"Pink urine" in morbidly obese patients following gastric partitioning

MERVYN DEITEL, MD, FRCS[C], FACS
DOUGLAS A. THOMPSON, MD, FRCP[C]
COLIN F. SALDANHA, MB, BS
PETER J. RAMSHAW
MAXWELL C. PATTERSON, MD, FRCP[C]
KENNETH P.H. PRITZKER, MD, FRCP[C]

A pink coating on the inner surface of plastic urinary tubing, which gave the impression that the urine was pink, had frequently been noted 4 to 24 hours following gastric partitioning by means of a stapler in morbidly obese patients. A study was therefore done in 187 such patients as well as in 14 patients of normal weight who had undergone abdominal surgery of comparable magnitude. Postoperatively "pink urine" was observed in 32% of the obese patients but in none of the nonobese patients; however, a pink sediment remained following centrifugation of urine collected postoperatively from all the obese patients. Microscopy of this sediment showed crystals of uric acid dihydrate; these were infrequent in the preoperative specimens but present in high concentration in the postoperative specimens, particularly those of "pink urine". X-ray diffraction analysis confirmed the nature of the crystals.

Preoperatively the obese patients had high-normal serum levels of uric acid. Postoperatively in all the groups of patients the serum levels of uric acid decreased while the urine levels and the urinary clearance of uric acid increased; the last two values, however, were significantly greater, both preoperatively and postoperatively, in those who were morbidly obese. Compared with the patients who did not have "pink urine" the patients with "pink urine" were significantly more obese and had a significantly lower postoperative urine pH. The latter also had a marked postoperative increase in urine osmolality and were the only patients to have a significant postoperative decrease in urine output. Thus, the pink colour of this group's urine was attributed to precipitation of uric acid crystals, fostered by a decrease in pH and an increase in concentration of the urine.

Une pellicule rose à la surface interne de la tubulure de plastique des sondes urinaires avait souvent été observée de 4 à 24 heures après cloisonnement gastrique par agrafage chez des patients souffrant d'obésité pathologique, donnant l'impression que l'urine était rose. Une étude a donc été entreprise chez 187 de tels patients de même que chez 14 patients de poids normal ayant subi une chirurgie abdominale d'importance comparable. En postopératoire une "urine rose" a été observée chez 32% des patients obèses mais chez aucun des non obèses; toutefois, un sédiment rose a pu être observé après centrifugation des urines prélevées en postopératoire chez tous les patients obèses. L'examan microscopique de ce sédiment a révélé la présence de cristaux d'acide urique dihydraté; ceux-ci étaient rares dans les prélèvements préopératoires, mais présents à forte concentration dans les prélèvements postopératoires, particulièrement dans ceux d' "urine rose". La cristallographie par diffraction de rayons x a confirmé la nature de ces cristaux.

En préopératoire les patients obèses avaient une uricémie élevée mais dans les limites de la normale. En postopératoire tous les groupes de patients ont montré une diminution de l'uricémie et une augmentation de la concentration et de la clairance urinaires de l'acide urique; ces deux dernières valeurs étaient toutefois significativement plus élevées, en préopératoire comme en postopératoire, chez les patients souffrant d'obésité pathologique. Comparativement aux patients qui n'avaient pas d' "urine rose", ceux dont l'urine était "rose" étaient significativement plus obèses, et le pH de l'urine prélevée en postopératoire était significativement plus faible. Ces patients-ci ont aussi enregistré en postopératoire une augmentation sensible de l'osmolalité urinaire, et étaient les seuls à subir en postopératoire une diminution significative du débit urinaire. En conséquence, la coloration rose prise par l'urine de ces patients a été attribuée à la précipitation de cristaux d'acide urique, favorisée par la baisse du pH et la concentration accrue de l'urine.

