Kentucky Poison Control Center

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Provider Update

There are no old, bold mushroom hunters.

Unintentional mushroom ingestions account for a small but steady percentage of poison center consultations. Cumulative data from the National Poison Data System (NPDS) indicates that mushrooms represent less than 0.25% of reported human exposures, and combined NPDS and Mushroom Poisoning Registry data estimate approximately five toxic mushroom exposures per 100,000 persons per year. Although more than 100,000 species exist, fewer than 0.1% are known to be toxic; moreover, in 75% to 95% of reported exposures the exact species is unidentified.[1]

The weight of epidemiologic evidence demonstrates that most mushroom exposures are benign. In most exposures individuals do not develop symptoms, most exposures are managed at home, and major toxicity is rare. During a 35-year review period, fewer than 100 deaths were attributed to mushroom ingestion. All reported deaths were in adults and most were associated with either Amanita sp., some hallucinogens, Boletus sp., or gyromitrin-containing varieties. The most common toxin groups are the hallucinogens and gastrointestinal (GI) irritants but these comprise less than 10% of all reported mushroom exposures, with other toxin categories representing under 2% of identified cases.[1]

Staff Safety Alert: Emerging Drug Threats in Clinical Setting

Several dangerous substances are increasingly present in prehospital and emergency department settings. These include BTMPS, medetomidine, xylazine, and carfentanil. Each poses unique risks to patients and providers, especially through handling or close contact

For more information visit: https://kypoisoncontrol.com/wp-content/uploads/2025/10/High-Risk-Street-Drug-Contaminants.2025.pdf

Who We Are

Clinical Toxicologists:

Director
Ashley Webb, PharmD, MSc, DABAT, FAACT, AFACMT

Clinical Operations
Jay Adams, PharmD, DABAT

Clinical Pharmacy Specialist, Editor
Jan Scaglione, PharmD, MT, DABAT

Medical Toxicologists:

Medical Director
Peter Akpunonu, MD, FAAEM, FACEP, FACMT

Consultants:
Drew Micciche, MD
Jan Sullivan, MD, FAAP, FCCM, CPI

Specialists in Poison Information:

Jordon Blanton, BSN, CSPI
Chris Boroomand, PharmD, CSPI
Terra Brown, BSN
Brad Chevalier, BSN, CSPI
Whitini Hartsell, BSN
Kaila Hollkamp, PharmD, CSPI
Callie Kappesser, BSN
Sam Katzman, PharmD
Nicole Kirchner, RN
Bryan Murphy, PharmD, BSN, CSPI
Jessica Purser, BSN, CSPI
Sara Reinke, BSN, CSPI
Lois Taurman, ASN, CSPI
Michelle Vitols, BSN, CSPI
Jay Vowels, BSN, CSPI

Poison Prevention Coordinator:

Maria Chapman, BA

Gyromitra (False Morel) Toxicity: Overview

Gyromitra esculenta (false morel) is notable among toxic mushroom species due to its characteristic toxidrome. Exposures often result from its mistaken identity as a true morel (Morchella sp.) by foragers. Gyromitrin — the mushroom's principal toxin — hydrolyzes to monomethylhydrazine (MMH), a metabolite that inhibits pyridoxal phosphokinase, thereby reducing pyridoxal-5′-phosphate (PLP) availability and impairing GABA synthesis; the resulting GABA depletion predisposes the patient to CNS excitation and seizures.[2]

Etiology

Gyromitrin is a polar, water-soluble, volatile mycotoxin found in G. esculenta and certain related Gyromitra species (Gyromitra gigas and Gyromitra fastigiata may contain gyromitrin, though human poisonings are not commonly attributed to those species). Fresh G. esculenta can contain 50–300 mg/kg gyromitrin; washing, boiling, and drying substantially reduce this content, and parboiling has been cited to remove up to ~99% of gyromitrin in some reports. However, fumes from sauteing the mushrooms has led to significant toxicity.[8,9,17] Gyromitrin is hydrolyzed to N-methyl-N-formylhydrazine (MFH) and then oxidized to the active MMH metabolite via cytochrome P450 enzymes.[3]

Epidemiology of Gyromitra Poisonings

Documented poisonings associated with Gyromitra species date back centuries, with evolving nomenclature and progressive chemical identification of gyromitrin in the 20th century.[3] Geographic clustering of cases is common: Eastern Europe (Germany, Poland, Finland) reports higher incidence in coniferous forest regions, whereas in North America cases have been reported most often in Michigan; less toxic varieties appear to grow west of the Rockies (Idaho, Western Canada). Exposures typically occur in spring, distinguishing them from some other hepatotoxic species that are more prevalent in fall.[3] North American registry data suggest Gyromitra accounts for a small proportion of mushroom toxin cases, with few documented fatalities in modern series.[3]

