Down's syndrome associated with two Robertsonian translocations, 
45,XX,-15,-21,+t(15q21q) and 
46,XX,-21,+t(21q21q)

Summary. A female infant with 
Down's syndrome was found to be a 
chromosomal mosaic with two cell lines 
in both blood and skin cells. One line 
carried a balanced 15/21 translocation, 
and the other line was effectively trisomic 
for chromosome 21 with a 21/21 translo-
cation.

This report describes a child with Down's syn-
drome associated with an unusual type of mosaicism 
involving two cell lines each with a different type of 
Robertsonian translocation.

Case report

The patient, a female, was born on 23 December 1968 
after a 33-week gestation. Birth weight was 2600 g. 
Spontaneous breathing occurred 10 min after delivery. 
Because of cyanosis noted at birth she was placed in an 
incubator for 5 days where she received oxygen for the 
first 48 hours. Mild neonatal jaundice appeared on the 
third day of life, and it subsided by the eighth day. 
Subsequently, there were occasional cyanotic spells for which 
she was first seen at 20 days of age. Physical examina-
tion at that time showed a round face, microcephaly, 
mongoloid slanting of the palpebral fissures, hypoth-
telorism, epicanthal folds, and a protruding tongue. 
There was cyanosis with crying. The heart was en-
larged with a loud ejection type pansystolic murmur 
audible along the left sternal border and apex with 
radiation to the back. An apical mid-systolic rumble was present. 
The findings were interpreted as evidence of 
congenital heart disease, most likely an atrioventricular canal defect. 
The hands showed incurring of the fifth digit bilaterally with normal transverse palmar creases. 
The axial triradii were normal. Dermatoglyphic patterns showed five ulnar loops on the fingers of the left 
hand, a double loop on the right thumb, wholets on the 
right second and third fingers and ulnar loops on the 
right fourth and fifth fingers.

On the basis of the physical findings the diagnosis of 
Down's syndrome was made (Fig. 1).

Subsequently, there were two episodes of severe pneu-
monia. The heart continued to enlarge despite digitalis 
therapy. Physical and psychomotor development were 
retarded. At 33 months of age she weighed 10·9 kg; 
length was 87 cm; and the head circumference was 47·2 
cm (all below the 3rd centile). Her mental develop-
ment was estimated to be at the 11–12 month level, she 
could not walk without support, and she used only one or two words. Radiology of the dorsal spine showed 
scoliosis.

At 4½ years length was 99 cm and weight 13·1 kg (3rd 
centile).

At the time of the child's birth the father's age was 33, 
and the mother was 30. There had been three previous 
spontaneous abortions, and there were two subsequent 
abortions all occurring between the second and third 
months of gestation. A normal boy was born when the 
proposita was 4 years old. The parents are not related, 
and the family history is negative for any known birth 
defects, mental retardation or known genetic disorders.

<table>
<thead>
<tr>
<th>Age</th>
<th>Tissue</th>
<th>45</th>
<th>90(4n)</th>
<th>46</th>
<th>92(4n)</th>
<th>Total Cells Counted</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 wk</td>
<td>Blood</td>
<td>12</td>
<td>-</td>
<td>42</td>
<td>-</td>
<td>54</td>
</tr>
<tr>
<td>2 mth</td>
<td>Blood</td>
<td>14*</td>
<td>-</td>
<td>35</td>
<td>-</td>
<td>40</td>
</tr>
<tr>
<td>21 yr</td>
<td>Blood</td>
<td>14</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>19</td>
</tr>
<tr>
<td>21 yr</td>
<td>Skin</td>
<td>41</td>
<td>-</td>
<td>59</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td>4 yr</td>
<td>Blood</td>
<td>38</td>
<td>-</td>
<td>25</td>
<td>-</td>
<td>65</td>
</tr>
<tr>
<td>4 yr</td>
<td>Skin</td>
<td>7</td>
<td>1</td>
<td>41</td>
<td>1</td>
<td>50</td>
</tr>
</tbody>
</table>

* One cell with a C-group chromosome missing.