Morbid obesity is frequently associated with hypertension, cardiorespiratory problems, glucose intolerance, debilitating osteoarthritis of weight-bearing joints, venous stasis, hyperlipemia, urinary stress incontinence, cholelithiasis, foul intertrigo, somnolence, and major psychosocial and economic problems. In an attempt to ameliorate these sequelae after conservative attempts at weight loss have failed, surgery has been performed.[1] The morbidly obese patient, being at high risk, is monitored closely following gastric stapling procedures. A Foley catheter is usually introduced after the patient is anesthetized to monitor urine output. We observed that following surgery the plastic urinary tubing frequently became pink or even red, and the urine was deep amber. This caused considerable concern and led to the following prospective study.

Materials and methods

At St. Joseph's Health Centre jejunoileal bypass surgery was performed on 65 patients between 1973 and 1979. Between 1979 and 1983 gastric partitioning was performed on 384 patients, many of whom had been referred from out of town. These patients were at least twice the ideal weight, had failed to sustain weight loss with exhaustive conservative treatment over the years and suffered from the sequelae of morbid obesity.

In the first 258 patients who underwent gastric

From the departments of surgery, medicine and laboratories, University of Toronto and St. Joseph's Health Centre, Toronto, and the department of pathology, Mount Sinai Hospital, Toronto

Reprint requests to: Dr. Mervyn Deitel, St. Joseph's Health Centre Research Foundation, 30 The Queensway, Toronto, Ont. M6R 1B5

partitioning the division was made horizontally, with the stapler applied twice to prevent breakdown of the partition.[1] The last 126 patients underwent vertical banded gastroplasty, with two vertical applications of the stapler.[2] The staples crush stomach tissue and likely result in a degree of devitalization of the tissue between the two lines of staples.

Studies were performed on 187 consecutive patients undergoing a gastric restriction operation, of whom 162 were women and 25 were men. The ages of the women ranged from 21 to 51 (mean ± standard deviation [SD] 32.4 ± 7.1) years and those of the men from 18 to 46 (mean ± SD 36.6 ± 6.3) years. Urine was collected for 24 hours preoperatively and postoperatively, and the uric acid level, the pH, the volume and the osmolality were determined; the urine was also subjected to x-ray crystallography and was cultured before removal of the catheter. The urinary tubing was changed at intervals to determine how long pinkness of the urine persisted. The patients' dietary histories were recorded, and all the patients received a standard hospital diet from the time of admission. The drugs given before, during and after surgery were also recorded. Plastic urinary tubing from five manufacturers was used; samples of tubing were analysed by the manufacturers.

For comparison, 14 nonobese patients undergoing abdominal surgery were also studied. The operations included colon resections in three patients, repair of a large ventral hernia (in three), cholecystectomy (in two), gastrogastrostomy (in two), exploratory laparotomy (in two), small bowel resection (in one) and duodenojejunostomy (in one). Eight of these patients had been morbidly obese and had undergone gastric partitioning 5 to 18 months previously; they now required an abdominal operation after reaching their ideal weight. The two gastrogastrostomies were performed to overcome strictures of the gastroplasty channel.

The pre- and postoperative data on the individual patients were analysed by the paired *t*-test, and the data for the various groups were compared by the *t*-test for independent samples.

Results

Centrifugation of urine collected on the first postoperative day from all 187 of the obese patients studied showed that in each case a strawberry-pink sediment precipitated out, leaving a clear supernatant (Fig. 1). The urine samples collected on the second postoperative day, as well as those collected preoperatively, also produced a pink sediment, but much less.

In 59 patients (32%), those whose urine produced the greatest amount of sediment, the precipitate coated the inner surface of the urinary tubing and thus gave the impression that the urine was pink (Fig. 2). The precipitate, which varied in shade, appeared as early as 4 hours postoperatively and continued forming for as long as 48 hours. Precipitation was especially noticeable along the dependent parts of the urinary collection apparatus (Fig. 3). The urine was frequently deep amber. The pink deposit on a 25-cm length of the plastic tubing from each of the 59 patients was rinsed with 9 mL of distilled water into a test tube. After the tube had stood, a pink precipitate appeared at the bottom; the overlying fluid was pink. When one drop (0.025 mL) of concentrated (14 *N*) sodium hydroxide was added to 1 mL of this mixture the precipitate dissolved completely, leaving a clear, pale yellow solution.

