Rattlesnake Envenomation in Arizona

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Clinical Education Director
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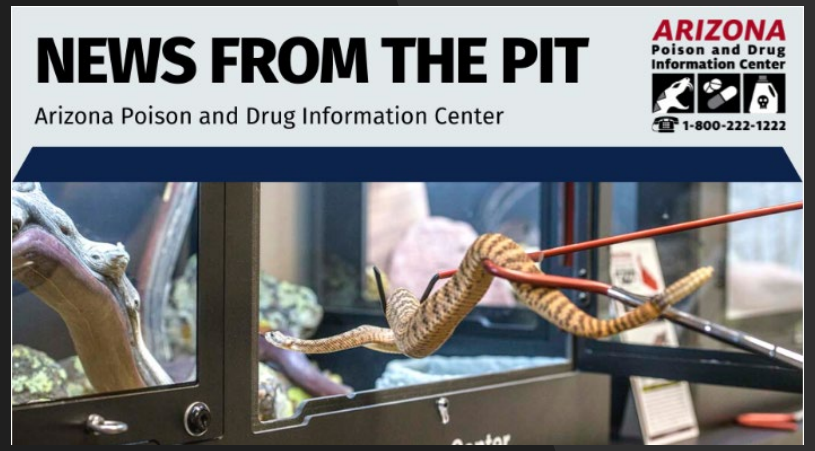
1-800-222-1222



https://azpoison.com/content/news-pit

- **Department of Health and Human Services**
  - AZ Rev Stat § 36-1161 (2015)
  - Poison Prevention
  - **Data Collection** IRB #2108137685
  - **Education**
  - **Management of Poisoned Persons**
  - Drug Information Services

- **Staff Members**
  - Medical Director — Mazda Shirazi
  - Managing Director — Steven Dudley
  - Clinical Education Director — **Geoffrey Smelski**
  - Mother to Baby Director — Chris Stallman
  - Public Health Educators
  - Specialists in Poisoning Information
  - Toxicology Fellowship
  - Pharmacist Internship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Rattlesnake Features

