Postoperatively, she rapidly recovered spontaneous respiration. Within minutes after extubation she developed acute respiratory failure followed by cardiovascular collapse. There was no evidence of further bleeding. She was rapidly reintubated and resuscitated, and on her return to the unit her girth had increased to 1·4 m and her abdomen was tympanic on percussion. Air was aspirated by suction on the Sengstaken tube and her cardiovascular system restabilised. She was extubated and returned to the ward.

CASE 2

A 40 year old man with alcoholic liver disease was admitted after a massive haematemesis. Anaesthesia was induced with etomidate 10 mg and suxamethonium 100 mg and maintained with alcuronium 15 mg, 0·6% enflurane, oxygen, and 60% nitrous oxide and intermittent positive pressure ventilation. At emergency endoscopy his varices were injected and a Sengstaken tube left in place.

Postoperatively, residual neuromuscular blockade was antagonised by atropine 1·2 mg and neostigmine 2·5 mg and spontaneous respiration returned. He was extubated in the left lateral position but, when turned on to his back, became apnoeic with circulatory collapse. He was again turned to the left lateral position, reintubated, and ventilated. Air was aspirated from the stomach via the Sengstaken tube and intermittent positive pressure ventilation was continued for two days before he could maintain adequate spontaneous respiration.

## Discussion

Many abdominal conditions restrict diaphragmatic movement. These include simple obesity, pregnancy, ovarian cysts, and peritoneal dialysis, as well as ascites and gastric distension. Our two patients were already severely compromised by their ascites and the reduction in functional residual capacity that occurred in the supine position and after anaesthesia. Air insufflated by the endoscopist during variceal injection was retained in the stomach, which was already distended with the gastric balloon of the Sengstaken tube containing 400 ml air. This may have tipped these patients into acute respiratory failure. The clinical improvement after gastric decompression would tend to support this hypothesis. A pilot study investigating respiratory function in the presence of gross ascites has shown a reduction in vital capacity by up to 50% of predicted values, and we propose to study this further.

High intra-abdominal pressures are known to reduce venous return and impair myocardial performance.[2] The cardiovascular collapse seen in these two patients may have been due partly to compression of the inferior vena cava, the so called "supine hypotension syndrome" of pregnancy. Certainly the second patient (case 2) showed some clinical improvement when he was turned to the left lateral position before resuscitation.

Patients with ascites who undergo endoscopy should have all air aspirated at the end of the procedure, and careful respiratory supervision should be continued in an intensive care unit during the early postoperative phase.

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# Pseudoporphyria associated with consumption of brewers' yeast

C K LIM, J M RIDEOUT, T J PETERS

## Abstract

**A case of pseudoporphyria associated with excessive consumption of brewers' yeast was studied. Detailed analysis of the yeast tablets by high performance liquid chromatography showed the presence of dicarboxylic deuteroporphyrin, mesoporphyrin, and protoporphyrin; coproporphyrin I and III isomers; and uroporphyrin I and III isomers. The faecal porphyrin concentration of the patient taking yeast tablets was significantly increased, resembling the excretion pattern in variegate porphyria.**

**Any patient showing an unusual porphyrin excretion pattern on high performance liquid chromatography should be investigated for a possible dietary cause.**

**Division of Clinical Cell Biology, MRC Clinical Research Centre, Harrow, Middlesex HA1 3UJ**
C K LIM, PHD, scientific officer
J M RIDEOUT, FIMLS, chief research officer
T J PETERS, PHD, FRCP, professor and head of division

## Introduction

Brewers' yeast is sold as vitamin enriched tablets with added thiamine, riboflavine, and nicotinic acid. Although certain strains of yeast are known to accumulate porphyrins,[1 2] there have been no reports of porphyrins in commonly taken vitamin enriched yeast tablets. Diagnosis of the porphyrias requires the routine identification and determination of porphyrins in blood, urine, and faeces. In recent years this has been carried out increasingly by high performance liquid chromatography.[3-6]

We report a case of pseudoporphyria associated with consumption of brewers' yeast and describe the detailed analysis of porphyrins in these tablets and their relation to the biochemical identification of the porphyrias.

