Deadly Animals of the World

Joseph Pauly MD, MPH, DTM&H

Emergency Medicine
Yale University

https://www.youtube.com/watch?v=emisZUHJAEA

Definitions

An animal is *poisonous* when its toxins are passively deployed

An animal is *venomous* when it directly injects you or their prey with a toxin

The Median Lethal Dose (LD50): is how much venom is needed to kill 50 percent of a test population of lab mice

On the land


Case 1

Introduction

Félix is a 35-year-old male who presented to the emergency department with complaints of severe pain and swelling on his left hand.

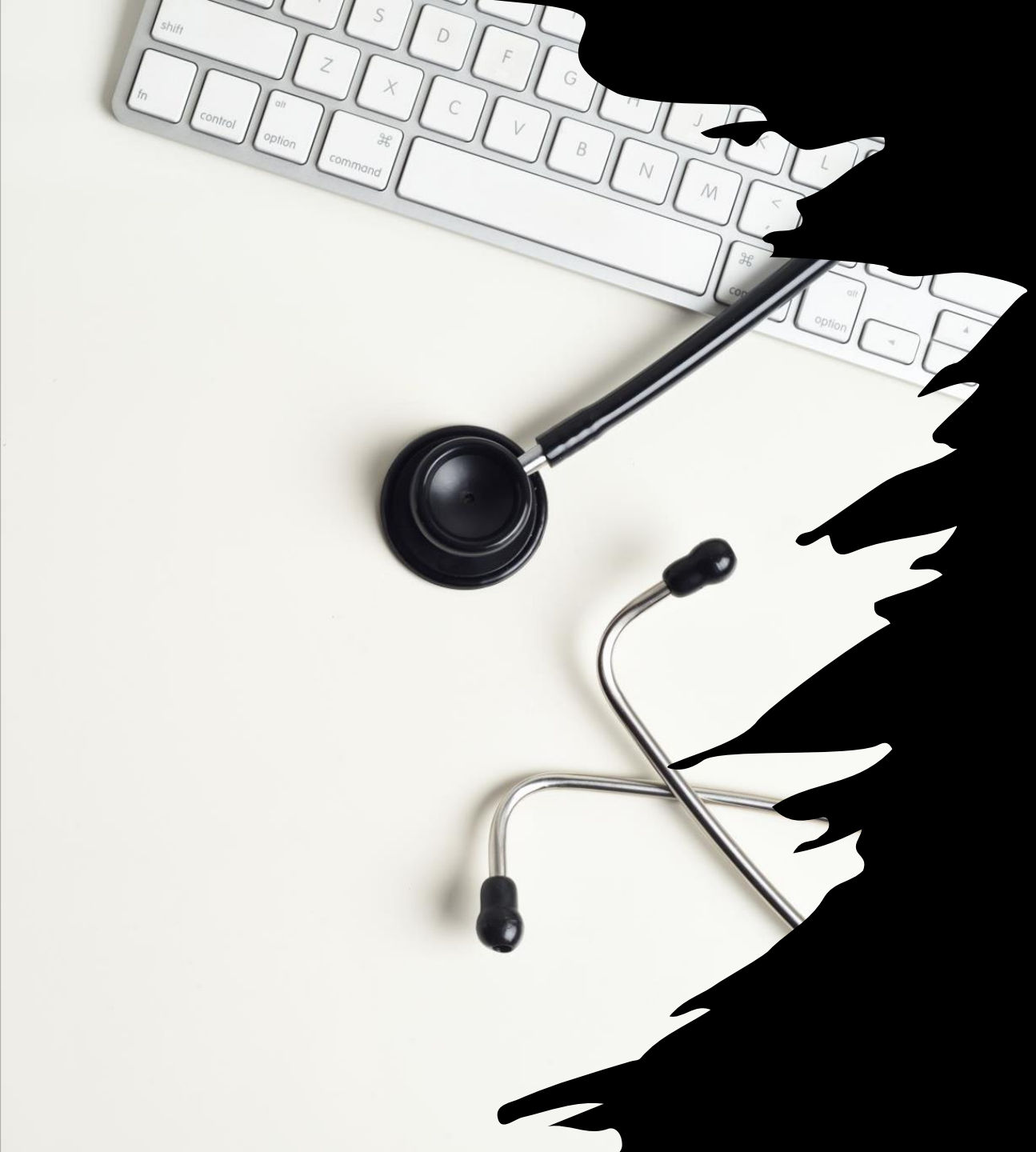
He reported being bitten on the hand while working construction overnight in a village outside of São Paulo, Brazil. The patient reported that he thinks it was a spider, brown in color and had red stripes on its legs. The patient reported no other medical history or allergies.

Upon physical examination: the patient was found to be in mild distress and had significant swelling and erythema on his left hand.

<u>Vital signs:</u>
Blood pressure 140/90 mmHg
Heart Rate 110 beats per minute
Respiratory Rate 20 breaths per minute
Temperature 37°C

Physical Exam

- **General appearance**: Patient appears **uncomfortable**, holding left hand in a dependent position, with **mild sweating and tachycardia**.
- **Skin:** Mild **erythema and edema** present at the site of the bite on the **left hand**, approximately 2 cm in diameter.
- **Neurological exam:** Neurological exam: No focal deficits noted. Patient reports mild **paresthesia** in the affected hand.
- **Cardiovascular exam**: **Tachycardic**, regular rhythm, no murmurs or gallops noted.
- **Respiratory exam**: Clear to auscultation bilaterally.
- **Abdominal exam**: Soft and non-tender, no hepatosplenomegaly or masses palpated.
- **Genitourinary exam**: **Painful and persistent erection is noted**, suggestive of priapism. No other genitourinary abnormalities noted
- **Musculoskeletal exam**: **Mild weakness** noted in the left hand **with decreased grip strength.** No obvious signs of compartment syndrome or necrosis.