Light microscopy showed that the pink sediment from the urine of the obese patients was composed of irregular birefringent aggregates 10 to 50 × 20 μm that were composed of crystals 1 to 5 μm in diameter. The aggregates looked like clusters of fine uric acid crystals (Fig. 4).[3] Scanning electron microscopy confirmed that the material consisted of aggregates of crystals 1 to 5 μm in diameter. Energy-dispersive x-ray analysis failed to demonstrate calcium or phosphate in the crystals. X-ray diffraction analysis identified the crystals as uric acid dihydrate (Fig. 5).

No one in the nonobese group of patients had "pink urine" or a pink urinary sediment postoperatively, nor was the urinary tubing of any other patient in the hospital reported to be pink.

The pink urine was not related to diet, drugs, bacteria in the urine (organisms were rarely cultured) or any material in the plastic tubing (tubing from all five manufacturers was affected, and all the manufacturers reported their tubing to contain only inert material).

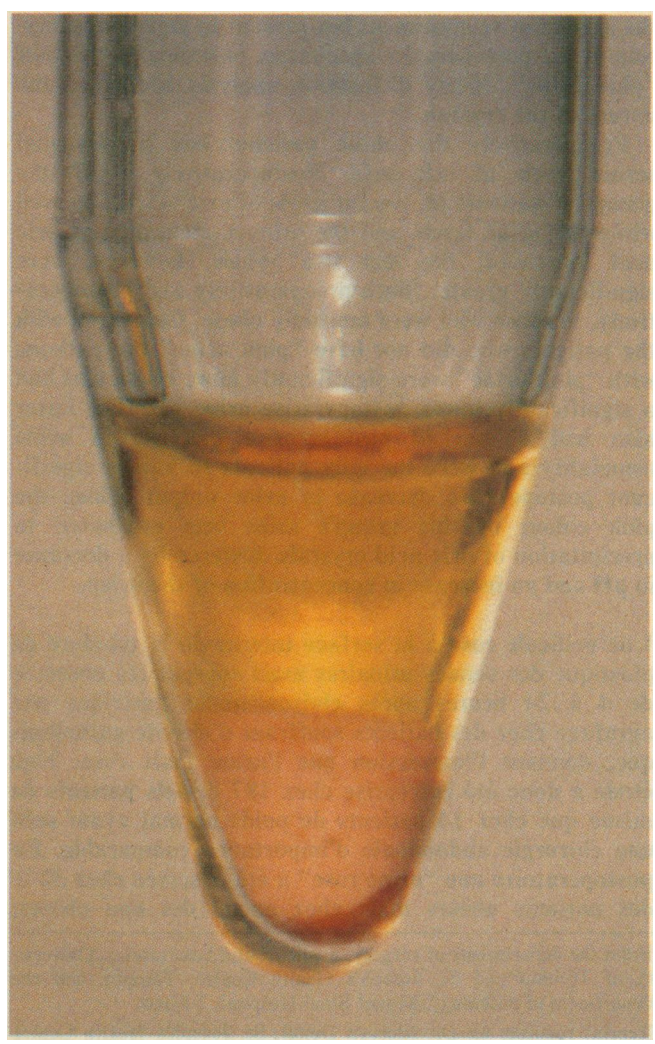

Fig. 1—Pink sediment evident following centrifugation.

Hemoglobinuria, myoglobinuria and significant hematuria were not present in any of the 59 patients with pink urine.

