essentially in agreement with and complement those obtained in a double-blind contraceptive field trial carried out in the Netherlands with Lyndiol and Conovid (tablets with 5 mg. norethynodrel and 75 μ g. mestranol). The trial comprised 500 women, and each preparation was given during six months; liver-function tests were performed monthly in 30 women receiving Lyndiol and 30 receiving Conovid. The results confirmed that no impairment of hepatic function throughout these first months of treatment had occurred (Swaab, 1964a, 1964b).

In a recent paper from the Finnish investigators Eisalo *et al.* (1964) reversible elevations of serum transaminase levels and bromsulphthalein retention were reported immediately after the administration of Lyndiol or mestranol, but not that of Orgametril, in a series of 12 post-menopausal women. Other tests of liver function (total serum bilirubin and serum alkaline phosphatase) remained normal in nearly all the cases investigated. These results appear to be strikingly different from those obtained in the Netherlands and show only some partial agreement with the changes, much more benign, briefly mentioned for Orgametril and Lyndiol in some cases of endometriosis by two other Scandinavian investigators (Soiva and Castrén, 1963; Borglin, 1964). Although it seems difficult to account for such a discrepancy, one might speculate whether the high age (59 to 80 years) of the women in the study of Eisalo *et al.*, or perhaps other characteristics of the population sample chosen, may have played a part in the results obtained. Our own data in a fairly large series of women of fertile age do not indicate that long-term administration of Orgametril, Lyndiol, or Lyndiol 2.5 results in any influence upon the status of liver function.

SUMMARY

Liver-function tests were carried out on 52 women who had been receiving long-term treatment with a progestational and ovulation-inhibiting substance (Orgametril), or its combination with oestrogen in two different concentrations (Lyndiol and Lyndiol 2.5), for the management of menorrhagia, endometriosis, or dysmenorrhoea or for contraceptive purposes. No laboratory or clinical indication of hepatic dysfunction during treatment with these products could be found.

Thanks are due to Dr. C. F. G. Lehr, Apeldoorn, who performed most of the laboratory work. The products Orgametril, Lyndiol, and Lyndiol 2.5 were provided by Organon, Oss, Netherlands.

G. LINTHORST, M.D.,
Consultant Gynaecologist,
Juliana Ziekenhuis and St. Liduina,
Ziekenhuis, Apeldoorn, Holland.

REFERENCES

- Borglin, N. (1964). *Int. J. Fertil.*, **9**, 17.
Drill, V. A. (1959). *Fed. Proc.*, **18**, 1040.
Eisalo, A., Järvinen, P. A., and Luukhainen, T. (1964). *Brit. med. J.*, **2**, 426.
Garcia, C., and Pincus, G. (1964). *Int. J. Fertil.*, **9**, 95.
Lancet, 1962, **1**, 1056.
Marquardt, G. H., Fisher, C. I., Levy, P., and Dowben, R. M. (1961). *J. Amer. med. Ass.*, **175**, 851.
Perez-Mera, R. A., and Shields, C. E. (1962). *New Engl. J. Med.*, **267**, 1137.
Rice-Wray, E., Schulz-Contreras, M., Guerrero, I., and Aranda-Rosell, A. (1962). *J. Amer. med. Ass.*, **180**, 355.
Sherlock, S. (1962). *Brit. med. J.*, **1**, 1359.
Soiva, K., and Castrén, O. (1963). *Ann. Chir. Gynaec. Fenn.*, **52**, 376.
Swaab, L. (1964a). *Int. J. Fertil.*, **9**, 107.
— (1964b). *Ned. T. Geneesk.*, **108**, 1070.

Medical Memoranda

Haemoglobin J_{Baltimore} in a Kent Family

Brit. med. J., 1964, **2**, 921-922

Details of a variant of adult haemoglobin not previously reported in an English person are given here.

CASE REPORT

A widow of 66 was admitted to Lewisham Hospital in December 1963 with acute bronchitis. She gave a history of recurrent bronchitis and vague ill-health for the past 12 years. The only relevant finding on routine examination and investigation was a severe hypochromic anaemia, for which no obvious cause could be found. Further films suggested a haemolytic process. Investigations showed: haemoglobin 6.2 g./100 ml.; M.C.H.C. 25%; test for occult blood negative; direct Coombs test negative; haemoglobin electrophoresis showed an abnormal haemoglobin but no cause for haemolysis. There was haemosiderinuria and a Ham acid serum test (19% haemolysis) was positive. The diagnosis of paroxysmal nocturnal haemoglobinuria having been made, interest now centred on the results of electrophoresis. On occasion a "fast"-moving haemoglobin fraction, presumably haemoglobin A₃, had been seen on electrophoresis in other patients with paroxysmal nocturnal haemoglobinuria. This one, however, proved to have the mobility of haemoglobin J—that is, on paper electrophoresis at pH 8.6 and 8.9 it moved more slowly than haemoglobin N but faster than haemoglobin K (Fig. 1).

IDENTIFICATION OF HAEMOGLOBIN J VARIANT

Globin was prepared from the purified abnormal haemoglobin using acid/acetone according to Anson and Mirsky (1930). The globin was digested with trypsin in 0.5 M ammonium hydrogen carbonate buffer and the digestion products "finger-printed" according to Ingram (1958) and Baglioni (1961). The "finger-print" showed that the spot corresponding to peptide β TpII which

FIG. 1.—Paper electrophoresis at pH 8.9 of the propositus's haemoglobin, showing haemoglobin A and haemoglobin J.

contains the 9-17 amino-acid sequence of the β -chain of haemoglobin A was missing and that a new spot moving more slowly towards the cathode had appeared (Fig. 2). A second very faint new spot was observed moving towards the anode. Ehrlich reagent (Smith, 1953) showed that both the new spots contained tryptophan. These observations were identical with those reported by Baglioni and Weatherall (1963) for the "finger-print" of haemoglobin J_{Baltimore}. These authors found that in the 9-17 amino-acid sequence of haemoglobin J_{Baltimore} an aspartic-acid residue had been substituted for a glycine residue in position 16 (Table I).

