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Case Report

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# Pink Urine Syndrome

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## Abstract

Discolouration of the urine is commonly encountered in clinical practice, ranging from brown dirty urine from urine infection to blood-stained urine from haematuria. Awareness of urine discolouration and its associations is important for diagnosis and appropriate treatment. This case report explores the rare occurrence of pink urine in a 35-year-old obese patient following a surgery under general anaesthesia with propofol. Despite the absence of associated symptoms or abnormalities in renal function, the urine exhibited amphourous pink urate crystals, leading to discolouration. The phenomenon, known to be associated with propofol use, resolved spontaneously after four days without any complications. The case highlights the importance of recognising and understanding urine discolouration with propofol usage.

**Keywords**: Urine discolouration, Propofol, Uric acids, Urate crystals

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## INTRODUCTION

Urine discolouration is common in clinical practices and the most common are reddish discolouration or bright red from haematuria to dirty brown urine from urinary tract infections. [1] Additionally, there are many less common discolouration reported in the literatures.[1] Causes include bleeding resulting in red staining, medications such as rifampicin causing orange discolouration to infection causing dirty brown urine and purple urine syndrome. (*Refer to the Supplementary text for types of discolouration of urine, aetiologies and pathophysiology*—**Table I**).

The colour, opacity, and odour of urine have been used for decades to help clinicians diagnose diseases. Urine discolouration secondary to chemicals is always a cause of concern, as it may indicate potentially dangerous conditions. Propofol (2,6-diisopropylphenol) is becoming the anaesthetic of choice used for induction of anaesthesia and in the intensive care unit settings for sedation due to its rapid hypnotic effects and associated antiemetic effects.[2] Among anaesthetic agents, propofol is infrequently associated with a self-limiting urine discolouration, which may seem alarming for those unfamiliar with the phenomenon.

## CASE REPORT

A 35-year-old morbidly obese gentleman, with no prior medical or urological history, suddenly developed pink sedimented urine after undergoing sigmoid colectomy for severe diverticulosis under general anaesthesia with propofol as the induction agent. He was managed post-operatively in the intensive care unit and was kept ventilated and sedated using propofol. On post-operative day one, he was noted to have asymptomatic pinkish discolouration of his urine with a cloudy pink substance lining the tubing of the urinary catheter (**Figure 1a**).

Clinical examination did not reveal any abnormalities. A urinalysis showed a low urinary pH of 5.0, specific gravity of 1.030, the absence of blood, leukocytes, or nitrate. His serum creatinine level was within the normal range. Cultures of the urine were sterile, and the ultrasonography of his urinary system was normal. Interestingly, his urine microscopic examination revealed amphourous urate crystals and no blood cells. His serum uric acid level was high at 450umol/L. A pink sediment rapidly precipitated in the urine following centrifugation (**Figure 1b**).

This condition spontaneously resolved after four days with recurrence or complications. The patient was discharged following recovery from surgery on post-operative day seven and was followed up in clinic for three months, during which he did not experience any urinary complications.

## DISCUSSION

Propofol is a commonly used intravenous anaesthetic agent due to its rapid onset of action and relatively safe therapeutic window.[2] Propofol acts by modulating the inhibitory function of the GABA (gamma-aminobutyric acid) neurotransmitter.[2] It is primarily metabolised by the liver through glucuronidation and to a smaller extent via cytochrome P450 enzymes. The metabolites are then excreted through the kidneys. [2,3]

Pink discolouration of the urine or pink urine syndrome, now commonly associated with propofol, is a rare condition first reported in the 1800s by Louis Proust, who described it as “substance rosacée” or “acid rosacique.”[2] The syndrome is characterised by the presence of uric acid crystals in the urine, which can appear pink due to their interaction with urinary pigments like uricine, a metabolite of bilirubin.[4] The lack of blood or haem and presence of uric acid crystals on urine microscopy can differentiate this condition. Pink urine syndrome was first recognised in 1984 among patients

