Hirschhorn, K. (1971). Trisomy 22: a clinical entity. *Journal of Pediatrics*, **79**, 12-19.
Latta, E., and Hoo, J. J. (1974). Trisomy of the short arm of chromosome 17. *Humangenetik*, **23**, 213-217.
Nielsen, J., and Rasmussen, K. (1975). Extra marker chromosome in newborn children. *Hereditas*, **81**, 221-224.
Norwood, T. H., and Hoehn, H. (1974). Trisomy of the long arm of human chromosome 1. *Humangenetik*, **25**, 79-82.
Salamanca, F., and Armendares, S. (1974). C bands in human metaphase chromosomes treated by barium hydroxide. *Annales de Génétique*, **17**, 135.
Sanchez, O., Yunis, J. J., and Escobar, J. I. (1974). Partial trisomy 11 in a child resulting from a complex maternal rearrangement of chromosomes 11, 12, 13. *Humangenetik*, **22**, 59.
Smith, D. W. (1976). *Recognizable Patterns of Human Malformation*. pp. 12-15. Saunders, New York.

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Ring chromosome 8 in a boy with multiple congenital abnormalities and mental retardation

SUMMARY A ring chromosome 8 was found in peripheral blood cells in a boy, whose chromosomes were studied because of multiple congenital anomalies. Examination of skin cells revealed a 46,XY/46,XY,8r pattern. Application of several banding techniques suggested a duplication of the most distal bands of both arms in the ring. The terminal end of 8q appeared to have been retained as could be shown by R-banding.

The anaesthesia and surgery the mother underwent in the first month of her pregnancy is considered as a possible cause of the chromosome abnormality.

Ring chromosomes derived from unidentified C chromosomes have been reported in several cases.

After the development of the banding techniques the possibility of identifying the origin of C ring chromosomes led to the publication of reports of 4 patients with a ring chromosome 6 (Moore *et al.*, 1973; Van den Berghe *et al.*, 1974; Fried *et al.*, 1975; Wurster-Hill and Hoefnagel, 1975), 2 patients with a ring chromosome 7 (Zackai and Breg 1973), 1 patient with a ring chromosome 8 (Pfeiffer and Lenard, 1973), and 5 patients with a ring chromosome 9 (Kistenmacher and Punnett, 1970; Jacobsen *et al.*, 1973; Fraisse *et al.*, 1974; Zdansky *et al.*, 1975; Nakajima *et al.*, 1976). In the case of Kistenmacher and Punnett the identification was based on morphology and study of the exchange pattern induced by mitomicin C.

In this paper a ring chromosome 8 is described in a patient who was studied because of multiple congenital abnormalities.

Case report

The propositus (born 13 October 1967) is the first of two children. At birth his mother was 25 and his father was 28 years old. There were no abortions or stillbirths. Unaware of her pregnancy the mother underwent an appendectomy on account of chronic appendicitis on the 18th day of her last menstrual cycle (premedication: 0·5 mg atropine, 25 mg promethazine, 20 mg pantopon; narcotics: thiopenthone-sodium, suxamethonium-chloride, nitrous oxide, and fluothane).

Gestation was uneventful and ended 13 days after term. Birthweight was 2770 g, length 47 cm. Feeding was very difficult in the neonatal period.

At 1½ years of age the boy suffered from feverish convulsions. When he was 2 years old he was operated on for bilateral hernia inguinalis. Because of an impending dislocation of the right hip, he was treated with a stretch bandage at the age of 2½ years. He suffered from recurrent infections of the upper respiratory tract. Psychomotor development was very retarded.

At the age of 5 5/12 years the boy was admitted to our institution. Physical examination at that time disclosed the following (Fig. 1A and B): dwarfism, dolichocephaly, prominent occiput, asymmetry of the viscero-cranium, bilateral strabismus convergens alternans, bilateral epicanthic folds, asymmetric ears, tight upper lip, thin lips, gothic palate, asymmetry of the upper dental arch, micrognathia, pectus excavatum, scapulae alatae, wide-spaced areolae mammae, long thorax, bilateral inguinal scars from herniotomy, sacral dimples, and dimples dorsal of the elbows, camptodactyly of both fifth fingers, hypotonia, and cutis marmorata.

The electroencephalogram was normal. Opthalmological examination revealed a distinct bilateral hypermetropia and minor astigmatism of the right eye, which seems to be affected by amblyopia.