Table I shows the results of the laboratory investigations performed preoperatively and postoperatively. All the groups of obese patients had high-normal mean serum levels of uric acid preoperatively, the levels ranging from 341 to 480 (normally 180 to 420) μmol/L. There was no significant difference between the patients with and without "pink urine", but the men had significantly higher ($p < 0.05$) preoperative levels than the women. The nonobese patients had normal mean serum levels preoperatively. Postoperatively the serum levels of uric acid decreased while the urine levels and the urinary clearance of uric acid increased in both the obese and the nonobese patients. Again, there was no significant difference in the values between the obese patients with and without "pink urine". However, the obese patients had significantly higher ($p < 0.05$) urine levels and urinary clearance of uric acid than the nonobese patients both preoperatively and postoperatively. The men (both the obese and the nonobese) had significantly higher ($p < 0.05$) urine levels of uric acid than the women both preoperatively and postoperatively.

The urine osmolality increased significantly after surgery only in the obese women with "pink urine"; however, there was a trend toward increased urine osmolality in the obese men with "pink urine". There was no significant change in the urine osmolality of the patients without "pink urine". The obese men had significantly higher ($p < 0.05$) pre- and postoperative urine osmolality than the obese women.

Only in the patients with "pink urine" was there a

Fig. 2—Strawberry-pink urine in collection apparatus.

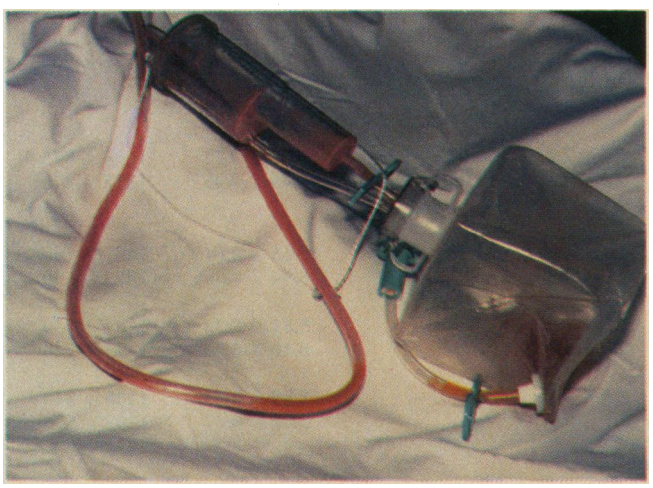

Fig. 3—Urine that appears red but does not contain blood.

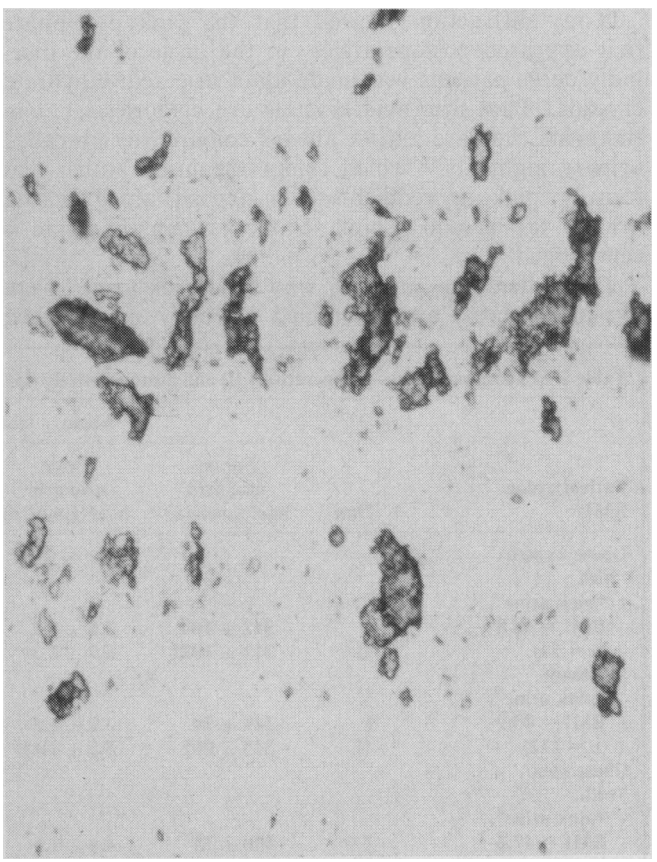

Fig. 4—Aggregates compatible with clusters of fine crystals of uric acid (×40).

