Review Article

# Abnormal Urine Color

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**Abstract:** A change in urine color can be distressing for patients and physicians alike. Many of the causes of abnormal urine color are benign effects of medications and foods; however, a change in urine color may be a sign of an underlying pathological condition. The good news is that in many cases the diagnosis can be determined from a thorough history and urinalysis. This article presents many of the conditions physicians may encounter and will help them form a narrow differential diagnosis and treatment plan.

**Key Words:** drug toxicity, hemolysis, urinary tract infection, urine

Abnormal urine color can be distressing to patients, their family members, and clinicians alike. Patients expect an explanation for any alterations in the color of their urine, and rightfully so. Unfortunately, little original research exists regarding urine discoloration. Much of the information comes from case reports. Further complicating the issue is that there is no objective, standardized way to describe urine color.[1] One author may use the term "dark" to describe findings without fully defining the term to mean either a bolder shade of yellow, muddy brown, orange, or even a crimson red.[2]

More than 20 years ago, the *Southern Medical Journal* published a review article on the differential diagnosis of various urine colors.[3] Although useful at that time, clinicians are unlikely to perform benchtop chemistry tests such as adding hypochlorite bleach to urine samples to determine the presence of aminosalicylic acid. The present review attempts to list many of the conditions physicians may encounter and help them form a narrow differential diagnosis and treatment plan. The Fig. lists many of the potential causes of different urine colors that are described in detail in the review.

## Red Urine

The first problem we encounter with word "red" is that the term is broad enough to encompass the colors pink, shades of red, orange, brown, or black, depending on which clinician views the sample.[4] Whenever a patient develops red urine, the physician should always order a urine dipstick and urinalysis to look for the presence of red blood cells or hemoglobin. If blood is truly present, then the differential is broad and includes disorders of the renal collecting system[5] and hematologic system,[6,7] and contamination from menstrual blood. Additional workup will be guided depending on the patient's history and physical examination. A computed tomography scan may elucidate an anatomical problem such as entrapment of the left renal vein between the superior mesenteric artery and the aorta, also known as Nutcracker syndrome.[8] A transfusion reaction, glucose-6 -phosphate dehydrogenase deficiency,[9,10] sickle cell anemia, or thalassemia can lead to a hemolytic anemia and darken the urine to a deep reddish color.

Even without the presence of blood, dark red urine could be an ominous sign. The classification of diseases collectively known as porphyria can present with dark urine,[11] abdominal pain, photosensitive rashes, or neuropsychiatric complaints.[12] The disease is difficult to detect because it is rare. In addition, many hospital laboratories are ill equipped to perform porphyrin analysis on urine, further delaying treatment.

A relatively new development in US toxicology practice is the use of hydroxocobalamin for cyanide poisoning.[13] The traditional treatments for cyanide poisoning—amyl nitrite, sodium nitrite, and sodium thiosulfate—can induce methemoglobinemia, further reducing the oxygen-carrying capacity of red blood cells. Hydroxocobalamin works by combining with cyanide to form cyanocobalamin (vitamin $B_{12}$).[14] An unintended yet benign consequence of its administration is to color the skin and urine red.[15] The effects usually wear off after a few days.[16]

Other medications associated with red urine development include warfarin,[17] phenazopyridine,[18] rifampin,[19] ibuprofen, and deferoxamine.[20] Certain foods such as carrots (carotene),[21] blackberries, and beets can occasionally cause red urine.[22,23] Curiously, beeturia seems to be linked to the co-ingestion of oxalate-containing foods such as rhubarb, spinach, and oysters.[24]

### Key Points

- Diagnosing the cause of abnormal urine color usually can be made using a patient's history alone.
- When encountering abnormal urine color, a physician must, as the first step, order a urinalysis.
- Treating the underlying condition leads, in general, to resolution of urinary symptoms.

