

Phenazopyridine Monograph

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Phenazopyridine

Phenazopyridine Hydrochloride, or 2,6-Pyridinediamine, 3-(phenylazo), monochloride, is classified as a urinary tract analgesic and is FDA approved in adults for the symptomatic relief of urinary burning, itching, urgency and frequency associated with the lower urinary tract caused by infection, trauma, surgery, endoscopic procedures or the passage of sounds or catheters.^{1,2,3} Non-FDA approved uses include symptomatic relief of the urinary tract in children, diagnosis of premature rupture of membranes in pregnant women and diagnosis of stress incontinence in women, where phenazopyridine was considered an unreliable diagnostic tool for either finding.⁴ Phenazopyridine is commercially available as a prescription medication as the trade name Pyridium and as generic hydrochloride salt in 100mg and 200mg tablets. It is also available as an over-the-counter medication as Azo-Gesic, Azo-Standard, and Uristat (95mg tablets), ReAzo (97mg tablets), and UTIRelief and Baridium (97.2mg tablets).² In the United States, phenazopyridine hydrochloride is manufactured by Vintage Pharmaceuticals, Breckenridge Pharmaceutical, Qualitest Pharmaceuticals, West-Ward, Able Laboratories, Novartis Generics, Copley Pharmaceutical, Quantum Pharmics, Trinity Technologies, Geneva Generics, Actavis Totowa, Zenith Goldline Pharmaceuticals, Barr Laboratories, Contract Pharmacal, Superior Pharmaceutical, Schein Pharmaceutical, and Superior Pharmaceutical. Phenazopyridine is also available in combination with Sulfisoxazole as a 50mg tablet (Amide Pharmaceuticals) and as Phenazopyridine Plus with hyosciamine hydrobromide and secbutarbarbital in a 150mg tablet (Contract Pharmacal).^{1,5} As a single agent, phenazopyridine is also available in tablet form in Argentina (Cistalgina), Belgium (Uropyrine), Brazil (Pyridium; Urologin; Urotril), Canada (Phenazo; Pyridium), Chile (Nazamit; Nordox; Pyridium), Hong Kong (CP-Pyridin; Phenazo; Pyridium), India (Pyridium), Israel (Sedural); Mexico (Azofur; Bioferina; Pimir; Urezol), South Africa (Pyridium), Singapore (Urogesic), Thailand (Ammilazo, Anazo; Phendiridine; Sumedium), and Venezuela (Pyridium). Phenazopyridine is supplied as a multi-ingredient agent in Argentina (Bacti-Uril; Nor 2; Priper Plus; Urisept NF; Uro-Bactrim), Brazil (Minazol; Uretil; Urizal; Uro Bac Septin; Uro Duoctrim, Uro-Baxapril; Urobiotic; Urotrin Urofar; Urofen; Uromix, Uroneotrim; Uropac; Uropielon; Uropirite; Uropol; Uroseptin), Chile (Uro-Micinovo), Germany (Urospasmon), India (Nephrogesic), Mexico (Azo-Uronalin; AzoWintomylon; Azogen; Mictasol; Nalixone; Naxilan-Plus; Pirfur; Urovec), Spain (Micturol Sedante), and Venezuela (Azo-Mandelamine; Bacteal).¹

Phenazopyridine is an azo dye which serves as a urinary tract analgesic as it is excreted in the urine where it exerts a local anesthetic effect on the urinary tract mucosa. The exact mechanism of action is unknown.^{2,3} The usual dose is 100-200mg orally three times per day after meals in adults and the elderly and 12mg/kg/day in 3 divided doses after meals in children.⁶ The recommended dose should only be given for 2 days when used concomitantly with an antibacterial agent for the treatment of urinary tract infection to relieve associated symptoms during the interval before the antibacterial agent controls the infection. The continuation of phenazopyridine with antibacterial therapy has not shown to be more efficacious than just using the antibacterial alone.³ No hepatic adjustments are necessary. Renal adjustments are recommended if the creatinine clearance is 50-80ml/minute, in which the dosing interval may be adjusted to every 8-16 hours. Use of phenazopyridine should be avoided if creatinine clearance is less than 50ml/min.²