X-ray examination revealed that the right caput femoralis was located laterally in the acetabulum and that the right femur was adducted, the right side

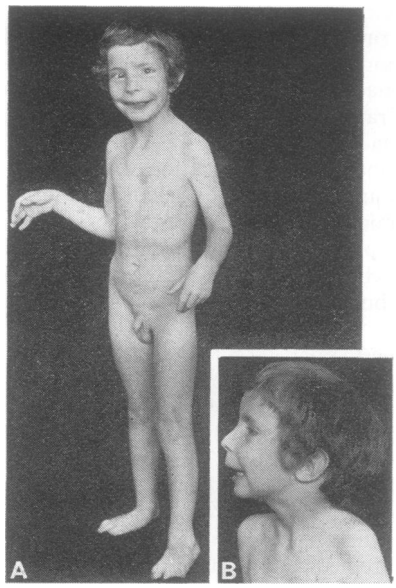

Fig. 1 *(A) Propositus at the age of 6 years. (B) Profile of the propositus at the age of 6 years.*

of the pelvis was in a higher position than the left side, both tibiae showed minor exostosis, and the sacral arches were cleft. The chest organs showed no abnormalities.

Results of biochemical examination of blood and urine were normal.

With the Griffiths Mental Development scales the General Quotient proved to be 36.

The dermatoglyphic data of the propositus and his parents are pictured in Fig. 2 and summarised in the Table.

CYTOGENETICS

Chromosome examinations were carried out on peripheral blood cells and by means of a skin fibroblast culture of the patient.

G-banding of the chromosomes was studied with the trypsin-Giemsa technique, Q-banding by fluorescent staining with atebrin, and R-banding with acridine orange with and without BrdU pretreatment. The total number of leucocytes examined was 120. In 118 of these cells 46 chromosomes were present. One had a normal complement but in 117 cells a C chromosome was missing and replaced by a ring (Fig. 3). Of two further cells one had 45 chromosomes without a ring and one had 47 chromosomes with two rings.

Ring size and morphology were constant. In only 5 cells were double rings found, indicated by two blocks of heterochromatin (Fig. 4b). In most of the cells microscopical examination suggested that the circumference of the ring was somewhat greater than the length of the normal chromosome 8.

In 72 fibroblasts examined the ring was found only in 8 cells, 5 of which had 47 chromosomes while in 3 cells random elements were missing. The remainder of the cells had a normal set of chromosomes.

In cells with a ring the banding techniques revealed that in the C-X group there was only one normal number 8 chromosome (Fig. 3). To get a more precise insight into the number and origin of the bands present in the ring, BrDU pretreated cells were photographed after AO staining and rephotographed after C-banding the same cells. In this way the location of the centromere in the R banded ring could be clearly traced back (Fig. 5). Comparison of the bands on the ring with these on the normal chromosome 8 showed that all bands detectable in the latter were present in the ring. Besides that, suitable cells suggested that the most distal bands on both arms were wider in the ring than in the normal homologue. This impression was strengthened by reflection photometer scanning which indicated that these bands were present in duplicate in the ring. The most striking feature of the ring revealed by the R-banding was that the terminal end of 8q appears to have been retained in the ring (Fig. 4c).

The chromosomes of both parents were normal.

Discussion

Ring chromosomes are thought to be the result of double terminal deletions followed by reunion of the

Table *Dermatoglyphs of propositus and his parents*

		Finger-tip patterns					*TRC*	*Palmar formulae*	*Maximal atd*	*Palmar creases*
		I	*II*	*III*	*IV*	*V*				
Propositus	L	UL	UL	UL	UL	UL	113	7.5″.5′1−t″−A^{c}.O.O.O.L	61°	Proximal transverse crease
	R	W	UL	UL	W	UL		9.9.5′.1−t″−A^{c}.O.O.L.O	70°	Proximal transverse crease
Mother	L	UL	UL	UL	W	W	168	11.7.7.4−t′t^{b}−L^{r}/A^{c}.O.O.O.L	47°	Normal
	R	UL	W	W	W	W		11.9.7.5′−t′−A^{c}.O.O.L.O	47°	Normal
Father	L	W	RL	UL	W	UL	193	11.9.7.1−t′−A^{u}.V.O.L.O	47°	Partial simian crease
	R	W	W	UL	W	W		11.11.9.3h−t′t^{b}−L^{r}.O.O.L.O	49°	Partial simian crease

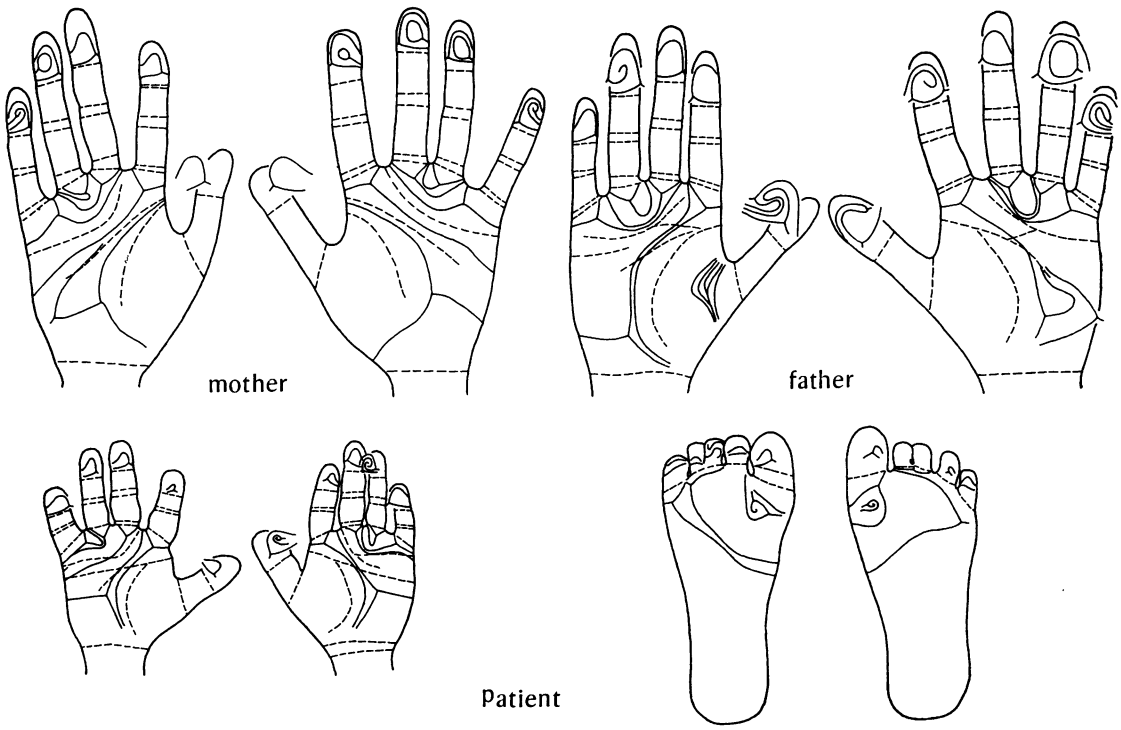

Fig. 2 *Dermatoglyphic patterns of the propositus and his parents.*

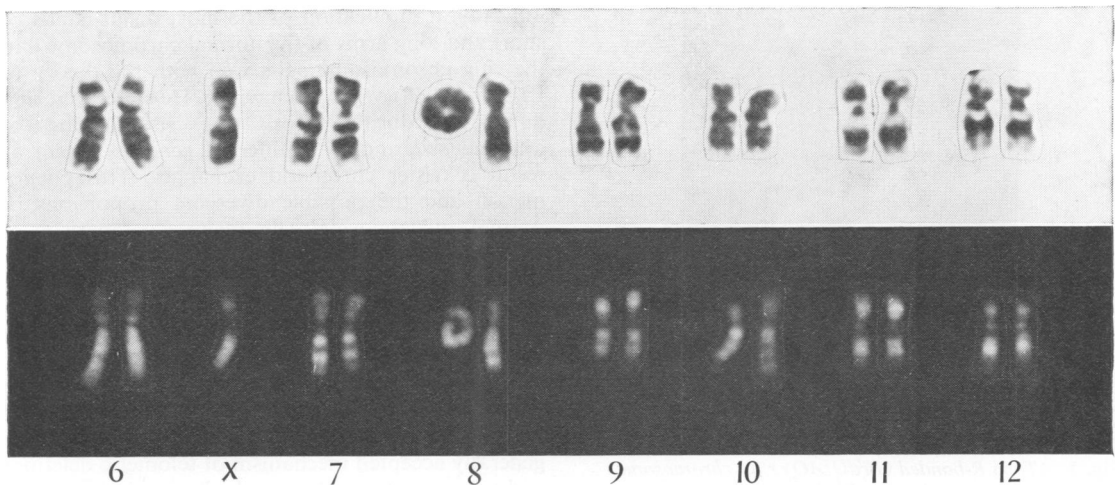

Fig. 3 *G-banding (above) and Q-banding (below) of the C-X chromosomes of the propositus.*