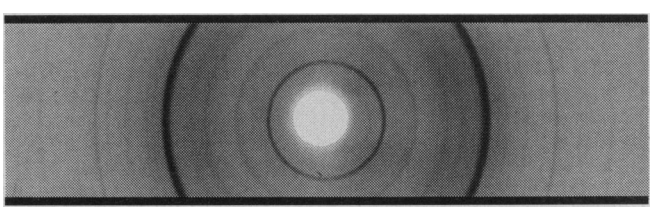

Fig. 5—Results of x-ray diffraction analysis: d-spacings characteristic of crystals of uric acid dihydrate.

postoperative mean urine pH of 5.4 or less, and only in the women with "pink urine" was there a considerable postoperative decrease in the urine pH. Compared with the obese patients who did not have "pink urine" the patients with "pink urine" had a similar preoperative urine pH but a significantly lower ($p < 0.05$) postoperative urine pH.

The postoperative 24-hour urine output decreased markedly (to 1312 mL or less) only in the obese patients with "pink urine". In the remaining obese patients and in the nonobese patients the postoperative urine output either increased or was unchanged compared with the preoperative output.

The serum creatinine level, the 24-hour creatinine clearance and the arterial pH were within normal limits in all the patients both pre- and postoperatively.

The men and the women with "pink urine" had a significantly higher ($p < 0.025$) body mass index than the patients without "pink urine".

Discussion

X-ray diffraction showed that the pink precipitate that appeared postoperatively in the urine of the morbidly obese patients was made up of uric acid dihydrate crystals.[4] Pure uric acid crystals are colourless, but in the urine they are almost always coloured by absorbed urinary pigments,[5,6] which colour the urine amber and form a pink to reddish-brown deposit along plastic urinary tubing and a pink sediment when the urine is centrifuged.

The patients in our study who had "pink urine" were the most obese, as determined by body mass index, which has a high correlation with assessments of body fat by body density and skinfold measurement.[7,8] It has been observed that obese patients have a greater rate of purine biosynthesis and an exaggerated rate of uric acid production.[9,10] Therefore, the greater the obesity, the higher is the potential baseline level of uric acid in the urine. Thus, factors conducive to precipitation of the uric acid would have greater effects in the obese.

In our study the urine levels of uric acid increased significantly after the operation in both the obese and the nonobese patients, but there was no significant difference in the postoperative levels between the obese patients with and without "pink urine". However, it is likely that the measurements in the patients with "pink urine" were falsely low because the uric acid dihydrate crystals that had precipitated along the urinary tubing were not taken into account. In a study of 10 patients of normal weight who underwent gastric operations for peptic ulcer disease Snaith and Scott[11] also found a postoperative increase in the urine levels of uric acid.

A postoperative increase in the urine level of uric acid may be related to a nonosmotic release of antidiuretic hormone (ADH) due to the stress of surgery. An increase in the circulating level of ADH would cause expansion of the extracellular fluid volume, which in turn will increase the urinary clearance of uric acid by changing the rate of reabsorption in the proximal tubule.[12-14] The increased secretion of ADH would also explain the reduced urine volume and increased urine osmolality of the patients with "pink urine". A further reaction to the stress of surgery is the activation of the adrenal cortex; the released corticosteroids would increase the clearance of uric acid through their uricosuric

Table I—Laboratory values preoperatively (I) and postoperatively (II)

