

# D<sub>1</sub> Ring Chromosome in Newborn with Peculiar Face, Polydactyly, Imperforate Anus, Arrhinencephaly, and Other Malformations

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Previously the occurrence of a D ring chromosome replacing a D chromosome has been reported in 15 cases (Wang *et al.*, 1962; Bain and Gauld, 1963; Turner, 1963; Macintyre *et al.*, 1964; Reisman, Darnell, and Murphy, 1965; Adams, 1965; Jacobsen, 1966; Gerald *et al.*, 1967; Teplitz *et al.*, 1967; Gilgenkrantz, Peters, and Streiff, 1967; Sparkes, Carrel, and Wright, 1967; Lejeune *et al.*, 1968; Mikkelsen and Niebuhr, 1969). A collection of the physical findings in patients with ring chromosomes is of special interest, to see whether there is a correlation between clinical signs and certain chromosomal anomalies.

## Case Report

The patient was a newborn male infant, born to a 25-year-old mother and a 33-year-old father. Both were Caucasians and were physically and mentally well. A 6-year-old daughter was perfectly normal. There is a questionable history of radiation exposure when the father worked with radioactive substances for 3 months.

Prenatally, poor fundal development was noted and placental insufficiency suspected. Before delivery, x-ray films suggested foetal demise; however, foetal heart tones remained audible. Spontaneous delivery produced a liveborn infant weighing 2000 g. One umbilical artery was present. The head was small and conically shaped, measuring only 12 cm. in circumference. The posterior fontanelle was large and open, the anterior fontanelle quite small. The occiput was hairless and there was a round moon face with receding forehead and chin, a small nose the root having no indentation, hypertelorism, small lid folds, and microphthalmia on the left (Fig. 1). The ear lobules were deeply seated and both auricles deformed. Both hands were clinodactylous with extra digits. The right hand had 4 metacarpals and the left hand 5. Both feet were rockerbottom in appearance. The left scrotal sac was poorly developed and the left gonad palpable in the superficial inguinal pouch. The penis was normal, but small. There was

atresia ani. An excretory urogram revealed an absent left kidney.

The infant died on his 7th day of life due to intestinal obstruction and bronchial pneumonia. At necropsy, the infant was 1740 g. and 44 cm. long. Bilateral bronchial pneumonia was noted. The right ventricle was enlarged with a large oval defect in the interatrial septum. There was narrowing of the ostium of the left coronary artery. The left pelvic kidney measured one-third the size of the right ptotic kidney. Gonads on the left were not found. The brain was arrhinencephalic.

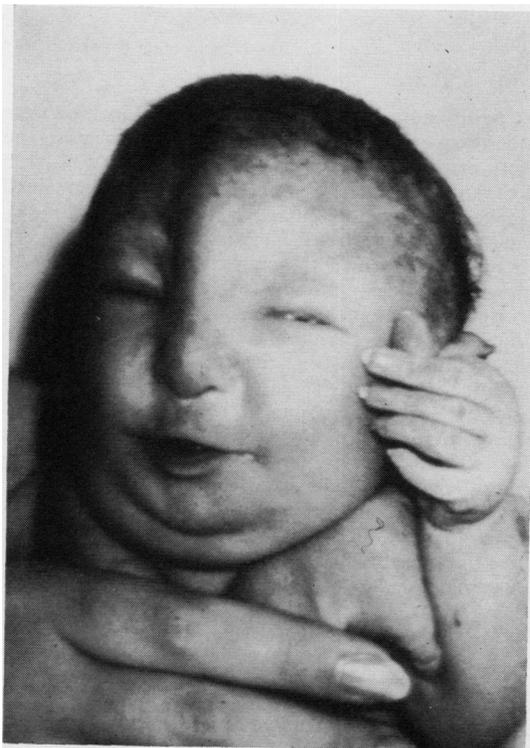


FIG. 1. Peculiar facies.

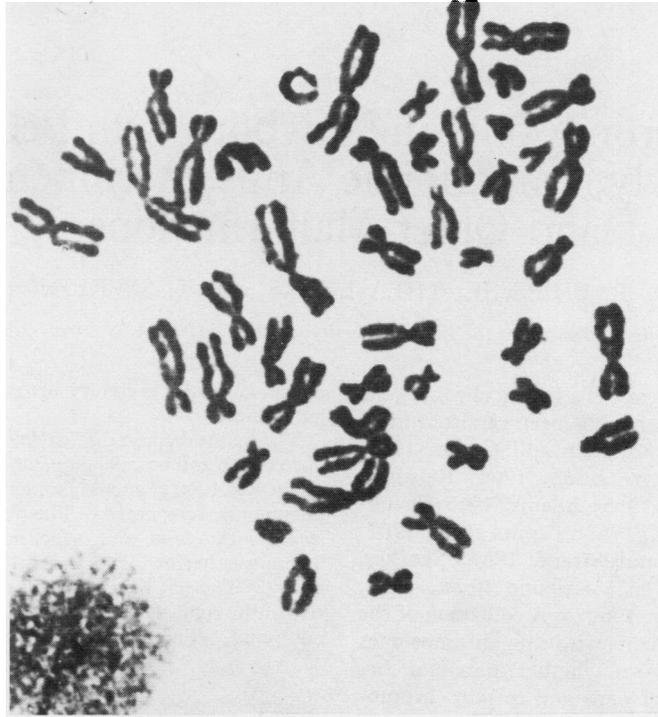


FIG. 2. One of the 88 metaphases with a ring chromosome in the D group.