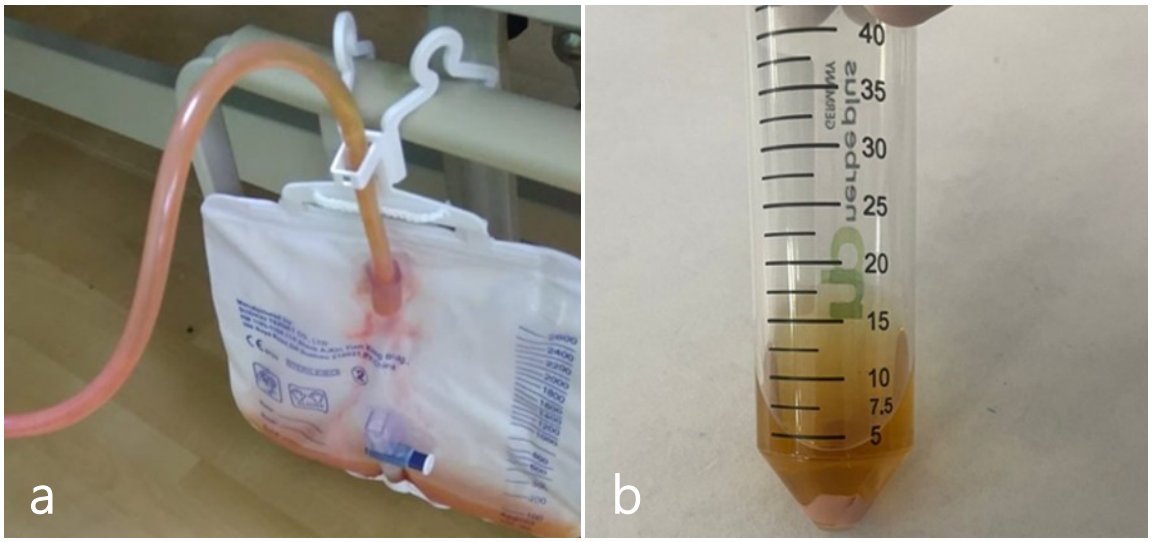


**Figure 1: a) Pink discolouration of the urine and b) pink urate sedimentations at the bottom of the tube.**

undergoing gastric partitioning,[4] and its association with propofol was identified in 1996, in nine Japanese patients presenting with milky pink urine following anaesthesia with propofol.[5] Apart from causing pink urine syndrome, propofol can also cause other discoloration- white due to oil-in-water emulsion and green due to the phenolic metabolites of propofol produced by the liver.[4]

The combination of propofol usage, male gender, obesity, and insulin resistance was noted in all reported cases, consistent with our findings. They were noted to have increased excretion of urinary uric acid. Low urine pH is an important factor that influences urate crystallisation.[6] Acidic urine is common in patients with insulin resistance. Populations with insulin resistance often have lower urine pH due to ammoniagenesis defects, leading to lowered ammonia production.[7] Several hypotheses have been put in place to explain the lowered ammonia production in individuals with insulin resistance, including reduced intracellular signalling strength in the proximal tubule and the upregulation of the nuclear erythroid 2 related factor 2 (Nrf2) antioxidant pathway.[8] Activation of the Nrf2 pathway is also demonstrated by propofol on its own, without the presence of insulin resistance.[2,9] This pathway activates a series of antioxidants that promote pink urinary pigment production through bilirubin metabolism. Obesity also increased purine metabolism and uric acid production, further contributing to increased uric acid excretion.[10]

Pink urine discolouration although self-limiting, can be distressing for patients and similarly to healthcare providers who are not family with this condition. It is a benign and self-limiting condition associated with uric acid precipitation. Reported cases have all been self-limiting and resolved with increased hydration and monitoring.

