any recognized abortions. From the point of view of genetic counselling, it is desirable that the proportion of conceptions which will have unbalanced karyotypes be established. Before the birth of the proposita it would have been reasonable to suppose, from the evidence in generation III, that unbalanced karyotypes were likely to occur with low incidence or not at all. It should be remembered that Jacobs (1972) has shown that the incidence of unbalanced karyotypes is low or nil in families in which the reciprocal translocation has not been ascertained through an abnormal individual. The present family, ascertained through the chromosomally abnormal propositi, provides an example of a translocation in which unbalanced zygotes are produced, but the incidence cannot be calculated. Therefore, prenatal chromosome diagnostics through amniocentesis should probably be advocated in future pregnancies of the translocation carriers or their spouses.

This study was aided by grants from the Sigrid Jusélius Foundation, the Finnish National Research Council for Medical Sciences and the Ella and Georg Ehrnrooth Foundation.

ALBERT DE LA CHAPELLE, MAILA KOIVISTO, and JIM SCHRÖDER

Folkhälsan Institute of Genetics, Helsinki and the Department of Paediatrics, University of Oulu, Oulu, Finland

REFERENCES

Caspersson, T., Zech, L., Johansson, C., and Modest, E. J. (1970). Identification of human chromosomes by DNA-binding fluorescent agents. *Chromosoma*, **30**, 215–227.

Jacobs, P. A. (1972). Human population cytogenetics. In *Human Genetics. Proceedings of the Fourth International Congress of Human Genetics*, ed. by J. de Grouchy, F. J. G. Ebling, and I. W. Henderson, pp. 232–242. Excerpta Medica, Amsterdam.

Paris Conference (1971). Standardization in human cytogenetics. *Birth Defects: Original Article Series*, **8**, pt. 7, pp. 1–46, 1972. The National Foundation, New York.

Seabright, M. (1971). A rapid banding technique for human chromosomes. *Lancet*, **2**, 971–972.

Shaw, M. W., Cohen, M. M., and Hildebrandt, H. M. (1965). A familial 4/5 reciprocal translocation resulting in partial trisomy B. *American Journal of Human Genetics*, **17**, 54–70.

Cryptophthalmos in Two Families from Bahia, Brazil*

Summary. Two families with cryptophthalmos are reported. Both families came from the same town in Bahia State, Brazil. Consanguinity was known between the parents themselves, but not between the individual families reported here. However, a common ancestor for both families is very likely because the four parents were born in the same 'municipio'. There was one affected girl in family 1 and four affected sibs in family 2. A pair of affected monozygotic twins and a case of possible low expressivity of the syndrome are described in family 2.

Congenital fusion of eyelids was described by Zehender and Manz (1872) as an isolated anomaly. In 1969, François made an extensive review of the subject showing that cryptophthalmos is not a localized malformaton but a syndrome characterized by cryptophthalmos, anomalies of the head, ears, nose, syndactyly, and genital abnormalities. Up to 1969 there were 43 cases reported in the world literature (Ide and Wollschlaeger, 1969). No chromosomal anomalies have been demonstrated, but parental consanguinity has been observed in 15% of the cases and it has therefore been suggested that autosomal recessive inheritance is likely (François, 1969). In the present paper we report two affected families from Bahia State in Brazil.

Received 1 November 1972.

* This work was supported by the Conselho Nacional de Pesquisas (CNPq) TC 10343 and TC 11503.

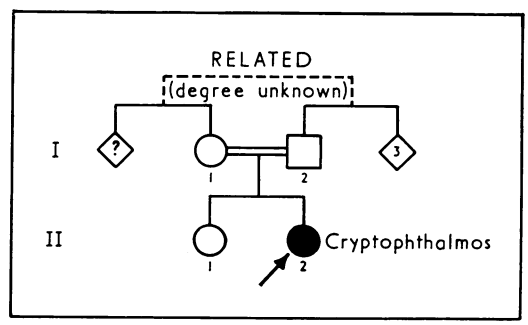

FIG. 1. Pedigree of family 1.

