ACQUIRED PORPHYRIA IN WHITE PATIENTS

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A number of studies during the past 20 years have shown that porphyria is relatively common in White and Bantu members of the South African community.[1-6] The main clinical and biochemical features of the disorder in the two groups may be similar or differ as indicated below:

PRESENTING FEATURES OF PORPHYRIA IN SOUTH AFRICAN RACIAL GROUPS

White	*Bantu*
Cutaneous lesions of the epidermolysis bullosa type are common, especially in males, less often in females	Similar erosive lesions are the commonest clinical manifestation in both sexes. Hyperpigmentation of exposed skin and facial hirsutism are more common than in White patients
Acute porphyric episodes (abdominal pain, neurological disturbances, psychological changes) occur in both sexes, but are more common in females	These acute episodes are virtually unknown in Bantu patients with cutaneous manifestations
Faecal excretion of copro- and protoporphyrin markedly raised, irrespective of clinical status	Faecal porphyrins normal or only moderately increased; coproporphyrin principally affected
Urinary porphyrins increased during acute episodes, slightly increased and sometimes normal in remission	Urinary porphyrins greatly to moderately increased when skin lesions are active, at other times slightly increased
Porphyrin precursors markedly increased during acute episodes, almost invariably normal in remission	Precursors slightly increased when urinary porphyrins are highest, otherwise normal

It has been shown that the form of porphyria seen in White patients develops in subjects with susceptible constitutions inherited as a Mendelian dominant.[7] No satisfactory evidence has been obtained that there is a genetic basis for porphyria in the Bantu and it is regarded as acquired. The two forms are considered to be separate clinical entitities.

In our records, collected over a number of years, there is a small group of White patients whose laboratory findings resemble those of the acquired form more closely than the variegate; several of them were not of South African stock. These have presented in different hospitals and in panel and private practices. Detailed studies with a view to publication were not made at the time, and the clinical information presented was obtained later from the patients' private doctors, to whom thanks are due. Specimens of urine had been investigated for porphyrin by spectroscopic examination of layers of varying thickness, and for porphobilinogen by the Watson-Schwartz test.[8] Any positive findings were regarded as indicative of an excess of the substance concerned. Acetic acid-ether extracts of small fragments of stool examined under ultraviolet light enabled a rough assessment of the porphyrin content to be made. Quantitative determinations of porphyrin in some of the urines and stools were carried out by the procedure described by Rimington.[9]

Sufficient information was collected about 12 of these patients to indicate that they can and should be differentiated from the very much more numerous White patients in this country with the genetically determined variegate form of porphyria.

CASE REPORTS

Case 1

Male, aged 56, born in Russia and came to South Africa at age of 7. Father died of heart failure at 50 years, mother died in childbirth. Sister had died 2 years previously from cerebral tumour, two brothers alive and healthy.

There was no history of serious illness, operations or accidents. Three-and-a-half years previously the patient felt unwell and noted fragility of the skin on his hands with blistering on the dorsal surfaces. He was referred to a dermatologist who made a diagnosis of epidermolysis bullosa. Urine contained 182 μg. of copro- and 6,400 μg. of uroporphyrin in a 24-hour specimen; stool coproporphyrin 125 μg. and protoporphyrin 78 μg. per G. dry weight.

He was then proprietor of a hotel and admitted having taken up to 12 whiskies a day for the previous 2 years. Appetite was normal. His liver was 2 fingers enlarged and flocculation tests were positive.

He changed his occupation and his alcohol consumption was reduced. The rash cleared and he remained well for 3 years. He then consulted his doctor because of dizziness, weakness and unsteady gait. Laboratory tests showed — Blood: serum albumin 3·7 and globulin 3·9 G. per 100 ml., A/G ratio 0·95; thymol turbidity 7, flocculation +++, total serum bilirubin 0·9, one minute 0·3 mg. per 100 ml.; haemoglobin 17·5 G. per 100 ml., PCV 55, MCHC 32; leucocytes 9,400 per c.mm. Urine: coproporphyrin 362, uroporphyrin 1,830 μg. per litre. Stool: coproporphyrin 153, protoporphyrin 106 μg. per G. dry weight. There were no active skin lesions.

Further investigation showed a mass in the chest, almost certainly a bronchial carcinoma, and possible metastases. The subsequent course was downward and death occurred 5 months later.

