Biological poisonings

Snake envenomations

Snake envenomation worldwide is primarily related to occupational exposure, such as in farmers and hunters, but is also seen among tourists exploring the outdoors. When **snake** envenomation occurs in humans, the initial damage is local around the site of the bite and may spread to systemic toxicity depending on the species.

Snakes primarily use their venom production for targeting prey, but it is also a form of self-defense. Some species can selectively release their venom leading to the occurrence of "dry **bites**," in which there is the delivery of no venom. When venom gets released with their bite, the overall toxicity is dependent on both the volume of the venom released and the median lethal dose (LD50) of the venom.

Patients with venomous snakebites present with signs and symptoms that can include superficial puncture wounds, localized pain and swelling, nausea, vomiting, muscle cramping, dizziness, numbness, tingling around the mouth, dyspnea, life-threatening coagulopathy, and shock. Pre-hospital treatments, including the application of ice, alcohol consumption, and wound incisions and oral suction of venom, are not recommended. Evidence supports initial conservative management, such as immobilization. the use of lymphatic constriction bands is not advised as these are reserved for venoms with significant neurotoxic effects only. Otherwise calming the patient and encouraging oral fluid intake prior to rapid evacuation to an emergency center where definitive care can be rendered. Antivenom is the definitive treatment, although the specific type of antivenom depends on the snake species.

The symptoms seen from **snake** envenomations are mainly due to the toxic components in their venom. The exact composition ranges from species to species and can vary significantly from localized tissue destruction to profound coagulopathies. The clinical effect on humans is related to both the potency and the volume of the toxin released during the **snake** bite.

The composition of **snake** venom from a single species of venomous **snake** can consist of up to 100 different toxic elements. Local tissue destruction is primarily due to hyaluronidase and proteolytic enzymes in the **snake** venom,

which can lead to local tissue edema, blistering, and tissue necrosis. Phospholipase A2 is a common component of **snake** venom and causes local tissue damage. This compound has both local effects of the surrounding tissues as well as systemic effects on the vascular system and nerve endings. There are a variety of other proteins and polypeptides with toxic effects, such as neurotoxins and hemotoxins.

Most of the neurotoxic effects are secondary to damage at both the presynaptic and postsynaptic terminals of the neuromuscular junction. Presynaptic neurotoxins, such as phospholipase A2, damages the terminal axon, which prevents the release of acetylcholine, causing diffuse paralysis. In contrast, the postsynaptic neurotoxins, such as alpha neurotoxin, responds well to antivenom and anticholinesterase administration as the toxin binds directly to the acetylcholine receptor.

There are a wide variety of hemotoxins with effects on the coagulation cascade, platelet activation, and fibrin clot formation. Most of the toxins lead to an increased bleeding tendency secondary to a consumptive coagulopathy and defibrination. There are, however, some hemotoxins that promote clotting and thrombosis.

A detailed history of a patient suspected of having a **snakebite** is essential. Information to obtain includes the timing and location of the bite, the onset of any symptoms the patient has been experiencing, and any first aid administered in the field. Factors that contribute to the severity of the bite include size of the victim, with larger patients doing better, part of the body bitten, exertion following the bite, depth of the bite, species of **snake** causing the bite, time to the presentation at the hospital, and initial first aid given at the scene.

There could be local tissue damage, such as ecchymosis, blistering, or even tissue necrosis. Neurotoxic effects will initially present with generalized weakness, ptosis, and ophthalmoplegia; this may progress to paralysis of the facial muscles, and eventually, respiratory failure secondary to obstruction or paralysis of the diaphragm. Significant bleeding from the puncture site, epistaxis, or evidence of spontaneous bleeding could indicate a hemotoxic effect. Patients may present with signs of shock secondary to venom-induced vasodilation, hypovolemia, or even anaphylaxis in some patients.

Symptoms that may suggest systemic effects of the envenomation include nausea, vomiting, abdominal pain, lethargy, muscle weakness, muscle fasciculation, and severe headache. It is important to recognize these symptoms early to prompt initiation of antivenom administration.

