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**Overview of Today's Talk**

- General Approach to Venom
- Rattlesnakes
- Insects and Marine Creatures
- Cobra Wrestling Demo / Q and A

**The Venom Menagerie**

*Terrestrial Creatures*
- Snakes
- Gila Lizards
- Spiders and Scorpions
- Insects

*Marine Creatures*
- Jellyfish and Cone Snails
- Scorpionfish
- Stingrays

**Background**

- Venom Injuries occur worldwide

- A Neglected Tropical Disease:
  - Approximately 2.5 million cases/year of snakebites
  - Approx 35 K – 50 K deaths/year (up to 95K)
  - In AMERICA: 8-15 K cases of snakebite with 5 deaths
  - BEESTINGS KILL ABUT 25/YEAR IN THE US

- Venoms are still poorly understood in many species
- Venom-specific therapies lacking for most species
- We still have A LOT to learn about venomous creatures

- Let's focus clinically by discussing venom effects

**Venom: “Nature’s Polypharmacy”**

Venom = digestive and defensive MIXTURE
- Small molecules and monoamines
- Digestive Enzymes and Proteases
- Vasoactive/Neuroactive/ Allergenic peptides
- Venom components are HIGHLY variable
• Different responses in different patients
• Envenoming apparatus → Mechanical Injury
  - Fangs, hairs, stingers and barbs: “Nature’s jailhouse shivs”
• Mechanical Injuries
  • Fangs: Specialized venom-channels
    - Curved vs Straight → can be hard to track venom injection
    - Dead snakes may still injure and ENVENOMATE
    - Rattlesnake fangs do not penetrate into deep muscles
  • Teeth
    - Most spiders cannot penetrate human skin
    - Gila Monsters are notoriously destructive
  • Impalers: Sea Urchins, Stingrays
  • Jellyfish nematocysts
  • Stingers: Bees, Wasps, Ants
  • Telsons: Venom bulbs on Scorpions
  • Hairs/Setae: Caterpillars and Tarantulae
    - Uveitis and dermal irritation
    - Oral injury/irritation if swallowed

7 Neurotoxins
  Major Effects:
  • Rapid Paralysis
    - Alpha and Beta Bungarotoxins
    - Cobras, Kraits, Aust. Snakes
  • Fasciculations (myokymia)
  • Muscle contractions
    - Black widow spider venom
  • Rhabdo (multifactorial)
  Minor Effects:
  • Tingling/Paresthesias
  • Vomiting/Metallic taste (snakes)
  • Facial edema (spiders)
  • Oculogyric Crisis/Ataxia (scorpions)

8 Venom: Tissue Toxins
  • Enzymes
    - Metalloproteinases
    - Hyaluronidases
    - Phospholipase A2
  • Locally destructive: blebs, necrosis
  • Tourniquets worsen ischemia and injury
  • Spitting cobras: corneal injuries
• Found in:
  - Viper Snakes
  - Some elapids (mamba, cobras)
  - Gila Monsters
  - Massive beestings
  - Scorpionfish

Hematotoxins

• Laboratory Effects
  - Fibrinogen depletion
  - Low Platelets
  - INR increases

• Clinical Effects
  - Spontaneous hemorrhage
  - DIC-like syndrome
  - Rarely thrombosis

• Pit Vipers & Viperids
  - Asian Vipers: Pituitary Hemorrhage and Apoplexy
  - South American Vipers: Hematuria, nailbed/ hair root bleeding, ICH, ARDS
  - Lonomia species caterpillars (Brazil)

Complications of Snakebites

Generally manifest over 24 hrs

• Hemorrhage
• Consumptive Coagulopathy
• Renal Failure
• Respiratory Paralysis
• Infections/Tetanus
• ARDS/ MI/ Stroke
• Allergic Reactions

Venomous Medicines

• Bothrops jararaca (South Am): Hypotension
  - Bradykinin Potentiating Factor (BPF)
    - research led scientists to discover ACE-inhibitors
• Gila Monster Saliva: glucagon-like peptides
  - Gila-derived antidiabetic medication (exenatide) recently FDA-approved for DM type 2
• Cone Snails: Potent non-opioid analgesic
  - Ziconatide, (Prialt) N- CCB