Case 2

Male, aged 55, born in South Africa. Miner (classified as having 1st stage pulmonary disability). In March 1955 he was referred to a physician for a crusted rash on both hands and the right forearm which had recurred for 4 years and had been more severe for the last 3. The initial lesion was vesicular. He had noted a dark reddish urine for 6 months. In 1917 he had had malaria and in 1948 a heart attack. For the past 3 years he had been on light work.

He was markedly obese and had dyspnoea on walking. There was peripheral paraesthesia, but no pain in the legs. BP 156/110 mm.Hg.

Laboratory tests: In April 1955, January 1958 and June 1960 his urine contained a slight excess of porphyrin, but the Watson-Schwartz test for porphobilinogen was negative. Stool in June 1960: coproporphyrin 90, protoporphyrin 47 μg. per G. dry weight.

Case 3

Male, aged 59, born in Scotland, had lived in South Africa for 48 years. Turner.

His father was killed in an accident. His mother had a right hemiplegia and subsequently died in renal failure. A brother and two sons were healthy. The patient admitted to drinking 3 - 4 brandies a day. In 1939 he suffered a fractured femur which was plated, and in 1944 he developed

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jaundice. Skin lesions commenced in 1954, limited to hands, forehead and neck, and diagnosed as epidermolysis bullosa. When seen in 1959 the eruptions were worst on the forehead, and the hands improved somewhat though blisters still formed. In 1959 his chest was injured in an underground accident at work. Because of persistent pain he was investigated for coronary thrombosis, but the ECG was normal. There were fractured ribs and the liver was enlarged 1 inch on deep inspiration.

The skin condition improved on cortisone tablets, but 2 months later was worse and the lesions were suppurating.

Laboratory tests in December 1958: serum albumin 3·2 and globulin 3·6 G. per 100 ml., A/G ratio 0·89. Modified Ide test negative. Urine: slight excess of porphyrin and urobilinogen; porphobilinogen doubtful. In February 1959 2 specimens of urine contained excess porphyrin, but no porphobilinogen (Watson-Schwartz test); stool analysis showed coproporphyrin 29, protoporphyrin 35 μg. per G. dry weight. March 1959: haemoglobin 17·5 G. per 100 ml., haematocrit 52·0, leucocytes 5,700 per c.mm.; thymol turbidity 6·5, flocculation ++, cephalin-cholesterol flocculation ++++; Takata-Ara reaction +++; zinc-sulphate turbidity 24; serum albumin 2·7 and globulin 4·9 G. per 100 ml., A/G ratio 0·55. April 1959: haemoglobin 17·2 G. per 100 ml., haematocrit 49, leucocytes 6,500 per c.mm.; thymol turbidity 6·5, flocculation +++; cephalin-cholesterol flocculation ++++; Takata-Ara reaction +; zinc-sulphate turbidity 21·6; serum albumin 3·9 and globulin 4·3 G. per 100 ml., A/G ratio 0·89.

Case 4

Female, aged 41, born in South Africa, but has lost touch with her family. Housewife.

Appendicectomy as a child. Fractured head of femur 9 years previously, vitallium cap applied. 'Ptomaine poisoning' 4 years before, after which muscles wasted. In 1954 complained of inability to move her limbs; after thorough neurological investigation peripheral neuritis was diagnosed. At this time porphyrin was detected in the urine, but no porphobilinogen. Skin lesions were not recorded in the notes. The letter from the referring practitioner stated '... there is no history of alcohol', but the patient admitted taking occasional beer and stout. In 1957 she was admitted to hospital for treatment of hypertension, but soon discontinued the treatment given. Again admitted to hospital in December 1959 with injuries to hip after a fall; she was then very thin with markedly wasted muscles. X-ray revealed old fractures of the right 8th, 9th, and 10th ribs, the capping of the left femoral head and a recent fracture of the neck of the right femur.

Scarring of forearms, face, forehead and neck were attributed to epidermolysis bullosa. There were no active lesions, but she acknowledged past blistering on these sites.

On admission the smell of alcohol was noted in her breath and she confirmed heavy alcohol consumption. Her liver was enlarged 1 finger. During this admission several specimens of excreta were examined. Two specimens of urine contained slight excess of porphyrin, but no porphobilinogen; the third, a 24-hour specimen, contained coproporphyrin 148 and uroporphyrin 334 μg. One stool was normal in respect of porphyrin, a second contained coproporphyrin 62 μg. and protoporphyrin 53 μg. per G. dry weight. Excreta from the patient's daughter, an only child, showed no abnormal amounts of porphyrin.