- Triangular Head
- Elliptical Pupils
- Heat Sensing Pits

- Fangs
- Forked Tongue

- Rattle
- Ambush Predator

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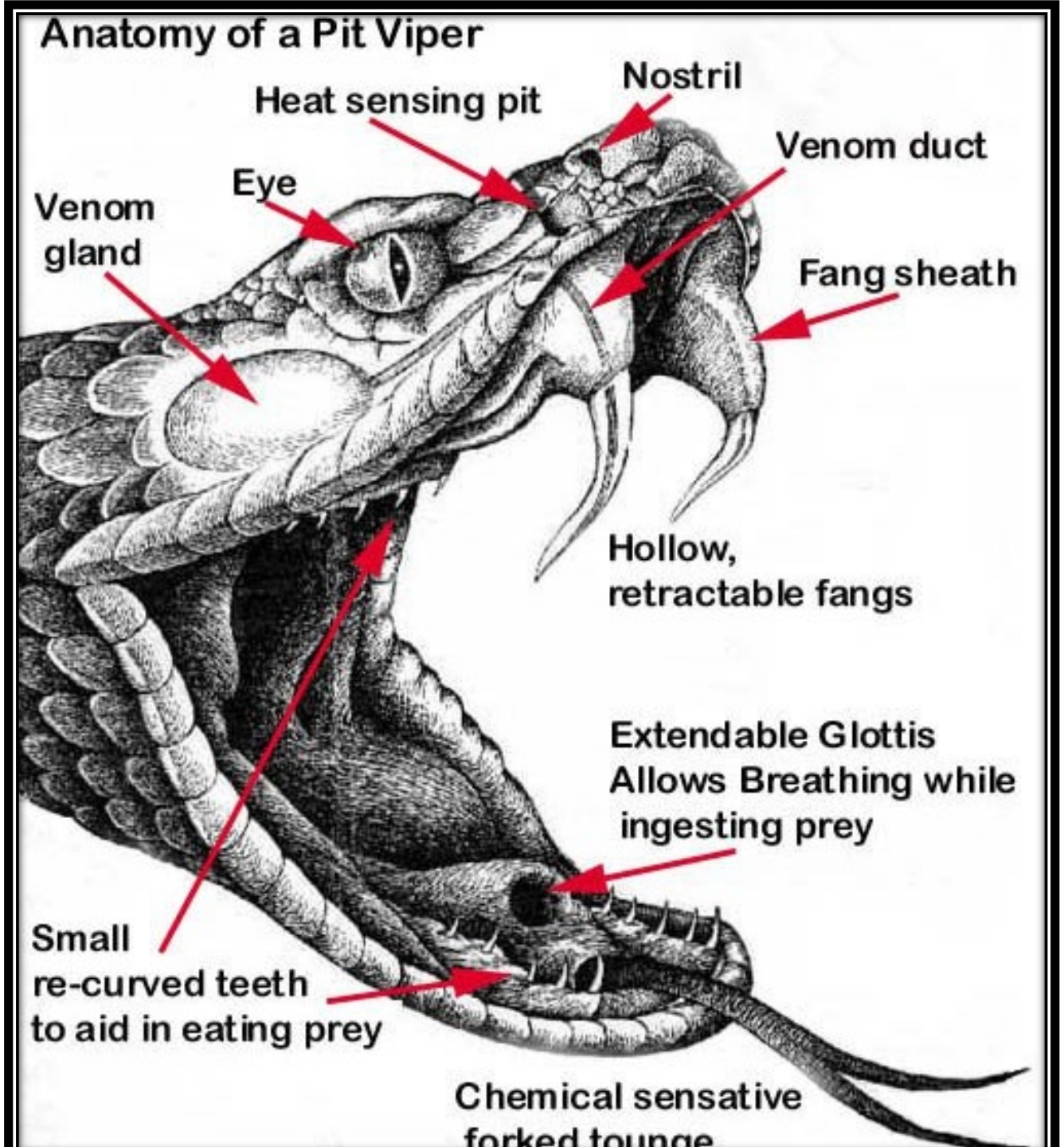
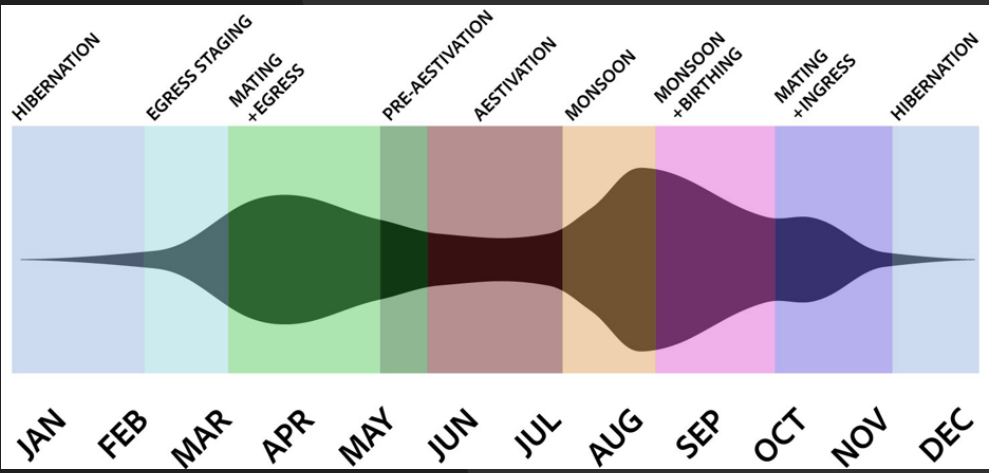
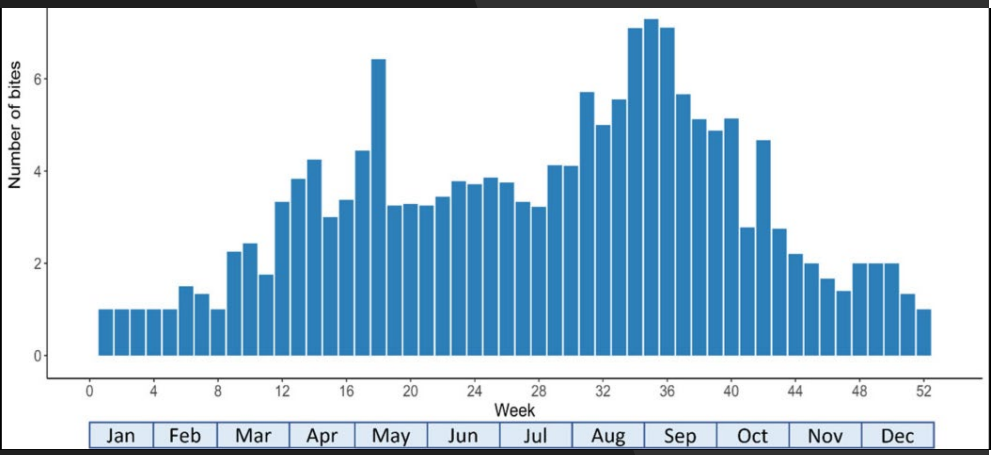


