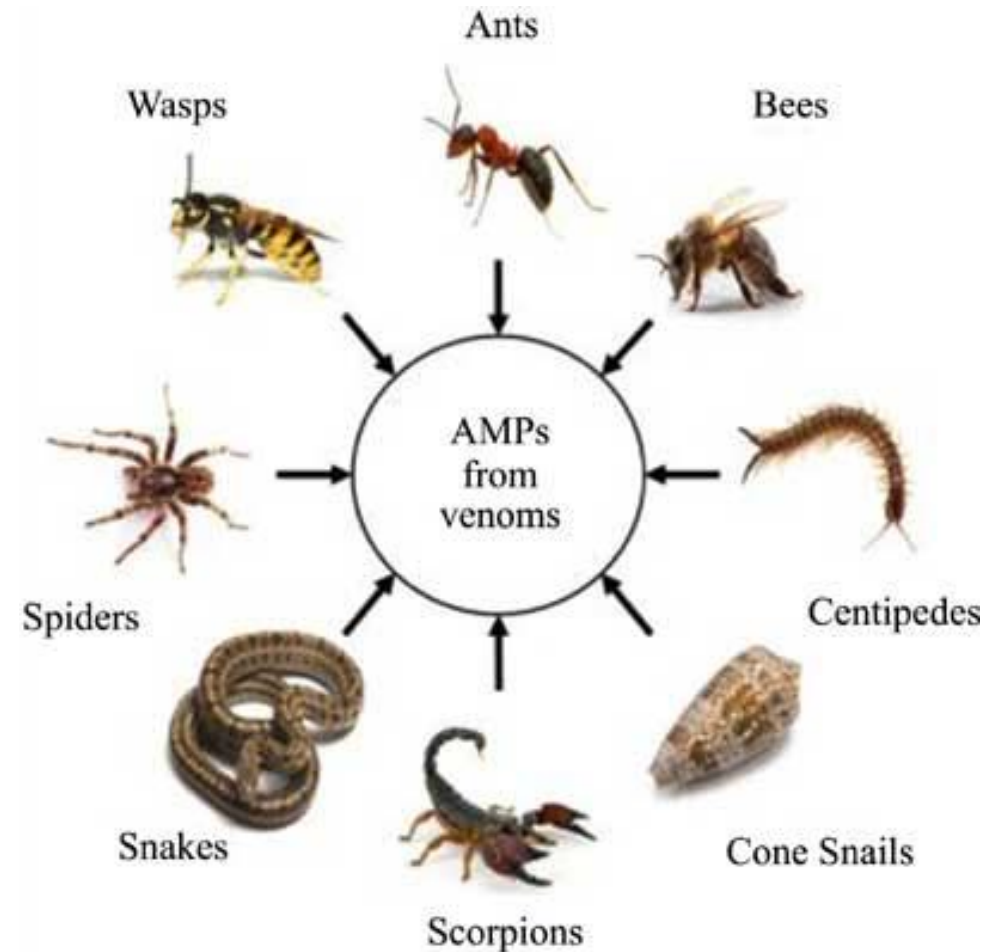


# Toxicology course

- Part 8:

- ❖ Toxicology of animal poisoning



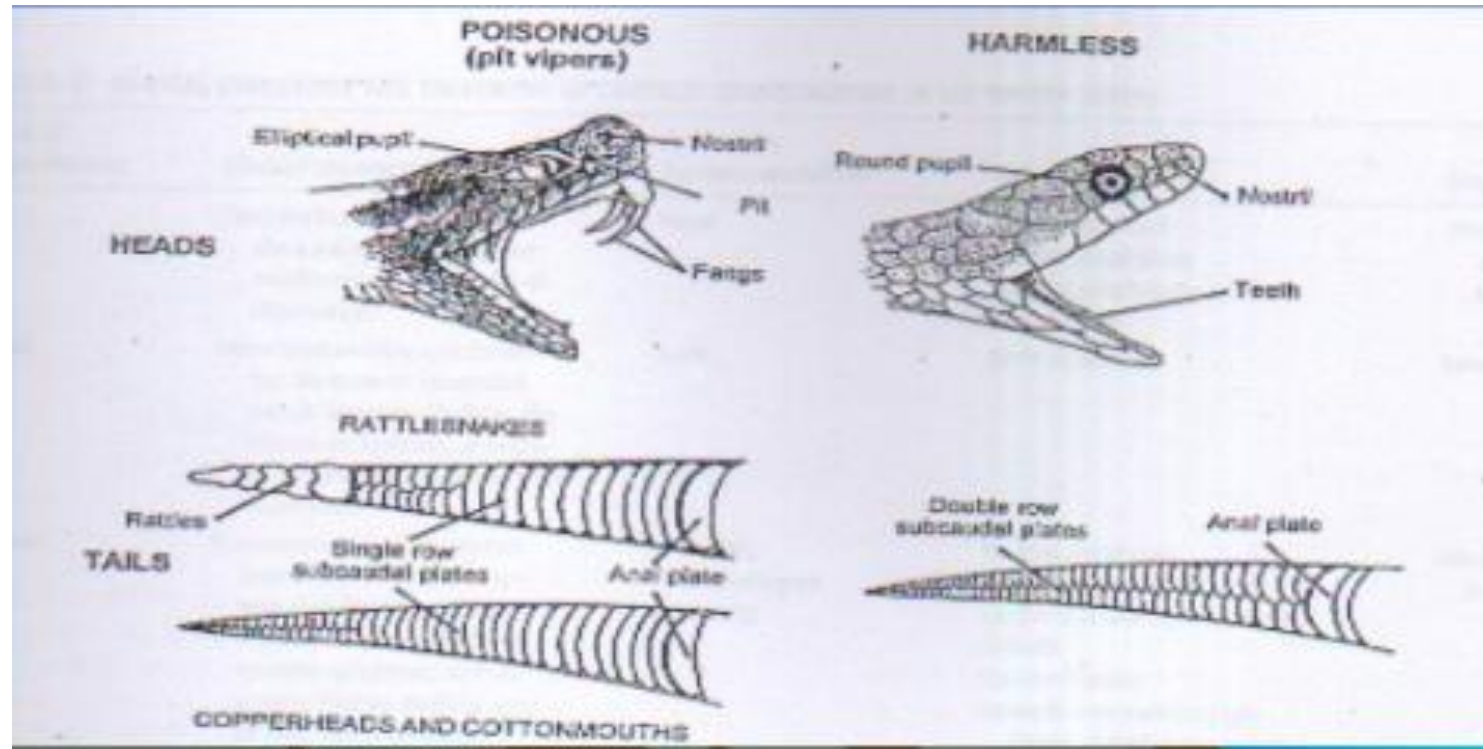
# Definition

- **Venom** is an animal poison contains different types of antigens as: (proteins enzymatic as protease, phosphodiesterases, hyaluronidases, phospholipase) .
- Proteins toxics: acids amines, polypeptides. has to be injected into circulation.



# Snakes

- Snakes are nocturnal reptiles & undergo hybridization, classified into:



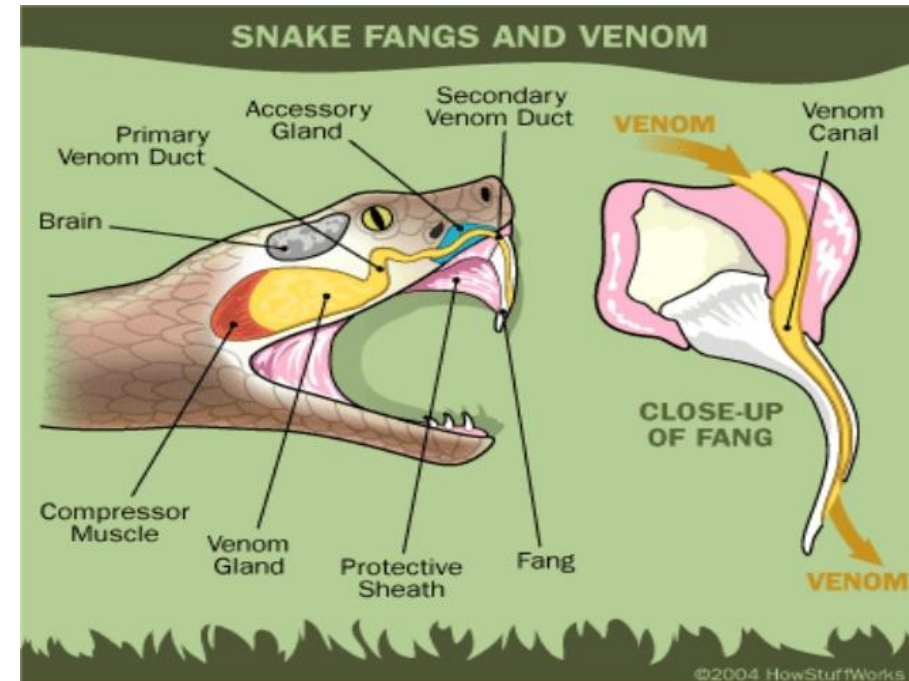
# Classifications of snakes

- According to the dominant venom:
  - Snake venom: Mixture of specific toxins (peptides & small proteins as hemotoxin, neurotoxin, cardio toxin, ...) and spreading factors (enzymes as hyaluronidase, phospholipase A, ...)
1. Hemotoxic: vipers
  2. Neurotoxic : cobra
  3. Myotoxic : sea snakes



- **Neurotoxic venom:**
- Dominant in cobra venom
- 50-75% have low MW so are dialyzable.
- Act mainly on neuromuscular junctions --> weakness
- Dangerous when affecting respiratory muscles -> respiratory failure.

- **Hemotoxic venom :**
- Dominant in viper snake venom
- Have high MW so, not dialyzable
- Mainly composed of hemolysin, thromboplastin, cardiotoxin
- Can cause: hemolysis, destruction of vascular endothelium → cerebral and intestinal hemorrhage, hypotension & shock, and tissue necrosis.



# Snake Venom composition

- Snake venom consists of proteins, enzymes, substances with a cytotoxic effect, neurotoxins and coagulants.
1. **Phosphodiesterases**: are used to interfere with the prey's cardiac system, mainly to lower the blood pressure .
  2. **Phospholipase A2**: causes hemolysis through esterolysis of red cell membranes and promotes muscle necrosis . Snake venom inhibits cholinesterase to make the prey lose muscle control.
  3. **Hyaluronidase**: increases tissue permeability to increase the rate that other enzymes are absorbed into the prey's tissues.
  4. **Amino acid oxidases and proteases** are used for digestion. Amino acid oxidase also triggers some other enzymes and is responsible for the yellow color of the venom of some species.
  5. **ATPases** which are used for breaking down ATP to disrupt the prey's energy fuel use.

