TABLE II.—*Injected Cases: Number of Days Elapsing Between Entry into Trial and Injection*

		Class 1		Class 2	
		Neuro- tomized	Unneuro- tomized	Neuro- tomized	Unneuro- tomized
No. of cases Entry- injection interval (days)	Maximum	22	14	7	3
	Average	85	148	204	25
	Interval	21.4	22.1	93	18
	Minimum	4	0	12	16

the unneurotomized, but here the total of 21 patients, injected and uninjected, was too small for this comparison to be very significant.

Uninjected cases numbered 14. In class 1 they represent one "success" out of a possible 23 for neurotomy and two "successes" out of a possible 16 for doing nothing; in class 2, five "successes" out of a possible 12 for neurotomy and six out of a possible nine for doing nothing. The follow-up periods, for what little they are worth with so few cases, can be compared in Table III; the three

TABLE III.—*Uninjected Cases: Length of Follow-up*

		Class 1		Class 2	
		Neuro- tomized	Unneuro- tomized	Neuro- tomized	Unneuro- tomized
No. of cases Length of follow-up (days)	Individuals	1	2	5	6
	Maximum	250	321	—	—
	Average	—	322	314	271
	Minimum	—	—	189	125

patients in class 1 all happened to enter the trial before any of the 11 in class 2, which is the only reason why they were followed up longer.

The patient needing bilateral treatment said when first interviewed, and again on the day of his right-sided neurotomy, that the left side needed treatment rather more than the right, so that it was for left-sided injection, as we thought, that he was admitted to hospital. He then said, however, that the right-sided pain had become worse than the left, and asked for a right-sided injection, which was given. About three and a half months later he began to have a bout of severe left-sided pain, which continued for two to three weeks and then abated. During that bout he asked for left-sided injection, but changed his mind before it could be given. Thereafter until his latest follow-up, 322 days after entry, his left-sided pain was not severe enough to make him want injection.

In all of those 12 cases in which the pain had both affected the tongue and been treated by neurotomy, it continued not only in the tongue but also in other structures, and in 10 out of the 12 cases injection was carried out.

A few neurotomized patients found the numbness in and round the ear unpleasant, especially when lying in bed with the affected area in contact with a pillow. The 29 neurotomized patients who required injection nearly all said in effect that neurotomy had been worth trying, but had made no difference whatever to their pain.

Comment

Controls apart, it would be hard to praise any treatment for tic douloureux which in 22 out of 23 severe cases left the patient in need of injection within 85 days.

The search for a cure without trigeminal sensory loss must continue, but each proposed new remedy ought, in the very first cases in which it is used, to be subjected to a controlled clinical trial. This precaution is especially necessary in any disease which is so chronic and remittent as tic douloureux. The two features of the present inquiry which we have found most valuable are (1) preliminary classification of the severity of each case by the patient himself, through his response to a standard offer of radical treatment, and (2) assessment of the efficacy of the method

under trial by the patient himself, through his decision when to undergo radical treatment. By these means, and with an adequate supply of patients; reliable results can be obtained within 12 months.

Summary

Between August, 1954, and May, 1955, 23 severe cases of tic douloureux, strictly diagnosed, were treated by great auricular neurotomy, and 16 other severe cases, comparable in all essentials with the first 23, were left untreated. In each of these 39 severe cases the patient when first interviewed had his name put on a waiting-list for trigeminal injection, which he was left free to postpone if his pain had abated enough. In 22 of the 23 neurotomized cases (95.7%) trigeminal injection had to be carried out at most 85 days later, and in 14 of the 16 unneurotomized (87.5%) it had to be carried out at most 148 days later. The average interval between entry into this clinical trial and injection was 21.4 days in the 22 neurotomized and 22.1 days in the 14 unneurotomized cases. One severe neurotomized case and one equally severe unneurotomized case, instructively, were on the right and left sides of a single patient. Twenty-one other patients with milder tic douloureux were similarly divided into 12 neurotomized and 9 unneurotomized and left to decide when they must undergo trigeminal injection, with similar results. Great auricular neurotomy, to judge from this trial, has no effect on tic douloureux.

