Review Article

Mushroom Poisoning

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Summary

Background: Poisonous mushrooms are eaten by mushroom hunters out of ignorance, after misidentification as edible mushrooms, or as a psychoactive drug. Mushroom poisoning commonly leads to consultation with a poison information center and to hospitalization.

Methods: This review is based on pertinent publications about the syndromes, toxins, and diagnostic modalities that are presented here, which were retrieved by a selective search in PubMed. It is additionally based on the authors' longstanding experience in the diagnosis and treatment of mushroom intoxication, expert consultation in suspected cases, macroscopic identification of wild mushrooms, and analytic techniques.

Results: A distinction is usually drawn between mushroom poisoning with a short latency of less than six hours, presenting with a gastrointestinal syndrome whose course is usually relatively harmless, and cases with a longer latency of six to 24 hours or more, whose course can be life-threatening (e.g., phalloides, gyromitra, orellanus, and rhabdomyolysis syndrome). The DRG diagnosis data for Germany over the period 2000–2018 include a total of 4412 hospitalizations and 22 deaths due to the toxic effects of mushroom consumption. 90% of the fatalities were due to the death cap mushroom (amatoxins). Gastrointestinal syndromes due to mushroom consumption can be caused not only by poisonous mushrooms, but also by the eating of microbially spoiled, raw, or inadequately cooked mushrooms, or by excessively copious or frequent mushroom consumption.

Conclusion: There are few analytic techniques available other than the qualitative demonstration of amatoxins. Thus, the diagnosis is generally made on the basis of the clinical manifestations and their latency, along with meticulous history-taking, assisted by a mushroom expert, about the type(s) of mushroom that were consumed and the manner of their preparation.

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The incidence of mushroom poisoning varies from region to region, season to season, and depending on the weather. In routine clinical practice mushroom poisoning is rare, so clinicians often lack experience in its diagnosis and treatment. Mushrooms (fungi, *μύκης*) are heterotropic eukaryotic organisms, the fungi, which form their own kingdom alongside the animals and plants in the biological classification of life.

This article deals particularly with poisoning by the fruiting bodies of higher fungi that occur in Europe and can lead to symptoms that are persistent and non-self-limiting, or at least not quickly self-limiting. Of the approximately 5000 kinds of fungi known worldwide, about 20 are excellent eaters, a few hundred are edible, and in Europe around 150 are known to be poisonous—including a few that are potentially deadly (*Table 1*).

Mushroom foragers ingest poisonous mushrooms out of ignorance, or after confusing them with another, edible kind (*Table 1*), or misuse them as intoxicating drugs. Along with medical drugs, household chemicals, and plants, mushrooms are among the noxa that often give rise to enquiries at Poison Centers (*Giftinformationszentren*, GIZ) (see annual reports of the Munich [1] and Göttingen Poison Centers [2]).

Methods

Using the search terms "mushroom [and] poisoning" and the term "analytic" combined with the individual toxins, the PubMed database was searched for articles published up to January 2020. Also fed into the data analysis were opinions and experience from experts from the Society of Clinical Toxicology (Gesellschaft für Klinische Toxikologie e. V., the professional association of Poison Centers in the German-speaking countries and of clinical toxicologists; www.klinitox.de) and from the Clinical Toxicology Working Group of the

TABLE 1

Overview of mushroom poisoning syndromes, their most important causative species, and species with which they may be confused