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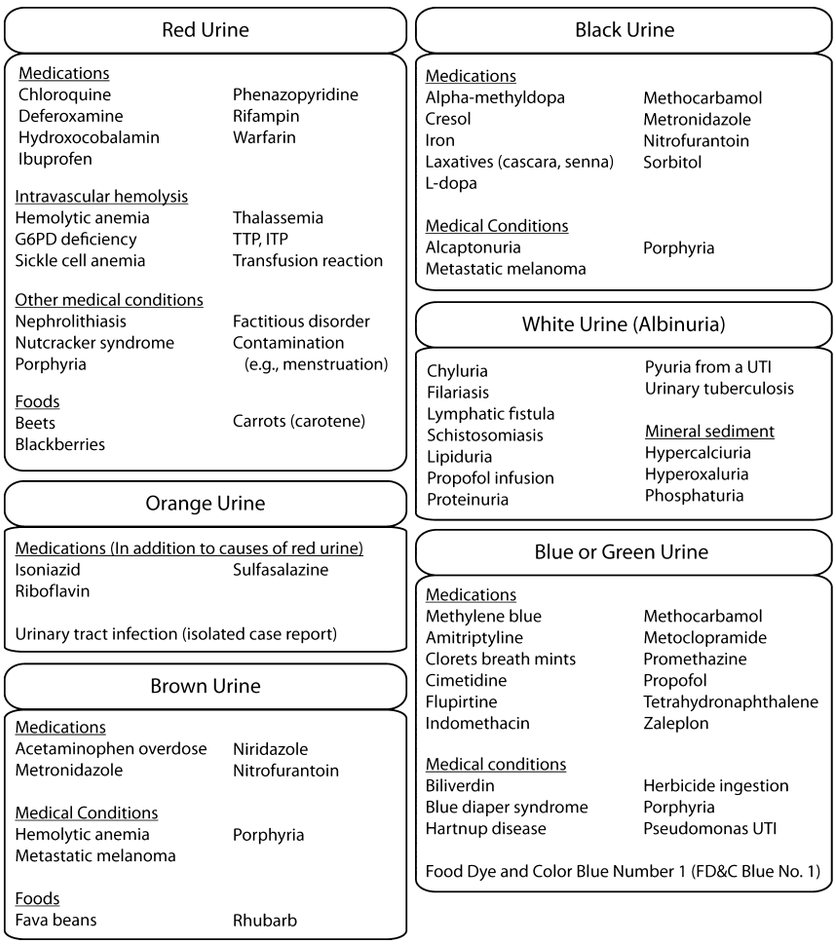


**Fig. Differential diagnosis of disorders and ingestions that can lead to abnormal urine colors.**

Finally, a patient with factitious disorder may present with red urine from adding blood or another red-colored material directly to his or her sample.[25–27] These patients may present with otherwise nonspecific complaints and will undergo an extensive but futile workup. Malingering is difficult to diagnose and may require repeat urine samples obtained under direct observation to finally uncover the disorder.

## Orange Urine

Continuing along the spectrum of red disorders, orange urine may be a manifestation of one of the above-named conditions or ingested substances such as high-dose riboflavin,[28] phenazopyridine,[29] and isoniazid. According to one study, 50% of isoniazid users will notice discoloration, making the finding common but insensitive when checking for compliance.[30] The discovery is harmless and requires no further workup if there are no additional complaints.

Curiously, one case report mentions an infant with orange urine caused by a urinary tract infection.[31] The apparent cause was a Gram-negative bacillus that produces indole from tryptophan. The conclusion reached by the authors is peculiar in that indole reactions usually produce blue, green, or purple urine.

## Brown Urine

As red urine becomes darker, some clinicians may interpret the color as brown. As a result, any of the disorders or ingestions listed above should be considered whenever a sample is thought to be brown. In the 1980s, a case series on acetaminophen overdose demonstrated that in addition to hepatorenal failure, three patients developed brown urine because of the buildup of the metabolite p-aminophenol.[32]

Brown urine could be a sign of melanocytes in the urinary system. Metastatic melanoma can lead to a rare condition called diffuse melanosis, causing dark skin, distant lesions to the internal organs, and brown or black urine.[33] One case report mentions a patient with acute kidney injury from melanin accumulation in the tubular system.[34] The prognosis is poor at this point.

## Black Urine

Black urine rounds out the discussion of causes of reddish urine discoloration. Many of the conditions listed above can present with black urine if the discoloration is dark enough; however, several of the conditions listed below are dangerous enough that the presence of black urine requires additional

workup. Example causes include metronidazole,[35] nitrofurantoin, cascara or senna laxatives, methocarbamol, sorbitol, and the phenol derivative cresol,[36] a common disinfectant ingested by alcoholics, which often is debilitating and leads to severe systemic toxicity.[37] Intramuscular iron injections are also associated with black urine as a benign effect of the medication. Patients in this case simply need reassurance.[38]

The presence of melanin in the urine can cause brown discoloration, as discussed above, or with a black tint. α-Methyldopa and L-dopa can induce urinary melanin in alkalotic urine, which is a known adverse effect of these medications.[39]

Alcaptonuria is a rare hereditary disease in which the body has a weakened ability to catabolize tyrosine, leading to an accumulation of homogentisic acid in the body.[40] It presents clinically with arthritis and darkening of the skin and urine.[41] The diagnosis is made by measuring homogentisic acid in the urine.[42] There is no cure, however, and treatment consists of high-dose vitamin C and limiting protein intake.

