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Relevance of Twin Data to Intrauterine Selection

Special case of childhood cancer

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The purpose of this paper is to draw attention to the statistical implications of abortion risks being greater for twins than singletons, greater for MZ than DZ twins, and greater for one member of a twin pregnancy than both members. This last fact is important, because if one twin aborts the other is usually mistaken for a singleton at birth; thus allowing a given number of nonconcordant abortions to have a marginally greater effect on twin frequency than double the number of concordant abortions.

This feature of abortion hazards is shown in Tab. I, which is based on Sandon's calculations of concordance effects. The figures show how much greater is the effect of a high rate of nonconcordant abortions (Case B) than the effect of an equally high rate of 90% concordant abortions (Case A) or a lower rate of 60% concordant abortions (Case C). In other words, a low frequency of twins in general (and MZ twins in particular) should be typical of an abortion-ridden population and might be a means of recognizing diseases whose prevalence rates are misleading, because they are associated with an abortion hazard (i.e., inherited diseases and diseases acquired during embryogenesis).

Low Frequency of Twin Births among American Indians

In a consecutive series of 36 964 live and stillborn children, 96% of whom were of American-Indian parentage, there were 267 pairs of twins, or fewer than one would expect if the babies had been of American-European parentage. For twins of like sex and for MZ twins the difference between the two groups was in the region of 36% and 50% respectively, and for twins of unlike sex and for DZ twins it was less than 20% (cf. Tab. II). Since inbreeding is commoner among American-Indians than American-Europeans, these findings are probably indicative of a higher proportion of nonviable genotypes among the former than among the latter.

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Tab. I. Effect of various assumptions on the joint survival rate of twin pairs

	Assumed variables	3 sets of 4 assumed variables*		
		Case A	Case B	Case C
	Affected pairs of twins			
1	Survival rate of individual twins	0.3446	0.3446	0.6554
2	Intrapair correlation**	+0.90	+0.00	+0.60
	Joint survival rate	0.2784	0.1187	0.5200
	Unaffected pairs of twins			
3	Survival rate of individual twins	0.6554	0.6554	0.8413
4	Intrapair correlation**	+0.90	+0.90	+0.90
	Joint survival rate	0.5892	0.5892	0.7981
	Deficiency of twins in a population of affected survivors	53%	80%	35%

* Under Case A, $53\% = \frac{100\ (0.5892 - 0.2784)}{0.5892}$;

Under Case B, for r = 0.00, $0.1187 = (0.3446)^2$;

When r>O, joint survival rate exceeds square of individual survival rate.

** i.e., twin concordance for the abortion risk.

Tab. II. Comparative frequency of twin births in White and Indian populations of the USA

	Twin frequency ‰ births			
	As counted, by sex composition		Weinberg estimate by zygosity	
	Like sex	Unlike sex	MZ	DZ
Indians of Arizona, New Mexico and Oklahoma 1954-58	4.46	2.49	1.97	4.98
Whites, 1956	6.99	3.08	3.91	6.16
Deficiency of twin-born subjects in Indian, compared with White population	36%	19%	50%	19%

Low Frequency of Twins with Trisomy 21

Even before the chromosomal basis of mongolism was known, epidemiologists were aware that twin concordance was rare, and they even entertained a false hope of identifying " causes " of this condition among gestational period events (Smith, 1960). We now know that the basic cause is already present in the zygote and that MZ pairs are usually concordant. Hence, a deficiency of MZ twins with trisomy 21

should now be interpreted as evidence of an associated abortion hazard. There are, in fact, two pointers in this direction.

In an analysis of congenital malformations in New York State, Gittelsohn and Milham (1965) gave the following figures for the birth certificate incidence of mongolism: (1) ♂♂ and ♀♀ twins, 28/100 000; (2) ♂♀ twins, 37/100 000; and (3) single births, 38/100 000.

In this series there were only 12 " affected " twins because the recording of mongolism on birth certificates only applied to about 20% of the affected children. However, in a study focused specifically on twins with trisomy 21, McDonald (1964) found that only 5 of 67 affected pairs were concordant, when 10.46 concordant pairs were expected.

Low Frequency of Twins among Juvenile Cancers (Nonradiogenic Cases)

In a consecutive series of 166 twins who died from malignant diseases before the age of 10 years and were included in a nation-wide cancer survey (Stewart and Kneale, 1968) there were 118 children who were X-rayed shortly before birth and 48 other children (cf. Tab. III). In the non-X-rayed group only 54% of the children

Tab. III. Sex composition of certain series of twin pairs

Twin sets	N. of pairs	% distribution			
		Like sex			Unlike sex
		♂	♀	Subtotal	
Pairs containing a child who died from a cancer before the age of 10 years and had a cotwin of known sex					
Total	166	33	28	61	39
With antenatal X-ray	118	35	29	64	36
Balance	48	29	25	54	46
Both members live-born. All such pairs born in England and Wales during:					
1955	7707	32	32	64	36
1960	8396	33	32	65	35
1965	9068	34	32	66	34

had a cotwin of like sex, compared with 64% in the X-rayed group and 65% in the population from which the two groups of cases were drawn. In the X-rayed group approximately 40% of the cases were radiogenic in origin (i.e., were caused by an event which is usually much too late to be the cause of an abortion). In the non-X-rayed group there were none of these cases and the mean age at death was younger than in the X-rayed group. So, the inference is that a deficit of like sex twins among the nonradiogenic cancers of childhood is typical, and is the result of selective

elimination of twin zygotes whose malignant neoplasms are the result of cell damage incurred at or shortly after conception.

It is also possible to derive from the same cancer survey (and from official statistics) evidence that selective elimination of "tumour bearing" embryos, or the forerunners of infant cancers, not only applies with greater force to twins than singletons, but also with greater force to males than females. For instance, although all forms of cancer were commoner in boys than in girls (sex ratio 1.3) nevertheless more girls developed neoplasms during infancy than boys (sex ratio 0.94). Less than 2% of healthy controls gave a history of a threatened abortion, whereas the corresponding figures for children who developed cancers within a year of birth or between 1 and 10 years were 4.5% and 2.5% respectively. This excess of near-abortions among the infant cancers was achieved in spite of there being a marked deficit of boys with the relevant experiences. Thus, 25 children, whose birth was preceded by a threatened abortion, developed cancers within six months of birth, but only 7 of them were boys (sex ratio 0.39).

Finally, in the absence of any other hypothesis accounting for lethal congenital defects with an unusual sex bias, selective elimination during embryogenesis should be considered as a possible reason for the low sex ratios which characterize stillbirths due to congenital defects in general (0.63) and anencephaly in particular (0.42); and also for the small numbers of boys among the 135 "normal" children in 55 sibships containing two or more children with juvenile cancers (sex ratio 0.69 — cancer survey data).

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