The pharmacokinetic properties of phenazopyridine are not completely known. It is absorbed orally from the gastrointestinal tract.⁴ Metabolism may be hepatic or via other tissues.² The following metabolites have been found in the urine: N-acetyl-P-aminophenol (acetaminophen), P-aminophenol, and alanine.⁴ The drug is excreted up to 65% in the kidney as unchanged drug and 18% as paracetamol.^{1,3} Ninety-percent of a single dose is cleared within 24 hours with approximately 40% unchanged drug.⁷ Besides most of the drug entering the urine as unchanged drug, distribution was not described

Adverse reactions associated with therapeutic doses of phenazopyridine include headache, pruritis, rash, gastrointestinal disturbances (nausea, vomiting, diarrhea), orange to red urine discoloration, and staining of soft contact lenses. In cases of insufficient renal function, phenazopyridine can tinge the skin, sclera, or fluids yellow due to accumulation of drug, which may warrant drug discontinuation. Hemolytic anemia and methemoglobinemia have been seen at both therapeutic doses and in overdose. Reports of nail damage (deep lemon yellow nails), nephrolithiasis, and renal failure have been observed with chronic use of the medication. Occurrence of sulfmethemoglobinemia, thrombocytopenia, neutropenia, and agranulocytosis have also been described with therapeutic doses. Hepatitis following therapeutic doses may be related to a hypersensitivity reaction to the drug, and may resolve with discontinuation of the drug.⁴ An anaphylactoid reaction to phenazopyridine has been seen, but exact occurrence is unknown. With long-term use in rats and mice, carcinogenicity was observed with neoplasia in the large

intestines of rats and in the livers of mice. No association between phenazopyridine use and occurrence of human neoplasia have been reported. Phenazopyridine is contraindicated in patients with known hypersensitivity to the drug or its components and impaired renal function, described as creatinine clearance $< 50\text{ml/minute}$.³ Patients with hepatitis and glucose-6-phosphate dehydrogenase deficiency should use phenazopyridine with caution.⁴

Phenazopyridine is currently classified in pregnancy category B and has limited human data. Although the drug crosses the placenta, there is little fetal risk. Other than a possible decrease in fertility during the first trimester, there is no evidence of risk during later trimesters.⁴ The Collaborative Perinatal Project monitored 50,282 mother-child pairs in which 1,109 exposures anytime during pregnancy and 219 exposures during the first-trimester were documented. Results indicated no individual defects or large categories of minor or major malformations could be attributed to phenazopyridine. In a second surveillance study of Michigan Medicaid recipients, 229,101 pregnancy exposures, 469 newborns being exposed during the first semester, saw a 5.4% occurrence of major birth defects. These birth defects included cardiovascular defects and an oral cleft defect; however, data did not support an association between phenazopyridine administration and congenital defects.⁸ In pregnant rats, phenazopyridine at doses of 50mg/kg/day have also shown no harm to the fetus or impairment on fertility. Because of limited human data, use of the drug during pregnancy is only recommended if clearly necessary.³ However, these defects were found not to be associated with exposure to the drug. Phenazopyridine safety in breast feeding is unknown with no human data or description of the drug or metabolites entering the human milk.⁸

Considering phenazopyridine's synthesis in 1914 and compared to its widespread use, relatively few reports of phenazopyridine toxicity exist.⁹ In a review of all case reports before 1979 conducted by Green et al.,¹⁰ there were seven cases of acute accidental ingestion, nine cases of chronic overdose, four cases of phenazopyridine-induced hypersensitivity hepatitis, and no deaths directly due to phenazopyridine toxicity. The majority of acute accidental ingestion were children. Elderly patients compromised the majority of chronic overdose cases.¹⁰ Case reports after 1979 included at least two acute accidental ingestions, four chronic overdoses, three toxicities at therapeutic doses, and four intentional acute ingestions as suicide attempts. (See Table). Phenazopyridine's availability as both a prescription and over-the-counter (OTC) medication may also contribute to the number of reports of toxicity.¹¹ A cross-sectional study,

surveying consumers who bought OTC phenazopyridine, found that only 57% knew phenazopyridine was a urinary tract analgesic, and 43% thought phenazopyridine possessed other actions, including antibacterial and curative effects. In addition, 19% knew neither the cause of their urinary symptoms or the action of the drug.¹² From a toxicology standpoint, the lack of consumer knowledge of the drug as well as its accessibility can lead to the improper use of the drug chronically or acutely as with suicide attempts.