Epidemiology





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- **Demographics**
  - Male Sex 62.0%
  - Age 65+ 26.7%
  - Unaware of Snake **83.0%**
  - Lower Extremity 55.4%
- **Encounter Circumstances**
  - Residential Property **59.0%**
  - 4:00pm – 10:00pm **50.5%**
  - Summer Months 47.2%
- **Disease Burden**
  - Bites per Year 250 - 300
  - Disability at 14 Days **65.3%**
  - Psychiatric Sequelae **33% - 40%**
  - Avg Hospital Bill $120,000

Rattlesnake Envenomation 01/01/2017 – 12/31/2021

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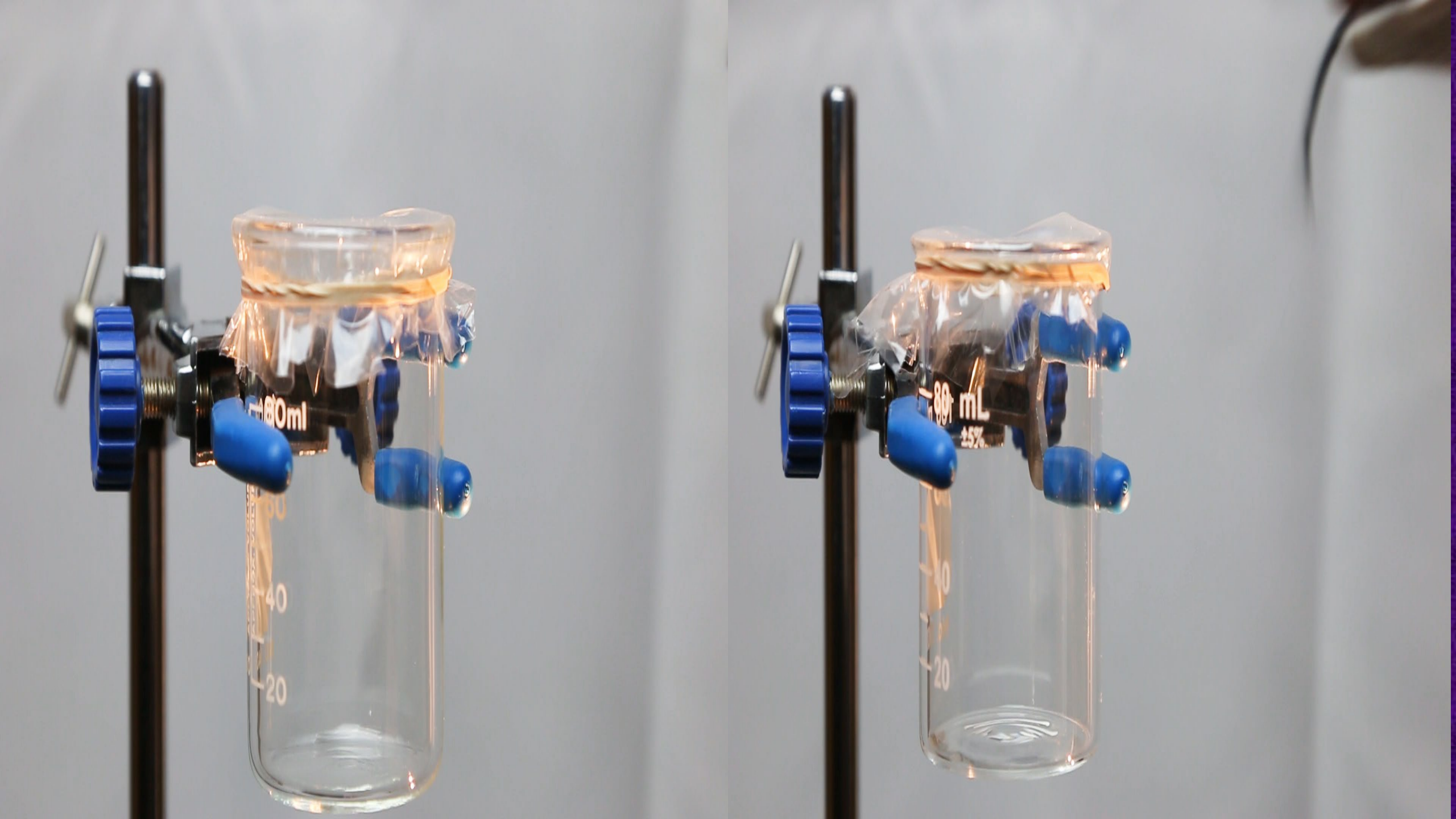
Age Groups	Children < 12 yr (n = 57)	Adolescent 12-17 yrs (n = 23)	Adults 18-39 yrs (n = 128)	Middle Aged 40-64 yrs (n = 214)	Older Adults ≥ 65 yrs (n = 154)	Total All Ages (n = 576)
Wound Healing, No. (%)						
Antibiotics	5 (8.8)	2 (8.7)	24 (18.8)	33 (15.4)	23 (14.9)	87 (15.1)
Necrotic Debridement	2 (3.5)	0 (0.0)	3 (2.3)	6 (2.8)	2 (1.3)	13 (2.3)
Surgical Repair/Amputation	1 (1.8)	0 (0.0)	3 (2.3)	3 (1.4)	1 (0.6)	8 (1.4)
Day 7 – Full Recovery	16 (28.1)	1 (4.3)	16 (12.5)	16 (7.5)	9 (5.8)	58 (10.1)
Day 7 – Disability Confirmed	41 (71.9)	21 (91.3)	106 (82.8)	185 (86.4)	144 (93.5)	497 (86.3)
Day 14 – Full Recovery	29 (50.9)	8 (34.8)	40 (31.3)	40 (18.7)	45 (29.2)	162 (28.1)
Day 14 – Disability Confirmed	27 (47.4)	13 (56.5)	75 (58.6)	154 (72.0)	107 (69.5)	376 (65.3)
Day 90 – Full Recovery	39 (68.4)	16 (69.6)	67 (52.3)	96 (44.9)	87 (56.5)	305 (53.0)
Day 90 – Disability Confirmed	8 (14.0)	2 (8.7)	31 (24.2)	61 (28.5)	49 (31.8)	151 (26.2)
Day 180 – Full Recovery	42 (73.7)	17 (73.9)	70 (54.7)	108 (50.5)	102 (66.2)	339 (58.9)
Day 180 – Disability Confirmed	1 (1.8)	0 (0.0)	11 (8.6)	20 (9.3)	15 (9.7)	47 (8.2)