# Spitting of the venom



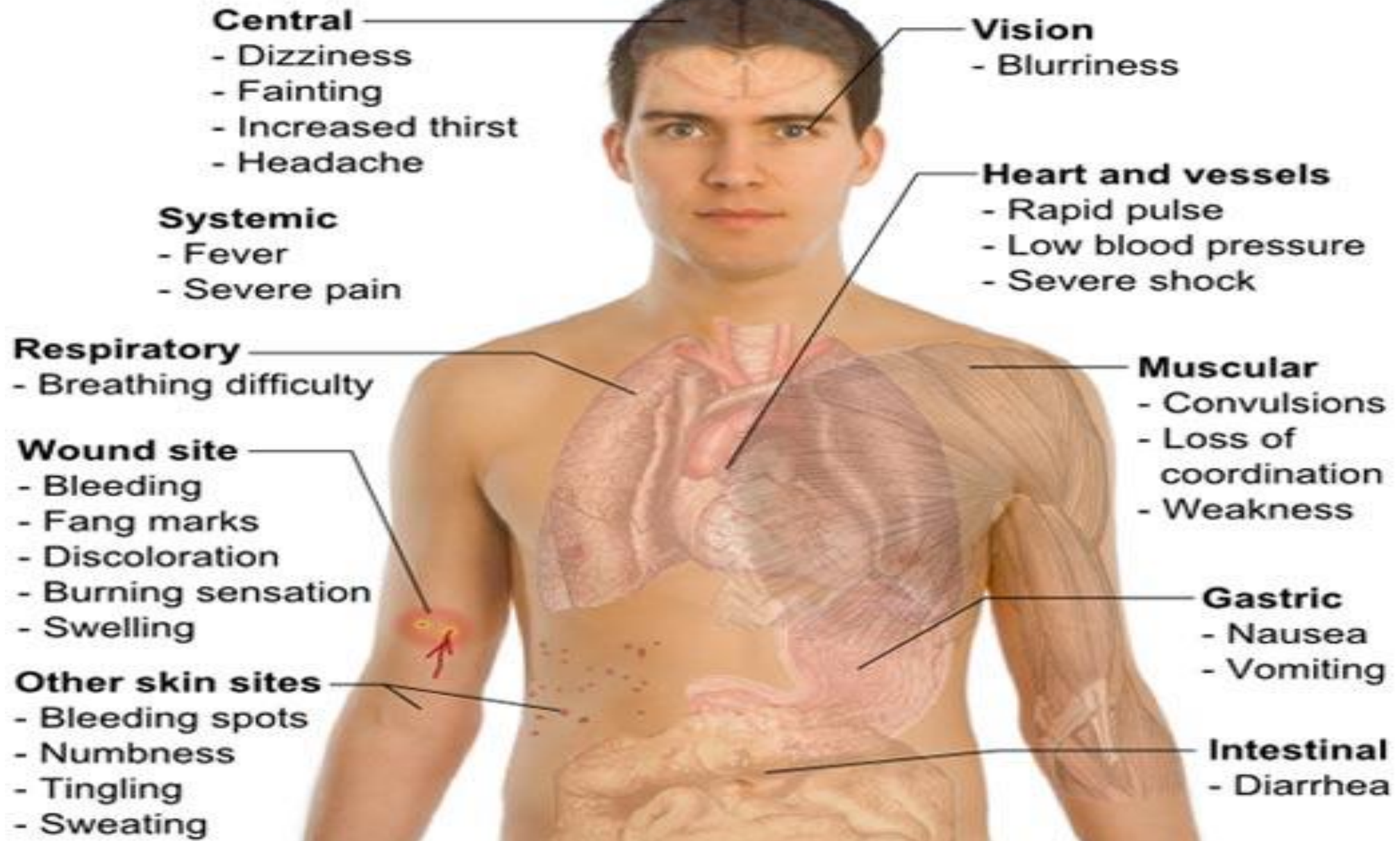
- Is a defensive reaction.
- The snake tends to aim for the eyes of a perceived threat.
- A direct hit can cause temporary shock and blindness through severe inflammation of the cornea and conjunctiva.
- While there are no serious results if the venom is washed away at once with plenty of water, the blindness caused by a successful spit can become permanent if left untreated.
- Contact with the skin is not in itself dangerous, but open wounds may become envenomed.

# Clinical Manifestations

- The manifestations & severity of the case are depended on:
  1. Amount of venom injected.
  2. Species of snake & nature of venom.
  3. Site of bite.
  4. Time of bite.
  5. Condition of fangs.
  6. Pathogens in mouth of snake.
  7. Death may occur immediately due to neurogenic shock.



