Autosomal Trisomy Syndromes: A Detailed Study of 27 Cases of Edwards' Syndrome and 27 Cases of Patau's Syndrome

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The three autosomal trisomy syndromes, which appear to be specific and well documented, are Down's syndrome (trisomy 21), Edwards' syndrome (trisomy 18), and Patau's syndrome (trisomy 13-15). Down's syndrome was described in 1866 (Down, 1866), and the chromosomal nature of the disorder was demonstrated by Lejeune, Turpin, and Gautier in 1959. The rarer Edwards' and Patau's syndromes were described only in 1960 by Edwards et al. (1960) and Patau et al. (1960). Down's syndrome is well known and will only be discussed where a comparison of the three syndromes is relevant.

Since 1960 many cases of Edwards' and Patau's syndromes have been reported: owing to the rarity of the two conditions, most described only one or two cases. Series of cases have been reported by Weiss, DiGeorge, and Baird (1962), Warkany et al. (1964), Taylor and Polani (1964), Giambattista and Jacobson (1965), Butler et al. (1965), Snodgrass et al. (1966), Conen, Erkman, and Metaxotou (1966), and Ricci et al. (1966), and study of these series of cases allows the spectrum of clinical signs of these conditions to be assessed.

Data have been collected in a standard fashion in order to assess the clinical overlap between the two syndromes, and to date 54 infants have been studied.

Material and Methods

The case material has been collected during the five-year period from 1962-1967 from the South East of England and part of East Anglia. In that part of the area administered by the South East Metropolitan Regional Hospital Board, a survey of all N.H.S. live births has been in progress since June 1965, so that from this date, data from the region can be referred to a specific population. Cases of suspected autosomal chromosome abnormality are notified to the Paediatric Research Unit and then studied in standard fashion. With the exception of 6, all 54 cases in this report have been seen by the author.

In all, 27 cases of Edwards' syndrome and 27 cases of Patau's syndrome were investigated and confirmed. Each of the 54 infants was assessed for 46 clinical and 24 post-mortem findings, irrespective of the initial clinical diagnosis. Any additional findings in individual subjects were also noted. When possible, blood was taken from the propositus and parents for full blood group analysis, and analysis of haemoglobins, haptoglobins, transferrins, and serum Gc groups. Each infant had a dermatoglyphic examination, and was photographed. Sex chromatin and chromosome studies were also carried out. Chromosome studies were done on peripheral blood leucocytes, and also, in some instances, on skin fibroblasts. In general, 20 cells from each tissue were counted, 5 of these being fully analysed. Blood smears were examined for the excess of granulocyte nuclear projections often found in Patau's syndrome (Powars, Rohde, and Graves, 1964). In a few instances a neurological examination of the infant was possible. Results of all these studies are presented in the Tables and in the individual case reports (see Appendix).

Results

Clinical findings are summarized in Table I, and presented in detail in the case reports. Of 46 features scored, 44 occur in both syndromes, a considerable degree of overlap. An attempt has been made to measure this overlap: the right-hand column of Table I gives the discriminating ratio, which is calculated as the percentage of Edwards' syndrome cases with features divided by the percentage of Patau's cases with the same features. Taking two arbitrary cut-off points at ratios <0.5 and >1.5, it is possible to separate 'Patau's' features, an area of major overlap, and 'Edwards' features. Features separated in this fashion are presented in Table II.
TABLE I

<table>
<thead>
<tr>
<th>Occurrence</th>
<th>Edwards</th>
<th>Patau</th>
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<th>Patau</th>
<th>% Edwards</th>
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<td>6/23</td>
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<td>26</td>
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<td>11/26</td>
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<td>38</td>
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<td>58</td>
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<td>6/24</td>
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<td>25</td>
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<td>1/23</td>
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<td>4/25</td>
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<td>23/26</td>
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<td>15/26</td>
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<td>18/26</td>
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<td>13/22</td>
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<td>79</td>
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<td>72</td>
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<td>19/25</td>
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<td>76</td>
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<td>12</td>
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<td>5/23</td>
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<td>68</td>
<td>13</td>
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<td>9/24</td>
<td>63</td>
<td>37</td>
<td>17</td>
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<td>17/25</td>
<td>16</td>
<td>68</td>
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<td>90</td>
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<tr>
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<td>16/25</td>
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<td>64</td>
<td>95</td>
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<td>14/19</td>
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<td>Arches on fingers-tips</td>
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<td>Short dorsiieflexed big toe</td>
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<td>Fibular S</td>
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<td>5/10</td>
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<td>4/21</td>
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<td>19</td>
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<td>12</td>
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<td>10/25</td>
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<td>19/26</td>
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<td>13/14</td>
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TABLE II

<table>
<thead>
<tr>
<th>Discriminating Features of Edwards' and Patau's Syndromes</th>
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<tr>
<td>Edwards' Features</td>
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<tr>
<td>Microcephaly</td>
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<td>Eye defects</td>
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<td>Microphthalmos</td>
</tr>
<tr>
<td>Low-set normal ears</td>
</tr>
<tr>
<td>Hare-lip</td>
</tr>
<tr>
<td>Capillary</td>
</tr>
<tr>
<td>Haemangioma</td>
</tr>
<tr>
<td>Talipes equino-varus</td>
</tr>
<tr>
<td>Fibular S-shaped phallic arch</td>
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</table>

* Note: 27 cases of Edwards' syndrome and 27 cases of Patau's syndrome were scored for the same 46 features. The discriminating ratio is calculated as % of Edwards' cases with feature / % of Patau cases with feature.

† Features marked thus are the only features that do not appear in both syndromes.

Pregnancy Order. No effect of pregnancy order on the frequencies of these syndromes has been detected. Up to and including the propositi, the mothers of children with Edwards' syndrome in this series have had 73 pregnancies, of which 7 (9.6%) ended in known abortions. The mothers of children with Patau's syndrome have had 68 pregnancies, of which 5 (7.4%) ended in known abortions. Assuming that 15% of all pregnancies end in spontaneous abortion (Carr, 1965), the proportion of abortions in this series may be lower than normal.

Maternal Age. In Edwards' syndrome and Patau's syndrome maternal age is raised, and birth order is inevitably correlated with maternal age, but there are not sufficient data to separate the effects of these two factors.

Survival. Very few infants with these two conditions survive the first six months of life. Survival is related to the severity of the congenital malformations and, to some extent, to the availability of paediatric care.

Season of Birth. This series indicates an
cess of winter conceptions. Although the data are small, the same trend is seen in six successive years (Table VI). 66-6% of all cases of Edwards' syndrome and 79% of all cases of Patau's syndrome were conceived between September and February. The mean maternal ages differ in the winter and summer conceived groups. In Edwards' syndrome the summer conceived group had a mean maternal age of 25-2±1-3, compared with 31-8±1-7 in the winter group. In Patau's syndrome the summer conceived group had a mean maternal age of 28-6±2-9, compared with 32-7±1-8 in the winter group.