The initial first aid at the scene should be minimal and aim at getting the patient to the nearest treatment center quickly. Removal of jewelry and any constrictive clothing on the affected limb is necessary due to the possibility of swelling and circulatory compromise. The patient should be kept calm and encouraged not to exert themselves as this could increase the **snake** venom absorption. If the identity of the **snake** species is known to cause neurotoxicity and no local tissue damage, the application of a pressure bandage could slow the spread of the venom. However, if the venom is known to cause local tissue damage, the implementation of the pressure bandage may worsen the damage inflicted to the extremity. The use of venom extractors has also demonstrated to be ineffective. Local wound manipulation, such as incision or washout, is generally not suggested.

1.ABCDE/CPR if required
2.treat hypoxia/hypovolemia- oxygen/aggressive fluid resuscitation
3.analgesia/sedation
4.symptomatic treatment – coagulation disorders, AKI, steroids
5.Apply specific antisnake serum only if high grade envenomation
Mind that adverse allergic reactions are possible when administering ASS

ARTHROPODES

Arthropod species use toxins for defense and to kill prey. Some individuals are poisonous (e.g., certain beetles release toxins when pressed or crushed), whereas others inject venom using an apparatus, which can cause systemic repercussions in the prey, as observed with the stings of certain spiders and scorpions

Bees and wasps stings only cause local inflammation in most people. Most deaths result from immediate hypersensitivity reactions and anaphylaxis.

honey bees, bumble bees, among others) are usually not aggressive and only sting when threatened or provoked. However, there is a subset of “Killer Bees” or “Africanized bees,” that are very defensive, often aggressive, and tend to swarm. bees use stingers, which often remain attached in the skin after a single sting.

(wasps, yellow jackets, hornets) are known to be more aggressive.

Bees and wasps stings cause reactions by injecting venom via their ovipositors into their target. The venom have characteristics, consisting of a mixture of smaller, low-molecular-weight, proteolytic enzymes (hyaluronidase, proteases, phospholipase, acid phosphatase), lipids, carbohydrates, and also high-molecular-weight proteins which act as allergens. The low-molecular-weight components are responsible for local inflammatory reactions while the high-molecular-weight component is integral to the systemic reaction (in other words, anaphylaxis). When the venom is introduced into the skin, the proteolytic enzymes begin to degrade the surrounding tissue. The release of histamine from mast cells and basophil activation, in response to the venom, causes vasodilation and the ensuing inflammatory response: edema, pain, erythema, and increased warmth. Large, local reactions (LLRs) develop in about 10% of ***bee and wasp*** stings and are believed to be immune IgE-mediated. Anaphylaxis develops in people with preformed antibodies to the high-molecular-weight aspects of these venoms. These reactions, like other anaphylactic reactions to allergens, occur via a systemic IgE-mediated histamine release. The resulting mast cells and basophil activation can cause systemic vasodilation, angioedema, urticaria, hypotension/shock, and death.

Patients with uncomplicated, local reactions typically present complaining of pain and swelling after a presumed or witnessed sting. *Bee and wasp* stings usually cause immediate pain. The venom then causes a local reaction within minutes that can last for hours. Symptoms include pain, swelling, pruritis, bleeding. you may find erythema, edema, induration, increased warmth. In some instances, one may also see a stinger still attached in the skin. Stingers are usually still attached to the venom sac and so should be removed from the skin by scraping, not by squeezing or with tweezers).

Systemic reactions often present as severe anaphylaxis, are rapid in onset, and life-threatening. Patients may have a history of anaphylaxis or a similar systemic reaction in the past secondary to insect stings. Patients present in

extremis with rapidly worsening symptoms, including generalized urticaria, angioedema, flushing, difficulty breathing, wheezing, hypotension/shock.

Uncomplicated, local reactions can be treated with supportive care (ice packs, NSAIDs/APAP for pain, H1/H2 blocker). Within the first few minutes after the sting, the stinger should be removed via scraping with a credit card rather than squeezing/tweezing to avoid further venom exposure.