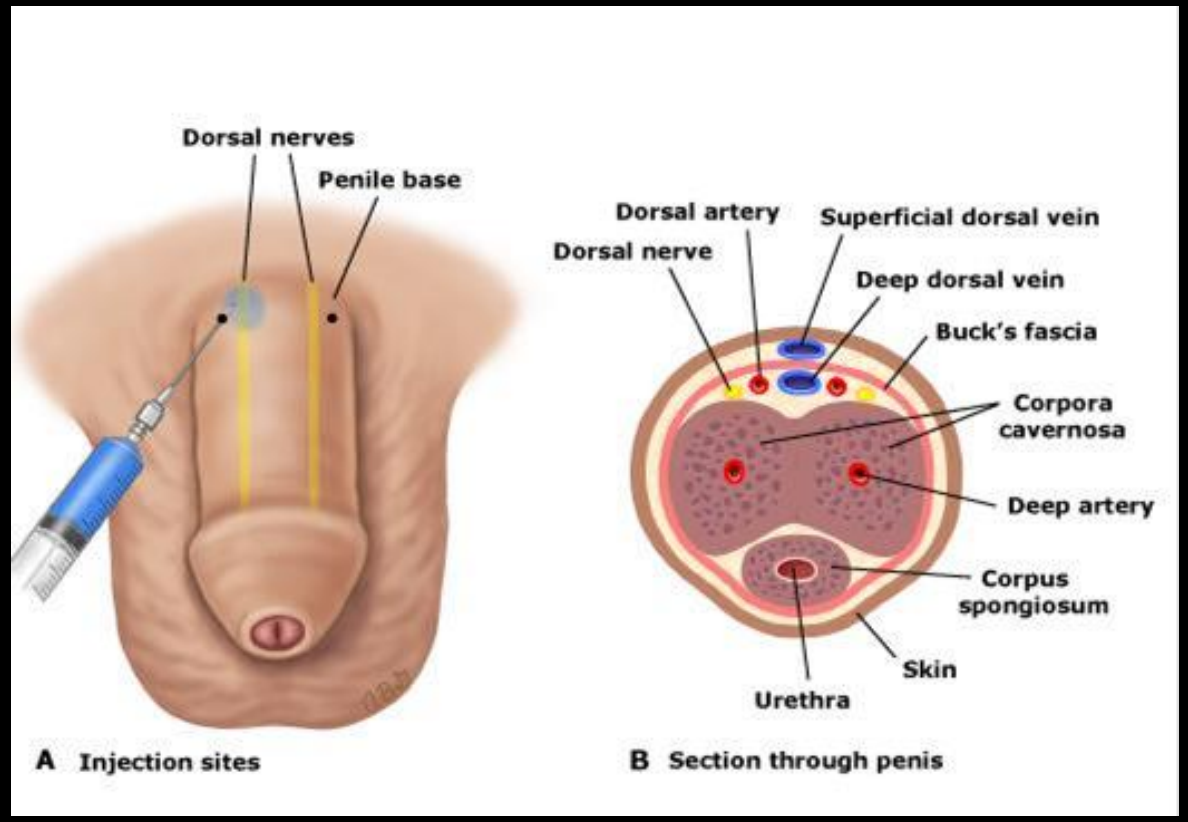


- He reported having an erection that has been present for the past six hours.
- Denies history of erectile dysfunction or use of medications
- Based on this history, the patient was diagnosed with priapism, a complication of the spider bite
- Overall, this physical exam suggests mild to moderate envenomation with evidence of priapism.
- Manage priapism urgently

Use phenylephrine and perform needle aspiration for the treatment of priapism:

- 1mL phenylephrine 0.1% injection into the corpus cavernosum (10 and 2 o’clock position)
- 19 gauge needle to aspirate blood from corpus cavernosum
- monitored for 30 minutes to ensure that the priapism was resolving
- Repeat process if not improvement

- Following this intervention, the priapism resolved, and the patient reported relief of pain



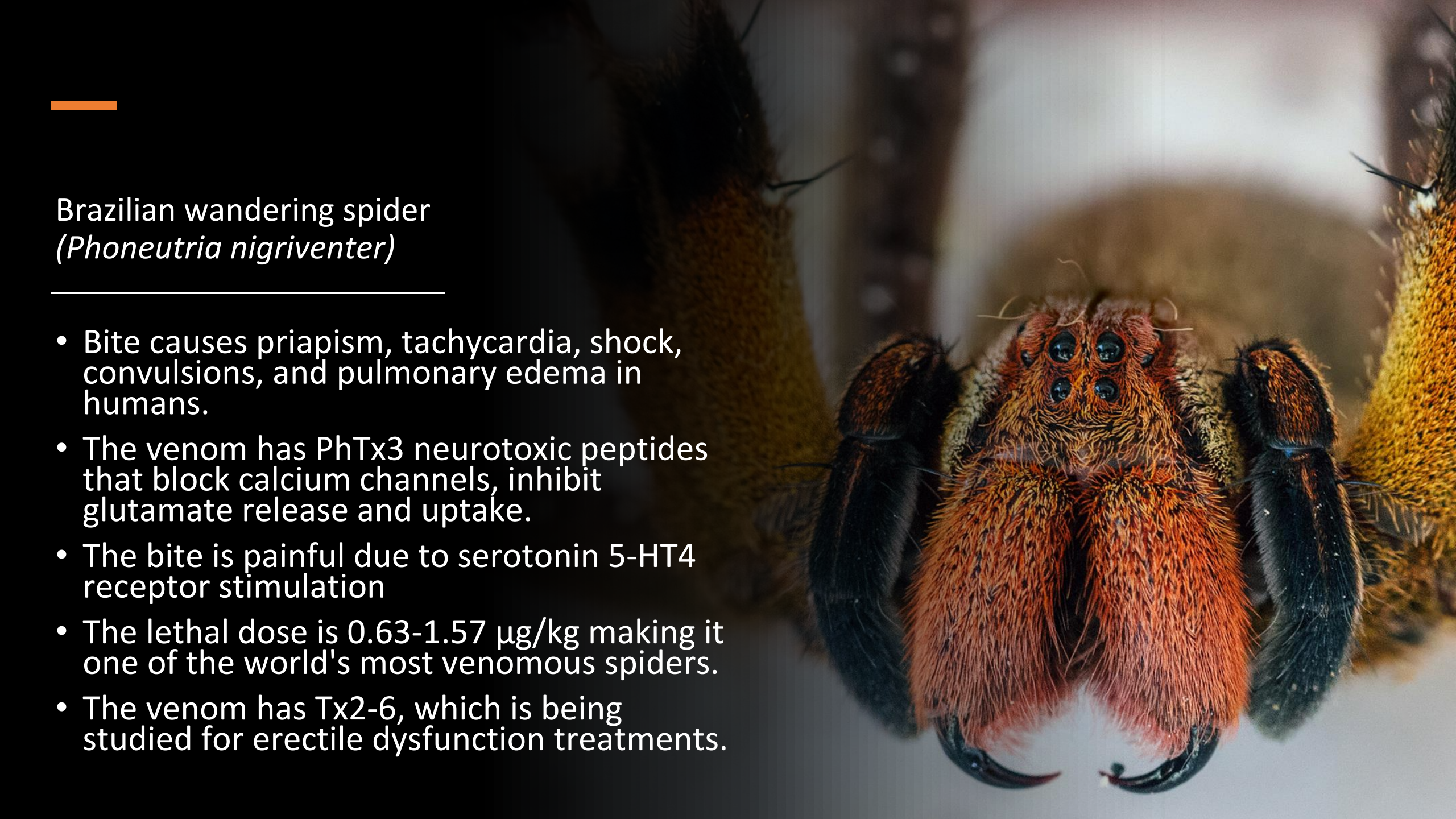
Antivenom Use

- Antivenom is used for severe or life-threatening envenomation
- Efficacy for treating priapism is uncertain
- In resource-limited settings, antivenom use for spider envenomation must be carefully considered due to:
  - limited availability
  - high cost
  - potential adverse effects/anaphylaxis

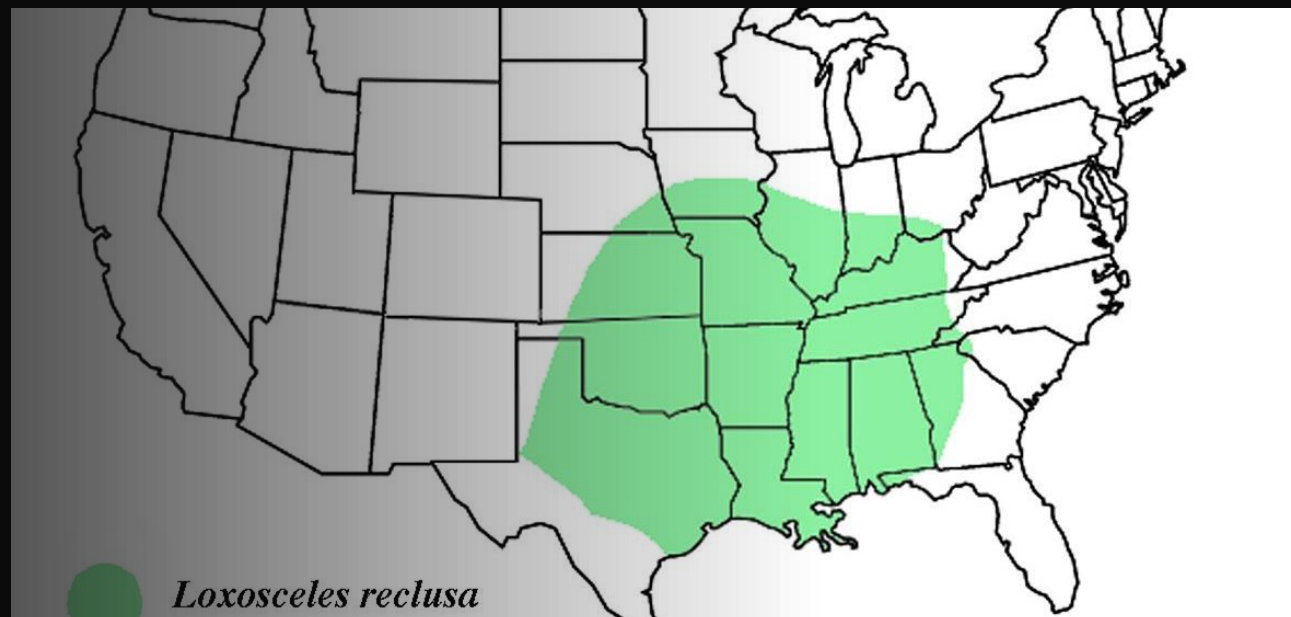
Brazilian wandering spider *(Phoneutria nigriventer)*