We thank Mr. Wylie McKissock for encouraging us to do this work in his department, Professor A. Bradford Hill for valuable guidance and criticism, Professor T. Crawford and Dr. N. F. C. Gowing for microscopy of the excised portions of nerves, Miss Audrey Gear for her skill and patience in organizing the case records and the follow-up, and members of the almoners' department of the Royal South Hampshire Hospital for their prompt efficiency in tracing a psychiatrically ill patient who would otherwise have defaulted.

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HAEMOGLOBIN C DISEASE AND TRAIT REPORT OF A FAMILY IN ENGLAND WITH HAEMOGLOBIN C

BY

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Abnormal, genetically determined haemoglobins are being recognized with increasing frequency as the cause of certain anaemias, generally of the haemolytic type. Their discovery has followed the application of electrophoretic techniques to the study of sickle-cell haemoglobin (S) by Pauling, Itano, Singer, and Wells (1949). The other human haemoglobins so far described are A (adult), C, D, E, F (foetal), G, H, I, and J; and the list is doubtless incomplete. The hereditary haemoglobinopathies occur almost exclusively in people of non-European descent, and principally in negroes.

Haemoglobin C was described by Itano and Neel (1950). Their cases were North American negroes, and the haemoglobin C was in the heterozygous state, with A or S. Homozygous haemoglobin C (haemoglobin C disease) was reported, again in North American negroes,

by Spaet, Alway, and Ward (1953). Haemoglobin C was first reported from outside the U.S.A. by Edington and Lehmann (1954), who found a high incidence in negroes from the Gold Coast; and by Portier, Cabannes, Massonat, and Duval (1954) in negroes from Algiers. Huisman, van der Schaaf, and van der Sar (1955) reported haemoglobin C disease from Curaçao, in an apparently white family of German-Dutch origin (but with possible negroid ancestry) and also in negroes. In general, haemoglobin C is found in West Africans, and in places where it may have been introduced by them. Diggs, Kraus, Morrison, and Rudnicki (1954) have, however, described its occurrence in a white family, of Italian origin, in the U.S.A.

Homozygous haemoglobin C generally causes a mild anaemia, of the haemolytic type. Heterozygous haemoglobin C, if paired with A (haemoglobin C trait), is usually symptomless.

Case Report

Mrs. P., a West Indian negress, 2-para, aged 39, arrived from Jamaica, with her family, in July, 1955. Apart from one attack of malaria, in 1936, and high blood pressure during her first pregnancy (1949), she had always been healthy.

On October 28, 1955, she attended an antenatal clinic, being then 15 weeks pregnant. On routine blood testing she was found to have a haemoglobin of 10.5 g. per 100 ml. (71%); R.B.C., 3,470,000; P.C.V., 30%; M.C.V., 88 cubic microns; M.C.H.C., 35%; W.B.C., normal. The film showed large numbers of target cells.

At her next visit, on November 25, her haemoglobin had dropped to 8.7 g. per 100 ml., and there was some hypochromia. She was admitted to hospital for investigation.

On examination, pregnancy was normal for 20 weeks. The liver and spleen were enlarged to four and two finger-breadths below the costal margin, respectively. There was no complaint of joint pains, and no other physical abnormality. Urine: Albumin +; deposit: a few red blood cells and hyaline and granular casts. Culture: no growth; urobilin and urobilinogen not demonstrated. The serum bilirubin was 0.6 mg. per 100 ml.; alkaline phosphatase, 6 K.-A. units; thymol turbidity, 2 units; zinc sulphate turbidity, 14 units; total serum protein, 5.8 g. per 100 ml.

