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CREATURE FEATURE: PHARMACOLOGIC MANAGEMENT OF BITES, STINGS & OTHER ANIMAL EXPOSURES

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Disclosures

- Neither the presenter nor her preceptor have conflicts of interests related to this presentation
- Note: This program may contain the mention of suppliers, brand products, services, or drugs presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes only and should not be perceived as an endorsement of any particular supplier, brand, product, service, or drug.

Pharmacist & Nurse Objectives

1

Review available drugs for the treatment and prophylaxis of bites, stings and other animal exposures

2

Discuss appropriate pharmacologic therapy depending on indication

3

Describe a treatment strategy based on patient presentation

Pharmacy Technician Objectives

1

Recall brand and generic names of drugs utilized in the setting of bites, stings, and other animal exposures

2

Identify various available dosage formulations for presented pharmacologic agents

3

Explain the preparation of medications used as treatment or prophylaxis for bites, stings, and other animal exposures

Presentation Outline

- Background
- Rabies virus
  - Post-exposure prophylaxis (PEP)
  - Pre-exposure prophylaxis (PREP)
- Envenomations
  - Snakes, scorpions, and spiders
- Skin and soft tissue infections

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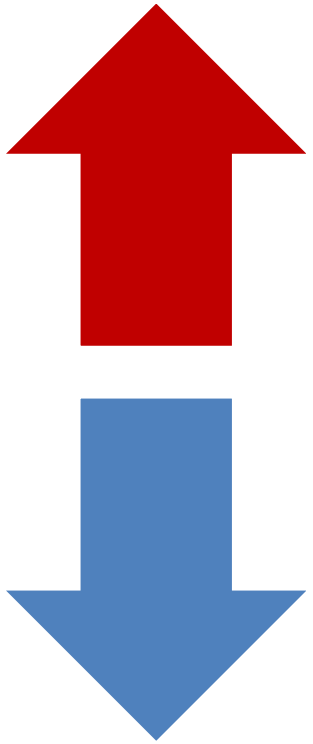
BACKGROUND

Animal Exposures

- Exposures
  - Dog bites most extensively studied
  - No routine regional or local tracking
  - Injury rate usually highest among children
- Morbidity and mortality
  - Infection, envenomation, disability
- High cost

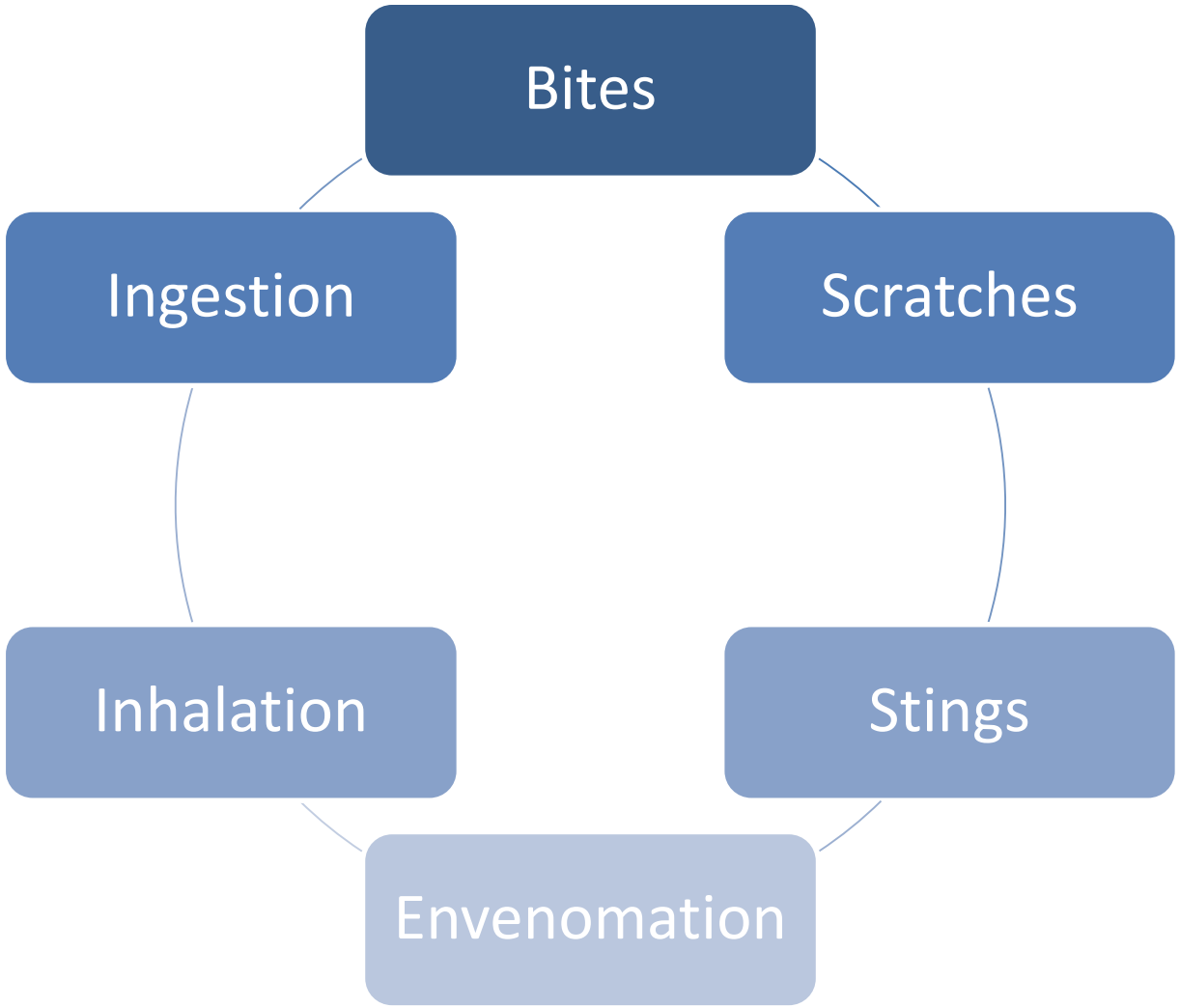


Warm Months

Cold Months

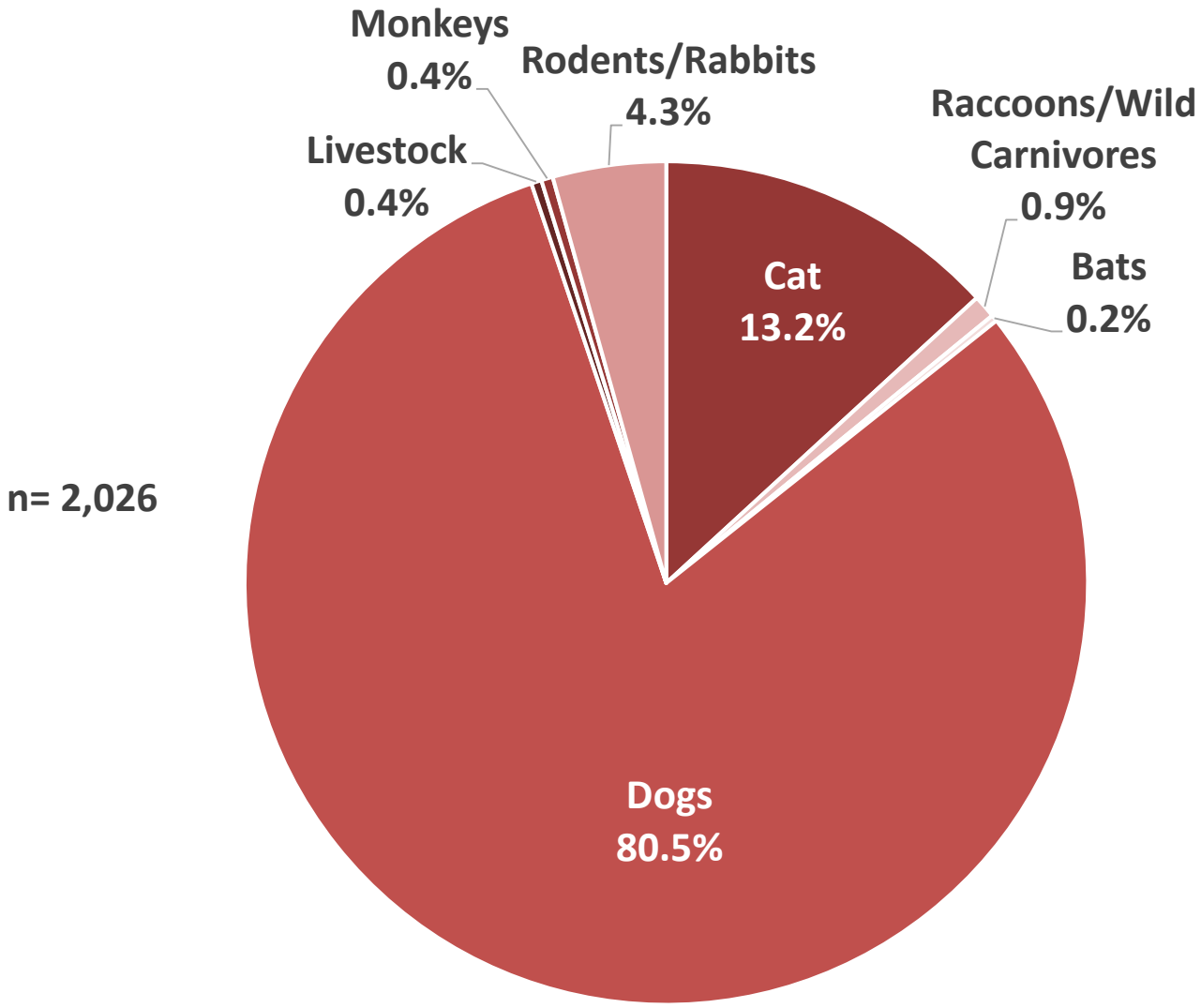
Sources: Kang AM, et al. *J Med Toxicol*. 2017 Jun;13(2):158-165.
Lyu C, et al. *Public Health Rep*. 2016 Nov;131(6):800-808.
Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep*. 2003 Jul 4;52(26):605-10.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2019 Jun 11. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/location/usa/cost.html.

Routes of Injury & Illness



Source: Stauffer K, et al. [Internet]. Atlanta: CDC; 2019 Jun 24. [cited 2021 Jan 29]. Available from: https://wwwnc.cdc.gov/travel/yellowbook/2020/noninfectious-health-risks/animal-bites-and-stings-zoonotic-exposures.