Brazilian wandering spider
(Phoneutria nigriventer)

- Bite causes priapism, tachycardia, shock, convulsions, and pulmonary edema in humans.
- The venom has PhTx3 neurotoxic peptides that block calcium channels, inhibit glutamate release and uptake.
- The bite is painful due to serotonin 5-HT4 receptor stimulation
- The lethal dose is 0.63-1.57 µg/kg making it one of the world's most venomous spiders.
- The venom has Tx2-6, which is being studied for erectile dysfunction treatments.



Brown Recluse
Loxosceles reclusa



Brown recluse

- found primarily in the southern and central United States
- typically light to dark brown in color and have a characteristic violin-shaped marking on their back.
- Venom contains sphingomyelinase D which causes tissue necrosis at bite site
- LD50 5-14 mg/kg usually not lethal to humans
- They are typically found in dark, quiet, undisturbed areas such as closets, attics, and basements.
- not aggressive and will usually only bite when they feel threatened or cornered.

Brown Recluse Spider bites

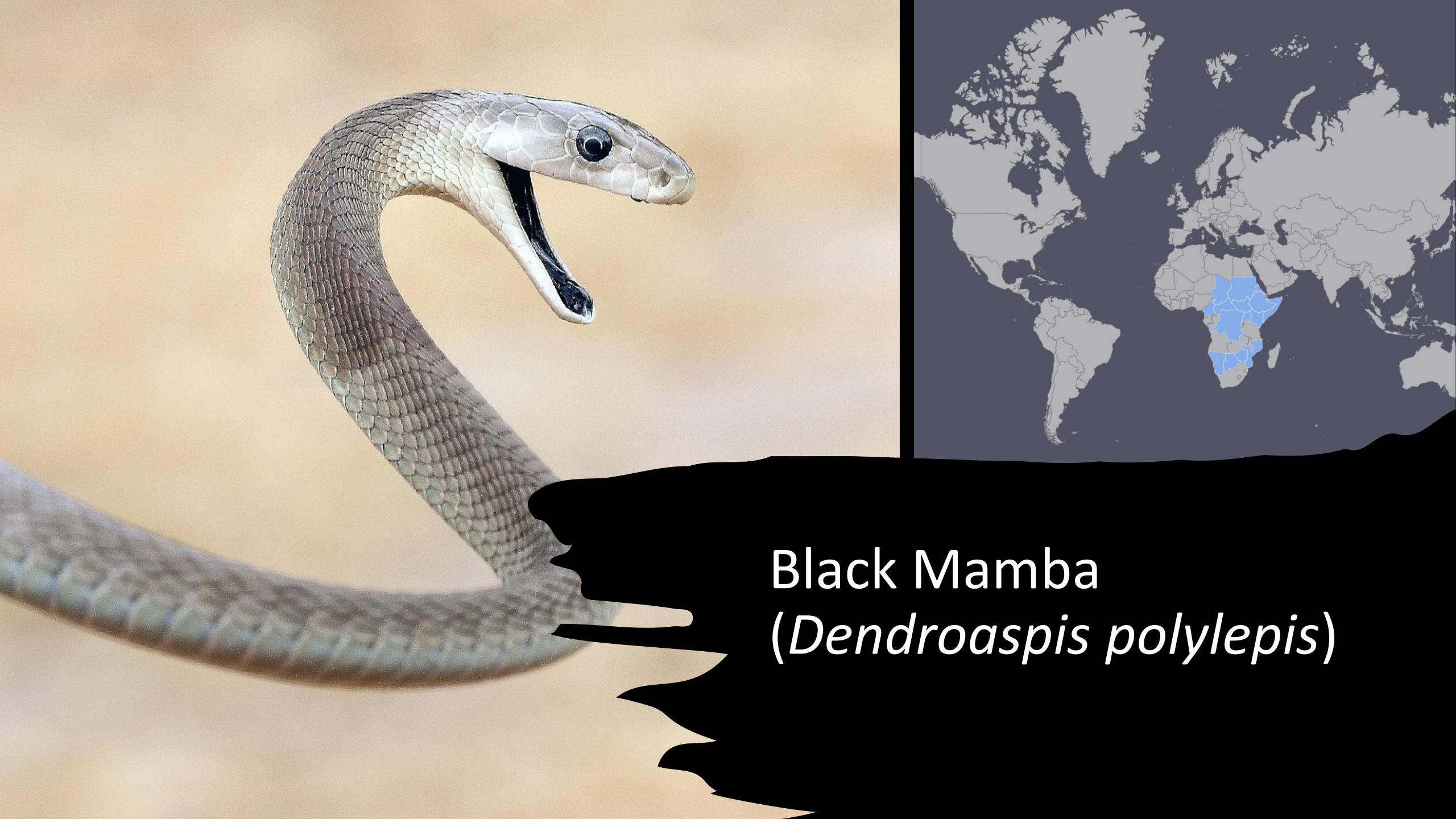
Black Widow Spiders
Latrodectus

Latrodectus hesperus

Black Widow
Latrodectus hesperus

- Distinctive red hourglass on the abdomen (Latrodectus hesperus) species found in Western US and Canada
- Typically found in dark, sheltered areas
- venom of the black widow spider contains a neurotoxin alpha-latrotoxin, which can cause muscle pain, cramps, spasms, and paralysis
- Symptoms typically begin within an hour of the bite
- LD50 0.16-0.36 mg/kg however not all bites result in symptoms and death is rare
- In some cases, symptoms can progress to include abdominal pain, high blood pressure, and difficulty breathing
- Pain control and benzodiazepines are first line, antivenom is reserved for severe cases ie. Respiratory distress