Syndrome	Poisonous mushroom species	Edible species with which poisonous species can be confused
Gastrointestinal irritant syndrome	Livid Pinkgill (Entoloma sinuatum) Yellow Stainer (Agaricus xanthoderma) Woolly Milkcap (Lactarius torminosus) Leopard Knight (Tricholoma pardinum) Omphalotus olearius	Clouded Funnel (Clitocybe nebularis) Field Mushroom (Agaricus campestris) Grey Knight (Tricholoma terreum) Chanterelle (Cantharellus cibarius)
Muscarinic poisoning	Fools' Funnel (Clitocybe rivulosa) Inocybes, e.g., Deadly Fibrecap (Inocybe erubescens)	The Miller (Clitopilus prunulus)
Panthercap /Fly Agaric poisoning	Panthercap (Amanita pantherina) Fly Agaric (Amanita muscaria)	The Blusher (Amanita rubescens) Caesar's Mushroom (Amanita caesarea)
Psilocybin /Magic Mushroom poisoning	Magic Mushroom (UK) / Liberty Cap (USA) (Psilocybe semilanceata) Banded Mottlegill (Panaeolus subbalteatus, syn. Panaeolus cinctulus)	
Coprine poisoning	Common Ink Cap (Coprinus atramentarius) Freckled Dapperling (Lepiota aspera) (= Echinoderma asperum)	Shaggy Ink Cap / Layer's Wig (Coprinus comatus)
Paxillus poisoning	Brown Rollrim (Paxillus involutus)	
Amatoxin / phalloides poisoning	Deathcap (Amanita phalloides) Destroying Angel (Amanita virosa) Small Dapperlings (Lepiota species) Poisonous Galerina species, e.g., Funeral Bell / Deadly Skullcap (Galerina marginata)	Field Mushroom (Agaricus campestris) Shaggy Parasol (Chlorophyllum rhacodes) Sheathed Woodtuft (Kuehneromyces mutabilis)
Gyromitrin poisoning	False Morel (Gyromitra esculenta)	Morel (Morchella esculenta)
Orellanine poisoning	Webcaps, e.g., Fool's Webcap (Cortinarius orellanus) Deadly Webcap (Cortinarius rubellus, syn. Cortinarius speciosissimus)	Chanterelle (Cantharellus cibarius)
Rhabdomyolysis / Tricholoma equestre poisoning	Yellow Knight (Tricholoma equestre) Russula subnigricans (found in East Asia)	

Society of Forensic and Toxicological Chemistry (Gesellschaft für Forensische und Toxikologische Chemie; www.gtfch.org). Epidemiological data were collected by searching the databases of the Munich and Göttingen Poison Centers and the Federal Health Reports information system for cases treated in German hospitals that were coded with the ICD-10 diagnosis T62.0 "Toxic effect of ingested mushrooms" (data for the years 2010–2018) (3).

Clinical aspects of mushroom poisoning

Diagnostic clues

Because experience is scarce and the subject only marginally touched on during medical training, there is always a danger that diagnosis and the start of treatment will be delayed. The diagnosis of mushroom poisoning rests on three pillars (in the order given below) (4):

- Identification of the ingested mushroom
- The time interval between mushroom ingestion and the onset of symptoms
- Confirmation by laboratory tests (if available).

The emergency doctor or emergency room clinician can start narrowing down the nature of a poisoning and coordinating the patient's further treatment by proceeding as follows:

The most reliable means of diagnosis is still macroscopic identification of the ingested mushrooms or uningested leftovers (gills current or decurrent; pores; stem shape; cap color), or microscopic identification of the spores in cooked mushroom remains, vomit, or feces, by a qualified mushroom expert (contact details may be obtained from the relevant Poison Center [5]). Other useful information includes how the mushrooms were cooked or prepared, the condition they were in, where they were collected, and how they were transported and stored, together with the latency period to symptom onset (using an interpreter if required). The checklist in *Table 2* can be helpful for structured questioning.

If the patient has eaten a gilled mushroom with a white or green cap, there is cause for extreme alarm. Nevertheless, caution is still needed if one has only

the patient's description to rely on, and it should always be borne in mind that there may have been other mushrooms in a dish apart from the samples brought in with the patient (4).

Mushroom poisoning can be divided into two major categories depending on the interval (latency) from mushroom ingestion to the onset of the first symptoms of poisoning:

- Latency < 6 hours: functional syndromes, usually with a mild course (the exception is Panthercap poisoning) (*Table 3a*)
- Latency > 6 hours: organ-damaging syndromes, often with fatal outcome (*Table 3b*).

It should be noted that in some cases gastrointestinal symptoms caused by mushrooms are due not to mushrooms that are poisonous in themselves, but to mushrooms that are microbially contaminated, or raw or inadequately cooked, or eaten in too large a quantity, or eaten too often at too frequent intervals.