Further laboratory tests included: thymol turbidity 2·5, flocculation negative; van den Berg reaction negative, total bilirubin 0·4, one minute 0·2 mg. per 100 ml.; serum albumin 3·3 and globulin 3·8 G. per 100 ml., A/G ratio 0·87; serum calcium 4·5 mg. per 100 ml., inorganic phosphorus 4·6 mg. per 100 ml., alkaline phosphatase 8·5, acid phosphatase 2·3 King-Armstrong units, blood urea 11 mg. per 100 ml., potassium 4·0, sodium 138 and carbon dioxide 17·5 mEq. per litre; haemoglobin 13·5 G. per 100 ml.; leucocytes 7,000 per c.mm., polymorphs 79%, monocytes 6%, lymphocytes 14%, and eosinophils 1%. Modified Ide test negative. Urine contained 39 and 37 mg. of calcium and 490 mg. of phosphorus in 24-hour specimens.

Case 5

Male, aged 46, born in South Africa. Wood machinist. He was referred to an outpatient department in January 1958 complaining of weakness with shooting pains and wasting of legs for 9 months. Skin pigmentation had increased over the past eight years. Seven weeks later he was admitted for investigation for possible cancer of the lung and porphyria. He admitted consumption of a quarter of a bottle of brandy almost every day for 5 years. His appetite was poor and he experienced dyspnoea on walking, and tingling and cramps under his feet and in his toes. He had a weight loss of 22 lb. in 2½ months. Liver 2 fingers enlarged, BP 140/90 mm.Hg.

Father had died at 56, cause unknown, mother was alive, aged 69; he had one sister who was healthy. Apart from rheumatic fever at 8 years his past health was good and there had been no admissions to hospital. His extremities were wasted and the skin was darkly pigmented, but no lesions or scars were recorded.

Laboratory tests: Modified Ide test negative. Thymol turbidity 2·5, flocculation negative; cephalin-cholesterol flocculation +, Takata-Ara reaction +++, zinc-sulphate turbidity 20·6. Serum bilirubin: total 1·0, 1 minute 0·4 mg. per 100 ml. Total serum protein 6·6 G. per 100 ml. Urine in January 1958: slight excess of porphyrin, no porphobilinogen. Stool in February: coproporphyrin 92 and protoporphyrin 71 μg. per G. dry weight.

Case 6

Male, aged 57, born in South Africa. Retired engine driver.

This patient was admitted to hospital in August 1959 with a long history of refractory anaemia for which he had already received over 90 blood transfusions. Subsequent examinations indicated that he had a refractory normoblastic anaemia.

The dorsal surfaces of his hands and wrists were hyperpigmented, but showed numerous irregular depigmented areas. He stated that blistering first occurred following burns some 10 years previously, but had recurred at intervals since then.

Laboratory examinations: August 1959, urine — slight excess of porphyrin, no porphobilinogen; stool — coproporphyrin 130 and protoporphyrin 41 μg. per G. dry weight. A week later, urine — coproporphyrin 133 μg. and uroporphyrin 1,610 μg. in a 24-hour specimen; stool — coproporphyrin 133 and protoporphyrin 52 μg. per G. dry weight.

Specimens of excreta were obtained from his mother, sister, son and daughter. None of these gave results compatible with variegate porphyria.

In March 1960 the patient was admitted to hospital in a distant town from where specimens were sent for analysis. Urine contained a small amount of porphyrin, but no porphobilinogen; stool — coproporphyrin 91 and protoporphyrin 20 μg. per G. dry weight. He died a few days later, presumably from cerebral haemorrhage. Information was later obtained from a sister that earlier in his life he had been a chronic alcohol addict for about 15 years.

Case 7

Female, aged 52, born in South Africa. Housewife.

She was referred to a physician in December 1957 with a history of having been treated with thyroid and iron for several months. There had been slow improvement of her myxoedematous appearance and anaemia, but she failed to maintain contact with her doctor and returned some months later looking worse again. There was a pronounced alcoholic history. Hypothyroid stigmata were evident and pigmentation of her skin suggested haemochromatosis.