## CONCLUSION

Pink urine syndrome is a rare manifestation of propofol, a commonly used anaesthetic agent. There are several hypotheses for the occurrence of pink urine with propofol usage. Male gender, obesity, insulin resistance, lowered urinary pH, and high serum uric acid were noted in all reported cases. Propofol increases uric acid excretion in the urine. Meanwhile, a lowered pH encourages sedimentation. This heightened urinary excretion of uric acid crystals is usually transient, without toxicity to the human body, and unnecessary testing should be avoided. It is important to be vigilant and be aware of not just the association of pink urine with propofol use but also causes of urine discolouration so that early diagnosis can be made and appropriate management instituted.

## Declarations

### Conflict of interests

The authors declare no conflict of interests.

### Consent

Consent has been obtained from patient's parents for publication.

### Acknowledgement

None.

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## *Supplementary Texts*

**Table I: Types of urine discolouration, aetiologies and the underlying pathophysiology.**

| Colour of urine | Aetiology | Pathophysiology |
|---|---|---|
| Orange | Rifampicin<br>Sulfasalazine<br>Carrots | Produce metabolites that cause bodily fluids such as tears, urine, and saliva to turn orange. |
| Bright yellow | Excess vitamin B supplementation | Riboflavin gives a lime-yellow colour to the urine |
| Purple | Urinary tract infection in patients with long-term urinary catheters and typically has constipation<br>Rick tryptophan diet | Caused by bacteria that produce sulfate (Sulfatase) and phosphates (Phosphatase), which lead to tryptophan metabolism to produce indigo and indirubin pigments that become purple<br><br>- *Providentia* species, *Proteus mirabilis*, *Enterococcus* species, *Escherichia coli*<br>- *Morgenella morganii, Citrobacter* species, *Proteus* species<br><br>Note: This list include some of the commonly reported bacteria associated with purple urine bag syndrome (PUBS) |
| Green/ blue | Pseudomonas urinary tract infection | Bacteria produce pigments such as pyocyanin and pyoverdine that turn urine green |
| Cloudy/ milky sediment in urine | Pyuria | Due to the presence of white blood cells, bacteria, and pus. |
| | Chyluria (high protein in urine, remains cloudy despite sedimentation) due to disruption of lymphatic flow | Lymphatic malformation<br>Filariasis infection<br>Granulomatous disease |
| | Hypercalciuria | Hyperparathyroidism<br>Paraneoplastic syndromes<br>Milk-alkali syndrome<br>Familial hypophosphatemic hypercalciuric rickets |
| Red | Dye (food or medicinal) | Beetroot, or food colouring that includes betacyanin<br>Blackberries |
| | Blood | Haematuria causes:<br>Urinary tract causes<br>Stones, Urinary tract infection, Interstitial nephritis Urinary tract tumors. Glomerular causes, Vasculitis<br>Systemic causes<br>Renal vein thrombosis Trauma, Arteriovenous malformations, Coagulation disorders, Haematological disorders and Medications (Cyclophosphamide, vincristine, anticoagulants, quinines)<br>Contamination<br>Menstrual contamination |
| Dark brown/ Tea coloured | Bilirubin | Excess conjugated bilirubin due to obstruction of the hepatobiliary system<br>Choledocholithiasis, Cholangiocarcinoma, Hilar tumours or nodes, Pancreatic mass, Duodenal or gastric mass, Choledochal cysts, |
| | Bilirubin and urobilinogen | Liver dysfunction causing variable levels of urobilinogen production<br>Hepatitis, Wilsons disease, Rotor syndrome, Gilbert syndrome, Haemochromatosis |
| | Haemoglobinuria | Excessive haemolysis<br>Hereditary and acquired forms of haemolytic anaemia<br>Infections |
| | Myoglobin<br><br>Can be dark- Coca cola urine | Metabolic<br>Rhabdomyolysis<br>Medications (Statins, Amphotericin B, Diazepam) |
| | Drugs:<br>Metronidazole<br>nitrofurantoin, and niridazole. | Metabolites that are excreted in the urine can oxidize, leading to dark brown discolouration |
| Black | Melanuria | Metastatic melanoma |
| | Porphyin | Porphyrias |

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