one can conclude that an antigen is a true family antigen. Particularly is this so if there is the possibility of immunization to an antigen of the Rh series.

This antigen is very infrequent in the English population; it might be that in other populations the frequency would be greater.

Summary

A description is given of a case of haemolytic disease of the newborn due to a new Rh antibody, anti-C^x.

Anti-C^x antibody gives very few positive results when tested with random blood samples from the English population. Out of 3,931 random samples tested, four positive results were obtained.

The C^x antigen is considered to be an allele of Rh at the C-c locus. Its inheritance has been demonstrated.

The desirability of including direct tests between the husband's cells and the maternal serum in suspected cases of haemolytic disease, as well as the need for extensive investigations on antibodies thought to be reacting with family blood groups, is discussed.

Our thanks are due to Dr. G. Komrower, paediatrician, St. Mary's Hospital, Manchester, for permission to publish the clinical details, and to Dr. R. F. Jennison, pathologist, St. Mary's Hospital, Manchester; to Dr. D. M. Parkin, of the Blood Group Reference Laboratory, London, for undertaking certain family groups; and to Dr. R. R. Race, of the Blood Group Research Unit, London, for his advice; also to our colleagues in the National Blood Transfusion Service for obtaining samples of blood for family studies.

REFERENCES

- Callender, S. T., and Race, R. R. (1946). *Ann. Eugen.*, **13**, 102.
Davidsohn, I., Stern, K., Strauser, E. R., and Spurrier, W. (1953). *Blood*, **8**, 747.
Graydon, J. J. (1946). *Med. J. Austr.*, **2**, 9.
Holman, C. A. (1953). *Lancet*, **2**, 119.
Levine, P., Stock, A. H., Kuhmichel, A. B., and Bronikovsky, N. (1951). *Proc. Soc. exp. Biol.*, N.Y., **77**, 402.
Medical Research Council (1952). Memorandum No. 27. "The Rh Blood Groups and their Clinical Effects." H.M.S.O., London.
Stratton, F. (1953). *Lancet*, **1**, 1169.

PORPHYRIN EXCRETION IN A PATIENT WITH DELAYED LIGHT- SENSITIVE PORPHYRIA

BY

A. BENSON

W. D. FOSTER, M.B., B.Chir.

AND

F. T. G. PRUNTY, M.D., F.R.C.P.

(From the Departments of Chemical Pathology,
St. Thomas's Hospital, and University College
Hospital, London)

Extensive knowledge based on modern techniques is becoming available on the porphyrin excretion in patients with acute porphyria (Nicholas and Rimington, 1953), but the present state of knowledge on the porphyrins of "delayed light-sensitive porphyria" is much less advanced. This term has been used (Prunty, 1952) in a suggested modified classification of porphyria to include cases referred to by previous authors as "porphyria cutanea tarda." The condition usually occurs in men of adult age and is not familial. Amongst the other changes, one important clinical manifestation is a bullous eruption of the skin produced by light and trauma. The present paper concerns additional data obtained from one of the rare cases of this condition seen by chance in this country.

Clinical Description of the Patient

A man aged 54, normally resident in South Africa, was admitted to St. Thomas's Hospital for investigation. He complained that he had had blisters on his hands for the past year. He has also suffered from arthralgia of the left hip, left knee, right ankle, and right shoulder for three years. There was no relevant family history. He had had blackwater fever in 1915, appendicectomy in 1924, and a cholecystectomy in 1945 for an illness accompanied by abdominal pain and jaundice. In 1952 radiological evidence of the presence of colonic diverticula had been obtained; at about this time he had had symptoms of diverticulitis. Apparently the porphyria became manifest a year before admission. Recurrent crops of blisters about 0.5 cm. in diameter occurred on the backs of his hands and fingers. They took four or five days to develop and then burst. They often contained a clear reddish fluid. This blistering did not appear to be related to exposure to sunlight. He had been treated with a sulphonamide for the diverticulitis without influencing the skin condition. There was some evidence that trauma to the skin favoured the production of these blisters. During the year his urine had been the colour of "dark ale," and had occasionally been dark during the last four years.

Physical examination showed a number of small circular scars on the backs of the hands and fingers, with a circular zone of slight pigmentation around some of them. When first seen three weeks before admission he had three blisters about 0.25 cm. in diameter on his hands, containing yellowish fluid, but these had disappeared by the time of his admission. There was a small rodent ulcer on the right cheek. The liver was enlarged one fingerbreadth below the costal margin, and scars from his two abdominal operations were present. There was a minor degree of osteoarthritis in the knees, hips, and right shoulder.