Laboratory investigations: Haemoglobin 14·4 G. per 100 ml., erythrocytes 4·8m. per c.mm., leucocytes 5,200 per c.mm. Modified Ide test negative. Serum protein-bound iodine 2·0 mg., iron 195 μg., and cholesterol 280 mg. per 100 ml.; thymol turbidity 6, flocculation +++, cephalin-cholesterol flocculation ++; Takata-Ara reaction negative; zinc-sulphate turbidity 18·0; serum albumin 4·4 and globulin 3·5 G. per 100 ml., A/G ratio 1·25.

She was treated with small doses of 'tertroxin' for several months, during which her blood pressure varied from 140/70 to 160/90 mm.Hg and her pulse rate from 88 to 108 per minute.

In February 1961 she was referred to a dermatologist who noted epidermolysis bullosa in addition to the myxoedematous appearance. The skin lesion had commenced about two years previously and had become much worse recently. She was one of 10 survivors in a family of 13; none of the others suffered from any skin trouble, but all declined to submit specimens for examination. One brother died following an industrial accident, an older sister from heart disease and a younger at 18 from unknown causes.

Two specimens of urine from the patient at this time contained slight excess of porphyrin, but no porphobilinogen. A stool contained coproporphyrin 61 and protoporphyrin 64 μg. per G. dry weight.

Case 8

Male, aged 55, born in Germany.

He was seen by a dermatologist in April 1956 who diagnosed epidermolysis bullosa affecting his hands, neck, face and legs, and which had commenced 8 weeks previously. A specimen of faeces contained coproporphyrin 32 μg. and protoporphyrin 76 μg. per G. dry weight, and the eruption was attributed to reaction to contact with asbestos cement. A year later he was referred for tests by another dermatologist with the information that he had been drinking heavily. Skin lesions were still active, the urine contained a slight excess of porphyrin, but no porphobilinogen, and the faeces contained coproporphyrin 41 and protoporphyrin 65 μg. per G. dry weight.

In June 1958 this patient was admitted to hospital complaining of worsening cough with blood-stained sputum. He then admitted recent heavy drinking. He had had pains in his legs for the past 2 years. Physical findings were of no significance apart from an enlarged liver (3 fingers) and a record of a generalized rash and abrasions on the legs. He stated that his skin abraded easily.

His status was considered indicative of incipient delirium tremens and he was treated accordingly, the treatment including 'seconal', gr. 1½ *nocte*. A few days later he volunteered the information that he was a porphyric and had been advised to avoid sleeping tablets. The seconal was stopped and excreta was sent for porphyrin examination. Two specimens of urine contained moderate excess of porphyrin and a slight excess of urobilinogen. The Watson-Schwartz test for porphobilinogen was doubtful in one of the specimens. A stool contained coproporphyrin 288 and protoporphyrin 470 μg. per G. dry weight.

Case 9

Male, aged 61, born in Britain. Professional.

This man had been troubled by a skin rash for some time, and more recently vesicles had developed on the dorsal surfaces of his hands. Several specimens of urine had been examined in other laboratories, and some were reported positive and others negative for porphyrin. Porphyria was suggested, but not accepted, in the differential diagnosis by his physician, since there had never been any systemic manifestations even when he had been given barbiturates intermittently for insomnia. In January 1959 a rather brownish specimen of urine was found to contain a slight excess of porphyrin, but no porphobilinogen; faeces contained coproporphyrin 64 and protoporphyrin 67 μg. per G. dry weight.

A detailed history is available which includes severe infective hepatitis at the age of 11, and pleurisy and pulmonary tuberculosis at 27 which was treated and healed completely. He had an attack of malaria in 1927 and amoebic dysentery in Egypt in 1944. The latter remained chronic for some years and an amoeboma developed in 1948. In 1954 he had severe herpes zoster affecting most of the right side of his trunk. Thereafter he noted easy abrasion of the skin on his hands. Rashes on various parts of the body, accompanied by itching, caused much discomfort for some years. Amoebic cysts were again found in 1957 and a course of treatment was given. 'Pentothal' was administered twice; in 1948 with no reaction, and in 1957, after which administration he says he felt 'ghastly' for a while. However, there were no frankly acute porphyric manifestations.

The diagnosis of porphyria was then accepted. The patient abstained completely from alcohol, which he had previously used in moderation, and no further barbiturates or sulphonamides were taken. A few months later he wrote that his health was much improved, though he still tired easily and bullae continued to form on his hands. These disappeared after increased precautions against sun exposure had been taken and a daily dose of triamcinolone (2 mg.) was administered. A later letter reported no lesions over a period of 7 months.