Major toxicities associated with phenazopyridine include methemoglobinemia, acute renal failure, and hemolytic anemia. Cases of hypersensitivity hepatitis were also reported as well as myelosuppressive pancytopenia. Methemoglobinemia, hemolytic anemia, and acute renal failure occurred in as little as therapeutic doses, 600mg/day.^{10, 11, 13} Therapeutic doses may have led to toxicity due to use in elderly patients with impaired renal function; however, some previously healthy patients also experienced these toxicities in the absence of renal impairment.^{13, 14} Hypersensitivity hepatitis has been shown to be non-dose-related, occurring after one tablet.¹⁵ Myelosuppressive pancytopenia was reported along with acute renal failure in an elderly male taking prescription strength phenazopyridine four times daily for 3 days.¹⁶ Death has not been directly associated with phenazopyridine toxicity; therefore, a lethal dose has not been documented. As an acute ingestion, doses as small as 50mg/kg have produced toxicity.¹⁷ A dose as high as 750mg/kg has not shown to be lethal in a previously healthy patient.¹⁰

Although small amounts of ferrous iron are normally oxidized to ferric iron, normal erythrocytic processes reduce ferric iron back to ferrous iron, stabilizing the met Hb level to <1mg/dL.¹⁸ Acquired methemoglobinemia may be caused by drugs including phenazopyridine and its metabolite aniline, which serve as a direct oxidants of hemoglobin to methemoglobin (met Hb).¹⁴ Tissue hypoxia and cyanosis result from methemoglobinemia as met Hb is unable to transport oxygen. In addition, the met Hb already bound to oxygen is less likely to release the oxygen at the tissues due to a left shift of the oxyhemoglobin dissociation curve, indicating an increase in affinity for the oxygen.¹⁰

Three pathophysiological mechanisms for phenazopyridine-induced acute renal failure have been described. Phenazopyridine may have a direct toxic effect on the renal tubules leading to acute tubular necrosis in the absence of hemolysis, seen in animal models as well as a case report.^{19,20} Acute renal failure may also be secondary to methemoglobinemia, a mechanism

tested in rats which develops as cast formation, interstitial edema, tubular degeneration and regeneration. Finally, hemolytic anemia may cause progressive renal failure, especially seen in patients with renal insufficiency.^{7,19} Dehydration as a result of nausea and vomiting may also contribute as a factor of renal failure.¹⁰ All case reports of renal failure were reversible except for one patient who progressed to chronic kidney disease.^{7,20}

Phenazopyridine may induce hemolytic anemia through several mechanisms. The red blood cell's reductase enzyme system, which normally prevents oxidation of sulfhydryl groups by providing reduced glutathione, may be overcome by phenazopyridine or aniline's oxidizing properties. Phenazopyridine may also act as an intermediate between molecular oxygen and hemoglobin, consequently leading to destruction of hemoglobin when oxygen is present.²¹

Myelosuppressive anemia was supported by all cell lines being suppressed but was not confirmed by a bone marrow biopsy. Mechanism of this toxicity is unknown. However, the patient had a history of prostate cancer which may have contributed to the cause of the toxicity.¹⁶

Methemoglobinemia patients may manifest with cyanosis, chocolate-colored blood, and unresponsive to oxygen therapy. Lethargy, confusion and somnolence may also be a result of methemoglobinemia, secondary to hypoxia to the brain.⁷ In cases of hemolytic anemia, patients may present with skin pallor. "Bite cells" or "degmacytes", erythrocytes with portions removed, may also be evident when hemoglobin is oxidized.¹⁹ Acute renal failure may or may not be accompanied by oligouria and is often progressive with peak serum creatinine levels between 3 and 10 days and usually resolves with discontinuation of phenazopyridine.⁷ In addition, presence of orange to red colored urine may suggest phenazopyridine exposure when causative agent is unknown.¹¹ Patients with liver toxicity usually presented with jaundice, epigastric pain, nausea, vomiting, hepatomegaly, elevated liver enzymes, and fever.¹⁰

