Case: A new antidote for an old problem

• A 30 year old man is envenomated by a rattlesnake.
• He has no history or asthma and takes no meds
• He has no allergies
RULE ONE:
Pleasing don’t kiss snakes
Penetrating Ocular Injury Caused by Venomous Snakebite
Chien-Chung Chen et al
AJOM

RULE TWO:
PLEASE DON’T HANDLE DEAD SNAKES
CroFab™ Dose

Patient with Indication for CroFab(TM) Administration

Establish Initial Control
By Administering 4-6 Vials of CroFab(TM)
Over 1 Hour

Initial Control Achieved?

No
Administer Additional 4 - 6 Vials of CroFab (TM)
Families of Poisonous Snakes

VIPERIDAE  ELAPIDAE  COLUBRIDAE  HYDROPHIDAE  ATRACTASPIDIDAE

- Rear lateral – direct-ed front fangs
- Fixed, rear fangs
- Fixed, front fangs
- Mobile, front fangs

US: Thousands of snake bites occur annually
Hundreds in Arizona
< 10 deaths per year

5 million snake bites
125,000 deaths
Families of Venomous Snakes

- Viperidae
- Elapidae (coral snakes)
- Hydrophiidae
- Atractaspididae
- Colubridae

Crotalinae subfamilies

Crotalinae

- New world or 'pit' vipers
- Front, mobile fangs
- Triangular shaped head
- Heat sensing pits
- >95% venomous bites in US

US Pit Vipers

- Rattlesnake
- Copperhead
- Cottonmouth
Arizona Rattlesnakes

Western diamondback
(C atrox)

Mojave
(C scutulatus)

Tiger Rattlesnake
(C tigris)

Massasauga
(Sistrurus catenatus)

Speckled Rattlesnake
(C mitchelli)

Northern Blacktail Rattlesnake
(C molossus)

Ridgenose rattlesnake
(C willardi)

Twin-spotted rattlesnake
(C pricei)

Rock rattlesnake
(C lepidus)

Sidewinder
(C cerastes)
Who are the victims?

Unlucky → Leg bites

unintelligent → Hand bites

About 60% of all bites illegitimate

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illegitimate Bites</td>
<td>97.9%</td>
<td>2.1%</td>
<td>56.0%</td>
</tr>
<tr>
<td>Legitimate Bites</td>
<td>72%</td>
<td>28%</td>
<td>16%</td>
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</tbody>
</table>
Location of Rattlesnake Bites

- Lower extremities: 39.3%
- Upper extremities: 60.2%
- Other: 0.4%

VIPERIDAE

**Crotalinae**
- Pit vipers
  - *Crotalus*
  - *Sistrurus*

**Viperinae**
- Old world vipers
  - *Agkistrodon*

**VIPERIDAE**

- Cottonmouths
- Copperheads

“Mighty Fighting Sun of Love and Ecstasy”
Legitimacy of Snakebite

- **Legitimate Bite**
  - did not recognize encounter with snake before being bitten
  - recognized encounter and immediately attempted to move away, but was bitten anyway

- **Illegitimate Bite**
  - recognized encounter with snake, but did not try to immediately move away
  - pet snakes, moving snakes, killing snakes, kissing snakes, playing with snakes, feeding snakes

Demographics and Characteristics

**236 patients**

**Population**
- male 81%
- female 19%
- children 22%

**Location**
- upper extremity 60.2%
- lower extremity 39.4%
- other 0.4%

Edema After Snakebite

- Swelling looks very scary
- Long, linear incisions on envenomated extremity would decrease tissue pressure and might "restore" blood flow
- Tissue necrosis would then be prevented
Rattlesnake Bite

- no swelling
- mild swelling
- severe swelling
- no insurance
- excellent insurance

long linear incisions

Compartment Syndrome

- Other management options
  - Antivenom
  - Antivenom and mannitol

Venom

- Enzymes
  - Proteolytic
  - Thrombin-like
  - Hyaluronidase
  - Phospholipase $A_2$
  - Many others...

- Non-enzymatic
  - Necrosis
  - Hematologic
  - Tissue
d  - Disrupts cell membranes
  - Amp

Tissue Hypertension

- Tissue hypertension quite exceptional despite edema
- Fasciotomies and SQ decompression do not prevent myonecrosis in animals receiving IM or SQ venom injections
- Noninvasive vascular studies demonstrate increased blood flow in envenomated extremities in most all patients
Local Tissue Effects

- Hemorrhagic bulla (blebs)
- Local necrosis
  - Tissue loss
  - Amputation
- VMPs and other digestive enzymes

Blebs
Blebs

Myotoxicity

• Digestive enzymes and metalloproteinases
• More specific myotoxins
  – myotoxin a and similar proteins
    • prairie rattlesnake (C. viridis viridis)
    • midget faded rattlesnake (C. viridis concolor)
    • common in other Crotalus and Sistrurus species
Myotoxicity

- Venom injection directly into muscle produces local myonecrosis
- Digestive enzymes, metalloproteinases, myotoxins
- Systemic absorption
- Subcutaneous systemic rhabdomyolysis

Coagulopathy

- About 60% of victims develop coagulopathy
- Hypofibrinogenemia with prolonged clotting times by far the most common

Coagulopathy

Normal Coagulation

- Clotting cascade: prothrombin → thrombin → fibrinogen → fibrin mesh
- Fibrinopeptide A & B
- Fibrin mesh
- Inhibited by heparin
- Active XIII
- Inactive XIII
- Cross linking
Coagulopathy
Crotalinae Thrombin-like Enzymes

- Thrombin-like enzymes
- Only split FP-A or FP-B from fibrinogen
- Fibrinogen
- Poorly-constructed fibrin chain
- Fibrinopeptide A OR fibrinopeptide B