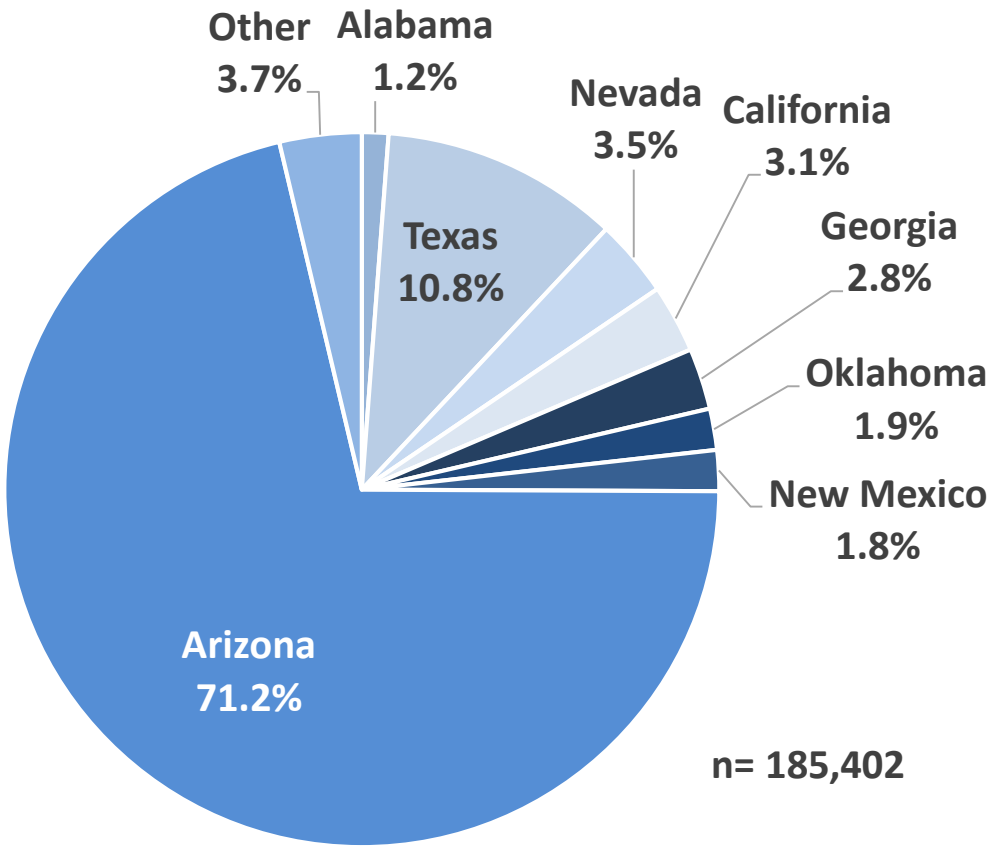
Emergency Department Mammalian Exposures



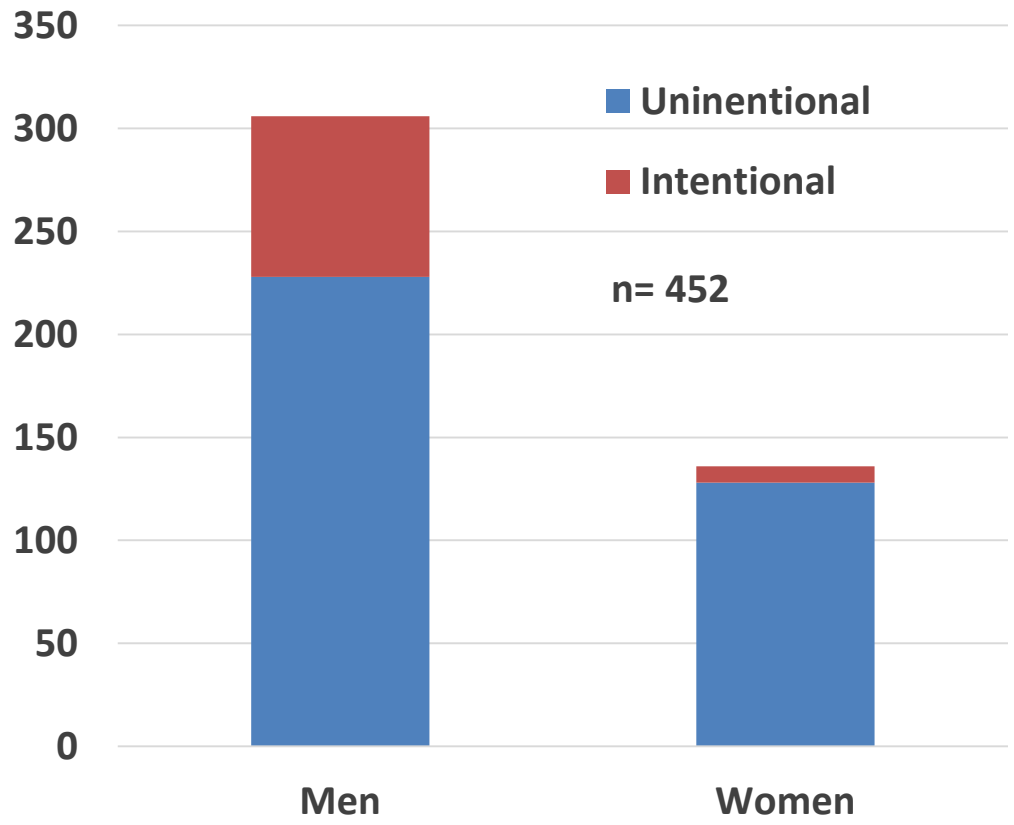
Source: Steele MT, et al.; EMERGEncy ID NET Study Group. *Acad Emerg Med*. 2007 May;14(5):398-403.

United States Envenomations

Nationwide Scorpion Exposures 2005 - 2015



North American Snake Bite Registry Exposures 2013 - 2015



Sources: Kang AM, et al. *J Med Toxicol*. 2017 Jun;13(2):158-165.
Ruha AM, et al. *J Med Toxicol*. 2017 Dec;13(4):309-320.

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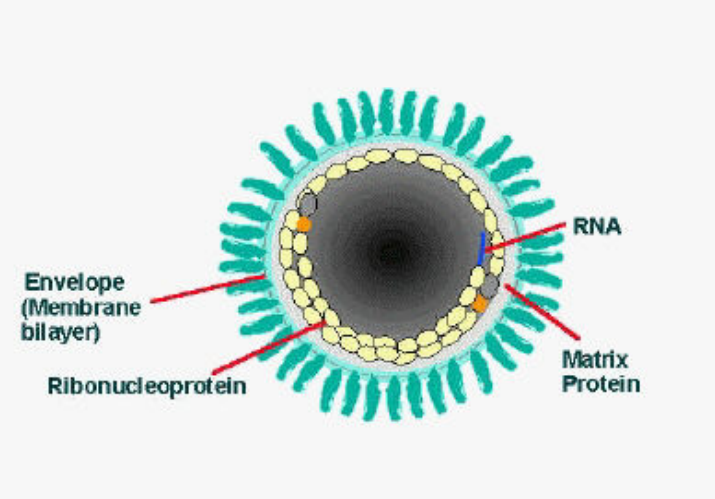
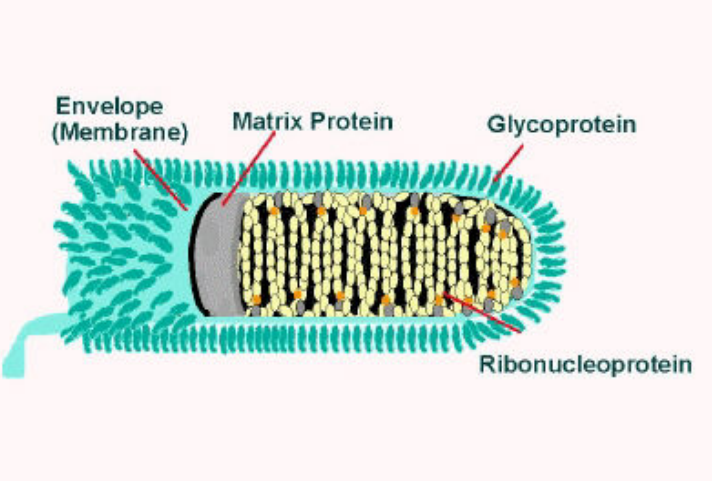
RABIES VIRUS

Rabies lyssavirus

- Non-segmented, negative-stranded RNA virus
- Annual United States cases: 1 to 3
- Transmission via saliva or central nervous system (CNS) fluid
- Typical incubation: 1 to 3 months





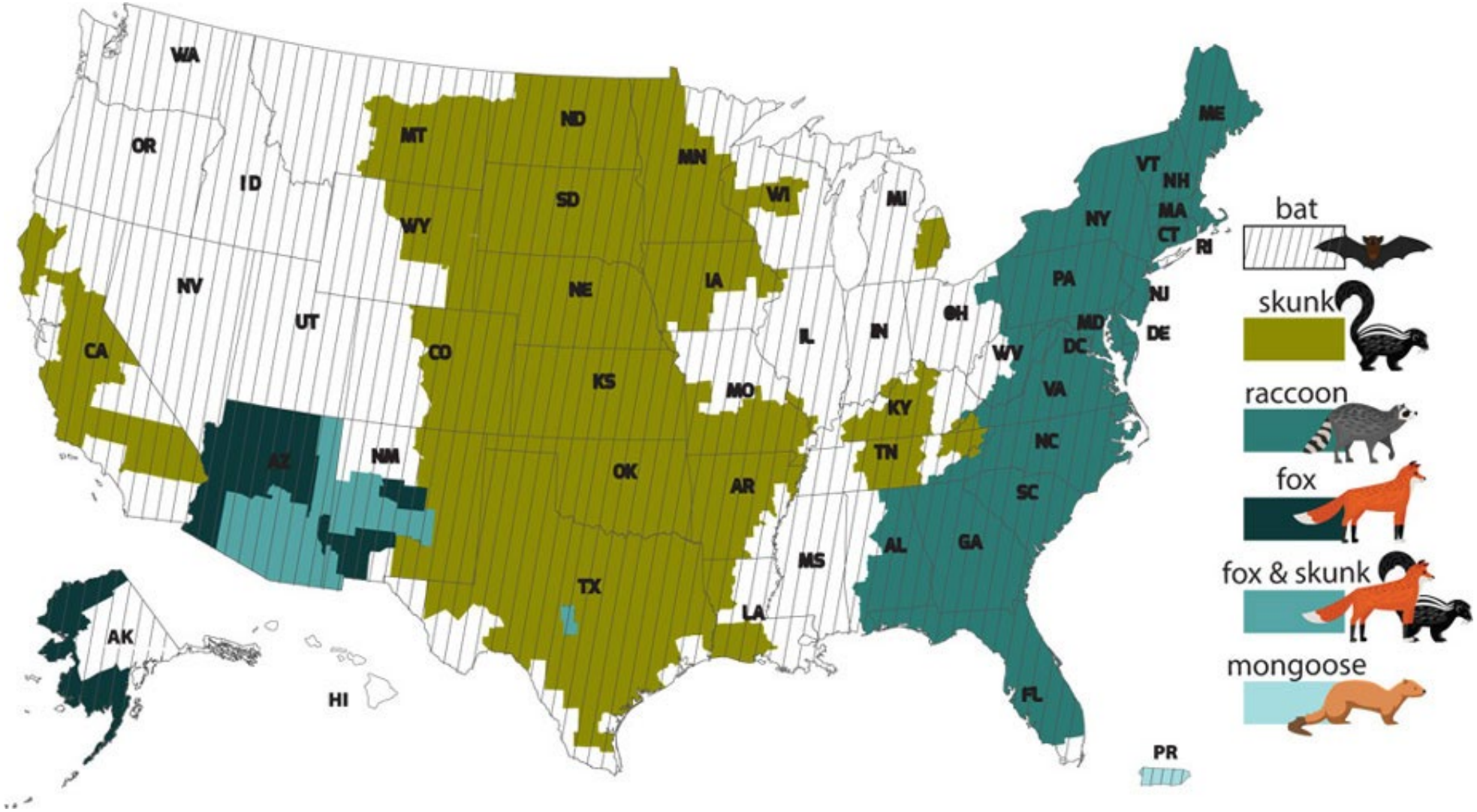
Sources: Rupprecht CE, et al. *MMWR Recomm Rep*. 2010 Mar 19;59(RR-2):1-9.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Nov 30. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/about.html.

