On March 24, 1956, the toxoplasmosis dye test was positive 1:256 and the C.F.T. 1:32. Repeat examination on April 3 gave positive results of 1:64 for the dye test and 1:32 for the C.F.T. Tests on her husband were negative.

Case 3

On March 16, 1956, a 36-year-old woman who worked as an assembler was seen in the out-patient department. She had noticed enlarged axillary glands since November, 1955, but had otherwise felt well. She was found to have enlarged axillary lymph nodes and a palpable spleen. Later, cervical and inguinal glands were also felt.

The blood count was normal. The E.S.R. in one hour was 9 mm. (Westergren) and the Paul–Bunnell test was negative. A lymph-node biopsy was performed and the histological report (Dr. D. Brewer) was: "An enlarged lymph node measuring 1.6 and 2.5 cm. It shows marked follicular lymphoid hyperplasia. It appears to be a reactive process. A prolonged search revealed no organisms."

On April 13 the toxoplasmosis dye test was positive to a titre of 1:64 and the C.F.T. to 1:8. Tests on this patient's daughter were negative.

Discussion

No history of contact with sick animals was obtained from any of these patients, though a cat was kept in two of the households. No specific treatment was given, as in each case the diagnosis was not made until the acute stage of the disease was over. *Toxoplasma gondii* is sensitive to sulphonamides, particularly sulphadiazine and sulphadimidine, and to pyrimethamine ("daraprim"), which appears to act synergistically with sulphonamides (Eyles, 1953).

There have now been numerous case reports of congenital toxoplasmosis and also of an increasing number of cases in adults. The three cases described here varied in acuteness and severity: the first two patients were ill, whereas the third complained only of lymph-node enlargement. None of these patients completely fulfils the serological requirements for diagnosis (Sabin *et al.*, 1952). However, the high titres in Cases 1 and 2, with the characteristic clinical picture, make the diagnosis of acute toxoplasmosis almost certain. In Case 3 the serological tests were done so long after the onset of lymphadenopathy that high values would not be expected.

The occurrence of the acute illness during the fourth month of pregnancy in Case 2 made foetal infection likely, but on May 11, 1956, she was delivered of a normal baby, which has since shown no signs of congenital toxoplasmosis. After birth the dye-test titre was 1:8 in the mother and 1:16 in the baby, and the C.F.T. in each was anti-complementary. On November 11 the dye test was positive to a titre of 1:8 in the mother and 1:4 in the baby and the C.F.T. was negative for each. These results probably indicate passive transference of immunity from mother to child and exclude active disease in the child.

Gard and Magnusson (1951) reported a case of acute illness in the first month of pregnancy associated with a dye-test titre rising to 1:4000. The child was normal, and the dye-test titre at 3 months was lower than at birth, indicating a passive immunity. Stanton and Pinkerton (1953) described the case of a woman who had cervical-gland enlargement in early pregnancy. Biopsy was performed and two pseudocysts were seen on histological examination of the material. The dye test for toxoplasmosis was positive in a titre of 1:1024 14 weeks after the onset of cervical-gland enlargement, falling to 1:64 after 43 weeks. Animal inoculation failed to reproduce the disease. The infant's dye test at birth was positive to a titre of 1:256. The child was normal and remained so. The authors suggested that the original toxoplasma infection of the mother might have occurred five years earlier when she had weakness, fever, lymphocytosis, and lymphadenopathy, and that the illness in pregnancy was an exacerbation of this.

Paulley *et al.* (1956) reported a normal pregnancy in a woman probably suffering from toxoplasmic myocarditis, but foetal infection would not be expected during the chronic stage of the disease in the mother. Sabin *et al.* stated that none of the 67 subsequent pregnancies in 45 mothers of congenitally affected children had shown evidence of toxoplasmosis. It has been assumed that transmission of disease to the foetus occurs during asymptomatic or unrecognized maternal infection in the early months of pregnancy. The cases reported here, and those of Gard and Magnusson and of Stanton and Pinkerton, show that infection of the child is not inevitable.

Summary

Three cases of illness with lymphadenopathy probably due to acute toxoplasmosis are described. In one the disease occurred in the fourth month of pregnancy and there has been no evidence of its transfer to the child. It is probable that acute toxoplasmosis is not so rare as is suggested by the comparatively small number of reported cases.

I thank Dr. Clifford Parsons and Dr. W. T. Cooke for permission to publish their cases and Dr. W. T. Cooke for advice and criticism. The serological tests were performed by Dr. I. A. B. Cathie, at the Hospital for Sick Children, Great Ormond Street, London.

