BBB - Mushroom toxins

Bad Bug Book: Foodborne Pathogenic Microorganisms and Natural Toxins Handbook
Mushroom toxins

A new version of the Bad Bug Book was released in 2012, below is a previous version.

1. Name of the Organism:
Mushroom poisoning is caused by the consumption of raw or cooked fruiting bodies (mushrooms, toadstools) of a number of species of higher fungi. The term toadstool (from the German Todesstuhl, death's stool) is commonly given to poisonous mushrooms, but for individuals who are not experts in mushroom identification there are generally no easily recognizable differences between poisonous and nonpoisonous species. Old wives' tales notwithstanding, there is no general rule of thumb for distinguishing edible mushrooms and poisonous toadstools. The toxins involved in mushroom poisoning are produced naturally by the fungi themselves, and each individual specimen of a toxic species should be considered equally poisonous. Most mushrooms that cause human poisoning cannot be made nontoxic by cooking, canning, freezing, or any other means of processing. Thus, the only way to avoid poisoning is to avoid consumption of the toxic species. Poisonings in the United States occur most commonly when hunters of wild mushrooms (especially novices) misidentify and consume a toxic species, when recent
immigrants collect and consume a poisonous American species that closely resembles an edible wild mushroom from their native land, or when mushrooms that contain psychoactive compounds are intentionally consumed by persons who desire these effects.

3. Nature of Disease:

Mushroom poisonings are generally acute and are manifested by a variety of symptoms and prognoses, depending on the amount and species consumed. Because the chemistry of many of the mushroom toxins (especially the less deadly ones) is still unknown and positive identification of the mushrooms is often difficult or impossible, mushroom poisonings are generally categorized by their physiological effects. There are four categories of mushroom toxins: protoplasmic poisons (poisons that result in generalized destruction of cells, followed by organ failure); neurotoxins (compounds that cause neurological symptoms such as profuse sweating, coma, convulsions, hallucinations, excitement, depression, spastic colon); gastrointestinal irritants (compounds that produce rapid, transient nausea, vomiting, abdominal cramping, and diarrhea); and disulfiram-like toxins. Mushrooms in this last category are generally nontoxic and produce no symptoms unless alcohol is consumed within 72 hours after eating them, in which case a short-lived acute toxic syndrome is produced.

4. Diagnosis of Human Illness:

A clinical testing procedure is currently available only for the most serious types of mushroom toxins, the amanitins. The commercially available method uses a 3H-radioimmunoassay (RIA) test kit and can detect sub-nanogram levels of toxin in urine and plasma. Unfortunately, it requires a 2-hour incubation period, and this is an excruciating delay in a type of poisoning which the clinician generally does not see until a day or two has passed. A 125I-based kit which overcomes this problem has recently been reported, but has not yet reached the clinic. A sensitive and rapid HPLC technique has been reported in the literature even more recently, but it has not yet seen clinical application. Since most clinical laboratories in this country do not use even the older RIA technique, diagnosis is based entirely on symptomology and recent dietary history. Despite the fact that cases of mushroom poisoning may be broken down into a relatively small number of categories based on symptomatology, positive botanical identification of the mushroom species consumed remains the only means of unequivocally determining the particular type of intoxication involved, and it is still vitally important to obtain such accurate identification as quickly as possible. Cases involving ingestion of more than one toxic species in which one set of symptoms masks or mimics another set are among many reasons for needing this information. Unfortunately, a number of factors (not discussed here) often make identification of the causative
mushroom impossible. In such cases, diagnosis must be based on symptoms alone. In order to rule out other types of food poisoning and to conclude that the mushrooms eaten were the cause of the poisoning, it must be established that everyone who ate the suspect mushrooms became ill and that no one who did not eat the mushrooms became ill. Wild mushrooms eaten raw, cooked, or processed should always be regarded as prime suspects. After ruling out other sources of food poisoning and positively implicating mushrooms as the cause of the illness, diagnosis may proceed in two steps. The first step, outlined in Table 1, provides an early indication of the seriousness of the disease and its prognosis.

