Haemoglobin H disease in Arabs in Kuwait

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SYNOPSIS  Three cases of haemoglobin H disease are described in Arabs, two of Syrian and one of Kuwaiti origin. Two were investigated on account of moderate anaemia, the third for splenomegaly not associated with anaemia.

Haemoglobin H disease was first reported in Greeks (Gouttas, Fessas, Tsevernis, and Xefteri, 1955) and Chinese (Rigas, Koler, and Osgood, 1955). In the Middle East haemoglobin H has been found in Trans-Jordanians (White, Beaver, and Ellis, 1956), in Oriental Jews (Ramot, Sheba, Fisher, Ager, and Lehmann, 1959), in Kurdish Jews, and in Jews originating from eastern Turkey (Horowitz, Cohen, Goldschmidt, and Levene, 1966). It has not been reported previously from the Gulf area.

Haemoglobin H, which has a beta_4 molecule (Jones and Schroeder, 1963), tends to be unstable and to precipitate as granules in the older red cells. It is best demonstrated by using brilliant cresyl blue which exaggerates the precipitation of the denatured haemoglobin H to form small round granules inside the red cells. Lehmann and Huntsman (1966) have suggested that this test is more sensitive than electrophoresis for demonstrating haemoglobin H. One (case 2) of the three cases of haemoglobin H disease to be described was found amongst 29 cases of thalassaemia major of 2,680 cases referred to this section for haematological investigation during 1967. This, however, may be an exaggeration of the frequency owing to preliminary screening in the clinics.

METHODS AND MATERIALS

The patients and their relatives were bled by venepuncture. The haemoglobin was estimated in duplicate as cyanmethaemoglobin using Drabkin's solution and a whole blood standard (Hyland). Blood films were stained by Leishman's method. For the haemoglobin H test a few drops of blood were placed in a 1% solution of brilliant cresyl blue in saline (Gouttas et al, 1955), incubated for one hour at 37°C, and the films made. Alkali-resistant haemoglobin was determined by the one-minute technique (Singer, Chernoff, and Singer, 1951). Electrophoresis was carried out on a cellulose acetate strip in a Beckman micro-zone tank using a barbitone buffer at pH 8.6. Other standard haematological examinations were performed according to the methods described by Dacie and Lewis (1963).

CASE 1  N.M.H., aged 8 years, the son of Syrian parents, presented with a history of crises during which marked anaemia developed. At the time of examination the spleen was just palpable but there was no jaundice. Haemoglobin was 9.9 g/100 ml (68%), PCV 36%, reticulocytes 12%; leucocyte and platelet counts were normal. The blood film showed slight macrocytosis with hypochromasia, anisopoikilocytosis, target cells, and small fragmented red cells (Fig. 1A). Haemoglobin F was not detected but granules of haemoglobin H were found in more than 50% of the red cells (Fig. 1B). The whole family was investigated (Fig. 2). No haemoglobin H was found in the parents or sisters but his father had a slightly increased level of haemoglobin F (3%).

CASE 2  S.F.B., a young Syrian, was referred during her second pregnancy for investigation of anaemia not responding to iron or other haematinics. Previously she had given birth to healthy twins. On examination she looked anaemic and appeared to be more distressed by it than would be expected by the haemoglobin level found. The spleen was not enlarged. Haemoglobin was 8.2 g/100 ml (56%); reticulocytes 8%. A blood film showed marked anisopoikilocytosis, hypochromasia, target cell formation, fragmentation of the red cells, and basophilic stippling (Fig. 1C). Haemoglobin F was not detected. Haemoglobin H preparations showed the characteristic stippling in
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**FIG. 1.** A (case 1) and B (case 1). The red cells with anisocytosis, poikilocytosis, target change, fragmentation, and hypochromasia (Leishman’s stain). Arrow shows fragmented red cell. C (case 2) and D (case 2), showing the typical HbH inclusion bodies. (Brilliant cresyl blue stain.) × 1,000.
about 10% of the red cells. No haemoglobin H was detected in either of her children but her parents were not available for investigation.

CASE 3  G.A.R., a Kuwaiti male aged 25 years, was sent for investigation on account of splenic enlargement and weakness for one year. Haemoglobin was 12 g/100 ml (82%), white blood cells 8,400/cmm, reticulocytes 7%. A blood film showed anisopoikilocytosis, hypochromasia, target change, and fragmented red cells. No haemoglobin F was detected on electrophoresis and a sickling test was negative. In haemoglobin H preparations about 70% of the red cells contained the characteristic granules. His mother was investigated but appeared to be normal haematologically and neither haemoglobin H nor haemoglobin F was detected in her blood. The father was not available for investigation.

DISCUSSION

The frequency of haemoglobinopathies in the immigrant populations in Britain is well recognized (Beard and Signy, 1965). Beaven, Dixon, and White (1966) investigated 352 immigrants and found 8·3% of the patients from the near and middle east had thalassaemia. In their series they did not detect a single case of haemoglobin H disease, but suggested that patients with persistently abnormal haematological findings, including a low haemoglobin A₂ level, may be considered as possible bearers of the alpha thalassaemia trait. It has been suggested that the gene for haemoglobin H does not express itself unless it is associated with the alpha thalassaemia gene (Motulsky, 1956). Lehmann and Huntsman (1966) suggested that the additional gene which converts alpha thalassaemia into haemoglobin H disease is infrequent in Great Britain. They also mention that there is less formation of haemoglobin H during a period of iron deficiency but that once the deficiency is corrected the red cells can be shown to contain haemoglobin H. It appears now that the additional gene required for haemoglobin H formation is not rare in the Gulf area, so that all the cases of thalassaemia should be screened for this abnormal haemoglobin. Further, as some cases of beta thalassaemia have a very high level of alkaline-resistant haemoglobin (HbF) the gene for high foetal haemoglobin may also be frequent in this area.

I am grateful to Professor Lehmann and his staff of the MRC Abnormal Haemoglobin Research Unit in Cambridge for the examination of blood samples from case 1 and some of his relatives; to Professor W. M. Davidson for help in preparation of the MSS; to Dr Signy, Director of the Group Laboratories, St Stephen's Hospital, for his advice; to my clinical and other colleagues who referred the cases to me and gave me technical assistance.

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doi: 10.1136/jcp.22.2.226

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