Obtaining phenazopyridine levels would not be beneficial as symptoms would have already developed. Furthermore, doses or levels have not been correlated with specific toxic effects. In cases of cyanosis, met Hb levels may be assessed and can be beneficial in determining whether the antidote, methylene blue, is effective at reducing the met Hb level, and whether a second dose is required. Met Hb levels can also be useful to correlate with patients' symptoms. However, met Hb may not be an adequate indicator of toxicity if laboratory analysis of met Hb are not performed immediately due to continued production and reduction of met Hb in vitro at varying rates creating falsely high or low values. If correctly analyzed, patients with

met Hb levels less than 25% may present with slight cyanosis. At met Hb levels of 25-50%, patients may exhibit headaches, weakness, lightheadedness, and cyanosis. With met Hb levels greater than 50%, patients may begin to have exertional dyspnea and increasing lethargy. Death, coma, and convulsions may occur at met Hb levels greater than 70%, which have not yet been described with phenazopyridine overdose.¹⁰ Other monitoring parameters to be assessed include CBC, renal and liver function tests, and urinalysis.

First aid measures to terminate toxic exposure is mainly discontinuation of the drug, early hydration, alkalization, and diuresis to prevent renal toxicity. Supportive care measures include supplemental oxygen to saturate remaining hemoglobin in patients with acquired methemoglobinemia, infusion of packed red blood cells for patients exhibiting hemolytic anemia, and hemodialysis for patients with acute renal failure. Hyperbaric oxygen originally was not recommended due to the potential to exacerbate methemoglobinemia.¹⁰ However, more recently therapy with hyperbaric oxygen for met Hb has been considered a reasonable treatment as it may increase availability of oxygen at hypoxic tissues.²² In the case where , met Hb levels of >70% are reached, airway management or benzodiazepines may be needed with development of coma or convulsion. Methemoglobinemia usually develops within 2 to 3 hours of ingestion, but may be delayed.⁶ Gold et al.¹⁷ recommends patients should be observed for at least 4-6 hours even after small ingestions. For acute renal failure N-acetylcysteine (NAC) and L-carnitine can be considered to prevent anoxic injury and have relatively low toxicity. NAC may act as an antioxidant and reduce interstitial injury, replenish intracellular glutathione, and improve kidney function. L-carnitine is beneficial by protecting mitochondrial metabolism, which may be affected by free oxygen radicals.⁷

Due to rapid absorption of phenazopyridine, activated charcoal, gastric lavage, and whole bowel irrigation may have limited efficacy in preventing absorption of phenazopyridine after overdose, but may be beneficial in large ingestions.^{7,9,18} Ipecac may be considered if there are no contraindications, there is no alternative to decrease gastrointestinal absorption, there will be a delay of greater than 1 hour to reach a health care facility, there is a substantial chance of serious toxicity, and it can be administered within 30-90 minutes. Activated charcoal can be considered in patients if it can be administered within one hour of ingestion, if there are no contraindications, and the patient consumed a potentially toxic ingestion.⁶

Methods for enhancing elimination include exchange transfusion. Exchange transfusion could be potentially beneficial in patients not responding to methylene blue and at risk for inducing methemoglobinemia by both removing offending agents and reducing met Hb levels.⁶ By similar mechanisms, hemodialysis may decrease aniline toxicity.