Rabies: Vectors Around the World

Sources: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2013 Sep 23. [cited 2021 Jan 29]. Available from: https://blogs.cdc.gov/global/2013/09/23/rabies-control-three-months-three-continents/.

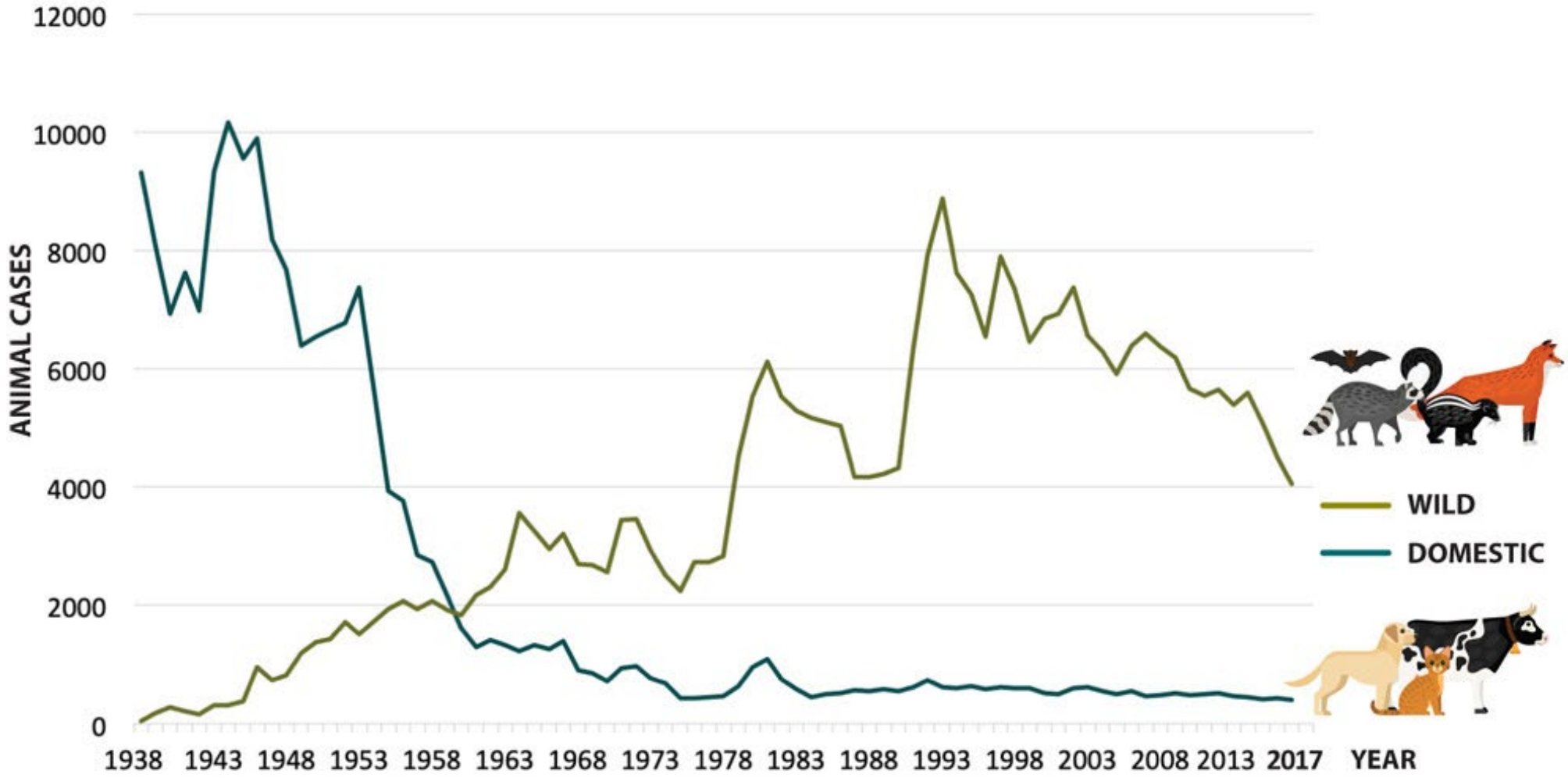
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Jul 29. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/location/world/index.html.

Rabies: Wildlife Reservoirs



Source: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2019 Jun 12. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/vitalsigns/rabies/index.html.

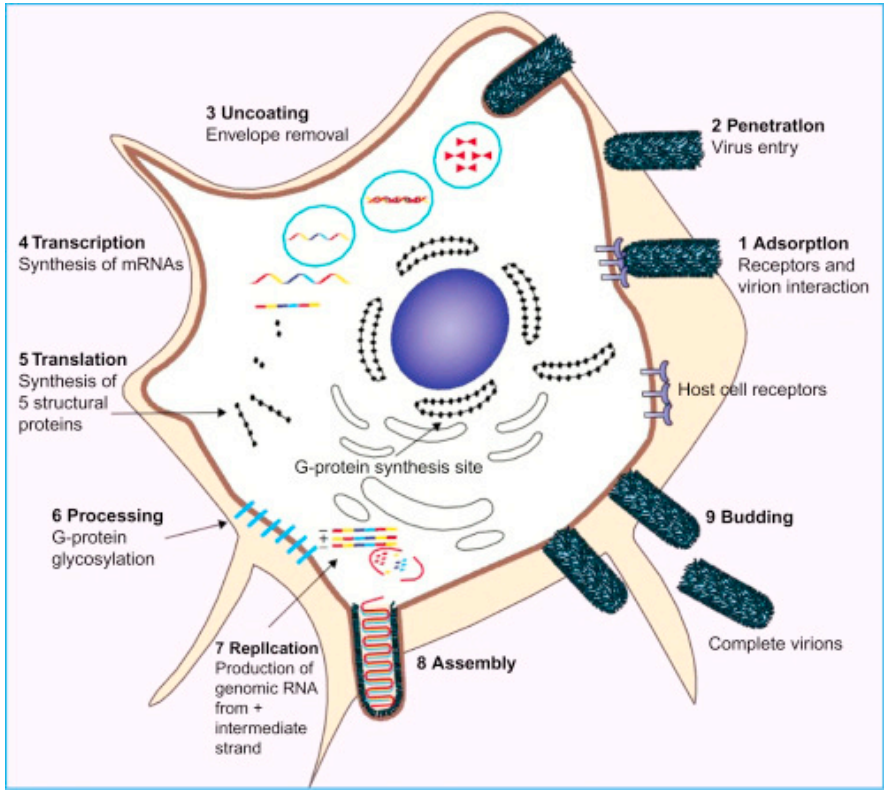
Rabies: Trends Over Time



Source: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2019 Jun 12. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/vitalsigns/rabies/index.html.

Pathophysiology and Diagnosis

- Pathophysiology
  - Replication in striated muscle
  - Direct nerve cell infection
  - Retrograde/anterograde neuronal transport
- Diagnosis
  - Clinical presentation
  - Exposure history
  - Fluorescent antibody testing
  - Polymerase chain reaction

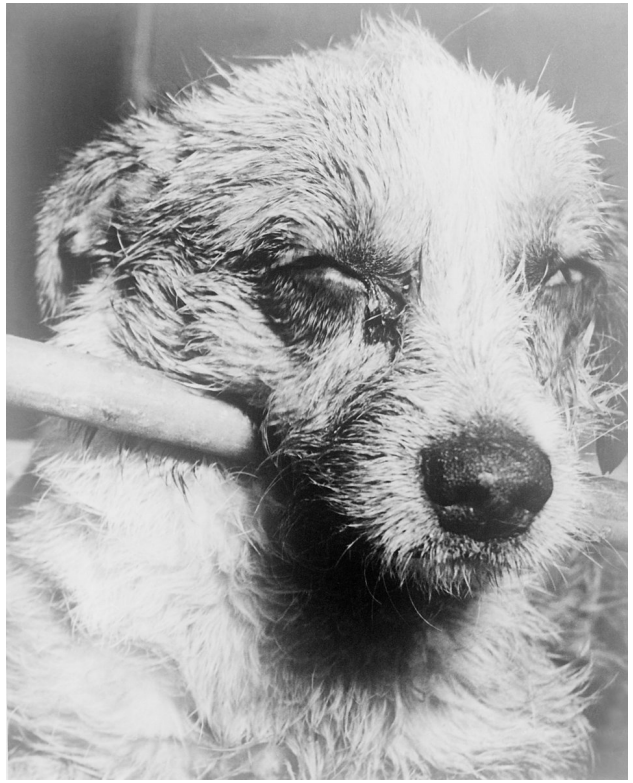


Sources: Dean DJ, et al. *Bull World Health Organ*. 1963;29(6):803-11.
Sami D, et al. In: *Emerging and Reemerging Viral Pathogens: Academic Press*; 2020. p. 259-75.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Nov 30. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/about.html.
Greenlee, J. [Internet]. Kenilworth: Merck Sharp & Dohme Corp.; 2020 Jul. [cited 2021 Feb 2]. Available from: https://www.merckmanuals.com/professional/neurologic-disorders/brain-infections/rabies.