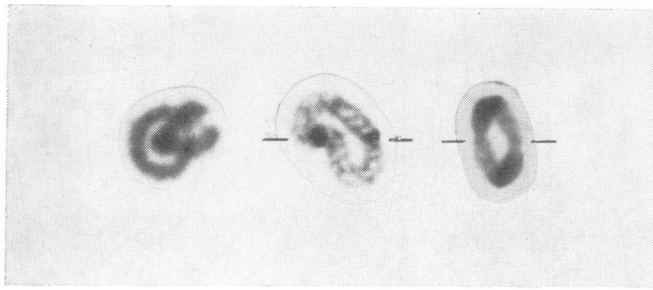

Fig. 4 *Three examples of dicentric ring chromosomes of the propositus: (a) orceine staining; (b) C-banding; (c) R-banding (note the distinct telomere bands of 8q).*

broken ends carrying the centromere. The results of the studies of Kunze *et al.* (1972) on the symptomatology of patients with a ring chromosome 18 support this theoretical mechanism. They found that a ring 18 syndrome cannot be exactly separated from the 18p– or 18q– clinical pictures and that in patients with a ring 18 chromosome the symptoms of both the deletion syndromes were overlapping. However, only three patients with a deletion of the short arm and none with a deletion of the long arm of chromosome 8 are known to us (Lubs and Lubs, 1973; Taillemite *et al.*, 1975; Orye and Craen, 1976). The features in common in these and our patient are, however, unspecific, and are seen in a wide variety of chromosomal disorders.

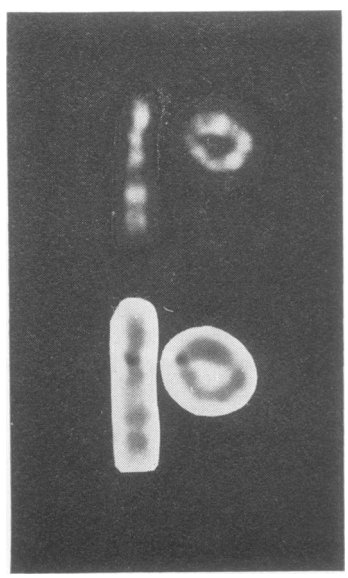

Fig. 5 *(Top) R-banded (BrdU/AO) ring chromosome and its normal homologue. (Bottom) Same chromosomes after C-banding.*

Nine case reports of unidentified C ring chromosomes are available from the literature, in two of which gonosomal origin could not be excluded. In 11 other patients described the ring was identified but was found to be derived from a C chromosome other than an 8. Only one patient with a ring 8 chromosome is known to us (Pfeiffer and Lenard, 1973). The phenotype of this patient does show some resemblance to the present case. Both have a low birthweight, short stature, a dolichocephalic skull, gothic palate, abnormal dentition, and micrognathia. Mental retardation seems to be more serious in our case.

Remarkably enough, in both patients most fibroblast cells have a normal karyotype so that in fact they are mosaics 46,XY/46,XY,8r.

The anaesthesia the mother of our proband underwent in the first month of her pregnancy during an appendectomy could be the cause of a mitotic disturbance early in embryogenesis giving rise to the abnormal cell line of the mosaic pattern.

The fact that the reflection photometer scanning indicated a duplication of the most distal bands of short and long arms of the normal chromosome 8 in the ring chromosome suits well with the theory of Lejeune (1968) on ring behaviour. He states that ring duplication during mitosis gives rise to rings of different size and with different genetic content as result of sister chromatid exchanges. This phenomenon and the possible divergent proportions of normal and abnormal cells make a comparison of the phenotypes of ring patients precarious.

An intriguing feature in the ring of the patient studied is the fact that the terminal bands of the long arms of the original chromosome appear to have been retained in ring formation.

H. E. Wyandt (1974, personal communication) found this in three other cases, where at least one end of the chromosomes appeared to be unaffected. The generally accepted mechanism of telomeric deletions and subsequent reunion, on the basis of this finding, needs revision or at least additional attention.

The authors are indebted to Dr J. B. Bijlsma (Amsterdam) for the reflexion photometer scanning and to Dr H. E. Wyandt (Portland) for carrying out the R-banding.

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References

Fraisse, J., Lauras, B., Ooghe, M. J., Freycon, F., and Rethoré, M. O. (1974). A propos d'un cas de chromosome 9 en anneau. Identification par denaturation ménagée. *Annales de Génétique*, **17**, 175-180.

Fried, K., Rosenblatt, M., Mundel, G., and Krikler, R. (1975). Mental retardation and congenital malformations associated with a ring chromosome 6. *Clinical Genetics*, **7**, 192-196.