Laboratory tests

Apart from the toxins contained in the Deathcap and the Destroying Angel, there are few mushroom toxins for which laboratory tests have been developed, and laboratory tests are not routinely used in the diagnostic workup. For retrospective confirmation of a diagnosis, it may be possible to request testing for some toxins from a specialist laboratory (overview in *Tables 3a and 3b*; information regarding these may be obtained through the Poison Centers).

By contrast, many laboratories provide testing for amatoxins, the presence of which can be shown in urine before the onset of symptoms after poisoning by the Deathcap or Destroying Angel. Qualitative evidence of amatoxin in the urine can be valuable, since a confirmed diagnosis allows aggressive treatment to be started early, thus probably reducing mortality rates.

Clinical chemical laboratory tests to determine, e.g., impairment of liver function, may not be very helpful towards obtaining a diagnosis, since often they do not yield pathological results until organ damage has already occurred. Because the analytic options are limited, the suspected diagnosis needs to be made primarily on a clinical basis, to allow intensive medical treatment, if required, to be initiated as early as possible.

Case numbers

To estimate case numbers, data from the Poison Centers relating to cases of suspected mushroom poisoning for Southern and Northern Germany and France were collated (*Table 4*). Depending on weather conditions, numbers can very greatly from one year to the next. There is no central registry in Germany, although efforts have been made to establish a database for monitoring at a national level (6). For this reason, only a generalized search could be made for the numbers of hospitalizations and deaths reported to the German Federal Statistical Office with the diagnostic code ICD-10 T62.0 "Toxic effect of ingested mushrooms."

TABLE 2

Information that is helpful for a diagnosis (checklist)

Macroscopic identification of the ingested mushrooms*1	Gills □ Pores □ Cap color:
Microscopic identification of spores in meal leftovers or vomit or stool sample*2	Any mushroom remains? Yes □ No □ Nature of remains/sample:
Nature of location where mushrooms were gathered	Coniferous woodland □ Mixed woodland □ Deciduous woodland □ Grassland □
Transport and storage	Dry, cool?
How the mushrooms were prepared (cooked)	Were they cooked for long enough (>20 min)? Yes □ No □
Condition of the ingested mushrooms	Fresh □ Warmed over □ Pickled □
Symptoms	Vomiting □ Diarrhea □ CNS □ Hepatic □ Renal □ Other:
Latency	<6 h □ >6 h □ >12–24 h □

*1 By reference to illustrated authoritative mushroom guides (7–9)
*2 An expert mycologist can identify the mushroom from spores present in mushroom remains (4).

All the numbers given in *Table 4* have limitations, since the data reflect either emergency call statistics or hospital statistics. The numbers of patients treated at local doctor offices or as hospital outpatients, or whose main or discharge diagnosis was coded as "acute liver or kidney failure," for example, are not included in these figures. Furthermore, mushroom poisoning is not a notifiable condition, so an unknown number of unrecorded cases must exist.

Mushroom poisoning syndromes and how to treat them

For quick reference, *Tables 3a and 3b* list the ten most important poisoning syndromes observed after the ingestion of mushrooms, showing their typical symptoms, latency period, treatment, and antidote if any. The mechanism of action, relevant toxins (if known), and any options for laboratory analysis are also given. *Table 1* lists the typical poisonous mushrooms and those they can be confused with. *Figure 1* shows the Deathcap mushroom (*Amanita phalloides*), *Figure 2* the Fool's Webcap (*Cortinarius orellanus*), and *Figure 3* the Frosty Funnel (*Clitocybe phyllophila*) . To identify other kinds of mushrooms, mushroom identification guides should be referred to (7–9).

In most cases treatment for mushroom poisoning is symptomatic. Depending on the toxin involved, fluid and electrolyte replacement, administration of antiemetics, activated charcoal, atropine, beta blockers, benzodiazepines, or neuroleptics, or hemodialysis/plasmapheresis may be used. To enable a quick overview, the therapeutic options for all except amatoxin poisoning are summarized in *Tables 3a and 3b*.