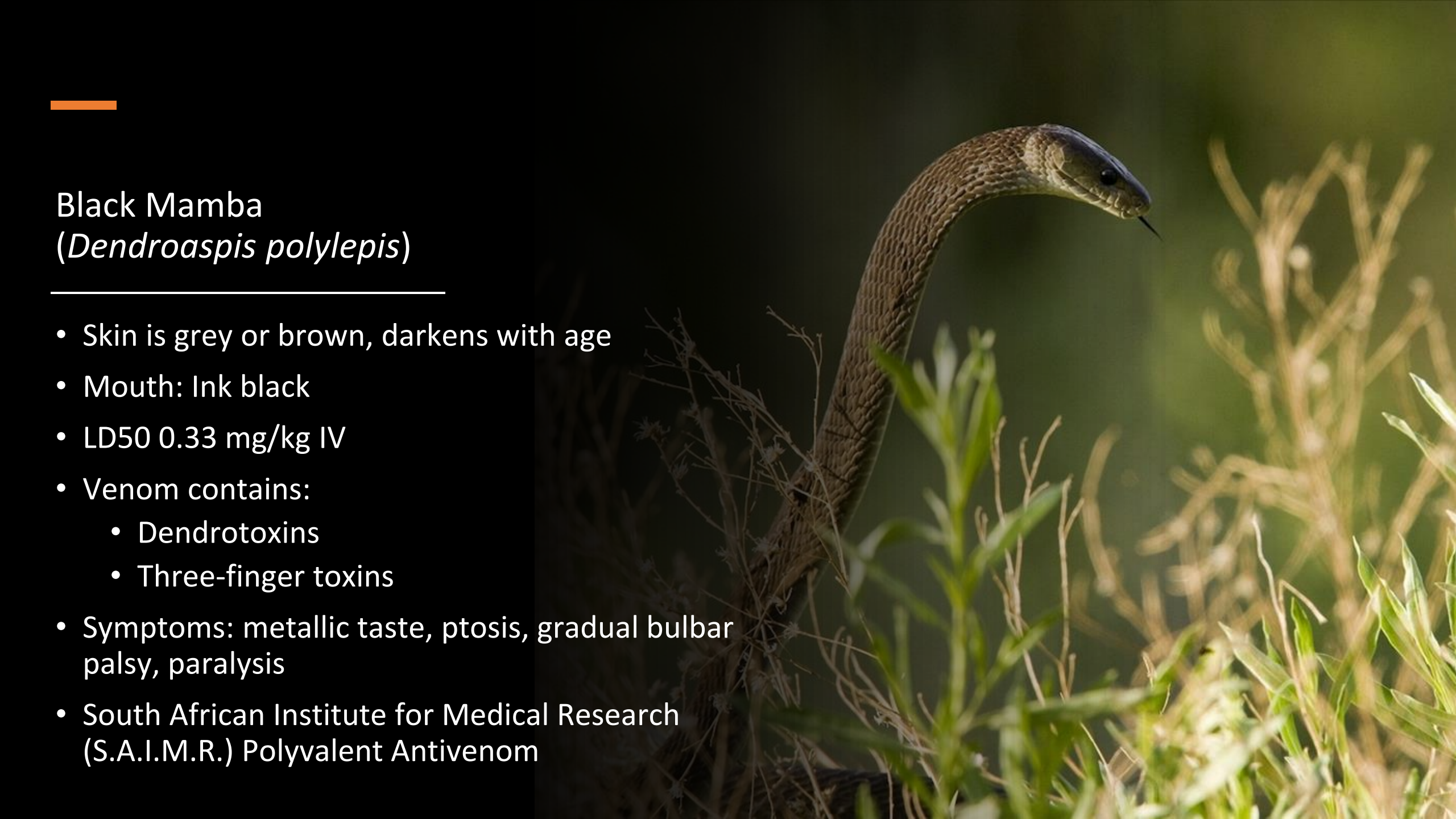
Elapidae (Ex: Mamba, Cobra, Kraits, Coral Snake)	Viperidae (Rattlesnake, Copperhead, Water moccasin)
Long cylinder bodies	Short, narrow neck
Head roughly same size as neck	Triangular head, wider than neck
Pupils: round	Pupils: vertical
Tail: round	Tail: tapering
Venom: typically neurotoxic, more likely systemic	Venom: digestive enzymes, proteases, local reaction



Black Mamba
(*Dendroaspis polylepis*)

Black Mamba (*Dendroaspis polylepis*)

- Skin is grey or brown, darkens with age
- Mouth: Ink black
- LD50 0.33 mg/kg IV
- Venom contains:
  - Dendrotoxins
  - Three-finger toxins
- Symptoms: metallic taste, ptosis, gradual bulbar palsy, paralysis
- South African Institute for Medical Research (S.A.I.M.R.) Polyvalent Antivenom



King Cobra
(Ophiophagus hannah)

King Cobra

- Longest venomous snake in the world (max of 19.2 ft.)
- 7 mL of venom can kill one elephant
- Similar composition to mamba venom but less lethal
- LD50 1.3 mg/kg
- Can spit toxin from a distance

Inland Taipan (*Oxyuranus microlepidotus*)

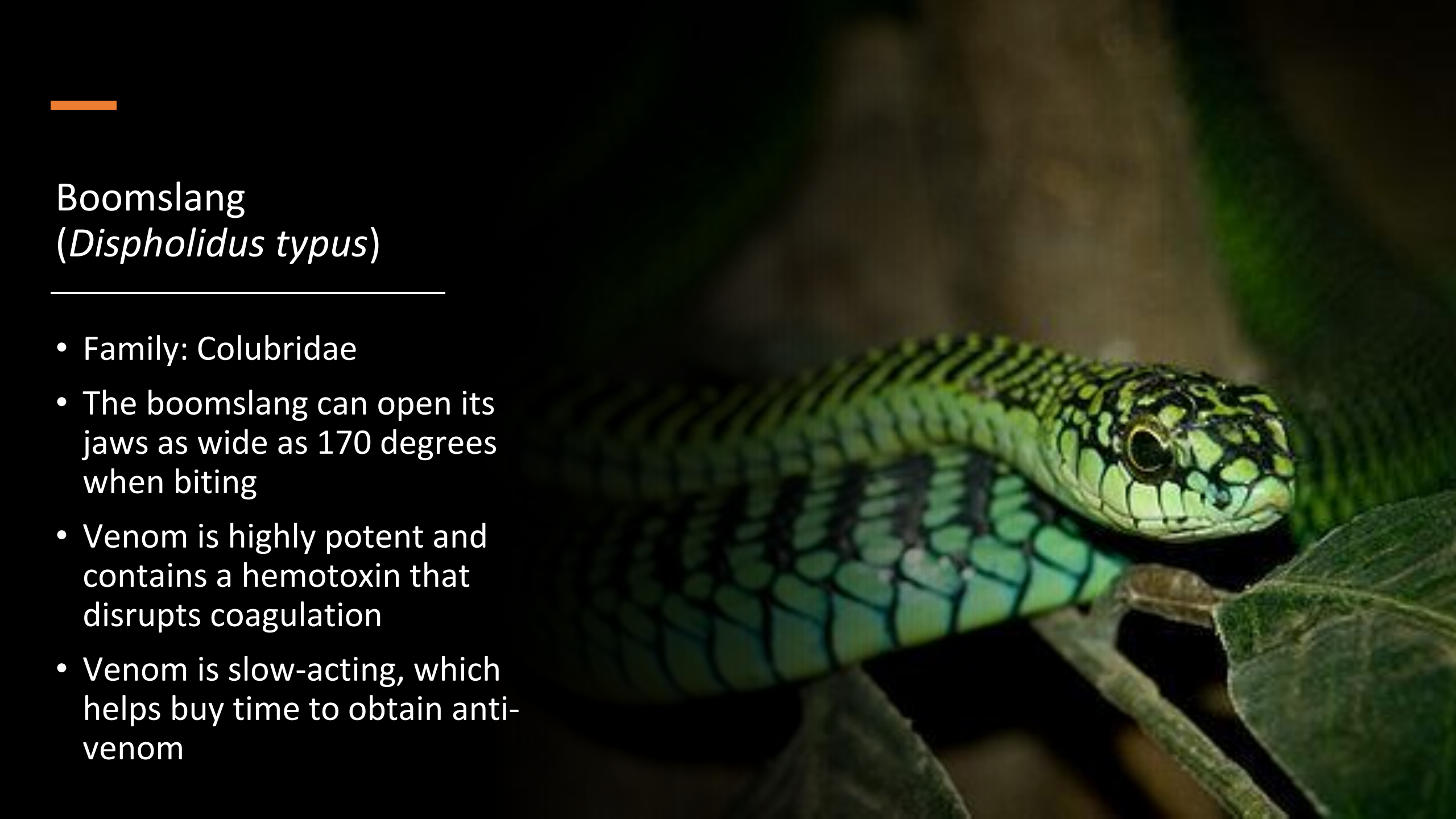
Inland Taipan (*Oxyuranus microlepidotus*)