Development of methemoglobinemia can be reversed with methylene blue administration at a dose to 1-2mg/kg of a 1% solution IV or 5mg/kg orally in less severe cases for children and adults. The dose for neonates is 0.3-1mg/kg. To avoid local pain, IV methylene blue should be administered slowly over 5 minutes and subsequently 15-30ml of fluid should be run through the IV rapidly. Doses may be repeated every 4 hours if necessary to reduce met Hb levels. If IV access is not possible, methylene blue may also be given intraosseously.⁶ Improvement should be evident within 1 hour of administration. Methylene blue is reduced via NADPH-dependent methemoglobin reductase to leukomethylene blue which then directly reduces the methemoglobin back to hemoglobin.¹⁷ Methylene blue can also induce methemoglobinemia at high doses. Furthermore, at doses >3mg/kg, or in patients with G-6-PD deficiency, methylene blue can cause hemolytic anemia.¹⁹ Therefore, initiation should not be considered until the met Hb level is 20 to 30% or symptomatic because of its toxicities.⁶ Methylene blue may also not be required in mild cases of methemoglobinemia due to normal reconversion back to hemoglobin via NADH-methemoglobin reductase within 24 to 72 hours, in which methemoglobin is decreased by approximately 15% per hour once the offending agent is removed and production of met Hb has ceased.¹⁷ Ascorbic acid can directly convert met Hb to hemoglobin; however, its effects are slow and requires high doses. Furthermore, ascorbic acid has been associated with hemolytic anemia and should only be considered for patients with hereditary enzyme deficient methemoglobinemia.¹⁰

Summary of Case Reports involving Phenazopyridine Overdose or Toxicity after 1979