TABLE 3a

Mushroom poisoning syndromes with short latency (<6 h)

Syndrome; latency	Mechanism of action	Symptoms	Treatment, antidote	Toxins, tests
Gastrointestinal irritant syndrome 30 min – 4(6) h	Toxins with a local irritant action on gastrointestinal mucosa; the mechanisms of the toxicity are not understood in detail	Vomiting, diarrhea, hypotension	Fluids and electrolyte replacement, antiemetics if required	Toxins unknown; analysis of serum/urine not available
Muscarinic poisoning 30 min – 2 h	Muscarine is similar to acetylcholine, but unlike acetylcholine it is not broken down by acetylcholinesterase, thus leading to overstimulation of the peripheral muscarinic cholinergic receptors (e1, e2).	Vomiting, diarrhea, miosis, sweating, bradycardia, hypotension	Activated charcoal may be given (19), fluid and electrolyte replacement, atropine	Muscarine; muscarine can be detected in urine, but this has little clinical relevance*1
Panthercap / Fly Agaric poisoning 30 min – 3 h	Ibotenic acid and muscimol are structurally related to the neurotransmitters glutamate and GABA in the central nervous system. Ibotenic acid is an agonist of NMDA-glutamate receptors; muscimol is a potent GABAA agonist.	Euphoria, hallucinations, myoclonus, cerebral seizures, mydriasis/miosis, tachy-/bradycardia, somnolence	Cardiovascular monitoring; benzodiazepines may be given to agitated patients;*2 role of flumazenil for patients in coma is unclear	Isoxazole derivatives such as ibotenic acid, muscimol, and muscazone (approx. 500 mg/kg) (e3–e5) It is possible to detect ibotenic acid and muscimol in serum and urine, but this is of largely forensic or academic interest.*1
Psilocybin / Magic Mushroom poisoning 15 – 60 min	The psychoactive effects are evoked by stimulation by psilocin as a partial agonist of the 5-HT2A receptor in the limbic system and frontal lobes, leading to increased glutamatergic transmission (e6).	Euphoria, hallucinations, nausea, tachycardia, hypotension, mydriasis, headache, psychotic states that can potentially lead to accidents	Observation, monitoring for danger to self or others; benzodiazepines may be given, neuroleptics if appropriate	Psilocybin (and its metabolite psilocin) (e7–e9). Methods are available in specialist laboratories to detect psilocin in urine.*1
Coprine poisoning 15 min – 2 h	The breakdown of ethanol is inhibited by coprine, an acetaldehyde dehydrogenase inhibitor, also known as the "Antabuse effect" or disulfiram–alcohol reaction	Flushing, sweating, tachycardia, nausea, vomiting; hypotension may occur	Cardiovascular monitoring; beta blockers may be given	Coprine No tests are available to detect coprine in serum or urine
Paxillus poisoning 60 min – 2 h	Involutin and other unknown antigens lead to the formation of antibodies (immunoglobulin G) that can result in hemolysis via an agglutinating antigen–antibody complex on erythrocytes (e10); however, the exact mechanism of action is not clear.	Vomiting, diarrhea, flank pain, kidney damage, hypotension; multiorgan failure may occur, especially after repeated ingestion (even after many years); hemolysis leading to death may occur (e10)	Activated charcoal may be given (19), hemodialysis*3/plasmapheresis is an option; blood product replacement	Involutin and others No serum/blood tests are available

*1 Poison Centers can provide contact details for the (specialist) laboratories that can offer this testing (5).
*2 Benzodiazepines should be used with caution, and intensive monitoring is required to watch for respiratory depression (e11).
*3 From a nephrological point of view, hemodialysis is *not* suitable for toxin elimination.
GABA, Gamma(γ)-aminobutyric acid; NMDA, *N*-methyl-D-aspartate

The symptoms of many kinds of mushroom poisoning often spontaneously disappear after 2 to 3 days at most. Although mushroom poisoning with a short latency period is usually not life-threatening, it should nevertheless not be underestimated, as often only the rapidly occurring signs of poisoning are paid attention to at first. A short latency period does not always rule out amatoxin poisoning (think mixed mushroom dishes). For this reason, patients with symptoms or who have eaten what were probably poisonous mushrooms should generally be kept under observation in hospital for at least 36 hours. Since many cases of mushroom poisoning occur in multiple persons who have shared the same mushroom dish, the other diners should also be examined and if appropriate admitted to hospital—even if they have not developed any symptoms.