Large local reactions should also be treated with supportive care along with glucocorticoids (usually a burst course of prednisone 40 to 60 mg per day for 3 to 5 days) to decrease the inflammatory response and improve symptoms.

Systemic reactions (anaphylaxis) are life-threatening and should be managed as such. ABCs first. The airway can be lost within seconds to minutes, so intubate early. As with any anaphylactic reaction, epinephrine, corticosteroids, H1 and H2 antagonists, and intravenous (IV) fluids should be given immediately. Epinephrine 0.3 to 0.5 mg should be given intramuscularly (IM) to the anterolateral thigh. This may be repeated every 5 to 15 minutes. The alpha1-mediated increase in vascular tone, beta1-mediated increase in inotropic/chronotropic cardiac activity, and B2-mediated bronchodilation all help to reverse anaphylaxis. Corticosteroids (prednisone, methylprednisolone, dexamethasone) act to decrease inflammation and immune response to the antigen. H1 and H2 antagonists block the effects of histamine decreasing pruritis, erythema, and urticaria.

Mushrooms

Mushroom poisonings can occur because of misidentification of a poisonous species as edible, although many cases are intentional ingestions. Mushroom poisonings may range from benign symptoms of generalized gastrointestinal upset to potentially devastating manifestations which include liver failure, kidney failure, and neurologic sequelae.

The clinical presentation differs depending on the species of mushroom and toxin ingested.

Acute gastroenteritis: Most often secondary to one of a variety of "backyard mushrooms" such as *Chlorophyllum molybdites.* Symptoms of nausea, vomiting, abdominal cramping and possibly diarrhea associated with ingestion account for the vast majority of reported poisonings. It manifests typically within 1-3 hrs.

Hallucinations: Caused by psilocybin and psilocin containing species which include *Psilocybe*, *Conocybe*, *Gymnopilus*, and *Panaeolus*. These agents act as agonists or partial agonists at 5-hydroxytryptamine (5-HT) subtype receptors. These are grown and abused for recreational purposes, though they may grow naturally in warm, moist climates. Ingestion may be of fresh mushroom caps or dried mushrooms. Altered sensorium and euphoria occur 30 minutes to 2 hours after ingestion and last typically 4–12 hours depending on the amount.

Cholinergic toxicity: Caused by muscarine containing species in various genera such as *Clitocybe* and *Inocybe*. Though *Amanita muscari* contains small amounts of muscarine, levels are typically not sufficient to cause a cholinergic presentation. Cholinergic effects of abdominal cramping, diaphoresis, salivation, lacrimation, bronchospasm, bronchorrhea, and bradycardia usually occur within 30 minutes. Duration is dose-dependent though typically short-lived when compared to other sources of cholinergic poisoning such as pesticides.

Liver toxicity: Caused by amatoxin in species of *Amanita*. They disrupt RNA polymerase II, leading to protein deficiency at the cellular level. Toxicity characteristically demonstrates three distinct phases. Gastrointestinal effects start typically 6-12 hours post-ingestion, followed by a latent interval 24-36 hours after ingestion with symptomatic improvement. During this phase, however, there may be laboratory signs of hepatotoxicity. After 48 hours, hepatic damage intensifies, leading to liver failure and its sequelae. Death may occur within a week in severe cases or require liver transplantation.

Nephrotoxicity: Members of the *Cortinarius* genus produce orellanine, a nephrotoxic agent. Renal symptoms may delay for 1-2 weeks after ingestion. The typical presentation includes acute gastroenteritis symptoms progressing to renal injury in 12-24 hrs. Although some patients will require hemodialysis, most patients have a full recovery with appropriate supportive care.

Seizures: Caused by gyromitrin present in *Gyromitra* species. Toxicity stems from a metabolite, monomethylhydrazine, that leads to pyridoxine (B6) and ultimately GABA depletion. Because of this, these seizures may be intractable to anticonvulsant therapy and may require supplemental treatment including pyridoxine.