As described above, the protoplasmic poisons are the most likely to be fatal or to cause irreversible organ damage. In the case of poisoning by the deadly Amanitas, important laboratory indicators of liver (elevated LDH, SGOT, and bilirubin levels) and kidney (elevated uric acid, creatinine, and BUN levels) damage will be present. Unfortunately, in the absence of dietary history, these signs could be mistaken for symptoms of liver or kidney impairment as the result of other causes (e.g., viral hepatitis). It is important that this distinction be made as quickly as possible, because the delayed onset of symptoms will generally mean that the organ has already been damaged. The importance of rapid diagnosis is obvious: victims who are hospitalized and given aggressive support therapy almost immediately after ingestion have a mortality rate of only 10%, whereas those admitted 60 or more hours after ingestion have a 50-90% mortality rate. Table 2 provides more accurate diagnoses and appropriate therapeutic measures. A recent report indicates that amanitins are observable in urine well before the onset of any symptoms, but that laboratory tests for liver dysfunction do not appear until well after the organ has been damaged.

5. Associated Foods:

Mushroom poisonings are almost always caused by ingestion of wild mushrooms that have been collected by nonspecialists (although specialists have also been poisoned). Most cases occur when toxic species are confused with edible species, and a useful question to ask of the victims or their mushroom-picking benefactors is the identity of the mushroom they thought they were picking. In the absence of a well- preserved specimen, the answer to this question could narrow the possible suspects considerably. Intoxication has also occurred when reliance was placed on some folk method of distinguishing poisonous and safe species. Outbreaks have occurred after ingestion of fresh, raw mushrooms, stir-fried mushrooms, home-canned mushrooms, mushrooms cooked in tomato sauce (which rendered the sauce itself toxic, even when no mushrooms were consumed), and mushrooms that were blanched and frozen at home. Cases of poisoning by
home-canned and frozen mushrooms are especially insidious because a single outbreak may easily become a multiple outbreak when the preserved toadstools are carried to another location and consumed at another time.

Specific cases of mistaken mushroom identity appears frequently. The Early False Morel *Gyromitra esculenta* is easily confused with the true Morel *Morchella esculenta*, and poisonings have occurred after consumption of fresh or cooked *Gyromitra*. *Gyromitra* poisonings have also occurred after ingestion of commercially available "morels" contaminated with *G. esculenta*. The commercial sources for these fungi (which have not yet been successfully cultivated on a large scale) are field collection of wild morels by semiprofessionals. Cultivated commercial mushrooms of whatever species are almost never implicated in poisoning outbreaks unless there are associated problems such as improper canning (which lead to bacterial food poisoning). A short list of the mushrooms responsible for serious poisonings and the edible mushrooms with which they are confused is presented in Table 3 ([Food/FoodborneIllnessContaminants/CausesOfIllnessBadBugBook/ucm072145.htm](http://www.fda.gov/Food/FoodborneIllnessContaminants/CausesOfIllnessBadBugBook/ucm072145.htm)).

Producers of mild gastroenteritis are too numerous to list here, but include members of many of the most abundant genera, including *Agaricus*, *Boletus*, *Lactarius*, *Russula*, *Tricholoma*, *Coprinus*, *Pluteus*, and others. The Inky Cap Mushroom (*Coprinus atrimentarius*) is considered both edible and delicious, and only the unwar who consume alcohol after eating this mushroom need be concerned. Some other members of the genus *Coprinus* (Shaggy Mane, *C. comatus*; Glistening Inky Cap, *C. micaceus*, and others) and some of the larger members of the *Lepiota* family such as the Parasol Mushroom (*Leucocoprinus procera*) do not contain coprine and do not cause this effect. The potentially deadly Sorrel Webcap Mushroom (*Cortinarius orellanus*) is not easily distinguished from nonpoisonous webcaps belonging to the same distinctive genus, and all should be avoided.

