

Drugs and False-positive Screening Tests for Porphyrria

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Patients with obscure abdominal pain are often screened by testing the urine with Ehrlich's reagent to exclude acute intermittent porphyria. The side-room test most commonly applied is that described by Watson and Schwartz (1941), in which the red colour due to porphobilinogen is not extracted into chloroform. It is not always realized that before extracting into chloroform the mixture of urine and Ehrlich's reagent should be buffered with an equal volume of a saturated solution of sodium acetate. In the Rimington (1958) modification the organic solvent is a 1:4 mixture of benzyl alcohol and amyl alcohol. With this the colour due to urobilinogen is entirely extracted into the organic layer, while most of that due to porphobilinogen remains in the aqueous layer.

An excess of porphyrins in the urine is suggested by finding a pink fluorescence in an amyl alcohol extract of acidified urine (Rimington, 1958). We report a case in which drug therapy was the cause of screening tests which suggested an excess of both porphobilinogen and porphyrins.

Case Report

A woman aged 28 was admitted to hospital complaining of pleuritic chest pain and pain in one calf. Pulmonary embolism was suspected. She was a divorcee and under severe domestic stress. Two years previously a pulmonary embolism had been diagnosed shortly after a laparotomy for acute abdominal pain and vomiting. No cause for the symptoms had been found. She had suffered other bouts of abdominal pain over several years and for two days before admission had been treated for a urinary infection with Uropol (tetracycline, sulphamethizole, and phenazopyridine).

On examination she was overbreathing and had tetany, which improved with rebreathing. There was slight tenderness in the left calf but no other abnormality. Subsequent investigation did not support the diagnosis of pulmonary embolism. Urine tests on admission, however, suggested acute intermittent porphyria, which could have been the explanation for many of her symptoms.

Ehrlich's Reaction.—Freshly passed urine had a bright-yellow colour, and on adding Ehrlich's reagent an orange-red colour appeared immediately. After extraction with chloroform the red colour remained in the aqueous layer. Subsequently the urine was tested with the Rimington (1958) procedure when it was noted that the red colour disappeared with the addition of sodium acetate. After extraction with the alcohol mixture the organic layer was yellow while the aqueous layer was colourless. We suspected that these colour changes were caused by an indicator and found that the addition of 10% hydrochloric acid to the urine gave a colour identical with that obtained with the (acid) Ehrlich reagent.

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Aqueous solutions of the three constituents of Uropol were tested with Ehrlich's reagent according to the Rimington procedure. Tetracycline and sulphamethizole gave yellow colours which were entirely extracted into the organic layer. Phenazopyridine gave an orange-red colour with Ehrlich's reagent (or with 10% hydrochloric acid) and the colour became yellow on buffering with sodium acetate. This yellow colour was extracted into the organic layer. We concluded that the false-positive Ehrlich test was caused by phenazopyridine in the urine. This substance behaves as an indicator.

Tests for Excess Porphyrins.—An amyl alcohol extract of acidified urine had a dull pink fluorescence under ultraviolet light at 254 nm. It was later noted that the fresh urine had a strong yellow fluorescence similar to that given by an aqueous solution of tetracycline. Phenazopyridine in solution gave no fluorescence but a mixture of solutions of tetracycline and phenazopyridine gave, after acidification, a dull pink fluorescence. Thus it is likely that the pink fluorescence observed with the patient's urine was due to the presence of tetracycline and phenazopyridine together.

The mean excretion of delta-aminolaevulinic acid was 4.0 mg/24 hours (Mauzerall and Granick, 1956), which is normal (Goldberg, 1966).

Comment

This patient did not have acute intermittent porphyria. The abnormalities in the screening tests were produced by the urinary excretion of drugs; the excretion of delta-aminolaevulinic acid was normal. Nevertheless, she had a history of recurrent abdominal pain (which could have been caused by porphyria), and the positive screening tests could have been a trap for the unwary. Phenazopyridine is included in a number of proprietary preparations for urinary symptoms (Pyridium, Uromide, and Uropol), and patients for whom these are prescribed may well have abdominal pain.

The false-positive "Ehrlich's" reaction with urine containing phenazopyridine has been noted once before (Stanley *et al.*, 1952). A suspicion might have been aroused by the fact that unlike urine containing porphobilinogen the patient's urine gave an orange-red rather than a cerise colour and that the colour appeared immediately. There would not, however, have been any confusion at all if the mixture of urine and Ehrlich's reagent had been buffered before extraction into organic solvents, as is recommended by Watson and Schwartz (1941) and by Rimington (1958).

The false-positive screening test for excess porphyrins in urine with a mixture of tetracycline and phenazopyridine has not, so far as we know, been described before but could presumably also occur with other drug combinations.

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References

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