

# **Chapter Six**

## **Toxic Effects of Some Animal Venoms and Plant Toxicants**

# Outline

- Objectives
- Poisons, Toxins, and Venoms
- Major Sites and Mechanisms of Toxic Action
- Toxins of Higher Plants
- Animal Venoms and Toxins

# Objectives

At the end of this chapter the student will be able to:

- Describe the Poisons, Toxins, and Venoms
- Differentiate the Major Sites and Mechanisms of Toxic Action
- Discuss the Toxins of Higher Plants
- Understand the Animal Venoms and Toxins

# 1. Poisons, Toxins, and Venoms

- A **poison** is any substance or mixture of substances which can be life-threatening mainly from non-biological origin
- **Poisonous organisms** either secrete or contain one or more chemicals (toxins) that seriously interfere with normal physiological functions
- A toxin is a single substance with definable molecular properties that interferes with normal function

# Poisons, Toxins, and Venoms cont'd

- Most toxins are exogenous substances made by an organism to adversely affect another organism
- **Venoms** are secretions containing a mixture of biologically active substances, including enzymes, toxins, neurotransmitters, and other compounds
  - The functional value of a venom for the procurement of prey or as a defense against predators

## 2. Major Sites and Mechanisms of Toxic Action

### Neurotoxic Actions

- Toxins act on electrically active tissues—muscle and neuronal cells that use neurotransmitter and voltage gated ion channels for generating their electrical signals
- The peripheral nervous and muscular systems are particularly vulnerable cellular targets for rapidly acting toxins, since no blood brain barrier protects them from exposure to toxins

# Major Sites and Mechanisms of Toxic Action cont'd

## Cardiovascular Toxins

- The cardiovascular system is also quite vulnerable to many natural toxins that act on ion channels in cardiac or smooth muscles or on autonomic nerve terminals
- Many lethal actions of venoms probably are due to rapid action on these excitable cells.
- Once the victim is envenomed, the active constituents spread locally according to their molecular size and other chemical properties.

# Major Sites and Mechanisms of Toxic Action cont'd

- Toxin entry into the systemic circulation will be greatly enhanced if they rapidly spread into tissues surrounding the bite:
  - This can be enhanced by a venom enzyme, **hyaluronidase**, which breaks down the **hyaluronic acid** in connective tissue
  - Some venoms also contain hemorrhage inducing, anticoagulant, and hemolytic proteins, which together can cause much loss of blood volume, tissue edema and cytolysis
  - Thus the cardiovascular system can be affected in many different ways by venoms and their toxic constituents

# Major Sites and Mechanisms of Toxic Action cont'd

## Toxins Affecting the Liver and Kidneys

- Two other organs that are especially vulnerable to toxins are the liver and the kidney
- These organs contain many catabolic enzymes and is thus capable of metabolizing practically any type of exogenous compound, usually to a less active or toxic form

# Major Sites and Mechanisms of Toxic Action cont'd

## Inflammatory and Carcinogenic Toxins

- Many sedentary organisms like plants and some marine animals synthesize inflammatory substances
- These may be similar to endogenous chemical mediators, such as **histamine, prostaglandins, or phospholipids**, or may liberate the endogenous mediators from basophils and other cells mediating inflammatory processes.
- Some of the most potent carcinogens are natural substances, like the ochratoxins

# Major Sites and Mechanisms of Toxic Action cont'd

## Cytotoxins

- This is the most common group of toxins
- Cytotoxins generally affect life requiring processes as protein synthesis, DNA replication, RNA synthesis, oxidative phosphorylation (metabolism), or cell electrolyte balance
- Cytolysins are cytotoxins that create an osmotic imbalance, causing cell swelling and subsequently cell lysis
- The most potent cytolysins create large holes in the cell membrane permitting the outlet of many proteins as well as low molecular weight substances

### 3. Toxins of Higher Plants

#### Mushrooms and Other Fungi

- Fewer than one percent of the mushroom species are poisonous to humans, but these can be extremely dangerous
- Mushrooms of the genus *Amanita* are the most dangerous
- These contain about equal amounts of two relatively small (seven amino acids) cyclic peptide toxins called **amatoxins** and **phallotoxins**
- Unfortunately these cyclic peptides are quite stable at high temperatures, so they survive cooking
- Consumption of a single *Amanita or phalloides* mushroom may be lethal

