IS WEINBERG'S METHOD VALID?

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Suppose that L like-sexed and U unlike-sexed twins have been observed. Weinberg's method estimates the numbers of DZ and MZ twins as DZ = 2U and MZ = L — U. This method is based on the assumptions that (1) the sex ratio in DZ twins is ½ and (2) the sexes of DZ twins are determined independently and with the same probability in all parents; in consequence there should, on average, be equal numbers of like-sexed and unlike-sexed DZ twins. The first assumption is not exactly true, but the necessary correction is negligible. Departures from the second assumption would probably lead to an excess of like-sexed over unlike-sexed DZ twins; in consequence, Weinberg's method would underestimate the numbers of DZ twins and overestimate the numbers of MZ twins. The literature on the frequencies of like-sexed and unlike-sexed pairs among twins known to be DZ through other genetic markers is reviewed. It is concluded that there is no evidence of an excess of like-sexed twins among them, and that there is therefore no reason to doubt the validity of Weinberg's method. The extension of Weinberg's method to estimate the zygosity types of triplets and quadruplets is described; it is shown that the resulting estimates agree well with the results of direct zygosity determination by blood grouping.

In most studies of the frequency of twinning, direct information about the zygosity of the twins is not available. The frequencies of the two types of twins (MZ and DZ) must therefore be estimated from information about the numbers of twins of like and unlike sex. Suppose that L like-sexed and U unlike-sexed twin pairs have been observed. All MZ twins must be like-sexed; if the sex ratio is ½, then half the DZ twins will, on average, be like-sexed and half unlike-sexed. The number of DZ twins can therefore be estimated by doubling the number of unlike-sexed twins: DZ = 2U. The remainder must be MZ, so that MZ = L — U.

This method was first systematically used by Weinberg in 1901 and is usually associated with his name. It was however known to Bertillon as early as 1874, but was rejected by him because the number of MZ twins estimated by this method is larger than the number of monochorial twins. It was then thought that all monochorial twins were MZ (which is true) and that all dichorial twins were DZ (which is untrue). It is now known that 25-30% of MZ twins are dichorial. Such twins arise if the embryo divides in the few days of pregnancy before the chorion is formed.

Weinberg's method depends on two assumptions, first that the sex ratio in DZ twins is ½ and second that the sexes of the two twins are determined independently and with the same probability in all parents. The first assumption is not exactly true, but the necessary correction is negligible. Suppose that the sex ratio in DZ twins is $p = \frac{1}{2} + \varepsilon$. If the second assumption is true, then the probability that DZ twins are unlike-sexed is: $P(U) = 2p(1-p) = \frac{1}{2} - 2\varepsilon^2$. The number of DZ twins should therefore be estimated as: $DZ' = U/(\frac{1}{2} - 2\varepsilon^2) = 2U + 8\varepsilon^2 U$, and the number of MZ twins as: $MZ' = L - (1 + 8\varepsilon^2)U$. Unfortunately, the sex ratio in DZ twins is not known. In Caucasoids the sex ratio in single births is about 0.514, and the sex ratio in all twins about 0.508. If we take the sex ratio in DZ twins to be the same as the sex ratio in all twins, then $\varepsilon = 0.008$ and $8\varepsilon^2 = 0.0005$.

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It is possible, however, that the reduction in the sex ratio in twins is due entirely to a reduction in MZ twins, caused by a slightly increased chance of division in the female embryo. In this case we should take $\varepsilon = 0.014$ and $8\varepsilon^2 = 0.0016$. In either case the correction is fortunately negligible and can be safely ignored.

The second assumption underlying Weinberg's method is that the sexes of the two twins in DZ twinning are determined independently and with the same probability of about ½ in all parents. This assumption would break down if some parents were, for some reason, more prone to have boys and others girls, though there is evidence that this factor is at most only of minor importance (Edwards and Fraccaro 1960, Edwards 1958 and 1966). It would also break down if, as suggested by James (1971*a*), the sex of offspring is related to the day of conception in the menstrual cycle, so that the sexes of the twins are not independently determined; the evidence for this suggestion seems to me to be very weak. In either case, more like-sexed than unlike-sexed DZ twins would be produced. In consequence, Weinberg's method would underestimate the numbers of DZ twins and overestimate the numbers of MZ twins. In view of the widespread use of Weinberg's method it is desirable to review the evidence which now exists about its validity.

The first line of evidence comes from sheep, in which nearly all twins are known to be DZ since two corpora lutea are almost always found. In an extensive survey of over 24,000 sheep twins, the proportion of like-sexed twins was 49.4%, which is not significantly different from the theoretical value of 50% (Rae 1956). There is thus no doubt of the validity of Weinberg's assumption in this species.

I turn now to the human evidence. Weinberg's method was criticised by Renkonen in 1967. He found that the proportion of MZ twins in Finland estimated by Weinberg's method from data on births was higher than the proportion found in a sample of twins in their thirties whose zygosity had been determined by blood grouping. He concluded that Weinberg's method was defective. However, it has been pointed out by several authors that the discrepancy can be explained by the higher mortality of MZ twins in the first few months of life; one would therefore expect to find a lower proportion of MZ twins in an adult sample than at birth. Weinberg's method can only be adequately tested by blood grouping a sample of twins at the same time as their sex combinations are recorded.