While this paper was being prepared news was received that this patient had undergone resection of part of the descending colon for diverticulitis. Any drugs which might have influenced or aggravated porphyria, barbiturates especially, were withheld. Morphine, chlorpromazine and 'librium' were used in small amounts for sedation. The postoperative course was satisfactory at first, but later he complained of a peculiar abdominal pain and troublesome frequency of stools; his temperature was slightly elevated. His urine was negative for porphobilinogen and porphyrin, but a few days later another laboratory reported positive findings for stool porphyrin and urinary porphobilinogen; uroporphyrin was not detected in the urine. For various reasons no quantitative analysis could be done at the time.

His condition did not improve, abdominal distension developed and he became mentally confused. All analgesics were stopped, the dose of triamcinolone was increased; vitamin B_{12} in large doses and 'largactil' were given. Over the week-end there was a rapid decline of all symptoms, and 6 weeks later he had recovered almost completely and returned to work. Stool analysis now showed coproporphyrin 20 and protoporphyrin 43 μg. per G. dry weight; neither porphyrin nor its precursors were detected in the urine by screen tests.

The patient stated that his forbears were noted for longevity — his father died of hypostatic pneumonia when he was 75 years of age, and his mother at 87 following cerebral haemorrhage. One brother who had been subject to prickly heat in India died in Burma, and another died of septicaemia. Five living siblings had no symptoms of porphyria. These family members were asked to provide excreta for examination and 4 complied. The patient's 3 children also supplied specimens.

The following results were obtained:

	Urine		*Stool*	
	Copro (μg./l.)	*Uro (μg./l.)*	*Copro (μg./G. dry wt.)*	*Proto (μg./G. dry wt.)*
Brother	40	?	70	117
Brother	13	—	17	50
Sister	—	—	10	64
	63	—	11	40
Sister	2	—	20	87
	8	—	17	166
Son	Negative on spectroscopic examination		26	100
	—	—	17	35
Daughter	Negative on spectroscopic examination		18	48
Son	91	?	5	7

Case 10

Male, born in South Africa. Miner.

He was referred to a dermatologist, with marked bullae, ulcers and scars on the dorsal surfaces of the hands and fingers. These had developed in the previous 6 months following a cat scratch. White scars on the forearm were attributed to injuries received in a blasting accident some years previously. Facial skin was coarse, but bore no lesions and there was no hypertrichosis.

Urine contained a slight excess of porphyrin, and the Watson-Schwartz test for porphobilinogen was negative. Stool

contained coproporphyrin 41 and protoporphyrin 40 μg. per G. dry weight, and a later specimen 52 and 41 μg. of these pigments respectively.

No mention was made in available notes of habits with regard to alcohol, and 15 months after the above results were obtained his general practitioner said he had no reason to doubt the veracity of the patient's denial. He had been seen recently and the lesions had healed.

Case 11

Male, aged 38, born in South Africa. Semi-skilled labourer, unemployed.

This man was referred to a dermatologist in November 1957 with manifestations of epidermolysis bullosa of 6 months' duration. An enlarged liver was noted and a specimen of urine contained a moderate excess of porphyrin, but no porphobilinogen.

In February 1959 the urine again showed a trace of porphyrin but no precursor, the faeces contained coproporphyrin 53 and protoporphyrin 227 μg. per G. dry weight. In October 1960 he was transferred to the Johannesburg General Hospital from Potchefstroom where he had been intensively treated for pain in the anus with a rectal discharge. Repeat examinations of excreta showed small amounts of porphyrin in two specimens of urine, but no porphobilinogen; the stool contained coproporphyrin 130 and protoporphyrin 39 μg. per G. dry weight. The anal abscess was opened and drained and the patient discharged in November. The abscess recurred in January 1961, necessitating readmission. Incision for drainage was performed immediately, and a fortnight later a sphincterotomy was carried out. Pentothal was inadvertently administered on this occasion, but there was no post-operative episode of acute porphyria. He progressed well and was discharged in February 1961. He admitted taking a few drinks.

Case 12

Male, aged 46, born in Portugal.