**Sex Proportions.** The sex proportions in Edwards' syndrome are grossly abnormal. Of 143
cases, 113 (77.0%) were female. Within this group an unexpectedly high proportion of double aneuploids occurs: four 48,XXX,18+ females and three 48,XXY, 18+ males. The discrepancy between liveborn males and females is not accounted for by the reverse situation in abortions; of 6 reported 17–18 trisomic abortions, 4 were female and 2 were male (Aisters-Bauer and Kleinheng, 1963; Carr, 1963; Thiede and Salm, 1964; Szulman, 1965). J. L. Hamerton (personal communication, 1965) suggested that males and females might have different postnatal survival values. In 21 females and 4 males, mean survivals are 134.5 and 14.7 days, respectively, so there is a difference. However, the number of males is small and, as pointed out above, survival is determined by availability of paediatric care and actual policy concerning treatment, though this should not be expected to differ between the sexes.

The sex proportion in Patau's syndrome is much nearer to normal, and mean survival is similar in the sexes, but still longer in females, 38–0 days as opposed to 22–7 days in males.

**Chromosomal Findings.** Of 27 cases of Edwards' syndrome, 21 (78%) had primary trisomy 18, and 2 (7.4%) were double aneuploids with XXX and XXY sex chromosomes respectively (4.8% of females and 20% of males). One (3.7%) had 46 chromosomes with only 1 chromosome 18 and an extra, structurally abnormal medium-sized chromosome (46,XX,E−,?Ep+q+) (Fig. 1), 2 (7.4%) had mosaic, and 1 (3.7%) had normal chromosomes.

Of 27 cases of Patau's syndrome, 19 (70.4%) had primary trisomy 13–15(D), 3 (11.1%) had D/D interchange D trisomy, 1 (3.7%) was a mosaic, 1 (3.7%) had 46 chromosomes with a deleted short arm of a B chromosome (46,XY,Bp−) (Fig. 1), and 2 (7.4%) had normal chromosomes. One girl with absolutely typical features of Patau's syndrome (see Fig. 3b) had 46 chromosomes with a deletion of about half the long arm of a D chromosome (46,XX,Dq−) (Fig. 1). Cytogenetic findings in the propositi and most of their parents are summarized in Tables VII and VIII, and the complex structurally abnormal karyotypes in Fig. 1. (Cytogenetic results are described as recommended by the Chicago Conference (1966).)

**Dermatoglyphs.** Dermatoglyphic abnormalities are very common in both syndromes. Examination of the fingertips and palms is usually difficult, especially when the fingers are abnormally flexed. The fingers and palms are inspected using an auriscope, and the fingertip patterns and positions of the palmar triradii are noted. Prints of the soles are usually feasible.

Of 25 patients with Edwards' syndrome, 24 had

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**TABLE VI**

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<tr>
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<td>1966</td>
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<td>3</td>
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<td>1967</td>
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<td><strong>Totals</strong></td>
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<td>4</td>
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Fig. 1. Partial karyotype of 3 cases with structurally abnormal chromosomes. (a) D group showing (Dq−) in GH 051267/4308; (b) E group showing (18−,?18p+q+) in ES 231265/3020; (c) B group showing (Bp−) in LB 290367/3855.
### TABLE VII

CYTOGENETIC FINDINGS IN 27 CASES OF EDWARDS' SYNDROME WITH FAMILY STUDIES WHERE COMPLETED

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<tr>
<td></td>
<td>Propositus</td>
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<tr>
<td>HD</td>
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<td>46,XY</td>
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<tr>
<td>EF</td>
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### TABLE VIII

CYTOGENETIC FINDINGS IN 27 CASES OF PATAU'S SYNDROME WITH FAMILY STUDIES WHERE COMPLETED

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<td>46,XY</td>
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</tbody>
</table>
at least 3 simple arches on fingertips and often 10. Partial or total dysplasia of the dermal ridges is a frequent finding. Three or more simple arches were also seen in 7 out of 21 cases of Patau's syndrome.

A distally placed t triradius occurred in 12 out of 21 cases of Edwards' and 14 out of 20 cases of Patau's syndromes. In a few instances all or part of the palm was dysplastic, and in the remainder the triradii were normally situated.

A fibular S-shaped hallucal arch was present in 7 out of 18 cases of Patau's syndrome and in 1 out of 20 cases of Edwards' syndrome. Recently, Penrose has pointed out that a fibular S-shaped hallucal arch is not the most frequent finding in Patau's syndrome. The more typical configuration found in 13 of 28 cases is a tibial loop in the proximal thanar region associated with an f triradius (Penrose, 1966).

**TABLE IX**

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of Newborns</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Edwards/Patau</td>
<td>Edwards/Patau</td>
</tr>
<tr>
<td>Hecht et al. (1963b)</td>
<td>999</td>
<td>2</td>
</tr>
<tr>
<td>Smith (1964)</td>
<td>10,345</td>
<td>3</td>
</tr>
<tr>
<td>Taylor and Moores (1967)</td>
<td>9,688</td>
<td>1</td>
</tr>
<tr>
<td>A. I. Taylor and J. A.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fraser Roberts (unpublished)</td>
<td>94,000</td>
<td>11</td>
</tr>
<tr>
<td>Totals</td>
<td>115,032</td>
<td>17</td>
</tr>
<tr>
<td>Rates</td>
<td>1 per 6766</td>
<td>1 per 7602</td>
</tr>
</tbody>
</table>

**Birth Frequencies.** The highest estimate of the incidence of Edwards' syndrome is that of Hecht et al. (1963b) who reported 2 cases in 999 newborns. Marden, Smith, and McDonald (1964) found 1 case in 4412 newborns, and Smith (1964) extended the same survey for another 2 years, finding 3 cases in 10,345 newborns. Conen and Erkman (1966b) found 8 cases in 89,309 live births, and after complex adjustments for missed cases estimated the incidence as 1 per 4500. Combining the data of Hecht et al. (1963b), Smith (1964), Taylor and Moores (1967), and A. I. Taylor and J. Fraser Roberts (unpublished) allows an assessment of incidence based on data from newborn populations where total ascertainment was attempted. This estimate is a minimum one and is 1 per 6766 live births (see Table IX).

With the exception of Hecht et al. (1963b), the same authors have estimated the incidence of Patau's syndrome. Marden et al. (1964) reported 2 cases in 4412 newborns and the extension of the same survey to 10,345 newborns revealed no more cases (Smith, 1964). Conen and Erkman (1966b) found 5 in 224,460 live births, and after corrections estimated the incidence of Patau's syndrome as 1 per 14,500. Taylor and Moores (1967) found 2 cases among 9688 newborns, and the survey in progress in South East England has yielded 11 cases in 94,000 live births (A. I. Taylor and J. Fraser Roberts unpublished). The incidence of Patau's syndrome in newborns is 1 per 7602 live births (see Table IX).