## Present study

CASE REPORT

A 24 year old man suffered persistently from episodic abdominal pain. Since no other abnormalities were found, screening tests for porphyrias were performed. He had normal urinary concentrations of 5-aminolaevulinate (15 μmol/l (201 μg/100 ml); normal range 0-40 μmol/l (0-536 μg/100 ml)), porphobilinogen (1·6 μmol/l (36 μg/100 ml); normal range 0-8 μmol/l (0-181 μg/100 ml)), and total

porphyrins (85 μg/l; normal range 50-250 μg/l). Results of haematological and serum biochemical studies including liver and renal function tests were normal. His erythrocyte hydroxymethylbilane synthase activity (32·6 nmol (27 μg) porphyrin/ml red cells/hour; normal range 20-42) was also normal. An acid solution of the faecal specimen, however, showed intense fluorescence typical of porphyrins. Detailed analysis of the faecal porphyrins by high performance liquid chromatography was therefore carried out resulting in the detection of raised concentrations of dicarboxylic porphyrins and coproporphyrin, together with a small amount of uroporphyrin. In addition, several unidentified fluorescent components not normally found in faecal porphyrin profiles[3] were detected.

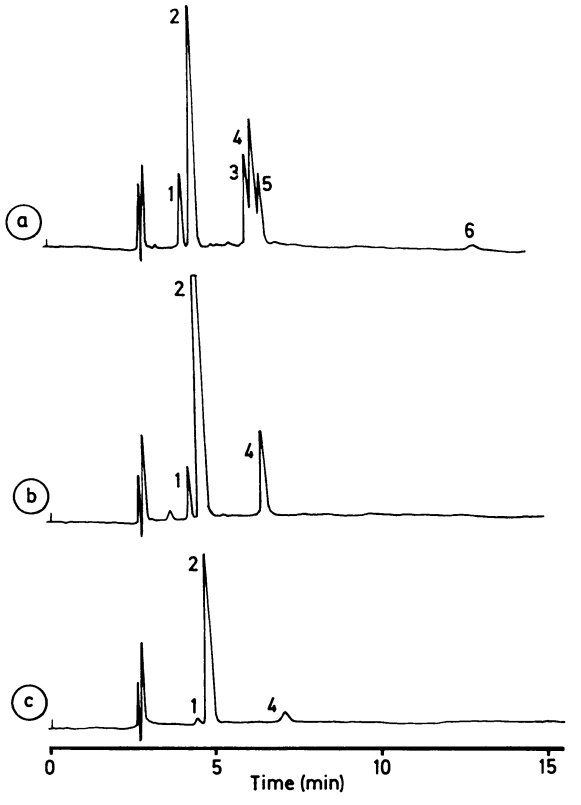


FIG 1—Separation by high performance liquid chromatography of porphyrin methyl esters from faeces of (*a*) present patient consuming brewers' yeast tablets, (*b*) typical patient with variegate porphyria, and (*c*) present patient after stopping yeast tablets. Peak 1 represents mesoporphyrin, 2 protoporphyrin, 3 unknown, 4 coproporphyrin, 5 unknown, 6 uroporphyrin. Column: μ-Porasil (30 cm × 4·6 mm); solvent: N-heptane-methyl acetate (60/40 vol/vol); flow rate: 1 ml/min; detector: ultraviolet 404 nm.

LABORATORY INVESTIGATIONS

*Materials and reagents*—Vitamin enriched brewers' yeast tablets (Phillips Yeast Products Ltd, London) were purchased from the local pharmacist. Porphyrin standards were from Sigma Chemical Co, Poole, Dorset. Ammonium acetate, glacial acetic acid, hydrochloric acid, and diethyl ether were AnalaR grade from BDH Chemicals, Poole, Dorset. Acetonitrile and methanol were high performance liquid chromatography grade from Rathburn Chemicals, Walkerburn, Peebleshire.