Full Recovery: Patient Reported Resolution of all Pain, Swelling, and Functional Impairment.


80ml
60
40
20
80 mL
±5%
60
40
20

Envenomation

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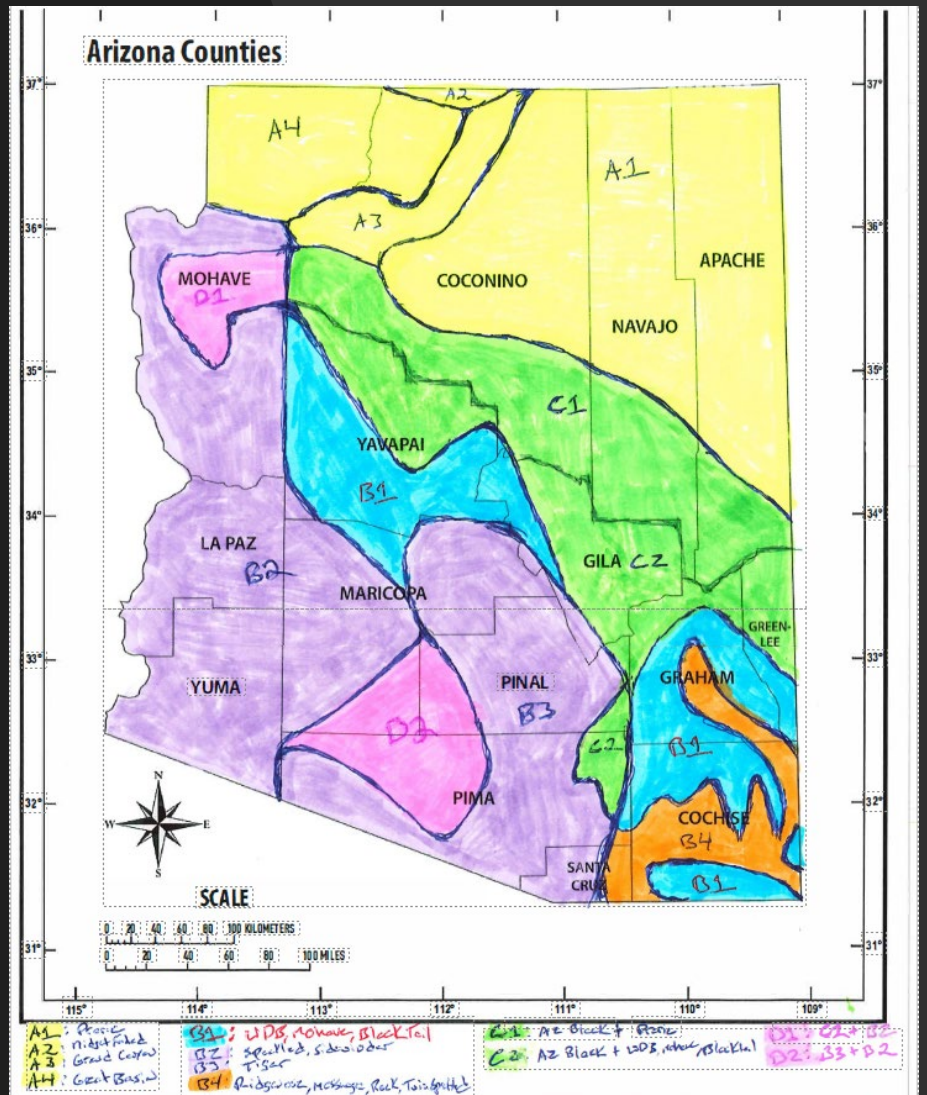
Venom Composition