Family Reports

Family 1

Case 1 (A.L.J., II.2, Fig. 1). A mulatto female was born with bilateral cryptophthalmos and was first seen at the age of one month. Her eyes were small (Fig. 2), had an abnormal shape, and the distance between them was increased. Eye movements were present with some indication of light perception. Eyelashes and eyebrows were absent. The frontal hairline was high in the centre, but laterally extended towards the orbits. Her nostrils were elongated upward. There was a longitudinal fissure extending down the midline to include the nose, upper lip and tongue. The palate was high. Both ears were normal in shape and size but low set. Skull radiology was normal. Her chest was normal apart from the nipples which were widely spaced. There was syndactyly between the second, third, and fourth fingers on both hands with a typical simian crease on the right hand and an atypical one on the left. Syndactyly was also present on both feet from the second to the fifth toes. The clitoris was enlarged but otherwise the genitalia were normal.

The patient was the second child of a young couple (Fig. 2). The pregnancy and delivery were uneventful. The first child was said to be normal, but was not

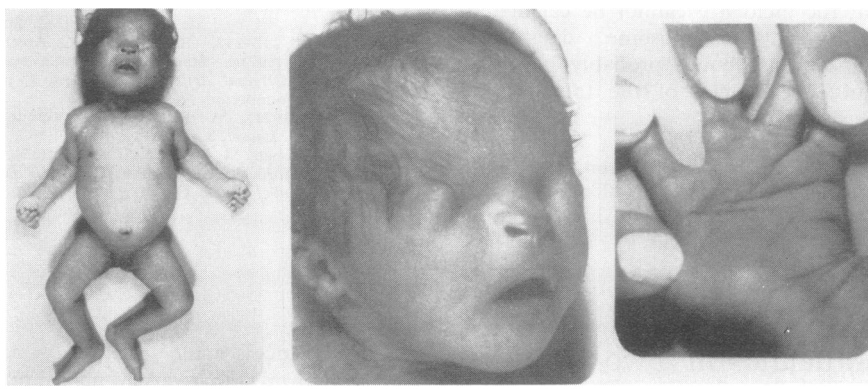

FIG. 2. Case 1 (family 1) at 30 days of age.

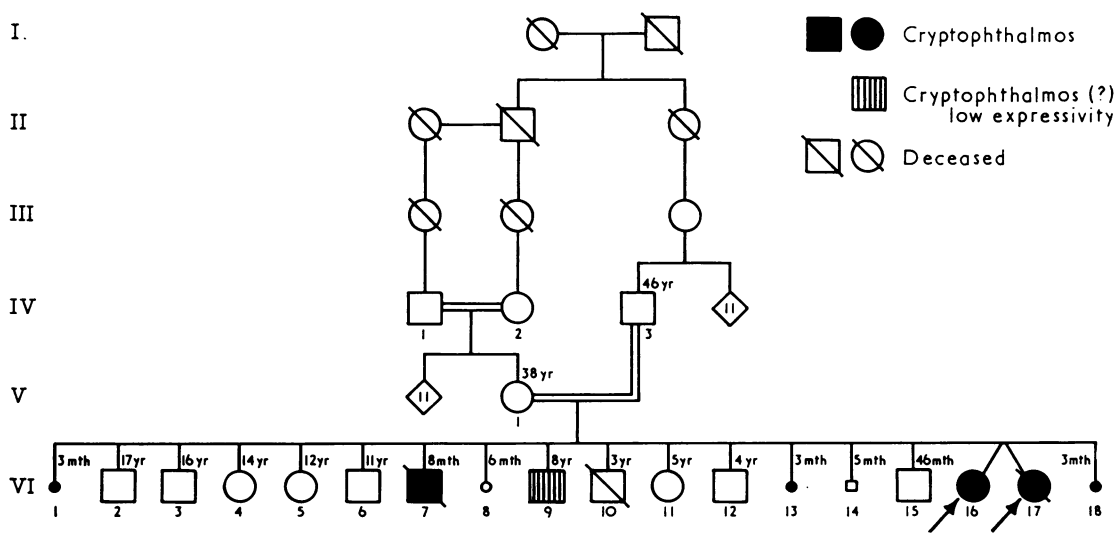

FIG. 3. Pedigree of family 2.

examined by us. The parents said they were related to each other but were unable to state the precise degree of relationship.

Family 2 (Fig. 3). Female mulatto twins (Figs. 4 and 5) were first seen at the age of two days.