Presentation: Mammalian Animals

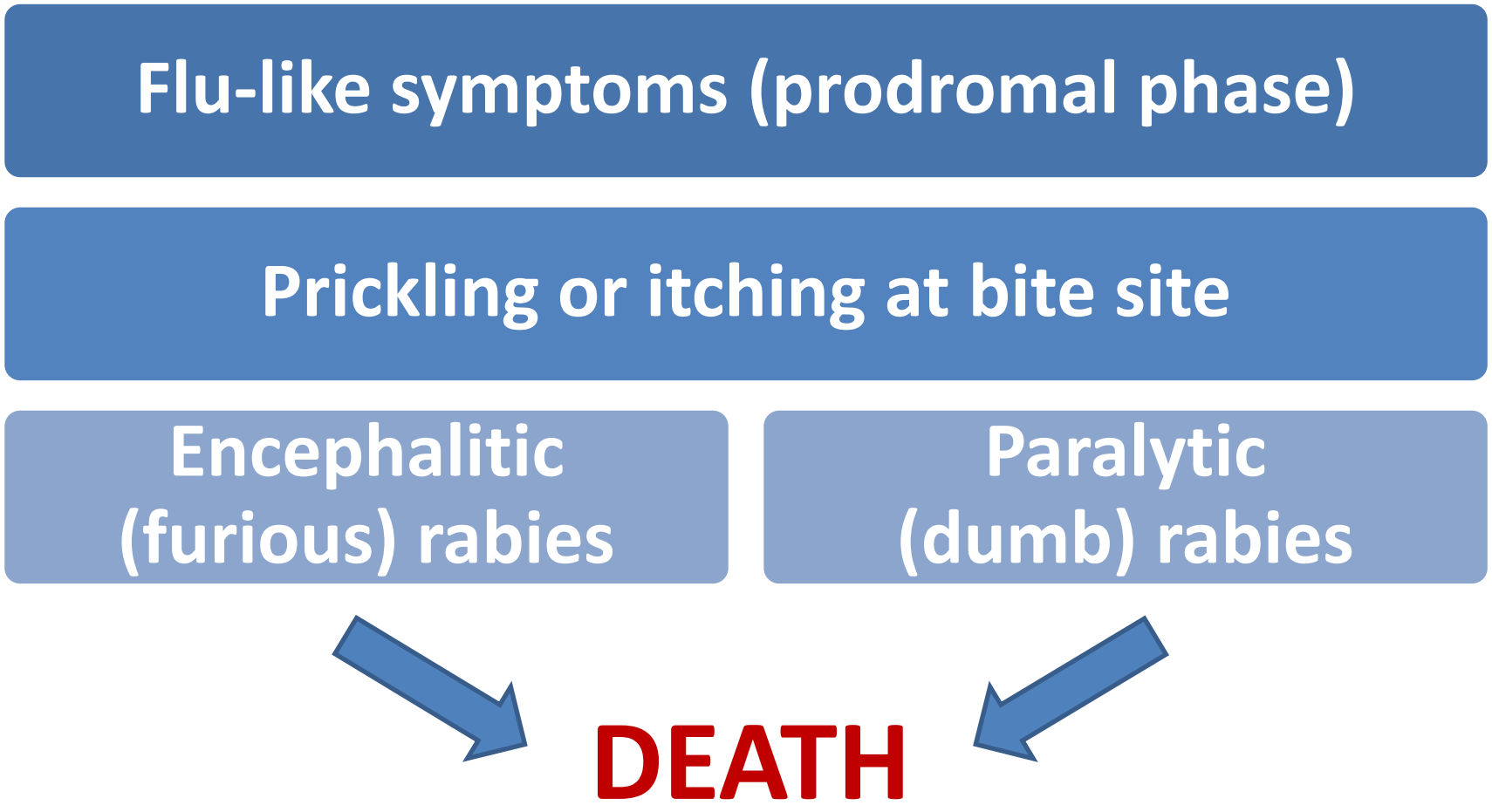
Infected Animals

- Lethargy, fever, vomiting
- Aggression, biting, self-mutilation
- Uncharacteristic tameness
- Excessive drooling; difficulty breathing or swallowing
- Movement issues, seizures, paralysis



Sources: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Jun 10. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/animals/index.html.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2017 Mar 10. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/vaccines/vpd/rabies/public/photos.html.

Clinical Presentation: Humans



Sources: World Health Organization. [Internet]. Geneva: WHO; 2020 Apr 21. [cited 2021 Jan 29]. Available from: https://www.who.int/news-room/fact-sheets/detail/rabies.
Greenlee, J. [Internet]. Kenilworth: Merck Sharp & Dohme Corp.; 2020 Jul. [cited 2021 Feb 2]. Available from: https://www.merckmanuals.com/professional/neurologic-disorders/brain-infections/rabies.

Post-exposure Prophylaxis Considerations

- General
  - Specific exposure
  - Area epidemiology
  - Animal availability for testing
- Rabies vaccination series ± immune globulin and/or tetanus
  - Vaccination status
  - Immunocompetence status

Source: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Jun 10. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/animals/index.html.

Animal Type Considerations

Animal Type	Disposition Status	Vaccination?
Dogs **Cats** **Ferrets**	Observe health for 10 days	Delay
	Suspected or confirmed rabid	✓ **Immediately**
	Unknown	**Consult public health officials**
Raccoons **Skunks** **Foxes** **Wild Carnivores** **Bats**	**Regarded rabid** unless tested otherwise	✓ **Immediately** May discontinue if animal later tests negative.
Livestock **Horses** **Rodents** **Hares** **Other Mammals**	Rarely require PEP; consider individually	**Consult public health officials**

Sources: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2017 Jul 5. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/exposure/animals/domestic.html.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2021 Jan 25. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/exposure/animals/other.html.

Bats

- Documented disease in 49 states
- Bites: minor or unrecognized
- PEP recommended with:
  - ANY bite, scratch, or mucous membrane exposure
  - Direct exposures
  - Inability to confirm direct exposure
  - +/- if found indoors with no history of contact
- May withhold if bat tests negative

Sources: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2017 Jul 5. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/exposure/animals/bats.html.

Rabies Vaccinations

- Dose: 1 mL (≥2.5 IU of rabies antigen)
- Administration: intramuscular injection
  - Adults: deltoid muscle, never gluteal
  - Children: anterolateral aspect of thigh
- Serologic testing not routine
- Adverse effects:
  - Injection site reactions
  - Mild systemic effects

Products	Formulation	Additives	Similarities
RabAvert®	Purified chick embryo cell vaccine (PCEC)	Neomycin, albumin (human), amphotericin B, bovine gelatin, egg and chicken protein, and chlortetracycline	• Reconstitution • Route • Dosing schedule • Inactivated virus • Interchangeability
Imovax® Rabies	Human diploid cell vaccine (HDCV)	Neomycin, albumin (human), phenol (formulation with preservatives)	

Sources: Briggs DJ, et al. *Vaccine*. 2000 Dec 8;19(9-10):1055-60.
RabAvert® (rabies vaccine). Package insert. GlaxoSmithKline; 2019.
Imovax® Rabies (rabies vaccine). Package insert. Sanofi Pasteur Inc.; 2019.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Jun 10. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/animals/index.html.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2019 Oct 2. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/specific_groups/hcp/biologic.html.

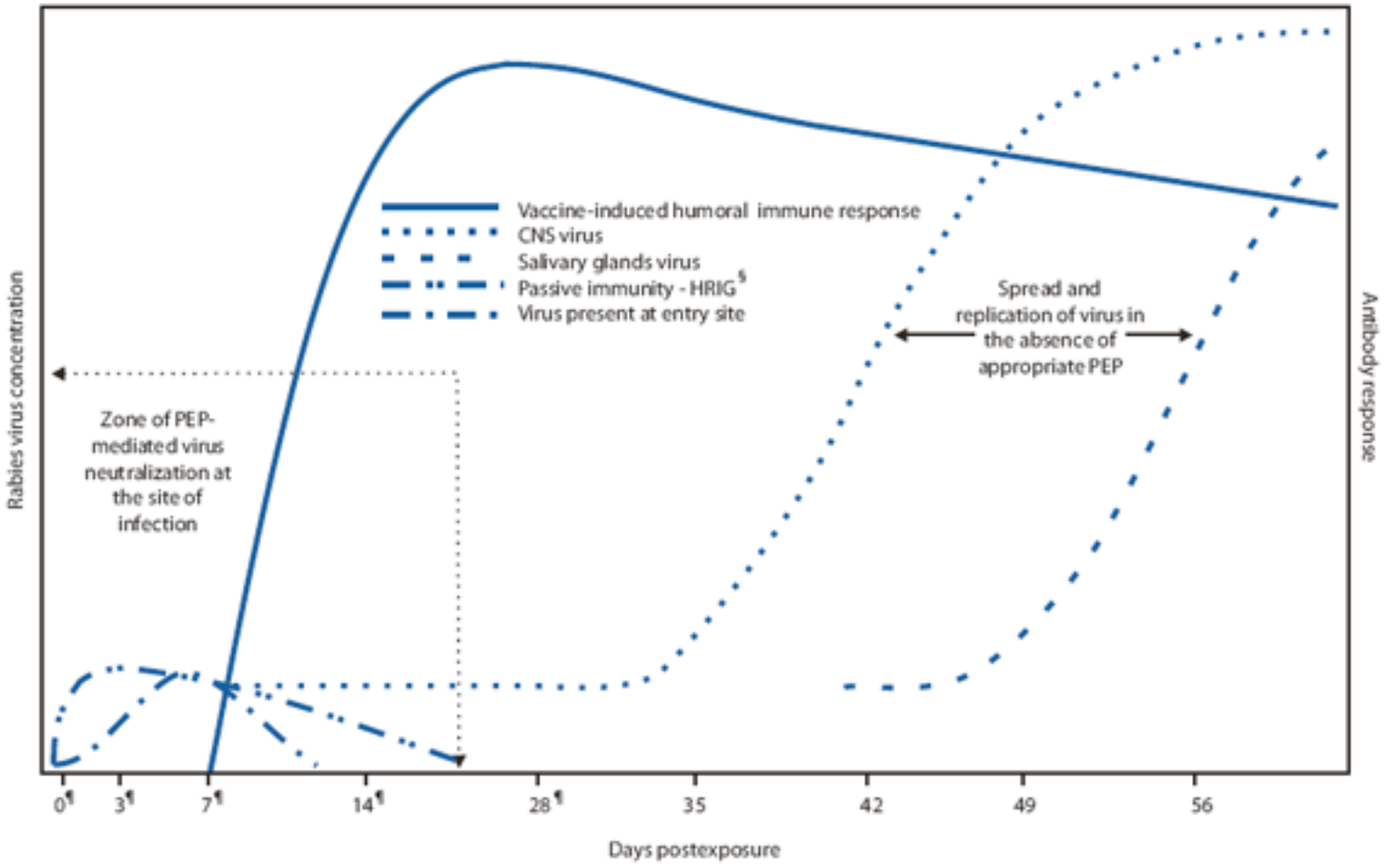
Vaccination Schedule

Day*	Unvaccinated Persons		Previously Vaccinated Persons
	Immunocompromised	Immunocompetent	
0	✓	✓	✓
3	✓	✓	✓
7	✓	✓	X
14	✓	✓	X
28	✓	X	X

*If dose missed on scheduled day, administer as soon as possible. After catch-up dose, space remaining doses at same intervals. Consider serologic testing with significant deviations.

