Envenomation and Antivenom:
Snakes, Scorpions, Spiders and Companion Animals

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Did you know?

- The incidence rate of snake bites and insect bites/stings
- In 2014 VPI Pet Insurance received

VPI® and Pet Poison Helpline®
working together

- Shared mission in highlighting the importance of preparing for accidents and poisonings in small animals
- Addressing the cost of veterinary care
  - VPI covers the $49 Pet Poison Helpline fee when a pet is brought in to your hospital for care
- Enabling best medicine
  - Pet owners with VPI pet insurance spend 60% more on veterinary care than those without pet insurance
Introduction
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Envenomation and Antivenom
Snakes, Scorpions, Spiders and Companion Animals
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Envenomation - Antivenom

Pharmacological and Pathophysiological Venom effects → Observed Clinical Manifestations → Veterinary Medical Management

Venom - Toxins

Cytotoxic
Cardotoxic
Hemotoxic
  Clotting Factors
  Fibers
  Platelets
Hemorrhagic
Myotoxic
Necrototoxic
Nephrotoxic
Neurotoxic

Enzymatic and non-Enzymatic Proteins
Non-protein components

Keyler ©
## VENOM

**PROTEINS & POLYPEPTIDES**

<table>
<thead>
<tr>
<th>ENZYMATIC</th>
<th>NON-ENZYMATIC</th>
<th>NON-PROTEIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholinesterase</td>
<td>Bradykinin-potentiating Peptides</td>
<td>Amino Acids</td>
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<tr>
<td>Arginine Ester Hydrolase</td>
<td>Cardiotoxins</td>
<td>Biogenic Amines</td>
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<tr>
<td>Collagenase</td>
<td>Cholinesterase Inhibitors</td>
<td>Carbohydrates</td>
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<tr>
<td>Hydrolase</td>
<td>Complement System Proteins</td>
<td>Lipids</td>
</tr>
<tr>
<td>Lactic dehydrogenase</td>
<td>Cytotoxic</td>
<td>Nucleosides-ribosides</td>
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<tr>
<td>L-Amino acid oxidase</td>
<td>Lectin</td>
<td>Riboflavin</td>
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<tr>
<td>Phosphodiesterase</td>
<td>Lactate dehydrogenase</td>
<td>Amine</td>
</tr>
<tr>
<td>Phospholipases</td>
<td>L-Amino acid oxidase inhibitors</td>
<td>Cations</td>
</tr>
<tr>
<td>Phosphomonoesterase</td>
<td>Phospholipase A2, C, D inhibitors</td>
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<tr>
<td>Proteases</td>
<td>Phospholipase Inhibitors</td>
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</tr>
<tr>
<td>Thrombin-like enzyme</td>
<td>Platelet Function Proteins</td>
<td></td>
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<tr>
<td>Proteinase Inhibitors</td>
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</tbody>
</table>

## ENVENOMATION FACTORS

- Site of bite
- Victim Age, Size, Health
- Species
- Venom Quantity
- Venom Quantity
- Time post Envenomation
- Venom Delivery Route

Spiders, Scorpions, Snakes

**Antivenom Pharmacotherapy**
### Antivenom Sources (traditional)

- **Horses (equine)**
- **Sheep (ovine)**
- **Goats (caprine)**

### Antivenom Sources (Novel Sources)

- **Chicken eggs (avian)**
- **Camels (camelid)**

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### Antivenom - Antibodies

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Molecular Wt.</th>
<th>Venom antigen species</th>
<th>Immunization host species</th>
<th>Specificity</th>
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</thead>
<tbody>
<tr>
<td>F(ab')2</td>
<td>102 kD</td>
<td>Crotalids-various spp.</td>
<td>Horse</td>
<td>Polyspecific</td>
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<tr>
<td>IgG</td>
<td>150kD</td>
<td>Coral snake</td>
<td>Horse</td>
<td>Monospecific</td>
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<tr>
<td>Fab</td>
<td>50kD</td>
<td>Eastern Diamondback</td>
<td>Sheep</td>
<td>Polyspecific</td>
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<tr>
<td></td>
<td></td>
<td>Western Diamondback</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mojave Rattlesnake</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Water Moccasin</td>
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</tr>
</tbody>
</table>

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Antibodies – Antivenom - Pharmacokinetics

<table>
<thead>
<tr>
<th></th>
<th>Distribution (hrs)</th>
<th>Elimination (hrs)</th>
<th>Tissue affinity</th>
<th>Complement Reaction</th>
<th>Excretion</th>
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</thead>
<tbody>
<tr>
<td>Fab’/Fab</td>
<td>3</td>
<td>≥ 3</td>
<td>Mod-high</td>
<td>(-)</td>
<td>Immune tissue</td>
</tr>
<tr>
<td>Fab</td>
<td>1</td>
<td>&gt; 100</td>
<td>High</td>
<td>(+)</td>
<td>Immune tissue</td>
</tr>
<tr>
<td>IgG IgG</td>
<td>10-12</td>
<td></td>
<td>Low</td>
<td>(-)</td>
<td>Renal</td>
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</tbody>
</table>