REFERENCES

Eyles, D. E. (1953). *Amer. J. trop. Med. Hyg.*, **2**, 429.
Gard, S., and Magnusson, J. H. (1951). *Acta med. scand.*, **141**, 59.
Paulley, J. W., Jones, R., Green, W. P. D., and Kane, E. P. (1956). *Brit. Heart J.*, **18**, 55.
Sabin, A. B., Eichenwald, H., Feldman, H. A., and Jacobs, L. (1952). *J. Amer. med. Ass.*, **150**, 1063.
Stanton, M. F., and Pinkerton, H. (1953). *Amer. J. clin. Path.*, **23**, 1199.

HAEMOGLOBIN L: A NEW HAEMOGLOBIN FOUND IN A PUNJABI HINDU

BY

J. A. M. AGER, M.B., B.S.
Lecturer in Clinical Pathology, St. Thomas's Hospital, London

AND

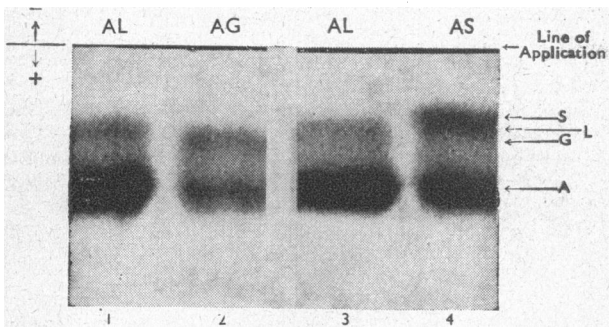
H. LEHMANN, M.D., Ph.D., F.R.I.C.
Senior Lecturer in Chemical Pathology, St. Bartholomew's Hospital, London

On examining the blood of an East Indian patient admitted to hospital for investigation of erythema nodosum it was seen that his haemoglobin consisted of two fractions. One of them was normal adult haemoglobin (haemoglobin A), and the other a minor component moving on paper electrophoresis at *p*H 8.6 more slowly than haemoglobin A. Six haemoglobins are known to move more slowly than haemoglobin A under these conditions; they are in order of increasing mobility C, E, S and D, G, F. The minor component of the patient's haemoglobin moved differently from all these. On paper electrophoresis in barbiturate buffer of *p*H 8.6 using a hanging-strip technique (for details see Lehmann and Smith, 1954) or horizontal paper electrophoresis between glass plates (for details see Smith and Conley, 1953), and on zone electrophoresis using starch blocks (Kunkel and Wallenius, 1955; for details see Kunkel, 1954), the abnormal component moved between haemoglobin S (or D) and haemoglobin G (See Figure).

Following paper electrophoresis the separated fractions were dried on the paper, stained with light green (Danger-

field and Smith, 1955), and eluted. Following starch electrophoresis the haemoglobin fractions themselves were eluted. On measuring the colour of the eluates it was found that the abnormal component formed 28% of the total haemoglobin. The proportion of haemoglobin A_2 (Kunkel and Wallenius, 1955) was within normal limits.

On paper electrophoresis in phosphate buffer of *p*H 6.5 no separation occurred. The difference in appearance from haemoglobins A+G mixtures was insignificant, but a difference could always be discerned between the patient's haemoglobin and haemoglobin A or mixtures of haemoglobins



Comparison of patient's haemoglobin (1 and 3) with haemoglobin mixtures AG (2) and AS (4) respectively. The cells were washed in isotonic saline solution, packed, lysed with water and toluene, and centrifuged to separate the haemoglobin from the stroma. Paper electrophoresis was carried out by the hanging-strip method: Whatman filter paper No. 3 "for chromatography," barbiturate buffer *p*H 8.6. At the end of the electrophoretic run the strips were dried and the haemoglobin bands were stained with light green. It will be seen that the abnormal component in the patient's haemoglobin (haemoglobin L) migrates faster than haemoglobin S and more slowly than haemoglobin G.

A+S, A+E, and A+C. On paper electrophoresis in cacodylate buffer of *p*H 6.5 again no separation occurred, but with this buffer a difference could be seen in the appearance of the patient's haemoglobin and haemoglobin A+G mixtures.

The patient's haemoglobin mixture was rapidly denatured by alkali (Singer, Chernoff, and Singer, 1951), and it was resistant to cold denaturation (Rigas, Koler, and Osgood, 1956). The absorption spectra of his carboxyhaemoglobin and of a normal control showed identical peaks of extinction in the visible and ultra-violet ranges.