Most of the psychotropic mushrooms (*Inocybe* spp., *Conocybe* spp., *Paneolus* spp., *Pluteus* spp.) are in general appearance small, brown, and leathery (the so-called "Little Brown Mushrooms" or LBMs) and relatively unattractive from a culinary standpoint. The Sweat Mushroom (*Clitocybe dealbata*) and the Smoothcap Mushroom (*Psilocybe cubensis*) are small, white, and leathery. These small, unattractive mushrooms are distinctive, fairly unappetizing, and not easily confused with the fleshier fungi normally considered edible. Intoxications associated with them are less likely to be accidental, although both *C. dealbata* and *Paneolus foenisicii* have been found growing in the same fairy ring area as the edible (and choice) Fairy Ring Mushroom (*Marasmius oreades*) and the Honey Mushroom (*Armillariella mellea*), and have been consumed when the picker has not carefully examined every mushroom picked from the ring. Psychotropic mushrooms, which are larger and therefore more easily confused with edible mushrooms, include the Showy Flamecap or Big Laughing Mushroom (*Gymnopilus spectabilis*) which has been mistaken for Chanterelles (*Cantharellus* spp.) and for *Gymnopilus ventricosus* found growing on
wood of conifers in western North America. The Fly Agaric (Amanita muscaria) and Panthercap (Amanita pantherina) mushrooms are large, fleshy, and colorful. Yellowish cap colors on some varieties of the Fly Agaric and the Panthercap are similar to the edible Caesar's Mushroom (Amanita caesarea), which is considered a delicacy in Italy. Another edible yellow capped mushroom occasionally confused with yellow A. muscaria and A. pantherina varieties are the Yellow Blusher (Amanita flavorubens). Orange to yellow-orange A. muscaria and A. pantherina may also be confused with the Blusher (Amanita rubescens) and the Honey Mushroom (Armillariella mellea). White to pale forms of A. muscaria may be confused with edible field mushrooms (Agaricus spp.). Young (button stage) specimens of A. muscaria have also been confused with puffballs.

6. Relative Frequency of Disease:

Accurate figures on the relative frequency of mushroom poisonings are difficult to obtain. For the 5-year period between 1976 and 1981, 16 outbreaks involving 44 cases were reported to the Centers for Disease Control in Atlanta (Rattanvilay et al. MMWR 31(21): 287-288, 1982). The number of unreported cases is, of course, unknown. Cases are sporadic and large outbreaks are rare. Poisonings tend to be grouped in the spring and fall when most mushroom species are at the height of their fruiting stage. While the actual incidence appears to be very low, the potential exists for grave problems. Poisonous mushrooms are not limited in distribution as are other poisonous organisms (such as dinoflagellates (Dinoflagellida)). Intoxications may occur at any time and place, with dangerous species occurring in habitats ranging from urban lawns to deep woods. As Americans become more adventurous in their mushroom collection and consumption, poisonings are likely to increase.

7. Course of Disease and Complications:

The normal course of the disease varies with the dose and the mushroom species eaten. Each poisonous species contains one or more toxic compounds which are unique to few other species. Therefore, cases of mushroom poisonings generally do not resemble each other unless they are caused by the same or very closely related mushroom species. Almost all mushroom poisonings may be grouped in one of the categories outlined above.