Snakes: The Global Challenge

• Viper snakes:
  - Rattlesnakes/ Copperheads
  - Bushmasters, Bothrops (South America)
- Ecchis, Bitis, Cerastes (Africa, Asia, Middle East),
- Habu, Mang Mountain, and Russell’s Vipers (Asian vipers)
- Taipans and Puff Adders

- Neurotoxic snakes:
  - Coral Snakes in the USA
  - Naja species: cobra, king cobra, and spitting cobras
  - Kraits
  - Mamba
  - Brown/tiger snakes (Australia)
  - Sea Snakes and Kraits

- Coral snakes (elapids) are neurotoxic, mainly in Southern and Southeastern USA

North American Snakes
- Pit Vipers of North America
  - Pits are sensitive, infrared heat sensors
  - Rattlesnakes, cottonmouths/copperheads
  - Very complex venoms and fang apparatus

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First Aid Measures
- DOs:
  - Determine the genus of animal
  - Reassure the patient, remove rings, etc.
  - Not necessary to bring in the animal
  - In USA, not necessary to identify the species
  - Pressure Wrap bitten extremity if long txport

- DO NOTs:
  - Shock, freeze, heat, suck, or cut the wound!
  - Tourniquets are harmful with tissue-toxic venom (rattlesnakes, vipers, adders)

- DONUTs:
  - Mmmm, donuts.

Snakebite Physical Exam
- Neurotoxic Snakes:
  - Assess for peripheral and respiratory weakness
  - Cobras and mambas CAN cause tissue damage; mambas can cause MI!
  - Ptosis can be initial symptom

- Viperid Snakes
  - 5-25% Rattlesnake bites are “dry” d/c in 4 hrs
- Local tissue necrosis causes most morbidity
- Fasciculations>> paralysis in rattlesnakes
- Hemorrhagic complications (South AM, Asia)
- Superinfection (South Am, Asia/Africa)

19 **Snakebite Treatment Initial Steps**

- Pain meds and IVFs
- MEASURE and MARK SWELLING of limbs
- Lab abnormalities indicate venom effects
  - Platelets, CBC, fibrinogen, coag panel
  - Renal function, lytes, CK
  - Can occur prior to significant swelling
  - Can help track inpatient progress and treatment responses
- Fasciotomy: JUST SAY NO!! Give Antivenom
  - VERY RARE to get a compartment syndrome in RSB
  - Number of reported cases of ischemic contractures= 0!
  - Local debridement of digits may be done in 3-5 days

20 **Antivenoms**

- Made by “milking” snake venom(s)
- Inoculate into horse/sheep--> Antivenom
- Antivenom is purified, sometimes fragmented
- FAB= fragmented antibody AV (less allergy)

21 **CroFab (Crotaline polyvalent immune ovine fab)**

- Sheep-derived F-ab fragments
  
  - Approved for moderate crotalid envenomations
  - 4-6 vials initial dose then 2 vials q 6 hrs x3
  - Less antigenic than whole IgG AV
    - 17% allergic reactions, mostly mild
  - Can use machines to gently mix solution
  - Rewash vials with extra saline to get all the foamy residues and improve product yield
  - No upper limit despite package insert (“18 vials”)

22 **Case: Fussy, Target lesion, Belly Pain**

- 2 yo child with irritability and abdominal tenderness, was playing outdoors
- VS bp 140/85, hr 160’s, temp 100 f
- Macular eruption on the face, periorbital edema, and dime-sized red lesion without central
pallor on the right buttock
• No oral erythema, no tremors, no rigidity

27 What was the toxin?
28
29
• 30,000 spider species worldwide…and all are venomous!!!
• Good news: envenomation apparatus is usually insufficient to penetrate human skin
• Some venoms are specific to insect receptors/ tissues.
• So the vast majority of spiders are not harmful from a venom standpoint.
• Widows, Aus funnelwebs, recluses,

