

able for examination, but his paternal uncle showed the same peculiarity of his Y chromosome. The patient himself was an only child, and the paternal uncle was childless. At the other extreme, another patient in our series had a large Y chromosome of about the same size as an ordinary D chromosome. Possibly further examination of the meiotic chromosomes of our series will make it necessary to modify these interpretations, which were based mainly on the analyses of mitotic chromosomes.

A comprehensive report of this investigation will be published elsewhere.

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### HERMAPHRODITE WITH MOSAIC XX/XY/XXY

SIR,—In a recent review de Grouchy<sup>1</sup> compiles the following karyotypes described in true hermaphroditism: 46 XX, 46 XY, 46 XX/46 XY, 45 XO/46 XY, 46 XX/47 XXY, 46 XX/47 XXX, 46 XX/46 XY/45 XO, 46 XX/47 XXY/49 XXXYY, and 45 XO/46 X *iso*Y/47 XY *iso*Y.

We have studied the chromosomes of a true hermaphrodite with a new mosaicism, 46 XX/46 XY/47 XXY, which might throw some light on the possible multiple pathogenesis of this clinical entity.

A boy, aged 9 years, was seen in the endocrinological outpatient department of Hospital de San Pablo, Barcelona (Professor Vilaclara). He was an only child after 10 years of marriage. The family history was not contributory, and there was no history of miscarriages. The patient had a normal body proportion with masculine features. The external genitalia showed a phallus 1 cm. long, with a perineal urethra between two folds which resembled the labia majora. There was no vagina. Laparotomy revealed, on the right side, a gonad resembling an atrophic testis which was in the scrotum, and from which a biopsy specimen was taken. There was an ovary on the left which was removed. Pathological study confirmed an atrophic testis with poorly developed seminiferous tubules and germinal aplasia, and an ovary with primary follicles and normal ovarian stroma. Blood-group studies (R. R. Race and R. Sanger) did not reveal a double erythrocyte population.

Leucocytes from peripheral blood were cultured by the method of Moorhead et al.<sup>2</sup> with the following results:

Karyotype	No. of cells
46 XX	49
46 XY	8
47 XXY	7
	—
	64

Recently Gartler et al.<sup>3</sup> described a case of true hermaphroditism, with XX/XY mosaicism, possibly due to a double fertilisation demonstrated by two erythrocyte populations. In a similar case de Grouchy et al.<sup>4</sup> found a double type of haptoglobins indicating a possible double fertilisation.

Since in our case double fertilisation has not been proven by the erythrocyte studies, this mosaicism could perhaps result from an initial XXY zygote (resulting from a meiotic non-disjunction), with posteriorly a double mitotic loss of an X and a Y chromosome. Thus it is possible that a potential Klinefelter zygote (XXY) could evolve into true hermaphroditism during embryogenesis.

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- de Grouchy, J. *Sem. Hôp. Paris*, 1964, **40A**, 1088.
- Moorhead, P. S., Nowell, P. C., Mellman, W. J., Battips, D. M., Hungerford, D. A. *Exp. Cell. Res.* 1960, **20**, 613.
- Gartler, S. M., Waxman, S. H., Giblett, E. R. *Proc. natn. Acad. Sci. U.S.A.* 1962, **48**, 332.
- de Grouchy, J., Moulicc, J., Salmon, Ch., Josso, N., Frezal, J., Lamy, M. *Annls Génét.* 1964, **7**, 25.

### CHROMOSOMAL ANALYSIS IN HERMAPHRODITISM

SIR,—In 1963 we published a report of a chromosome analysis of the blood of a true hermaphrodite.<sup>1</sup> The interesting feature in this chromosome analysis was a chromosomal fragment in 84% of the cells analysed. Chromosomal fragments have been reported in other cases of hermaphroditism, and there has been considerable speculation as to whether the chromosomal fragment was genetically important. We have now succeeded in obtaining a chromosome analysis on the parents.

The father had a normal count with normal XY chromosomes. The mother's karyotype was a normal XX, but one cell did show the presence of a small chromosomal fragment, although it was felt to be quite insignificant in her genotype. Failure to find this fragment in either parent seems to exclude them as carriers, and suggests that its presence in the patient's cells is of no clinical significance.

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### PALM-PRINTS AND A RING-D CHROMOSOME

SIR,—Abnormal dermatoglyphics have been described in many patients with chromosomal aberrations.<sup>2,3</sup> The significance of these abnormal prints is not understood. I here present studies on the palm-prints of an infant girl with a ring-D chromosome. Because of the unusual occurrence of aplasia of the thumbs, these prints may provide a reference for interpreting abnormal friction-ridge patterns in other pathological conditions.

