Discussion

The final cause of persistent priapism is thought to be thrombosis of the dorsal veins draining the corpora cavernosa into the pelvic plexus of veins. The initial cause may be spasm of the erectile musculature, or possibly trauma, which could occur during coitus. Thrombosis of the corpora appears to be delayed for some time, and this delay can be prolonged indefinitely by anticoagulant therapy. Resolution may occur in the early stage by relief of the muscular spasm. This is presumably what occurred in the second case in the earlier attacks. After thrombosis has occurred resolution can be achieved only by recanalization of the dorsal veins, and this, too, may occur spontaneously after a considerable time, as in the case quoted by Tripe (1845). If the thrombosis persists, the rational approach to the problem would appear to be a direct attack on the vein to perform a disobliterative operation. This would be a very difficult and uncertain procedure. The problem is simplified if the thrombus could be persuaded to move on into a part of the pelvic venous plexus where it does not produce such drastic effects. This is presumably what happens after forcible massage, the dorsal veins being cleared of thrombus, allowing adequate drainage to occur.

In our second case the disobliteration of the vein was produced after 30 days, and this resulted in a partial recovery of normal function. I feel that if the procedure had been attempted earlier a better result might have been possible.

Summary

Two cases of persistent priapism are presented. The first resolved after five days on anticoagulant treatment alone. The second partially resolved after 30 days on anticoagulant therapy followed by forcible massage of the penis under general anaesthesia.

It is suggested that this non-operative method of management should be tried in the early stages of the condition.

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The Pakistan Medical Research Council has now established the quarterly *Pakistan Journal of Medical Research*. The chairman of the editorial board is Dr. M. JAFAR, and the editor Dr. M. M. SIDDIQ HUSAIN. The overseas subscription rate is 24 Pakistan rupees (£1 16s.) a year, and inquiries should be sent to the Editor-Secretary, Director, Bureau of Laboratories, Government of Pakistan, Karachi Cantt.

HAEMOGLOBIN H DISEASE WITH PERSISTENT HAEMOGLOBIN "BART'S" IN AN ORIENTAL JEWESS AND HER DAUGHTER

A DUAL ALPHA-CHAIN DEFICIENCY OF HUMAN HAEMOGLOBIN

BY

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Haemoglobin H was discovered in 1955 (Rigas, Koler, and Osgood, 1955; Gouttas, Fessas, Tseveren, and Xefteri, 1955), and its appearance in the phenotype is associated with the inheritance of thalassaemia (Motulsky, 1956). Oriental Jews are known to harbour the thalassaemia gene, particularly those from Kurdistan (Schieber, 1945; Matoth, Shamir, and Freundlich, 1955). We can now report the finding of haemoglobin H disease (haemoglobin H thalassaemia) in a Babylonian (Iraqi) Jewess and her daughter. The case presents two further points of interest. There was a decreased glutathione stability of the red cells in the mother, and, in addition to haemoglobin H, an abnormal foetal haemoglobin "Bart's" (Ager and Lehmann, 1958) was present in both mother and daughter.

Case Report

A 40-year-old Jewish woman from Bagdad was sent to the Tel Hashomer Hospital because of dizziness and increasing fatigue for the previous six months. There was no contributory history, and the patient had never been jaundiced. On physical examination the only positive findings were pallor and hepatosplenomegaly, both liver and spleen being palpable for two fingerbreadths below the costal margin. No skeletal abnormalities were found on x-ray survey.

Blood Examination

Plasma: serum proteins were normal in amount and distribution (paper electrophoresis). Serum lability (liver-function) tests showed nothing abnormal. Serum bilirubin: total 1.1 mg./100 ml., direct 0.4 mg./100 ml. Serum iron 165 µg./100 ml. White cells: total count 6,200/c.mm.; differential count normal. Red-cell count 4,540,000/c.mm.; haemoglobin 7.7 g./100 ml.; P.C.V. 34%; M.C.V. 75 cubic microns; M.C.H. 17 µg.; M.C.H.C. 23%; reticulocytes 7.8%. Inclusion bodies were seen in the red cells on incubation with brilliant cresyl blue. Osmotic fragility was reduced and the bone-marrow showed an erythrocytic hyperplasia. The stained smear (Fig. 1) showed marked poikilocytosis, many target cells, and 4 nucleated red cells per 100 white cells. Coombs test was negative. Glutathione stability was reduced: 27 mg./100 ml. red cells; glucose-6-phosphate dehydrogenase activity 9.1 OD units/g. haemoglobin (Szeinberg, Sheba, and Adam, 1958).