30
• Black widows are endemic to California
• Venom (alpha-latrotoxin) induces calcium pores in nerve endings, releases NTs
• Acetylcholine, NE, epi, dopamine released
• Sympathetic signs predominate

31 Black Widow Spider Envenomation
Effects of Excess Ach and NE release:
• HTN, tachycardia, cramps
• diaphoresis (can localized to bite site)
• SEVERE PAIN: “acute” abdomen, back, legs
• Target lesion at the bite site-red/pale/red.
• Nausea, vomiting, pulm edema, weakness.
• Facial edema, conjunctivitis, trismus (facies latrodectesma).
• Rare– priapism, MI can result.

32 Black Widow Bite Therapy
Great analgesia + Muscle relaxation
• Morphine and ativan→may require high doses for relief.
• 70-90% pts will require only these meds.
• Avoid calcium... no benefit, potential worsening of symptoms
• IgG Antivenom: only for severe symptoms, young and older pts

33 Scorpions
• Centruroides genus in US, many others globally
• 12000 stings in US, mainly Arizona
• Venom causes increased sodium ion-channel activity in the nerves
  – Local Pain, hypersalivation, tachycardia, HTN Crisis
  – NEUROMOTOR Toxicity is Unique
    • Ocular gyric crisis, ataxia
    • Dysphonia and dysarthria
    • Choreiform and ballismus activity
• Treatment: Symptomatic
  – Benzodiazepines, analgesics
  – Antivenoms used rarely in Mexico and AZ

34 Hymenoptera
• Bees, wasps, ants, yellowjackets
• Most allergenic of all known venoms
• Thousands of deaths/year from anaphylaxis
• Localized hives, sterile pustules
• Secondary infection
• Massive envenomations (20 stings/kg) from bees can cause critical illnesses (rhabdo)

Gila Monster/Mexican Beaded Lizard
• Heloderma horridum and H. suspectum
• Jaws can grip very tightly
• Venom Effects
  – Severe hypotension
  – Hypoglycemia??
  – Arrhythmias may manifest
  – Severe tissue swelling and loss
• No antivenoms available
• Treat as complex animal bite and involve plastic surgeon for delayed repairs

CATERPILLARS
• Setae (hairs) allow venom into SC tissues
• Pain with Megalopyge (puss caterpillar)
• Others usually produce pruritus
• Grids/lines of urticaria/hemorrhage;
• Dermal edema and lymphangitis

Opthalmia Nodosa
• Tarantula/caterpillar hairs
• Inflammatory eye reaction
• Mechanical/chemical injury to the eye tissues
• Effects may be seen for months, and recur if setae are left in ocular tissue
• Steroids and (Surgical) removal of foreign body may be indicated

Venomous Marine Life
• Fish (scorpion, puffer)
• Coelenterates
• Corals/Urchins
• Rays

Wilderness First Aid
• Preparation/Prevention
  – Clothing, boots and walking sticks
• Treatment and Stabilization
  – Wrap/Litter Transport (treat like a fracture)
  – Allergy/Pain/Itching treatment (insects)
  – Hot water/foreign body tx (marine venoms)
• Evacuation
  – Transport all venomous snakebites
  – Evac. sickest spider/scorpion/marine attacks

Summary
• Venoms are complex molecular mixtures
• Simple clinical observations can identify most envenoming syndromes and severity
• Most injuries are not lethal
• Antivenom: most useful for snakes
• Anaphylaxis risk from AV is real– know how to TX!
• Know your “local critters”

Venom Resources
• UCSD SnakeBite Protocols → updates coming soon
  - Txs for snakes from all over the world
  - See me if you would like to help update!
  - http://drdavidson.ucsd.edu/Portals/0/snake/proinde.htm

• AZA Antivenom Index (www.aza.org)
  - Needs a poison center password for access

• www.Toxinology.org
  - (Australian, some free info, good first aid and basic antivenom info)
• Miami Fire-Rescue (Venom-1) Webpage