Case 1 (M.C., VI.16). Bilateral cryptophthalmos was present. Her facial abnormalities were very similar to those found in case 1, family 1, except for the presence of a line of fine hair along the facial midline. Eye movements were present, but there was no indication of light perception. Her ears were abnormal and low set. The hands were grossly abnormal due to syndactyly uniting all her fingers. There was a single crease on the fifth finger of both hands. On her feet there was mild syndactyly, the second and third toes being fused. Examination of the genitalia showed that the clitoris was enlarged.

Case 2 (N.C., VI.17). The second twin had cryptophthalmos on the left side. Her right eye had no upper lid, the skin of the forehead being directly attached to the sclera. She had neither eyelashes nor eyebrows on either side. The visible part of the right eye was heavily opaque. All these findings agree well with François' description (1969) of 'abortive cryptophthalmos'.

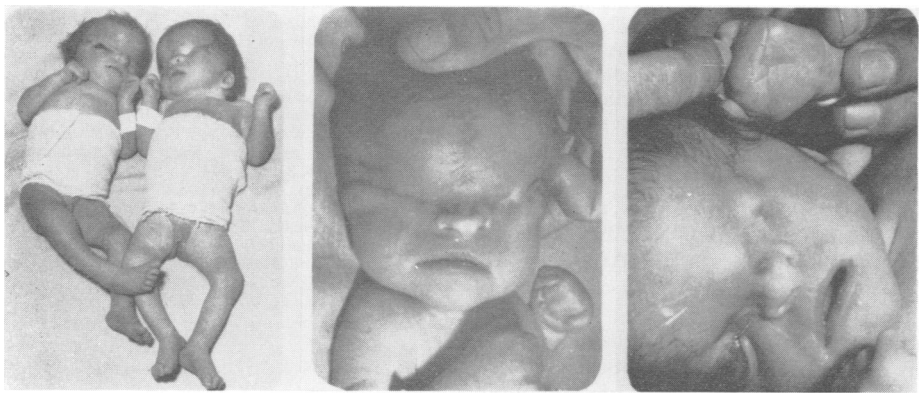

FIG. 4. Twin girls, cases 1 and 2 (family 2).

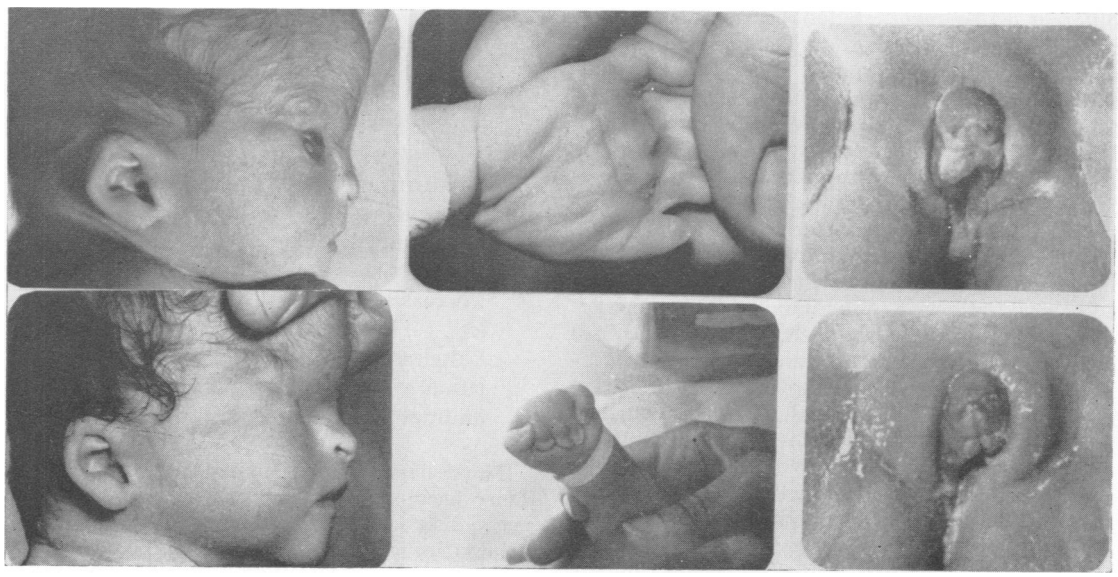

FIG. 5. Cases 1 and 2 (family 2).

The abnormalities of ears, nose, genitalia, hands, and feet were similar in both twins.

