MONGOLISM IN BOTH OF MONOZYGOTIC TWINS

BY

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Mongolism in more than one member of a family is a rare event; mongolism in both of twins is even rarer and merits interest. Warner (1949) collected from the literature two families, each having four mongoloid siblings, and four families, each having three mongoloid siblings, and 42 families each having two mongols per family. He mentioned two cases of special interest, (Lahdensuu, 1937; Sirkin, 1937) in which each mother, after having a series of normal children, had two successive children with mongolism by different fathers. Excluded from the data were families in which mongols constituted one or both of twins. In addition he collected from the literature data on 101 sets of twins in which one or both members were affected. He added a case of mongolism in one of twins and in another sibling. An analysis of these 102 authenticated cases of mongolism in twins showed 30 cases of unlike-sex twins in which one was affected, 15 cases of unknown sex in which one was affected, 37 cases of like sex in which one was affected, and 20 cases of like-sex twins in which both were affected. Of this latter group Warner considered that 10 sets of twins were monozygotic.

It was, however, often uncertain whether the twins were mono- or dizygotic and it is interesting that up to the present mongolism in both twins of different sex has not been described.

Subsequent to Warner's comprehensive review further cases of mongolism in one of twins have been recorded by Crozier and Campbell (1950), Cook (1950) two cases, Dawson (1950), Brown (1950), Graham (1950), Posteraro (1951), Robertson (1952), Engler (1952) three cases, Morris and MacGillivray (1953) and Lang-Brown, Lawler and Penrose (1953) three cases.

Bencini (1952) and Lang-Brown et al. (1953) have reported instances of mongolism in both members of a monozygotic twin pair.

The purpose of this communication is to put on record an additional example of a pair of apparently monozygotic twins in which both members were affected by mongolism.

Case Report

There was no consanguinity in the family pedigree and no knowledge of the presence of mongolism in the family on either side. The father, aged 45 years, was alive and in good physical and mental health. The mother, aged 29 years, was a twin. She had had scarlet fever, measles and mumps in childhood but otherwise had been free from illness. The mongol twins reported here were the result of a second pregnancy during which her health was good. A first pregnancy, three years previously, had resulted in the birth at full term of a normal 9 lb. male infant, still alive and healthy. There was no history of stillbirths or miscarriages.

She was admitted to the Jubilee Maternity Hospital as a case of twin pregnancy, the membranes having ruptured 24 hours before admission. The amniotic fluid was stained bright red but the patient, a qualified midwife, insisted that the loss was bloodstained liquor and not a haemorrhage. She was well nourished and clinical examination revealed no signs other than those expected at a 36 weeks' pregnancy. After a labour lasting three and a half hours she gave birth to twin boys weighing 4 lb. 12 oz. and 3 lb. 4 oz. respectively. There were two separate placentas.

Examination showed that each infant had the characteristic appearance of mongolism; oblique palpebral fissures, marked over-development of the epicanthic folds, and a tongue which was frequently protruded. Each child had blue irides with numerous white spots. The hands were short and the fifth digits short and incurved. The palms and soles showed the markings considered to indicate mongolism. Both twins showed a facies typical of mongolism, and all who saw them had no doubt that the diagnosis of mongolism was correct. Though each twin had the characteristic stigmata of mongolism they were not identical in appearance as may be seen from the photograph taken on the fourth day of life (Fig. 1).

At birth, the first twin (a) weighed 4 lb. 12 oz. and measured 17½ in. in length. The colour was fairly good. On the third day of life the infant became jaundiced, was drowsy and had to be fed by tube. On the tenth day drowsiness and jaundice were marked, but on the fifteenth day the infant became a little brighter and by the eighteenth day was feeding fairly well from a baby-type feeder. On the twenty-second day the jaundice began to clear and this had completely disappeared on the thirtieth day by which time the infant was feeding well from a bottle. The baby continued to gain weight steadily.
and was discharged home aged 7 weeks. No cardiac murmur or other evidence of a cardiac lesion was detected at any time during this period. The child developed pneunonia and died when aged 8 months. A necropsy was not carried out.

At birth, the second twin (b) was 3 lb. 14 oz. and measured 17 in. in length. There was blue asphyxia but on admission to the nursery his general condition was only fair. On the second day of life melaena was present. At this time a systolic murmur was audible over the praecordium with maximum intensity at the third left intercostal space. The second pulmonary sound was accentuated and split. A systolic thrill was palpable at the site of maximum intensity of the murmur. On the third day the infant became jaundiced and his general condition was weak. Jaundice deepened, the general condition deteriorated, and he died on the seventeenth day.