PROTOPLASMIC POISONS

Several mushroom species, including the Death Cap or Destroying Angel (*Amanita phalloides*, *A. virosa*), the Fool’s Mushroom (*A. verna*) and several of their relatives, along with the Autumn Skullcap (*Galerina autumnalis*) and some of its relatives, produce a family of cyclic octapeptides called **amanitins**. Poisoning by the amanitins is characterized by a long latent period (range 6-48 hours, average 6-15 hours) during which the patient shows no symptoms. Symptoms appear at the end of the latent period in the form of sudden, severe seizures of abdominal pain, persistent vomiting and watery diarrhea, extreme thirst, and lack of urine production. If this early phase is survived, the patient may appear to recover for a short time, but this period will generally be followed by a rapid and severe loss of strength, prostration, and pain-caused restlessness. Death in 50-90% of the cases from progressive and irreversible liver, kidney, cardiac, and skeletal muscle damage may follow within 48 hours (large dose), but the disease more typically lasts 6 to 8 days in adults and 4 to 6 days in children. Two or three days after the onset of the later phase, jaundice, cyanosis, and coldness of the skin occur. Death usually follows a period of coma and occasionally convulsions. If recovery occurs, it generally requires at least a month and is accompanied by enlargement of the liver. Autopsy will usually reveal fatty degeneration and necrosis of the liver and kidney.


Certain species of False Morel (*Gyromitra esculenta* and *G. gigas*) contain the proplasmic poison gyromitrin, a volatile hydrazine derivative. Poisoning by this toxin superficially resembles *Amanita* poisoning but is less severe. There is generally a latent period of 6 - 10 hours after ingestion during which no symptoms are evident, followed by sudden onset of abdominal discomfort (a feeling of fullness), severe headache, vomiting, and sometimes diarrhea. The toxin affects primarily the liver, but there are additional disturbances to blood cells and the central nervous system. The mortality rate is relatively low (2-4%). Poisonings with symptoms almost identical to those produced by *Gyromitra* have also been reported after ingestion of the Early False Morel (*Verpa bohemica*). The toxin is presumed to be related to gyromitrin but has not yet been identified.

The final type of protoplasmic poisoning is caused by the Sorrel Webcap mushroom (Cortinarius orellanus) and some of its relatives. This mushroom produces orellanine, which causes a type of poisoning characterized by an extremely long asymptomatic latent period of 3 to 14 days. An intense, burning thirst (polydipsia) and excessive urination (polyuria) are the first symptoms. This may be followed by nausea, headache, muscular pains, chills, spasms, and loss of consciousness. In severe cases, severe renal tubular necrosis and kidney failure may result in death (15%) several weeks after the poisoning. Fatty degeneration of the liver and severe inflammatory changes in the intestine accompany the renal damage, and recovery in less severe cases may require several months.

**NEUROTOXINS**

Poisonings by mushrooms that cause neurological problems may be divided into three groups, based on the type of symptoms produced, and named for the substances responsible for these symptoms.

Muscarine Poisoning: [CDC/MMWR](http://www.cdc.gov/search.do?action=search&direction=desc&queryText=Muscarine&sort=date&subset=mmwr) [Agricola](http://agricola.nal.usda.gov/cgi-bin/Pwebrecon.cgi?DB=local&CNT=25&Search_Arg=muscarine&Search_Code=GKEY&STARTDB=AGRIDB)

Ingestion of any number of Inocybe or Clitocybe species (e.g., Inocybe geophylla, Clitocybe dealbata) results in an illness characterized primarily by profuse sweating. This effect is caused by the presence in these mushrooms of high levels (3-4%) of muscarine. [Muscarine](http://www.fda.gov/Food/FoodborneIllnessContaminants/CausesOfIllnessBadBugBook/ucm074156.htm) Muscarine poisoning is characterized by increased salivation, perspiration, and lacrimation within 15 to 30 minutes after ingestion of the mushroom. With large doses, these symptoms may be followed by abdominal pain, severe nausea, diarrhea, blurred vision, and labored breathing. Intoxication generally subsides within 2 hours. Deaths are rare, but may result from cardiac or respiratory failure in severe cases.