There are now several investigations in which twins have been blood grouped at birth. Weinberg's method can be tested by considering the numbers of like and unlike-sexed twins in a sample of twins known to be DZ because of differences in blood groups or other genetic markers apart from sex James (1971*b*) reviewed evidence of this kind and concluded that there was an excess of like-sexed twins. The evidence available today is summarised in Table 1.

There is no significant evidence of heterogeneity between the Caucasoid and Nigerian figures ($\chi^2 = 3.33$, 1 DF). The pooled data shows no significant departure from a 50/50 ratio ($\chi^2 = 2.71$, 1 DF). There is nevertheless a suspicion of an excess of like-sexed twins in the Nigerian, though not in the Caucasoid, data. If this difference is genuine we may estimate (in the Yoruba) that $p(\mathrm{U}) = 0.454$. To estimate the numbers of DZ and MZ twins in the Yoruba we should therefore take: $\mathrm{DZ}' = = \mathrm{U}/0.454 = 2.2\mathrm{U}$; $\mathrm{MZ}' = \mathrm{L} - 1.2\mathrm{U}$.

To test whether the excess of like-sexed twins in the Nigerian data is genuine or merely a sampling accident, I have used both the Weinberg estimate and the modified estimate on three other sets of data for the Yoruba for which only sex is known; the results are shown in Table 2. In fact, Nylander (1970), by direct zygosity determination, found the percentage of MZ twins among all twins to be 8.3%. This agrees much better with the Weinberg estimates than with the modified estimates. I therefore suggest that the excess of like-sexed twins in Nylander's data is a sampling accident and that there is no reason to doubt the validity of Weinberg's method.

Weinberg's method has been extended by Allen (1960) to estimate the frequencies of the three types of triplets. All MZ triplets must be of the same sex, half the DZ triplets will be of the same sex and half of unlike sex (either two boys and one girl or one boy and two girls), while one quarter of the trizygotic (TZ) triplets will be of the same sex and three quarters of unlike sex (cf. Table 3).

Unfortunately, there are three types of triplets and only two sex types, so that some further assumption must be made to obtain estimates of the zygosity types from the sex types. It seems reasonable

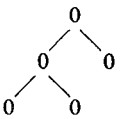
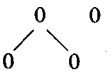
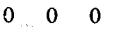
Table 1. *Numbers of like-sexed and unlike-sexed pairs among twins diagnosed as DZ through differences in other genetic markers*

Like-sexed	Unlike-sexed	Race	Author
79	71	Caucasoid	Potter 1963
38	22	Caucasoid	Walsh and Kooptzoff 1955
84	88	Caucasoid	Corney et al. 1968
180	202	Caucasoid	Strong and Corney 1967
381	383	Caucasoid subtotal	
383	318	Nigerian (Yoruba)	Nylander 1970
764	701		Total

Table 2. *Twinning in Yoruba* (Bulmer 1960, Knox and Morley 1960, Nylander 1969)

			Weinberg's estimates			Modified estimates		
L	U	N	MZ	MZ/N	%MZ	MZ′	MZ′/N	%MZ′
512	417	20,045	95	4.7‰	10.2%	12	0.6‰	1.3%

Table 3. *The three types of triplets*

Type	Monozygotic	Dizygotic	Trizygotic
Origin			
Like-sexed	1	½	¼
Unlike-sexed	0	½	⅓

to suppose that if m and d are the MZ and DZ twinning rates, then the frequency of DZ triplets will be $2md$; for the probability that two ova will be released is d and the probability that one or other of them will divide to produce DZ triplets is $2m$. We may therefore estimate the number of DZ triplets as $T_2 = 2Nmd$, where N is the total number of births. Now $\frac{1}{2} T_2$ will be unlike-sexed DZ triplets; the remaining unlike-sexed triplets will represent three quarters of the TZ triplets. Hence we estimate the TZ triplets as: $T_3 = 4/3 (U - \frac{1}{2} T_2)$. The remainder are MZ triplets, so that: $T_1 = L - \frac{1}{3} U - \frac{1}{3} T_2$.

This method has been used to estimate the frequencies of the three types of triplets in Caucasoid populations, and it was found that they were in the ratio of 1 : 3 : 2. Among like-sexed triplets the ratio should be 2 : 3 : 1. A series of 54 like-sexed Swedish triplets were typed by blood grouping by Hauge et al. (1967), and it was found that the numbers of MZ, DZ, and TZ triplets were 17, 28

and 9, which is in almost perfect agreement. Recently, Nylander and Corney (1971) have published the results of an investigation of 44 Yoruba triplets. The frequencies of the three types estimated by Allen's extension of Weinberg's method were 4, 16 and 24; the estimates obtained by direct zygosity determination for 40 of the 44 troplets were 2, 14 and 24. The agreement is again excellent.
Finally, similar arguments have been used to extend Weinberg's method to estimate the four zygosity types of quadruplets from data on the three possible sex types. Details of the method which I propose, which differ slightly from Allen's method, are given in Bulmer (1970). The estimates obtained agree well with the frequencies of 28 quadruplets in the literature whose zygosity has been determined directly.

In conclusion, Is Weinberg's method valid? Yes.

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