This patient was referred from a neighbouring territory to a dermatologist, who diagnosed epidermolysis bullosa. The lesions had been present a year. Urine contained a moderate excess of porphyrin and a slight excess of urobilinogen, but no porphobilinogen. The screen test of faeces did not indicate an excess of porphyrin. He left Johannesburg the following day and this precluded further investigation, but he gave information that syphilis had been diagnosed at the age of 14 for which he had had intensive treatment. He had also had diabetes mellitus for 18 years and was in the habit of drinking wines.

DISCUSSION

One patient showed hyperpigmentation as the only cutaneous feature — all the rest had had vesicular or bullous lesions, which in 8 were frankly described as epidermolysis bullosa. The duration of these lesions varied from 8 weeks to 10 years; the age at onset in the majority was over 40 years, so that the condition fits into the classification of porphyria cutanea tarda in this respect. In our experience of variegate porphyria, skin lesions are most often seen in the third and fourth decades and are known to have commenced in 1 patient at the age of 6 months. Four of the patients complained of pains suggestive of peripheral neuritis and others of symptoms possibly associated with acute porphyric episodes. This will be discussed more fully later.

Findings in the Urine

Porphyrin was detected on spectroscopic examination of one or more specimens of urine from all these patients. The amounts varied from a slight to moderate excess as assessed by the depth of the column of urine at which the characteristic spectral absorption bands became visible. Quantitative analysis of 3 24-hour specimens (2 from case 1 and 1 from case 4) showed normal or slightly increased coproporphyrin and markedly increased uroporphyrin. The Watson-Schwartz test for porphobilinogen was negative in 20 of these specimens and doubtful in 1 each from cases 3 and 8; repeat tests on both these patients were negative.

More extensive follow-up studies will be required to determine whether or not these biochemical abnormalities persist.

Findings in the Faeces

The screen test indicated that the single specimen available from case 12 was normal with regard to porphyrin; quantitative determinations of coproporphyrin and protoporphyrin were carried out on from 1 to 3 stools from each of the 11 other patients. The findings are clearly lower than the usual run of figures in patients with variegate porphyria, in which several hundred, and sometimes over a thousand, micrograms of these fractions are commonly found. Only 1 specimen (the third from case 8) stands far apart from the rest in this respect and indicates that more data are required on this point.

It is quite impossible to fix strict normal ranges for these pigments when expressed in terms of dry faecal solids. For working purposes we have adopted upper limits of 15 and 45 μg., for coproporphyrin and protoporphyrin respectively. Eales regards these as too low, since he has found total porphyrin (C + P) to be between 100 and 132 μg. in several normal subjects.

It is thus our practice to allow considerable margins of doubt above the working normal limits mentioned above. By these criteria 6 of the specimens of faeces were 'normal' with regard to protoporphyrin, but none with regard to coproporphyrin. It follows that if both fractions are taken into consideration, all these stools must be considered as 'abnormal'. By Eales' criterion about half of them would be considered abnormal.

In cases 8, 9 and 11 the presence of blood in the gastro-intestinal tract may have been a complicating factor in this connection.

It is pointed out that the findings on urine alone do not permit any distinction to be made between variegate and acquired porphyria. When the results of stool and urine examinations are considered in conjunction, the findings reported show more resemblance to those in the acquired than in the variegate form.

Familial Incidence

Information given by patients about the medical histories of their relations is often unreliable, and in this particular connection its value is still further reduced by the possibility of latent porphyria. Nevertheless this information should not be entirely ignored. Eight of the patients gave information about 45 immediate blood relations in whom there was no definite indication of porphyria. Histories of terminal hemiplegia in the mother of case 3, prickly heat in a brother of case 9, and death from unknown causes of the father of case 5 and a sib of case 7 are possible exceptions which cannot now be assessed.

Specimens of excreta were obtained for analysis from

near relations of 3 of the patients. The findings have been mentioned in the individual case notes. In all these relations the urinary findings were normal, and though stools from several contained slightly increased amounts of porphyrin, these were never as high as is commonly found in variegate porphyria. There is thus no support for this diagnosis in respect of patients 4, 6 and 9.