ANTIVENOM – IMPORTANT CONSIDERATIONS

- **DOSE** – Antibody type
- **FLUID LOAD**
- **ADVERSE REACTIONS**
  - Rate of administration – too fast ↑ risk
  - Concentration of Preparation – too concentrated ↑ risk
ANTIVENOM INDICATIONS

Significant Venom Effects:

• Neurological & Cardiac
• Coagulopathy
• Hypotension (major concern)
• Nausea, Vomiting,
• Paresthesia, Muscle Fasciculation (Myokymia) - Remote to Bite
• Extension of Local Swelling

ANTIVENOM – THRESHOLD for TREATMENT

• Antivenom administration before toxic symptoms develop or worsen will prevent severe complications
• Can’t always reverse a venom-induced process
• You don’t know how severe symptoms will become
• You may treat to prevent unknowingly of how severe envenomation symptoms will become

ANTIVENOM ADMINISTRATION

Diphenhydramine 50 mg

Antivenom

Epinephrine
**Scorpion Envenomation – North America**

![Image of a dog and a cat]

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**SCORPIONS – North America**

- Centruroides sculpturatus
- Hadrurus arizonensis

- Arizona Bark Scorpion
- Desert Hairy Scorpion

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**SCORPION ENVENOMATION IN USA**

- *C. sculpturatus* - Primary Toxic Species

- Venom – Neurotoxic
  - Low MW Proteins
  - Depolarization at NM Junction
  - Na⁺ Ion Channel Permeability
### Signs & Symptoms of Envenomation

- Sharp local pain
- Paresthesia - At Sting Site & Remote to it
- Tachycardia
- Hypertension, Hypersalivation
- Hyperactivity, Thrashing, Flailing, Writhing, Dysphagia, Vocalization, Ocular

*Systemic Toxicity May Persist for Many Hours (> 24 hrs)*

### Scorpion Envenomation

**Symptomatic Treatment**

Limited to First Aid (94% of Cases):

- Ice - cooling
- Elevation
- Analgesics

### Treatment of Scorpion Envenomation

**Veterinary Medical Management**

*Antivenom vs. Other Med*

- Midazolam (Continuous IV)
  - For Cranial and/or Skeletal Neuromuscular Dysfunction
  - Median Dose to Stop Agitation-Involuntary Motor Activity = 0.3 mg·kg⁻¹·hr⁻¹
Treatment of Scorpion Envenomation
Veterinary Medical Management

Antivenom

ANASCORP® (Rare Disease Therapeutics, Inc.)
Centruroides (Scorpion) Immune F(ab')² (Equine) Injection

3 vials (15 mL) diluted to 50 mL
Infuse over 10-15 min

SPIDERS

SPIDER IDENTIFICATION IS CRUCIAL TO DIAGNOSIS

NO PATHOGENOMIC CLINICAL SIGNS CONFIRM DIAGNOSIS OF SPIDER ENVENOMATION
WITHOUT A SPECIMEN

BLACK WIDOW - Latrodectus mactans
BLACK WIDOW BITE

Initial Bite - Sharply Painful

Bite Site - Dull Ache - Numb

Venom - Latrotoxin = Neurotoxin

2786 Cases (15 % Significant, 0.4 % Severe) - 2002

SPIDER ENVENOMATION

DIFFERENTIAL DIAGNOSIS

LOCAL LESION

- Fungal
- Bacterial
- Viral
- Lyme disease
- Arthropod-borne
- Foreign Body Reactions
- Systemic Conditions
- Diabetes
- Lupus

SYSTEMIC

- Scorpion or Snake Toxins
- Pesticide Toxicity
- Sepsis
- Meningitis
- Hemolytic Anemia
- Acute Abdomen

BLACK WIDOW BITE SYMPTOMS

- Diaphoresis - Localized to Bite Site Region
- Hypertension - Seizures
- Neuromuscular: Fasciculations, Involuntary Spasms, R rigidity Large Muscle Groups (Abdominal-Back)
- Respiratory Depression
- Weakness - Ptosis - Priapism - Thready Pulse - Vocalization - Vomiting
**BLACK WIDOW ENVENOMATION**

**SYMPTOMATIC MANAGEMENT**

Local Wound Pain: Cleansing, Ice
Muscle Spasms - Severe Pain: Benzodiazepines & Narcotics
Hypertension: Responds to Pain Control

**ANTIVENOM**

LABS:
- CK
- Troponins
- AST

**BLACK WIDOW ENVENOMATION**

**MEDICAL MANAGEMENT**

Severe or Life-Threatening Symptoms

1 vial / 50-100 mL NS over 15-30 min

**Other Spiders**

- **Lycosidae species**  Wolf spiders
- **Chiracanthium species**  Sac spiders
- **Tegenaria agrestis**  Hobo spider
VENOMOUS SNAKEBITE

Snakebite Victim - Where's the Bite?

