Snake Envenomation in the Southeast US

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Incidence in the US

- Venous snake bites
  - Estimates of 150-300,000 in animals
- 99% are Crotalid
- Crotalids
  - Crotalis (rattlesnakes)
  - Sistrurus (pygmy rattlesnakes, massasaugas)
  - Agkistrodon (water moccasins, copperheads)
- < 1% are coral snakes

A Bit about Snakes...

- Vital role in controlling rodent population
- The venom apparatus was developed to obtain food
  - Use in defense is a last resort

A Bit about Snakes...

- Defensive bites inject less venom than offensive bites
  - Size of snake is often not positively correlated to amount of venom injected
  - 20-30% bites are thought to be dry bites

Snake Season

- April to October

  - Where?
    - Fallen brush, pine straw, wood piles
    - Woodlands
    - Adjacent to bodies of fresh water

Venomous Snake in SC, NC, GA, and FL

- Family Viperidae (Vipers)
  - Copperhead (Agkistrodon contortrix)
  - Cottonmouth/Water Moccasin (Agkistrodon piscivorus)
  - Eastern Diamondback rattlesnake (Crotalus adamanteus)
  - Canebrake/Timber rattlesnake (Crotalus horridus)
  - Pygmy rattlesnake (Sistrurus milliarius)
- Family Elapidae (Coral Snakes)
  - Coral snake (Micrurus fulvius)
Anatomy and the Snakebite

- Absorption of venom from bites to extremities is minimized by local swelling
- Bites to torso have more rapid absorption
- Lingual and vascular bites have rapid and severe envenomation
- Dogs
  - Most bites to head and legs
- Cats
  - Most bites to torso

Envenomation Syndrome

- Severe pain is often the 1st sign... but swelling is often the initial complaint on presentation
- Focal and spreading bruising and serosanguinous drainage
  - Progressive for up to 36 hours

Envenomation Syndrome

- Lethargy, hiding
- Ptyalism
- Vomiting
- Obtundation
- Generalized weakness
- Cervical ventroflexion
- Respiratory muscle weakness

Venom

- 90% water
- 10 different enzymes in individual snake venom
  - Over 50 different pit viper enzymes identified
- 3-12 proteins and non-enzymatic peptides
  - ‘killing fraction’ of venom
    - Up to 50 times more toxic than crude venom

Venom

- 3 broad classifications
  - Cytotoxic
  - Neurotoxic
  - Coagulopathic

Venom – Cytotoxic Effects

- Endothelial cell damage increases vascular permeability and venom spread
  - Phospholipases

- Necrosis helps venom spread to regions remote from the puncture
  - Proteolytics
  - Hyaluronidase
  - Collagenase
Venom - Neurotoxic Effects

- 9 subspecies of rattlesnakes can have venom containing Mojave toxin A
  - Timber rattlesnake (C. horridus)
- Varying ion channel inhibition results in respiratory muscle paralysis
  - Phospholipase A2 + acidic subunit

Rattlesnake – Neurotoxicity

- Fairly rare
  - 5.4% over a 5 year period (34 of 627 cases receiving Antivenom)
  - 61% of the patients had neurologic signs on presentation
    - Altered mentation > nonambulatory tetraparesis > extensor rigidity > CP deficits > ataxia > ambulatory tetraparesis
  - All progressed to neurologic signs within 24 hours
  - 11% (4/34) required mechanical ventilation
  - Mortality rate 17%

Venom - Coagulopathy

- Venom Induced Consumption Coagulation (VICC)
  - Consumption of fibrinogen and factors V and VIII
  - Fibrinogenases, Fibrinolytics
  - Protein C, Metalloproteases
  - Increased PT, aPTT
  - Treatment is antivenom, NOT fresh frozen plasma

