# Suspected Hepatotoxic Mushroom Ingestion*: Quick Treatment Tips

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People who have eaten foraged mushrooms should be evaluated and treated for suspected hepatotoxic mushroom ingestion if:

a) New vomiting begins more than 5 hours after the mushroom ingestion.
b) Significant vomiting and diarrhea persists or worsens more than 5 hours after mushroom ingestion.
c) Laboratory evidence of hepatitis exists after mushroom ingestion.
d) An ingested mushroom was suspected, by identification, to be a hepatotoxic species.

***Principles of Management:***

## I. Hydration

Dehydration and hypovolemia are common and may be severe. Amatoxins are excreted by the kidney so it is extremely important to give fluids to prevent acute tubular necrosis and to promote good urine production.

- Obtain laboratory studies with IV placement: basic metabolic panel, serum liver enzymes (and ammonia if CNS depression is evident) and albumin, pancreatic enzymes, PT/PTT/INR, complete blood count, urinalysis, consider plasma lactate.
- Chemistries and coagulation should be monitored at regular intervals.
- Use 0.9% saline boluses to quickly restore intravascular volume.
- Treat hypoglycemia, maintain electrolyte balance.
- Provide appropriate IV fluid to promote brisk urine output yet maintain normal serum sodium concentrations.
- Anti-emetic therapy, such as ondansetron (if no long QT risk factors), may be used to reduce vomiting.

## II. GI Decontamination

Mushroom toxins are rapidly absorbed by the intestine, and patients typically come to medical attention with significant vomiting and diarrhea. No additional GI decontamination is likely to be warranted in this clinical setting (patients presenting "early" after hepatotoxic mushroom exposure should be discussed with a clinical toxicologist).

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## III. Prevention of Amatoxin Uptake / Binding by Hepatocytes

- *Silibinin dihemisuccinate*, a milk thistle extract, inhibits hepatic amatoxin uptake. As silibinin has promising benefit and low risk of harm it can be considered reasonable to administer silibinin as early after mushroom ingestion as possible. In the U.S. it is available only through an open NIH clinical trial by calling 1-866-520-4412.** Dose is 5 mg/kg followed by a continuous infusion of 20 mg/kg/day.
- *Silymarin* is a nutritional supplement from the milk thistle that contains silibinin, and is available at stores that sell such supplements. Quality control of the silymarin capsules is inconsistent, and gastroenteritis may limit the ability to tolerate enteral capsule administration. Nonetheless, some authorities recommend silymarin (50 mg/kg to max 1g, q8 hrs) if IV silibinin is unavailable.
- High dose *penicillin G* (500,000 U/kg/day by continuous infusion) or *ceftazidime* (adult dose 4.5g q2 hrs) have been suggested by some authorities. These high doses are associated with toxicity, especially in the context of renal insufficiency, and demonstrated benefit is currently weak. We do not routinely recommend these therapies.
- *Polymyxin B* has been suggested to block genetic transcription injury from amatoxins. Due to insufficient human clinical experience we are unable to recommend for or against this therapy (see citation by Garcia, 2015).

## IV. Interruption of Enterohepatic Recirculation of Amatoxins

60% of ingested amatoxins are excreted in the bile and may be recirculated to the liver to continue hepatocellular damage.

- If tolerable in the context of mushroom-induced gastroenteritis, consider *activated charcoal* (0.5 g/kg, max 10g) orally or via NG tube every 4 hours (if silymarin is given, it should be given at the midpoint between charcoal doses).
- Some authorities have suggested biliary drainage as an alternative to enteral activated charcoal. Such protocols suggest octreotide to prevent gall bladder emptying, and percutaneous aspiration of the gall bladder or placement of a nasobiliary tube. Currently, data are insufficient for us to routinely recommend this invasive procedure.

## V. Antioxidant Liver Support

- *N-acetylcysteine* (NAC) therapy has been associated with reduced mortality in a large case series. It is reasonable to administer NAC per the prescribing information for acetaminophen poisoning: 150 mg/kg IV over 1 hour, then 12.5 mg/kg/hr over 4 hours, then 6.25 mg/kg/hr until recovery is evident.
- *Cimetidine* (10 mg/kg, max 300mg, every 8 hours) and *Vitamin C* are relatively safe but have little evidence for benefit. We do not routinely recommend these therapies.

## VI. Additional Notes

- As liver injury is delayed after mushroom poisoning, no patient suspected of hepatotoxic mushroom ingestion should be "medically cleared" until asymptomatic and serum aminotransferases are demonstrated normal at 24-36 hours.
- Amatoxins may be found in the urine for 3-4 days after ingestion. If liver injury occurs, therapies should be continued until clear evidence of liver recovery can be documented (decreasing serum aminotransferases, improving hepatic synthetic function).
- Patients with evidence of dysfunction of hepatic synthesis should be managed by an experienced hepatologist at a facility with liver transplantation capability. Hepatotoxic mushroom poisoning has a 5-15% mortality rate, and approximately 2% of cases proceed to liver transplantation.
- Mushroom specimens are not necessary to provide treatment. If mushroom specimens are available they should be photographed from the top, side and bottom; a description of where they were collected (date, town, and "woods/lawn/mountaintop/etc") should be obtained; and the mushrooms should be frozen (in a paper bag) until their possible inspection can be arranged by The Poison Control Center.

*Good clinical trials are not currently available to guide treatment of hepatotoxic mushroom poisoning. These guidelines are based upon in vitro and animal studies, analysis of published observational data, and expert opinion accumulated from a number of sources. These guidelines are informational but not intended to establish a standard-of-care. Health care providers should be prepared to make independent clinical decisions for their patients on an individual basis.

** The principal investigator of the IV silibinin trial has extensive experience in managing hepatotoxic mushroom poisoning cases. His recommendations for treatment may vary from this guide, and from recommendations provided by other academic authorities, and have not been vetted by The Poison Control Center. His protocol may include administration of octreotide to prevent gall bladder contraction until silibinin can be delivered, and may involve discussion of biliary drainage. Health care providers should be prepared to carefully consider his recommendations and to make independent clinical decisions for their patients on an individual basis.

## References: Hepatotoxic Mushroom Poisoning

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