The solubility of his haemoglobin was within normal limits (Itano, 1953). We repeatedly found a slightly lower solubility of the ferrohaemoglobin than 5 g./l. when using a 2.24 *M* phosphate buffer. In Itano's solubility test all haemoglobin mixtures other than those containing haemoglobin S have a solubility of at least 5 g./l. at this buffer concentration. We thank Dr. H. A. Itano for measuring the solubility of our patient's haemoglobin. He found a normal solubility in 2.58 *M* phosphate buffer (1.8; 1.9 g./l.) and a slightly lowered solubility in 2.24 phosphate buffer (4.6; 4.7 g./l). Dr. Itano informs us that he does not place much confidence in such a small reduction in solubility approaching 5 g./l. in 2.24 *M* phosphate buffer, since that figure represents all the haemoglobin added in his test. A small amount of precipitation might occur before the concentrated buffer (2.8 *M*) is completely mixed. Dr. T. H. J. Huisman obliged us by testing the solubility of our patient's haemoglobin by a salting-out technique; he also found it to be normal. We are grateful to Dr. Huisman for his permission to quote that the abnormal component of this haemoglobin moves on chromatography (Huisman and Prins, 1955) between haemoglobins S and C, whereas haemoglobin G moves between haemoglobins A and S, and to Dr. Itano for informing us of differences seen on open boundary electrophoresis between the haemoglobin of our patient and mixtures of haemoglobins A+S and A+G respectively.

Our patient was born a Hindu of the Khashtri caste in the Mianwali District, Pakistan. He is 27 years old and is now a citizen of India temporarily resident in London. He is not anaemic and there is nothing remarkable in his blood picture, excepting a slight eosinophilia. The osmotic fragility of his red cells is within normal limits. By the kindness of Dr. Ishwar Chandar we have examined the blood of our patient's parents and of one brother and one sister. The mother's haemoglobin consisted of haemoglobin A and of a component moving more slowly than haemoglobin A, but faster than haemoglobin S or D. The other three bloods contained haemoglobin A only.

New haemoglobins are allotted letters which are in general in alphabetical order of discovery (Statement on Haemoglobin Nomenclature, 1953). The accepted symbols for the haemoglobins so far identified are A, C, D, E, F, G, H, I, J, K, and S. The abnormal component in our patient's haemoglobin should therefore be called haemoglobin L.

REFERENCES

Dangerfield, W. G., and Smith, E. B. (1955). *J. clin. Path.*, **8**, 132.
Huisman, T. H. J., and Prins, H. K. (1955). *J. Lab. clin. Med.*, **46**, 255.
Itano, H. A. (1953). *Arch. Biochem.*, **47**, 148.
Kunkel, H. G. (1954). "Zone Electrophoresis" in *Methods of Biochemical Analysis*, edited by D. Glick. Interscience Publishers, New York.
—— and Wallenius, G. (1955). *Science*, **122**, 288.
Lehmann, H., and Smith, E. B. (1954). *Trans. roy. Soc. trop. Med. Hyg.*, **48**, 12.
Rigas, D. A., Koler, R. D., and Osgood, E. E. (1956). *J. Lab. clin. Med.*, **47**, 51.
Singer, K., Chernoff, A. I., and Singer, L. (1951). *Blood*, **6**, 413.
Smith, E. W., and Conley, C. L. (1953). *Bull. Johns Hopk. Hosp.*, **93**, 94.
Statement on Hemoglobin Nomenclature (1953). *Blood*, **8**, 386.

RELATIONSHIP BETWEEN HAEMOGLOBINS C AND S AND MALARIA IN GHANA

BY

G. M. EDINGTON, M.D., D.C.P., D.T.M.&H.
Specialist Pathologist in charge of Medical Research Institute and Laboratory Services, Ghana

AND

W. N. LAING, M.B., Ch.B., D.T.M.&H.
Medical Officer attached to Laboratory Services, Ghana

Haemoglobin C was first described in a North American negro by Itano and Neel (1950) and was later found in high incidence in Ghana by Edington and Lehmann (1954). Allison (1956) and Edington and Lehmann (1956) discussed its incidence and distribution in West Africa. It would appear that the gene responsible for haemoglobin C occurs in high frequency in the tribes of Northern Ghana and declines in frequency from this focus to Nigeria and Sierra Leone, where low frequencies are recorded. Haemoglobin S is also found in Ghana, the incidence of the trait being high (19%) in the Southern regions, where the incidence of the C trait is low (10%), and low in the Northern regions (7%), where the incidence of C is high (21%). There are thus present in the country in high frequency two genes which in their homozygous and combined heterozygous expression are disadvantageous to their bearers. Other abnormal haemoglobins have been detected in Ghana, but their incidence is low. The common genotypes seen are listed in Table I.

The S gene is thus being eliminated from the population at large by individuals suffering from sickle-cell anaemia, sickle-cell haemoglobin C disease, microdrepanocytic-like disease (Edington and Lehmann, 1955), and perhaps in certain unspecified instances by bearers of the sickle-cell trait. It is difficult under these circum-