A necropsy showed congenital heart disease, with a widely patent foramen ovale and patent inter-ventricular septum; pulmonary congestion, oedema and focal atelectasis; and persistent extra-medullary haemopoiesis of the liver and spleen.

Evidence of Monozygosity.—It is known that 20-30% of monozygotic twins are born in dichorial placentas so that the knowledge that there were two distinct placentas at birth is valueless. To be of any value in determining zygosity the foetal membranes, even when fused, must be properly examined grossly and microscopically and with adequate tissue sections (Morison, 1949). In the presence of two separate placentas it is only possible to make a comparison of blood groups, hair colour, skin colour and texture, irides colour, prints of the palms and soles, and the general features.

Detailed blood group studies (Table 1) showed complete concordance between the twin blood groups but some dissimilarities between the blood groups of the father and the mother. This was taken as conclusive evidence that the twins were monozygous.

The colour of the hair, eyebrows and irides, and the skin colour and texture of both twins were similar. The first twin was ¹⁄₈ in. longer, 1 lb. 8 oz. heavier, and more round-faced than the second twin. It is known, however, that like twins may differ in size at birth, and Schatz (quoted by Newman, Freeman, and Holzinger, 1937, and referred to by Morison, 1949) found that at about the middle period of pregnancy the size difference in monozygotic twins was greater than at term. The difference in general features of the twins, which were premature, is therefore not significant.

Electrocardiograms showed no significant dissimilarities. In the second twin, with clinical signs of a congenital heart lesion, SI and AVL were marked, and R VI suggested right ventricular preponderance. T was flat in limb leads. The R segment of VI was late but the total duration of the QRS group was only 0·8 second, so there was no bundle branch block. In the first twin, without any abnormal clinical signs in the cardiovascular system, differences in electrocardiogram were minor, namely, there was better voltage in T VI but the voltage of T in limb leads was low, and there was similar right ventricular predominance.

The presence of a congenital heart lesion in only one of the twins is not evidence against the twins being monozygous, as instances of congenital heart disease in one of monozygotic twins have been reported. Weitz (1936) reported patent ductus arteriosus in one of monozygotic twins, and Forsyth and Uchida (1951) noted an auricular septal defect in one of uniovular twin girls. Morison (1949) presented convincing evidence that congenital malformations may occur in one of monozygotic twins.

TABLE 1

<table>
<thead>
<tr>
<th>Sera Used</th>
<th>ABO Group</th>
<th>C⁺</th>
<th>C⁻</th>
<th>D⁺</th>
<th>D⁻</th>
<th>E⁺</th>
<th>E⁻</th>
<th>c⁺</th>
<th>c⁻</th>
<th>e⁺</th>
<th>e⁻</th>
<th>Most Probable Rh Genotype</th>
<th>M</th>
<th>N</th>
<th>S</th>
<th>Le⁺</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Twin</td>
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<td>cde/cde</td>
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<td>2nd Twin</td>
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<td>Father</td>
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<td>CDe/cde</td>
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<td>Mother</td>
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The palm and sole prints of the twins (Fig. 2) were made on the eighth day of life. The characteristic trends elucidated by Cummins (1939) as being distinctive of mongols were present in both twins. In addition, the homologous hands and feet of the twins were more nearly alike in pattern than the two hands or two feet of either twin.

'It is generally accepted as a criterion of monozygotic twinning that the difference between the right and the left hand of either twin should be greater than the difference between the two corresponding hands of the pair of twins' (Ford and Frumkin, 1942).

Detailed digital, palmar and plantar formulae could not be obtained, as in the early neonatal period the papillary ridges are not sufficiently raised to hold a thin film of ink and there is no known method of obtaining a satisfactory impression of the ridge system in this age period.

The evidence, based on blood typing, that the twins were monozygous was thus collaborated by the studies of the dermatoglyphic patterns and the colour of the hair, eyebrows and irides of the twins.

**Discussion**

Intrapair variations in dizygotic twins may be due to both heredity and environment, but environment only can be responsible for intrapair variations in monozygotic twins.

The occurrence of a congenital heart lesion in one twin should be similar to that of its normal partner, the malformations arise from an arrest of normal development when the placenta of one twin is at some environmental disadvantage in obtaining nutrition from the utero-placental site for a short period early in intra-uterine life'. That there was unequal sharing of nutrient may be deduced from the twin with the congenital heart lesion being 1 lb. 8 oz. lighter than the twin with a clinically normal heart. Morison was careful to point out that while environment may be a cause of congenital malformation, there are other causes.