Venom - Coagulopathy

- Thrombocytopenia
  - Platelet aggregation (venom)
  - Platelet sequestration (wound)
  - Phospholipases (direct effect on PLT membrane)
  - Antivenom is the treatment
  - Platelet levels normalize within 3-4 days

Rattlesnake – Coagulopathy

- Coagulation times not associated with survival
  - ~70% thrombocytopenic (mean 95 K)
  - ~68% echinocytosis
  - 60% prolonged PT
    - 50% > 25% prolonged
  - 53% prolonged PTT
    - 35% >25 % prolonged
- Hypokalemia is common

Venom – Cardiovascular Effects

- 3rd spacing, vascular leak and hemorrhage → hypovolemia, hypotension, tachycardia
  - Phospholipases
  - Systemic Inflammatory Response Syndrome
- Hypovolemia triggers catecholamine release
  - ↑HCT (spleen)
  - Hypokalemia
Venom – Cardiovascular Effects

- Decreased DO2
  - Echinocytes (global hypoxemia)
  - Tissue edema/microvascular leak (local hypoxemia)
    - Tachypnea, tachycardia, hyperlactatemia
- Cytotoxic venom → necrosis, SIRS
  - Proteolytics, Hyaluronidase, Collagenase, AA

Envenomation - Incidence of Infection

- Although multiple bacterial species are cultured from the oral cavity in Rattlesnakes and non venomous snakes, infections are uncommon
  - Antimicrobial effects of the venom
  - Toxin is sterile
  - Low inoculum from the rapid bite
  - Inflammatory response to the venom
  - Bacteria may be very host adapted (snake)
- 1 of 102 dogs with Rattlesnake envenomation developed infection (JVECC 2015)
- 0 of 263 humans

First Aid for Owners

- Keep the patient calm and still
- Immediate transport to veterinary facility
- Avoid tourniquets, ice, succioning the wound, alcohol etc.
- If transport is long or delayed can consider recommending administration of diphenhydramine (mild sedation)
- Picture of the snake or bring the deceased snake to the DVM for identification

Emergency Assessment

- Triage
  - TPR, respiratory effort
  - Baseline blood pressure
  - ECG
- Bloodwork
  - CBC, Chemistry, Electrolytes
  - PT/PTT
  - Blood smear for platelet count, echinocyte %

Snake Bite Severity Score

- 0-3 scale
- Baseline (0 hr), 6 hr, 12 hr, 24 hr
- 6 body systems
  - Pulmonary
  - Cardiovascular
  - Wound
  - Gastrointestinal
  - Hematologic
  - CNS

ER Treatment of Envenomation

- Focus on hemodynamic stabilization
  - Crystalloids
    - 10-20 ml/kg boluses with frequent reassessment
      - Shock dose 80 ml/kg (dog), 60 ml/kg (cat)
  - Colloids (Vetstarch, Hetastarch)
    - Limited use if thrombocytopenia (PLT < 75 K)
    - Contribute to edema with vascular leak?
    - Boluses: 5 ml/kg (Hetastarch), 10 ml/kg (Vetstarch)
      - Max 24 hr dose: 20 ml/kg/d (Hetastarch), 40 ml/kg/d (Vetstarch)
ER Treatment of Envenomation

- Diphenhydramine can be used for mild sedation but no other envenomation indication
  - Pretreatment for antivenom administration
- Antibiotics on a case by case basis
- Steroids are contraindicated

ER Treatment of Envenomation

- Snake bites are PAINFUL
  - Antivenom is one of the best treatments for pain
  - Opioids
    - Fentanyl CRI
    - Hydromorphone (dogs)
    - Oxymorphone (cats)
    - Avoid morphine – histamine release mimics anaphylaxis
  - Avoid NSAIDS

Antivenom

- 2 broad categories
  - Whole IgG
  - Antibody fragments
- Equine origin
- Ovine origin

Crotalide Polyvalent Equine Origin Serum (ACP)

