Short communication

Journal of Medical Genetics (1976). **13**, 62-63.

A note on the inheritance of the hereditary persistence of fetal haemoglobin and the δ -chain variant Hb-A₂'

The most common form of the condition known as the hereditary persistence of fetal haemoglobin (HPFH) is characterized by a continued synthesis of Hb-F and an absence of β - and δ -chain synthesis by the chromosome carrying the HPFH determinant. This conclusion is based on observations made in homozygotes who produce Hb-F only; in subjects heterozygous for the β -chain variant Hb-S and for the HPFH condition who produce Hb-S, Hb-F, a decreased amount of Hb-A₂ and no Hb-A₁; and in one subject who is heterozygous for the HPFH condition and the δ -chain variant Hb-A₂', producing Hb-F, Hb-A, Hb-A₂', and no Hb-A₂ (Huisman *et al*, 1971; Huisman, 1972). Recently we were able to study a large family in which the HPFH anomaly and the Hb-A₂' variant occurred separately and in combination with each other, thus allowing a further evaluation of the inheritance of these two conditions.

The family consisted of the parents, three sons, and five daughters. Blood samples were analysed by routine haematological procedures using a Coulter Counter Model S. Haemoglobin in red cell haemolysates was analysed by starch gel electrophoresis at pH 9.0 (Efremov *et al*, 1969), by an alkali denaturation procedure to determine the percent Hb-F (% F_{AD} (Betke *et al*, 1959)), and by DEAE-Sephadex chromatography to quantitate the levels of Hb-A₂ and Hb-A₂' (Huisman and Dozy, 1965; Dozy *et al*, 1968). The data are given in the Table. The father appears to have a HPFH heterozygosity and the mother a heterozygosity for the δ -chain variant Hb-A₂'. Three of their children are normal, one has the Hb-A₂' heterozygosity, two have the HPFH heterozygosity, and two have the HPFH heterozygosity as well as the Hb-A₂' heterozygosity. The level of Hb-A₂ in

TABLE
HAEMATOLOGICAL AND HAEMOGLOBIN
COMPOSITION DATA ON FAMILY MEMBERS

	Age	Hb (g/dl)	PCV	RBC ($\times 10^{12}/l$)	F _{AD} (%)	A ₂ (%)	A ₂ ' (%)
Father	58	12.7	38	4.31	21.5	2.2	0
Mother	52	11.9	36	4.03	1.0	1.3	1.1
Son	27	13.5	40	4.79	0.6	2.7	0
Daughter	25	12.2	37	4.05	1.1	2.4	0
Daughter	23	13.7	41	5.00	21.7	0	2.0
Daughter	20	12.1	36	4.27	0.6	1.7	1.3
Daughter	19	11.9	36	4.68	21.0	1.7	0
Son	18	14.1	42	4.89	23.4	1.6	0
Son	15	12.9	39	5.05	21.7	0	1.8
Daughter	12	11.9	35	4.41	0.7	2.7	0

the three normal family members (2.4, 2.7, and 2.7%) is comparable to that of the sum of Hb-A₂ and Hb-A₂' in the two Hb-A₂' heterozygotes (2.4 and 3.0%) and is distinctly more than that of Hb-A₂ in the HPFH heterozygotes (1.6, 1.7, and 2.2%) and of Hb-A₂' in the two persons with the Hb-A₂' HPFH condition (1.8 and 2.0%) who do not produce any Hb-A₂.

The complete absence of Hb-A₂ in the two individuals with the Hb-A₂'-HPFH combination confirms previously published, rather incomplete, data (Huisman *et al*, 1971) and offers additional evidence that δ -chain production is absent on the chromosome carrying this HPFH determinant.

These studies were supported in part by US Public Health Service Research Grants HL-01568 and HL-15158.

T. H. J. HUISMAN,* MARSHA E. GRAVELY,*
and ROBERT SOX†

* Laboratory of Protein Chemistry, and Comprehensive Sickle Cell Center, Medical College of Georgia, Augusta, Georgia 30902, USA.

† South Carolina State Board of Health, Columbia, South Carolina, USA.

REFERENCES

- Betke, K., Marti, H. R., and Schlicht, I. (1959). Estimation of small percentages of foetal haemoglobin. *Nature*, **184**, 1877-1878.
- Dozy, A. M., Kleihauer, E. F., and Huisman, T. H. J. (1968). Studies on the heterogeneity of hemoglobin. XIII. Chromatography of various human and animal hemoglobin types on DEAE-Sephadex. *Journal of Chromatography*, **32**, 723-727.
- Efremov, G. D., Huisman, T. H. J., Smith, L. L., Wilson, J. B., Kitchens, J. L., Wrightstone, R. N., and Adams, H. R. (1969). Hemoglobin Richmond, a human hemoglobin which forms asymmetric hybrids with other hemoglobins. *Journal of Biological Chemistry*, **244**, 6105-6116.
- Huisman, T. H. J. (1972). Normal and abnormal human hemoglobins. *Advances in Clinical Chemistry*, **15**, 149-253.
- Huisman, T. H. J. and Dozy, A. M. (1965). Studies on the heterogeneity of hemoglobin. IX. The use of tris-(hydroxymethyl)-aminoethane-HCl buffers in the anion-exchange chromatography of hemoglobins. *Journal of Chromatography*, **18**, 160-169.
- Huisman, T. H. J., Schroeder, W. A., Charache, S., Bethlenfalvay, N. C., Bouver, N., Shelton, J. R., Shelton, J. B., and Apell, G. (1971). Hereditary persistence of fetal hemoglobin. Heterogeneity of fetal hemoglobin in homozygotes and in conjunction with β -thalassemia. *New England Journal of Medicine*, **285**, 711-716.

Announcements

Data on cytogenetic registers

The International Advisory Committee on Cytogenetic Registers to the Standing Committee on Standardization in Human Cytogenetics was charged with the responsibility of compiling, updating, and publishing a list of cytogenetic registers, together with summaries of aims, objectives, and key elements. The committee has developed a form for the collection of such data and invites individuals who operate Cytogenetic Registers (either in isolation or as part of a larger register system) to write for these data forms as soon as possible to Dr James R. Miller, Department of Medical Genetics, The University of British Columbia, Vancouver, B.C., V6T 1W5, Canada.

Eighth Stadler Genetics Symposium

The eighth Stadler Genetics Symposium will be held in the University of Missouri, 9-10 April 1976. Information and detailed programmes can be obtained by writing to: Conferences and Short Courses, University of Missouri, 347 Hearnes Building, Columbia, MO 65201, U.S.A.

Teratology Society: 1976 Annual Meeting

The Teratology Society will hold its Sixteenth Annual Meeting 20-23 June 1976 at Highlands Inn, Carmel, California, U.S.A.

Further information can be obtained by writing to Dr Lucille S. Hurley, Department of Nutrition, University California, Davis, California 95616, U.S.A.