Jacobsen, P., Mikkelsen, M., and Rosleff, F. (1973). A ring chromosome, diagnosed by quinacrine fluorescence as no. 9, in a mentally retarded girl. *Clinical Genetics*, **4**, 434-441.

Kistenmacher, M. L., and Punnett, H. H. (1970). Comparative behaviour of ring chromosomes. *American Journal of Human Genetics*, **22**, 304-318.

Kunze, J., Stephan, E., and Tolksdorf, M. (1972). Ring-Chromosom 18. Ein 18p−/18q− -Deletionssyndrom. *Humangenetik*, **15**, 289-318.

Lejeune, J. (1968). De la duplication de structures circulaires. *Annales de Génétique*, **11**, 71-77.

Lubs, H. A., and Lubs, M. L. (1973). New cytogenetic technics applied to a series of children with mental retardation. In *Nobel Symposia. Chromosome Identification Techniques and Applications in Biology and Medicine*, pp. 241-250. Ed. by T. Caspersson and L. Zech. Academic Press, New York.

Moore, C. M., Heller, R. H., and Thomas, G. H. (1973). Developmental abnormalities associated with a ring chromosome 6. *Journal of Medical Genetics*, **10**, 273-303.

Nakajima, S., Yanagisawa, M., Kamoshita, S., and Nakagome, Y. (1976). Mental retardation and congenital malformations associated with a ring chromosome 9. *Human Genetics*, **32**, 289-293.

Orye, E., and Craen, M. (1976). A new chromosome deletion syndrome. Report of a patient with a 46,XY,8p- chromosome constitution. *Clinical Genetics*, **9**, 289-301.

Pfeiffer, R. A., and Lenard, H. G. (1973). Ringchromosom 8 (46,XY,8r) bei einem debilen Jungen. *Klinische Pädiatrie*, **185**, 187-191.

Taillemite, J. L., Chanarond, J., Tinel, H., Mulliez, N., and Roux, Ch. (1975). Délétion partielle du bras court du chromosome 8. *Annales de Génétique*, **18**, 251-255.

Van den Berghe, H., Fryns, J. P., Cossiman, J. J., and David, G. (1974). Chromosome 6 en anneau. Caryotype 46,XY,r(6)/45,XY,-6. *Annales de Génétique*, **17**, 29-35.

Wurster-Hill, D. H., and Hoefnagel, D. (1975). Banding identification of chromosomal abnormalities in four patients: ring (6), translocation (2q−;15q+), translocation (21q;21q) and deletion (22q−). *Journal of Mental Deficiency Research*, **19**, 145-150.

Zackai, E. H., and Breg, U. R. (1973). Ring chromosome 7 with variable phenotypic expression. *Cytogenetics and Cell Genetics*, **12**, 40-48.

Zdansky, R., Andrle, M., Bühler, E., Tsuchimoto, T., Mayer, W. R., and Rett, A. (1975). Irregular phenotypic expression of ring-chromosomes. *Humangenetik*, **26**, 193-198.

An interstitial deletion of chromosome 9 in a girl with multiple congenital anomalies[1]

SUMMARY An infant with peculiar facies, coloboma of both eyes, and developmental retardation was found to have a *de novo* interstitial deletion of the secondary constriction and some adjacent euchromatin on one of her No. 9 chromosomes, del(9) (q11q21). Since studies on duplications, variants, and the molecular composition of the secondary constriction suggest that it contributes little if any information necessary to normal development, deletion of the euchromatin alone is most probably responsible for the clinical findings.

An extensive literature now exists on the various trisomies of chromosome 9 and their clinical significance (Sutherland *et al.*, 1976). In contrast relatively few data are available regarding deletions of this chromosome. Alfi *et al.* (1976) have studied 6 patients with deletions of the short arm distal to 9p22 and have found consistency in the resulting clinical malformations. Smith *et al.* (1973) reported a unique long arm deletion with associated persistent fragments in a severely malformed boy. In this case, specific identification of the deleted material was difficult. An institutionalised male with a 46,XY,9q− karyotype was reported by Newton *et al.* (1973). The deleted segment in this patient was identified as the secondary constriction. Ring chromosomes resulting from elimination of small amounts of distal chromosomal material have been reported by Jacobsen *et al.* (1973) and Kistenmacher *et al.* (1975).

We wish to report our observations on a child with a new deletion, one which resulted in loss of the secondary constriction and a small amount of adjacent euchromatin. The patient presented with developmental retardation and multiple congenital anomalies.

[1]This work was supported in part by the National Foundation—March of Dimes Grant No. 1-298.