*Sample preparation*—Powdered yeast tablets (0·5 g) in concentrated hydrochloric acid (2 ml) were sonicated in the dark for five minutes. The mixture was then vortex mixed with 6 ml ether. Water (6 ml) was added and the mixture again vortex mixed. After centrifugation at 2000 *g* for 10 minutes the aqueous acid solution was used for porphyrin analysis by high performance liquid chromatography. Faecal specimens were similarly processed.

*High performance liquid chromatography*—A Pye Unicam (Cambridge, UK) PU 4010 liquid chromatograph was used. Injection was by a Rheodyne 7125 injector fitted with a 100 μl loop. A variable wavelength ultraviolet light detector (Pye Unicam PU 4020) set at 404 nm or an LS-3 fluorescence detector (Perkin Elmer, Beaconsfield, Bucks) set at excitation and emission wavelengths of 404 and 618 nm, respectively, was used. The dicarboxylic porphyrins were separated on a 15 cm × 5 mm SAS-Hypersil column (5 μm spherical silica chemically bonded with trimethylsilyl groups) with 65% methanol in 1·0M ammonium acetate (pH 6·85) as the mobile phase. Uroporphyrins and coproporphyrins were analysed on a 25 cm × 5 mm ODS-Hypersil column (5 μm spherical silica chemically bonded with octadecylsilyl groups) eluted with 13% and 30% (vol/vol) acetonitrile in 1·0M ammonium acetate buffer pH 5·15, respectively. Faecal porphyrin methyl esters were analysed as described.[3]

## Results

Figure 1 shows the faecal porphyrin excretion patterns analysed as methyl esters by high performance liquid chromatography (*a*) of the patient consuming brewers' yeast tablets and (*b*) in a typical case of variegate porphyria. The dicarboxylic porphyrins (112 μg/g dry weight; normal range 5-75) and coproporphyrin (68 μg/g; normal range 5-50) of the patient were slightly but clearly increased. These findings together with his episodic abdominal pain suggested variegate porphyria. Nevertheless, the absence of dermatological symptoms, the normal urinary 5-aminolaevulinate and porphobilinogen concentrations, and the presence of other, unidentified compounds (peaks 3 and 5, fig 1) with ultraviolet absorption in the Soret region led us to suspect that these compounds—and possibly some of the porphyrins—might be of dietary origin. In addition, these unidentified compounds had not been observed in faecal profiles[3] of patients with well defined porphyrias. The total amount of faecal porphyrins estimated spectrophotometrically (450 μg/g dry weight) was also much higher than that measured by specific methods of high performance liquid chromatography. This again strongly indicated that much of the absorbance and fluorescence was not due to porphyrins. On close questioning the patient eventually admitted to ingesting more than 30 tablets (about 10 g) of brewers' yeast a day as part of a health diet. He was advised to stop the yeast tablets, and this was accompanied by a return to normal of his porphyrin excretion (fig 1 (*c*)) and disappearance of abdominal pain.

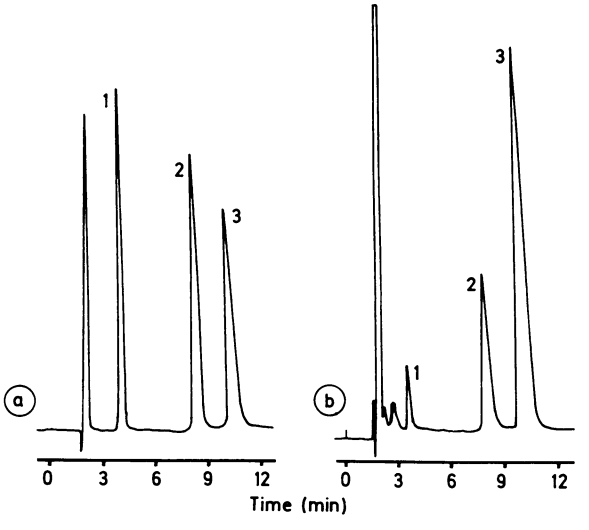


FIG 2—Separation by high performance liquid chromatography of deuteroporphyrin (1), mesoporphyrin (2), and protoporphyrin (3). (*a*) Standard mixture. (*b*) Yeast tablet extract. Column: SAS-Hypersil (15 cm × 5 mm); eluent; 65% (vol/vol) methanol in 1·0M ammonium acetate; flow rate: 1 ml/min; fluorescence detector: excitation 404 mm, emission 618 mm.