His urine on examination had a rosy hue and not the brownish-purple appearance of acute porphyria urine containing porphobilin. Porphobilinogen was never detected. On three consecutive days his pigment excretion measured:

Day	Urobilinogen mg./day	Total Porphyrin mg./day	Total Porphyrin Minus Uroporphyrin µg./day
1	9.4	2.4	37
2	6.6	4.8	80
3	3.0	4.4	126

The serum and cerebrospinal fluid contained no porphyrin. Faecal urobilinogen excretion was 295 mg. a day—a normal quantity. Serum total protein was 7.7 g. per 100 ml. (albumin 4.3 g. and globulin 3.4 g.). Thymol turbidity was 4 units; serum bilirubin 0.7 mg. per 100 ml.; cholesterol 159 mg. per 100 ml., of which 65% was esterified. The prothrombin time was 12 seconds (normal). The blood urea was 21 mg. per 100 ml., and endogenous creatine clearance 83 ml. a minute. The haemoglobin was 16.2 g. per 100 ml., and the packed cell volume 48%.

Urine Porphyrin

The porphyrin was isolated as previously described (McSwiney, Nicholas, and Prunty, 1950). Chromatography of the esters on columns of Al₂O₃ (Savory and Moore) and MgO Grade III (Nicholas, 1951) (see Diagram) to clean up the porphyrin gave a single main band (1), which on further chromatography on MgO Grade IV yielded a main band (1a) and traces of two other bands. This main fraction was crystallized, and the product had a melting-point at 211 to 213° C., and its α band at 624.3 m μ . Each band obtained from these three columns was submitted to paper chromatographic analysis, with the results shown in the Diagram. It should be noted that most of the urinary porphyrin was lost during preliminary purification.

There were two very faint bands, 1c and 1e, too little for any paper chromatography at all.

Fractionation of Urine Porphyrins

Urinary porphyrin. 24 mg. total from 6 litres of urine	Results of Paper Chromatographic Analyses		
	Method 1 (Nicholas and Rimington, 1949)	Method 2 (Falk and Benson, 1953)	Method 3 (Chu <i>et al.</i> , 1951)
	1. Mainly 8*† + trace 6, 5, and 4		
	1. Mainly 8* + some 6 and 7 and trace 4	Like Uro III, but Rf slightly greater	Strong spot between uro and copro I position
	1d. Mainly 4 and trace 3 1b. Mainly 6 + 7 and trace 8* 1a. Mainly 8* and some 6 and 7	Like Uro III, but Rf slightly greater	Strong spot between uro and copro I position

* All octacarboxylic spots had relative fronts (Rf's) slightly greater than pure uroporphyrin; the appearance of these spots also was different, and the material cannot be regarded as typical uroporphyrin.

† The numerals indicate that porphyrins bearing this number -COOH groups in side-chains were found by the paper chromatographic method (cf. Nicholas and Rimington, 1949).

Faecal Porphyrin

This was extracted as ester (McSwiney *et al.*, 1950). Paper chromatography in the lutidine-water system (Nicholas and Rimington, 1949) of the crude ester extract showed only an atypical octacarboxylic porphyrin. Chromatography on MgO Grade III gave two small green-brown bands which were discarded and a main band (α band 620.8 $m\mu$). This main fraction, derived from material which originally appeared to contain only octacarboxyl porphyrin, now on paper chromatography showed spots corresponding to a major component with either 6 or 7 carboxyl groups, together with traces of porphyrins with 3, 4, and 5 carboxyl groups. The evidence for degradation on the MgO column to substances with fewer -COOH groups was in this instance very clear. On paper chromatography after Chu, Green, and Chu (1951) there were three spots. The major component ran in the same position as pure coproporphyrin III, and there were two smaller amounts of material, one behaving like protoporphyrin, the other moving slightly slower than coproporphyrin III.