Patient group, BMI*	Time	Mean ± standard deviation†					
		Serum uric acid level (μmol/L)	Urine uric acid level (mmol/d)	Uric acid clearance (mL/min)	Urine osmolality (mmol/kg)	Urine pH	Urine volume (mL/d)
Obese women with "pink urine", BMI = 48.8	I	342 ± 104	3.5 ± 0.9	4.7 ± 1.3	552 ± 308	5.72 ± 0.80	1492 ± 860
(n = 51)	II	311 ± 102‡	5.2 ± 2.3‖	8.8 ± 5.3‖	694 ± 212§	5.30 ± 0.51‡	1156 ± 515‡
Without "pink urine", BMI = 43.9	I	341 ± 90	3.2 ± 1.5	5.6 ± 4.1	641 ± 213	5.60 ± 0.82	1515 ± 760
(n = 111)	II	315 ± 96‡	5.2 ± 2.4‖	8.9 ± 5.3‖	664 ± 149	5.75 ± 0.93	1581 ± 760
Obese men with "pink urine", BMI = 47.3	I	480 ± 70	4.4 ± 1.5	4.7 ± 2.1	802 ± 230	5.47 ± 0.21	1596 ± 573
(n = 8)	II	460 ± 43§	4.8 ± 1.2§	7.2 ± 0.8§	850 ± 174	5.40 ± 0.48	1312 ± 270§
Without "pink urine", BMI = 46.3	I	422 ± 65	4.5 ± 2.6	4.9 ± 2.4	782 ± 59	5.55 ± 0.61	1557 ± 1008
(n = 17)	II	412 ± 110	5.8 ± 2.3‡	8.8 ± 4.5§	730 ± 97	5.94 ± 0.88§	1473 ± 530
Nonobese women, BMI = 24.6	I	261 ± 101	2.0 ± 0.9	4.3 ± 2.5	–	5.81 ± 0.38	1187 ± 530
(n = 8)	II	212 ± 154§	3.1 ± 1.5§	5.0 ± 8.2	–	6.10 ± 0.40	1495 ± 740
Nonobese men, BMI = 23.0	I	305 ± 66	2.1 ± 0.3	5.3 ± 3.0	–	5.82 ± 0.23	1100 ± 340
(n = 6)	II	282 ± 45§	4.0 ± 0.7‡	6.1 ± 0.7	–	5.91 ± 0.47	1308 ± 576

***Body mass index (BMI) = weight (in kilograms)/height squared (in metres).**
†Different from preoperative value at $p <$ ‡0.01, §0.05 or ‖0.001.

effect.[11,12,15,16] The urine levels of uric acid could also be increased by the crushing of stomach tissue through gastric stapling, which would release nucleotides; when the purines were metabolized, uric acid would remain as the end product.[12,13]

In our study the "pink urine" had a significantly lower pH than the postoperative urine of normal colour from obese patients and the postoperative urine of the nonobese patients. Uric acid has a pKa of 5.75, and its undissociated form is highly insoluble; therefore, it is more likely to precipitate in acidic urine.[12,13,17] Alkalinization with sodium hydroxide caused dissolution of the pink precipitate, which is characteristic of uric acid crystals,[4] owing to the dissociation of uric acid into urates, which are much more soluble. The urine of patients with uric acid calculi has a lower pH than the urine of control subjects or patients with calcium oxalate stones; the low pH has been attributed to an observed defect in ammonium excretion.[17,18] The cause of the lower postoperative urine pH in our patients has not been determined.

Postoperatively the patients in our study with "pink urine" had the lowest urine volume of any of the groups of patients and a significant increase in urine osmolality; thus, the tendency of the uric acid in their urine to precipitate would have been increased.

Crystalluria and urine supersaturated with crystalloid material are precursors of stone formation. The "pink urine" in our patients occurred 4 to 48 hours after surgery. Had the high urine levels of uric acid plus the decreased urine pH, decreased urine volume and increased urine osmolality not been transient, the supersaturation of the urine with uric acid dihydrate crystals might have led to urolithiasis.

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