- Numerous Uniquely Acting Toxins
- Varies Between & Within Species

- **Deposition**
  - Subcutaneous (usually)
  - Toxins Initially “Inactive”
- **Low MW Toxins Absorbed into Circulation**
  - Rapid Onset of Systemic Effects
  - **Severity is Dose Dependent**
  - Departure Activates Higher MW Toxins
- **Higher MW Toxins Act Locally**
  - Variable Onset(s) of Tissue Injury
  - Progressive Inflammatory Injury
- **Targeted Vascular Damage**
  - Delayed Onset (usually)
  - Undermines Injury Containment

Distribution Map



- 15 Rattlesnake Species in AZ
  - 4 Located only in North
  - 4 Isolated in Southeast
  - 7 Broadly Distributed
  - 24 Individual Toxins of Interest (Combined)

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	Bradykinin Potentiating Peptides	Kallikrein-Like	Ficolin	Natriuretic Peptides	Phospholipase A2 β-Neurotoxin	Vespryn (Ohanin)	Nerve Growth Factor	Kunitz-Type Inhibitor	Myotoxin (Defensin)	Three Finger Toxin	Phosphodiesterase	Waparin	Vascular Endothelial Growth Factor	Cysteine-Rich Secretory Protein	Phospholipase B	Phospholipase A2 Cytotoxin	L-Amino Acid Oxidase	5'-nucleotidase	Adenosine Triphosphatase	Arginine Ester Hydrolase	C-Type Lectins / SNACLEC	Thrombin-Like Enzyme	Snake Venom Metalloproteinases	Hyaluronidase
Western Diamondback	Y	Y	-	Y	Y	-	-	-	Y	-	-	-	Y	Y	-	Y	Y	-	-	-	Y	Y	Y	Y
Mohave	Y	Y	-	-	Y	Y	Y	Y	Y	-	Y	-	Y	Y	-	Y	Y	Y	Y	Y	Y	Y	Y	Y
Black-tailed	-	Y	-	-	-	-	-	-	Y	-	-	-	-	-	-	Y	Y	-	-	-	-	Y	Y	Y
Prairie	Y	Y	-	-	Y	Y	-	-	Y	-	Y	-	Y	Y	Y	Y	Y	Y	Y	-	Y	Y	Y	-
Midget Faded	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Y	-	-
Grand Canyon	-	-	-	Y	-	Y	Y	Y	Y	-	-	-	Y	Y	-	Y	Y	-	-	-	Y	Y	Y	Y
Great Basin	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Y	-	-
Southwestern Speckled	-	Y	-	-	Y	-	-	-	-	-	-	-	-	-	-	Y	Y	-	-	-	-	Y	-	-
Sidewinder	Y	-	Y	-	-	Y	Y	-	Y	Y	Y	Y	Y	Y	-	Y	Y	Y	-	-	Y	Y	Y	-
Tiger	-	-	-	-	Y	-	-	-	-	-	-	-	Y	Y	-	Y	-	-	-	-	-	Y	Y	-
Arizona Black	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Y	Y	-
Ridge-nose	-	Y	-	-	-	-	-	-	-	-	Y	-	-	Y	-	Y	Y	-	-	-	Y	Y	Y	-
Rock	-	Y	-	-	-	-	-	-	-	-	Y	-	-	Y	-	Y	Y	Y	-	-	Y	Y	Y	-
Twin-spotted	Y	Y	-	-	-	-	Y	-	-	-	Y	-	-	Y	Y	Y	Y	Y	-	-	Y	Y	Y	-
Massasauga	-	Y	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Y	-	-

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Rattlesnake Envenomation Model