The occurrence of mongolism in both of monozygotic twins makes pertinent a study of the causation of mongolism.

From a study of the ages of the mothers of 2,822
mongols, Bleyer (1938) compiled evidence that maternal age is a significant aetiological factor, the peak age of the mothers in his series being 41 years. However, normal children have been born in families both before and after the birth of a mongol child, and Tredgold (1952) gives an instance of a mongol child being born to a girl aged 16 years. The age of the mother, therefore, is not the sole determining factor.

A pituitary or thyroid imbalance in the mother was suggested by Benda (1949) to be of importance in the production of mongoloid infants. In a series of 50 patients he found a degree of thyroid disorder in over one-third of the mothers. He did not, however, define his criteria of thyroid disorder. He mentioned three patients in whom there was a high basal metabolic rate and an overactive thyroid, and in another case he noted ‘thyroid deficiency suspected’. It seems extremely unlikely that mongolism could be produced by either an excess or deficiency of thyroid secretion. Furthermore, any theory of endocrine imbalance would not explain why mongolism has occurred in only one of 97 sets of twins.

The nidation theory postulates that the lesion occurs after fertilization during implantation of the ovum (Bennholdt-Thomsen quoted by Jervis, 1943). The division of the embryo into twin cell groups, however, has already occurred when implantation takes place. Therefore, if this theory were true, and the aetiological factors entirely environmental, the incidence of discordant monozygotic mongol twins should equal the incidence of discordant dizygotic mongol twins. Many instances of discordant dizygotic mongol twins have been reported but no instance of discordant monozygotic mongol twins has yet been reported.

Complete concordance of monozygotic twins and discordance of a high number of dizygotic twins are inconsistent with the hypothesis that mongolism is due to exogenous agents acting in early embryonic life.

The mutation theory (Bleyer, 1934) is consistent with the presence of concordance in monozygotic twins and discordance in dizygotic twins. Warner considered that of the 20 sets of concordant twins reviewed by him, 10 were dizygotic. It would have to be assumed that mutation, which is a rare occurrence, has taken place in two different ova at the same time, in the same place and in 10 instances, a highly improbable assumption (after Jervis, 1942). It should be pointed out that the 10 pairs of dizygotic concordant twins were of the same sex type when it would be expected that about half should be of different sex. In accounts of some of those twins an inadequate analysis of the type of twinning was made so that the number of monozygotic twins may be higher than that accepted by Warner.

The genetic hypothesis (Macklin, 1929) assumes that mongolism is due to an alteration of the chromosomes recessively or dominantly inherited. This is consistent with the finding of concordance in monozygotic twins and non-concordance in dizygotic twins and also with the finding of a certain number of discordant dizygotic twins. The only real evidence, however, in favour of an explanation involving transmission of a gene is that although mongolism is uncommon, it is more common in siblings than in the general population. If this is to be explained on a genetic basis then the gene must very often be non-penetrant, that is, present but not exerting its effect. Otherwise one in four or one in one of siblings would be affected or unaffected. Therefore on such a hypothesis it would not be very surprising if there were many pairs of monozygotic twins where only one was affected.

Penrose (1946, 1951) discussed the possibility that mongolism could be partly determined by some unknown antigenic factors. The same author, working with Lang-Brown et al. (1953), subsequently carried out detailed blood typing of 148 cases of mongolism and their parents and siblings. They concluded that mongolism could not be due to antigenic incompatibility between mother and foetus within the known blood group antigen-antibody systems.

Halbertsma (1923) was the first to suggest that mongolism is germinal in origin and not acquired by the foetus. Jenkins (1933) postulated a plasmatic defect of the germ cell. He concluded that ‘in the population of ova there is continually a certain mortality rate. In a period between that of complete viability and failure of reproductive function ova pass through a mongolian-genetic stage’. Fertility diminishes as the age of the mother increases. Jenkins related this diminished fertility to a diminished reproductive viability of the ova. This theory would appear to be the one most consistent with the data on mongolism in twins and with the increasing incidence of mongolism in the older age group of mothers.

**Summary**

A case history of mongolism in both of twins is recorded. Though the placentas were separate the evidence from blood groups, prints of the palms and soles, hair colour, skin colour and texture, and colour of the irides strongly suggested that the twins were monozygotic.
MONGOLISM IN BOTH OF MONOZYGOTIC TWINS

The data on mongolism in twins and the increasing incidence of mongolism in the older age group of mothers support the hypothesis that mongolism is germinal in origin.

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