Source: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Jun 10. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/animals/index.html.

Vaccination Response



Source: Rupprecht CE, et al. *MMWR Recomm Rep*. 2010 Mar 19;59(RR-2):1-9.

Evidence: Four Dose Regimen

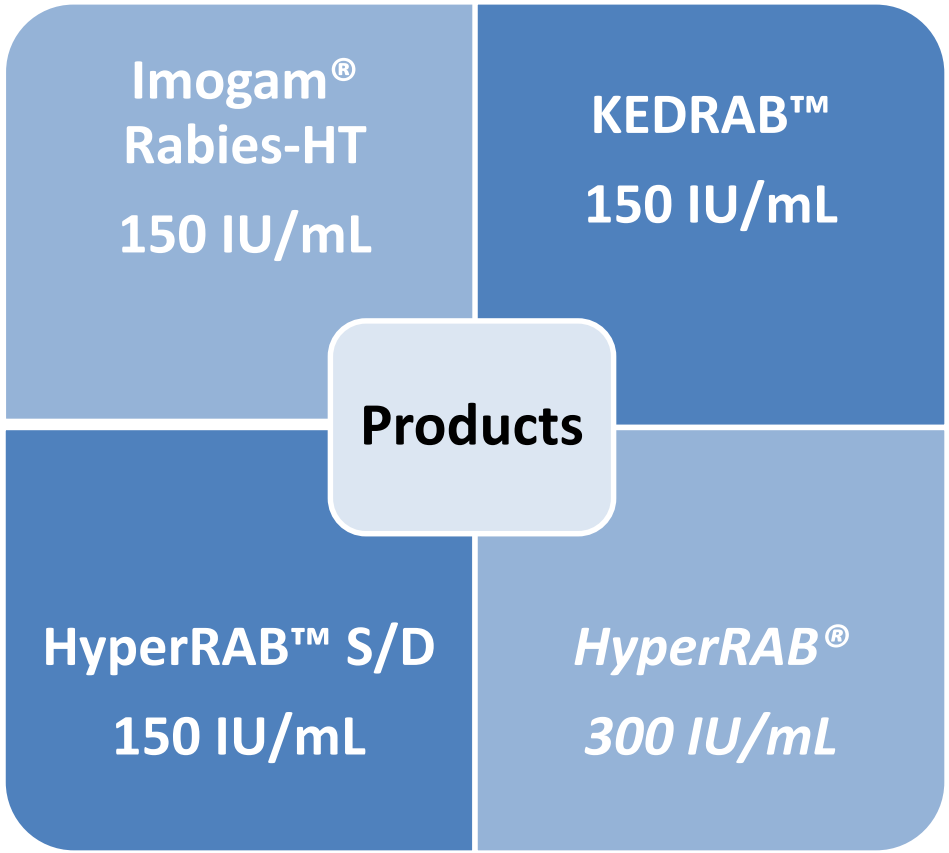
Study	Population	Regimen	Schedule	Adequate Titers?
Bahmanyar M, et al.	n= 45	HDCV	0, 3, 7, 14, 30, 90	All after 4 doses
Kuwert EK, et al.	n= 16	HDCV + RIG	0, 3, 7, 14, 30, 90	All by day 14
Aoki FY, et al. (1989)	n= 24	HDCV ± RIG	0, 3, 7, 14, 28	All after 3 doses
Aoki FY, et al. (1992)	n= 42	HDCV + RIG	0, 3, 7, 14, 28	All after 3 doses
Wasi C, et al.	n= 27	PCECV ± RIG	0, 3, 7, 14, 28, 90	All after 3 doses
Seghal S, et al.	n= 37	PVCV	0, 3, 7	All ≥1.2 IU/L at 10-15 days after dose 3
	n= 62		0, 3, 7, 14 **OR** 0, 7, 14, 30	All ≥1.2 IU/L at 10-15 days after dose 4
Lang J, et al.	n= 32	HDCV ± RIG	0, 3, 7, 14, 28	All; max at day 14
Jones RL, et al.	n= 680	HDCV or CPRV + RIG	0, 3, 7, 14, 28	All by day 14
Briggs DJ, et al.	n= 57	PCECV ± RIG	0, 3, 7, 14, 30, 90	All after dose 4
Bakker AB, et al.	n= 23	PCECV ± RIG	0, 3, 7, 14, 28	All by day 14

HDCV: human diploid cell vaccine; **RIG**: rabies immune globulin; **PCECV**: purified chicken embryo cell vaccine; **PVCV**: purified vero cell vaccine; **CPRV**: chromatographically purified rabies vaccine

Sources: Rupprecht CE, et al. *Vaccine*. 2009 Nov 27;27(51):7141-8.
Rupprecht CE, et al. *MMWR Recomm Rep*. 2010 Mar 19;59(RR-2):1-9.

Rabies Immune Globulin (RIG)

- Indicated in PEP regimen when:
  - Inappropriate or lack of PREP
  - Inappropriate past PEP
- Dose: 20 IU/kg via local wound infiltration
  - Remaining via intramuscular injection
  - Site distant from vaccination
- Adverse effects:
  - Injection site reactions
  - Mild systemic reactions



Sources: HyperRAB® (rabies immune globulin). Package insert. Grifols Therapeutics Inc.; 2018.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2011 Apr 22. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/medical_care/hrig.html.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2019 Oct 2. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/specific_groups/hcp/biologic.html.

Other Considerations

- Immediate, thorough wound cleansing
- Tetanus toxoid if last booster >5 years prior
- PREP: three vaccinations on days 0, 7, 21 **OR** 28

Risk	Population	Action
Continuous	Research laboratory, biologic production workers	Primary vaccination course + Serologic testing every 6 months + Boosters for low serologic titers
Frequent	Diagnostic laboratory workers, wildlife workers, or veterinary staff	Primary vaccination course + Serologic testing every 2 years + Boosters for low serologic titers
Infrequent	Veterinary staff or travelers	Primary vaccination course

Sources: Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2014 Sep 24. [cited 2021 Jan 29]. Available from:https://www.cdc.gov/rabies/medical_care/vaccine.html.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2020 Jun 10. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/rabies/specific_groups/travelers/pre-exposure_vaccinations.html.

Knowledge Check 1: Technicians

A physician requests a dose of rabies immune globulin for a patient with a recent raccoon bite. Which of the following products is **NOT** a brand of rabies immune globulin?

A. Imogam® Rabies-HT
B. HyperRAB®
C. Imovax® Rabies
D. KEDRAB™

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C. Imovax® Rabies

D. KEDRAB™

Knowledge Check 2: Technicians

The pharmacy is looking to purchase rabies vaccinations from the hospital's distributor. Which of the following products is/are appropriate?

A. Imovax® Rabies
B. RabAvert®
C. Imovax® Rabies and/or RabAvert®
D. None of the above

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Knowledge Check 1: Pharmacists & Nurses

A 34-year-old male presents to the emergency department after waking up to a bat flying in his bedroom. He has no past medical history, medications, or allergies (last tetanus vaccination in 2014, no prior rabies vaccinations). Select the most appropriate treatment for this patient.

A. No treatment; observe for rabies signs and symptoms for 10 days
B. RIG and rabies vaccination on days 0, 3, 7, and 14
C. RIG, tetanus vaccination, and rabies vaccination (days 0, 3, 7, and 14)
D. RIG, tetanus vaccination, and rabies vaccination (days 0, 3, 7, 14, and 28)

Knowledge Check 1: Pharmacists & Nurses

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A. No treatment; observe for rabies signs and symptoms for 10 days
B. RIG and rabies vaccination on days 0, 3, 7, and 14
C. **RIG, tetanus vaccination, and rabies vaccination (days 0, 3, 7, and 14)**
D. RIG, tetanus vaccination, and rabies vaccination (days 0, 3, 7, 14, and 28)

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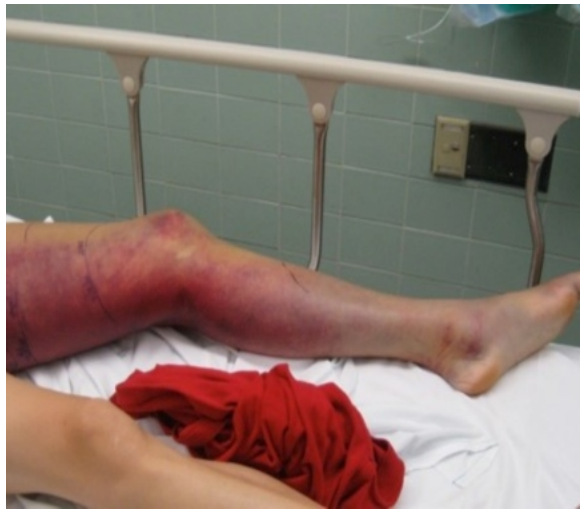
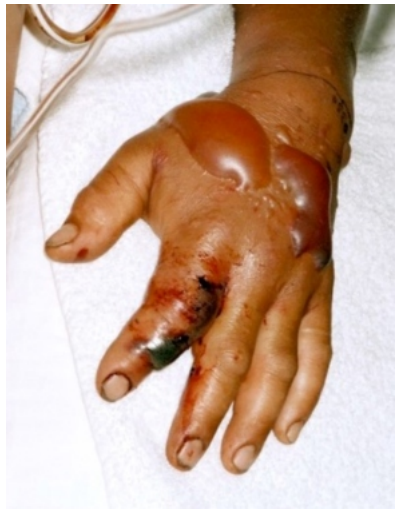
ENVENOMATIONS

Snake Envenomations

- Annual cases: 7,000 - 8,000
- Disability and injury common
- Men comprise 75% of bites
- Majority occur in April to September





Signs and Symptoms

- Bite site:
  - Puncture marks
  - Bruising, bleeding, blistering, erythema
  - Severe pain
- Tachycardia, hypotension
- Nausea, vomiting, diarrhea
- Labored breathing
- Blurred vision
- Metallic, mint, or rubber taste
- Salivation, sweating
- Numbness or tingling
- Muscle twitch or spasm

Sources: Ruha A, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2018 May 31. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/niosh/topics/snakes/default.html.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2018 May 31. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/niosh/topics/snakes/symptoms.html.

Venomous Snakes

Rattlesnakes

Water Moccasins

Copperheads

Coral Snakes

Family: *Viperidae*

Family: *Elapidae*

Sources: Ruha A, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2018 May 31. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/niosh/topics/snakes/types.html.