Toxidrome	Signs & Symptoms (Incidence)	Pathology	Toxin	Mass (kDa)
Venom Induced Shock	Angioedema (3.0%), Dyspnea (3.3%), Metallic Taste, Systemic Paresthesia, Syncope (3.3%), Hypotension (5.6%), Bradycardia (8.5%), Chest Pain (2.3%), Erythema (19.6%), Pruritis/Hives (70.8%), Nausea/Vomiting (30.2%), Diarrhea (3.0%)	↑Bradykinin	Bradykinin Potentiating Peptides	1
			Kallikrein-Like	27
		↑Histamine	Ficolin	?
			Natriuretic Peptides	3-4
			Phospholipase A2 β-Neurotoxin	24
Neurotoxicity	Dizzy, Orthostasis (6.4%), Blurry Vision, Salivation, Lacrimation, Diaphoresis (3.8%), Piloerection, Urinary Retention	Autonomic Instability	Vespryn (Ohanin)	?
			Nerve Growth Factor	25-54
			Kunitz-Type Inhibitor	7
	Myokymia (5.2%), Weakness (1.6%), Ptosis	Cholinergic Dysfunction	Myotoxin (Defensin)	4-5.3
			Three Finger Toxin	6-9
Progressive Inflammatory Injury	Pain (33.3%), Edema (47.0%), Functional Impairment (55.2%)	↑Capillary Permeability	Phosphodiesterase	98-120
			Waparin	?
			Vascular Endothelial Growth Factor	25
			Cysteine-Rich Secretory Protein	20-30
	Lymphadenopathy (18.2%), Lymphangitis (4.2%), Renal Injury (3.5%), Rhabdomyolysis (3.8%)	Necrosis	Phospholipase B	?
			Phospholipase A2 Cytotoxin	13-19
			L-Amino Acid Oxidase	50-70
			5'-nucleotidase	53-82
Hemotoxicity	Thrombocytopenia (44.4%), Deep Vein Thrombosis (0.0%), Pulmonary Embolism (0.0%), Stroke (0.2%)	↑/↓ PLT Aggregation	Adenosine Triphosphatase	?
			Arginine Ester Hydrolase	25-36
			C-Type Lectins / SNACLEC	27-29
	Hypofibrinogenemia (36.3%), Hypocoagulation (14.6%)	Consumptive Coagulopathy	Thrombin-Like Enzyme	29-35
			SVMP P-I	20-30
			SVMP P-II (Disintegrin)	30-60 (5-10)
	Blisters/Blebs (34.2%), Ecchymosis (24.0%), Anemia (5.0%)	Vascular Injury	SVMP P-III (Cysteine)	60-100
			Hyaluronidase	52-55, 73

Systemic Toxicity

- Angioedema 3.0%
- SBP < 120 5.6%
- HR < 60 8.5%
- Syncope 3.3%
- Orthostasis 6.4%
- Myokymia 5.2%

Progressive Inflammatory Injury

- Opioid Refractory Pain 33.3%
- Edema > ½ Extremity 47.0%
- Erythema > ½ Extremity 19.6%
- Lymphadenopathy 18.2%
- Lymphangitis 4.2%
- CK > 1,000 U/L 3.8%

Hemotoxicity

- Platelet < 150 k/mm^3 44.4%
- Fibrinogen < 150 mg/dL 36.3%
- INR > 2.0 14.6%
- Hemoglobin < 10.0 mg/dL 5.0%