The Fly Agaric (*Amanita muscaria*) and Panthercap (*Amanita pantherina*) mushrooms both produce **ibotenic acid** and **muscimol**. Both substances produce the same effects, but muscimol is approximately 5 times more potent than ibotenic acid. Symptoms of poisoning generally occur within 1 - 2 hours after ingestion of the mushrooms. An initial abdominal discomfort may be present or absent, but the chief symptoms are drowsiness and dizziness (sometimes accompanied by sleep), followed by a period of hyperactivity, excitability, illusions, and delirium. Periods of drowsiness may alternate with periods of excitement, but symptoms generally fade within a few hours. Fatalities rarely occur in adults, but in children, accidental consumption of large quantities of these mushrooms may cause convulsions, coma, and other neurologic problems for up to 12 hours.

Psilocybin Poisoning: CDC/MMWR, NIH/PubMed, Agricola. A number of mushrooms belonging to the genera *Psilocybe*, *Panaeolus*, *Copelandia*, *Gymnopilus*, *Conocybe*, and *Pluteus*, when ingested, produce a syndrome similar to alcohol intoxication (sometimes accompanied by hallucinations). Several of these mushrooms (e.g., *Psilocybe cubensis*, *P. mexicana*, *Conocybe cyanopus*) are eaten for their psychotropic effects in religious ceremonies of certain native American tribes, a practice which dates to the pre-Columbian era. The toxic effects are caused by psilocin and psilocybin. Onset of symptoms is usually rapid and the effects generally subside within 2 hours. Poisonings by these mushrooms are rarely fatal in adults and may be distinguished from ibotenic acid poisoning by the absence of drowsiness or coma. The most severe cases of psilocybin poisoning occur in small children, where large doses may cause the hallucinations accompanied by fever, convulsions, coma, and death. These mushrooms are generally small, brown, nondescript, and not particularly fleshy; they are seldom mistaken for food fungi by innocent hunters of wild mushrooms. Poisonings caused by intentional ingestion of these mushrooms by people with no legitimate religious justification must be handled with care, since the only cases likely to be seen by the physician are overdoses or intoxications caused by a combination of the mushroom and some added psychotropic substance (such as PCP).

**GASTROINTESTINAL IRRITANTS**
Numerous mushrooms, including the Green Gill (*Chlorophyllum molybdites*), Gray Pinkgill (*Entoloma lividum*), Tigertop (*Tricholoma pardinum*), Jack O’Lantern (*Omphalotus illudens*), Naked Brimcap (*Paxillus involutus*), Sickener (*Russula emetica*), Early False Morel (*Verpa bohemica*), Horse mushroom (*Agaricus arvensis*) and Pepper bolete (*Boletus piperatus*), contain toxins that can cause gastrointestinal distress, including but not limited to nausea, vomiting, diarrhea, and abdominal cramps. In many ways these symptoms are similar to those caused by the deadly protoplasmic poisons. The chief and diagnostic difference is that poisonings caused by these mushrooms have a rapid onset, rather than the delayed onset seen in protoplasmic poisonings. Some mushrooms (including the first five species mentioned above) may cause vomiting and/or diarrhea which lasts for several days. Fatalities caused by these mushrooms are relatively rare and are associated with dehydration and electrolyte imbalances caused by diarrhea and vomiting, especially in debilitated, very young, or very old patients. Replacement of fluids and other appropriate supportive therapy will prevent death in these cases. The chemistry of the toxins responsible for this type of poisoning is virtually unknown, but may be related to the presence in some mushrooms of unusual sugars, amino acids, peptides, resins, and other compounds.

**DISULFIRAM-LIKE POISONING**

The Inky Cap Mushroom (*Coprinus atramentarius*) is most commonly responsible for this poisoning, although a few other species have also been implicated. A complicating factor in this type of intoxication is that this species is generally considered edible (i.e., no illness results when eaten in the absence of alcoholic beverages). The mushroom produces an unusual amino acid, coprine, which is converted to cyclopropanone hydrate in the human body. This compound interferes with the breakdown of alcohol, and consumption of alcoholic beverages within 72 hours after eating it will cause headache, nausea and vomiting, flushing, and cardiovascular disturbances that last for 2 - 3 hours.