Case 3 (J.C., VI.9). An 8-year-old male brother of the twin girls. He did not have cryptophthalmos but there was flattening of the supraorbital ridges with pseudohypertelorism, cleft palate, abnormal teeth, unilateral cryptorchidism, and syndactyly. Assuming autosomal recessive inheritance these findings suggest either that he was a homozygote with less severe manifestation or a heterozygote.

Case 4 (G.C., VI.7). A stillborn male delivered prematurely. From his parents' description it seems likely that he had bilateral cryptophthalmos, syndactyly, and genital abnormalities.

Family History showed that the parents were second cousins once removed and the mother's parents were first cousins. Clinical examination (by E.S.A.) of all individuals shown in the pedigree did not disclose any abnormality. The mother said that the abortions (VI.8 and VI.14) did not show any features to suggest the syndrome.

Discussion

The twins in family 2, their parents, and two normal sibs were studied for ABO, DCEce, MN, P, Kell, and Duffy blood types. The ABO and MN were segregating allowing an overall estimation of 0·976 probability for monozygosity.

The clinical descriptions of the cases reported by Key (1920), Ashley (1947), Gupta and Saxena (1962), Sugar (1968), François (1969), and Ide and Wollschlaeger (1969), together with those described here, show cryptophthalmos to be a syndrome with a wide range of expressivity. In addition, the finding of different ocular manifestations in the monozygotic twins suggests that genetical factors alone do not account for this syndrome. The anomalies described in case 3 in family 2 may represent one of the mildest cases of the syndrome so far reported. Unfortunately, there is no way available to investigate whether the case with mild anomalies is one of low expressivity in a homozygous individual or partial manifestation in a heterozygous one.

The finding of consanguinity between the parents in both families increases the evidence favouring autosomal recessive inheritance. Both families came from the same town in the State of Bahia, had different family names, and were not known to be related. However, their birthplace was within the same 'municipio'. Because the kinship coefficient is higher for individuals born at shorter distances in this region, north-eastern Brazil (Azevêdo, 1969), it is easier to assume a common ancestor for both families than to admit independent mutations.

We are grateful to Dr G. Corney for reading and commenting on the manuscript and to Professor George Fraser and Dr Salma Assemany for providing us with references and copies of some papers on cryptophthalmos. Miss Elisabeth Peixoto and Mr Braz Orrico are gratefully acknowledged for typing the manuscripts and drawing the pedigrees, respectively.

ELIANE S. AZEVÊDO, JESULINO BIONDI, and LUIZ M. RAMALHO

Laboratory of Medical Genetics, Department of Preventive Medicine, Hospital Prof. Edgard Santos, Federal University of Bahia, Brazil

REFERENCES

Ashley, L M. (1947). Bilateral anophthalmos in a brother and sister. *Journal of Heredity*, **38**, 174–176.

Azevêdo, E. S. (1969). *Erythrocyte Isozymes, other Polymorphisms, and the Coefficient of Kinship in North-Eastern Brazil.* PhD Thesis, University of Hawaii.

François, J. (1969). Syndrome malformatif avec cryptophtalmie. *Acta Geneticae Medicae et Gemellologiae*, **18**, 18–50.

Gupta, S. P. and Saxena, R. C. (1962). Cryptophthalmos. *British Journal of Ophthalmology*, **46**, 629–632.

Ide, C. H. and Wollschlaeger, P. B. (1969). Multiple congenital abnormalities associated with cryptophthalmie. *Archives of Ophthalmology*, **81**, 638–644.

Key, S. M. (1920). Report of a case of cryptophthalmia. *American Journal of Ophthalmology*, **3**, 684–685.

Sugar, H. S. (1968). The cryptophthalmos-syndactyly syndrome. *American Journal of Ophthalmology*, **66**, 897–899.

Zehender, W. and Manz (1972). Eine Missgeburt mit hautüberwachsenen Augen oder Kryptophthalmus. *Klinische Monatsblätter für Augenheilkunde*, **10**, 225–249.

The Genetic Variability of Thalassaemia. A Family Study

Summary. Two step-brothers, homozygotes for β-thalassaemia, have been studied. One of them showed the characteristics of Cooley's anaemia, whereas the other was almost symptomless. The existence of two different β-thalassaemic genes is discussed in relation to the haematological and clinical findings.

The thalassaemia syndromes are a group of hereditary haemolytic anaemias due to a more or less severe disorder in haemoglobin synthesis (Weatherall and Clegg, 1972). Molecules of the main human

Received 8 June 1973.