Milne *et al.* was not observed in Y. Though a sharp rise occurred by the first hour and again by the fifth hour and the total excretion over 24 hours was 6.2% of the tryptophan load (normal 1.1%), this pattern is not similar to that reported by Milne *et al.* The marked increase in urinary indican after a tryptophan load in Hartnup cases has been ascribed to bacterial degradation of a greater proportion of tryptophan which reaches the colon consequent on incomplete absorption from the small intestines. In the subject studied here, the rise in urinary indican after the tryptophan load began even by the second or third hour, by which time the tryptophan would still not have reached the colon for bacterial action. Such a trend is evident also from the results of Milne *et al.* The increase at such an early period therefore has to be explained on some other basis. While there was a higher level of the total indican excretion in Y (6.2% against 1 and 1.3% of tryptophan load in normals), in the asymptomatic R the excretion was almost normal—1.8%. The observation that urinary indican levels were not maintained at high levels over a long period is regarded as complementary to the observation that tryptophan could not be detected in the faeces.

The excretion of indole acids in R was abnormally high (3.9%) but almost normal in Y (1%). These observations are dissimilar to the observation of Milne *et al.* (1960), who found that, like indican, indolyl-acetic acid excretion after the load is abnormally elevated and maintained over long periods. The absence of prolonged maintenance of high levels of indican and indole acids in urine, the elevation of blood tryptophan to the levels found in normals after the tryptophan load, and the presence of marked tryptophanuria indicate that in the subjects here studied there was no defect in the absorption of tryptophan from the gut. On the other hand, the marked loss of tryptophan through the kidney at blood levels comparable to that in normals denotes a pronounced failure of tubular reabsorption of the amino-acid. It is possible that the condition studied here is a variant of Hartnup disease. Milne *et al.* (1960) suggested that Hartnup disease is essentially due to a failure of transport of

tryptophan across the cell membrane and that this can explain both the tryptophanuria and the alteration in indican-indole acid metabolism. The absence of marked changes in indican-indole acid metabolism seen in the above case cannot be explained on this basis unless it is postulated that the absorption of tryptophan from the gut and that from the renal tubule are controlled by independent processes. One could then suggest that in Hartnup disease a defect in the absorption from the renal tubule is always present but the defect in absorption from the gut is variable. The latter consideration will then govern the pattern of changes in the metabolism of indole compounds.

A comparison of the results in Y with those in R suggested that the absence of the pellagra-like rash in R may have been due to the relatively less amount of tryptophan lost in her urine.

The presence or absence of tryptophan pyrrolase could not be established in this case as urinary kynurenine levels after tryptophan load were not determined.

Summary

A case of Hartnup disease is described and some biochemical aspects of the disorder are investigated. The clinical manifestations leave little doubt that the subject was suffering from Hartnup disease, but the biochemical data suggested that he might be a genetic variant of the trait.

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REFERENCES

- Albanese, A. A., and Irby, V. (1944). *J. biol. Chem.*, **153**, 583.
Baron, D. N., Dent, C. E., Harris, H., Hart, E. W., and Jepson, J. B. (1956). *Lancet*, **2**, 421.
Milne, M. D., Crawford, M. A., Girao, C. B., and Loughridge, L. W. (1960). *Quart. J. Med.*, **29**, 407.
Weissbach, H., King, W., Sjoerdsma, A., and Udenfriend, S. (1959). *J. biol. Chem.*, **234**, 81.

Medical Memoranda

Black Urine After "Jectofer" Injections

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Discoloration of the urine has always roused interest, and this has especially been so with black urine. We report here another cause for this in the hope that the knowledge of its occurrence may save anxiety to patients and doctors and avoid unnecessary investigation.

CASE REPORT

A 54-year-old woman was receiving daily intramuscular injections of iron-sorbitol-citric-acid complex ("jectofer"). A 24-hour specimen of her urine had been collected for an unrelated investigation, and on chance inspection some three hours after completion it was noted to be black. The patient was not receiving any other drugs and denied taking any unusual sweets, drinks, or medicaments. She had not previously noted any discoloration of her urine and there was no family history. A previous routine urinalysis had

been negative and culture of a mid-stream specimen of urine gave no growth of organisms.

Laboratory Investigations.—The urine in the bottle was uniformly black throughout. In a test-tube, however, it was more a dark olive colour. On standing for a few hours a dark-grey deposit appeared. The pH of the urine was 8. Tests on this sample and on a fresh specimen for reducing substances, ketones, protein, bilirubin, urobilin, haem pigments, porphyrins, melanogens, and homogentisic acid all gave negative results. Centrifugation of the original urine provided a dark-grey deposit which was readily resuspended on agitation. Addition of 2 N hydrochloric acid to the deposit dissolved it and produced hydrogen sulphide, detected by its effect on lead acetate paper. The solution gave a strong Prussian-blue reaction, indicating the presence of iron.

It was accordingly concluded that the black coloration was due to the formation of a fine precipitate of iron compounds, partly as iron sulphide. The original urine was found to contain 2.5 mg. of iron per 100 ml., presumably as a result of the administration of jectofer.

To see if the phenomenon was peculiar to this patient, single 24-hour specimens of urine were collected from each of 10 other patients receiving jectofer therapeutically and kept in clean but not sterile bottles. The patients presented no evidence of infection of the urinary tract. Urine colours were within the normal range initially, but in five cases the urines turned black within 24 hours.

Another four urines turned black within four days, but the remaining urine did not go black within 10 days.