Up until 1990, about a dozen different kinds of mushroom poisoning were known in Germany. After 1990, another half dozen additional types of poisoning were published (overview in 3, 9–14).

For example, mushroom intolerances can arise on an individual basis in immunosuppressed patients, young children, pregnant women, and older persons—including intolerance to mushrooms generally regarded as good to eat, such as the Clouded Funnel (Clitocybe nebularis).

Poisoning syndromes with a short latency period (<6 hours) include gastrointestinal irritant syndrome, muscarinic poisoning, Panthercap/Fly Agaric poisoning, Psilocybin or Magic Mushroom poisoning (hallucinogenic syndrome), coprine poisoning, and paxillus poisoning (Brown Rollrim) (*Table 3a*).

Poisoning syndromes with a longer latency period (6 to 24 hours) include amatoxin poisoning (described at greater length below), gyromitrin poisoning, orellanine poisoning, and rhabdomyolysis syndrome (*Table 3b*).

TABLE 3b

Mushroom poisoning syndromes with long latency (6 to 24 h)

Syndrome; latency	Mechanism of action	Symptoms	Treatment, antidote	Toxins, tests
Amatoxin / phalloides poisoning 6–12 h (max. 24 h)	Inhibition of RNA polymerase II inhibits the transcription of DNA to mRNA, thus blocking the biosynthesis of many proteins (enzymes, structural proteins, peptide hormones, membrane receptors).	Vomiting, profuse diarrhea, hypotension, acute renal and liver failure, coagulopathy, encephalopathy	Activated charcoal may be given (19), aggressive fluid and electrolyte resuscitation, coagulation factors; other options include hemodialysis/albumin dialysis, with liver transplantation as a last resort. Silibinin is the antidote of first choice; it may be given in combination with N-acetylcysteine (NAC).NAC may be given alone if silibinin is not available	Amatoxins are a group of 10 heat-stable bicyclic oligopeptides. The main active substances, α-amanitin and β-amanitin, are resistant to gastrointestinal peptidases. Immunoassay (ELISA) and chromatographic techniques to demonstrate α-amanitin in urine are available at several laboratories.*1 Note the window of opportunity: from 6 to a maximum of 36 hours after the mushrooms were ingested) (27–29)
Gyromitrin poisoning 6–12 h	Gyromitrin is broken down to monomethylhydrazine (MMH) by a long period of drying, cooking, or by gastric juices. MMH inhibits pyridoxal phosphokinase and leads to reduced production of pyridoxal 5-phosphate (vitamin B6), with neurotoxic effect (vitamin B6 is a key cofactor in the synthesis of GABA). MMH after massive ingestion of gyromitra mushrooms leads to oxidative stress and thus to methemoglobinemia.	If MMH builds up rapidly, the damage caused is mainly to the liver; if it builds up slowly, CNS symptoms are seen (acetylator type) (e12); nausea, vomiting, impaired consciousness, CNS excitation, cerebral seizures, liver and kidney damage (e14); methemoglobinemia may occur	Activated charcoal may be given (19) Intravenous pyridoxine, or alternatively, e.g., levetiracetam	Gyromitrin, which is metabolized to MMH (e13). MMH is volatile, heat-sensitive, and water-soluble, and these mushrooms were therefore long regarded as edible so long as they were well cooked (in fact, multiple cases are known of severe or even fatal poisoning even when the mushrooms were correctly prepared!) (e12). No serum or urine tests are available
Orellanine poisoning 36 h – 17 days	Orellanine, or its metabolite, causes oxidative stress leading to formation of superoxide ions and thus to inhibition of alkaline phosphatase and DNA and RNA polymerases, which in turn results in inhibition of protein biosynthesis in renal tissue (e15–e18)	Thirst, flank pain, weakness, oliguria or even acute renal failure, tubulointerstitial nephritis; there may be irreversible terminal renal failure requiring dialysis	Symptomatic treatment, treatment of renal failure, hemodialysis if indicated*2, steroids	Orellanine No published serum or urine tests; only testing of renal tissue is available (e19–e21)
Rhabdomyolysis / Tricholoma equestre poisoning 1–3 days	Substances that damage striated muscle. The mechanism of action is not entirely understood (e22, e23).	Muscle pains, rhabdomyolysis (raised CPK values), arrhythmias, myocarditis, renal failure	Urine alkalinization may be carried out; hemodialysis*2	Not identified with certainty; among others, cyclopropylacetyl (R)-carnitine (found in Russula species [e24] but not in Tricholoma equestre [e25]) No serum or urine tests available

