; A = among pair; W = within pair.
*P < 0.05.
**P < 0.01.

TABLE 4. Analyses of Variance for Unlike-Sexed Twin Pairs Within Sex/Chorion-Type Categories[a]

	Male-female		Female-male				
	df	Ms	df	MS	F_A	F_W	F_{A+W}
Dichorionic fused DZ							
A	20	314,788	16	258,028	1.2	1.3	1.2
W	20	127,151	16	98,389			
Dichorionic separate DZ							
A	23	259,414	31	292,185	1.1	1.2	1.1
W	23	67,842	31	57,922			

[a]MS = mean squares; A = among pair; W = within pair.

category. This is in contrast to what would have been expected under the assumptions of the classical twin model if genetic effects are important in the expression of the trait. No significant heterogeneity in total variance was found in any comparison between males of any category. However, significant heterogeneity in total variance was found in comparisons of MC MZ females with DCF MZ females, DCF MZ females with DCF DZ females and DCS MZ females with DCS DZ females. The differences in intrapair variation observed between sex/zygosity/chorion-type categories were significant in comparisons of female MC and DCS MZ twins and in comparisons of female DCS MZ with female DCS and DCF DZ twins. Variation within MZ pairs, as reflected by the within-pair mean squares, appears to be inversely associated with the degree of prenatal proximity of pair members. An identical pattern of variation was observed in the DZ pairs when the sex of the twins was ignored, and fused and separate placental types were compared. However, the pattern was inconsistent when DZ pairs were partitioned by sex.

Table 5 gives intraclass correlation coefficients for birthweight within each sex/zygosity/chorion-type classification. Two trends are evident from the information on like-sexed twin pairs presented in this table. First, the magnitude of the intraclass correlation appears to increase with decreasing prenatal association of pair members. Second, female twin pairs appear to be characterized by a lower intraclass correlation than are male pairs.

Mean intrapair differences in birthweight for each sex/zygosity/chorion-type category are shown for like-sexed pairs in Table 6 and for unlike-sexed pairs in Table 7. The trends evident in these tables are consistent with those reflected by the differences observed in intrapair variation over sex/zygosity/chorion-type categories. These trends also suggest

TABLE 5. Intraclass Correlation Coefficients for Birthweights (g) of Twin Partners

	Monochorionic	Dichorionic-fused	Dichorionic-separate
MZ cotwins			
Male	0.70 ± 0.08	0.72 ± 0.13	0.74 ± 0.16
Female	0.52 ± 0.09	0.34 ± 0.22	0.70 ± 0.14
DZ cotwins			
Male		0.54 ± 0.15	0.72 ± 0.11
Female		0.45 ± 0.15	0.47 ± 0.15
Unlike-sexed cotwins		0.43 ± 0.14	0.63 ± 0.08

TABLE 6. Mean Intrapair Differences in Birthweight (g) Within Like-Sexed Zygosity/Chorion-Type Categories

	Male pairs	Female pairs
MZ cotwins		
Monochorionic	312.67	286.56
Dichorionic fused	291.00	239.13
Dichorionic separate	234.56	179.29
DZ cotwins		
Dichorionic fused	332.65	333.77
Dichorionic separate	300.25	340.72

TABLE 7. Mean Intrapair Differences in Birthweight (g) Within Unlike-Sexed/Chorion-Type Categories

	Male-female pairs	Female-male pairs
Dichorionic fused DZ	441.62[a]	322.29
Dichorionic separate DZ	247.96	302.44

[a]Mean difference not adjusted for effects of sex.

that the intrapair differences seen in MZ twin pairs may be inversely related to the degree of proximity of pair members during prenatal development. While the lack of statistical significance of these differences may be a result of small sample size, it may also suggest that effects of chorion type on birthweight are of a subtle rather than an overt nature.

DISCUSSION

Of the variables examined in this study using regression techniques, gestational age was found to have the greatest effect on variation in birthweight. The consistent, though insignificant, differences in birthweight between males and females suggest that sex, in itself, is also an important factor in determining birthweight. Further, males in a given zygosity/chorion-type category outweighed their female counterparts despite adjustment for length of gestation. This suggests that sex exerts an independent overall effect on birthweight beyond that which might be attributed to variation in length of gestation between males and females. Naeye et al [14] have pointed out that twins born early in gestation tend to be characterized by greater intrapair differences than those born closer to term. In our study, analyses did not reveal the existence of any relationship between length of gestation and intrapair difference. Also, while the greatest intrapair differences were seen for monochorionic MZ and dichorionic DZ twins, these categories were not characterized by the shortest mean length of gestation. Even though these results suggest that differences in length of gestation are not responsible for the differences seen in intrapair variation between categories, it is difficult to assess the degree to which the existence of a cause and effect relationship between intrapair difference and length of gestation might be important in explaining the results obtained in this study because of the small size of our sample population. The lack of information with respect to this relationship, per se, further complicates an interpretation of results. At present, it is not known if intrapair differences remain stable after some point in gestation or if they increase or decrease with its duration.