# General symptoms of Snakebite



# Neurotoxic Venom:

Neurotoxin and myotoxin are taken to the blood stream faster than the hemotoxin which results in massive LOCAL effects



- Start 15-45 minutes after biting.
- Local : fang mark (2 punctures), pain, redness, hotness, swelling, & may wet gangrene (generally less prominent than with hemotoxic venom)
- Systemic : 1 st sign is ptosis & numbness in lips & tongue – giddiness – heaviness in bitten limb – salivation & vomiting – blurred vision – dysarthria – dysphagia – bradypnea – convulsions – coma & death due to respiratory failure

# Hemotoxic Venom:

- **Local:** prominent and include: fang marks, severe pain, redness, ecchymosis, hotness, edema and swelling of affected limb & dry gangrene.
- **Systemic:** nausea, vomiting – hypotension with rapid weak pulse – bleeding from mucous membranes – acute renal failure due to hemoglobinuria – coma and death due to circulatory collapse.



# MANAGEMENT OF TOXICITY

- Reassurance of patient is important.
- First step is to examine the site of bite and decide if the bite is poisonous or not to avoid unnecessary use of polyantivenom as it is risky and expensive.
- Immobilize the affected limb.
- Stop venom absorption as possible using tourniquet proximal to bite (just enough to obstruct lymph drainage not venous drainage) and {make 2 small incisions over fang marks, and suction; not recommended nowadays}.
- **Don't** use ice fomentations to avoid gangrene or give aspirin to avoid bleeding.

## **SUPPORTIVE TREATMENT:**

1. Open IV line and correct fluid, electrolytes and acid-base balances.
2. In all cases of snake bite either poisonous or nonpoisonous, we have to give broad spectrum antibiotics and anti-tetanic serum owing to pathogens found in snake mouth.

# SPECIFIC TREATMENT:

- **Antivenoms** can be classified into:

1. Monovalent (when they are effective against a given species' venom)
2. Polyvalent (when they are effective against a range of species, or several different species at the same time).

- **Indication:**

- Envenomated bite with systemic manifestations.

- **Dose:** depends on severity of bite not age or body size so a pediatric dose equal an adult dose:

- Mild; give 3-5 vials

- Moderate; give 5-10 vials

- Severe cases; give 10 vials & maintain with more vials according to situation

- Antivenoms are purified by several processes but will still contain other serum proteins that can act as **antigens** .
- Some individuals may react to the antivenom with an immediate hypersensitivity reaction ( anaphylaxis ) or a delayed hypersensitivity (serum sickness ) reaction and antivenom should, therefore, be used with caution.
- Despite this caution, antivenom is typically the sole effective treatment for a **life-threatening condition**
- The side effects are manageable, and antivenom should be given as rapidly as the side effects can be managed.

# SCORPIONS

- Belong to Arthropods.
- All of them are poisonous.
- Their venoms are more potent than that of snakes, and numerically more than snakes, so they represent more public health problem especially in southern areas.
- Generally, more dangerous and causing more morbidity and mortality in children.

Ex: *Androctonus amoreuxi*. [African fat-tailed]





# DANGEROUS SCORPIONS



Deadly red Indian scorpion



Middle east fat tailed scorpion

# SCORPION VENOM

- Generally more toxic, more variability of specific toxins & more multiplicity of antigens than snake venom.
- Consists of amino acids, peptides & small proteins (mainly neurotoxin, nephrotoxin, cardiotoxin, hemolytic toxin, histamine, serotonin, anti-ACh-esterase) & enzymes as phospholipases, hyaluronidases, phosphodiesterase.
- Inject able LD: few up to 50  $\mu\text{g}$ .
- Human have unique variable susceptibility to scorpion venom.