The child who has been fully described<sup>4</sup> was referred to the University of Michigan Medical Center because of multiple congenital anomalies, including microcephalus, holistic prosencephalon, ocular hypertelorism, ptosis of eyelids, epicanthal folds, malrotated right pinna, micrognathia, hypoplastic left nipple, interventricular septal defect, congenital hip dysplasia, widely spaced first and second toes, aplasia of thumbs, and failure to thrive. Leucocyte cultures revealed only five chromosomes in the D group (13-15) and a ring chromosome. The rest of the karyotype was normal.

The friction ridges of the patient's right palm are represented in figure b for comparison with a generalised schema of the normal configuration (figure a). Superimposed on the

- Lonsdale, D., Mercer, R. D., McCullagh, E. P. *Cleveland Clin. Q.* 1963, **30**, 207.
- Uchida, I. A., Patau, K., Smith, D. W. *Am. J. hum. Genet.* 1962, **14**, 345.
- Cummins, H. *Anat. Rec.* 1939, **17**, 407.
- Juberg, R., Adams, M. S., Venema, W., Hart, M. Unpublished.

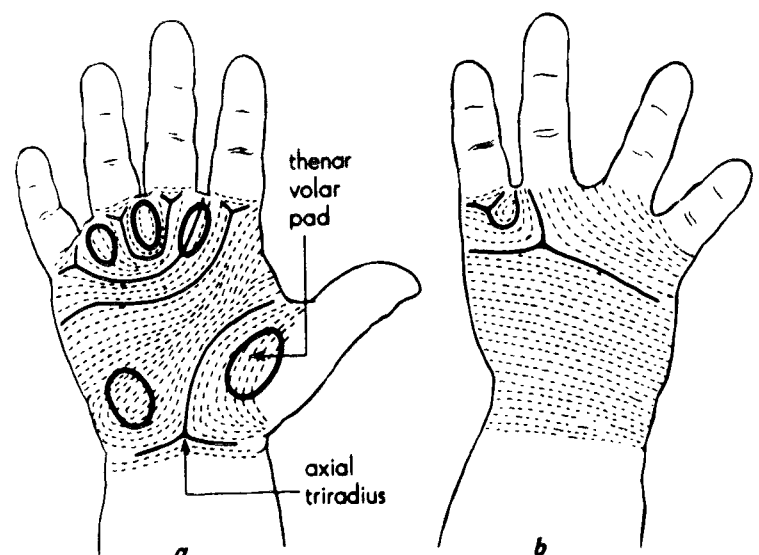


Diagram of palmar friction ridges on: (a) left normal hand, with volar pads of 10-week human foetus superimposed; (b) right hand of patient.

generalised drawing is the distribution of volar pads as found on the 6-13-week human embryo. On the patient's palm the axial triradius is missing, and the friction ridges course the hand horizontally.

The pattern of palmar friction ridges depends upon the size, shape, time of appearance, and time of regression of the embryonic volar pads.<sup>5</sup> There is considerable variation in these aspects of the volar pads. Embryos of this age showed that the developing friction ridges conformed to the contours of these dermal prominences, and that when the volar pads regressed the dermatoglyphics remained as a reflection of earlier reliefs.

The interaction of friction-ridge systems (related to volar pads) is thought to result in the particular dermatoglyphics of an individual. In this way loops, whorls, and arches are formed depending upon the relative contribution of ridges proliferative from opposing systems. There is normally a volar pad on the thenar eminence which did not develop in this patient's hand. The absence of this volar pad, and consequently the ridge system formed around it, has provided an opportunity to study the unopposed growth of the other ridge systems.

The most apparent manifestation of the interaction of opposite ridge systems is the formation of a triradius. It is accepted that a triradius represents the meeting of three such independent systems. In this patient, where one of these systems is absent, no triradius was formed. The axial triradius is occasionally absent in the prints of normal individuals,<sup>6</sup> and its absence has been recorded in association with various abnormal conditions.<sup>7</sup> But in these cases three ridge systems were present, and their failure to meet was due to an extremely longitudinal course of their ridge systems.

The general course of the palmar friction ridges is another indication of the forces active during the differentiation of the patterns. In the normal situation the ridges are diverted by elevations in their paths of formation, and are displaced by ridges centering on these elevations. This accounts for the usual vertical alignment of ridges on the palm. In our patient, however, there was no elevation at the thenar eminence, thus allowing the ridges to proliferate horizontally rather than be diverted into the long axis.

These considerations emphasise the importance of physical forces, coincident with other developmental processes, in shaping the configuration of friction ridges. Many separate (although probably related) gene sequences control these developmental processes. It is not surprising that statistical studies have shown dermatoglyphics to be controlled by a number of additive genes.<sup>8</sup>

This discussion suggests that the abnormal dermatoglyphics seen in pathological traits such as chromosomal aberrations should be considered as reflections of physical forces coincident with the many disturbed gene sequences controlling the differentiation of the entire hand or foot. They are further evidence of the genic imbalance imposed by aneuploidy or structural aberration.