**Discussion**

**Clinical Features.** Both syndromes are clinical entities though there is a considerable degree of overlap of features. Individuals with autosomal trisomies are known in other species, both plant and animal. Generally these trisomics have a distinctive phenotype, but in drosophila the triplo-IV individual cannot be distinguished by phenotype alone (Bridges, 1921). In Datura there are 12 chromosomes, and all theoretically possible 12 trisomics are known (Blakeslee, 1928). All are phenotypically distinct and all are fertile. Similar considerations apply to the complex trisomics in *Oenothera lamarckiana* (Catcheside, 1936).

Autosomal trisomies in man determine marked variations from normal embryogenesis. The degree of overlap in the two syndromes is considerable, and this is probably related to the times of disturbance of embryogenesis. The characteristic features are presumably determined by specific effects of the chromosomes involved. Most cases have a distinct facies which allows a rapid diagnosis, but a minority of cases have an intermediate facies (Fig. 2 and 3), and full clinical appraisal is needed to establish diagnosis. Each syndrome also has features in common with Down's syndrome (trisomy 21), but the facies of Down's syndrome is quite different. In Tables I and II a preliminary attempt is made to assess the degree of overlap in Edwards' and Patau's syndromes. In order to gain significant results, it is necessary to weight the individual features, and data are being assembled for a discriminant function analysis by computer.

Post-mortem findings are extremely variable. In some cases careful study reveals no abnormality, either microscopical or macroscopical, which was not detectable on clinical examination; in others, every system is demonstrably abnormal.

After a simple separation, the features that emerge as mainly 'Patau's features' are microcephaly, unspecified eye defects, microphthalmos, iris colobomata, low-set normal ears, hare-lip, and cleft palate. Also more frequently present in
Patau's syndrome are capillary haemangiomata, polydactyly, long hyperconvex fingernails, talipes equino-varus, and a fibular S-shaped hallucal arch. With the exception of iris colobomata all these findings occur also in Edwards' syndrome. 21 out of 46 findings occur with a similar frequency in both syndromes. Feeding difficulty is common though it may be due to different causes. In Edwards' syndrome the palate is deformed and is often partially paralysed, making sucking difficult or impossible. In Patau's syndrome severe clefts of the lip and palate often cause feeding problems. Developmental retardation is universal, and jaundice, hypotonia, and failure to thrive are common. Jitteriness, apnoeic attacks, and seizures are frequently found. Failure to respond to 'auditory attention' (a low tone sound stimulus of approximately 100 kc/sec. which should result in an
Angela I. Taylor

FIG. 3. Patau's syndrome (a) LA 080467/3921, microcephaly, severe cleft lip and palate (47,XX,D +); (b) PM 200867/4124, microcephaly, oblique palpebral fissures (47,XY,D +); (c) LG 231165/2967, hypertelorism, cleft lip, malformed ear (46,XX,Dp +); (d) MF 080167/3761, intermediate facies, contracture of fingers (47,XX,D +); (e) TP 210667/4092, polydactyly (47,XX,D +); (f) MR 020464/1492, 'old' face (46,XX,D +,DqDq +); (g) PS 120767/4072, low-set ears, micrognathia, polydactyly (47,XY,D +); (h) GH 051267/4308, typical face (46,XX,Dq -); (i) LB 290367/3855, hypertelorism, cleft lip (46,XY,Bp -).
Autosomal Trisomy Syndromes

interruption in the crying cycle if the baby is crying) is common. This is a test of hearing and, to some extent, of cortical function. Facial features include ocular hypertelorism, epicantal folds, strabismus, low-set malformed ears, and micrognathia. The neck is short with extra skin at the nape. Fingers show a flexion deformity with axial deviation and an overriding index finger. Inguinal and especially umbilical hernias are common. Males almost invariably have undescended testes, and often the penis is reduced in size. The external genitalia in females are somewhat ambiguous, with enlargement of the labia and clitoris, but not sufficiently to give rise to doubt about the sex of the infant. Congenital heart disease occurs quite often but a proportion of cases have normal hearts. Dermatoglyphic examination often reveals a distal triradius and a single palmar crease, and here there is overlap with findings in Down’s syndrome.

In the group of ‘Edwards’ syndrome features’ are hypertonia, antero-posterior elongation of the skull, webbed neck, partial syndactyly of the toes, and distally implanted, often rudimentary, and retroflexible thumbs. The toe-nails are often hypoplastic. The halluces are often short, broad, and dorsiflexed. Feet often have a calcaneovalgus deformity or a prominent calcaneus. Abnormal hip and shoulder abduction is common. The sternum is often short, and the chest may be narrow or shield shaped. There is often a high-pitched cry, probably due to an abnormally shaped palate and micrognathia. Simple arches on finger-tips are diagnostic. With the exception of neck webbing, all these features also occur in Patau’s syndrome.

There is an even greater degree of overlap when the post-mortem findings are considered. Congenital heart disease is common, with major atrial and ventricular septal defects, dextroposition of the heart, coarctation of the aorta, pulmonary stenosis, and other defects. However the heart may be normal in either syndrome. Renal anomalies are quite common, and include cystic kidneys, double ureters, hydronephrosis, hydroureretes, horseshoe kidneys, and unilateral absence of a kidney. A normal renal tract may also occur in both syndromes. Malrotation of the intestine occurs in both syndromes, and Meckel’s diverticulum occurs more frequently in Edwards’ syndrome, as does pyloric stenosis. A biseptate or bicornuate uterus occurs in Patau’s syndrome, and in two cases in the present series the latter was associated with an absent ovary and tube.

The brain may be superficially normal in Edwards’ syndrome or it may have abnormally few convolutions or dilated cerebral ventricles. In Patau’s syndrome the olfactory nerves are usually missing or, if present, are reduced in size. The optic nerves may be absent or very small. The corpus callosum is often abnormally small.

Maternal Age (see above). This is raised with similar mean values in all three autosomal trisomic syndromes. It is of interest to look at the shape of the age distribution curves (Fig. 4). In both Edwards’ and Down’s syndrome the curve is markedly bimodal. The peaks are at 20–24 and 35–39 years in Edwards’ syndrome, and 25–29 and 35–39 years in Down’s syndrome (Richards, 1967). So in both these conditions there is a large group of maternal age-independent births. Ageing of cells in the ovary, with consequent reduced meiotic efficiency, is a possible reason for the increased risk of chromosomally abnormal offspring with advancing age. Chromosome studies on populations suggest that even mitotic efficiency is reduced with age (Jacobs et al., 1963; Hamerton et al., 1965). In the maternal age-independent group of Down’s syndrome cases, there is a concentration of those due to complex cytogenetic variants such as translocations and mosaicism. No such concentration is as yet apparent in the maternal age-independent group of Edwards’ syndrome, but the data are much less. In Patau’s syndrome the maternal age distribution is unimodal, with a very large peak at 25–29 years. The curve has a slight kink at 40–44 years. However, the larger data of E. Magenis and F. Hecht (personal communication, 1967) of 172 cases have a much more bimodal distribution, with peaks at 25–29 and 35–39 years. It seems that a proportion of cases of Edwards’ syndrome and a majority of those of Patau’s syndrome are maternal age independent.