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Cytogenetic studies
Routine studies of cultured leucocytes and skin cells of the proposita are summarized in Table I. Mosaicism was present in all specimens. One cell line contained 45 chromosomes including three small acrocentrics, five large acrocentrics, and an extra C-group chromosome which was interpreted as a balanced D/G translocation. The other cell line showed 46 chromosomes including three small acrocentrics and an extra F-group chromosome interpreted as a G/G translocation. Trypsin banding (Seabright, 1972) confirmed the presence of a 15/21

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Fig. 2. Trypsin-banded karyotype showing a balanced 15/21 translocation.
translocation in the 45-chromosome line (Fig. 2) and a 21/21 translocation in the line with 46 chromosomes (Fig. 3). The remainder of the karyotype in each cell line appeared normal.

Chromosome studies of the leucocytes of both parents and the normal male sib showed no abnormalities. The chromosomes of the parents were not studied with any of the banding techniques.

**Fig. 3.** Trypsin-banded karyotype showing an unbalanced 21/21 translocation.
Discussion

Zellweger and Abbo (1963) described different translocations in the cells of the same individual with Down's syndrome. Their case was a girl with mosaicism including four different cell lines. One line contained a balanced D/D translocation, an unbalanced D/G translocation and a 45,X sex-chromosome constitution. Another cell line contained a balanced D/D translocation. A third line contained an unbalanced D/G translocation with a 45,X sex-chromosome constitution. A fourth line was normal. Chromosomal mosaicism was observed in several other members of the family. The findings were attributed to an autosomal dominant gene.

In the case under discussion the presence of a balanced 15/21 translocation in one cell line and an unbalanced 21/21 translocation in another line effectively results in normal/trisomy-21 mosaicism. The possibility of an isochromosome for the long arm of a No. 21 cannot be excluded. The relationship of these two different translocations to another, if any, is unknown. The mother's history of five spontaneous abortions suggests some predisposing factor for the chromosomal abnormalities. If a translocation were present in a parental gonad and inherited one would expect all of the cells in the child to have the same abnormality. A plausible explanation for the findings could be postzygotic chromosomal breakage within two different cells in an early cleavage division with the resulting translocations. The cause for the breakage is unknown.

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References


48,XXX, +18 double trisomy*

Summary. An infant who died at 127 days with gross congenital deformities is described. Cytogenetic analysis showed double trisomy of 18 and X which was confirmed by autoradiography and fluorescent banding techniques.

Double trisomies are not of common occurrence in man. The most prevalent double trisomy involving one of the sex chromosomes is a 48,XXY,+G male having Klinefelter’s and Down’s syndromes. Only four cases involving X and 18 have been reported (Uchida and Bowman, 1961; Haas and Lewis, 1966; Ricci and Borgatti, 1963; Engel et al, 1967).

This report concerns another case of 48,XXX, +18 double trisomy in a female infant.

Case history

A female infant was born on 14 January 1972 after full-term normal pregnancy to a 22-year-old mother, who had a normal 34-year-old child from her previous pregnancy. The father was 21 years old. The birth weight was 1560 g. There were several gross malformations. The head was long with a pronounced occiput, the ears were low set, and the right pinna was deformed with the absence of an external meatus. The index fingers of both hands were flexed and curved over the middle fingers and there were bilateral palmar creases. The chest was shield-shaped. There was a loud systolic murmur present over the precordium. The child had rocker bottom deformity of both feet. The genitalia were unusual with part of the labia giving the appearance of a clitoris. The baby died of cardiac arrest at 127 days of age. No necropsy was performed.

Materials and methods

Chromatin mass. Squamous cell smears were prepared from inside the cheeks. Barr bodies were counted in 500 cells.

Chromosome analysis. Leucocyte chromosomes from the peripheral blood samples (two) were prepared according to Moorhead et al (1960). Fifty cells were counted from each sample. Skin fibroblast chromosome slides were also prepared and a sample of 30 well-spread metaphases was taken and analysed.

Autoradiography. Autoradiographs were prepared from 72-hour cultures and from skin culture chromosomes according to the method described by Schmid (1963).

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