**MISCELLANEOUS POISONINGS**

http://www.fda.gov/Food/FoodborneIllnessContaminants/CausesOfIllnessBadBugBook/ucm070853.htm
Young fruiting bodies of the sulfur shelf fungus *Laetiporus sulphureus* are considered edible. However, ingestion of this shelf fungus has caused digestive upset and other symptoms in adults and visual hallucinations and ataxia in a child.

8. **Target Populations:**

All humans are susceptible to mushroom toxins. The poisonous species are ubiquitous, and geographical restrictions on types of poisoning that may occur in one location do not exist (except for some of the hallucinogenic LBM, which occur primarily in the American southwest and southeast). Individual specimens of poisonous mushrooms are also characterized by individual variations in toxin content based on genetics, geographic location, and growing conditions. Intoxications may thus be more or less serious, depending not on the number of mushrooms consumed, but on the dose of toxin delivered. In addition, although most cases of poisoning by higher plants occur in children, toxic mushrooms are consumed most often by adults. Occasional accidental mushroom poisonings of children and pets have been reported, but adults are more likely to actively search for and consume wild mushrooms for culinary purposes. Children are more seriously affected by the normally nonlethal toxins than are adults and are more likely to suffer very serious consequences from ingestion of relatively smaller doses. Adults who consume mushrooms are also more likely to recall what was eaten and when, and are able to describe their symptoms more accurately than are children. Very old, very young, and debilitated persons of both sexes are more likely to become seriously ill from all types of mushroom poisoning, even those types which are generally considered to be mild.

Many idiosyncratic adverse reactions to mushrooms have been reported. Some mushrooms cause certain people to become violently ill, while not affecting others who consumed part of the same mushroom cap. Factors such as age, sex, and general health of the consumer do not seem to be reliable predictors of these reactions, and they have been attributed to allergic or hypersensitivity reactions and to inherited inability of the unfortunate victim to metabolize certain unusual fungal constituents (such as the uncommon sugar, trehalose). These reactions are probably not true poisonings as the general population does not seem to be affected.

9. **Food Analysis:**

The mushroom toxins can with difficulty be recovered from poisonous fungi, cooking water, stomach contents, serum, and urine. Procedures for extraction and quantitation are generally elaborate and time-consuming, and the patient will in most cases have recovered by the time an analysis is made on the basis of toxin chemistry. The exact chemical natures of most of the toxins that produce milder symptoms are unknown. Chromatographic techniques (TLC, GLC, HPLC)
exist for the amanitins, orelanine, muscimol/ibotenic acid, psilocybin, muscarine, and the gyromitrins. The amanitins may also be determined by commercially available 3H-RIA kits. The most reliable means of diagnosing a mushroom poisoning remains botanical identification of the fungus that was eaten. An accurate pre-ingestion determination of species will also prevent accidental poisoning in 100% of cases. Accurate post-ingestion analyses for specific toxins when no botanical identification is possible may be essential only in cases of suspected poisoning by the deadly *Amanitas*, since prompt and aggressive therapy (including lavage, activated charcoal, and plasmapheresis) can greatly reduce the mortality rate.

10. Selected Outbreaks:

For more information on recent outbreaks see the Morbidity and Mortality Weekly Reports from CDC (http://www.cdc.gov/search.do?action=search&direction=desc&queryText=mushroom,amanitin,gyromitrin,orellanine&sort=date&subset=mmwr).

11. Education and Background Resources:

Literature references can be found at the links below.

Available from the GenBank Taxonomy database, which contains the names of all organisms that are represented in the genetic databases with at least one nucleotide or protein sequence.

12. Molecular Structural Data:

Amanitin

Orellanine

Muscarine

Ibotenic Acid

Muscimol

Psilocybin

Gyromitrin

Coprine

These structures were created by Fred Fry, Ph.D, CFSAN.

More in Bad Bug Book