## Blue and Green Urine

Blue urine most typically appears to be caused by ingestion of methylene blue.[43,44] This substance is used in the United States for diagnostic tests, treatment of methemoglobinemia,[45,46] or as a treatment for refractory hypotension.[47] Outside the country, however, oral methylene blue may be found in medications and home remedies because it has antimicrobial properties.[48,49] True blue urine seems to be exceedingly rare, possibly because blue pigments combine with urochrome, the major contributor to urine's normal yellow hue, to create a green color before urine's elimination. In that regard, there are many case reports in which methylene blue turns urine green.[50–52]

Other medications associated with green urine may contain phenol groups and include promethazine,[52] thymol,[53] cimetidine,[54] and propofol.[55–58] The mechanism of action appears to be caused by phenol's conjugation by the liver and subsequent excretion by the kidneys.[59,60] The strength of the green seems to be dose related.[58] Curiously, propofol also is associated with pink[61] and white urine.[62]

Some nonphenol drugs noted to produce green urine are metoclopramide,[63] amitriptyline,[64] and indomethacin. In any event, the urinary findings of all of the above medications are benign effects and do not acquire further workup once urinalysis results are normal.

There are isolated case reports of parenteral absorption of tetrahydronaphthalene (Cuprex),[65] a pesticide that was used in the 1980s as an over-the-counter treatment for lice, and ingestions of the herbicides mefenaceta and imazosulfuro producing green urine.[66] A patient who has come in contact with these compounds should be treated as if he or she were poisoned and deserves full toxicology workup, stabilization, and possible admission to the intensive care unit.

In the critical care setting, patients receiving enteral tube feeds have on occasion been noted to produce green urine. The belief is that the food coloring additive Food Dye and Color Blue Number 1 (FD&C Blue No. 1) is absorbed from the gastrointestinal (GI) tract in high enough concentrations to cause dark green urine.[67,68] In animal models, <1% of FD&C Blue No. 1 is found in rat urine.[69] This finding is harmless and disappears with changes in tube feeds.

Not all causes of green urine are innocuous, however. *Pseudomonas*-causing bacteremia and urinary tract infections can present with green urine.[60,64] In this case, the patient's history and physical examination should point to an infectious disorder and urine and blood cultures may make the diagnosis. Treatment is centered on clearing the infection rather than on urine color.

Bile pigments in the urine represent a rare but worrisome cause of discoloration. Upon discovering biliverdin, clinicians must take a careful and thorough history to determine the location of the leak. Radiographs or invasive imaging may even be required. A case report of an enterovesical fistula caused by pelvic radiation therapy provides one such source of bile.[70]

Other rarer causes of blue and green urine include conditions that impair amino acid absorption from the GI tract. Blue diaper syndrome[71] and Hartnup disease[60] are autosomal recessive disorders in which tryptophan builds up in the GI tract, causing bacteria to metabolize it to indole, leading to a buildup of indican in the urine. The blue coloring by itself is not dangerous, but it does point to another underlying condition that requires investigation.

## Purple Urine

The only known cause of purple urine is purple urine bag syndrome. This usually benign condition is thought to arise from a series of steps in which tryptophan in the GI tract is converted to indole,[72] the indole is then metabolized by the liver and excreted by the kidneys, and the final product undergoes transformation by bacteria in the urine to create indigo (a blue pigment) and indirubin (a red pigment).[73] These pigments combine to form purple urine that then stains the polyvinylchloride of a Foley catheter.[74] Purple urine is associated with Gram-negative bacteruria and typically resolves after treatment with antibiotics and changing the catheter.[75,76]

## White Urine (Albinuria)

Albinuria has a wide differential diagnosis and requires a more thorough investigation beyond a simple urinalysis. Sediment from minerals in the urine such as hypercalciuria, phosphaturia, or hyperoxaluria occasionally can be discovered after centrifugation and analysis.[77] Consultation with a nephrologist is recommended at this point because changes in dietary intake and medication initiation may be required.

Severe urinary tract infection is one possible cause of white urine because purulent fluid may enter the bladder.[78] In addition, caseous material from urinary tuberculosis also should be entertained. Careful urine culture is required, followed by antibiotic therapy.

Chyluria is another possible diagnosis. It arises from abnormal communication between the lymphatics to the urinary tract, most commonly as a result of filariasis,[78] but also can be the result of a lymphatic fistula.[79] Antiparasitic drugs are of no benefit because the urine is usually sterile by this point. Referral to a urologist is necessary because the patient may require intervention to close the communication.

## Conclusions

A change in urine color can be distressing for patients, their family members, and clinicians alike. This article presented many of the potential causes of urine discoloration. Luckily, many of these causes are benign effects and can be elucidated from a detailed history. At a minimum, however, physicians should order a urinalysis when confronted with an abnormal urine color because potential pathologies do exist.

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