- World's most venomous snake, untreated lethality >80%
- LD50 0.025 mg/kg
- Hemotoxins: Coagulopathic Kunitz peptides inhibit serine protease
- Paradoxin (PDX): Neurotoxic Three-finger proteins inhibit post-synaptic Ach nicotinic receptors
- Hyaluronidase: increases rate of venom absorption
- Taipan Antivenom and Polyvalent Snake Venom

Boomslang (*Dispholidus typus*)

Boomslang (*Dispholidus typus*)

- Family: Colubridae
- The boomslang can open its jaws as wide as 170 degrees when biting
- Venom is highly potent and contains a hemotoxin that disrupts coagulation
- Venom is slow-acting, which helps buy time to obtain anti-venom



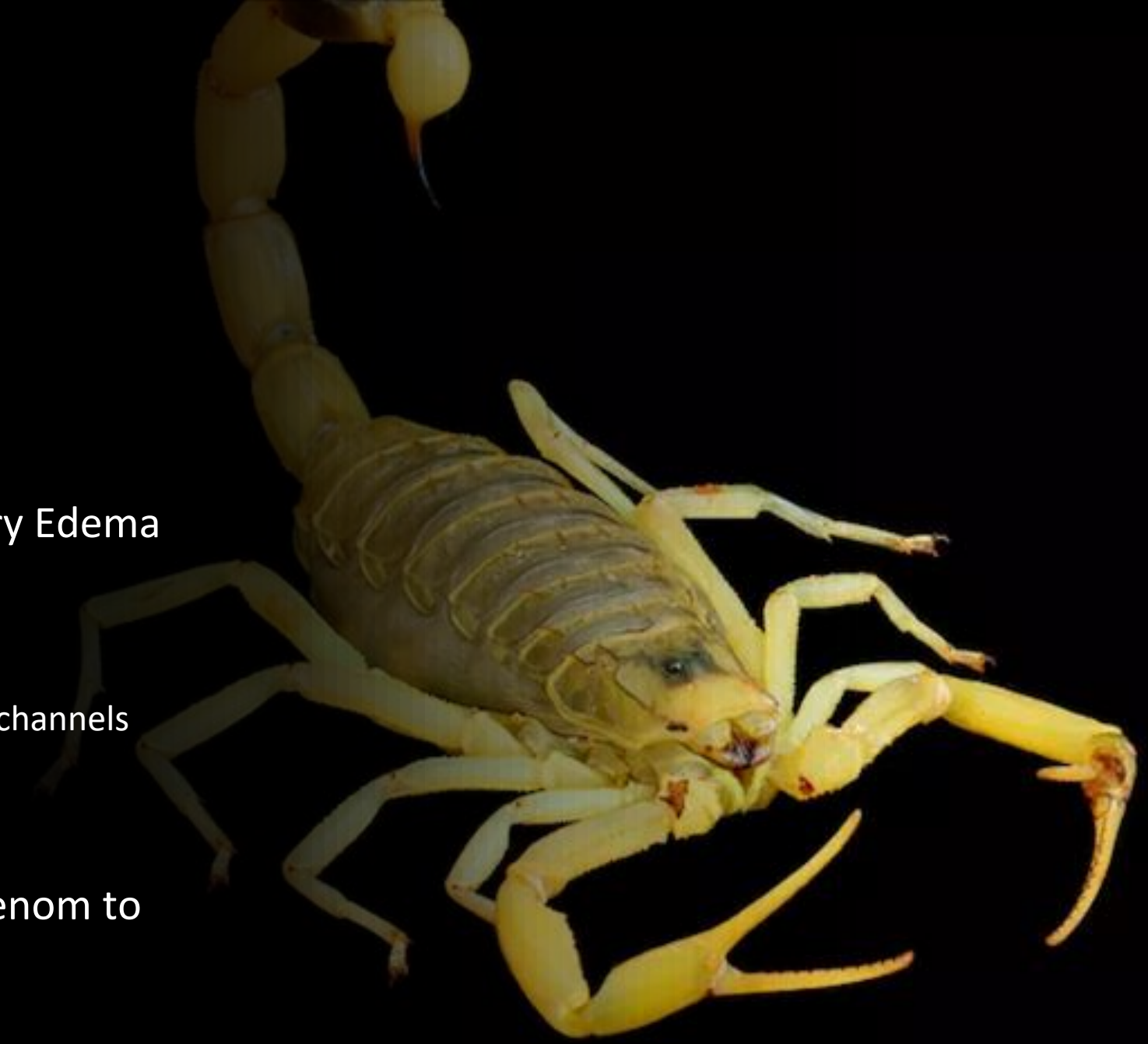
Deathstalker Scorpion (*Leiurus quinquestriatus*)

Deathstalker Scorpion (*Leiurus quinquestriatus*)

- LD50 of 0.25 mg/kg
- Can cause: Pancreatitis, Pulmonary Edema

Neurotoxin venom contains:

- Charybdotoxin:
  - blocks calcium-activated potassium channels
- Chlorotoxin:
  - used for human brain cancer
- Requires very high doses of antivenom to have any clinical impact



Indian red scorpion (*Hottentotta tamulus*)

Indian red scorpion (*Hottentotta tamulus*)

- Fatality rates of 8–40%; most victims are children
- Venom includes toxin tamapin: blocks SK2 channels
- Pulmonary edema, cardiopulmonary failure
- Scorpion antivenin (SAV) recommended but has little effect in clinical treatment
- **Prazosin** reduces the mortality rate to less than 4%
- Benzodiazepines and supportive care

Golden poison frog (*Phyllobates terribilis*)

Golden Poison Frogs
Phyllobates terribilis

- Color pattern is aposematic: a coloration to warn predators of its toxicity
- Four main color varieties:
  - Yellow
  - Mint Green
  - Orange
  - Orange Blackfoot
- Produce alkaloid batrachotoxin in skin glands
- Irreversibly opens sodium channels
- LD50 is 0.2 µg / kg

Underwater

Case Breakout 2

Melanie is on a family vacation in Northern Australia at the end of February for her birthday. While swimming, she feels a sharp pain on her leg. She quickly exits the water and seeks help. You are on the beach and she approaches you crying and in severe pain.