- Ecchymosis > ½ Extremity 24.0%
- Blisters/Blebs 34.2%

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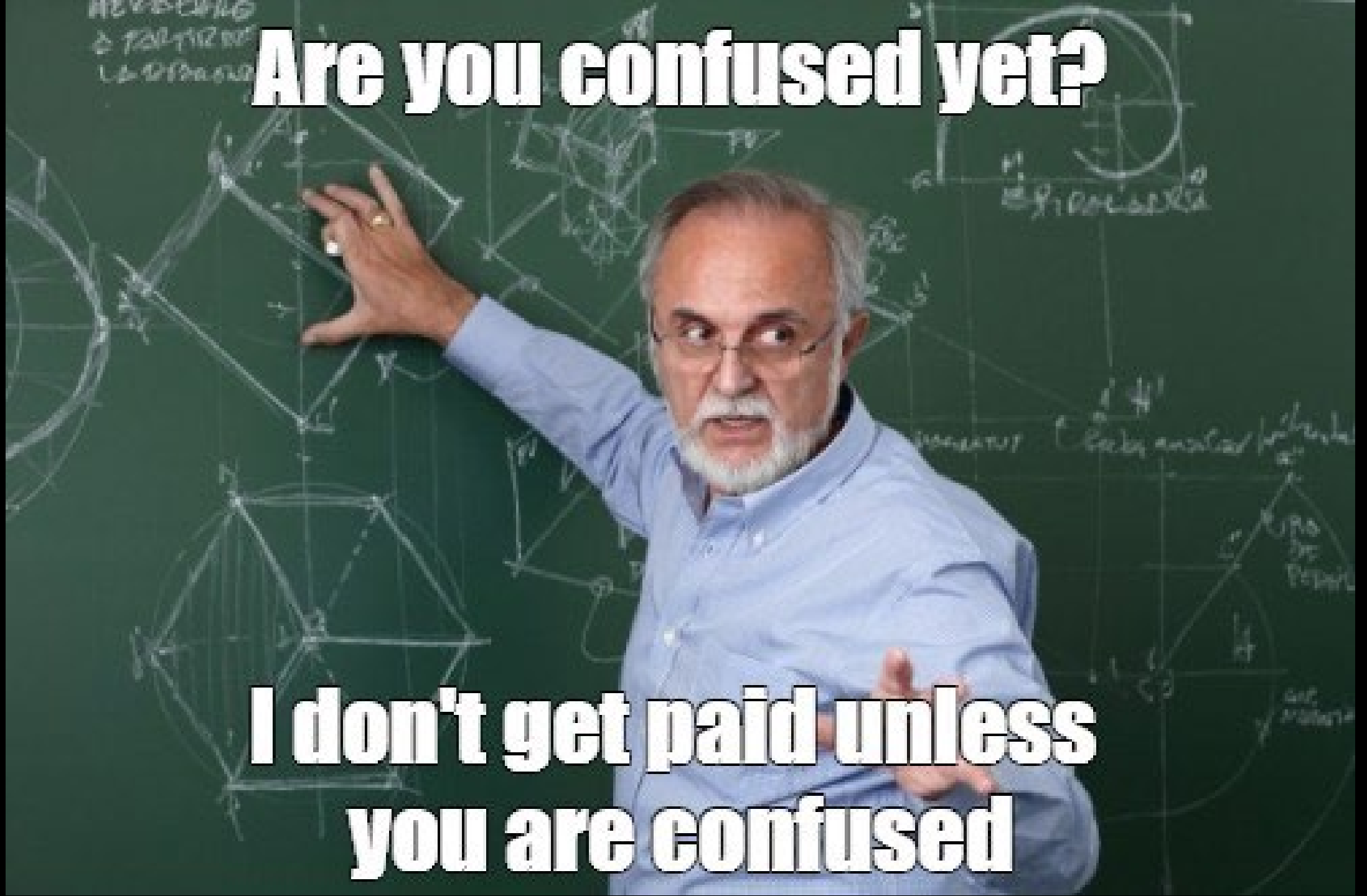
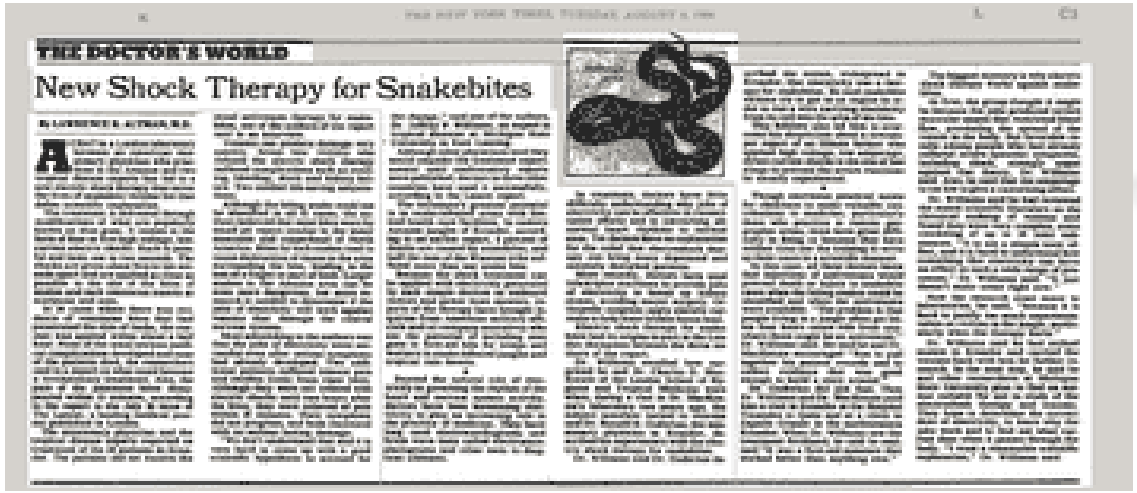
Vascular Injury Onset

Developed on Day 3

Presentation -> 4 Hours Later


Are you confused yet?
I don't get paid unless you are confused

Pre-Hospital Heroics



THE DOCTOR'S WORLD

New Shock Therapy for Snakebites

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- **Recommended by AzPDIC**
  - Just go to Hospital 88.4%
- **Discouraged by AzPDIC**
  - Restriction ("Tourniquet") **9.0%**
  - Removal (Cut, Suck, Extractor) 3.0%
  - Destruction (Electricity, Caustic) 0.2%

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Dry Bite?