On December 7 her haemoglobin was 8.4 g. per 100 ml.; R.B.C., 3,100,000; P.C.V., 27%; M.C.V., 87 cubic microns; M.C.H.C., 31.1%; reticulocytes, 2.2%; W.B.C. normal in number, type, and distribution; platelets normal. The red cells showed anisocytosis, with some hypochromia and polychromasia. Target cells, 56%; "boat" cells present (Fig. 1). The red-cell fragility was greatly reduced, commencing at

0.40% saline and incomplete at 0.10% (control 0.50% to 0.35%). (See Fig. 2.) Coombs's tests were negative. Tests for sickling were negative. Electrophoresis showed haemoglobin C only (Fig. 3). The sternal marrow was active, erythropoiesis being partially megaloblastic (occasional megaloblasts to 37% normoblasts). Granulopoiesis was normal apart from a maturation arrest at the myelocyte to metamyelocyte stage. M:E ratio 1.3:1. Platelet formation was normal.

Iron and folic acid therapy was started, and the haemoglobin level rapidly improved to 10.8 g. per 100 ml., which was maintained.

At 36 weeks the patient was admitted to another hospital for toxæmia, and a macerated foetus was delivered at 38 weeks, no blood specimen being submitted for examination.

On July 6, 1956, the haemoglobin level was 14.7 g. per 100 ml., and she felt well. Target cells were approximately 50%.

FIG. 2.—Red-cell fragility curve of Mrs. P., showing the characteristic decrease in osmotic fragility.

FIG. 3.—Electrophoretic patterns of the P. family, and of Mrs. P.'s half-brothers. The continuous line indicates the starting-point.

Investigation of the Family

Haemoglobin C Trait.—In addition to the P. family, consisting of Mrs. P., Mr. P., and two children (a boy, R.P., aged 7½, and a girl Y.P., aged 6), two of Mrs. P.'s half-brothers now live in this country. Three other half-brothers and a half-sister live in Jamaica. Mrs. P.'s father is alive and well, in Jamaica. Her mother died during Mrs. P.'s infancy. None of her family has ever complained of ill-health.

Hematology.—Mr. P.: Haemoglobin, 13.6 g. per 100 ml.; no target cells; electrophoresis showed haemoglobin A only. The P. children: On February 20, 1956, R.P.'s haemoglobin was 10.2 g. per 100 ml., target cells 2%; Y.P.'s haemoglobin 11.5 g. per 100 ml.; target cells 2.4%. On July 6, after treatment: haemoglobin—R.P. 12.3 g., and Y.P. 13.4 g. per 100 ml. Electrophoresis: Both children showed a mixture of A and C. Mrs. P.'s half-brothers: Blood samples were kindly obtained for me by Dr. J. N. Marshall Chalmers. On electrophoresis one brother (N.K.) showed a mixture of haemoglobins A and C; the other (D.K.) showed A only (Fig. 3).

Electrophoresis.—This was carried out at pH 8.6, on filter-paper, by the method of Smith and Conley (1953). Our

FIG. 1.—Blood film of Mrs. P., showing the high proportion of target and boat cells. (×900.)

findings were kindly confirmed by Dr. H. Lehmann, of St. Bartholomew's Hospital, who also demonstrated 1.9% of foetal haemoglobin (F) in Mrs. P.'s blood. Haemoglobin C moves characteristically slowly at pH 8.6 (the slowest of all the haemoglobins so far described). It is readily denatured by alkali.

Discussion

Since Mrs. P. is homozygous (CC), both of her parents, who were pure-blooded negroes, must have had Hb C. The brothers K. have the same father but a different mother, and, since D.K. has Hb A only, the father must have heterozygous C (AC). Fig. 4 summarizes the genetic data available.

FIG. 4.—Incidence of haemoglobin C in the P. and K. families.