<u>Patient Profile:</u>

- Name: Melanie
- Age: 12 years old
- Weight: 40kg
- Occupation: Tourist
- Medical history: No significant medical history

She is complaining of intense burning pain at the site of the sting with numbness and tingling

Vitals: HR 120, RR 18

On the beach so no BP cuff available, no O2 sat available, no temp available

Physical Exam:

- Airway intact
- Bilateral breath sounds, symmetric, mildly labored
- 2+ radial pulses present, capillary refill 1 second
- GCS 15, in acute pain
- you notice a box jellyfish tentacle sticking to her skin

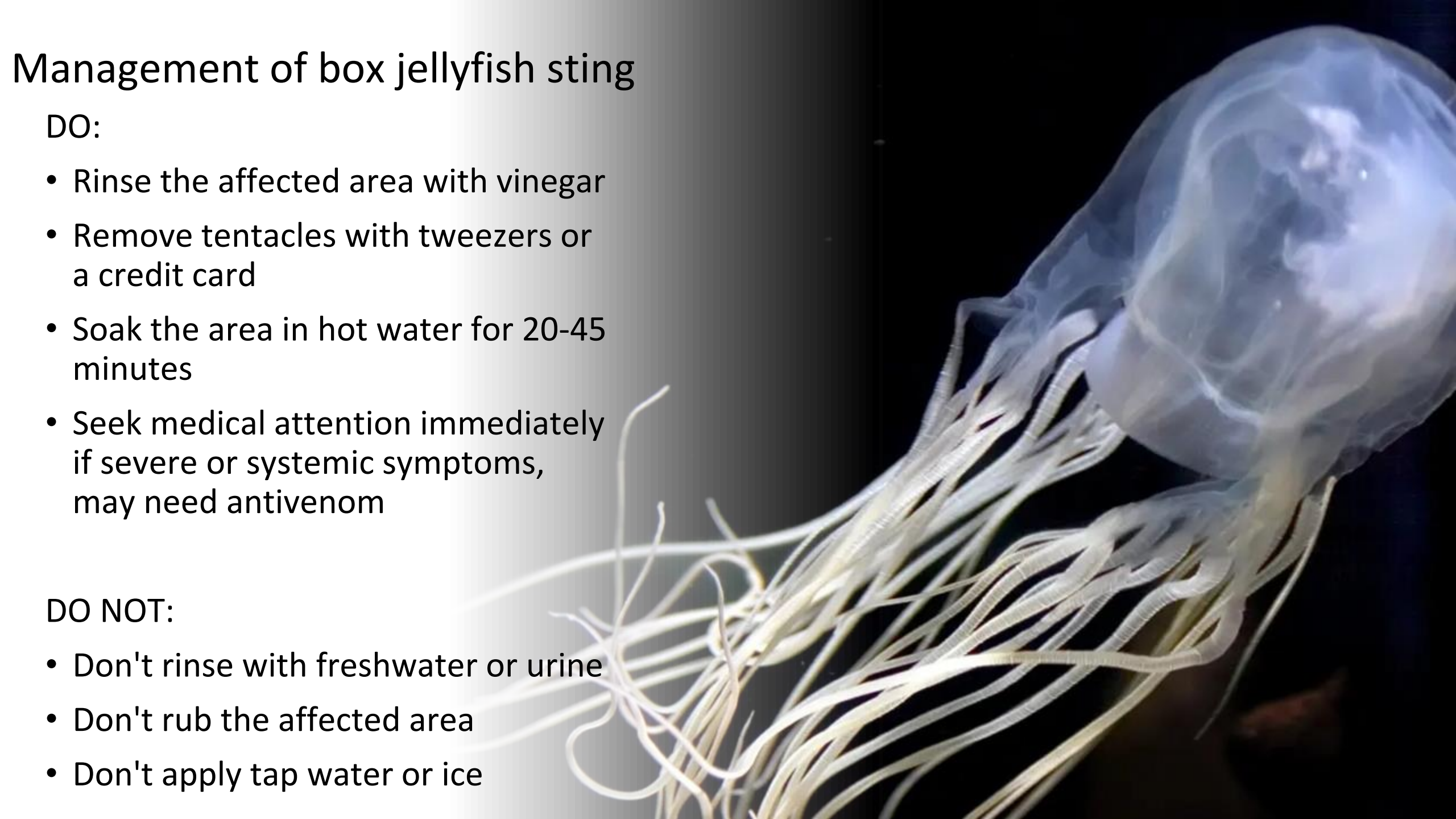
Management of box jellyfish sting

DO:

- Rinse the affected area with vinegar
- Remove tentacles with tweezers or a credit card
- Soak the area in hot water for 20-45 minutes
- Seek medical attention immediately if severe or systemic symptoms, may need antivenom

DO NOT:

- Don't rinse with freshwater or urine
- Don't rub the affected area
- Don't apply tap water or ice

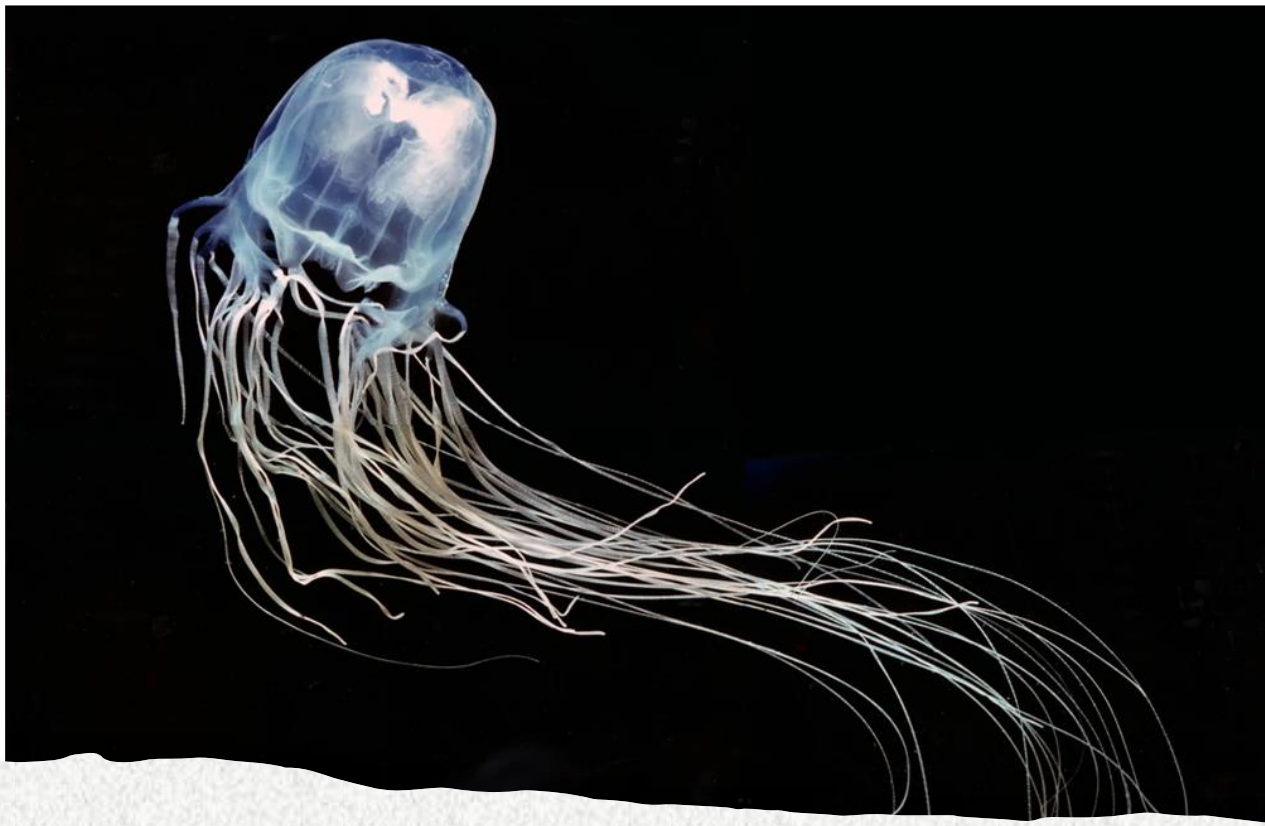


Clinical Presentation

She starts to develop:

- Nausea and vomiting with abdominal cramps
- Difficulty breathing
- Confusion and disorientation