Snake Venom

- Various components:
  - Proteins, peptides, lipids, carbohydrates, metal ions
  - Target receptors, ion channels, enzymes, proteins
- Deposited via subcutaneous fat
- Treatment considerations
  - Elevation, extension, and immobilization
  - Transfusions if indicated
  - Consider antivenoms

Clinical Effects

- Local tissue damage
- Coagulation effects
- Platelet effects
- Neurotoxicity

Source: Ruha A, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

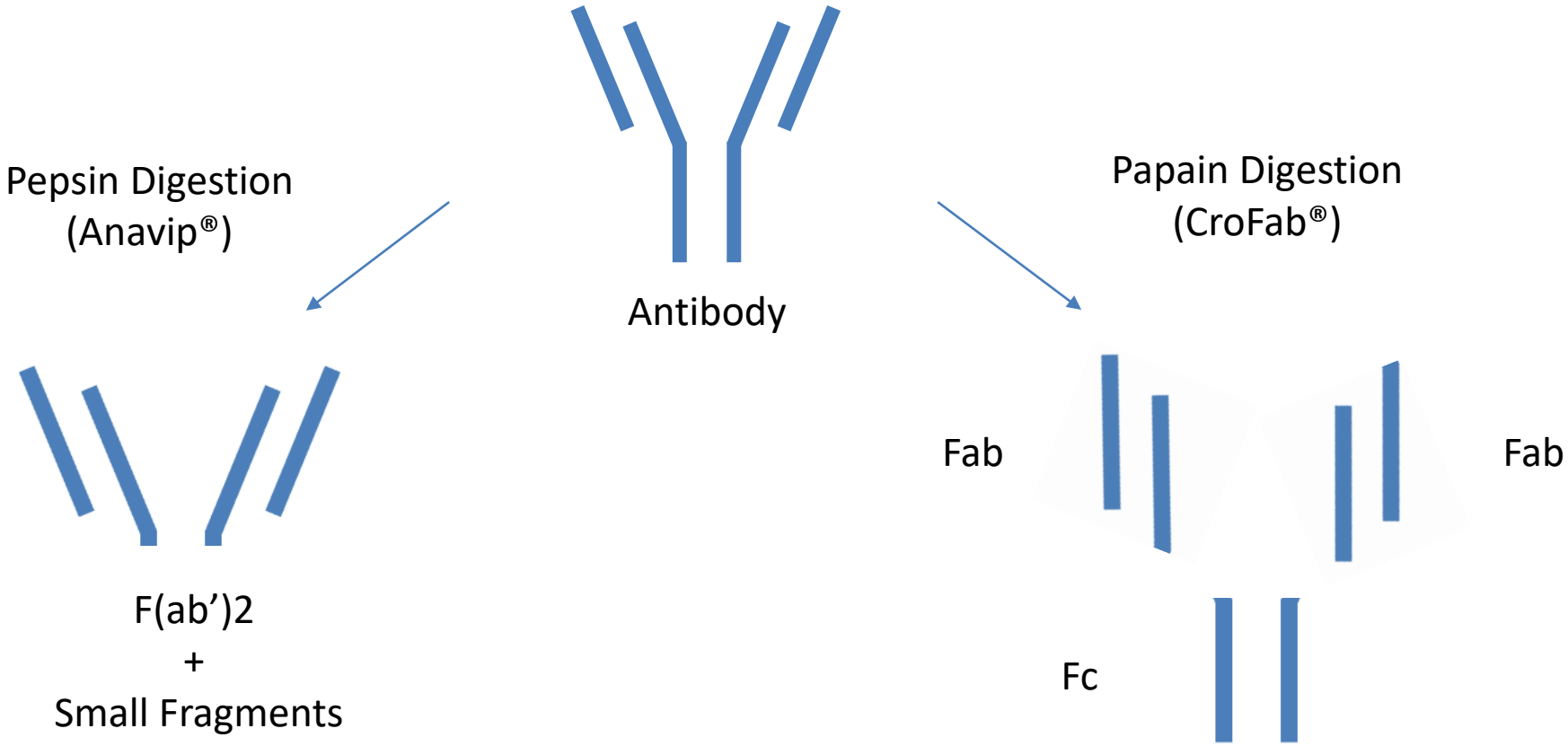
Antivenoms

- Indications: moderate-to-severe envenomation
  - Progressive swelling
  - Significant coagulopathy and/or thrombocytopenia
  - Neuromuscular toxicity
  - Hemodynamic compromise

Brand	Generic	Venom
CroFab®	*Crotalidae* polyvalent immune fab (ovine)	North American *Crotalidae*: Western and Eastern diamondback rattlesnakes (*Crotalus atrox* and *adamanteus*), Mojave rattlesnake (*Crotalus scutulatus*), **and cottonmouths (*Agkistrodon piscivorus*)**
Anavip®	*Crotalidae* immune F(ab')2 (equine)	North American *Crotalidae*: Lancehead (*Bothrops asper*) and tropical rattlesnake (*Crotalus durissus*)
Wyeth® Antivenin (*Micrurus fulvius*)	North American coral snake (*Micrurus fulvius*) antivenin (equine)	Elapidae; *Micrurus fulvius*

Sources: Wyeth® Antivenin (Micrurus fulvius) (equinine). Package insert. Wyeth Laboratories Inc.; 2001.
CroFab® (crotalidae polyvalent immune Fab (ovine)). Package insert. BTG International Inc.; 2017.
Anavip® (crotalidae immune F(ab')2 (equine)). Package insert. Rare Disease Therapeutics, Inc.; 2015.
Pizon AF, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

Pharmacology



Source: Pizon AF, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

Administration

- Reconstitution and further dilution for each antivenom
- Sensitivity testing?
- Dosing and administration
  - Initial slow injection to determine immunogenicity
  - Repeat doses until symptoms controlled (+/- maintenance)

Brand	Initial Dosing	Additional Dosing
CroFab®	4 to 6 vials	Repeat doses until controlled; then 2 vials every 6 hours for 3 doses
Anavip®	10 vials	Repeat doses until controlled; 4 vials as needed for maintenance
Wyeth® Antivenin (*Micrurus fulvius*)	3 to 5 vials	Repeat doses as needed for improvement; no maintenance recommended

Source: Wyeth® Antivenin (Micrurus fulvius) (equinine). Package insert. Wyeth Laboratories Inc.; 2001.
Crofab® (crotalidae polyvalent immune Fab (ovine)). Package insert. BTG International Inc.; 2017.
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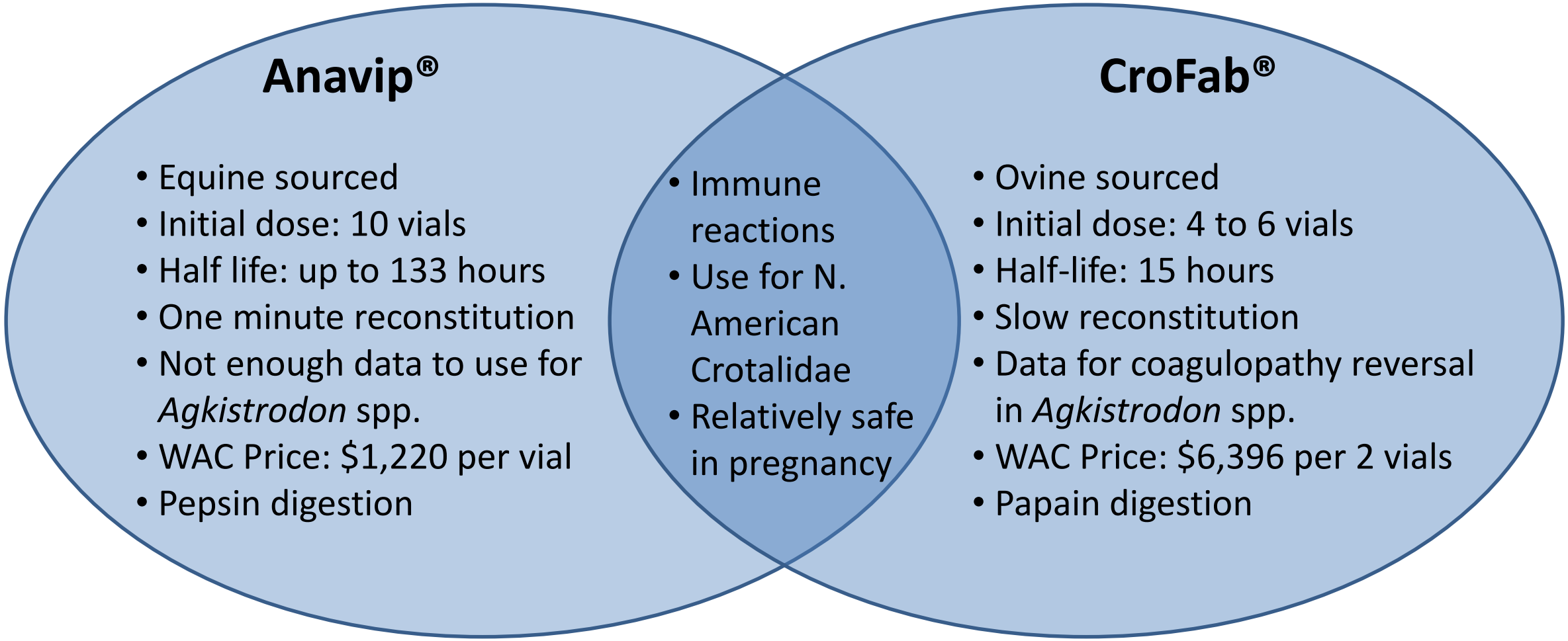
Available Products



Source: Mazer-Amirshahi M, et al. *J Med Toxicol*. 2018;14(2):168-171.
Anavip® (crotalidae immune F(ab')2 (equine)). Package insert. Rare Disease Therapeutics, Inc.; 2015.
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RED BOOK Online. IBM Micromedex [Online database]. Truven Health Analytics/IBM Watson Health; 2021. [cited 2021 Mar 5]. Available from: https://www.micromedexsolutions.com.

Bush, et al.

Comparison of $F(ab')_2$ versus Fab antivenom for pit viper envenomation: A prospective, blinded, multicenter, randomized clinical trial	
Population	Patients presenting for emergency treatment with Crotalinae envenomation aged 2 - 80 years (n= 114)
Intervention	1. Crotalidae equine immune F(ab')2 antivenom (Anavip®) with placebo maintenance 2. Crotalidae equine immune F(ab')2 antivenom (Anavip®) with F(ab')2 maintenance
Comparison	3. Crotalidae ovine polyvalent immune Fab (CroFab®) with Fab maintenance
Outcome	Coagulopathy between end of maintenance dosing and study day 8: 10.3% (Group 1) vs. 5.3% (Group 2) vs. 29.7% (Group 3) **Absolute risk reduction (95% CI): 0.195 (Group 1), 0.245 (Group 2)**

Source: Bush SP, et al. *Clin Toxicol (Phila)*. 2015 Jan;53(1):37-45.