Seasonal Incidence. Clustering of cases in time has been reported in mongolism (Stoller and Collman, 1965) and has recently been described in Edwards’ syndrome (Heinrichs, Allen, and Nelson, 1963; Conen and Erkman, 1966b) and in Patau’s syndrome (Conen and Erkman, 1966a).

The present series from South East England and East Anglia shows a seasonal incidence, with 67% of cases of Edwards’ syndrome and 79% cases of Patau’s syndrome born in June to November inclusive. The repetition of this trend over the six years studied to date, and the different mean maternal ages in the summer and winter conceived groups (see above), increases the probability that this is a real phenomenon. That the apparent excess of Edwards’ and Patau’s syndrome births in
June to November is not due to an excess of total live births at this time is seen by inspection of the Registrar General's Quarterly Returns (Registrar General, 1966). Of 5,876,277 live births in the period 1960–66, 2,999,682 were in January–June. There were 2,876,597 in July–December, which period compares most nearly with the June–November period in the present series. Clustering in Conen and Erkman's series was mainly of January–June births in both syndromes, but regional clusters can probably only be related to environmental variations. Parents of the propositi were closely questioned about radiation and illnesses, especially near the time of conception, and there is no history of undue radiation exposure or viral or other illness in this series. If a viral infection is to be implicated, it must be a subclinical one.

**Sex Proportions.** The abnormal sex proportion in Edwards' syndrome is difficult to explain. The discrepancy between the sexes is so large that it must be the result of differential survival at some stage. As noted above, 17–18 trisomic abortions are extremely rare, and of 6 known, 4 were female. It is possible that male 18-trisomic foetuses are early resorptions or 'missed abortions', or even that Y-bearing sperm with two No. 18 chromosomes are poorly viable.
Work on the T-locus in the mouse (Braden and Weiler, 1964) has shown that the genotype of the egg may influence the sex of the sperm that is able to fertilize it. It may be that a similar type of gametic selection is operating in man, and that a disomic-18 egg is more readily fertilized by an X-bearing sperm.

Amongst infants with Edwards' syndrome, Conen and Erkman (1966b) demonstrate a significantly longer survival in females, and this is confirmed in the present series. Yet there is no difference in birth data in the sexes, and the females seen by the author are in no way less severely affected than the males. The longest survivor in the present series lived for 1670 days, but she was a mosaic with minor normal and tetrasomic cell lines. At the time of writing, two cases of Edwards' syndrome are still alive: a primary trisomic boy aged 3½ months, and a girl, also a primary trisomic, aged 2½ months.

Chromosomal Findings. Chromosome studies on children with clinical features of Edwards' and Patau's syndromes reveal a surprising variability of findings. In Down's syndrome about 6% of cases are due to complex cytogenetic variants such as translocations and mosaics (Richards, 1967). Down's syndrome with normal chromosomes is unknown. It is difficult to assess the frequency of 'complex' variants from the literature as they are more likely to be published singly than single cases of primary trisomy. The present series, selected on clinical grounds alone, allows a provisional estimate of these complex variants: 18.5% in Edwards' syndrome and 22.2% in Patau's syndrome.

Double aneuploids with 48,XXX,18+ and 48,XXY,18+ occur with an unexpectedly high frequency in Edwards' syndrome, in 3.5% of females and 10% of males. In Patau's syndrome 48,XXX,D+ females are unknown, but there was a 6–8-week abortus with a 48,XXY,D+ chromosome complement (Pergament and Kadotani, 1965). In Down's syndrome 48,XXX,21+ is extremely rare. 48,XXY,21+ occurs with a frequency of 1 in 11,614 live male births (Taylor and Moores, 1967).

Translocations or structural rearrangements of unknown origin are well known in the two syndromes (Brodie and Dallaire, 1962; Hecht et al., 1963a; Rohde, Lee, and Sapin, 1963; Therman et al., 1963) and many others. In the majority of cases these are not familial. In Patau's syndrome sporadic D/D translocations are common; 4 out of 9 in Conen and Erkman's (1966a) series and 3 out of 27 in this series. Familial transmission of a D/D translocation chromosome is well known, but only very rarely does this lead to production of a child with D/D translocation D trisomy (K. Hirschhorn and J. R. Miller personal communication to Conen et al., 1966). The majority of cases of Patau's syndrome with D/D translocation D trisomy have parents with normal chromosomes.

One of the present cases of Patau's syndrome had 46 chromosomes and a normal D group but with a deletion of most of the short arm of one of the B chromosomes. A look at the literature reveals further cases with a deleted B chromosome associated with features resembling Patau's syndrome or a 'midline syndrome' (Wolf et al., 1965; Miller et al., 1966; Sidbury, Schmickel, and Gray, 1964; Giorgi, Ceccarelli, and Paci, 1966; Hirschhorn, Cooper, and Firschein, 1965; Hijmans and Shearin, 1965). Autoradiographic studies on 2 of these cases showed that chromosome No. 4 was the deleted one (Wolf et al., 1965; Miller et al., 1966). A further case in this series had an apparent deletion of about half the long arm of a D chromosome, 46,XX,Dq-.

Mikelsaar (1967) has reported a child with many features of Patau's syndrome, who was a mosaic, 46,XY/46,XY,Dq-.

Mosaics occur in Edwards' and Patau's syndromes, and, as in Down's syndrome, there may be a 'dilution' of clinical features leading to increased difficulty in diagnosis. Though the mosaic cases may survive slightly longer, there is no real improvement in prognosis.

The most interesting cytogenetic finding in Edwards' and Patau's syndromes is that of normal chromosomes. Published reports are all too infrequent but include those of Hook and Yunis (1965), Marshall et al. (1964), Szotowa and Kowalewska (1965), and Burks and Sinkford (1964). In this series, 1 child with Edwards' syndrome and 2 children with Patau's syndrome had normal chromosomes. The child with Edwards' syndrome was typical in every sense, including the presence of simple arches on finger-tips. She had an older sib who died at the age of 5 days with multiple congenital anomalies, and who may also have had Edwards' syndrome. Both parents had normal chromosomes. It is possible that an unknown factor interfered at the appropriate stage of embryogenesis and produced phenocopies of Edwards' syndrome. Of the 2 children with Patau's syndrome and normal chromosomes, one had a marker D chromosome with an enlargement of the short arm (46,XX,Dp+). It has not been possible to study the parents of either of these 2 children.