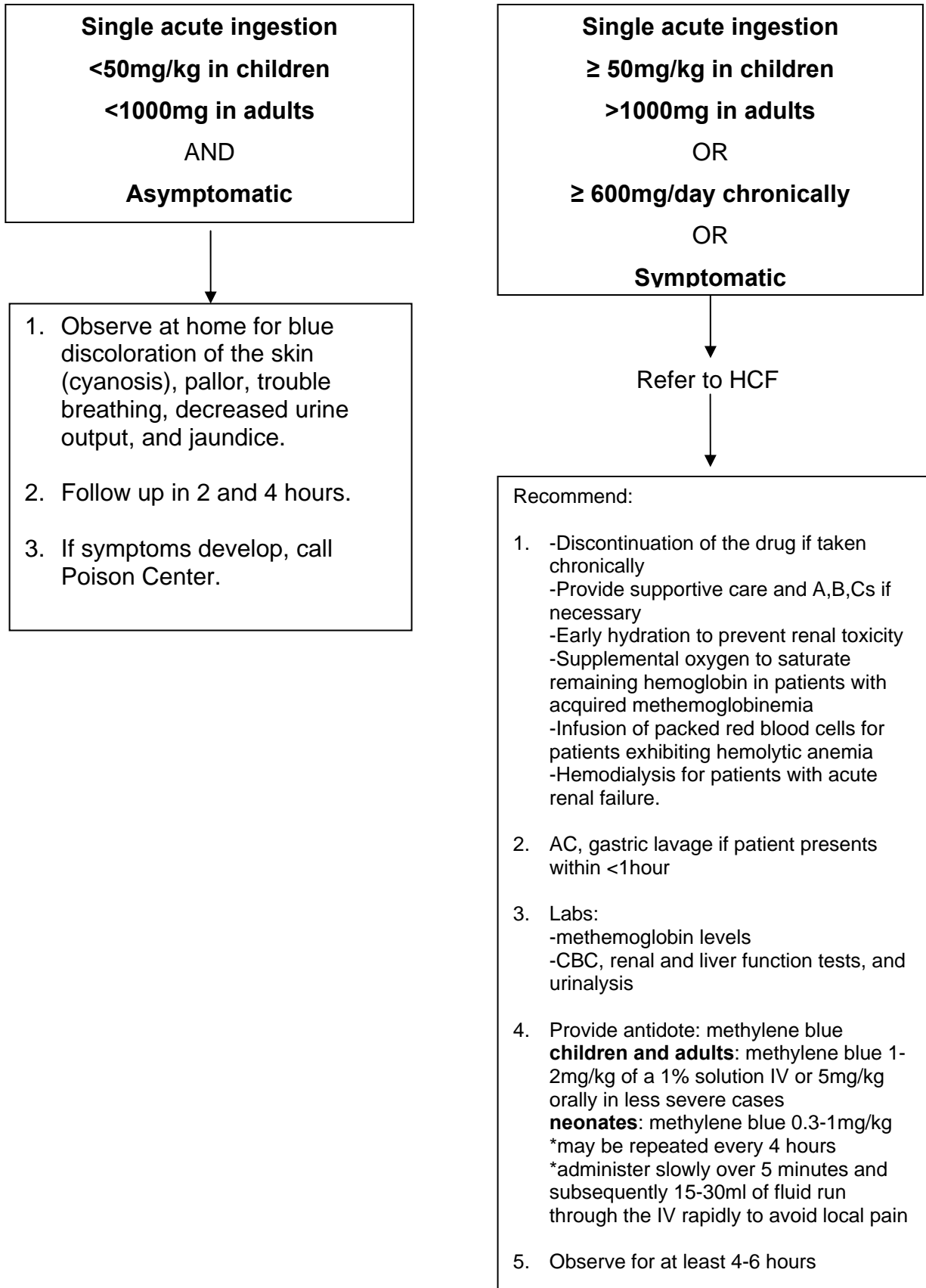
Patient age and gender	Amount ingested	Potential Co-ingestants	Clinical manifestations	Treatment	Outcome
17yo female (HIV+) with normal urine function ⁷	1200mg (suicide attempt)	Antiretroviral therapy (noncompliant) Marijuana	Progressive nonoliguric renal failure max SCr: 4.2mg/dl Methemoglobinemia resolving w/in 24hrs w/o treatment (methemoglobin level 8.7%) Acute tubular necrosis	N-acetylcysteine L-carnitine Sodium bicarbonate for urine alkalinization	Discharged on day 8 with normal renal function
87yo male ¹⁶	?mg Rx strength 4 times daily x 3 days	Home medications: digoxin, prednisone, Lasix, Ditropan	Fatigue and yellow skin Myelosuppressive pancytopenia Acute renal failure Orange-colored urine	Pyridium discontinued Rehydration Two units packed-red-blood cells	Discharged on day 5 in satisfactory condition Sin color and urine color returned to normal
58yo female ¹¹	Chronic use for ? duration	Prescription medications; Wellbutrin, Xanax, Synthroid, and Prilosec OTC medications: Tylenol and Motrin	Acute renal failure (Scr 3.0mg/dL with baseline 0.9mg/dL 2mo prior) Anemia (Hct 27.9 with baseline 37.5 2 mo prior) Dark orange urine	Discontinuation of phenazopyridine Day 2 and 4: 1 unit of packed red blood cells	Resolution of renal failure, anemia, lethargy within one month
2yo female ¹⁷	600mg 50mg/kg		Orange color on face and lips Alert, active and in no distress Vomited once (some orange particulate matter visible) Orange urine Methemoglobinemia: s/p 5 hours from arrival: slight grayish color of the face; 75-85% O2 Sat; methemoglobin level 29.1%	Activated charcoal 1mg/kg s/p methemoglobinemia: 1mg/kg methylene blue slow IV push	O2 sat improved 15-30 min after methylene blue administration, increasing to 91% 1 hour later No further methylene blue required
28yo female ¹⁴	100mg TID restricted to 2-3 day courses 1 100mg tablet morning of cytoscopy		Methemoglobinemia (cyanotic and Oxygen saturation 84%)	2mg/kg IV methylene blue	Oxygen saturation improved to 99% w/ methemoglobin level 2.3%
8.5 month old ¹⁸	2000mg (227mg/kg)		Asymptomatic presentation throughout	Gastric lavage (1 hour after	11 hours after the third dose of the methylene