In another series of experiments, 30 mg. of jectofer was added to each of 26 24-hour specimens of urine collected from various patients. Four turned black within four hours and a further six turned black within 24 hours. Within four days all but two urines had turned black. Most of the urines were initially acid to litmus. All black urines were found to be alkaline, although alkaline urines were not invariably black. Control samples without added jectofer did not turn black nor did six mid-stream specimens kept with added jectofer in sterile containers for up to seven days.

Several batches of jectofer were tested during these studies. All behaved similarly.

Since blackening of the urines appeared to be associated with bacterial contamination, some of the urines which had turned black were cultured. All were found to contain organisms, some of which were subsequently isolated and incubated in a peptone-water medium containing 0.2 mg. of jectofer per ml. Altogether 73 cultures of various organisms were obtained, of which 24 produced a black deposit in the jectofer-peptone-water medium. These 24 cultures were of various members of the coliform group, except for one *Streptococcus faecalis*.

DISCUSSION

Reports of jectofer as an iron preparation for parenteral use have been favourable (Andersson, 1961; Pringle *et al.*, 1962; Scott, 1963), so that it will probably be used more often in the future except for patients with a history of infection of the urinary tract or untreated folic-acid deficiency, where its use is contraindicated (Briggs *et al.*, 1963; Scott, 1963). It is therefore important that those prescribing the preparation should be aware that the urine of patients receiving it may turn dark on standing and that this phenomenon itself has no sinister significance.

Acute Renal Failure Due to Bilateral Renal Artery Emboli: Case Report

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Occlusion of both main renal arteries is an uncommon cause of renal failure. This may occur in dissection of the aorta, and as a sequel to thrombi arising on plaques within the aorta near the renal ostia (Fischer, Huffman, and Blount, 1959); less rarely occlusion is due to renal artery emboli. The source of such emboli may range from the exotic, as in the patient of Gill and Dammin (1958) with paradoxical bilateral renal artery embolism due to phlebothrombosis in the calf, to the commoner intracardiac lesions giving rise to thrombi. The original description of renal artery emboli in a youth with aortic incompetence is attributed to Traube (1856) by Regan and Crabtree (1948), who give an extensive review of the literature on renal infarction.

When both main renal arteries are blocked early embolectomy would seem to offer the only chance of the patient's survival; Duncan and Dexter (1962) describe the case of a patient with ischaemic heart disease and atrial fibrillation who suffered acute renal failure; he survived for over two months after the emboli blocking both his main renal arteries had been removed, and eventually died in heart failure.

CASE REPORT

A 41-year-old married Armenian woman suffered sudden severe pain in the right flank on 16 January 1963; in the next 24 hours

Although the urine has been observed to be dark at the time of peak excretion of jectofer (Andersson, 1961), it has not previously been reported to become black on standing. This is presumably because previous workers have used sterile containers or have carried out their studies soon after completion of the urine collections.

The mechanism of the change which involves the formation of insoluble iron compounds has not been fully elucidated. Jectofer is an iron-sorbitol-citric acid complex, and it is known that about 30% of an injected dose is excreted in the urine (Andersson, 1961; Pringle *et al.*, 1962). Presumably the iron is freed from the sorbitol-citric acid complex in urine by the action of contaminating bacteria and then forms iron sulphide with hydrogen sulphide generated by bacteria. Formation of ferric phosphate and other insoluble ferric compounds may also occur.

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REFERENCES

- Andersson, N. S. E. (1961). *Brit. med. J.*, 2, 275.
 Briggs, J. D., Kennedy, A. C., and Goldberg, A. (1963). *Ibid.*, 2, 352.
 Pringle, A., Goldberg, A., Macdonald, E., and Johnston, S. (1962). *Lancet*, 2, 749.
 Scott, Jean M. (1963). *Brit. med. J.*, 2, 354.

pain extended to the left flank and also forwards to the right subcostal margin. Urine examination at the time apparently showed a trace of protein and the presence of red and white cells with a few hyaline casts.

Two days later, when her symptoms had improved, she again suffered sudden sharp pain in the right flank and her urine output began to decline. Plain x-ray examination of the abdomen at this time disclosed no abnormality, and a retrograde pyelogram on 23 January showed a normal caliceal pattern and urinary tract on each side. She had become anuric by the sixth day of her illness (22 January), passing only a very few drops of blood. Her blood urea was 84 mg./100 ml., and she was flown from Iraq to England on 25 January, nine days after the onset of symptoms.

On examination she appeared remarkably fit and showed no signs of dehydration or overhydration. All peripheral pulses were present; the pulse was regular at this stage; the second heart sound appeared widely split. Her anuria continued, and the only other abnormal signs were slight tenderness in the right loin and the presence of bilateral severe cataracts.

Investigations.—Blood urea 144 mg./100 ml. Plasma sodium 129, potassium 4.9, chloride 92, CO₂ 25.6 mEq/l. Hb 12.9 g./100 ml. P.C.V. 41%; E.S.R. 42 mm./hour. Plasma albumin 2.8 g., globulin 2.8 g./100 ml.—electrophoresis showed decreased albumin and increased α_1 -globulin. No L.E. cells seen on blood film.

A radioactive renogram using 43 μ C ¹³¹I sodium iodohippurate (Fig. 1) showed no function on the left side, with no rise beyond the initial 30-second level (reflecting the general tissue blood flow). On the right side some function was shown by an increasing concentration after 30 seconds, but with only a low peak, maximal at two minutes. The renogram excluded absolutely an acute obstruction as cause for the anuria, and suggested very severe parenchymal damage consistent with a vascular occlusive lesion affecting both kidneys, more complete on the left.