The occurrence of 'marker' chromosomes in
children with Edwards’ and Patau’s syndromes and their families is worthy of comment. Among 27 cases of Edwards’ syndrome, 2 had marker chromosomes, one with a D with very large satellites and one a telocentric D. In both cases the marker was present in at least one other generation. In addition, the father of a girl with primary 18-trisomy had a marker chromosome 18 in which the short arm appeared to be satellited (46,XY,18ps+). This marker was not present in the proposita. In another case, also a girl with primary 18-trisomy, the baby’s mother and maternal grandmother had unusually polymorphic No. 16 chromosomes. The baby’s father and paternal grandmother had a D chromosome with deleted short arms. Neither of these two marker chromosomes was present in the proposita.

In the 27 cases of Patau’s syndrome, the only marker was that discussed above, and was in a child with normal chromosomes. The marker chromosomes are regarded as within the normal range of variation and their incidence in a random adult population is 2–3% (Court Brown et al., 1966). In this small group of cases of Edwards’ syndrome, the incidence of marker chromosomes is much higher than the population figure; this may be due to chance or to an increased risk of meiotic errors induced by the marker chromosome.

Blood Group and other Marker Gene Studies. These were undertaken in an attempt to locate gene loci on the trisomic chromosomes. To date, the results have been non-contributory.

An interesting finding is the occurrence in this series of two of the extremely rare instances of anomalous inheritance of Xg (Noades et al., 1966). MR 020464/1492, a case of Patau’s syndrome with karyotype 46,XX,D−,t(DqDq)+, was Xg(a−). Both parents were Xg(a+). Other blood groups showed no anomalies. CO 211263/1428, a case of Edwards’ syndrome with 47,XX,18+, was Xg(a−), and Xg(a−) mother and an Xg(a+) father. Paternity was confirmed by the occurrence of Hb D Punjab in the proposita and her father; an extremely rare occurrence in this country (H. Lehmann, 1967, personal communication).

The majority of cases studied had high values of foetal Hb, but most were tested within a few days of birth when such values are normal. Cases that survived longer showed an abnormal persistence of foetal Hb; in LA 080467/3921 the value was 50% at 2 months and 31% at 3 months, and in JN 240767/4119 the value was 80% at 1 month of age. This is further evidence of retarded embryonic development, with a delay in the switching on of adult haemoglobin synthesis.

Dermatoglyphs. Dermatoglyphic abnormalities are common in the two syndromes, and in general confirm the impression of retarded embryonic development, even to the extent of partial or total failure of dermal ridge development. Simple arches are the most striking finding, especially as they occur in Edwards’ and Patau’s syndromes, but not in Down’s. Occurrence of a distal tri-radial is easier to understand as it results from delayed elongation of the hand, and is a common finding in Down’s syndrome.

Studies on Spontaneous Abortion. Foetuses with 18-trisomy and 13-15-trisomy are known from studies of abortion material (Aisters-Bauer and Kleinhenz, 1963; Carr, 1965; El-Alfi, Biese1, and Smith, 1964; Szulman, 1965; Thiede and Salm, 1964). Such foetuses are rare and are seldom sufficiently well preserved for anatomical studies. However, Singh and Carr (1967) studied a small group of foetuses with 13–15 trisomy and found none of the usual malformations of Patau’s syndrome. There is much to suggest from these and other studies, however, that more of these trisomic concepts are lost as abortions than survive to live birth.

Identification of Trisomic Chromosomes. Autoradiographic studies have established the identity of the trisomic chromosome in Patau’s syndrome as 13 or D1 (Giannelli, 1965; Büchner, Pfeiffer, and Stupperich, 1965), and this has been confirmed by use of autoradiography combined with measurement (Giannelli and Howlett, 1966). Yunis, Hook, and Mayer (1964) were the first to demonstrate that Edwards’ syndrome was associated with trisomy 18.

Live Birth Frequencies. Using data uncorrected for missed cases, both syndromes occur with a frequency of approximately 1 in 7000 live births, but these are minimum estimates, and further prospective studies on newborn populations will provide a more exact figure. Certainly the referral of equal numbers of each syndrome to the Paediatric Research Unit indicates that the incidence of the two conditions is similar.

Summary

Twenty-seven cases of Edwards’ syndrome (trisomy 18) and 27 cases of Patau’s syndrome (trisomy 13–15) are described in detail, with particular reference to overlap of clinical features. Birth and
survival data are discussed and compared with larger data from the literature. The range of cytogenetic findings and the high frequency of complex variants are described. The population incidence of the two conditions is estimated.

I should like to thank all the paediatricians, obstetricians, and pathologists without whose help this study would have been impossible. Much of the material was derived from the survey of live births in the area administered by the South East Metropolitan Regional Hospital Board, and I am particularly grateful to the Consultants in this region for their prompt notification of cases and helpful co-operation. Cases were referred by: Drs. E. Addenbrooke, R. E. Bonham Carter, S. Carter, P. J. N. Cox, A. B. Donnison, M. Dysniki-Klein, Mr. B. R. Eaton, Mr. H. B. Eckstein, Drs. O. D. Fisher, J. L. Greaves, M. H. K. Haggie, M. C. Joseph, S. J. R. Macoun, R. C. Mac Keith, T. P. Manz, R. H. Mayone, White, D. O. Morris, F. W. Nash, A. P. Norman, C. H. Nourse, T. E. Oppé, A. Robinson, T. S. Rodgers, L. G. Scott, C. E. Stroud, P. N. Swift, M. A. Warley, and D. A. J. Williamson. I should also like to thank all staffs of Maternity and Premature Baby Units for their help. Skilled, technical help was provided by Miss V. M. McGuire, Mrs. B. Scott, and Miss D. Garrett, and secretarial help by Miss B. J. Alexander, Miss S. Burnett, Mrs. J. L. Hinton, and Mrs. H. M. Aggett. Blood group, genetic marker, and haemoglobin studies were undertaken by Drs. R. Race, R. Sanger, E. Robson, and H. Lehmann. I am indebted to Mr. J. L. Hamerton, Professor P. E. Polani, and Dr. J. A. Fraser Robert for their advice and constructive criticism. The work was supported by the Spathics Society and the Medical Research Council.

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Appendix

This appendix consists of 54 individual case reports and a table of birth and survival data in the 54 subjects (Table A). The subjects are identified by initials, date of birth, and unit number as recommended by the Chicago Conference (1966). For the sake of brevity, birth and survival data, summarized in Table A, are not repeated in the individual case histories. Cytogenetic findings are reported as in the Chicago nomenclature. Full blood group analysis and analysis of G6PD, haptoglobins, haemoglobins, transferrins, and serum Xn and Gc groups were undertaken on the majority of subjects and their parents. Most of the data are non-contributory and are referred to only if they are of interest.