8.8 kg			<p>Increasing PCO₂, HCO₃, and methemoglobin. Decreasing O₂ saturation and hemoglobin level.</p> <p>Negative for G6PD deficiency</p> <p>Protracted methemoglobinemia: methemoglobin level increased to 24.7%. (Methemoglobin peak at 25 hours)</p> <p>second increase in methemoglobin levels from 18.8% to 19.3% 5 hours after the first dose</p> <p>Next morning methemoglobin levels were 26.3%</p>	<p>ingestion) of 300ml of yellow liquid with brown tablet fragments</p> <p>10 grams (1gm/kg) activated charcoal in 35% sorbitol solution via nasogastric tube</p> <p>1mg/kg methylene blue over 5 min and intravenous fluids (20mEq potassium chloride in L 5% dextrose and 0.2% sodium chloride at 40ml/hr) were started at peak methemoglobin level</p> <p>Additional 1mg/kg methylene blue after second increase</p> <p>Third dose of 1mg/kg methylene blue the next morning</p>	<p>blue, methemoglobin level was 1.9 % with all other labs wnl</p> <p>No evidence of hemolysis</p> <p>Normal renal and hepatic function at 1 week.</p>
19 yo female w/ no history of renal or hematological impairment ²³	<p>200mg TID x 2 days</p> <p>6 grams on day of admission (suicide attempt)</p>		<p>Severe muscle and abdominal pain, nausea, and jaundice (1-2 hours before admission)</p> <p>On admission, jaundiced and cyanosis of the skin and lips and periorbital edema</p> <p>Methemoglobinemia, muscle damage (increased CPK), rhabdomyolysis, acute renal failure.</p>	<p>Supportive care, no hemodialysis (no signs of uremic pleuritis or pericarditis)</p>	<p>Methemoglobinemia resolved within 24 hours</p> <p>Muscle enzymes returned to normal on the 4th day.</p> <p>Fully recovered after 3months (normal renal function tests)</p>
18 yo female ²⁴	<p>10-15 200mg tablets</p>		<p>Transient renal failure</p> <p>5- day history of N/V</p>	<p>Treated at home with promethazine</p>	<p>Follow-up ten days later: asymptomatic; BUN 10mg and</p>

	(2000-3000mg) prior to admission		At admission (5 days after ingestion), mild dehydration and hyperactive bowel sounds; renal failure Scr=9.1mg and BUN 52mg Third hospital day: CrCl= 35ml/min; urine protein <100mg/24 hours Sixth hospital day: Scr and BUN decreased to 2.4 and 15	suppositories and dimenhydrinate; admitted to the hospital b/c could not ingest ampicillin orally (E.Coli UTI)	Scr=1.1mg/100ml. Six months later: Scr=1.0mg/100ml
89 yo male ²¹	100mg BID x 5months increased to 400mg TID x 3 weeks prior to admission for chronic urinary frequency and bladder spasm	Ibuprofen 300mg TID for degenerative joint disease Trimethoprim/ Sulfamethoxazole 2 tablets BID x 3 days Fava beans regularly for 40 years	Increasing SOB and anginal-type chest pain x several weeks Hemolytic anemia; Pale, dyspnea, pulse 110, BP 120/70 w/o orthostatic changes; serum lactic dehydrogenase 449 IU/L (100-230); bilirubin 2.1mg/dL (0.1-1.0) and Scr (1.3); hematocrit 28 (39.5 before phenazopyridine dosage increase)	Phenazopyridine discontinued; 2 units PRBC	Became asymptomatic and hematocrit became stable at 37.5.
46 yo male w/ hx of schizophrenia and poly-pharmacy abuse ²⁵	30-40 100mg tablets x 1 week		Methemoglobinemia, acute renal failure Deep yellow pigmentation of sclerae, mucous membranes, and skin; cyanosis of lips, malar eminences, and ears; Scr 9.2mg/dL (1.1 mg/dL 2 years earlier); Hgb 13.9g/dL, Hct 44%) Methemoglobin: 26.1% (normal 0-3% in nonsmoker) First 18 hours: oligouric (15cc/hr)	400mg IV furosemide over 4 hours one oral dose 10mg metolazone 100mg hydrocortisone sodium succinate every 6 hours 1mg/kg (70mg) of methylene blue IV Discharged with oral folate supplement for hemolytic episode	Urine output increased to 200-300cc/hr; Scr decreased to 1.8mg/dL (over 10 days); methemoglobin level decreased to 10% (8 hours after methylene blue) and then to 3% (ten days later); skin and urine pigment gradually returned to normal; asymptomatic (day 7) w/ Hgb 9.2 and Hct 27%, reticulocyte count 5% 2-month follow-up: Hgb 14.2g/dL, Scr 1.0mg/dL, reticulocyte 1.0%, methemoglobin 0.3%
67yo female/ 56 kg ¹³	200 mg TID x 10 days prior to hospitalization	Nitrofurantoin 50mg TID x 10 days prior to hospitalization Other	Methemoglobinemia, Hemolytic anemia Turned blue 2 days after starting the drugs	Discontinued phenazopyridine and nitrofurantoin (7/18) folic acid	(7/22) no methemoglobin was detected; reticulocyte count 6.8%

