father and G trisomy in the two mongol children, but
revealed 5 cells with 47 chromosomes among 70 cells
counted from the mother. In 4 of these cells the extra
chromosome was from the G group, and in the remaining
cell it was a C group chromosome. On these results
maternal mosaicism with karyotype 46,XX/47,
XX,G+ was diagnosed.
In 1971 the couple elected to have a further child
despite the risks involved. A male mongol was born
in December 1971. His karyotype has been confirmed
as 47,XY,G+.

Discussion
The difficulty of excluding chromosomal mosaici-
sm has long been recognized, and this family re-emphasizes the need to study large numbers of
cells from several tissues of both parents when two
or more regular mongols are born to a couple.
In this family, studies concentrated on the mother
because she showed some clinical features of
mongolism, but the initial investigations failed to
reveal the mosaicism despite counting 59 cells
from two tissues. Fortunately, appropriate genetic
advice was still given.
The occurrence of another regular mongol in the
family is also of interest, but his mother was 40
years old at his birth, so this may represent a
chance occurrence.

Summary
A case of maternal mosaicism leading to the produc-
tion of three mongol children is reported.
The difficulty of detecting the trisomic cell line
and the need to examine large numbers of cells is
emphasized.

We thank Drs. Ann Morgan, David Pitt, and Saul
Wiener for their assistance with this study; Dr. O.
Margaret Garson for the bone marrow studies and
confirming the trisomic state of the third child; and
the Mental Health Authority for permission to publish
this paper.

REFERENCE
propositi. Journal of Mental Deficiency Research, 14, 342.

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Dizygotic Twins with Down’s Syndrome
It is rare for both members of a twin pair to be
concordant for Down’s syndrome. The reported
incidence of such twins is lower than expected and
it is postulated that intrauterine death of one or
both members of the pair may often occur (Keay,
1958; Richards, 1971). To our knowledge, when
twins have been monozygotic both have always been
affected except in one case documented by de
Wolff, Schärer, and Lejeune (1962). In contrast,
the great majority of dizygotic twins have been
discordant for Down’s syndrome. A few exceptions
have been recorded in twins of the same sex con-
sidered to be dizygotic (Russell, 1933; MacKay,
1936; Jervis, 1943). Röhmer et al. (1970) reported
dizygotic twins, the one 47, XX, 21+ and clinically
mongoloid, the other 46, XX/47XX, 21+ and clini-
cally nonmongoloid. We know of only one case of
twins of opposite sex, both of whom were considered
on clinical grounds alone to have Down’s syndrome
(Nicholson and Keay, 1957). The purpose of this
paper is to put on record dizygotic twins of opposite
sex with unequivocal Down’s syndrome substan-
tiated by chromosome analyses.

Case Report
The parents of the twins were not related before
marriage. The mother was 39 years and the father 46
years of age when the twins were born.
The mother was one of a family of six, four brothers
living and one having died in an accident. She married
at the age of 19 years. The father has three brothers
and one sister, all of whom are alive and well. Both
parents are of average intelligence. No history of
Down’s syndrome or mental subnormality was discovered
on inquiry into the family history.
The mother has had 4 previous pregnancies, 2 of which
resulted in normal male infants, the other 2 in first
trimester miscarriages. At the time of the birth of
the twins, the brothers were aged 20 and 10 years,
respectively. They are of normal intellect and have good school
records.
The present pregnancy was uneventful but the pre-
sence of twins was not suspected until delivery which
took place at home. The female twin weighed 2.13
kg (4 lb 11 oz) at birth and at the age of 11 months
weighed 7.06 kg (15 lb 9 oz). A systolic murmur could
be heard over the precordium compatible with a
ventricular septal defect. The male twin weighed
2.18 kg (4 lb 13 oz) at birth and at 11 months weighed
10.8 kg (23 lb 13 oz). His cardiovascular system was
clinically normal.

No immediate comment about features of Down’s
syndrome was made during the neonatal period, but a
growing doubt as to the normality of the female twin
prompted referral, together with her brother, to a
paediatrician and then to our genetic counselling clinic for chromosome investigation. At this time, aged 9 weeks, several stigmata of Down's syndrome suggested that both twins were affected. The Fig. taken when the twins were 8 months old, supports this view, though the boy has fewer stigmata than his sister.

**Dermatoglyphs.** Inspection of the twins' palms did not reveal any 'simian' creases and two interphalangeal creases were seen on the fifth digit of each hand. All axis triradii were displaced distally and the sum of right and left ad angles was 160 degrees in the female twin and 172 degrees in the male. Dermal ridge patterns showed a high incidence of ulnar loops, 90% in the female and 80% in the male. Small distal loop patterns were present in the hallucal areas of the female twin, and tibial arch patterns in the male twin.

**Cytogenetics.** Blood specimens from the twins and their parents were cultured for chromosome study. Analysis confirmed that each twin had trisomy-G Down's syndrome (Table). Cells with less than 47 chromosomes did not show consistent losses and therefore mosaicism was not suspected.