**Chromosome studies.** Chromosomal analyses were undertaken on lymphocytes cultured for 3 days, using the micro-method of Arakaki and Sparkes (1963). 100 metaphase plates were examined. Many cells contained a monocentric and occasionally a dicentric ring chromosome of various sizes. Karyotypes showed that 88 metaphases contained the ring chromosome and were missing one D chromosome (Fig. 2). The location of the ring chromosome in the metaphase plates was generally peripheral. One cell contained 2 ring chromosomes. Eleven cells were missing one D chromosome without any ring (Table).  $^3\text{H}$ -thymidine labelling showed the ring chromosome to be heavily labelled in all cells examined (Fig. 3). It seems most probable that the ring is formed from a  $\text{D}_1$  chromosome (No. 13). Occasional polyploid cells were apparent, in which, depending on the number of chromosomes, two or more monocentric or dicentric ring chromosomes were observed. The chromosomes of the parents and the older sib are normal.

### Discussion

In all cases of D ring chromosome there are differences and similarities in structural patterns as well as in the clinically associated picture, but a common feature of all investigations is a high percentage of cells containing a ring. We believe, as suggested

by Lejeune (1968), that the various sizes of ring chromosomes result from sister-strand exchange.

Of particular interest is the comparison of malformations in patients with D ring chromosomes and in patients with other aberrations in the D group such as total and partial D trisomy. In all cases the identification of the D group chromosome must be considered. In the case of Sparkes *et al.* (1967), the autoradiographic findings suggest a  $\text{D}_2$  chromosome, while in our patient and those of Bloom, Gerald, and Reisman (1967), and of Mikkelsen and Niebuhr (1969) a  $\text{D}_1$  chromosome is considered to be involved. Infants with  $\text{D}_1$  trisomy (Patau syndrome) seldom survive the first few days of life. Common features are microphthalmia with narrowing of the eyelids and the lips, cleft palate and auricular deformities. Often associated are defects in the skull

TABLE  
CHROMOSOME COUNTS

$46,\text{XY},\text{D}^-, \text{Dr}^+$	$47,\text{XY},\text{D}^-, \text{Dr}^+ \text{Dr}^+$	$45,\text{XY},\text{D}^-$	Total Cells Examined
88	1	11	100

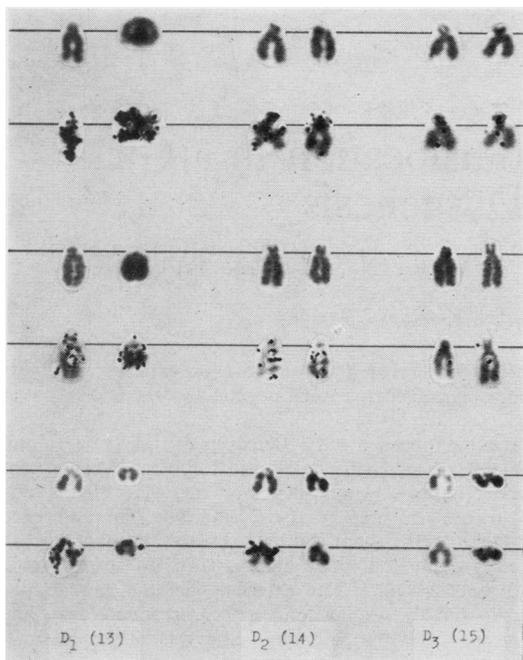


FIG. 3. Autoradiographic study from three cells. Only the D group is shown. The labelled chromosomes are located beneath the corresponding unlabelled ones.

one must consider, may have lost variable amounts of chromosome material during ring formation, and alteration of the size of the ring can occur either by loss or doubling of chromosome segments. This results in the presence of different amounts of genetic material in different cases. The loss of the ring chromosomes during mitoses in an individual cell may result in the formation of a monosomic cell line which might be clinically important.

### Summary

In a newborn boy cytogenetic and autoradiographic studies showed a D<sub>1</sub> ring chromosome in 88% of the metaphases (46,XY,13r). One metaphase contained 2 rings. The rest of the cells were missing one D<sub>1</sub> chromosome without rings (45,XY,13-). The infant exhibited multiple malformations, very similar to those reported in the D<sub>1</sub> ring chromosome literature, especially concerning the profile line with the prominent nose bridge.

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bones, skin angiomas, and often there are additional digits. Of special interest is the arrhinencephaly. Cardiovascular and genito-urinary abnormalities are also noted. Arrhinencephaly was also present in patients of Bain and Gauld (1963) and our own. There seems to be however greater conformity between the physical findings in our ring case and partial D<sub>1</sub> trisomy (Witkowski, 1968) than in total D<sub>1</sub> trisomy. We found no cleft palate, seldom seen in partial D<sub>1</sub> trisomy, but found atresia ani which is seen in about half the cases of partial D<sub>1</sub> trisomy. It is interesting to speculate whether increased information will result in describing a D<sub>1</sub> ring chromosome syndrome. Lejeune *et al.* (1968) described the peculiar facial structure in their 3 patients, which was also described by Gilgenkrantz *et al.* (1967). As an important feature of patients with a D<sub>1</sub> ring chromosome this included hypertelorism, typical Greek profile, receding chin, abnormal eyes, and large, deep-seated, deformed ears. These findings were also reported by Mikkelsen and Niebuhr (1969) and are found in the present case.

Generally, it can be assumed that ring chromosomes will show wider clinical variation than the trisomics. In trisomics there is always an intact extra chromosome present. Ring chromosomes,