- Previously the only veterinary licensed antivenom in the US
  - Equine origin
  - Eastern and Western Diamondback, Fer-de-lance and South American Rattlesnake
- Whole IgG antibody + other proteins
  - Only 20% of the IgG is active antivenom
- Up to 50% incidence of acute and delayed hypersensitivity
  - Long circulating half life
  - Lyophilized

CroFab

- Crotalidae Polyvalent Fab
  - Ovine
  - Western and Eastern Diamondback and Mojave Rattlesnakes, Cottonmouth
- Short half live
  - Recurrent signs of envenomation
  - Frequent reassessment after discharge is needed
- Lyophilized

Venomvet

- Licensed in the US for use in dogs
  - Equine (MT Venom, LLC, Argentina)
    - Central American Rattlesnake, Fer-de-lance, Bushmaster viper.
      - Cross protection
        - Except Mojave, Southern Pacific Rattlesnake
- Half life 2-4 days preventing recurrent envenomation signs
  - Liquid
Rattler Antivenin

- PLASMA based Crotalidae polyvalent Antivenom
  - Equine
    - Western Diamondback, Eastern Diamondback, Prairie Rattlesnake, Mojave Rattlesnake

- High potential for hypersensitivity
- No published peer reviewed studies to evaluate safety
  - Package insert: safety study “In house” in which all 6 dogs had type I hypersensitivity reaction
  - Website: sold 1200 doses and adverse events reported < 1%
  - Frozen plasma

Coral Snake Envenomation

- Micrurus fulvis fulvis
  - FL to Southern NC and Eastern GA
  - Less effective venom delivery due to fixed position of the hollow fangs
    - Chewing action
  - Size of snake is correlated to amount of venom delivery
    - Large adults can deliver >4-5X the lethal human dose of venom
  - Have the most toxic venom per mg dry weight of any snake

Coral Snake- Venom

- Post synaptic alpha-neurotoxins that block the nicotinic Ach R and result in Curare-like syndrome
  - Vasomotor instability, LMN paralysis and CNS depression

- Phospholipases
  - Myotoxic and cardiotoxic resulting in decreased skeletal and cardiac mm contractility, muscle fiber swelling
  - In some cases, hemolysin effects noted experimentally (coagulopathy not appreciated clinically)

Coral Snake- Clinical Signs

- Dogs
  - Generalized muscle weakness
  - Vomiting
  - Pytalism
  - Hyporeflexia, quadraplegia
  - Respiratory depression
  - Severe hemolysis has been uncommonly reported

- Cats
  - Rapid ascending flaccid paralysis
  - Decreased nociception
  - Hyperthermia
  - Decreased spinal and cutaneous trunci mm reflexes
  - Respiratory mm paralysis noted within 3 hrs (experimentally)

Coral Snake - Antivenom

- Recommended for all humans ASAP with confirmed bite
- Monitoring for 12-36 hrs as signs may not be noted for 12+ hrs

- Coralymin
  - Produced in Mexico
  - Equine
    - Black banded coral snake

When to Consider Coral Snake Envenomation

- Acute onset flaccid paralysis and respiratory muscle depression
  - FL, SC, southeastern GA
  - Increased ALT and CK
  - Pigmenturia, hemolysis (Dogs)
  - Vomiting/pytalism
  - Onset of CS ~1.5 hrs but up to 12 hrs noted in humans/dogs
  - Recommend monitoring for 48 hrs ➔ delayed reoccurrence of CS even after coral snake antivenom

- Differential Diagnoses
  - Tick paralysis, botulism, polyradiculoneuritis, metabolic/toxic neuropathies, adverse drug reactions/overdose
Coral Snake Treatment and Prognosis

- Antivenom administration
- Mechanical Ventilation
  - Impossible to know on presentation which patients will progress to respiratory muscle paralysis
- Monitoring and supportive care for 36 hours

- Survival:
  - 71% in U FL study
  - Improvement over 4-7 days

Questions?

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