Poisonous Mushroom Toxicity in Veterinary Medicine

Refer lecturer for course updated notes.

Students are oblidged to follow the courses for evaluation process and presented notes are preliminary drafts for the whole evaluation process.

General Information

- Amanita sp. – most deaths in dogs (for mushroom poisoning)
- Can affect multiple organ at the same time
- Early diagnosis is important
- Management is generally supportive
- Exposure is by ingestion

- According to toxins and toxidrome classes
  - Ibotenic acid/Muscimol
  - Cyclopeptide
  - Muscarine
  - Hallucinogens
  - Monomethyl hydrazine
  - GI Irritants
  - Acute renal failure

Liver toxic mushrooms

- Amanita phalloides (Death Cap Mushroom)
- Amanita ocreata (Angel of Death)
- Lepiota (False Parasol)
- Galerina

Hallucinogenic Mushrooms

- Conocybe
- Gymnopilus
- Psilocybe
- Panaeolus

- **Toadstool Mushrooms**
- - Amanita pantherina (Panther Cap)
- - Amanita muscaria (Fly Agaric)
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- **Mushrooms Containing Muscarinic Agents**
- - Inocybe
- - Clitocybe

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- **False Morel Mushrooms**
- - *Gyromitra esculenta* (Beefsteak)
- - *Gyromitra caroliniana*
- - Mushrooms in the *Verpa* genre
- - Mushrooms in the *Helvella* genre
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- **Mushrooms That Cause Gastrointestinal Distress**
- - Boletus
- - Chlorophyllum
- - Entolomo

Physical Characteristics of Common Poisonous Mushrooms

Genus and Species	Color of Cap/Spores	Habitat	Season	Range
Amanita muscaria	Red-tan to yellow/orange/ white	Ground-pine, spruce, birch, poplar, and oak trees	Autumn/winter: June–Nov	Widespread, common in East and California
A pantherina	White with whitish patches; dark to yellow-brown/white at margin	Ground under conifers (Douglas fir)	Autumn/winter: June, Sept–Oct, Nov–Feb (California)	Rocky Mountains/West coast; rare in East
A phalloides	Yellow/green or green/white	Ground under conifers, hardwoods; junipers and oaks	Autumn: late Sept–Nov, Nov–Jan	Massachusetts to Virginia west to Ohio; Pacific northwest to California
A virosa	White/white	Ground; mixed woods; grass, near trees	Autumn: late June–early Nov	North America
Chlorophyllum molybdites	White/green or grayish white	Lawn, pastures, meadows, fairy rings	Summer: Aug–Sept	Florida to California, common in Denver, reported in New York and New Jersey

Classification

Group	*Key Species*
Cyclopeptide	*Amanita phalloides*, many *Amanita* sp., *Galerina* sp.
Monomethyl hydrazine (MMH)	*A. muscaria* (fly agaric), *A. pantherina* (panther cap), *Gyromitra* sp., *Lycoperdon* sp.
Muscarine	*Clitocybe* sp., *Inocybe* sp., *A. pantherina*
Ibotenic acid/muscimol	*Coprinus atramentarius*, *A. pantherina*, *A. muscaria*
Hallucinogens	*Psilocybe* sp., *Panaeolus* sp., *Gymnopilus* sp., *Stropharia* sp., *Conocybe* sp.
GI irritants	*Chlorophyllum* sp., many others
Acute renal failure	*Cortinarius* sp.

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- contain diverse secondary metabolites (cyclopeptides, monomethylhydrazine, orelline/orellanin, muscarine, ibotenic acid and muscimol, psilocybin, and unknowns) that on ingestion/absorption result in mild to severe illness and even death.

Mechanism of action

Group	*Mechanism*
Cyclopeptide	Amatoxins inhibit RNA polymerase II blocking RNA and DNA transcription. Targets are exposed rapidly, dividing cells (intestinal crypt epithelium, hepatocytes, and renal tubular epithelia) Phallotoxin irreversibly polymerizes actin filaments in the hepatobiliary tree, resulting in cholestasis
MMH	Gyromitrin hydrolyses to MMH, which causes ↓ CNS GABA
Muscarine	Post-ganglionic M_1 and M_2 cholinergic agonist
Ibotenic acid/muscimol	Ibotenic acid, a glutamate agonist, is rapidly metabolized to muscimol, a GABA-B agonist
Hallucinogens	Psilocybin metabolized to psilocin, a 5-HT_{1A} and 5-$HT_{2A/2C}$ serotonin agonist
GI irritants	Irritants, allergens
Acute renal failure (orellanine)	Toxins are 2,2-bipyridine and compounds resembling paraquat and diquat—redox cycling is likely mechanism

Target tissues- Symptoms

Cyclopeptide	Gastrointestinal—severe gastroenteritis 6–24 h post-ingestion
	Hepatobiliary—delayed-onset (3–4 d) centrilobular hepatic necrosis
	Renal—delayed onset (3–4 d) acute renal tubular nephrosis
	Metabolic—hypoglycemia
	Hemic—coagulopathy
	Immune—prone to sepsis
	Nervous—cerebral edema, hepatorenal encephalopathy, coma
MMH	Gasrointestinal—vomiting/diarrhea 6–8 hrs post-ingestion
	Nervous—CNS excitation, seizure
	Neruomuscular—ataxia, tremor
	Hepatobiliary—hepatic necrosis and failure (rare)
Muscarine	Gastrointestinal—diarrhea, emesis, excessive lacrimation
	Urinary—frequent urination
	Ophthalmic—miosis, cycloplegia
	Respiratory—bronchorrhea, bronchoconstriction
	Cardiovascular—bradycardia, hypotension
Ibotenic acid/muscimol	Nervous—cycles of CNS stimulation followed by depression, visual hallucinations, confusion, agitation, aggression, pointless motor activity, seizure, coma, sympathomimetic signs
	Ophthalmic—mydriasis
	Metabolic—hyperthermia
Hallucinogens	Nervous—dysphoria, anxiety, confusion, agitation, aggression, pointless motor activity, seizure, coma, sympathomimetic signs
	Neuromuscular—ataxia, hyperreflexia
GI irritants	Gastrointestinal—emesis, diarrhea
Acute renal failure (orellanine)	Renal—delayed-onset (up to 20 d) tubulointerstitial nephrosis