Treatment of the vast array of possible symptoms primarily consists of supportive care.

Depending on the timing of ingestion, activated charcoal may provide some benefit.

Acute gastrointestinal effects may benefit from rehydration and antiemetics in addition to correction of any electrolyte derangements. For those patients with adverse hallucinations, benzodiazepines may provide anxiolysis. Cholinergic toxicity may benefit from the administration of anticholinergic agents such as atropine. Consider Atropine 0.5-1mg IV adults or 0.01mg/kg for pediatric patients.

Amatoxin Toxicity

Amatoxin toxicity is caused by the ingestion of mushrooms containing these cyclopepeptide toxins, especially *Amanita phalloides*, commonly known as the death cap.

The clinical manifestations of an *A phalloides* ingestion are caused by the cyclopeptide phallotoxins and amatoxins. Phalloidin, a cyclic heptapeptide, causes gastroenteritislike effects 6-12 hours after initial ingestion. It interrupts the actin polymerization-depolymerization cycle and impairs cell membrane function. Phalloidin has limited gastrointestinal (GI) absorption, and symptoms improve within hours of supportive care.

The cyclic octapeptide amanitins, primarily alpha-amanitin, are responsible for the hepatic, renal, and encephalopathic effects. Amatoxins inhibit RNA polymerase II, thereby interfering with DNA and RNA transcription. These toxins mainly affect tissues with high rates of protein synthesis, including the liver, kidneys, brain, pancreas, and testes.

About 60% of absorbed alpha-amanitin is excreted into the bile. The liver is exposed to high concentrations of toxin through the portal system and via the enterohepatic circulation. Hepatocytes are damaged early, with sparing of the hepatic sinusoids. In these cases, fatty degeneration of the hepatic parenchyma and patterns of centrilobular necrosis with hemorrhage are typical.

Amatoxin is eliminated in the urine, gastroduodenal fluids, and feces for several days after ingestion. The toxins of *A phalloides* are stable to cooking and remain active in dried mushrooms.

The clinical course of amatoxin poisoning can be divided into 3 stages. The first stage is preceded by a characteristic latent period that lasts for 6-12 hours following ingestion. After this asymptomatic period, abdominal cramping, vomiting, and profuse watery diarrhea (rice-water or choleralike) occur. Fluid losses may be severe enough to cause profound dehydration and even circulatory collapse.

Once this acute GI phase is over (usually after about 24 hours), the second stage begins. Although the patient appears to have improved clinically, ongoing liver damage is occurring, as indicated by laboratory abnormalities (eg, elevation of serum aminotransferase levels and lengthening of the prothrombin time [PT]). This stage may last as long as 2-3 days.

In the third and final phase, hepatic and renal injury become clinically apparent and may progress to fulminant hepatic failure (FHF). Death may occur in 3-7 days.

History

In patients with suspected amatoxin poisoning it is important to attempt to collect the following information:

- Time of mushroom ingestion - Patiens who develop GI symptoms (abdominal cramping, nausea, vomiting, and diarrhea) within 5 hours of the ingestion of the mushroom are unlikely to have ingested an amatoxin containing mushroom. GI symtpoms which manifest more the 6 hours from ingestion should make health care providers suspicious for ingestion of a possible amatoxin containing mushroom.
- Time of onset of symptoms – Phalloidin causes gastrointestinal (GI) symptoms about 6-12 hours after ingestion; renal and liver toxicity caused by amanitin is evident 24-48 hours after ingestion.