North American Coral Snakes
*Micrurus and Micruroides*

Range of U.S. Coral Snakes

Photo: Howard Richard. Used with permission.
CORAL SNAKE ENVENOMATION SYMPTOMS - NEUROLOGICAL

- Weakness/Faintness
- Nausea/Vomiting
- Drooling
- Ptosis
- Tremors
- Numbness/paresthesia
- Fasciculations
- Respiratory arrest
- Cardiac
- Neurological

North American Coral Snake - Antivenom

Antivenin (Micrurus fulvius) (equine origin)

IgG

Coralmyn Antivenom (Instituto Biocon, Mexico)

F(ab')2

Animal data indicate efficacy against

M. fulvius and M. tener

Anticoral Antivenom (Instituto Clodomiro Picado, Costa Rica)

IgG

Animal data indicate efficacy against

M. fulvius

Antivenoms – Alternate Options

North American Coral Snake (Micrurus spp)
**North American Pit Vipers**

- **Timber Rattlesnake**
  Crotalus horridus
- **Western Diamondback**
  Crotalus atrox
- **Massasauga**
  Sistrurus catenatus

- **Copperhead**
  Agkistrodon contortrix
- **Cottonmouth**
  Agkistrodon piscivorus

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**Crotalus, Sistrurus, Agkistrodon - Envenomation Characteristics**

20-25% of bites are “dry”

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**Rattlesnakes and dogs don't mix very well**

By Wally Jordan in Prescott has made that point clear. The dog was bitten by a rattlesnake on his leg. The dog was taken to a veterinarian who treated the wound. The veterinarian said that the dog was in a lot of pain. The dog was put on antibiotics and recovered. The owner said that they didn’t know the dog could be bitten by a rattlesnake. The veterinarian said that it’s important to know the risk of envenomation. The owner said that they were surprised to learn that the dog could be bitten by a rattlesnake. The veterinarian said that the dog was lucky to survive. The owner said that they would be more careful in the future.
MAINTAIN AIRWAY

SYMPTOMS

Edema – erythema
Local swelling - spreads proximally/radially
Inflammation – tenderness
Enlarged regional lymph nodes

Dry Bite
Oozing Fang Punctures
Ecchymosis

Pulmonary hemorrhage

All Labs Normal
Coag Lab Changes

LABS - COAGUALTION - HEMATOLOGY

PT
APTT
INR
FDPs

CBC
△
DIFF

PLTs
HCT
HGB
FIB
VETERINARY MEDICAL TREATMENT

**IMMUNOTHERAPY** = ANTIVENOM (Passive Immunization)

- Analgesics
- Respiratory
- Wound Care
- Antibiotics
- IV Fluids
- Surgery/Fasciotomy ?
- Antihistamines
- Tetanus

ANTIVENOM (Veterinary) – NA Pit Viper

ANTIVENOM (Non-Veterinary) – NA Pit Viper
Recurrent Thrombocytopenia
Platelets vs. Time & Fab Antivenom Dosing

Platelets x 10^3/mm³

0 24 48 72 120

Hrs/Day Post Bite

Day 5

Day 8

Day 9

Day 13

2AV (+ plts)

2AV (+1 u BL)

ANTIVENOM INDEX ONLINE
EXOTIC ENVENOMATOINS

Regional Poison Centers & Emergency Dept. - Locate Appropriate AV

Conclusions – Antivenom

- True antidote for Latrodectus spider, Centuroides scorpion, Crotalus, Sistrurus, Agkistrodon, Micrurus snake envenomations
- Produced by hyperimmunization of host animal – usually horses or sheep
- Composed of IgG, F(ab')₂, or Fab Antibody forms
- Severity of envenomation symptoms and clinical judgment determine the threshold for administration
- Acts primarily by binding venom toxins directly
THE END

They Both Got Bitten!!
What would you do?

When in doubt, call for the bad ones
800-213-6680

- Something you’re not familiar or comfortable with
- Odd clinical signs
- Animals with preexisting disease
Introducing…

Pet Poison Helpline’s new video series:

1. Subscribe to our YouTube Channel (petpoisonhelpline)
2. Follow the blog on our website for updates
3. Sign up for our program (email coming soon!) or contact us for more info: info@petpoisonhelpline.com

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Comments? Questions? Email us: info@petpoisonhelpline.com