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Differential Diagnosis

Cyclopeptide	GI phase—infectious gastroenteritis, GI irritants and corrosives Hepatorenal phase—white phosphorus, hepatotoxic mycotoxins and hepatotoxic algal toxins, hepatotoxic plants
MMH/Gyrometrin	GABA antagonists, CNS stimulants, seizure agents, isoniazid
Muscarine	Anticholinesterase pesticides, cholinergic medications and toxins
Ibotenic acid/muscimol	Other hallucinogens, stimulants, head injury, CNS infection
Hallucinogens	LSD and other hallucinogens, head injury, CNS infection
GI irritants	Infectious gastroenteritis, GI irritants and corrosives
Acute renal failure (orellanine)	Ethylene glycol, diquat, plants affecting the kidneys

Poisonous Mushrooms: Onset of Action and Organs Targeted

Mushrooms	Toxin	Onset Time	Organ/System
Latent Period >6 hr After Ingestion; Life-threatening			
Amanita phalloides; A virosa	Cyclopeptides, α and β amanitins, phallotoxins, virotoxins	6–24 hr, rarely >24 hr	Primarily liver, kidney secondary
Conocybe filaris	α and β amanitins	6–14 hr, rarely >24 hr	Primarily liver
Cortinarius gentilis	Orellanin, orelline	3–14 days (days/weeks)	Primarily renal[a]
Galerina autumnalis; G venenata	α and β amanitins	6–14 hr, rarely >24 hr	Primarily liver
Gyromitra esculenta	Monomethylhydrazine	6–24 hr	CNS
Lepiota spp	α and β amanitins	6–14 hr, rarely >24 hr	Primarily liver

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Mushrooms	Toxin	Onset Time	Organ/System
Latent Period ≤3 hr After Ingestion; Not Life-threatening			
Amanita muscaria; *A pantherina*	Isoxazoles: ibotenic acid muscimol	30 min–2 hr; recovery 4–24 hr	CNS
Chlorophyllum molybdites	Unknown	30 min–3 hr; recovery 1–2 days	GI
Clitocybe dealbata; *Clitocybe* spp; *Inocybe* spp	Muscarine	30 min–2 hr; recovery 6–24 hr	Autonomic nervous system
Paxillus involutus	Unknown	1–3 hr; recovery 2–4 days	Immune system
Psilocybe spp; *Conocybe smithii*; *Gymnopilus spectabilis*; *Panaeolus subbalteatus*	Psilocybin and psilocin	30–60 min; rarely 6 hr	CNS
Russula emetica	Unknown	30 min–3 hr; recovery 1–2 days	GI

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- Depending on the type of mushroom, the quantity eaten, the time elapsed since eaten, and several other factors, the signs of toxicity will vary. But common signs might include any of the following:
- Vomiting
- Diarrhea
- Abdominal pain
- Weakness
- Lethargy
- Yellowing of the skin (jaundice)
- Uncoordinated movements
- Excessive drooling (ptyalism)
- Seizures
- Coma

Diagnosis

- Anamnesis (onset and nature of the symptoms)
- Complete blood count, biochemistry profile, and *urinalysis* --
  - abnormally low blood glucose levels (*hypoglycemia*)
  - abnormally high levels of liver enzymes due to liver damage
  - sample from the stomach to identify the type of mushroom.
- Experinced mycologist required- no simple test to distinguish poisonous from nonpoisonous from clinical perspective

- Inexperience in harvesting wild mushrooms
- Owner substance abuse
- Cultivation/trafficking of hallucinogenic
- species Mushroom picking season

Treatment

- With no proven antidotes to treat mushroom poisonings, treatment is primarily directed at decontamination, mushroom identification when possible, and intensive supportive care

Group	*Target*
Cyclopeptide	None proven effective Thioctic acid (1–2 mg/kg q6h) credited with xyxy↓ human mortality Silibinin (50 mg/kg/day q6h); combine with n-acetylcysteine Penicillin theoretically beneficial, but limited practical effectiveness
MMH	Pyridoxine 25 mg/kg
Muscarine	Atropine to effect (endpoint is drying of secretions)
Ibotenic acid/muscimol	N/A
Hallucinogens	N/A
GI irritants	N/A
Acute renal failure (orellanine)	N/A

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Treatment cont’ed

Cyclopeptide

- IV glucose or dextrose
- Fresh frozen plasma
- Blood transfusion
- Vitamin K
- Potassium (hypokalemia)
- Furosemide
- Dopamine

MMH

- Diazepam
- Muscarine
- Atropine

Ibotenic acid/Muscimol

- Diazepam

Hallucinogens

- Diazepam

Acute renal failure

- Furosemide, Dopamin

- Check North American Mycological Association
- https://namyco.org/
- Turkey- Mushroom Flora
- http://www.mantarlaralemi.com/kategori/turkiyedeki-mantar-turleri/