Pathophysiology

MMH directly interacts with enzymatic systems, including cytochrome P450, amino oxidases, and glutathione pathways. This leads to reduced PLP, impaired function of glutamic acid decarboxylase, decreased GABA synthesis, and a state of relative neuronal hyperexcitability manifesting as delayed seizures. MMH also produces hepatocellular injury via free radical formation and unstable diazonium intermediates and may cause direct renal toxicity and dehydration-related kidney injury.[3] GABA is the principal inhibitory neurotransmitter in the CNS. Disruption of GABA synthesis or function — such as that produced by MMH or INH-related inhibition of pyridoxal phosphokinase — removes inhibitory tone and can precipitate seizures.

Clinical Presentation and Evaluation

The Gyromitra syndrome generally begins with gastrointestinal symptoms occurring several hours after exposure followed by confusion and CNS excitation in moderate to severe cases; refractory seizures can occur after substantial exposures. Specific tests for gyromitrin detection are currently unavailable in the clinical setting. Imaging is typically unrevealing for early CNS findings but indicated for persistent focal signs or status epilepticus.[3]

Management and Treatment

Secure IV access, correct fluid and electrolyte disturbances, monitor hepatic and renal function daily, and provide symptom-directed care. Specific antidotal therapy focuses on pyridoxine replacement to overcome MMH-induced PLP depletion and restore GABA synthesis. Pyridoxine can be administered intravenously to control or prevent seizures; benzodiazepines are recommended for ongoing seizures despite pyridoxine replacement, as many conventional anticonvulsants (eg, phenytoin) are often ineffective. Most patients recover within several days with appropriate supportive care and pyridoxine therapy.

Pyridoxine (Vitamin B6): Antidotal Role, Pharmacology, and Clinical Use

Introduction and Mechanism

Pyridoxine is converted in vivo to its active coenzyme form, pyridoxal-5′-phosphate (PLP). This is an essential cofactor for >100 enzymatic reactions including decarboxylation and transamination of amino acids and the conversion of glutamate to GABA.2 Xenobiotics such as isoniazid (INH), hydrazine, and methylated hydrazines inhibit pyridoxine phosphokinase or form hydrazone adducts with PLP, thereby depleting PLP and impairing GABA synthesis; pyridoxine administration replenishes PLP and reverses seizure propensity.[2]

Pharmacokinetics

Pyridoxine itself is not protein bound, has a volume of distribution ~0.6 L/kg, and rapidly crosses into tissues; PLP is largely bound to albumen. After 100 mg IV, PLP rises quickly in serum and erythrocytes; oral absorption is rapid (eg, 50% of a 600 mg dose absorbed within 20 minutes), with peak concentrations within hours. Baseline PLP may be reduced in chronic alcohol users due to enhanced degradation.[2]

Experimental and Human Evidence

Robust animal data demonstrate pyridoxine's protective and therapeutic efficacy against INH- and hydrazine-induced seizures across species (dogs, rats, cats, primates).2 For hydrazine and methylated hydrazine (ie, MMH, UDMH) poisoning, there is no established dose. However, in case reports, efficacy has been achieved using similar doses of pyridoxine as that used to treat INH toxicity.4 Pyridoxine has also restored consciousness in patients with prolonged postictal or comatose states after INH overdose, and case reports document neurologic improvement after pyridoxine administration for MMH or hydrazine exposures.[5,6,7,8]

Adverse Effects, Pregnancy, and Safety

Chronic high-dose pyridoxine administration (eg, 200 mg to multiple grams daily over weeks) can cause sensory neuropathy and axonopathy; volunteers receiving 1–3 g/day developed neuropathic findings within months. However, acute toxicity is uncommon.. Pyridoxine is FDA pregnancy category A and is used safely in low doses for hyperemesis gravidarum; gram-dose therapy in pregnancy is unstudied but the benefit in life-threatening INH seizures outweighs theoretical fetal risks.[9]

Dosing and Logistics

For INH overdose, recommended dosing is 1 g pyridoxine per gram of INH ingested, up to 5 g IV in adults (or 70 mg/kg in children up to the adult maximum). In actively seizing patients, IV infusion at ~0.5 g/min until seizure cessation is reasonable, with the remainder infused over 4–6 hours; repeat dosing is indicated for recurrent seizures or persistent depressed mental status. For MMH/Gyromitra exposures, an empiric dosing strategy similar to INH (e.g., 25 mg/kg IV to control seizures) is commonly used though formal human dosing trials are limited. The IV formulation (100 mg/mL) commonly contains chlorobutanol as a preservative and requires multiple vials for high-dose therapy, emphasizing the need for adequate ED and pharmacy stock.[9]

Conclusion and Practical Points for Poison Center Staff

• Mushroom exposures are uncommon but recurrent; a syndrome-based clinical approach is pragmatic given frequent lack of species identification.
• Gyromitra esculenta causes delayed GI symptoms, hepatotoxicity, and neurotoxicity via MMH-mediated inhibition of PLP and subsequent GABA depletion; pyridoxine is the principal antidote for associated seizures.
• Most mushroom exposures are benign and managed conservatively; however, progressive systemic signs warrant laboratory evaluation and close monitoring.
• Pyridoxine dosing of 25 mg/kg IV (max 5g) is reasonable for seizure control in combination with benzodiazepines for gyromitrin toxicity. This dosing is primarily derived from its use in INH toxicity

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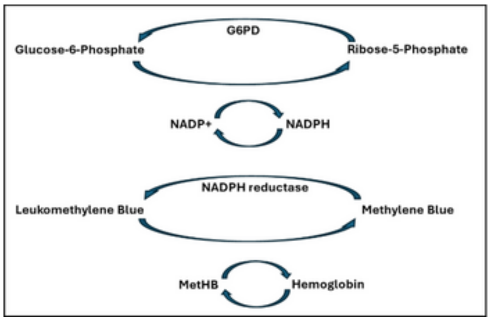
A Remedy for the Blues

Methylene blue is not a new drug, having been used as early as 1891 for medicinal purposes. The deep blue colored dye was useful in coloring textiles in the 1870's and was used to treat malaria among members of the military in 1891, but the side effect of blue urine wasn't well received. Of historical interest, psychiatrists added methylene blue to drugs administered to patients as the presence of blue urine was a visible indicator of compliance. In 1933, Williams and Challis reported that methylene blue had been successfully used as an antidote for aniline dye-induced methemoglobinemia. Methylene blue has been used for cystitis, urethritis, vasoplegic syndrome, cyanide and carbon monoxide poisoning, and ifosfamide-induced encephalopathy. In 1933, Williams and Challis successfully used methylene blue to treat aniline dye-induced methemoglobinemia. Regardless of this history, the FDA only approved methylene blue for the single indication of acquired methemoglobinemia in 2016.

A thiazine dye, methylene blue oxidizes methemoglobin to hemoglobin. Methylene blue is reduced by an enzyme, methemoglobin reductase, and nicotinamide adenosine dinucleotide phosphate (NADPH), to leukomethylene blue, and this in turn reduces methemoglobin to hemoglobin. The enzyme glucose-6-phosphate dehydrogenase (G6PD) is needed to generate NADPH.

G6PD-deficient individuals may not generate enough NADPH to reduce methylene blue to leukomethylene blue and therefore may not mount an adequate antidote response. They may go on to develop methylene blue-induced hemolysis or additional induction of methemoglobinemia with excess doses. Caution should be used if considered for these patients when G6PD deficiency is known or suspected.



Methylene blue has been used to treat symptomatic methemoglobinemia from a wide variety of sources including local analgesics (lidocaine, benzocaine), antimicrobials (dapsone, chloroquine) nitrates and nitrites (amyl nitrite, potassium nitrate), pharmaceuticals (phenazopyridine, metoclopramide), natural toxins (monomethylhydrazine) and industrial pesticides and chemicals (potassium permanganate, indoxacarb, naphthalene). There are many substances that may oxidize hemoglobin to methemoglobin.

Recently, methylene blue has been used off-label for refractory hypotension due to vasodilatory shock following calcium channel blocker or beta-blocker overdose. While methylene blue is not currently considered a first line therapy for these overdoses, there are numerous case reports showing favorable response.

Methylene blue is often given as an antidote to patients showing systemic signs and symptoms (often with a MetHB concentration >20%, although percent MetHB alone does not indicate treatment). The dose of methylene blue for methemoglobinemia is 1-2mg/kg body weight (maximum: 100mg) IV, infused slowly over a five-minute period. If given too quickly, it can result in pain at the site of infusion. If pain results, flushing the line with 15-30mL of fluid afterwards often helps reduce the severity of the reaction. Clinical improvement of methemoglobinemia is usually noted within 30 minutes of administration.

The most common side effects include pain at the injection site (described above), nausea, diaphoresis, dizziness, headache, and blue colored skin and urine. If a dose higher than 2mg/kg body weight of methylene blue is given, there is potential for significant side effects such as a paradoxical induction of methemoglobinemia or hemolytic anemia.

Methylene blue has been utilized in medicine and toxicology for more than a hundred years for a number of clinical indications, in addition to use for methemoglobinemia. The onset of action of methylene blue for methemoglobinemia is fast, often within minutes, with resolution within 30 min. of administration. As methylene blue is trialed and utilized for new medical and toxicological purposes, it could prove to be a versatile change agent for improving outcome.

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