Edwards' Syndrome

HD 291065/2976


EF 111265/3002

EH 290865/2835 ♀


KJ 060166/3042 ♀


RL 041065/2895 © (Fig. 2a)


PS 210466/3247 ©


ES 231265/3020 ©

Clinical features: elongated skull (head circumference 33 cm.), wide-set eyes with epicantic folds, large primitive low-set ears, extreme micrognathia. Palate high and arched, mouth small. Neck short, excess nape skin. Flexion deformity of fingers, retroflexible distally implanted thumbs. Calcaneo-valgus feet, hypoplastic toe-nails. Chest-shield shaped, short sternum, limited hip abduction. Slight umbilical hernia. Generally—hypertonia, jittery, opisthotonic posture. Respiratory distress soon after birth, recovered. Failed to thrive, died at 35 days. Necropsy: heart dextroposed, ventricular septal defect. Diaphragm abnormally thin. Brain macroscopically normal. Sections showed slight ventricular dilatation. One eye sectioned, normal. 56% foetal Hb. Dermatoglyphs: simple arches on 7 digits; positions of palmar triadri not seen; bilateral single palmar creases. Chromatin positive. Chromosomes: 46 chromosomes, with a single chromosome 18 and a chromosome resembling a 12 (Fig. 1b), also a D chromosome with very large satellites; 46,XX,Ds +,+18 −,?18p +q +. (Parents—normal chromosomes except baby's mother and maternal grandmother had marker D chromosome: 46,XX,Ds +.)

CW 300965/2887 ©


TW 130864/2353 ©


SA 031164/2492 © (Fig. 2i)

number 48 with additional chromosomes in C and E groups. Oral smear—cells with two Barr bodies, autoradiography confirmed two late-labelling Xs, 48,XXX,18+.

BC 240262/57 ♀

AT 211062/1105 ♀ (Fig. 2e)

SM 010763/1308 ♀

BC 231163/1418 ♀

(Case previously published, Taylor and Polani, 1964, Case 4.)

CO 211263/1428 ♀

CG 170561/1077 ♀

JT 280766/3427 ♀
Pregnancy complicated by hydranmios. Apgar score 3 at birth. Clinical features: elongated skull, low-set malformed ears, micrognathia. Unilateral neck webb-
Autosomal Trisomy Syndromes

MK 030567/3945 ♀


JV 240867/4140 ♀ (Fig. 2f)


BP 260867/4134 ♂


**TS 251166/3658 ♀**

Paternal grandfather was a twin. Pregnancy complicated by threatened miscarriage at 2 months. **Clinical features**: antero-posterior elongation of skull, wide-set eyes, epicantid folds. Pupils of both eyes eccentric, did not react to light. Low-set malformed ears, high-arched palate, microstomia, micrognathia. Neck short with extra skin laterally (webbing) and behind. Flexion deformity of fingers, extremely hyperconvex finger-nails. Fifth finger left hand had missing phalanx. Thumbs distally implanted. Calcaneo-valgus feet, short dorsi flexed big toes. Abduction of hips and shoulders limited. Chest very wide, asymmetrical, right nipple about 1·3 cm. below level of left nipple. Sternum had a bony prominence at end. Cyanosed after feeds, congenital heart disease suspected. Generalized hypotonia, retarded, failed to thrive, died at 89 days. **Necropsy**: ventricular septal defect, left atrium very small, under-developed. Brain superficially normal. 55-8% foetal Hb. **Dermatoglyphs**: 3 simple arches, 7 digits with ridge dysplasia; t triradii in t' position bilaterally; simian crease on left hand. Chromatin positive. **Chromosomes**: 46,XX,18+. Unusually polymorphic. No. 16 chromosomes present in baby's mother and maternal grandmother but not in proposita. A marker D chromosome (Dp−) present in baby's father and paternal grandmother but not in proposita.

DC 020167/3735 ♂ (Fig. 2c)

Pregnancy uneventful, labour induced at 42 weeks. Normal delivery, vertex presentation. Apgar score 4 at birth. **Clinical features**: antero-posterior elongation of skull, microphthalmos, hypertelorism, epicantid folds, normally placed malformed ears, micrognathia. Neck short with extra nape skin. Capillary haemangiomas on both eyelids. Flexion deformity of fingers with distal implantation of thumbs. Second, third, fourth toes webbed bilaterally. Halluces short, dorsi flexed, calcaneovalgus feet (Fig. 2g). Hip abduction limited. Testes undescended, umbilical hernia. **Neurologically** hypertonia, no auditory attention. Heart sounds normal, but cyanosis during feeds. Jaundiced, would not suck—paresis of palate suspected. Failed to thrive, frequent apnoeic attacks, died at 9 days. **Necropsy**: atelectasis of right lung, retention cyst at upper pole of right kidney. Heart normal. **Dermatoglyphs**: 7 simple arches, 1 whorl, 1 ulnar loop; ridge dysplasia on right fifth digit and both palms; bilateral simian creases. Chromatin negative. **Chromosomes**: 47,XY,18+.
ML 050767/4103 ♀


BW 150967/4182 ♀ (Fig. 2d)


SW 230767/4136 ♀


AW 011067/4237 ♀


Dermatoglyphs: 4 simple arches, 3 ulnar loops, 3 radial loops; normally situated t triradii; simian crease, right hand. Chromatin positive. Chromosomes: 47,XX,18+.

SC 120766/3465 ♀ (Fig. 2b)


Patau's Syndrome

SE 190765/2778 ♀

Autosomal Trisomy Syndromes

PF 160866/3461 ♂

**Clinical features:** Microcephaly, wide-set eyes, epicanthic folds, low-set malformed ears, cleft lip and palate, micrognathia. Short neck with excess nape skin. Capillary haemangiomas on forehead, eyelids. Flexion deformity of fingers, long hyperconvex finger-nails. Mild equino-varus feet. Abduction of hips, shoulders limited. Six digits on hands. Exomphalos, undescended testes, hypospasias. Generalized hypertonia. Heart sounds normal. Large scalp defect about 5 cm. square. Fed with difficulty, failed to thrive, died at 9 days. No necropsy. **Dermatoglyphs:** 5 simple arches, 4 loops, 3 digits with ridge dysplasia; t triradius extremely distally situated bilaterally; simian crease on left hand; no fibular S-shaped hallucal arch on sole. Chromatin negative. **Chromosomes:** 47,XX,D+.

LG 231165/2967 ♀ (Fig. 3c)

Umbilical cord only 18 cm. long. **Clinical features:** Microcephaly (head circumference 31 cm., crown-heel 44 cm.), skull elongated antero-posteriorly, with prominent occiput and prominent supraorbital ridge. Eyes wide-set, epicanthic folds (West Indian baby). Bilateral cataracts, in right eye very large. Ears low-set, malformed. Severe bilateral cleft lip and palate, extreme micrognathia. Neck short but no excess skin folds. Capillary haemangioma on eyelids. Long hyperconvex finger-nails, particularly right hand, retroflexible thumbs, also more marked on right. Bilateral double halluces (Fig. 5c), hypoplastic toe-nails. Thorax shield-shaped, with very wide-spaced nipples. Neurologically, ‘twitches’, general hypotonia, opisthotonic posture. Congenital heart disease suspected. Died at 6 days. **Necropsy:** Valvar foramen ovale but no other cardiac abnormality. Brain—underdeveloped olfactory bulbs but an intact cribiform plate. **Dermatoglyphs:** Ridge dysplasia on fingertips, palms, soles. Oral smears chromatin positive. Blood smears chromatin positive but negative for granulocyte nuclear projections usual in Patau’s syndrome. **Chromosomes:** 46 chromosomes, normal female with a marker D chromosome: 46,XX,Dp+. Parents not available for study.