## Toxins of Higher Plants cont'd

- The amatoxins are about 20 times more toxic than the phallotoxins
- They are particularly hepatotoxic because of their ability to be taken up through the bile acid transport mechanism
- Other species of mushrooms produce alkaloidal toxins, Muscarine are much less life threatening
- Muscarine, used in classifying cholinergic receptors, is one example
- Fortunately, specific antidotes such as the muscarinic antagonist atropine exist

# Toxins of Higher Plants cont'd

- Other mushrooms produce biogenic amines such as bufotenin (originally isolated from venom glands of the toad *Bufo*) and psilocybin
  - These are hallucinogenic compounds which primarily stimulate certain serotonin receptors in the brain

## Ergot

- It is a fungus that grows upon certain grains in damp climates
- Ergot produces a variety of biogenic amines which act as agonists on alpha type adrenergic receptors including **ergotamine**, which is used to treat migraine headaches

# Toxins of Higher Plants cont'd

- Methysergide, a serotonin antagonist, is the major hallucinogenic component of ergot

## Mold

- Some molds have been found to produce carcinogenic substances called *aflatoxins* and *ochratoxins*
- Proper storage of vegetable crops susceptible to these molds eliminates conditions favorable for their growth

# 4. Animal Venoms and Toxins

## Snake venoms

- There are four families of poisonous snakes:
  - The pit vipers (family Crotalidae)
  - The vipers (Viperidae)
  - The cobra (Elapidae) and
  - The sea snake (Hydrophiidae)
- Many pit vipers occur in North and South America, whereas vipers occur only in Africa and Europe
- Pit viper and viper venoms have greater local effects on the tissues where the bite occurs and on the cardiovascular system