<table>
<thead>
<tr>
<th>Number of Cells with Counts of</th>
<th>Total No. of Cells Counted</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>45</td>
<td>46</td>
</tr>
<tr>
<td>Female twin</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Male twin</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Mother</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Father</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

The chance of producing dizygous twins, both of whom have Down's syndrome, is very small. As there is no indication of mosaicism in either parent, though this cannot be entirely excluded, the most likely reason for the birth of the twins in this case would be due to a chance event which is maternal-age dependant. The random risk for a mother aged 39 giving birth to a child with Down's syndrome lies between 1/260 and 1/100 (Carter and Evans, 1961), and the empirical recurrence risk approximately double this, though this may be increased for concurrent births due to environmental factors. The chance of dizygous twins being born in this country is approximately 1/100 (Carter, 1969), but this increases with maternal age and is expected to be approximately 1 in 60 in this case. Hence in this instance for both twins to be affected by Down's syndrome the risk may be expected to be less than 1/300,000 (1/100 x 1/50 x 1/60) live births.

An alternative possibility for the birth of dizygous twins, both with the same chromosomal abnormality, may be the result of nondisjunction at first meiotic division in the female, followed by dispermous fertilization of a single ovum. Fusion of a sperm with the egg nucleus and a different sex chromosome carrying sperm with the second polar body, followed by separation of the two
fertilized products, could give rise to effective dizygous twins.

**Summary**

The presence of unequivocal Down’s syndrome in dizygotic twins of opposite sex is recorded. To our knowledge, this has been documented only once before, and at that time no chromosomal analyses were available for confirmation.

We wish to thank Dr. F. P. Hudson, who initially referred this family to our genetic counselling clinic, for permission to publish details of this case.

**References**


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**Septo-optic Dysplasia with Growth Hormone Deficiency (De Morsier Syndrome)**

The association of hypoplasia of the optic discs with absence of the septum pellucidum was described by De Morsier (1956). Few examples have been described outside the ophthalmological literature until recently, but it is now becoming apparent that the condition is not as rare as was once considered. It is now recognized that growth retardation is a feature of the condition, and it is the purpose of the present report to describe an example of septo-optic dysplasia with the classical features of the syndrome and an associated growth hormone deficiency in a female child.

**Case Report**

The patient was born after a normal pregnancy at term to an 18-year-old primipara. The birthweight was 2.84 kg. She was reported to have been jaundiced for a month after birth, but she was not seen by a paediatrician at that time. No investigations were carried out. Initially her progress was considered normal. Blindness was discovered at the age of 7 months when she was referred to hospital for the first time because she was unable to see.

Examination at this time showed a left-sided hemiplegia. There appeared to be no vision. Hearing was normal. She was unable to sit up spontaneously and her sitting balance was poor, but in spite of this she handled objects well and could play with a rattle.

Ophthalmoscopic examination under anaesthesia showed abnormal discs on both sides. On the right side the vessels all appeared on the temporal side of the disc. The disc had a deep pale cup and there was fine pigment stippling surrounding it. On the left side there was a small coloboma present, and fine pigmentary disturbance surrounding the optic nerve head.

The patient was treated with regular physiotherapy, and the mother instructed to afford the child as much stimulation as possible to compensate for the lack of vision. She quickly caught up developmentally and at the age of 10 months she was sitting unsupported. She spoke at the age of 2, and walked unsupported at the age of 3. Her hemiparesis improved steadily with physiotherapy and by the time she was 2 this had disappeared completely.

Initially she appeared to grow normally and at the age of 3 years 9 months her height was 91.5 cm just at the 3rd centile. From then on she stopped growing. This was first noted when she was admitted to hospital at the age of 5½ with a fractured skull. She was then extensively investigated at the Torbay Hospital and at the Royal Devon and Exeter Hospital. Obvious causes for growth retardation due to intercurrent disease, such as chronic infection and malabsorption, were excluded, nor did there appear to be any obvious endocrine cause; there was a normal response to tetraacosactrin stimulation.

**TABLE**

**Growth Hormone Levels After Stimulation with Bovril and Insulin-induced Hypoglycaemia**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Bovril (Royal Devon)</th>
<th>Bovril (G.O.S.)</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (fasting)</td>
<td>1·3</td>
<td>3·3</td>
<td>2·8 (58)</td>
</tr>
<tr>
<td>15</td>
<td>6·9</td>
<td>3·9</td>
<td>1·6 (27)</td>
</tr>
<tr>
<td>30</td>
<td>6·1</td>
<td>5·4</td>
<td>1·3 (38)</td>
</tr>
<tr>
<td>45</td>
<td>8·5</td>
<td>6·2</td>
<td>1·8 (31)</td>
</tr>
<tr>
<td>60</td>
<td>6·1</td>
<td>5·1</td>
<td>1·9 (34)</td>
</tr>
<tr>
<td>90</td>
<td>8·5</td>
<td>6·2</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td>3·3</td>
<td>5·4</td>
<td></td>
</tr>
<tr>
<td>150</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: Bracketed figures refer to blood glucose levels (mg/100 ml).*

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Dizygotic twins with Down's syndrome.

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