		<p>medications: aspirin 650mg BID, dipyrimdamole 50mg TID, Mylanta 30cc QID, pentobarbital 100mg hs, diazepam 2 mg po prn, propoxyphen napsylate 100mg with acetaminophen 650mg prn, cimetidine 300mg TID, isosorbide dinitrate 5 mg po TID, nylidrin 12 mg TID.</p>	<p>Hct 34.7%, reticulocyte 11.1%; Hgb A1 95.1%/ A2 4.9% (at local hospital 7/8)</p> <p>(after transfer to UNMH 7/17) Cyanosis of tongue, lips, and pharynx Hgb 9.3g/dL, Hct 28.4%, reticulocytes 21%, MCV 102u, methemoglobin level 40.1%; BUN 16mg/dL, Scr 0.8 mg/dL</p>	<p>5mg/d and ascorbic acid 500mg/d</p> <p>(7/21) methylene blue 56 mg (1mg/kg) IV</p>	
<p>46yo female/ 44.5kg¹³</p>	<p>200mg TID (started on 10/13); reduced to 100mg BID (10/16)</p>	<p>Sulfamethoxazole/ Trimethoprim 800/160mg BID (started on 10/16)</p> <p>Other medications: diazepam 5mg po Q8H prn, acetaminophen 650mg po Q6H prn, and Riopan 30cc po with meals</p>	<p>(10/19) Malaise, muscle aches, and SOB</p> <p>(10/20) Methemoglobinemia, Hemolytic anemia Cyanosis of lips, tongue, and extremities, slight left/right CVA tenderness, no edema or clubbing of the extremities</p> <p>Methemoglobin 34.9%, Hgb 8.7g/dL, Hct 27.6%, MCV 94u, BUN 11mg/dL, Scr 0.8mg/dL, bilirubin 1.2mg/dL, normal G-6-PD activity</p> <p>(Hospital day 3) Reticulocytes 15.2%, methemoglobin 23.3%</p>	<p>(on admission) methylene blue 100mg IV and Ascorbic acid 500mg/d</p> <p>(Hospital day 2) one unit PRBC and methylene blue 100mg IV</p> <p>(Hospital day 3) methylene blue 100mg</p>	<p>(Hospital day 4) discharged</p> <p>(F/U 11/6) Hct 36.7%, methemoglobin 4.6%</p>
<p>16yo female/ 45 kg²⁶</p>	<p>28-200mg tablets (12 hours before admission)</p>	<p>Smokes 1ppd</p>	<p>Methemoglobinemia, hemolytic anemia</p> <p>Cyanosis of the skin, nail beds, and mucous membranes, but no acute distress; Pulse 130bpm; mild epigastric tenderness to deep palpation Hgb 13.2 gm/dl; Hct 39.9%; chocolate brown blood; methemoglobin level 56.9%</p>	<p>Oxygen by rebreather mask</p> <p>2mg/kg methylene blue IV over 5 inutes</p>	<p>(30min after methylene blue) decreased cyanosis; methemoglobin level 12.8% (24 hours later) methemoglobin undetectable (36 hours post ingestion) Hgb 11.1g/dL (F/U 10 days later) mild exertional dyspnea; Hgb 10g/dL, 11.7% reticulocytes, moderate "bite cell" Subsequently lost to F/U</p>

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Phenazopyridine Guideline

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