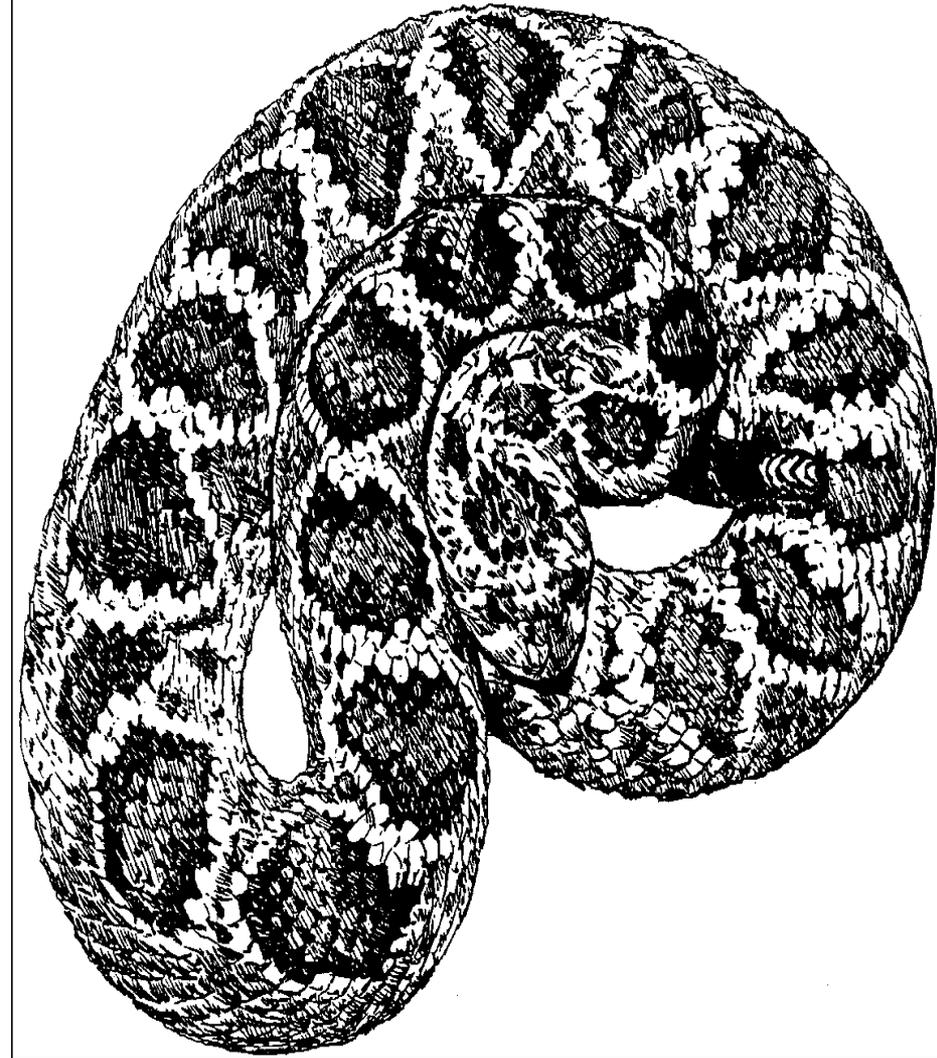
# Animal Venoms and Toxins cont'd

- Localized tissue swelling (edema) results from protein hemorrhagic toxins, which attack the capillary endothelium, making it leaky to blood cells as well as plasma proteins
- Protein myotoxins cause a pathological release of intracellular calcium stores in skeletal muscle, which may produce muscle necrosis
- The venom of the Brazilian rattlesnake, *Crotalu durissus terrificus*, possesses a potent neurotoxin
- Crotoxin paralyzes peripheral nerve terminals, causing loss of neuromuscular transmission and flaccid paralysis

# Animal Venoms and Toxins cont'd

## Figure:

- The Eastern diamondback rattlesnake (*Crotalus adamanteus*) is one of the most dangerous pit vipers
- On a weight basis its venom is not nearly as powerful as cobra or coral snake venom, but it compensates for this by injecting a much larger quantity of venom with an efficient venom delivery apparatus



# Animal Venoms and Toxins cont'd

- Cobra or sea snake envenomation often causes **respiratory arrest** before any signs of local tissue or systemic cardiovascular damage are apparent
- The major neurotoxin occurring in elapid and hydrophiid venoms is  $\alpha$ -neurotoxin
- The toxin acts as a competitive antagonist of the neurotransmitter acetylcholine (ACh) at the skeletal muscle neuromuscular junction

# Animal Venoms and Toxins cont'd

## ❖ Frog venoms

- alkaloidal toxin, histrionicotoxin, causes neuromuscular paralysis by binding to the open channel of the skeletal muscle nicotinic receptor
- **Toads** of the genus *Bufo* possess a very potent venom in their skin and parotid glands behind their eyes
- The major toxic constituents are cardiac glycosides called *bufotoxins*, but there also are biogenic amines, including epinephrine and bufotenin, a methylated form of the neurotransmitter serotonin

# Animal Venoms and Toxins cont'd

## Fish Venoms and Toxins

- Only a relatively small proportion of fish species are venomous, and in all cases the venoms are used defensively to discourage predators
- The most commonly encountered venomous fishes are the **catfishes** and **stingrays**
- The **stonefish** toxin has recently been isolated and shown to be a large protein that enhances **neurotransmitter release** from nerve terminals
- These stings are quite unpleasant, rarely life threatening, and can usually be treated with anti inflammatory drugs such as antihistamines and corticosteroids

# Animal Venoms and Toxins cont'd

## Arthropod Toxins and Venom

- This animal phylum consists of such different animals as **scorpions**, **spiders** and **insects**

### ❖ **Scorpion venom**

- It is one of the richest sources of peptide toxins
- Scorpions quickly immobilize their prey, generally insects, by injecting a complex mixture of **peptides** that act on the voltage gated sodium and potassium channels, which then produce action potentials

## Animal Venoms and Toxins cont'd

- There are two kinds (called *alpha* and *beta*) of toxins, that bind on the external surface of the sodium channel
- Both enhance electrical excitability by modulating the probability of sodium channel to be remain opened

### ❖ Spiders:

- Several spiders are exceedingly dangerous
- Their venom is primarily neurotoxic due to the presence of a powerful protein toxin called **alpha-latrotoxin**

# Animal Venoms and Toxins cont'd

- Spider venom (*Loxocceles* sp.) acts in an entirely different way because its venom primarily contains an enzyme, sphingomyelinase, which causes tissue damage
- While this venom is less dangerous than black widow venom, it can cause significant tissue necrosis at the site of the bite
- Although the bees, hornets, and wasps all belong to the order Hymenoptera, their venoms are different
- The most serious reactions to hymenopteran stings are hypersensitivity type and are due to an immune response from previous stings mediated by immunoglobulin E

# References and Suggested Reading

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