Coagulopathy
Crotalinae Thrombin-like Enzymes

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- Doesn't activate factor XIII
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Fibrin mesh not inhibited by heparin
Hypofibrinogenemia

- Two main mechanisms
  1. Thrombin-like enzymes
  2. Fibrinolysis/Fibrinogenolysis

  - degrade fibrinogen
  - degrade fibrin

Fibrinolysis
Fibrinogenolysis

- enzymatic degradation of fibrinogen and fibrin

Benign Defibrination

- hypofibrinogenemia and prolonged clotting times
- no abnormal intravascular coagulation
- significant bleeding unusual in absence of thrombocytopenia or trauma
- occasional blood loss into envenomated extremity requires transfusion
Venom-Induced Thrombocytopenia

• About 30% of victims experience thrombocytopenia

• Nadir in untreated patients commonly between 72 and 96 hours
Anaphylaxis

- Rare
- IgE mediated
- Pre-sensitized to crotalids
  - Previous bites
  - Dermal exposure
  - Ingestion of rattlesnake meat?
Case

- 25 yo man presents 25 min following RSB to hand
- SBP = 68/28 mmHg, intoxicated
- 20 min later develops tongue, facial, and neck edema with airway compromise

Case

- IVF, epinephrine (SBP 90 x 2 hr)
- Difficult intubation (sat>90%)

- Minimal swelling
- Mild coagulopathy
- Treated with AV

- Rhabdomyolysis (CPK = 120,000)
- Renal failure
- Hemodialysis

- Renal failure
- Hemodialysis
Outcome

- Complicated course
  - Recurrent large bowel enterocutaneous fistulas
  - Sepsis
  - Malnutrition
  - Died one year later in rehab facility

- History of capturing and cooking RS

Respiratory Failure

- Patient presents following RSB with muscle weakness and diplopia.

- Rapidly progresses to hypoventilation and respiratory failure.

- Despite antivenom treatment, patient requires intubation.

DIC

- Extremely uncommon
- Labs similar to venom-induced thrombocytopenia and defibrinination, with additional findings of:
  - Hemolysis
  - Red cell fragmentation
  - Organ infarction
  - Diffuse bleeding
ED Management

• IV fluids
• Pain control
• Measure circumference
• Neurovascular checks
• Elevate extremity

Antivenom?

Indications for Antivenom

• *Rapid* progression of swelling
• *Significant* coagulopathy or thrombocytopenia
• Neurotoxicity
• Shock

The Case of the Concerned Citizen

• A guy on I-17

The Alleged Scene
Venomous Lizards
Helodermatidae

Heloderma suspectum
Gila Monster
H. s. suspectum
H. s. cinctum

Heloderma horridum
Mexican Beaded Lizard
H. h. horridum
H. h. exasperatum
H. h. alvarezi

Gila Monster bite
Resulting in allergic rxn
...and tabloid story!
Gila Monster Distribution

- Banded Gila Monster
  - *H. s. cinctum*
- Reticulated Gila Monster
  - *H. s. suspectum*

Gila Monster Venom Delivery

- Venom glands on mandible
- Ducts lead to labial mucosa
- Venom flows through grooved teeth and into wounds
Removing a Gila Monster
• Pry mouth apart with pliers
• Jam screwdriver down monster's throat
• Dip monster in gasoline and set on fire
• Pour gasoline into mouth and set on fire
• Place fire under jaw without gasoline
• Strike back of lizard's head with large stone

Scorpions
• 40 species of scorpions in the US
• Only one dangerous, considered to be potentially fatal
  – Found in Arizona, some areas of Texas, New Mexico, California, and Nevada
• >6000 calls/year to Samaritan Regional Poison Control Center
• Most managed at home
The Bark Scorpion

- *Centruroides sculpturatus/exilicauda*
  - Yellow/tan/brown
  - Up to 5 cm in length
  - Hard exoskeleton
  - Segmented tail curves up, ends in a telson, containing venom glands and stinger

Exoskeleton

Telson
The Bark Scorpion

- Body fluoresces under UV light
- Resides in or near trees; wood
  - Climbs, but not up glass

Bark Scorpion

Envenomation

- Most stings cause only local pain
- Onset of symptoms immediate, progress up to 5 hours
- Children tend to be most severely affected
- No deaths reported in the US since 1968
Management

- Most symptoms improve within 9 to 30 hours without treatment
- Pain and paresthesias may last up to 2 weeks
- Options:
  - Antivenin (not currently available)
  - Sedation and pain control

Antivenin

- Recommended for Grade III and IV envenomations
- Results in rapid reversal of neurologic and respiratory toxicity within one hour
- Risks
  - Hypersensitivity reactions
  - Serum sickness

Scorpion Antivenin

- Goat serum derived
- Contraindications
  - Previous scorpion antivenin
  - Asthma
  - Beta Blockers
  - CAD
Black Widow
• *Latrodectus mactans*
• Female is 8-10 mm, black with red hourglass mark on ventral surface
• Live in woodpiles, crevices, barns…

Envenomation
• Female bite produces sharp pain
• Pair of fang marks with surrounding erythema
• 15 minutes to 6 hours following the bite, “latroductism”
Venom

• a-latrotoxin
  – Potent neurotoxin
  – Induces neurotransmitter release from nerve terminals

Latrodectism

– Neuromuscular
  • Muscle cramps – site, chest, abdomen (may mimic acute abdomen), thighs
  • Rigidity, tremor, weakness, priapism
– Systemic
  • Nausea, diaphoresis, pavor mortis (fear of death), salivation, urinary retention
– Cardiopulmonary
  • Hypertension, tachycardia, bronchorrhea
Management

• Airway
• Tetanus prophylaxis
• Pain control
• Antivenin to speed recovery