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#### A MONGOL CHILD WITHOUT TRISOMY G

SIR,—Neither the letter from Dr. Kahn and Dr. Cowie (Aug. 21) nor their camera-lucida drawings add any further evidence to their claim that they have found a new chromosome complement related to Down's syndrome; and until this is forthcoming I still maintain that the most reasonable explanation for their finding is that provided by the classical G<sub>21</sub>/G interchange, with an anomaly of the short arm of a G chromosome in the father and one brother. At present there is absolutely no evidence that the abnormal chromosome seen in the father is a deleted F-group chromosome. In fact, the little

that can be seen from the photographs provided in the original article by Dr. Kahn and Dr. Cowie (July 10) suggests that the short arms are elongated and heterochromatic—a typical picture seen in some G chromosomes with enlarged short arms. Autoradiographic studies might help to settle this question.

Assuming that we are in fact considering a case of Down's syndrome—and the evidence for this in the original article is not conclusive—the most reasonable explanation is that made in my previous letter (July 24) and mentioned again above. It is now up to Dr. Kahn and Dr. Cowie at least to provide reasonable evidence for their alternative hypothesis, for this raises a fundamental question on the causation of Down's syndrome by primary or interchange G<sub>21</sub> trisomy—an aetiology which is supported by the weight of cytogenetic and clinical evidence collected over the past seven years in many laboratories. The establishment of a different chromosome complement associated with Down's syndrome thus requires more extensive clinical and cytogenetic data than have so far been provided.

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#### NEONATAL JAUNDICE IN DOWN'S SYNDROME

SIR,—In 1961, Zuelzer and Brown<sup>1</sup> reported "prolonged and sometimes severe jaundice in mongolian idiots in early infancy", but concluded that "it remains to be seen whether this is a significant association". Their observation has been often cited in connection with neonatal jaundice; little attention, however, has been paid to severe neonatal jaundice in mongolism.

During 1961 and 1962 I examined routinely 2870 newborn in the obstetric clinics of the Universities of Sassari and Ferrara, and noticed a high incidence of hyperbilirubinæmia in newborn mongols. I found severe jaundice with serum-bilirubin levels above 15 mg. per 100 ml. in 124 of 2863 non-mongol, and in 5 of 7 mongol, newborn—a significant difference.

Since 1963, I have examined 6629 newborn in the obstetric clinic of the University of Pavia. Of these 12 had a clinical diagnosis of Down's syndrome. 2 were excluded because of their high degree of prematurity; the remaining 10 had weights ranging between 4 lb. 14 oz. (2200 g.) and 9 lb. 9 oz. (4350 g.) (mean 6 lb. 11½ oz. [3050 g.]) and gestation-times ranging between 226 and 296 days (mean 277 days). A control group was assembled by selecting, for every mongol infant, 4 normal ones of the same sex and of strictly similar weight (mean weight 6 lb. 12 oz. [3070 g.], mean gestation-time 271 days). In both mongol and non-mongol groups the course of bilirubinæmia has been followed from the 2nd to the 6th day of life. The mean of the highest levels of bilirubin (per 100 ml. serum) reached in each case was 15.2 mg. ± 5.1 for the mongol group, and 8.1 ± 4.2 for the control group. The difference is significant (P < 0.01).

Some hæmatological investigations were performed including glucose-6-phosphate-dehydrogenase determination, and isoantibody and erythrocyte incubation tests: the only relevant finding was that the mean hæmatocrit value was significantly higher (P < 0.05) in the newborn mongols. The relevance of this finding to the neonatal jaundice is not immediately obvious.

Naiman et al.<sup>2</sup> have suggested that the red-cell lifespan may be shortened in mongol idiots. This would easily explain neonatal hyperbilirubinæmia; but in 6 newborn mongols I measured red-cell lifespan and found their <sup>51</sup>Cr t<sub>1/2</sub> to range between 20 and 31 days. Similar data have been reported by Kaplan et al.<sup>3</sup> in full-term normal newborns. It seems therefore that shortened erythrocyte-survival can be excluded as a major causative factor of neonatal jaundice in these cases, and that mongol hyperbilirubinæmia can be considered metabolic rather than hæmolytic in nature.

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5. Cummins, H., Midlo, C. *Finger Prints, Palms and Soles*; p. 183. New York, 1961.

6. *ibid.* p. 173.

7. Wolf, U., Brehme, H., Reinwein, H. *Humangenetik*, 1964, 1, 149.

8. Holt, S. B. *J. forens. Sci. Soc.*, 1963, 4, 7.

1. Zuelzer, W. W., Brown, A. K. *Am. J. Dis. Child.* 1961, 101, 87.  
2. Naiman, J. L., Oski, F. A., Mellman, W. J. *Lancet*, 1965, i, 821.  
3. Kaplan, E., Hsu, K. S. *Pediatrics*, Springfield, 1961, 27, 354.