Discussion

The case described was fairly typical, but in relative remission at the time of the examination. The most interesting feature was the apparent absence of light sensitivity, although blisters which almost certainly had contained porphyrin had clearly been present at times. The large urobilinogen excretion in the urine and slight enlargement of the liver suggested hepatic abnormality, and it may be that the attack of jaundice and abdominal pain for which cholecystectomy had been performed was related to the porphyria. The other features worth mention were the rosy colour of the urine, due to increased porphyrin excretion, and the absence of porphobilinogen. Both of these are important points of differentiation from the findings in acute porphyria, in which condition the brown colour is largely due to porphobilin.

Of special interest were the porphyrins found in the urine and faeces. It has been most usual to find uroporphyrin in the urine (Waldenström, 1937), apparently the isomeric uroporphyrins I and III being present together (Macgregor,

Nicholas, and Rimington, 1952). These authors and Canivet and Rimington (1953) have together shown the presence of porphyrins with 2, 3, 4, 5, and 6 carboxyl groups, some of which have been more carefully characterized than others. Gray, Rimington, and Thomson (1948), however, in their case noted a remarkable instability of the ether-insoluble porphyrin fraction, and Macgregor *et al.* (1952) noted an unstable faecal porphyrin. This state of affairs was also apparent in the present case with regard to both urine and faecal porphyrins. The only stable porphyrin which could be isolated from the urine was a substance the ester of which had melting-point 211 to 213° C. and α band at 624.3 $m\mu$. Apart from these two differences it also differed from uroporphyrin on paper chromatograms (see Diagram). It appears to be identical, by all three paper chromatographic methods employed, with the octacarboxylic porphyrin isolated by Canivet and Rimington (1953) for the first time from the pooled urine of five similar patients. Its similarity to the porphyrin of these authors extends to likeness of α band and melting-point. Neither of these porphyrins appears to be a known uroporphyrin.

The faeces of our patient yielded some protoporphyrin and coproporphyrin III, as might be expected. In addition there was plenty of evidence of decomposition of more highly carboxylated porphyrins, and it is impossible to state with any certainty what the original porphyrins were.

Summary

A brief case report of a man with "delayed light-sensitive porphyria" (porphyria cutanea tarda) is presented. The urine porphyrins were very unstable. The only porphyrin which could be isolated was an atypical octacarboxylic porphyrin like that of Canivet and Rimington (1953). The more highly carboxylated faecal porphyrins present underwent decomposition during processing, but an atypical octacarboxylic porphyrin was observed on paper chromatography of an early fraction.

We are greatly indebted to Professor C. Rimington for his interest.

REFERENCES

- Canivet, J., and Rimington, C. (1953). *Biochem. J.*, **55**, 867.
 Chu, T. C., Green, A. A., and Chu, E. J. (1951). *J. biol. Chem.*, **190**, 643.
 Falk, J. E., and Benson, A. (1953). *Biochem. J.*, **55**, 101.
 Gray, C. H., Rimington, C., and Thomson, S. (1948). *Quart. J. Med.*, **17**, 123.
 Macgregor, A. G., Nicholas, R. E. H., and Rimington, C. (1952). *Arch. intern. Med.*, **90**, 483.
 McSwiney, R. R., Nicholas, R. E. H., and Prunty, F. T. G. (1950). *Biochem. J.*, **46**, 147.
 Nicholas, R. E. H. (1951). *Ibid.*, **48**, 309.
 — and Rimington, C. (1949). *Scand. J. clin. Lab. Invest.*, **1**, 12.
 — (1953). *Biochem. J.*, **55**, 109.
 Prunty, F. T. G. (1952). *Medical Annual*, p. 291. Wright, Bristol.
 Waldenström, J. (1937). *Acta med. scand.*, Suppl. 82.

The 54th annual report of the Liverpool School of Tropical Medicine records that a number of cases of leprosy in persons resident in Britain came to light last year. "All these patients had been imported into this country actually with the disease, as a result of the repatriation of British subjects from India and of the immigration of individuals from various parts of the world following the disturbance in populations due to the recent war. Leprosy is a very chronic disease, which may not display itself for many years after its acquisition and which, when unsuspected, may escape diagnosis for years. In spite of the frequent importation of cases of the disease over many years, it does not spread here, and no case of infection acquired in this country has been seen at the school during the last 50 years. Thus the risk to our own population of the presence of such imported cases of the disease can be ignored as a public health problem. Contrary to popular belief, leprosy is the least infectious of all infectious diseases. The results of treatment with the recently introduced sulphone series of drugs have been most encouraging; but the treatment must be sustained under expert supervision over very long periods to prevent relapse."