- Systemic symptoms and respiratory distress are indications for *Chironex fleckeri* antivenom



Box Jellyfish
(*Chironex fleckeri*)

Box Jellyfish (*Chironex fleckeri*)

- AKA Sea Wasp
- 60 tentacles each about 15-20 feet long
- 8 feet of one tentacle is enough to kill an adult human
- Billions of nematocysts (micro-harpoons) inject prey
- LD50: 0.025 µg/kg: most lethal in the world

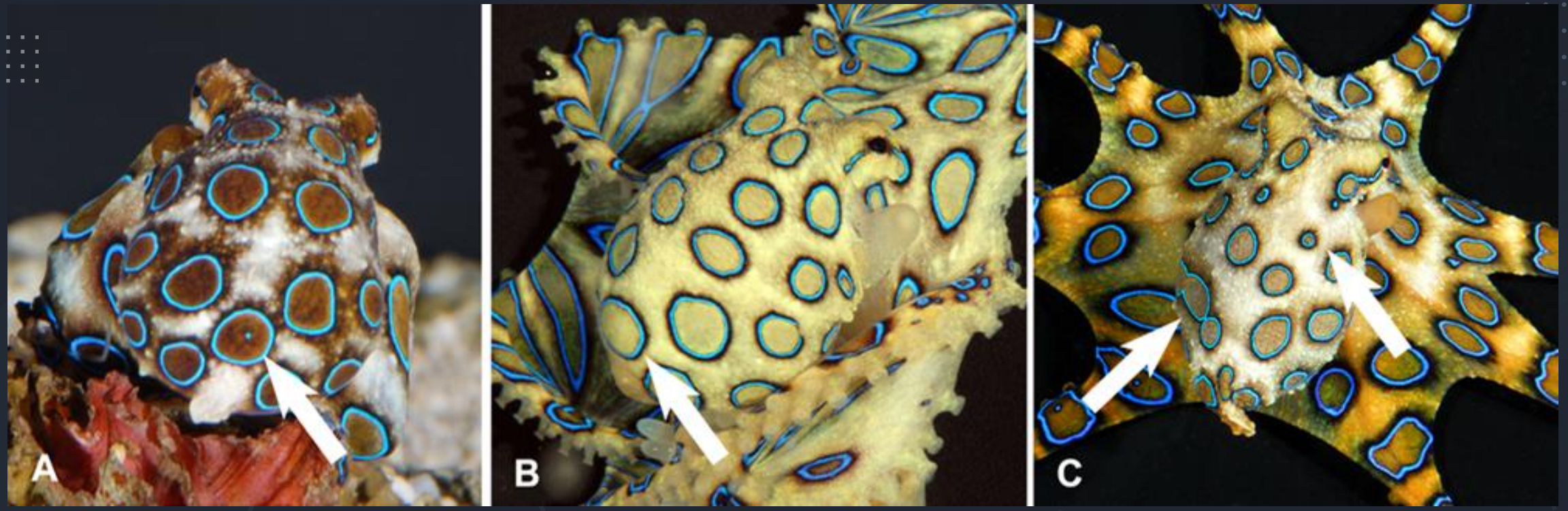
If Exposed:

- Use 5% acetic acid (vinegar) to inactive nematocyts
- Avoid tap water
- If nematocyst still in skin, apply flour or shaving cream
- Give antivenom for severe symptoms

Chironex fleckeri antivenom

- Box jellyfish antivenom is made from the plasma of sheep immunized with box jellyfish venom (Chironex fleckeri)
- Each vial of antivenom contains 20,000 units
- The product also contains phenol 2.2 mg, sodium chloride 8 mg, and water for injections to 1 mL in an aqueous solution
- Not all box jellyfish species have antivenom available
- Risk of anaphylaxis, observe after administration

Blue Ringed Octopus (*Hapalochlaena lunulate*)



Blue Ringed Octopus (*Hapalochlaena lunulate)*

- Yellow/brown skin with characteristic blue and black rings
- Changes colors when animal is threatened: 50-60 rings become iridescent blue
- Venom contains: tetrodotoxin, histamine, tryptamine, octopamine, taurine, acetylcholine and dopamine
- One bite can kill up to 26 people

Tetraodon fahaka

Hapaloclaena maculosa

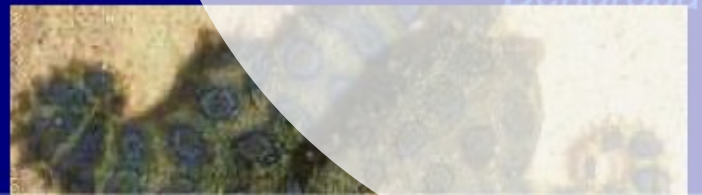
Babylonia japonica

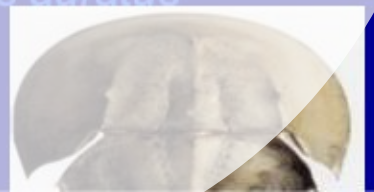
Scarus ghobban

Jania rubens

Dendrobates auratus

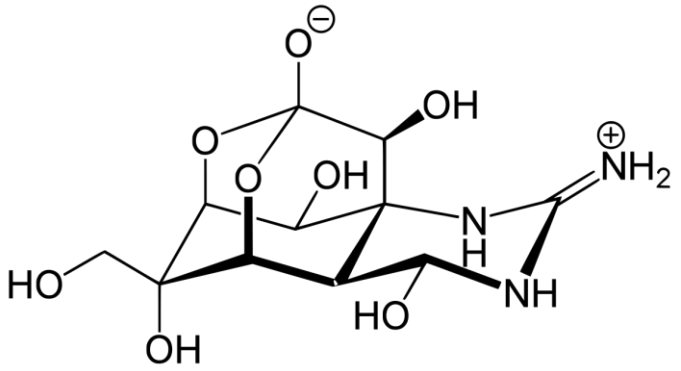
Tetrodotoxin

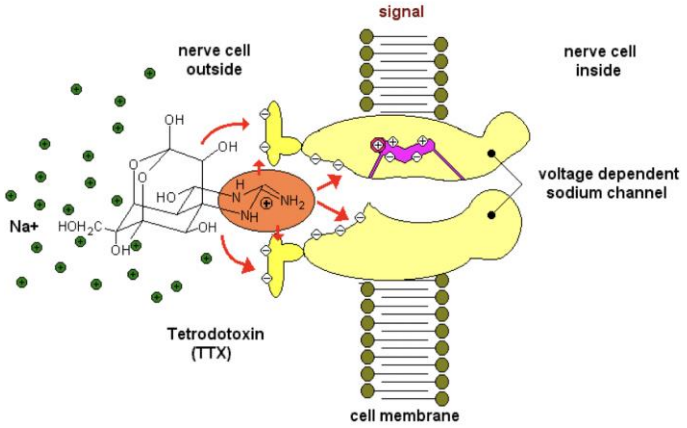


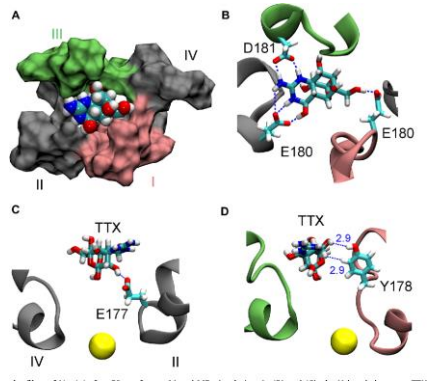


Tetrodotoxin

- Tetrodotoxin blocks voltage gated sodium channels
- Results in nausea, respiratory arrest, heart failure, paralysis, blindness
- Can lead to death within 30 minutes
- Death is usually from paralysis of the diaphragm
- The octopus's own sodium channels are adapted to be resistant to tetrodotoxin







