shown to have lungs with a smaller alveolar surface area and therefore presumed smaller capillary surface area,² which may predispose to the delayed clearance of lung fluid. That the effusion was a transudate is borne out by the scanty leucocyte count and protein content lower than plasma protein level.

Standard textbooks do not report an association of pleural effusions and chromosomal abnormalities, though Chernick and Reed³ commented on the association of chylothorax and Turner's syndrome and Yoss and Lipsitz⁴ reported chylothorax occurring in two infants with Down's syndrome.

Repeated needle aspiration is likely to be successful in ultimately controlling the reaccumulation of fluid. The insertion of a chest drain is therefore probably not justified in view of the hazards of infection and possible potentiation of high protein fluid loss.

We thank Miss Judith Simpkin of the Liverpool Congenital Malformations Registry for carrying out the literature search, Mr Ken Walters for the medical illustrations, and Mrs Dorothy Bolger for typing the manuscript.

References

- Yancy WS, Spock A. Spontaneous neonatal pleural effusion. *Pediatr Surg* 1967;2:313-9.
- Cooney TP, Thurlbeck WM. Pulmonary hypoplasia in Down's syndrome. *N Engl J Med* 1982;307:1170-3.
- Chernick V, Reed MH. Pneumothorax and chylothorax in the neonatal period. *J Pediatr* 1970;76:624-32.
- Yoss BS, Lipsitz PJ. Chylothorax in two mongoloid infants. *Genet* 1977;12:357-60.

Correspondence and requests for reprints to Dr Neena Modi, Regional Intensive Care Unit, Liverpool Maternity Hospital, Oxford Street, Liverpool L7 7BN.

Homozygosity in piebald trait

M A HULTÉN*, M M HONEYMAN*, A J MAYNE†, AND M J TARLOW†

*Regional Cytogenetics Laboratory, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST and †East Birmingham Teaching Unit and Department of Paediatrics and Child Health, University of Birmingham, Birmingham B15 2TT.

SUMMARY A severely affected child born to consanguineous parents is interpreted as being a homozygote for the dominantly inherited piebald trait. The striking phenotypic difference between the parents and the child implies intermediate inheritance of this condition, and the family also illustrates that consanguinity should not always be taken to indicate genetic heterogeneity and recessive inheritance.

Mendel defined a dominant character as one with identical or almost identical expression in the heterozygote and the homozygote.¹ A relevant comparison may be difficult in man as matings between heterozygotes may be rare and, in addition, a difference in phenotype may remain undetected because of early homozygote lethality. Thus, many human conditions classified as dominant may in fact be intermediately inherited, but there are comparatively few examples where heterozygotes have been

differentiated from the homozygote.²⁻⁴ We present here an Asian family with partial and complete albinism illustrating these points.

Case report

The proband and his family came from north-east Pakistan. He was born at term and weighed 3.2 kg. At birth he was noted to be an albino, but no other neonatal problems were reported. Over the subsequent months there was concern about his development, in particular his lack of response to sound and his slow motor development. He was admitted to hospital with a suspected febrile fit while visiting relatives in the UK at nine months of age. His growth was satisfactory (weight 10th to 25th centile, length 50th centile, head circumference 25th centile). He was hypotonic with poor head control, could not sit unsupported, and still possessed a primitive grasp reflex. He made no response to sound, hardly vocalised, and was considered totally deaf by his relatives. An EEG showed lack of physiological activity suggesting severe brain impairment. Apart from complete absence of hair and skin pigmentation and blue irides he showed some facial

dysmorphism, including severe brachycephaly, broad nasal root, synophrys, long philtrum, and full lower lip (fig 1a, b). The family returned to Pakistan before further investigations could be performed.

Family history

The proband was the second child of the marriage.

His older brother's development and hearing were said to be normal but he had depigmented skin patches. The father (fig 1c) and a number of other relatives (example in fig 1e) had a white forelock and patchy skin depigmentation without associated deafness. None of these family members have been examined. The full pedigree is shown in fig 2. The mother who accompanied the child appeared to

FIG 1 (a, b, c, d, e) The photographs of the proband (a, b) were taken during admission to hospital while those of his father (c), mother (d), and uncle (e) are from the family album. Note total albinism, broad nasal root, synophrys, bulbous tip to nose, full lower lip, and brachycephaly in the proband with absence of dysmorphic features in either parent. The white forelock is obvious in the father, but it is not seen in the mother because she has dyed her hair. The depigmented skin patches on the thigh and scalp are clearly seen in the uncle as a young child.

FIG 2 Family pedigree showing the proband (arrowed) and nine presumptive heterozygotes including his parents who are first cousins.

have a normal facial appearance (fig 1d). Only when pressed did she admit that she and her husband were first cousins and that in fact she had some depigmented skin patches on her thighs and had disguised her white forelock by dyeing her hair.