Our findings that male twins are heavier, on the average, than female members of like-sexed MZ or DZ pairs or female members of female-male pairs are consistent with those reported by several other investigators [7, 17]. The fact that males, in general, tended to be heavier than females and that second-born females of unlike-sexed dichorionic separate DZ twin pairs tended to be heavier than their like-sexed counterparts may suggest that the maleness or the presence of a male cotwin (in male-female pairs) in some way stimulates increased growth in the male or his female cotwin over that seen in like-sexed female pairs. There appears, however, to be great variability in this effect as manifested by the magnitude of the variance associated with male birthweight. There are several possible explanations for the sex effect observed here. One explanation is that the presence of the Y chromosome and the associated hormonal maleness in some way induces the male fetus to grow at a more accelerated rate than the Y-less female counterpart. This hypothesis does not seem likely, however, given that female members of certain unlike-sexed pairs also tend to have greater birthweights than do members of like-sexed female pairs, unless there is some degree of diffusion of fetal hormones between the placentae – again an improbable hypothesis, since female members of unlike-sexed pairs generally have not been found to be masculinized to any degree.

A second possible explanation for the increased birthweight of males over that of females could come from effects of interaction between H-Y antigen and the associated male hormones and maternal phenotype. This highly conserved antigen, which has been

https://doi.org/10.1017/S0001566000009326 Published online by Cambridge University Press

reviewed in great detail by Glasser and Silvers [4], has been hypothesized as being the essential inducer of testis differentiation in mammals. Mittwoch [12] has suggested that H-Y antigen exerts its effects on testis development by being responsible for the enhanced growth of the dominant heterogametic gonad at its critical stage of differentiation. If this is true, and if the presence of this antigen also indirectly stimulates overall development, it could explain, at least in part, the differences seen in birthweights of males and females. Further, if some of the hormones produced by the male fetus manage to enter maternal circulation and if their presence there has the ability to stimulate the production of a more optimal environment than is provided in their absence, male and female members of unlike-sexed pairs should be characterized by higher birthweights than female members of like-sexed pairs. The higher variance seen in birthweights of males could then be explained by variation, which could be genetic, in the ability of the maternal phenotype to respond to indirect H-Y antigen stimulation. Strong evidence in support of this hypothesis would be provided if male fetal hormones could be isolated in the serum of women carrying male offspring and if it could be shown that there is a dosage effect on birthweight with respect to the number of Y chromosomes present in a developing fetus. That is, if this hypothesis is accurate, XYY males would, on the average, tend to be heavier at birth than XY males. In the one report concerning birthweights of XYY males that we were able to locate in the literature [16], examination of seven XYY males revealed that these subjects were, on the average, 200 grams heavier than normal XY males. The reported difference, however, was not significant.

In comparisons of chorion types, no striking differences in birthweight were found which could be directly attributed to monochorionic or dichorionic placentation in MZ twins. While this could be a result of sampling, the consistency of results obtained for males and females suggests this is not the case. Even though the monochorionic twins examined in this study were characterized by the greatest intrapair difference and smallest intraclass correlation, these statistics were quite similar to those obtained for dichorionic fused MZ twins. The data, rather than demonstrating any massive differences between monochorionic and dichorionic MZ classes, instead reflected a gradation of decreasing intrapair variance and increasing intraclass correlation from monochorionic to dichorionic fused to dichorionic separate categories. This raises some doubt as to the importance of prenatal vascular anastomoses as the primary cause for variation in birthweights of monochorionic twins since these connections are almost always present in MC placenta, but are seldom found in DC placenta [19]. Our data suggest, rather, that chorionic effects may be attributable largely to the degree of proximity of placental implantation sites and that both MZ and DZ twins may compete for available nutrients in utero to a greater extent when the implantation sites are close to one another. The association seen between proximity of pair members during prenatal development is consistent for both male and female MZ twins, as well as for DZ pairs when sex is ignored.

While three monochorionic MZ pairs in the sample were characterized by extremely large ($< 40\%$) intrapair differences in birthweight ($> 1{,}050$ grams, with gestational ages > 37 weeks), there were three dichorionic fused sets characterized by an intrapair difference greater than 600 grams and five like-sexed DZ pairs which had intrapair differences greater than 1,200 grams. Thus, in this sample, at least, the monochorionic class was not alone in containing twin pairs characterized by marked intrapair differences. These results suggest that the magnitude of the intrapair difference in itself cannot be safely used as the criterion upon which zygosity or type of chorionic development is specified, nor as a criterion for diagnosis of fetal transfusion syndrome in the absence of other clinical information, since some dichorionic MZ pairs, as well as DZ pairs, are also characterized by large intrapair differences. These observations do not imply that the fetal transfusion syndrome cannot be the cause of large intrapair differences in birthweight, but suggest that other factors may be equally contributory to marked birthweight dissimilarities.

Genetic differences in the ability of a given maternal phenotype to respond to a twin pregnancy could explain some of the variation in birthweight observed among pairs and contribute to the within-pair variation as well. If maternal intrauterine environment is not a growth-limiting factor, one pair member may not be forced to compete or develop at the expense of his or her cotwin, whereas if the maternal environment is deficient in any way, competition may be enhanced. In the murine zygote transfer experiments reported by Hegmann et al [8], observed differences in the placental transport of amino acids appeared to be dependent on both the fetal and the maternal genotype, suggesting a possible mechanism for maternal effects on fetal growth.

While the study presented herein provides information with respect to the importance of chorionic effects on birthweight, it does not go very far in elucidating the nature and relationship of the factors which may influence fetal growth. The fact that the distributional characteristics of birthweights of MZ twins are quite similar to those of like-sexed dichorionic fused DZ twins suggests that variation resulting from the fetal transfusion syndrome and/or competition between monochorionic cotwins for available nutrients may be equivalent to that resulting from genetic differences and competition in DZ twins. For this reason, when the classical twin approach is to be used to estimate the relative importance of genetic and environmental effects on birthweight, perhaps the least biased results will be obtained when dichorionic separate MZ twins are compared with like-sexed dichorionic separate DZ twins. Failure to consider the placental type of both the MZ and DZ twins could lead to erroneous inferences.

REFERENCES

1. Chinnici JP, Sansing RC (1977): Mortality rates, optimal and discriminating birthweights between white and nonwhite births in Virginia (1955–1973). Hum Biol 49:335–348.
2. Corey LA, Kang KW, Christian JC, Norton JA Jr, Harris RE, Nance WE (1976): Effects of chorion type on variation in cord blood cholesterol of monozygotic twins. Am J Hum Genet 28:433–441.
3. Fraccaro M (1957): A contribution to the study of birthweight based on an Italian sample of twin data . Ann Hum Genet 21:224–236.
4. Glasser DL, Silvers WK (1972): Genetics and immunology of sex-linked antigens. Adv Immunol 15: 215–247.
5. Gedda L, Poggi D (1960): Importanza dell placentazione sul peso all nascita dei gemelli. Acta Genet Med Gemellol 9:271–281.
6. Hoffman HJ, Stark CR, Lundin FE Jr, Ashbrook JD (1974): Analysis of birthweight, gestational age, and fetal viability, US Births, 1968. Obstet Gynecol Surv 29:651–681.
7. Hoffman HJ, Bakketeig LS, Stark CR (1978): Twins and perinatal mortality: A comparison between single and twin births in Minnesota and in Norway, 1967–1973. In Nance WE, Allen G, Parisi P (eds): "Twin Research": Part B, Biology and Epidemiology." New York: Alan R. Liss, pp 133–142.
8. Hegmann JP, Blaklely A (1978): Gene differences alter placental transport of amino acids in mice. Behav Genet 8:98.
9. Karn M (1952): Birthweight and length of gestation of twins, together with maternal age, parity and survival rate. Ann Eugen 16:365–377.
10. McKeown TH, Record RG (1954): Influence of pre-natal environment on correlation between birthweight and parental height. Am J Hum Genet 6:457–463.

11. Meyer MB, Jonas BS, Tonascia JA (1976): Perinatal events associated with maternal smoking during pregnancy. Am J Epidemiol 103:464–476.
12. Mittwoch U (1977): H-Y antigen and the growth of the dominant gonad. J Med Genet 14:335–338.
13. Morton NE (1955): The inheritance of human birthweight. Ann Hum Genet 20:125–134.
14. Naeye RL, Benirschke K, Hagstrom JWC, Marcus CC (1966): Intrauterine growth of twins as estimated from liveborn birth-weight data. Pediatrics 37:409–416.
15. Nance WE, Corey LA, Boughman JA (1978): Monozygotic twin kinships: A new design for genetic and epidemiologic research. In Morton NE, Chung CS (eds): "Genetic Epidemiology." New York: Academic Press, pp 87–132.
16. Nielsen J, Fredrick U, Zeuthen E (1971): Stature and weight in boys with XYY syndrome. Humangenetik 14:66–68.
17. Ounsted M (1972): Gender and intrauterine gorwth: With a note on the use of sex of the probands as a reserach tool. In Ounsted C, Taylor DC (eds): "Gender Differences: Their Ontogeny and Significance." Edinburgh: Churchill Livingstone.
18. Snedecor GW, Cochran WG (1967): "Statistical Methods." Ames, Iowa: Iowa State University Press.
19. Strong SJ, Corney G (1967): The placenta in twin pregnancy. London: Pergamon Press.

Correspondence: Dr. L.A. Corey, Department of Human Genetics, Medical College of Virginia, MCV Station, Richmond, VA 23298, USA.