Aetiology

An association between alcoholism and cutaneous porphyria has often been stressed in papers published in other countries. According to some writers the association is strong, while others merely state the fact in their case notes. Two of the present patients denied the use of alcohol; in the others its consumption in larger or smaller amounts was either admitted or suspected by their medical attendants on grounds other than the finding of abnormal porphyrin metabolism. It is scarcely necessary to discuss the unsatisfactory nature of information usually given by the patient about alcohol consumption. It is, however, a matter which deserves closer study in future cases despite the reservation that it is not of decisive importance. To obtain a broader view of this aspect it is suggested that these and similar cases reported in the literature, the many Bantu patients with cutaneous porphyria and the still more numerous cases in South East Turkey,[10-12] be regarded as a homogeneous group until definite evidence to the contrary is obtained. Cutaneous manifestations form the common link and there is no tendency to acute episodes. Abnormal amounts of porphyrin are present in the urine, and porphobilinogen is almost invariably absent. Stool porphyrins have not been extensively studied, but this matter is worthy of further investigation because in the presence of raised porphyrins, the coproporphyrin fraction seems to be more affected than the protoporphyrin.

Berman[13] has reported a history of arsenical treatment in several patients with cutaneous porphyria, and this may have been a factor in our case 12. The Turkish 'epidemic' has been associated with ingestion of hexachlorobenzene, and in the Bantu patients the liquor consumed was usually an illicit brew with a variety of additives. There is often evidence of liver dysfunction and most of the aetiological agents discussed can be regarded as hepatotoxic. On these grounds it is suggested that enquiry and study should be directed in particular to further elucidation of previous illnesses likely to have damaged the liver, the nature and amounts of drugs used, exposure to industrial toxins, and the possibility of malnutrition as a predisposing factor. If a summation of several of these effects can lead to this type of porphyria, it is not necessary that the alcoholism should be of a severe grade. Our patient No. 9, with a long history of amoebiasis, severe jaundice in childhood plus prolonged self-medication, and only moderate consumption of alcohol, is a possible example.

The Significance of 'Acute' Symptoms

It is important to distinguish between acquired and variegate porphyria. The interpretation of symptoms which could be attributable to an acute episode sometimes presents very vexing problems. Berman,[14] reporting histories of 57 patients with porphyria cutanea tarda, mentioned several in whom this question arose. The point is often debatable, since abdominal pain could be produced by hepatic enlargement, peripheral neuritis could be the consequence of alcoholism, and psychiatric deviations could be explained in many other ways. Case 9, following the colonic resection, is of special interest. While the results of the screening tests during the episode lend some support to the suggestion that this was an acute porphyric attack, it remains possible that the excess of faecal porphyrin was derived from extravasated blood and that the positive porphobilinogen reaction was due to confusion with urobilinogen, which was also present in the urine. Uroporphyrin was not detected in this specimen and it is difficult to reconcile this with acute porphyria. The subsequent normal findings in urine and faeces also make it difficult to maintain this interpretation, and it is hoped that in similar future circumstances quantitative analyses will be carried out.

Barbiturates

Finally, a word may be said about the effects of barbiturates in these patients. Case 6 was sedated with seconal for several days; case 9 took courses of barbiturates repeatedly for insomnia and pentothal was administered twice; case 11 received pentothal at the time of his second operation. No symptoms compatible with acute porphyria were provoked in any of these patients.

Because of the grave risk of precipitating acute episodes by the administration of these drugs to patients with the 2 genetic forms, viz. variegate and the classical acute porphyria, their use is absolutely contraindicated in all known or suspected cases. There is, however, no evidence that this risk exists in the acquired form of porphyria. This condition is far from rare in large urbanized Bantu populations, and so far as is known no instance has yet occurred of acute porphyria developing after pentothal or other barbiturates in these people, though it is highly likely that opportunities for such incidents have taken place.

CONCLUSION

No apology is offered for the tentativeness of many of the observations in this paper. At this stage it is impossible to be more definite, but it is felt that this opportunity must be taken to show that not every case of porphyria in White members of the South African community belongs to the familial type. The speculations are interesting and possibly also important; they provide many indications for closer observation and study of future cases.

SUMMARY

The clinical manifestations and porphyrin excretion of 12 White patients with cutaneous porphyria are described. The implications with reference to the sub-classification of the porphyrias are discussed.

Much more information about these patients than is usually supplied with laboratory specimens was given by the many doctors involved. Analyses of some of the specimens from relatives were carried out by Prof. C. Rimington in London and Dr. I. C. Parsons in Melbourne, and I am grateful for this assistance. Laboratory facilities were provided by the Director of the South African Institute for Medical Research.

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