Haemoglobin.—The haemoglobin was examined by paper and starch electrophoresis, the first at pH 8.6 and at pH 6.5, the latter at pH 8.8. On paper electrophoresis three fractions were seen in the position of A, Bart's, and H (Fig. 2). On starch electrophoresis it was seen that

haemoglobin A₂ was present. On eluting the various fractions it was seen that Bart's amounted to 8% and H to 5%. Haemoglobin A₂ amounted to 1%. In the one-minute alkali denaturation test of Singer, Chernoff, and Singer (1951) on three different occasions 4.5, 5.7, and 3.5% respectively of the total haemoglobin was found to be alkali-resistant. Almost all of this could be accounted for by the Bart's component, which has about half the alkali resistance of haemoglobin F in this test. On chromatography in "amberlite IRC 50," however, traces of

FIG. 1.—Red cells of propositus. (Leishman. $\times 1,000$.)

FIG. 2.—Comparison by hanging-strip paper electrophoresis at pH 8.6 of haemoglobin A plus H and the patient's haemoglobin. In the patient's sample three components are visible—A, Bart's, and H. The strip was photographed unstained.

haemoglobin F could be demonstrated. The amount was the same or perhaps slightly more than that seen by this method in normal bloods.

Family Study.—The patient's sister had erythrocytes of the thalassaemia minor type: 4,460,000/c.mm.; haemoglobin 9.9 g./100 ml.; P.C.V. 30%; reticulocytes 4.4%; alkali-resistant haemoglobin 1.7% (just within the normal limits); serum iron 133 μ g./100 ml. Of the patient's four children, two (one son and one daughter) showed no abnormality; one daughter showed as the only abnormality 3.16% alkali-resistant haemoglobin in the one-minute test. The fourth child, a daughter, presented with a very similar blood picture to that found in her mother. Inclusion bodies were more numerous on incubation of the red cells with brilliant cresyl blue. On electrophoresis, haemoglobin A, Bart's, and H were found, but the proportion of H was greater than that of Bart's. On elution the first amounted to 9% and the second to 4%. Virtually no haemoglobin F was found.

Discussion

Haemoglobin H has mostly been found in people of Mongoloid extraction, the only non-Mongoloid popula-

tion in which this pigment has been seen with some frequency being Greeks. Similarly, haemoglobin Bart's has mostly been seen in Mongoloids and also in some Greek infants. The present case is the first instance of a haemoglobinopathy other than thalassaemia in a Jewish person. Haemoglobin H has been shown to consist purely of one of the two polypeptide chains forming the normal adult haemoglobin. Of the two, alpha and beta, only the second is present in haemoglobin H. Haemoglobin H is haemoglobin A without the alpha-chain (Jones, Schroeder, Balog, and Vinograd, 1959). Haemoglobin F has the same alpha-chain as haemoglobin A (Hunt, 1959), but the second chain is so different from the beta-chain that it has been called gamma-chain (Schroeder and Matsuda, 1958). Haemoglobin Bart's is the foetal equivalent of haemoglobin H; it consists solely of gamma-chain polypeptide and can be considered to be haemoglobin F with the alpha-chain missing (Hunt and Lehmann, 1959). As haemoglobins A and F share the same alpha-chain one would expect a deficiency of the alpha-chain to cause H to be found in adults and Bart's in infants. Infants with haemoglobin Bart's, however, do not form haemoglobin H when they grow up, and haemoglobin Bart's has been seen without H in a 14-year-old boy with thalassaemia (Choremis, Zannos-Marioleas, Ager, and Lehmann, 1959). Thus it might seem that the formation of the adult and foetal alpha-chains is controlled independently.

The present findings, however, suggest that the difference in the alpha-chain deficiency is quantitative rather than qualitative. While, for example, in the propositus suppression of the foetal alpha-chain is virtually complete, that of the alpha-chain production for haemoglobin A is much less, and more than 80% of the total haemoglobin consists of haemoglobin A. Furthermore, the presence of the two alpha-chain-deficient haemoglobins H and Bart's in a mother and her daughter while none of the other three children of the propositus has inherited either of these two singly, strongly suggests that the alpha-chain deficiency is one single genetic defect.