*1 Poison Centers can provide contact details for the (specialist) laboratories that can offer this testing (5).
*2 From a nephrological point of view, hemodialysis is *not* suitable for toxin elimination.
CPK, Creatine phosphokinases; GABA, gamma(γ)-aminobutyric acid; CNS, central nervous system

Amatoxin poisoning

Ninety percent of all fatal cases of mushroom poisoning are caused by *Amanita phalloides* (15), the symptoms and treatment of which will now be described in detail.

Symptoms

The symptoms go through three stages:

- A gastrointestinal stage with 6 to 24 hour latency: severe stomach pains, nausea, vomiting, cholera-like diarrhea
- A hepatic stage with 12 to 48 hour latency: cytolytic hepatitis with a rise in liver enzyme values, apparent clinical improvement
- Progressive acute liver and kidney failure after 24 to 72 h latency: coagulopathy, encephalopathy, nephropathy, seizures, hepatic coma, brain edema, possibly a fatal outcome.

Mechanism of action

Amatoxins are a group of ten heat-stable bicyclic oligopeptides. The main active substances -amanitin and β-amanitin are resistant to digestive peptidases. They inhibit RNA polymerase II and so prevent transcription of DNA to mRNA, thus blocking the biosynthesis of many proteins (enzymes, structural proteins, peptide hormones, membrane receptors). In addition, the presence of some other, temperature-sensitive

TABLE 4

Data on the incidence of mushroom poisoning in Germany and France

Source	Munich Poison Center (1)	Göttingen Poison Center (2)	France *1	Germany, hospital diagnostic data *2
Federal state(s)	Bavaria	Bremen, Hamburg, Lower Saxony, Schleswig-Holstein		16 federal states
Population	Approx. 13 million	Approx. 13 million	Approx. 67 million	Approx. 83 million
Enquiries/year	Approx. 40 000	Approx. 40 000	Approx. 350 000	
Study period	2014–2019	2014–2019	2010–2017	2010–2018
Enquiries about mushroom poisoning	3801	4750	10 625 *3	4441 patients who received hospital treatment
Deaths following mushroom poisoning	0	2 *4	22 *5	32
Cases of severe poisoning*6	19	66	217	NA
Cases of moderate poisoning*6	120 (n = 139; 3.7%) *7	366 (n = 434, 9.1%) *7	NA	NA
Minor *6/ asymptomatic/ could not be assessed	96.3%	90.9%	NA	NA

*1 Joint analysis by the eight regional French Poison Centers (Centres Antipoison) (15).
*2 Database query on ICD-10 T62.0 "Toxic effect of ingested mushrooms,"www.gbe-bund.de (3).
*3 Gastrointestinal symptoms occurred in 90% of all symptomatic patients.
*4 Deathcap or Destroying Angel in all cases.
*5 In 15 cases caused by amatoxin poisoning and in 7 cases caused by muscarinic poisoning.
*6 Assessed using the Poison Severity Score (PSS) (e26).
*7 Total of deaths and severe and moderate poisoning cases.
NA, not available

and acid-sensitive peptide toxins has been demonstrated.

Toxicity of α-amanitin

In animal trials, -amanitin has proved deadly (LD50, mouse) at doses as low as 0.3 mg/kg body weight. In humans, a fatal dose is assumed to be as low as 0.1 mg/kg body weight: that is, as little as 50 to 100 g mushrooms (containing 0.02% to 0.04% α-amanitin)—that is, roughly the amount of a mature fruit body—can be deadly for an adult; for a child the amount is 5 to 10 g mushrooms.