The characteristic haematological findings in haemoglobin C disease are: (1) marked reduction in the osmotic fragility of the erythrocytes; (2) numerous target cells, with boat cells (folded erythrocytes), in the blood film, owing to the abnormal thinness of the cells; (3) demonstration of haemoglobin C only, on electrophoresis. If the disease is in an active phase the features of a haemolytic anaemia are generally present in addition (anaemia, reticulocytosis, increase in serum bilirubin and faecal urobilin, etc.). All cases so far described have had enlarged spleens, and most have complained of joint pains.

The haematological findings in the case of Mrs. P. were complicated by her pregnancy. Although she was grossly anaemic her reticulocyte count was only 2.2%, and her serum bilirubin was normal. Marrow examination revealed a megaloblastic element. As she gives no history of previous ill-health attributable to anaemia the disease may not itself give rise to clinically detectable anaemia in her case. There must be many such persons, with virtually symptomless haemoglobin C disease, if estimates of the frequency of homozygous haemoglobin C are at all accurate. Terry, Motulsky, and Rath (1954) have suggested a frequency of 1 in 6,000 for CC, while Smith and Conley (1953) estimated the incidence of the C trait as 1 to 3%, in North American negroes. It would appear likely, therefore, that with the rapid increase of our negro population other cases of haemoglobin C disease must already be present in this country, and that we must be on the look-out for haemoglobinopathies in non-European patients with anaemia.

Summary and Conclusion

A Jamaican negress immigrant, found to be severely anaemic at routine antenatal investigation, proved to be a case of haemoglobin C disease (CC). Her husband has normal adult haemoglobin (A) only, and her two children have a mixture of A and C. Two of her half-brothers (co-paternal) have been investigated. One has heterozygous C (AC) and one A only.

The abnormal haemoglobins were demonstrated by electrophoresis on filter-paper at pH 8.6.

The characteristic diminished osmotic fragility of the erythrocytes and numerous target cells were well shown in this case.

An incidence of 1 in 6,000 has been suggested for haemoglobin C disease in North American negroes. This and other hereditary haemoglobinopathies should be considered when investigating non-European patients with anaemia.

I wish to thank Dr. H. Lehmann for his help and for confirming the results of electrophoresis; Dr. J. N. Marshall Chalmers for the blood specimens of the brothers K; Dr. J. D. Procter, the clinician in charge of the patient; and Mr. C. E. Vernon for the electrophoretic determinations. The first report of these cases, apart from the K. brothers, was made at a meeting of the Association of Clinical Pathologists in April, 1956.

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CARDIAC INFARCTION IN MALAYA

BY

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In the changing pattern of medicine in the tropics to-day the degenerative diseases, as elsewhere in the world, are found to be of growing importance. Before the second world war very little was written about cardiac infarction in South-East Asia, mainly because of the urgent need to study the important epidemic diseases, but also because cardiac infarction was still a young subject and because there were few electrocardiographs, without which investigations are unlikely to be carried out. Even to-day there is some difficulty in maintaining an electrocardiograph in good working order in a tropical climate, and servicing is not always possible.

In China an analysis of the incidence of disease in hospitals was given by Gear (1936), but heart disease was not common and degenerative heart disease not separately mentioned. In Canton Karcher (1936), whose patients were mainly female, analysed those who had heart disease. Only 2.1% were classified as having arteriosclerotic heart disease, but 17.7% had hypertensive disease. Snapper (1941) when working in China rarely encountered myocardial infarction. Tung (1948) saw nine patients with it at the Peiping Union Medical College Hospital in 1938-41 and nine patients in private practice in 1945-8. His opinion was that among Chinese, although hypertensive cardiovascular disease was prevalent, coronary thrombosis and angina pectoris were uncommon. Of his 18 patients, 15 were of the upper social and economic class.

In the Malaysian regions reports are also rare. Kouwenaar (1937) described a case, including a necropsy report, in a Javanese. Van Wesel (1939), in writing on cardiac infarction, reported five cases of coronary artery disease, but these were all in Europeans or Indo-Europeans. Soetano Tjokronegoro (1940) reported six