Toxins (Basel). 2017 Mar; 9(3): 75. Published online 2017 Feb 24. doi: 10.3390/toxins9030075

PMCID: PMC5371830 | PMID: 28245573

Acute Oral Toxicity of Tetrodotoxin in Mice: Determination of Lethal Dose 50 (LD50) and No Observed Adverse Effect Level (NOAEL)

Paula Abal,[1] M. Carmen Louzao,[1,*] Alvaro Antelo,[2] Mercedes Alvarez,[2] Eva Cagide,[2] Natalia Vilariño,[1] Mercedes R. Vieytes,[3] and Luis M. Botana[1,*]

Table 1: LD50 of oral tetrodotoxin

- The tetrodotoxin oral median lethal dose (LD50) for mice is around 232 µg/kg
- For comparison: the oral LD50 of potassium cyanide for mice is 8.5 mg/kg
- For IV injection of tetrodotoxin the lethal dose is 8 µg/kg

Table 2: shows tetrodotoxin side effects relative to administered dose

Table 1

Mortality induced by gavage administration of tetrodotoxin (TTX) to mice and survival times correspon with each treatment.

Dose (µg/kg)	Mortality	Survival Times (min)
1000	3/3	7, 18, 37
500	4/5	58, 3, 2, 1
250	4/7	100, 7, 19, 54
125	0/9	>120
75	0/9	>120
25	0/9	>120

Table 2

Symptoms registered after tetrodotoxin (TTX) administration. Ratio between mice with the symptom versus the total mice treated.

Symptoms	TTX Dose (µg/kg)					
	1000	**500**	**250**	**125**	**75**	**25**
Apathy	3/3	5/5	7/7	9/9	0/9	0/9
Piloerection	0/3	0/5	1/7	2/9	0/9	0/9
Paralysis of extremities	3/3	2/5	2/7	0/9	0/9	0/9
Seizures	3/3	2/5	2/7	0/9	0/9	0/9
Circling	0/3	2/5	1/7	0/9	0/9	0/9
Squint eyes	0/3	1/5	0/7	0/9	0/9	0/9

Pufferfish

Family: Tetraodontidae

Pufferfish

- 193 species of puffers in the family Tetraodontidae
- Tetrodotoxin isolated in organs of liver, gonads and skin in some species
- Puffer soup: fugu chiri
- Raw puffer meat: sashimi fugu
- Initial light-headedness, numbness of the lips and tongue
- Intestinal decontamination with gastric lavage and activated charcoal

Lionfish (*Pterois*)
Stonefish (*Synanceia*)

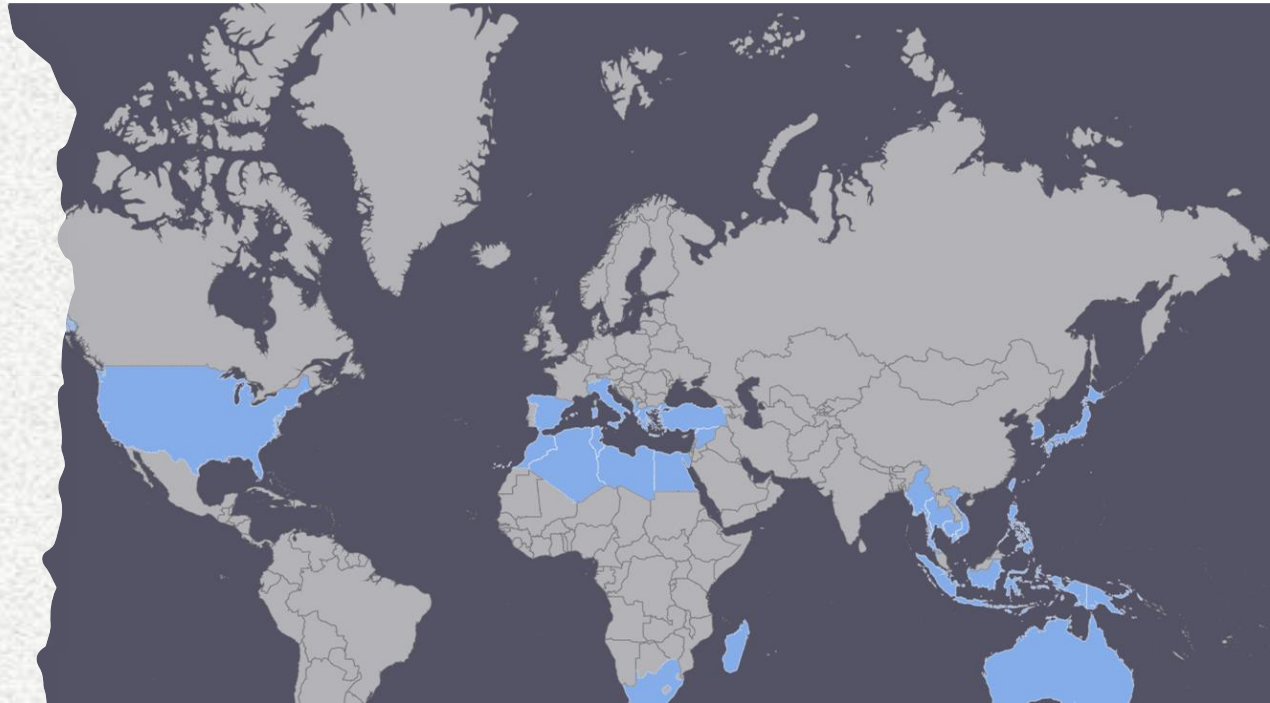
Lionfish

- Poisonous fin rays
- Suspected nitric oxide release
- Ionotropic and chronotropic effects in frog hearts
- Fatality in young children and elderly
- Fatality rare in healthy adults but pain can last days
- Anaphylaxis

Stonefish

- 13 dorsal spines with venom containing sacs at the base
- Most venomous fish (known), can be fatal
- Hot water denatures stonefish venom
- Synanceja trachynis Stonefish Antivenom (SFAV)
- Vinegar is said to lessen the pain

Cone Snails (*Conus)*



Cone Snails
Conus

- Uses a venomous harpoon called a toxoglossan radula
- Contains conotoxins
- Some cone snail venoms also contain a pain-reducing toxin
- Ziconotide: a pain reliever isolated from the venom of the magician cone snail
- Geography cone and tulip cone snails secrete insulin that can cause hypoglycemic shock
- Preclinical trials are using conotoxin for Alzheimer's disease, Parkinson's disease, depression, and epilepsy

Calculated LD50's (µg/kg)

Toxin Type	LD50 (ug/kg)
Box jellyfish (Chironex fleckeri)	0.025
Batrachotoxin (Poison Dart frog)	2
Taipoxin (Inland Taipan)	2
Tetrodotoxin (Puffer fish)	9
Saxitoxin (shellfish)	9
Scorpion toxin	17
Notexin (Tiger snake)	25
Cobra Neurotoxin	75
Sodium Cyanide	10,000

Summary

- Brazilian wandering spider causes priapism
- Recognize and distinguish between Elapids (neurotoxic, systemic toxin) vs. Vipers (typically locally toxic)
- Prazosin given for Indian Red Scorpion bite
- Tetrodotoxin: Blue Ringed Octopus and Pufferfish
- Stonefish venom is heat labile antivenom exists
- Vinegar and antivenom for Box jellyfish, avoid tap water
- Cone snails are pretty but have venomous harpoons
- **Don’t pick up any of the discussed animals in this talk**


THE END