Treatment

Treatment for amatoxin poisoning rests on four pillars (16–21):

- Volume replacement therapy (a)
- Toxin binding (b)
- Antidote therapy (c)
- Treatment for liver failure, including liver transplantation (d).

a) On admission to hospital, patients are dehydrated by vomiting and diarrhea. This needs to be compensated by copious fluid replacement including electrolytes. Patients should be monitored for adequate urine production, since the toxin is eliminated primarily through the kidneys.

b) Due to the long latency period before symptoms occur, it is usually too late for primary toxin elimination. Patients who attend hospital during the latency period can receive hemodialysis to remove the toxin. Another option for secondary toxin elimination which interrupts the enterohepatic circulation of the toxin is oral administration of activated charcoal 0.5 to 1 g/kg body weight or up to a maximum of 50 g as a bolus in adults (19).

c) Three medications are available as antidotes: penicillin G, silibinin, and *N*-acetylcysteine (NAC). Silibinin is derived from the milk thistle and is the pharmacologically active substance in the silymarin complex. No randomized clinical studies have been carried out on these substances, and indeed such studies are hardly possible owing to the low case numbers and ethical difficulties of withholding a plausibly effective treatment from patients. Penicillin G and silibinin act mainly by inhibiting uptake of the amatoxins by hepatocytes, which is mediated by the OATP-1B3 transporter (OATP, organic anion transporting polypeptide) (20). NAC has antioxidant and glutathione-regenerating effects. Mortality rates in a retrospectively studied group of patients were 22% with penicillin therapy alone (46/205) (21), 9% with combined penicillin and silibinin therapy (22/248), and 5% with silibinin monotherapy (6/118) (16). On this basis, silibinin monotherapy seems advisable. NAC can be given either as an alternative (if silibinin is not available) or as an adjunct to silibinin. There is a rationale for combining silibinin and NAC therapy, since these two substances have different mechanisms of action (22).

Photo: Robert Wennig, Luxembourg

Figure 1: The Deathcap (*Amanita phalloides*) is one of the most poisonous mushrooms in the world.

Photo: Bernd Fellmann, Munich

Figure 2: The Fool's Webcap (*Cortinarius orellanus*) has nephrotoxic properties.

Photo: Bernd Fellmann, Munich

Figure 3: The Frosty Funnel (*Clitocybe phyllophila*) contains the toxin muscarine.

d) Treatment for liver failure is the same as for liver failure of other etiologies. The Clichy criteria (23) and Munich criteria (24) both provide a suitable basis for decision making on whether a liver transplant is indicated. The Clichy criteria include the latency period, coagulopathy, and encephalopathy, while the Munich criteria are based on coagulopathy and renal function. Combining both scores together could be a reasonable option. Albumin-based dialysis techniques (e.g., MARS, Prometheus, ADVOS) have no significant effect in terms of toxin elimination, but can be a suitable interim measure until liver transplantation can be carried out (25, 26).

Laboratory tests

Various methods based on liquid chromatography–mass spectrometry (LCMS) are available to determine the presence of the main active substance α-amanitin and any other amatoxins that may be present (e.g., β-amanitin), but in Germany most of them are not available 24 hours a day. It is extremely important to note that a reliable result can only be obtained if the urine sample is taken within a window of 6 to, at the outside, 36 hours after the mushrooms have been ingested (27, 28). If there is uncertainty about suspected ingestion of Deathcap or Destroying Angel, an immunoassay can be a good alternative, and these are available almost everywhere in Germany (information from Poison Centers). Recently, the development of a rapid test has been reported, although it is not yet available commercially (29). Blood tests for functional liver impairment only give positive results after a considerable delay—usually after organ damage has already occurred. By contrast, amatoxins can be

demonstrated in urine even before the onset of symptoms. However, a negative test result does not indicate with any certainty that poisoning has not occurred, since amatoxins are only detectable in the urine for a short time.