MJ 100665/2739 ♀


SM 280466/3232 ♂

Family history of hydrocephalus and cleft palate in 2 of father’s relatives. **Clinical features:** Scalp defect, sloping temples, bilateral microphthalmos, hypertelorism, low-set malformed ears, bilateral cleft lip and palate. Capillary haemangioma on forehead. Short neck. Ulnar polydactyly on right hand, bilateral flexion deformity of fingers, finger-nails long, hyperconvex. Mild equino-varus feet, prominent heels. Ingual hernia, bilateral undescended testes. Failed to thrive, died at 6 days. **Necropsy:** Huge pentagonal defect of soft palate. Heart normal, foramen ovale, ductus arteriosus patent, aorta, pulmonary arteries normal. Kidneys enlarged, especially on right with a right hydrourereter and two separate ureters with separate connexions with the renal pelvis and bladder on left. Gallbladder large, lobulated. Right testis absent. **Brain:** Absent olfactory nerves. **Dermatoglyphs:** Total dysplasia of dermal ridges on finger-tips, palms, soles; no simian creases but abnormal palmar creases. Chromatin negative. **Chromosomes:** 46,XY,D-,-t(DqDq)+. (Parents: 46,XX,46,XY.)

HP 080966/3509 ♂

Placenta abnormally small (340 g.). **Clinical features:** Microcephaly (head circumference, 32 cm.), hypertelorism, epicanthic folds (negroid), left microphthalmos, low-set malformed ears, bilateral cleft lip and palate. Short neck with extra nape skin. Capillary haemangioma on forehead, eyelids. Six digits on hands, flexion deformity of fingers, long hyperconvex finger-nails. Feet normal except for hypoplastic toe-nails. Testes undescended, congenital heart disease suspected. Fed with difficulty, hypotonia, seizures, severe breath-holding spells requiring artificial respiration. Died at 3 days. **Necropsy:** Heart not examined. Seven accessory spleens. Double ureters. Intestine mralrotated. Brain—absent olfactory bulbs, reduction in size of parietal and frontal lobes. Foetal Hb 70%. **Dermatoglyphs:** 4 loops, 8 areas of dysplasia on 12 digits; dermal ridge dysplasia of palms. Chromatin negative. **Chromosomes:** 47,XY,D+.

CW 110665/2740 ♂

Three sibs well. No family history of congenital malformations. Pregnancy normal, spontaneous vertex
Fig. 5. Patau's syndrome. (a) TP 210667/4092, abdomen showing umbilical hernia and additional area of weak body wall musculature (47,XX,D+); (b) MR 020464/1492, back of head showing scalp defect (46, XX, D - t(DqDq)+); (c) LG 231165/2967, feet showing syndactyly-polydactyly (46, XX, Dp+); (d) LB 290367/3855, right eye showing iris coloboma (46,XY,Dp-); (e) MF 080167/3761, left ear showing accessory auricles (47,XX,D+); (f) LA 080467/3921, left hand showing hyperconvex finger-nails and polydactyly (47,XX,D+); (g) VN 080967/4158, liver showing intrahepatic gall-bladder (46,XX,D - t(DqDq)+); (h) MR 020464/1492, brain showing absent olfactory nerves (46,XX,D - t(DqDq)+) and small asymmetric optic nerves.
Autosomal Trisomy Syndromes


MR 020464/1492 ♂ (Fig. 3f)
Younger sib well. Pregnancy complicated by severe toxoaemia, labour induced at 34 weeks. Condition at birth poor. Clinical features: microcephaly, sloping temples, scalp defect (Fig. 5b), flat triangular nose, wide-set eyes with iris colobomata, low-set malformed ears, micrognathia. Capillary haemangiomata on eyelids, forehead. Flexion contractures of wrists, fingers. Short, very broad dorsiflexed halluces. Sucked poorly, had seizures, severe breath-holding spells, died at 6 hours. Necropsy (A. Claireaux): heart small, malrotated, coarctation of aorta. Kidneys very large, with microscopical appearance of polycystic disease. Brain—absent olfactory nerves, small asymmetrical optic nerves (Fig. 5h). Blood groups unremarkable except for anomalous inheritance of Xg. Proposita was Xg(−), both parents being Xg(a+). Other blood groups normally inherited. Foetal Hb 67%. No dermatoglyphs examined, but bilateral simian creases. Oral smears chromatin positive. Blood smears chromatin positive, did not show excess of granulocyte nuclear projections usual in Patau's syndrome. Chromosomes: 46,XX,D−,r(DqDq)+. Both parents had normal chromosomes.

NW 091063/1350 ♂

SC 300763/1322 ♂

JM 100862/1017 ♂

MR 030664/1541 ♂
empty. **Dermatoglyphs:** not studied. **Chromosomes:** 47,XY,D+.

**Birthweight** 3655 g. (placenta 708 g.), unusually high. **Clinical features:** wide-set eyes, epicanthic folds, bilateral microphthalmia, iris coloboma on right, coloboma and/or cataract on left. Ears low set, malformed, micrognathia. Neck short with excess nape skin. Severe flexion deformity of fingers, long hyperconvex finger-nails; 6 digits right hand, 7 left hand, 6 on both feet. Prominent heels, hypoplastic toe-nails. Hip abduction limited. Hypertonia, suspected congenital heart disease. No seizures, no apnoeic spells, auditory attention positive. Fed satisfactorily, gained weight. General impression—looked like Patau’s syndrome, but too robust. Began to vomit after feeds, had some cyanotic spells, died of aspiration pneumonia at 26 days. **Necropsy** (P. M. Forster): heart enlarged, globular due to dilatation of right atrium, right ventricle. Small high ventricular septal defect. Persistence of left superior vena cava. Pulmonary valve bicuspid. Uterus bicornuate. Brain macroscopically normal. **Dermatoglyphs:** 4 digits on left hand, simple arches; no pattern on fifth, sixth digits; patterns on right fingertips and palm could not be inspected due to severe flexion deformity; distal t triradius on left, bilateral single palmar creases. Oral smears chromatin positive. Blood smears also chromatin positive, showed excess of granulocyte nuclear projections usual in Patau’s syndrome. **Chromosomes:** 3 cell lines, 46,XX; 47,XX,D+; 46,XY,D+ . Tetrasomy cell line minor, not in skin. Other 2 lines present in both tissues (blood and skin): 46,XX/47,XX, D+/48,XX,D+,D+.