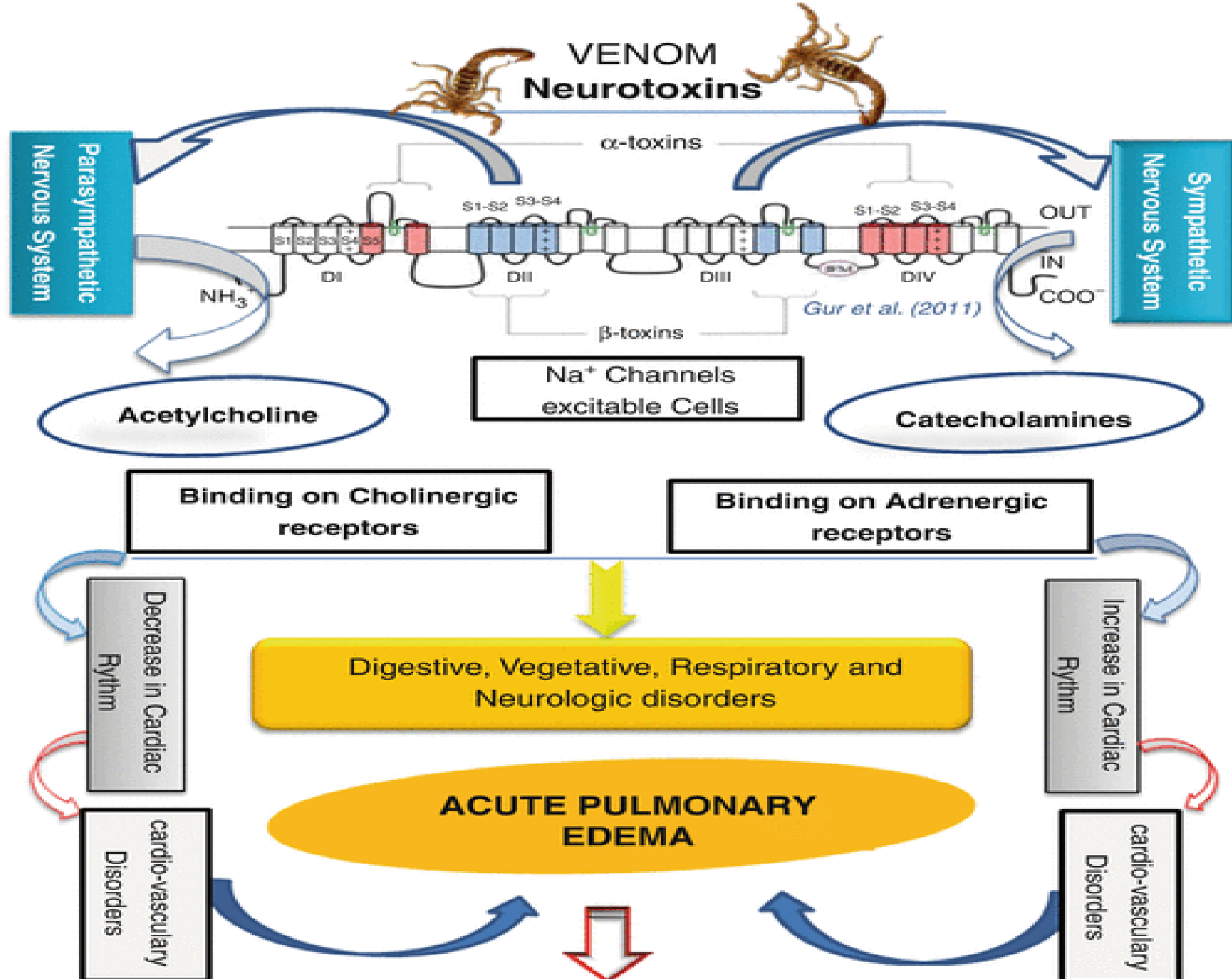


# TOXIC MECHANISM OF SCORPION VENOM

## Neurotoxin:

- **Blocks voltage-gated Na<sup>+</sup> & Ca<sup>++</sup> channels....**prolonged action potential & excessive release of catecholamine.....adrenergic manifestations
- The **long-chain polypeptide neurotoxin** causes stabilization of voltage-dependent sodium channels in the open position, leading to continuous, prolonged and repetitive firing of the somatic, sympathetic, and parasympathetic neurons. This repetitive firing results in autonomic and neuromuscular over-excitation symptoms, and it prevents normal nerve impulse transmissions

- The **short polypeptide neurotoxin** blocks the potassium channels.
- **Anti-cholinesterase**..... accumulation of Ach.....cholinergic manifestations.....this will lead to marked CV effects.
- **Autonomic excitation** leads to cardiopulmonary effects observed after some scorpion envenomations.
- **Somatic and cranial nerve hyperactivity** results from neuromuscular overstimulation.
- **Serotonin** may be found in scorpion venom and is thought to contribute to the pain associated with scorpion envenomation.
  