Discussion

In this report we have presented a Pakistani child with complete absence of skin, hair, and eye pigmentation, some facial dysmorphism, congenital deafness, and severe general developmental delay. His first cousin parents, who were of normal intelligence, both had a white forelock and patchy skin depigmentation, and the same features occurred in several other members of this Asian family (fig 2). These features indicate a dominantly inherited disorder such as piebald trait or Waardenburg syndrome.^{5,6}

The combination of white forelock and skin depigmentation is characteristic of both these disorders. The location of the depigmented patches in the affected family members did not discriminate with certainty between them. None of the family members had the additional typical features of Waardenburg syndrome (lateral displacement of the inner canthi, broad prominent nasal root, hyperplasia of the medial portion of the eyebrows or heterochromia irides) and deafness was only reported in the proband. Although Waardenburg syndrome has been described without dystopia canthorum (type II), the high penetrance of white forelock through three generations as documented by photographs from the family album is unusual in Waardenburg syndrome (either type I or type II).^{7,8}

We therefore believe that piebald trait is the most likely diagnosis.

We suggest that the reason for the child's severe clinical picture is that he has inherited the defective gene from both parents and is thus a homozygote. As we are certain that both parents are gene carriers we gave a 1/2 risk that any future child would have a similar phenotype as themselves and a 1/4 risk of having a severely affected child. From a pragmatic genetic counselling point of view, therefore, the severe defect is 'recessively inherited'.

Piebald trait is a classical example of a dominant disorder in man. The case described here has such a different phenotype from his parents that it would be difficult to accept this as an extreme variation in heterozygote expression and thus this child may represent the first example of homozygosity in this condition. Implicit in this argument is that the condition is inherited intermediately rather than as a true dominant. The same may well hold true for most other disorders in man classified as dominant but this may escape detection when the homozygote trait is lethal.

This family also illustrates the notion that consanguinity in itself is not necessarily an indication of recessive inheritance, albeit the risk of homozygosity is increased. It would be of interest to review cases where consanguinity between apparently unaffected parents has been taken to indicate a recessive form of a disorder previously recognised as dominant. Perhaps in some of these instances the impression of genetic heterogeneity is false and could simply be caused by the intermediate expression of one and the same gene defect with full expression in the homozygote. Had it not been for

the obvious white forelock in the father (or had he also dyed his hair), we might have concluded that we too were dealing with a new recessive pigmentary disorder with retardation and deafness.

Recombinant DNA techniques may in the future identify individual members of this family at the genotypic rather than the phenotypic level and this would be one way to investigate further the assumption that the proband is a homozygote in contrast to his heterozygote relatives. These methods may also help to clarify the genetic relationship between the recognised subtypes^{7 8} and the alleged recessive form^{9 10} of Waardenburg syndrome and separate these from the piebald trait, which may have a confusingly similar phenotype.^{5 11}

References

- ¹ Bateson W. *Mendel's principles of heredity*. London: Cambridge University Press, 1909:53, 324.
- ² Pauli RM. Dominance and homozygosity in man. *Am J Med Genet* 1983;**16**:455–8.
- ³ Hirschhorn K. Dominance and homozygosity in man. *Am J Med Genet* 1984;**18**:541.
- ⁴ McKusick VA. *Mendelian inheritance in man*. Catalog of autosomal dominant, autosomal recessive, and X-linked phenotypes. 6th ed. Baltimore, London: Johns Hopkins University Press, 1983.
- ⁵ Comings DE, Odland GF. Partial albinism. *JAMA* 1966;**195**:519–23.
- ⁶ Waardenburg PJ. A new syndrome combining developmental anomalies of the eyes, eyebrows and nose root with pigmentary defects of the iris and head hair with congenital deafness. *Am J Hum Genet* 1951;**3**:195–253.
- ⁷ Arias S. Genetic heterogeneity in the Waardenburg syndrome. *Birth Defects* 1971;**IV**(7):87–101.
- ⁸ Hageman MJ, Delleman JW. Heterogeneity in Waardenburg syndrome. *Am J Hum Genet* 1977;**29**:468–85.
- ⁹ Farndon RA, Bianchi A. Waardenburg's syndrome associated with total aganglionosis. *Arch Dis Child* 1983;**58**:932–3.
- ¹⁰ Shah KN, Dalal SJ, Desai MP, Sheth PN, Joshi NC, Ambani LM. White forelock, pigmentary disorders of irides, and long segment Hirschsprung disease: possible variant of Waardenburg syndrome. *J Pediatr* 1981;**99**:432–5.
- ¹¹ Reed WB, Stone VM, Boder E, Ziprkowski L. Pigmentary disorders in association with congenital deafness. *Arch Dermatol* 1967;**95**:176–86.

Correspondence and requests for reprints to Dr M Hultén, Regional Cytogenetics Laboratory, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST.