POISON PEARLS

Toxicology Topics for the Healthcare Team of a Poisoned Patient

For ALL patient recommendations call the Drug and Poison Information Center at 1-800-222-1222

Cyclopeptide Mushrooms

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Background

Cyclopeptide-containing mushrooms are a clinically important group of fungi responsible for mushroom poisonings worldwide. The most important toxins in this group are amatoxins, including α-amanitin, β-amanitin, and γ-amanitin. These toxins are found primarily in some Amanita species and also in some Galerina and Lepiota species. Amatoxins are bicyclic octapeptides that are highly stable and resistant to cooking, drying, and other common methods of mushroom preparation. Following ingestion, amatoxins are absorbed from the gastrointestinal tract and undergo extensive enterohepatic recirculation, contributing to prolonged systemic exposure. Their primary molecular target is RNA polymerase II inhibition, which blocks messenger RNA synthesis and ultimately impairs cellular protein production **(Luo et al., 2022).** Hepatocytes are particularly vulnerable, making the liver the principal target organ, although renal injury and gastrointestinal effects may also occur.

Clinical Presentation

Symptoms of poisoning typically have a characteristic delay in onset, with a latent period of approximately 6–24 hours preceding severe gastrointestinal symptoms including abdominal pain, vomiting, and profuse diarrhea. Patients may then enter an apparent period of clinical improvement while significant hepatocellular injury continues to develop, followed by acute liver failure in severe cases. Laboratory abnormalities commonly include markedly elevated aminotransferases, coagulopathy, hypoglycemia, metabolic acidosis, and hyperbilirubinemia as hepatic failure progresses **(Trakulsrichai et al., 2017)**.

Treatment Considerations

- Activated charcoal: Consider single- and multiple-dose activated charcoal since amatoxins undergo enterohepatic recirculation
- N-Acetylcysteine (NAC): Provides antioxidant effects and replenishes glutathione; commonly used despite limited clinical evidence
- Silibinin (Legalon SIL®): May inhibit amatoxin uptake into hepatocytes; early administration is preferred when available. It may be obtained through an FDA Emergency IND
- Penicillin G: Proposed to reduce hepatic uptake of amatoxin, although evidence of benefit is limited
- Cimetidine: P450 inhibition has been proposed to reduce formation of toxic metabolites; clinical benefit is unproven
- Vitamin C: Antioxidant therapy has been proposed, but clinical efficacy is not established
- Polymyxin B: Experimental therapy that may interfere with α-amanitin binding to RNA polymerase II; not established clinical treatment
- Liver transplantation: Early transplant-center consultation is essential in patients with progressive hepatic injury or acute liver failure; transplantation may be lifesaving **(Madhok et al., 2006)**.



Amanita Phalloides
*Not known to grow in Ohio



Amanita Bisporigera
Represents the button stage, mushrooms often change appearance as they mature

Key Points:

- Mycologists can help identify the ingested mushroom if photos or remanants exist
  - Mushrooms growing nearby are not a reliable surrogate for identification as non-toxic and toxic mushrooms can grow in close proximity
- The absence of symptoms during the initial latent period or apparent improvement after the gastrointestinal phase does not indicate resolution
- Patients can develop rapidly progressive hepatic failure after a period of clinical improvement
- Serial hepatic function testing and early toxicology/transplant consultation are essential

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