- **A smaller child, a lower body weight, and a larger ratio of venom to body weight lead to a more severe reaction**



# FACTORS AFFECTING SEVERITY OF SCORPION STING

- Age & body size of the victim.
- Species & size of scorpion.
- The amount of venom injected.
- Site & number of stings.
- Individual susceptibility to venom.

# CLINICAL MANIFESTATIONS

- **Local:** severe intense pain, edema, numbness & tenderness.
- **CVS:** sinus arrhythmias, hypertension, pulmonary edema, ischemic changes in ECG, complications are more in children with increased LDH & CPK.
- **CNS :** agitation, paresthesia ,irritability & (restlessness, severe involuntary shaking & jerking extremity due to somatic skeletal neuromuscular dysfunction). cerebral edema -> convulsions & coma.
- **Others:** nausea & vomiting, hypothermia , blurring of vision, tongue fasciculation slurred speech, diaphoresis, tearing.

# MANAGEMENT OF SCORPION STING

- **First aid:** like snake but, it is mandatory to control local pain (use local anesthesia) to make the patient calm which is very important procedure in management.
- **Specific treatment:** use polyantivenom as in snake.
- **Supportive treatment:**
  - Support CV functions to avoid complications
  - Symptomatic treatment: use Haloperidol to control agitation. use diazepam in convulsions .use diuretics in pulmonary edema



- Don't attempt to cut the wound and suck out the poison. This can cause infection or transfer the venom into the bloodstream of the person attempting to remove the poison.
- Scorpions cannot usually deliver enough venom to kill a healthy adult.
- While venom toxicity varies among species, some scorpions contain very powerful neurotoxins, which, ounce for ounce, are more toxic to humans than the venom of cobras.
- However, scorpions inject relatively small amounts of venom (compared to snakes), so the overall dose of toxins per sting is survivable.

# BLACK WIDOW SPIDER

- Belong to Arthropods
- Only **female bite** is clinically significant
- identified by a **red to orange hour-glass** on the thorax
- contains a potent **neurotoxin** which **destroy cholinergic nerve terminals** with massive release of **A Ch** especially at motor end plates causing severe muscle spasm & also, affect **adrenergic nerve** terminals that may cause increase in sympathetic outflow.



VectorStock®

VectorStock.com/1655658

# CLINICAL MANIFESTATIONS

- **Local:** bite usually painless & local reaction is very rare in the form of pain, redness, edema & itching.
- **Systemic:** develop 1-3 hours ranging from mild affection to serious troubles & mostly in the form of severe muscle spasm leading to chest & abdominal pain, tremors & muscle fasciculation followed by muscle weakness – hypertension – nausea, vomiting & salivation.

# MANAGEMENT OF SPIDER BITE

- IV **calcium gluconate** which controls pain and abdominal cramps, and is considered as an **antidote**.
- However, according to some recent studies, it is no longer recommended for widow **spider** envenomation. Studies suggest benzodiazepines are more efficacious than other muscle relaxant agents for the treatment of muscle pain related to widow **spider** envenomation.
- Prophylactic antibiotics are not indicated.
- **Latrodectus antivenin.**
- **Diazepam.**
- **Methocarbamol:** to relax muscles and relieve pain and discomfort caused by strains, sprains, and other muscle injuries. Methocarbamol is in a class of medications called muscle relaxants.
- **Opioid analgesics.**
- The **antivenin** is reserved for patient with severe cramps refractory to other therapy because it is an equine antivenin & may cause severe hypersensitivity and should be given very carefully with close patient observation.