Scorpion Envenomation

- Poison Control Centers calls: 11,000-19,000 (1995 to 2015)
- Southern and Southwestern United States
  - *Centuroides exilicauda* (bark scorpion)
  - *Centuroides viatus*
- Pathophysiology
  - Membrane excitability at neuromuscular junction
  - Repetitive depolarization
  - Catecholamines and acetylcholine release

Sources: Repplinger DJ, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Darracq MA, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2018 May 31. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/niosh/topics/insects/scorpions.html.

C. exilicauda Envenomation: Clinical Presentation

- Intense pain ("tap test") and parasthesias
- Autonomic findings:
  - Hypertension, tachycardia, and diaphoresis
  - Emesis and bronchospasm
- Somatic findings:
  - Restlessness, thrashing
  - Ataxia, fasciculations, opsoclonus
- Symptom onset is immediate

Grade	Findings
I	Pain or parasthesias at sting site
II	Grade I findings + Pain or parasthesias remote from sting site
III	Somatic skeletal neuromuscular dysfunction **OR** Cranial nerve dysfunction
IV	Somatic skeletal neuromuscular dysfunction **AND** cranial nerve dysfunction

Source: Repplinger DJ, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

C. exilicauda Envenomation Treatment

- Supportive and local wound care
  - Airway, breathing, circulation
  - Irrigation and washing
  - Pain management
  - Tetanus prophylaxis
- Corticosteroids, antihistamines, calcium
  - Considered but unproven benefit
- Antivenom for severe reactions
  - Grades III and IV

Sources: Kang AM, et al. *J Med Toxicol*. 2017 Jun;13(2):158-165.
Repplinger DJ, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

Antivenom: Anascorp®

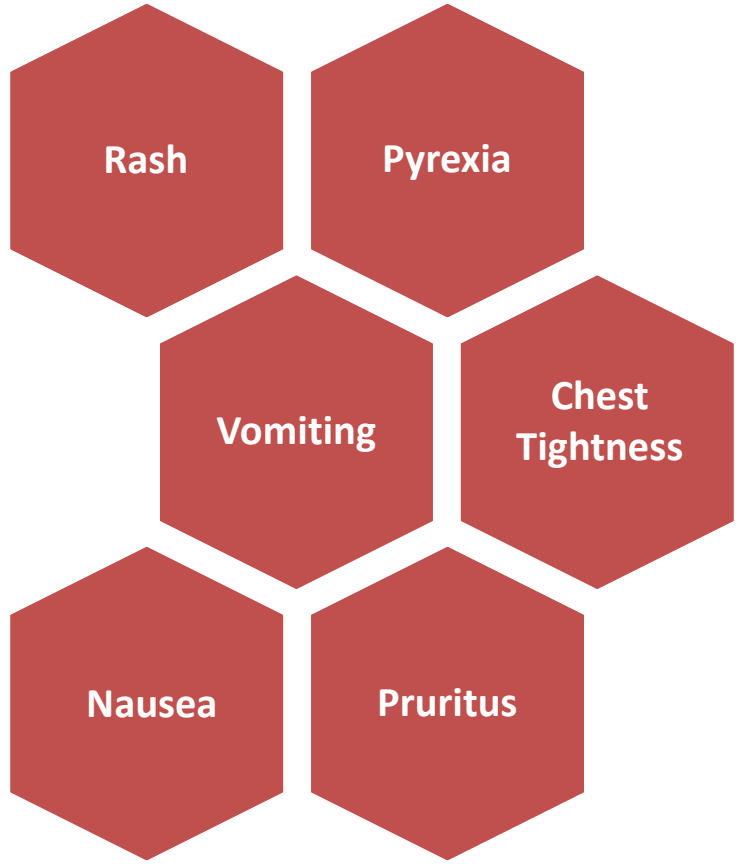
- Indications: severe envenomation or intractable pain
  - Neurotoxicity common in children <10 years

Antivenom for Critically Ill Children with Neurotoxicity from Scorpion Stings	
Population	Randomized, double blind study of children 6 months to 18 years of age admitted to pediatric intensive care with clinically significant scorpion envenomation signs (n= 15)
Intervention	Three vials Anascorp® administered intravenously (n= 8)
Comparison	Three vials of placebo administered intravenously (n= 7)
Outcome	**Resolution of Clinical Syndrome within 4 Hours:** Anascorp® (0%) vs. Placebo (86%) **p=0.001** **Mean Total Midazolam Dose (mg/kg):** Anascorp® (0.07 ± 0.1) vs. Placebo (4.61 ± 5.76); **p=0.01** **Mean Venom Plasma Levels at 4 Hours (ng/mL):** Anascorp® (0 ± 0) vs. Placebo (1.8 ± 1.9); **p=0.03**

Sources: Boyer LV, et al. *N Engl J Med*. 2009 May 14;360(20):2090-8.
Repplinger DJ, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Darracq MA, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

Anascorp®

- Reconstitution and dilution required
- Intravenous injection over 10 minutes
  - One vial neutralizes 150 mouse LD_{50}
  - FDA approved dose: 3 vials
  - Additional vials over 30- to 60- minutes each
- Warnings: hypersensitivity, serum sickness
  - Equine origin
- Cost: $3,750



Sources: Darracq MA, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Anascorp® (centuroides (scorpion) immune F(ab')2 (equine) injection). Package insert.Rare Disease Therapeutics, Inc.; 2020.

Coorg, et al.

Clinical Presentation and Outcomes Associated with Different Treatment Modalities for Pediatric Bark Scorpion Envenomation	
Population	Retrospective cohort of children (n=156) with Grades III or IV scorpion envenomation in Phoenix Children's Hospital Emergency Department (September 2011 – March 2014)
Intervention	1. 1- to 2-vial initial Anascorp® dose (n= 82)
Comparison	2. 3-vial initial Anascorp® dose (n= 16) 3. Supportive care only (n= 58)
Outcome	**Length of Stay (min):** Group 1 (259) vs. Group 2 (253) vs. Group 3 (261); **p=0.839** **Hospital Admission:** Group 1 (3.4%) vs. Group 2 (0%) vs. Group 3 (8.5%); **p=0.167** **Mechanical Ventilation:** Group 1 (2.4%) vs. Group 2 (0%) vs. Group 3 (0.5%); **p=0.607** **Aspiration:** Group 1 (2.4%) vs. Group 2 (0%) vs. Group 3 (0.5%); **p=0.607**

Source: Coorg V, et al. *J Med Toxicol.* 2017 Mar;13(1):66-70.

Latrodectus mactans Envenomation

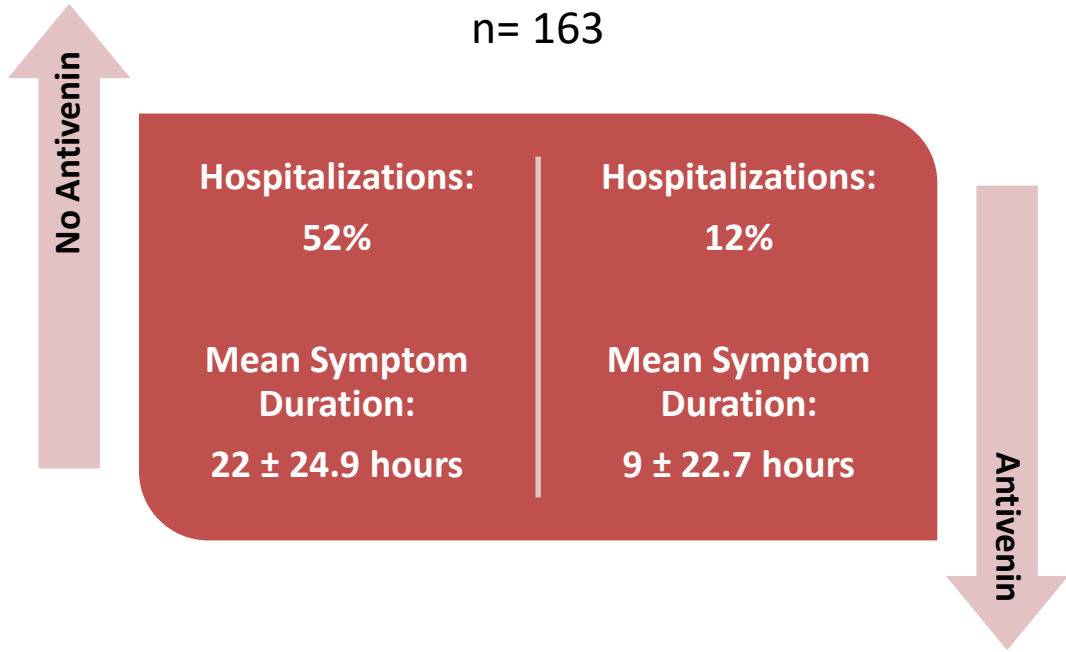
- Poison center calls: 40,000 in past 20 years
- Venom pathogenesis: 7 active components
- Grading system of severity
- Symptoms: gradually resolve over 2 to 3 days
  - Severe pain (bite site, abdominal, back)
  - Muscle cramping
  - Hypertension, tachycardia, tachypnea
- Treatment: symptomatic
  - Consider antivenom?

Sources: Offerman SR, et al. *Perm J*. 2011 Summer;15(3):76-81.
Repplinger DJ, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.
Centers for Disease Control and Prevention. [Internet]. Atlanta: CDC; 2018 May 31. [cited 2021 Jan 29]. Available from: https://www.cdc.gov/niosh/topics/spiders/types.html.

Antivenin *(Latrodectus mactans)* (equine)

- Indication: refractory severe symptomatic envenomation
- Administration (2.5 mL vial):
  - One vial IM or diluted IV over 15 minutes
  - Consider skin or conjunctival testing
  - Desensitization when life-saving
- Adverse Effects
  - Hypersensitivity reactions
  - Serum sickness

Clark et al.
Retrospective Chart Review
n= 163



Sources: Clark RF, et al. *Ann Emerg Med*. 1992 Jul;21(7):782-7.
Antivenin (*Latrodectus mactans* equine origin). Package insert. Merck Sharp & Dohme Corp.; 2020.
Darracq MA, et al. In: Nelson LS, et al. *Goldfrank's Toxicologic Emergencies, 11*e. New York, NY: McGraw-Hill Education; 2019.