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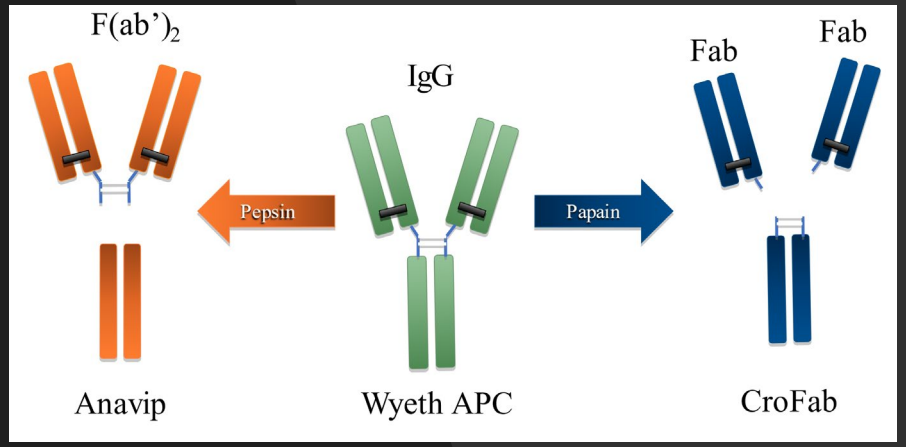
- **Emergency Department**
  - Primary Survey, Establish IV Access
  - Remove Restrictive Clothing / Jewelry
  - Wash Bite Site (Soap & Water)
  - Elevate Extremity
  - Mark Leading Edge q15-30 Min
  - Draw Labs – PLT, Fib, INR, Hgb
- **Envenomation Diagnosis**
  - Local Injury > Mechanical Puncture
  - Fibrinogen < 150 mg/dL or Platelets < 150 k/mm3
  - Dry Bite Diagnosed by EXCLUSION at 12hrs
- **Indication for Antivenom**
  - **All Envenomated Patients**

Antivenom



Antivenom	Crofab	Anavip
Host Animal	Sheep	Horse
FDA Approval	10/02/2000	10/08/2018
Half-life	15 hrs	133 hrs
Avg Total Dose	15 vials	18 vials

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- **"Control" of Envenomation**
  - Edema Progression < 1 inch per hour
  - Laboratory Values Normal or Clearly Improving
- **Loading Doses**
  - Administered q1h until Envenomation Controlled
  - Crofab 4-6 Vials (usually 6)
  - Anavip 10 Vials
- **Maintenance Dosing (Crofab Only)**
  - Administered AFTER Control Obtained
  - Crofab 2 Vials q6h x3 Doses
- **Loss of Control**
  - Crofab 4 Vials, Maintenance Dosing Starts Over
  - Anavip 4 or 10 Vials (usually 10)

Supportive Care

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- **Pain Control**
  - APAP + IV Opioids
  - Benzo's, Lidocaine, Ketamine
  - Toradol for Select Patients -> **Call PCC**

- **Wound Care**
  - Update Tetanus Vaccine
  - Empiric Antibiotics 15.1%
  - Lance or Deroof Blisters/Blebs 5.4%
  - Debridement of Necrotic Tissue 2.3%
  - DVT Prophylaxis for Select Patients -> **Call PCC**

- **Discharge Criteria**
  - Progressive Edema Halted, Fib > 150 & INR < 2.0
  - Stable > 18 Hours
  - PT/OT Assessment -> Walk Assist Device if Needed
  - Follow-up with PCP in 5-10 Days

Outpatient Monitoring

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- AzPDIC follows patients a minimum of every 1-2 days post discharge for 2 weeks.
- Patients are also contacted every 90 days until they report a full recovery.
- A standardized set of questions is asked at each point of contact.

- **Screening for Additional Care Needs**
  - Follow-up with PCP in 5-10 Days
  - Assess Wound Healing (necrosis?, infection?)
  - Ensure Adequate Pain Control
  - Order PT/OT if Needed
  - Consider Need for Surgical Repairs
- **Delayed Onset Complications**
  - Non-Healing Wounds ?
  - Serious Infections 1.4%
  - DVT/PE 0.2%
  - Anemia (Hgb < 7.0) 1.2%
  - Serum Sickness 40.5%

Questions?

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