FIG. 2.—"Finger-print" of the propositus's haemoglobin J. The left arrow shows the area where β TpII is found in haemoglobin A, and which is missing, and the right arrow shows an abnormal peptide corresponding to the major peptide of haemoglobin J_{Baltimore}. + = Point of application.

TABLE I.—Tryptic Peptide II of β -chain of Human Haemoglobin

Haemoglobin A	9	10	11	12	13	14	15	16	17
	Ser	Ala	Val	Thr	Ala	Leu	Try	Gly	Lys
Haemoglobin J _{Baltimore}	Ser	Ala	Val	Thr	Ala	Lcu	Try	Asp	Lys

The major new peptide was isolated by electrophoresis and chromatography, hydrolysed with 6 M HCl *in vacuo* at 110° C. for 20 hours and analysed for amino-acids on an automatic analyser (Spackman, Stein, and Moore, 1958). The normal peptide β TpII was prepared from haemoglobin A in a similar manner and also analysed for amino-acids (Table II).

TABLE II.—Molar Ratio of Amino-acids Formed after Acid Hydrolysis of β Tryptic Peptides II from Haemoglobin A and from Haemoglobin J of Patient Respectively

Amino-acid	β^A TpII	β^J TpII
Aspartic acid	<0.1	0.9
Threonine	1.0	1.1
Serine	1.1	1.2
Glutamic acid	<0.1	<0.1
Glycine	1.1	<0.1
Alanine	2.1	2.1
Valine	0.9	1.1
Leucine	0.9	0.9
Phenylalanine	<0.1	<0.1
Lysine	1.0	1.0
Tryptophan	+	+

The amino-acid analysis showed that in the abnormal peptide aspartyl had replaced the glycyl of the normal peptide.

As this variant of adult haemoglobin had not previously been reported in an English person, some of the patient's many relatives were approached with a view to establishing its lineage. One of the patient's brothers, two of her sisters, and two cousins on the

maternal side also showed this haemoglobin variant; none of them suffers from paroxysmal nocturnal haemoglobinuria. The mother's family has lived in the Folkestone area of Kent for at least five generations and no continental or other connexions have so far been recalled.

COMMENT

There have now been several reports of abnormal haemoglobins in English families. Haemoglobin Norfolk (Ager, Lehmann, and Vella, 1958) was the first to be discovered, but it was not seen again in a survey of 1,000 unrelated inhabitants of the Norfolk county (Huntsman, Hall, Lehmann, and Sukumaran, 1963), though two further examples of other abnormal haemoglobins were discovered. Thus abnormal haemoglobins must be expected to be seen from time to time in Great Britain.

The identification of haemoglobin J_{Baltimore} had been made in American negroes, and the finding of a J β is not entirely unusual in persons of negroid stock (Went and MacIver, 1959), but there has been one haemoglobin of that mobility seen in an Irishman (Gammack, Huehns, Lehmann, and Shooter, 1961), and, like J_{Baltimore}, this haemoglobin J also was an abnormal β -chain variant.

A haemoglobin J β has also been found in a Bengali family (Chatterjea and colleagues, in preparation), but other examples of haemoglobin J in South-East Asia so far examined have been found to be abnormal in the α -chain (Gammack *et al.*, 1961). It is at present useless to speculate whether sporadic findings of an identical abnormal haemoglobin indicate a relationship between different populations. These may well arise from independent mutations, and the somewhat more frequent finding of haemoglobin J_{Baltimore}, or a haemoglobin J β , which may or may not be the same, in persons with African ancestry could be due to a more intensive examination of their blood by electrophoresis.

Our thanks are due to Mr. L. Hanning, F.I.M.L.T., who screened the haemoglobin samples of this family, and to Dr. T. M. L. Price for permission and encouragement to study the patient.

C. A. HOLMAN, M.B., B.S., M.R.C.P., F.C.PATH.

A. J. SMITH, M.A., B.M., B.CH.

W. F. WHIMSTER, M.A., M.B., B.CHIR.

Lewisham Hospital,
London.

D. BEALE, B.SC.

H. LEHMANN, M.D., SC.D., F.R.C.P., F.R.I.C., F.C.PATH.

M.R.C. Abnormal Haemoglobin Research Unit,
University Department of Biochemistry,
Cambridge.

REFERENCES

- Ager, J. A. M., Lehmann, H., and Vella, F. (1958). *Brit. med. J.*, **2**, 539.
 Anson, M. L., and Mirsky, A. E. (1930). *J. gen. Physiol.*, **13**, 469.
 Baglioni, C. (1961). *Biochim. biophys. Acta (Amst.)*, **48**, 392.
 — and Weatherall, D. J. (1963). *Ibid.*, **78**, 637.
 Gammack, D. B., Huehns, E. R., Lehmann, H., and Shooter, E. M. (1961). *Acta genet. (Basel)*, **11**, 1.
 Huntsman, R. G., Hall, M., Lehmann, H., and Sukumaran, P. K. (1963). *Brit. med. J.*, **1**, 720.
 Ingram, V. M. (1958). *Biochim. biophys. Acta (Amst.)*, **28**, 539.
 Smith, I. (1953). *Nature (Lond.)*, **171**, 43.
 Spackman, D. H., Stein, W. H., and Moore, S. (1958). *Analyt. Chem.*, **30**, 1190.
 Went, L. N., and MacIver, J. E. (1959). *Brit. med. J.*, **2**, 138.