It was important to establish that the excess porphyrins excreted by our patient were of brewers' yeast origin since they had resulted in a false positive diagnosis of porphyria. Furthermore, interpretation of porphyrin excretion patterns, which are used for the differential diagnosis of porphyrias, may be confused if a patient is concurrently taking yeast tablets. In order to analyse in detail the nature of porphyrins present in the yeast tablets a novel, highly efficient system of high performance liquid chromatography was developed for the

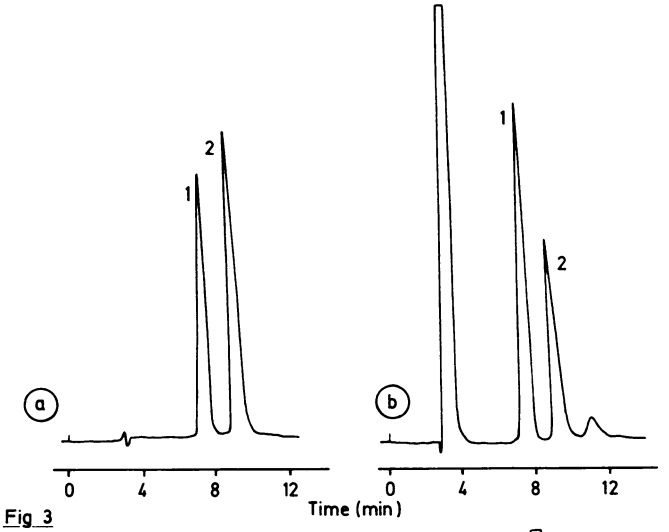


Fig 3

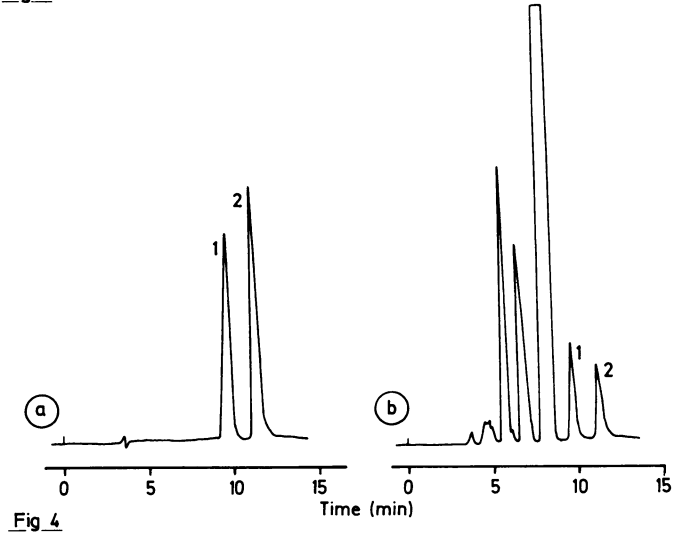


Fig 4

FIG 3—Separation by high performance liquid chromatography of coproporphyrin I (1) and III (2) isomers. (*a*) Standard mixture. (*b*) Yeast tablet extract. Column: ODS-Hypersil (25 cm × 5 mm); eluent: 30% (vol/vol) acetonitrile in 1·0M ammonium acetate pH 5·15; flow rate: 1 ml/min; fluorescence detector: excitation 404 mm, emission 618 nm. FIG 4—Separation by high performance liquid chromatography of uroporphyrin I (1) and III (2) isomers. (*a*) Standard mixture. (*b*) Yeast tablet extract. Column: ODS-Hypersil (25 cm × 5 mm); eluent: 13% (vol/vol) acetonitrile in 1·0M ammonium acetate pH 5·15; flow rate: 1 ml/min; fluorescence detector: excitation 404 nm, emission 618 nm.