- Other mushrooms or toxins concurrently ingested – GI symptoms occurring earlier than 6-12 hours after ingestion suggest that another mushroom is responsible, but if the patient's meal included several different mushrooms, earlier onset of symptoms does not rule out concomitant amatoxin ingestion; if the setting is an attempted suicide, every effort should be made to identify any other toxins that may have been ingested

Toxicity from amatoxin and other cyclopeptides occurs over several days and usually develops in the following stages:

- Stage I – Sudden onset of nausea, vomiting, watery diarrhea, and cramping abdominal pain between 6 and 12 hours after ingestion, potentially resulting in dehydration and hypotension; patients often present during this stage and, if misdiagnosed, may be erroneously discharged without further care. There is some evidence that in the development of early diarrhea (within 8 hours of ingestion) may protend more serious outcomes [16]
- Stage II – Clinical improvement with supportive care; however, despite the resolution of symptoms, hepatic and renal damage is ongoing, as evidenced by rising laboratory test values
- Stage III – If discharged, patients may return to the hospital 2-6 days later with severe hepatica injury or failure, severe coagulopathy, renal failure, and encephalopathy

Physical Examination

The examination findings depend on the stage of the poisoning. As a consequence of profuse vomiting and watery diarrhea, the patient may present in hypovolemic shock during the GI phase. Accordingly, assessing the patient's volume status is an important component of the initial evaluation. With delayed presentations, it is important to look for signs of hepatic dysfunction (eg, jaundice, lethargy, or bruising), renal injury, or central nervous system (CNS) dysfunction.

Examination findings may include the following:

- Vital signs – Tachycardia, hypotension

- Skin – Poor turgor, jaundice, bruising (with hepatic failure)
- Head, ears, eyes, nose, and throat – Epistaxis or scleral icterus that is related to hepatic failure may appear in a patient with delayed presentation
- Abdomen – The patient can have mild diffuse tenderness, and a rectal examination reveals occult bloody stool. Hepatomegaly results from hepatitis late in the course of the disease.
- Nervous system – Neurologic effects are related to hepatic failure; depending on the time elapsed since ingestion, the examination findings may range from normal to confusion, agitation, lethargy, somnolence, seizures, or coma.

Approach Considerations

The mainstays of treatment of amatoxin ingestion include aggressive IV fluid and electrolyte therapy to correct deficiencies and maintain adequate hydration. Serum electrolyte and glucose levels should be closely monitored. Gastric decontamination may be helpful if instituted promptly (within 1 hour after ingestion) but patients rarely present in this time frame. Liver transplantation may be indicated in selected cases, though the precise indications remain controversial.

Supportive Measures

Airway and fluid support

Early management of airway, breathing, and circulation (the ABCs) and prompt institution of IV access are vital in the treatment of *Amanita* poisoning. Supportive care with IV hydration and correction of electrolyte abnormalities leads to symptomatic improvement.

Gastric decontamination

If the patient presents less than 1 hour after known ingestion of cyclopeptide-containing mushrooms and has not already vomited, consider gastric decontamination via gastric lavage or nasoduodenal

suctioning. Patients who present with nausea and vomiting within 1-2 hours of ingestion of a mushroom most likely have consumed a less toxic mushroom.

Administer activated charcoal in all patients who are asymptomatic with suspected *Amanita* ingestion. Patients who are asymptomatic afer ingesting unknown or unidentified mushrooms may receive activated charcoal and observation for 6-12 hours. Most patients with confirmed *Amanita* poisoning arrive later than 6 hours after ingestion and are usually vomiting at presentation, which may eliminate the need for lavage. Control nausea and vomiting with antiemetics

Activated charcoal (1 g/kg) is recommended if the patient is not vomiting and has a protected airway. Multidose activated charcoal (typically 1gram/kg given every 2-4 hours)should be given as it may disrupt enterohepatic circulation and reduce toxicity [21] .

Hemodialysis and hemoperfusion

Hemodialysis and hemoperfusion have been proposed as methods for removing circulating amatoxin from the blood.

Pharmacologic Therapy

include benzylpenicillin (penicillin G), *N*-acetylcysteine (NAC), thioctic acid, vitamin K, cimetidine, cytochrome C, and hyperbaric oxygen.

NAC is given initially in an intravenous (IV) loading dose of 150 mg/kg IV infused over 15 minutes, diluted in 200 mL of 5% dextrose in water (D5W);