VET 433A: Toxic Mushrooms and House Plants

Amanitins overview

- Bicyclic octapeptides found in three genera of mushrooms:
  - Amanita spp.
  - Galerina spp.
  - Lepiota spp.
- Family of 8 known compounds
  - α/β/γ subtypes are the most prevalent
  - Responsible for nearly all fatal mushroom poisonings in people
  - A single good-sized mushroom is enough to kill an adult
  - NOT degraded by cooking, freezing, or the acidic stomach environment

Mushrooms

Toxin	Amanitin	Isoxazoles (psychoactive alkaloids)	Psilocybin-containing hallucinogenic mushrooms
Examples	*A. phalloides* (Death cap) *A. ocreata* (destroying angel)	Amanita muscarina (Fly Agaric) A. pantherina	*Psilocybe cyanescens, Conocybe, Panaeolus, Gymnopilus*
Relevant ADME	Utilizes the transport system for bile acids to enter hepatocytes OATP1B3 and NTCP Enterohepatic cycling maintains high intra-hepatocyte concentrations No known metabolism 80-90% is eliminated in the kidney Short plasma $t_{1/2}$		Toxin is metabolized to psilocin
Toxicity	Extremely toxic: α-amanitin IV LD_{50} in dogs of 0.1 mg/kg		Toxin = Psilocybin metabolized to psilocin

VET 433A: Toxic Mushrooms and House Plants

	Oral LD_{50} generally <1 mg/kg		
MOA	Binds eukaryotic DNA-Dependent RNA polymerase II which inhibits RNA elongation essential for transcription *Basically inhibits protein synthesis	Muscimol – GABA receptor agonist Ibotenic acid – Mimics glutamate	
Clinical Signs	Long asymptomatic incubation delay following ingestion (6-12 hours) GI phase 12-24 hours -diarrhea -vomiting -abdominal pain -dehydration Hepatotoxic phase 24-48h -liver damage and coagulopathy Hepato-renal phase -hemorrhage -convulsions -fulminant hepatic failure -coma -death <u>Presenting signs</u> Emesis, diarrhea, lethargy, anorexia Clin path findings HIGH ALT Hypoglycemia Coagulopathy	Occur within 30 min to 2 hours of exposure Disorientation, paresis, ataxia, seizures Deep sleep, coma, respiratory depression	Serotoninergic activity in the CNS **Humans**: hallucinations, increased HR, high BP **Dogs**: Ataxia, aggression, vocalization, nystagmus, seizures, increased temperature
Diagnosis	AMATOXtest		

VET 433A: Toxic Mushrooms and House Plants

	Ante-moretem -Serum, urine, GI contents CBC and chem panel Post-mortem tox testing Liver and kidney are + up to 2-3 weeks post-exposure Necropsy		
Lesions	Liver: Swollen Lungs: Petechiae Stomach: Ulceration Panlobular, uniform coagulative necrosis Pyknotic nuclei, eosinophilic cytoplasm Acute tubular necrosis is present in dogs that develop renal failure		
Treatment	Activated Charcoal Antiemetics IVF Correct hypoglycemia Vit. K_1 Plasma transfusions SAMe Octreotide Silymarin/Silibinin	Decontamination Seizure control Provide ventilation	Often not necessary due to the short duration of effects Decontamination Seizure control

VET 433A: Toxic Mushrooms and House Plants

Random Factoids and Images	Recommended dosages of silibinin (humans) 20 mg/kg/day IV 50 mg/kg of silibinin IV given 5 and 24h post-exposure to *A. phalloides* Small/Medium dog 1 tab: 24 mg silybin A+B Large dog 1 tab: 70 mg silybin A+B Poor bioavailability A. phalloides (Death cap)  A. ocreata (Destroying angel) 	Amanita muscaria (Flying Agaric) 	Psilocybe cyanescens  Panaeolus foenisecii (Haymaker's mushroom) 

VET 433A: Toxic Mushrooms and House Plants

Houseplants

Plant	**Cycad Palms** *Cycas spp., Zamia spp., Macrozamia spp.*	**Lilies** Tiger Lily, Asiatic Lily, Easter Lily, Day Lilies	**Macadamia Nuts**	**Oleander** *Nerium oleander*	**Dumbcane** *Dieffenbachia spp.* *Philodendron* *Epipremnum*
Toxin	Cycasin Leaves, seeds, and roots are toxic Seeds are the most toxic Dogs: 1-2 seeds can be lethal Sheep and cattle are also affected	Unknown Leaves, flowers and pollen are toxic Susceptible species: Cats Target organ: Kidney	Unknown Only reported in dogs Estimated toxic dose 2.4 g of nuts/kg BW 5-40 nuts/dog	Oleandrin As little as 0.005% of an animal's body weight in dry oleander leaves may be fatal	Insoluble Ca^{2+} -oxalated (raphide structure) All parts of the plant are toxic
MOA	-	Unknown	Unknown	Cardiac glycoside Similar to digitalis and inhibits cellular membrane Na^{+}/K^{+} ATPase by inducing conformational change in the enzyme and inhibiting its actions. This leads to an increase in extracellular potassium, intracellular sodium concentrations, and intracellular calcium resulting in disturbances in the	Bundle of needles within an idioblast cells Crystals are forcefully ejected when cells are chewed and cause mechanical irritation Penetrate oral mucosa, tongue and throat

VET 433A: Toxic Mushrooms and House Plants

				heart's electrical conductivity	
Clinical Signs	Within 24 hours Vomiting Diarrhea Depression Anorexia Liver Failure	Vomiting Depression within 12h followed by transient recovery Renal failure initiated within 48 hours of exposure	Within 12 hours of ingestion Weakness, especially in the hind limbs Tremors Stiffness Depression Vomiting	Vomiting Lethargy Diarrhea Arrhythmias	Rapid (within 2h of ingestion) <u>Mild</u> Hypersalivation Head shaking Chewing/pawing at mouth <u>Severe</u> Oropharyngeal edema Anorexia, vomiting, depression Dyspnea due to airway obstruction
Treatment	GI decontamination Activated Charcoal Supportive and symptomatic care GI protectants Fluids	GIT decontamination IVF diuresis Good outcome, low incidence of ARF	Recovery within 48 hours	Gastric decontamination Hemodynamic support Correcting electrolyte abnormalities Arrhythmia management Digoxin specific Fabs have been seen to be helpful in reducing mortality in humans	Supportive and symptomatic care Flush mouth with water Yogurt, milk, cottage cheese Dyspnea > go to clinic @ Clinic Flush mouth Antihistamine to decrease swelling Fluid therapy GI protectant Respiratory support