**MF 101166/3624 Δ**

Two sibs well. **Clinical features:** bilateral microphthalmos, low-set malformed ears, very severe cleft lip and palate, micrognathia. Neck short with excess nape skin. Hands and feet had 6 digits. Long hyperconvex finger-nails. Calcaneo-valgus feet, short dorsiflexed big toes. Chest shield-shaped. Testes undescended. Congenital heart disease, died at 8 hours. **Necropsy:** interventricular septal defect about 5 mm. diameter just below aortic and tricuspid valves. Foramen ovale patent, abnormally situated, led into very rudimentary left atrium. Ductus arteriosus patent. Renal and other systems normal. Brain—absent olfactory nerves. **Chromosomes:** 3 cell lines, 46,XX; 47,XX,D+; 46,XY,D+. Tetrasomy cell line minor, not in skin. Other 2 lines present in both tissues (blood and skin): 46,XX/47,XX, D+/48,XX,D+,D+.

**JC 131066/3781 Δ**

Older sister well. One macerated stillbirth. **Clinical features:** bilateral microphthalmos, bilateral cleft lip, cleft palate. Extra skin at nape, pilonidal sinus. Hypotonic, jittery, apnoeic spells. Exomphalos. Left hand had 6 digits. Fed poorly, jaundiced, bled from mouth, died at 3 days. **Necropsy:** heart, enlargement of right atrium, large atrial septal defect due to failure of development of septum secundum. Ductus patent. Kidneys enlarged, congested, cyst in upper pole left kidney. Tail of pancreas bifid. Brain—absent olfactory nerves. No dermatoglyphs. **Chromosomes:** 47,XX,D+. (Studied by W. M. Davidson.)

**MF 080167/3761 Δ** (Fig. 3d)

Sib has coeliac disease, other 2 sibs well. No family history of congenital malformations, 2 sets of twins in father’s family. **Clinical features:** antero-posterior elongation of skull, wide-set eyes, epicanthic folds, bilateral iris coloboma, low-set malformed ears with accessory auricles (Fig. 5e), micrognathia. High arched palate with calcified soft palate. Small tongue, uvula absent. Capillary haemangioma on eyelids, back of neck, abdomen near umbilicus. Both hands had 6 digits, flexion contracture of fingers. Finger-nails long, hyperconvex, toe-nails hypoplastic. Mild equino-varus feet. Narrow thorax, small umbilical hernia. Sucked poorly, bouts of jaundice, apnoeic attacks. Auditory attention negative. Muscle tone normal. Congenital heart disease suspected. Failed to thrive, died at 67 days. **Necropsy:** heart enlarged, no septal defects or coarctation of aorta. Ductus arteriosus patent. Kidneys bilaterally enlarged, lobulated. Uterus biseptate, absence of left cornu, tube, ovary. Accessory spleen. Brain—absent olfactory nerves. **Dermatoglyphs:** 9 simple arches, 1 narrow loop; sixth digits rudimentary; position of t triradius not recorded; fibular S-shaped hallucal arch on both soles; 2 palmar creases bilaterally. Chromatin positive. **Chromosomes:** 47,XX,D+.

**KA 20367/3856 Δ**

Sib had pyloric stenosis but well. **Clinical features:** microcephaly, wide-set very small eyes, low-set malformed ears, cleft palate, micrognathia. Neck short, excessive nape skin. Six digits on all hands and feet. Thumbs flexed abnormally, hip abduction tight. Thorax unusually narrow. Heart sounds normal. General hypertonia. Jaundiced, fed with difficulty, breath-holding spells, died at 4 days. **Necropsy:** abnormal heart, rudimentary atria, polycystic renal cortex, biseptate uterus, pyloric stenosis (also present in sib), Accessory liver lobules. Brain—absent olfactory tracts and bulbs, small optic chiasma. Both eyes, microphthalmos, aniridia, cataract, retrorenal retinal dysplasia, coloboma of retina, and choroid. Left eye had intracocular cartilage (G. Keith). **Dermatoglyphs:** 9 loops, 1 whorl, sixth digits dysplastic. Normally situated t triradius, 2 palmar creases bilaterally; complete ridge dysplasia of soles. Oral smears, chromatin positive; blood smears, characteristic granulocyte nuclear projections. **Chromosomes:** 47,XX,D+.

**LA 080467/3921 Δ** (Fig. 3a)

Younger brother well. No relevant family history. Delivery normal. Condition at birth fair. Pneumonia soon after birth, recovered. **Clinical features:** bilateral cleft lip and palate, poorly developed nose, microcephaly, microphthalmia, wide-set eyes with mongoloid
slant, epicanthic folds, micrognathia, short neck. Scalp defect. Normal ears. Capillary haemangioma on eyelids, forehead. Six digits on left hand (Fig. 5f). Neurologically—moved symmetrically, generalized hypotonia. Auditory attention negative. Heart sounds normal. Cyanotic spells followed feeds. No seizures or breath-holding attacks. Feeding difficulty due to hare-lip and cleft palate, but tried to suck, gained some weight. Died at 53 months. Necropsy: no abnormalities except brain which had enlargement of both lateral cerebral ventricles. Abnormal persistence of foetal Hb, 31%, at 2 months, 54%, at 3 months. Dermatoglyphs: 7 simple arches, 4 loops on 11 fingertips; t triradius in t' position, 2 palmar creases bilaterally. Oral smears chromatin positive. Blood smears showed excess of granulocyte nuclear projections typical of Patau's syndrome, chromatin positive. Chromosomes: 47, XX, D +.

PM 200867/4124 (Fig. 3b)


JN 240767/4119 (Fig. 3e)


BS 300867/4141 (Fig. 3e)

chiasma, deficient corpus callosum. Dermatoglyphs: no ridges on fingertips, palms or soles. Chromosomes: 47,XX,D+.

VN 080967/4158


LB 290367/3855 (Fig. 3i)

No relevant family history. Pregnancy ended at 30 weeks. Clinical features: cleft palate, unilateral cleft lip, microcephaly, wide-set eyes, bilateral iris coloboma (Fig. 5d), low-set malformed ears, micrognathia. Flexion deformity of fingers, retroflexible thumbs, limited hip abduction. Capillary haemangioma near anus. Testes undescended, glandular hypospadias. Generalized hypertonia, jittery, apnoeic spells. Congenital heart disease suspected. Fed with difficulty, died at 24 hours. Necropsy: (N. M. Davidson): lungs almost completely atelectatic, only demonstrable air in left lower lobe. Heart enlarged with large right atrium, minute left atrium. An ‘aorta’ arose from left ventricle, including coronary orifices, forming arch, branching only into carotid and subclavian arteries. Vessel arose from right ventricle, giving off pulmonary arteries, continuing as descending aorta on left. Large ventricular septal defect. Left kidney, ureter absent. Both testes pelvic. Dermatoglyphs: total ridge dysplasia on palms, fingertips; 2 palmar creases bilaterally. Chromatin negative. Chromosomes: (Fig. 1c) 46,XY,Bp−. The parents refused to be studied.

DW 301067/4271


GH 051267/4308 (Fig. 3h)