

# Mongolism in Twins\*

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It is now well established that persons with mongolism have an extra chromosome No. 21. Apart from a small proportion of cases in which a translocation is present, the anomaly is thought to arise from failure of a pair of No. 21 chromosomes to separate during meiosis in a gamete, or in an early mitotic division in a zygote. It was thought that a study of mongolism in twins might help to determine the stage at which this failure occurs.

There is no evidence that the prevalence of mongolism in twins is different from that in single children. Allen and Baroff (1955) found that the proportion of twins among patients with mongolism in institutions was similar to that in the general population. Making certain assumptions in cases of unknown zygosity, these authors found that in twins in which one or both had mongolism there was a slight but statistically insignificant excess of dizygotic pairs of unlike sex. Smith (1955) analysed 129 cases including 107 cases previously reported by Øster (1953) and found that the ratio of concordant twin pairs of like sex to all discordant pairs was significantly lower than the ratio of monozygotic to dizygotic twins in the population. Keay (1958) re-examined reported cases, including those of Allen and Baroff, and came to a similar conclusion. In a later report Smith (1960), with acknowledgements to Allen, indicated that he should have calculated the probability of mongolism occurring in zygotes rather than in children: with this correction the ratio of concordant pairs of like sex to all discordant pairs agreed closely with the expected ratio.

Published reports of twins with mongolism may have been biased in favour of concordant pairs, and it seems doubtful whether the true ratio of concordant to discordant pairs can be calculated from cases assembled in this way. A more accurate estimate would be expected from the cases obtained by Allen and Baroff (1955) from institutions for the mentally defective, but their series was small

and possibly biased by social factors and by the high mortality of mongolism in infancy. An attempt has therefore been made to collect a series of cases free from these sources of bias.

## Method

Letters were written in October 1961 to consultant obstetricians at maternity units in Britain with more than 30 beds, inviting them to report any twins born during the previous 10 years where mongolism was diagnosed or suspected in one or both infants before they left hospital. Reports on 71 twin pairs in which a diagnosis of mongolism was confirmed were received.

In 3 of the 71 pairs the co-twin of a child with mongolism was stillborn; of these, 2 were macerated and 1 was a foetus papyraceous; these 3 and a further pair in which the sex of the co-twin was unknown had to be excluded, leaving 67 pairs for study.

## Results

Some children had been kept under observation in paediatric departments, but others had not been seen since early infancy. Of the 74 children, 20 (27%) with mongolism from the 67 pairs were known to have died (Table I), mostly in the first few months of life. Mortality was a little higher in concordant than in discordant pairs, in children of younger mothers than in those of older mothers, and in males than in females; but none of these differences was significant at a 5% level.

Of the 67 pairs, 32 were of unlike sex and certainly dizygotic; 2 of these were concordant for mongolism. Of the remaining 35 pairs of like sex, 5 were concordant (Table II). Using the rates given by Carter and Evans (1961) for the prevalence of mongolism in children of mothers of different ages and assuming that, in dizygotic pairs, the probability of mongolism in the co-twin of an index case is not greater than normal, it was calculated that 0.14 concordant pairs would have been expected among the 32 pairs of unlike sex. The difference between the 2 observed and 0.14 expected is unlikely to have been due to chance ( $p < 0.01$ ).

One of the 5 concordant pairs of like sex was

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TABLE III

COMPARISON OF CONCORDANT TWIN PAIRS OF LIKE SEX OBSERVED AND NUMBER OF MONOZYGOTIC PAIRS EXPECTED ACCORDING TO MATERNAL AGE

Maternal Age (yr.)	Estimated Incidence per 1,000 Maternities*		Estimated Proportion (%) Monozygotes	Total Twin Pairs	Concordant Pairs of Like Sex	Expected Number of Monozygotic Pairs
	Monozygotic Pairs	Dizygotic Pairs				
20-24	3.32	5.32	23.78	3	—	0.713
25-29	3.39	8.26	17.03	16	2	2.725
30-34	3.62	11.02	14.15	10	—	1.415
35-39	3.68	13.22	12.22	19	1	2.322
40-44	3.63	9.44	16.13	18	2	2.903
45+	3.84	3.13	38.02	1	—	0.380
				67	5	10.458

\*From Waterhouse (1950) who calculated the rates from the Registrar-General's Statistical Reviews of England and Wales (1938-1948).

women have a tendency, over and above that due to maternal age, to produce affected children.

There were 5 pairs of twins of like sex concordant for mongolism; allowing for the known relation between maternal age and twinning, 10.5 monozygotic pairs would have been expected. Assuming that monozygotic twins are almost always concordant for mongolism, there were thus about half as many such pairs as expected ( $p=0.065$ ). Since in the 60 discordant pairs there was an equal number of pairs of like and unlike sex (30 of each), there was nothing to suggest the presence of monozygotic discordant pairs. The significance of these findings is discussed briefly.

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TABLE IV

SEX AND CONCORDANCE IN PREVIOUSLY REPORTED SERIES COMPARED WITH PRESENT SERIES

Source	Concordant				Discordant				Total	
	Like Sex		Unlike Sex		Like Sex		Unlike Sex		No.	%
	No.	%	No.	%	No.	%	No.	%		
Øster (1953)	19	17.8	—	—	50	46.7	38	35.5	107	100
Allen and Baroff (1955)	4	12.9	—	—	11	35.5	16	51.6	31	100
Keay (1958)	3	12.5	1	4.2	10	41.7	10	41.7	24	100
Total	26	16.1	1	0.6	71	43.8	64	39.5	162	100
Present series	5	7.5	2	3.0	30	44.8	30	44.8	67	100