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Conflict of interest statement
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► **Supplementary material**

For eReferences please refer to:
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Supplementary material to:

Mushroom Poisoning

by Robert Wennig, Florian Eyer, Andreas Schaper, Thomas Zilker, and Hilke Andresen-Streichert

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Questions on the article in issue 42/2020:

Mushroom Poisoning

cme plus+

The submission deadline is 15 October 2021. Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1

How many known poisonous mushrooms are there in Europe?

a) Around 50, b) around 250, c) around 150, d) around 500, e) around 400

Question 2

A patient is transferred to you from a receiving hospital after eating mushrooms. The patient has very high serum bilirubin (17 mg/dL), indicating hemolysis. Blood tests suggest renal damage. Which disease or poisoning syndrome is the most likely?

a) Deathcap poisoning
b) Wilson's disease (with coincidental simultaneous ingestion of mushrooms)
c) Orellanine poisoning (with renal involvement)
d) Hemolysis of unknown cause
e) Poisoning after eating *Paxillus involutus* (Brown Rollrim)

Question 3

Twelve hours after eating mushrooms, a patient suddenly develops severe vomiting and diarrhea. Deathcap poisoning is suspected. What do you do?

a) Perform liver function tests and wait for results to show whether damage to the liver has actually occurred.
b) Wait for results of urine test for amatoxin, since it could be a harmless case of food poisoning.
c) Start penicillin therapy, since no silibinin is available.
d) Start NAC therapy until silibinin can be obtained, and then give both combined.
e) Start penicillin therapy and combine it with silibinin once the latter has been obtained.

Question 4

What is the role of a urine test for amatoxin in the workup of a suspected case of Deathcap poisoning?

a) A urine test can give a positive result even before symptom onset, allowing specific treatment to be started early if required.
b) A negative test result rules out poisoning and purely symptomatic treatment can then be carried out.
c) In most cases, advanced organ damage has already taken place before the urine test gives a positive result.
d) Urine testing must be carried out within the first 6 hours after mushroom ingestion; later than that it is usually not possible to get a positive result.
e) The urine test gives a positive result for poisoning caused by other toxins as well, and is thus too nonspecific for diagnostic confirmation.

Question 5

A man presents to your office about 1 hour after eating mushrooms, suffering from diarrhea, vomiting, sweating, and miosis. When asked what mushrooms he has been eating, he says The Miller, picked and cooked by himself. You suspect he may have made a mistake in identification. What do you do?

a) Give beta blockers and antiemetics
b) Give fluids and electrolytes and atropine

c) Refer for hemodialysis and, if required, blood transfusion
d) Observe for 24 hours
e) Give benzodiazepines and antiemetics

Question 6

Which poisoning syndromes are among those with a long latency (6 to 24 hours)?

a) Magic Mushroom poisoning and Panthercap/Fly Agaric poisoning
b) Panthercap/Fly Agaric poisoning and amatoxin / phalloides poisoning
c) Coprine poisoning and gyromitrin poisoning
d) Gyromitrin poisoning and rhabdomyolysis / *Tricholoma equestre* poisoning
e) Gastrointestinal irritant syndrome and muscarinic poisoning

Question 7

A woman presents with flank pain, oliguria, and weakness. Four days previously, she ate what she believed to be chanterelles. What type of poisoning is she probably suffering from?

a) Paxillus poisoning, caused by the Brown Rollrim
b) Orellanine poisoning, caused by the Fool's Webcap
c) Coprine poisoning, caused by the Brown Rollrim
d) Gastrointestinal irritant poisoning, caused by excessive consumption of chanterelles
e) Magic Mushroom poisoning, caused by the Magic Mushroom / Liberty Cap (*Psilocybe semilanceata*)

Question 8

Which of the following mushroom toxins is considered to have a psychoactive effect that can be associated with hallucinations, nausea, and psychotic states?

a) Orellanine, b) muscarine, c) coprine, d) involutin, e) psilocybin

Question 9

Gyromitrin poisoning, which is life-threatening, is caused by a mushroom often held to be edible if correctly cooked, but which in Germany is no longer classified as edible. Which mushroom?

a) Shaggy Ink Cap, b) False Morel, c) Field Mushroom, d) False Morel e) Magic Mushroom / Liberty Cap

Question 10

What is the mechanism underlying the "Antabuse effect" that can occur in association with the toxin coprine?

a) Activation of $GABA_A$ receptors in the central nervous system
b) Activation of NMDA-glutamate receptors
c) Inhibition of acetaldehyde dehydrogenase
d) Increased renal excretion (polyuria)
e) CYP3A inhibition