separation of the dicarboxylic porphyrins. An SAS-Hypersil column with 65% (vol/vol) methanol in 1·0M ammonium acetate completely resolved deuteroporphyrin, mesoporphyrin, and protoporphyrin (fig 2 (*a*)). Figure 2 (*b*) shows the three dicarboxylic porphyrins present in the yeast tablet extract. Protoporphyrin was the main dicarboxylic porphyrin but a considerable amount of mesoporphyrin and a little deuteroporphyrin were also detected. The presence of deuteroporphyrin and mesoporphyrin was particularly interesting, as in man these are normally derived from protoporphyrin or protohaem by bacterial reduction in the gut. The total dicarboxylic porphyrin content was 9·2 μg/g yeast tablet. The content of coproporphyrins was 6·0 μg/g yeast tablet and consisted of 60% type I and 40% type III isomers (fig 3 (*b*)). The uroporphyrins (0·25 μg/g yeast tablet) were present in much smaller quantities. The isomer composition was 55% type I and 45% type III (fig 4 (*b*)).

## Comment and conclusion

The results in our patient suggested that much of the excess porphyrins excreted in his faeces was of yeast tablet origin. In analyses of brewers' yeast tablets from different sources we found that these porphyrins were always present, although the quantities varied considerably. An intake of 10 g of yeast tablets corresponds to approximately 150 μg of porphyrins. The abdominal pain in our patient appeared to be associated with constipation, probably due to the irritable bowel syndrome rather than as a direct effect of the porphyrins. Stopping the yeast tablets led to rapid relief of symptoms.

Porphyrin profiles obtained by high performance liquid chromatography are undoubtedly useful for the differential diagnosis of the porphyrias and other porphyrinurias. When unusual porphyrin excretion patterns are observed a possible dietary origin of porphyrins must be investigated. Brewers' yeast tablets contain uroporphyrin, coproporphyrin, and dicarboxylic porphyrin, which may lead to misinterpretation of results.

We are grateful to Ms Rosamund Greensted for secretarial help.

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ONE HUNDRED YEARS AGO It would appear that a general raid has lately been made upon the underground cisterns which exist in certain districts of London, on the ground that it is possible for them to be fouled by contaminated surface-water, or by infiltration from neighbouring drains. In Clerkenwell, a baker was recently summoned in respect of an underground cistern, which admittedly had not been cleaned out for two years, but the summons was eventually dismissed. There can be no doubt that underground cisterns are liable to pollution in many ways, and that it would be a most unwise thing, in London at least, to rely upon them for the supply of potable water, inasmuch as the covers of these underground cisterns are rarely raised above the surface of the ground, and are generally faulty in regard of their cementing rim round about the superior portion of the cistern-mouth. There is always a doubt, also, as to whether they leak or not, by reason of faulty ball-valves; and certainly they cannot be easily cleaned or flushed out, owing to their base being generally below the sewer, and only the overflow communicating with it in the ordinary shape of an overflow-pipe. Of course it is vexatious to be compelled, after taking a house, to erect at one's own proper expense a cistern above ground; but the propriety of so doing is undoubted, and one cannot wonder that the water-companies are making use of the powers which they possess by Act of Parliament for abolishing these underground cisterns, many of which are covered over by heavy stones, fitted inside by leaky ball-cocks, and sometimes in a very unsanitary state. It would appear that the search for these underground cisterns is becoming general, and we cannot say unwisely so. We know a case where such a cistern exists for carriage-washing in the yard of a West-End mews, and where the proprietor was peremptorily ordered to abolish it forthwith, and erect a cistern above ground, chiefly on the score of waste of water belonging to the Grand Junction Waterworks Company. By all means let the water-companies exercise their full powers in respect of these misplaced cisterns; only they should act once and for all, and make, while so employed, a house-to-house visitation, and by this means, and by dint of suitable expostulations, make evident to their clients that a certain amount of danger is likely to result from water stored underground. (*British Medical Journal* 1884;i:914.)