If the twofold alpha-chain deficiency is indeed the outcome of a single cause one would expect to find the combination of haemoglobin H with haemoglobin Bart's more often. There is an indication that this might indeed occur. A noteworthy difference between haemoglobin F and the adult haemoglobins is its high isoleucine content (Schaaf and Huisman, 1955). This must obviously be due to a high isoleucine content of the gamma-chain. It is therefore difficult to understand that Huisman (1959) found haemoglobin H—now known to be the beta-chain tetramer—to be unusually rich in isoleucine. Huisman had prepared his haemoglobin-H fraction by starch slab electrophoresis where H and Bart's are difficult to separate, and at a time when haemoglobin Bart's had not yet been discovered. The high isoleucine content of his haemoglobin fraction might therefore have been due to an undetected admixture of Bart's with the gamma-chain tetramer.*

*In a study of 415 cord bloods from Thailand by S. Tuchinda, C. Varenil, P. Bhanchit, and V. Minnich (*Pediatrics*, 1959, 16, 43) haemoglobin Bart's was found in 22 (two of the infants were twins). One infant with haemoglobin Bart's had a sister with haemoglobin H. On the other hand, the authors refer to a paper which is in preparation on "two 'fast' haemoglobin components found in thalassaemia hemoglobin H disease," and in their present paper they state that the abnormal foetal haemoglobin seen in the 22 babies has the properties of the second "fast" component which they had found in some patients together with haemoglobin H.

The decreased glucose-6-phosphate dehydrogenase deficiency in the propositus has probably no bearing on her haemoglobinopathy. It is found in about 20% of Iraqi Jews, and its presence in this patient can be presumed to be a coincidence.

Summary

Haemoglobin H disease in a Jewish woman from Bagdad is described. This is the first record of a haemoglobinopathy other than thalassaemia in a person of Jewish descent. In addition to haemoglobin H the abnormal foetal haemoglobin Bart's was found, and the significance of this association is discussed. One of the woman's four children also had haemoglobin H disease in association with haemoglobin Bart's.

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COMPARISON OF TWO ANALGESICS IN THE PROPHYLAXIS OF POST-EXTRACTION PAIN

BY

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A new synthetic, benzmethoxazone (Boehringer, Ingleheim), was presented to us as a mild analgesic of the aspirin type. Reported work showed that it had a relatively slow clearance rate and that adequate blood levels were maintained for more than half as long again as with acetylsalicylic acid (Beisenherz *et al.*, 1957).

Pain after extraction of teeth is a common complaint, and such a compound appeared to offer advantages for its relief, provided its pain-killing potency was at least as good as that of other analgesics in common use.

In this department it has been routine practice to give patients a small supply of codeine compound tablets following a difficult extraction, so a blind trial was set up to compare the new substance with this preparation.

The benzmethoxazone was made available under the name Ap. 674 as standard tablets of the same size, shape, and colour as the codeine compound tablets but containing 250 mg. of benzamethoxazone, 300 mg. of phenacetin, and 50 mg. of caffeine.

The analysis depends on the post-operative pain which some patients have been found to experience during the first 48 hours following the extraction of teeth.

The comparative trial reported here was made on 1,000 patients: 500 were given codeine compound tablets and 500 were given Ap. 674.

Method

A record of each patient was kept on a punched card. The patients involved were routine adult cases attending the local anaesthetic department requiring extraction of teeth.

Each patient involved in the series had two tablets just before the operation; further tablets for the post-operative period were given in an envelope with written instructions and a printed and stamped postcard on which to record the post-operative symptoms. The patients were asked to place a cross opposite the amount of pain experienced—none, mild, or severe. Those patients attending in the morning were to take 2 tablets at 4 p.m. and 2 at 10 p.m. The afternoon patients were to take two tablets at 9 p.m. In other words, each patient had two tablets between five and seven hours after their extraction. Cards posted more than 48 hours post-operatively were analysed separately, and the results are not included in this article.

In any one group of three consecutive patients one had no tablets, one had codeine compound tablets, and one had Ap. 674. The cards and appropriate tablet packets were numbered in series as the patients entered the clinic. The operator punched the index card while the local anaesthetic was given time to act, and at the same time gave the patient routine instructions.

Results

The postcard was returned adequately completed by 90.1% of the patients within 48 hours of the extraction. A further 6.3% returned the card at a later date. No account was taken of the latter group in this report, as it was felt that post-operative infection could confuse the issue after 48 hours had elapsed.

Table I shows a simple analysis of all patients. In the series of 500 patients taking no analgesic or placebo only 336 (67.2%) returned the postcard. Though the default of one-third of these patients is likely to make the "severe" group appear larger, the figures are included for the sake of completeness. Table II is a percentage analysis of cards returned derived from Table I. Though it would appear that the codeine compound was more effective, analysing the 3 × 2 table of codeine compound against Ap. 674 by a chi-square test it is found that $\chi^2=3.73$ with two degrees of

TABLE I.—Analysis of All Patients

	Pain			No Return Made	Total
	None	Mild	Severe		
Codeine compound tablets	268	156	19	57	500
Ap. 674	258	168	32	42	500
No tablets	137	160	39	164	500