Acquisition

- American Association of Poison Control Centers (AAPCC)
  - **1-800-222-1222**
- Online Antivenom Index
  - Association of Zoos and Aquariums (AZA)
- Manufacturers
  - Anavip®
  - Anascorp®
  - CroFab®

Knowledge Check 2: Pharmacists & Nurses

All of the following are differences between CroFab® and Anavip® products EXCEPT:

A. CroFab® is sourced from sheep whereas Anavip® is sourced from horses
B. The elimination half-life of Anavip® is longer than that of CroFab®
C. Anavip® has a significantly higher rate of immune reactions than CroFab®
D. CroFab® is approved for all North American Crotalids including *Agkistrodon* spp. whereas Anavip® is not

Knowledge Check 2: Pharmacists & Nurses

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D. CroFab® is approved for all North American Crotalids including *Agkistrodon* spp. whereas Anavip® is not

Knowledge Check 3: Pharmacists & Nurses

True or False: *Latrodectus mactans* antivenin is indicated in severe black widow envenomations presenting with muscle cramping, diaphoresis, and heart attack prior to the use of opiates and muscle relaxants.

A. True
B. False

Knowledge Check 3: Pharmacists & Nurses

True or False: *Latrodectus mactans* antivenin is indicated in severe black widow envenomations presenting with muscle cramping, diaphoresis, and heart attack prior to the use of opiates and muscle relaxants.

A. True

B. **False**

Knowledge Check 3: Technicians

Which of the following pharmacologic agents does not require reconstitution prior to administration?

A. Anascorp® (*Centruroides* (scorpion) immune f(ab')2 (equine) injection)
B. KEDRAB™ (Rabies immune globulin (human))
C. CroFab® (*Crotalidae* polyvalent immune fab (ovine))
D. Anavip® (*Crotalidae* immune f(ab')2 (equine))

Knowledge Check 3: Technicians

Which of the following pharmacologic agents does not require reconstitution prior to administration?

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B. KEDRAB™ (Rabies immune globulin (human))

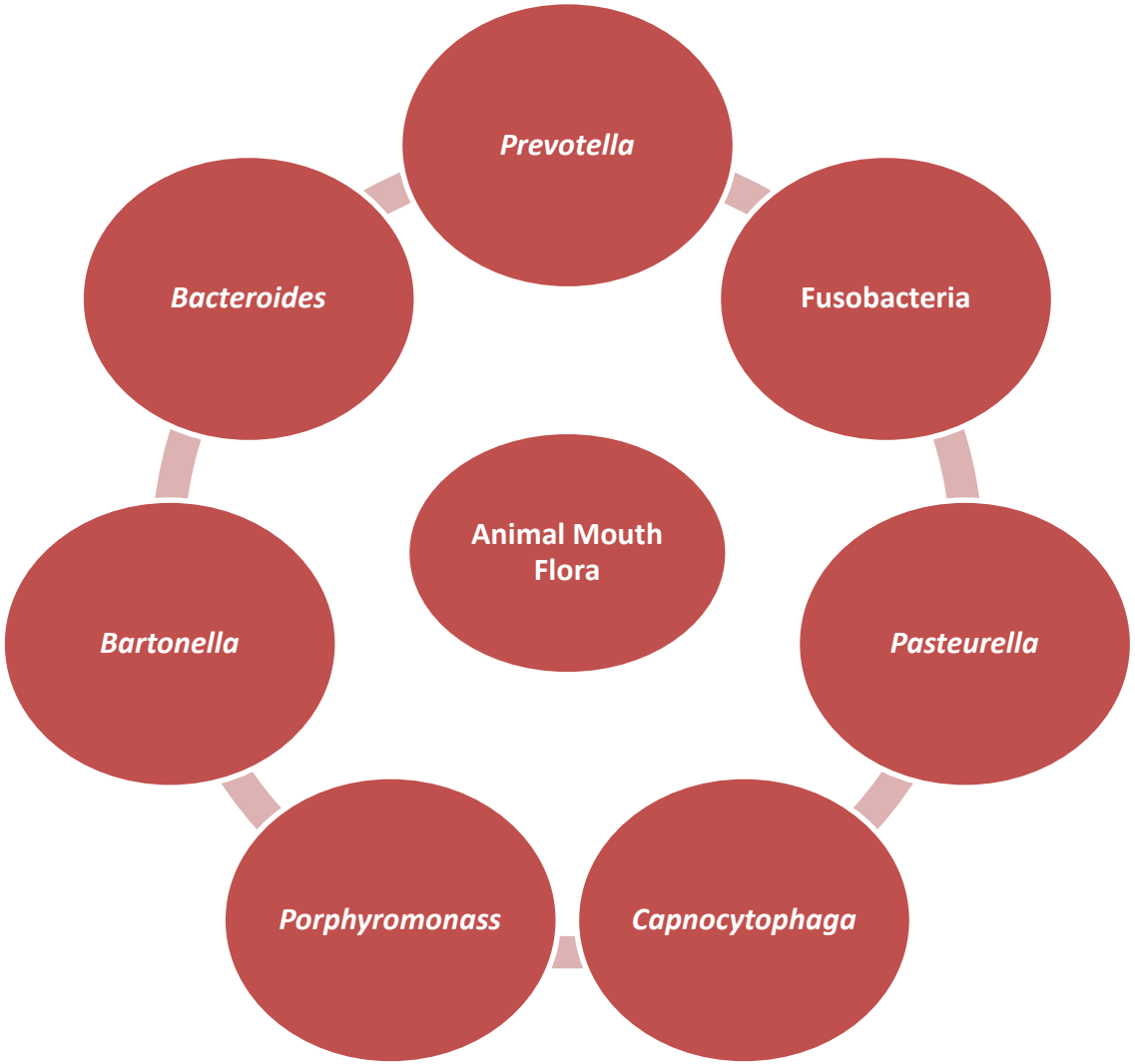
C. CroFab® (*Crotalidae* polyvalent immune fab (ovine))

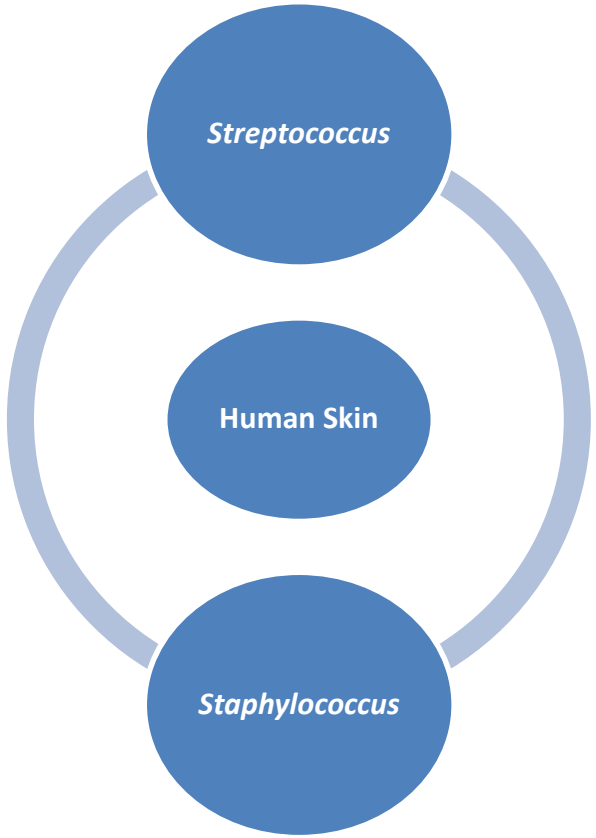
D. Anavip® (*Crotalidae* immune f(ab')2 (equine))

RWJBarnabas HEALTH

SKIN AND SOFT TISSUE INFECTION: ANIMAL BITES

Considerations: Pathogenic Organisms





Sources: Goldstein EJ, et al. *J Clin Microbiol*. 1978 Dec;8(6):667-72.
Talan DA, et al. *N Engl J Med*. 1999 Jan 14;340(2):85-92.
Butler T. *Eur J Clin Microbiol Infect Dis*. 2015 Jul;34(7):1271-80.
Goldstein EJ. *J Med Microbiol*. 1998 Feb;47(2):95-7.

Preemptive Early Antimicrobial Therapy

- Duration: 3 to 5 days
- Wound closure:
  - Avoid unless on face
  - Thorough irrigation and debridement
- Tetanus toxoid status
  - Tetanus, diphtheria, and pertussis (Tdap) preferred

Indications

- Immunocompromised state
- Asplenia
- Advanced liver disease
- Pre-existing new edema to bite site
- Moderate-to-severe, hand, or face injuries
- Injury penetration: periosteum or joint capsule

Source: Stevens DL, et al. *Clin Infect Dis*. 2014 Jul 15;59(2):e10-52.

Animal Exposure Antimicrobials

Animal	Pathogens*	Exposure	Primary Adult Regimen in Normal Renal Function
Dog	Pasteurella, Capnocytophaga, Staph, anaerobes	Bite	Amoxicillin-clavulanate 875/125 mg by mouth twice daily
Cat	Pasteurella, Capnocytophaga, Bartonella, Staph, anaerobes		
Rat	Streptobacillus moniliformis, Spirillum minus		
Pig	Actinobacillus suis, Pasteurella, Gram positive cocci, Gram negative bacilli, anaerobes		
Horse	Prevotella, Actinobacillus, Neisseria, Pasteurella, Staph, Strep, anaerobes, Campylobacter, Yersinia		
Camel	Staph, Strep, Bacillus, Pseudomonas, Aeromonas, Pasteurella, Actinobacillus	Bite	Piperacillin-tazobactam 4.5 grams intravenous every 8 hours
Bear	Staph, viridans strep, Aeromonas, Neisseria, Enterococcus, Enterobacteriaceae		
Monkey	Viral: Herpes simiae (Herpes B) Bacterial: Haemophilus, Fusobacterium, Peptostreptococcus, Actinomyces, Eikenella, Campylobacter, Capnocytophaga, Strep	Bite	Amoxicillin-clavulanate 875/125 mg by mouth twice daily **AND** Valacyclovir 1 gram by mouth every 8 hours (14 days)
Cat	Bartonella henselae	Scratch	Azithromycin 500 mg by mouth once, then 250 mg for 4 days

*Not all-encompassing

Source: Saag MS. *The Sanford Guide to Antimicrobial Therapy 2020*: Antimicrobial Therapy, Incorporated; 2020.

RWJBarnabas HEALTH

CONCLUSION

Conclusion

- Animal bites, stings, and other unwanted exposures burden millions of Americans each year.

Post-exposure therapies are available but not always indicated.

- Appropriate use of such therapies can maximize patient outcomes and minimize both cost and harm.

Acknowledgements

Patrick Bridgeman, PharmD, BCPS

Clinical Assistant Professor Ernest Mario School of Pharmacy

PGY-2 Emergency Medicine Pharmacy Residency Program Director

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Thank You!

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