



Toxicology

Snakes on the great
plains of Oklahoma:

-Managing envenomation-

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Oklahoma Osteopathic Association- 2023

Relevant Disclosure and Resolution

Under Accreditation Council for Continuing Medical Education guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

Claire Epperson, DO

I have no relevant financial relationships or affiliations with commercial interests to disclose.

“Every great story seems to begin with a snake.”

-Nicolas Cage



And snake bite season is here...

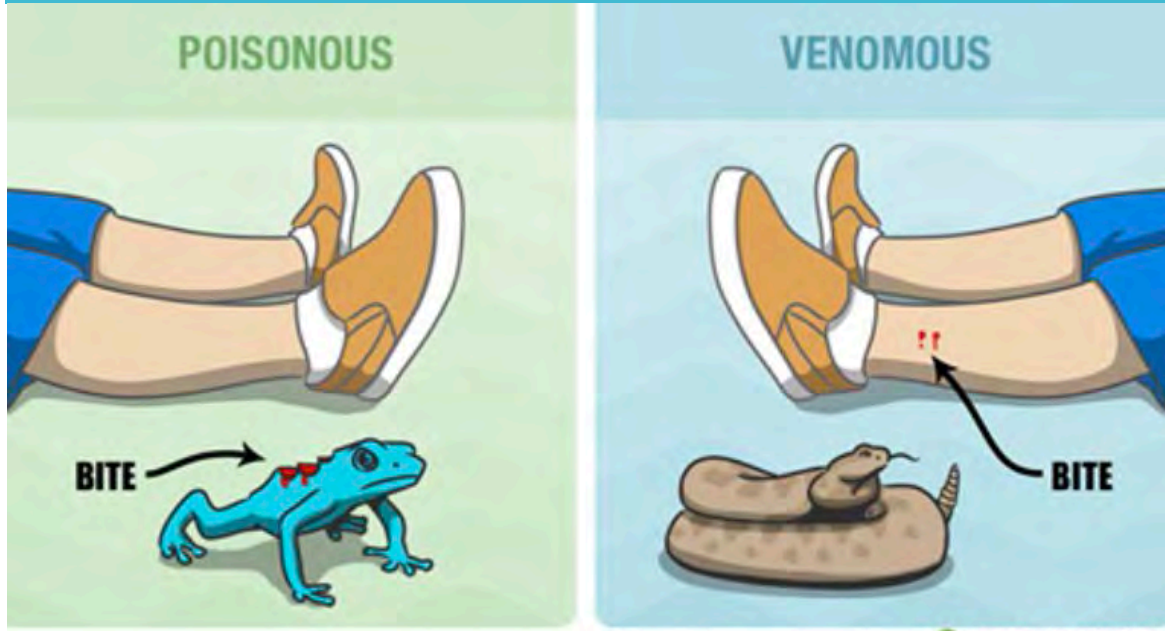
Objectives

1. Understand the difference between the terms venomous and poisonous
2. Discuss the treatment recommendations for the management of pit viper envenomation native to Oklahoma
3. Understand basic dosing differences between the two types of antivenom used in management of N. American Crotalid envenomation





If you eat it and you die, it's *poisonous*
If it eats you and you die, it's *venomous*



SnakeBuddies

Biting back: Boy in India kills cobra with his teeth after being bitten himself

—
Don't try this at home.

Snake guide

- Some of a snake's natural features can help determine if it has venom or not.
- However, it's safest to consider *ALL* snakes potentially dangerous.
- The Oklahoma Poison Center doesn't recommend getting within 5 feet of any snake.



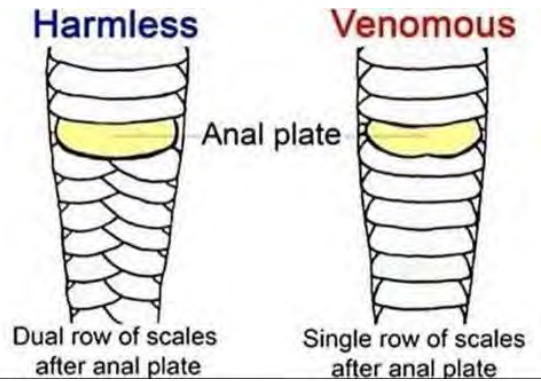
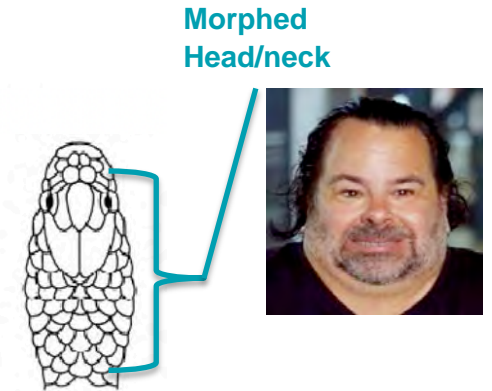
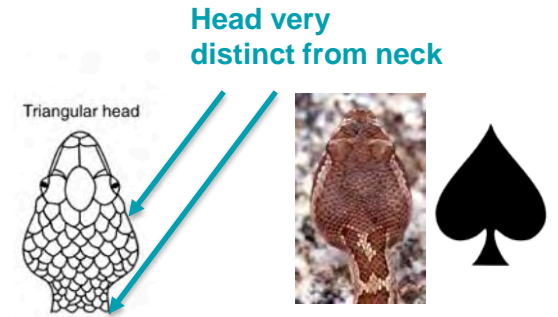
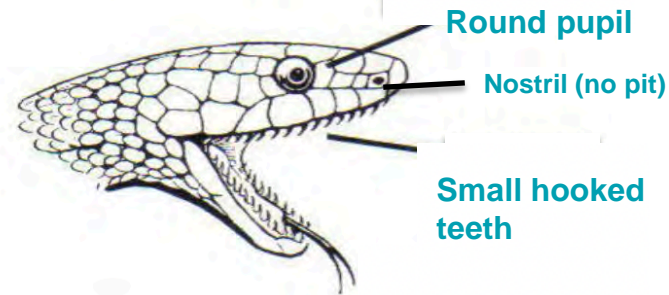
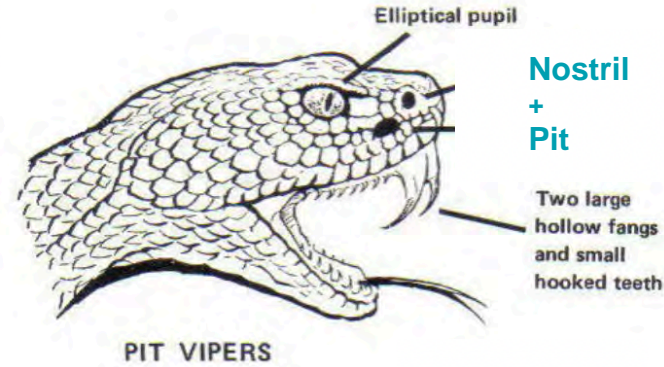
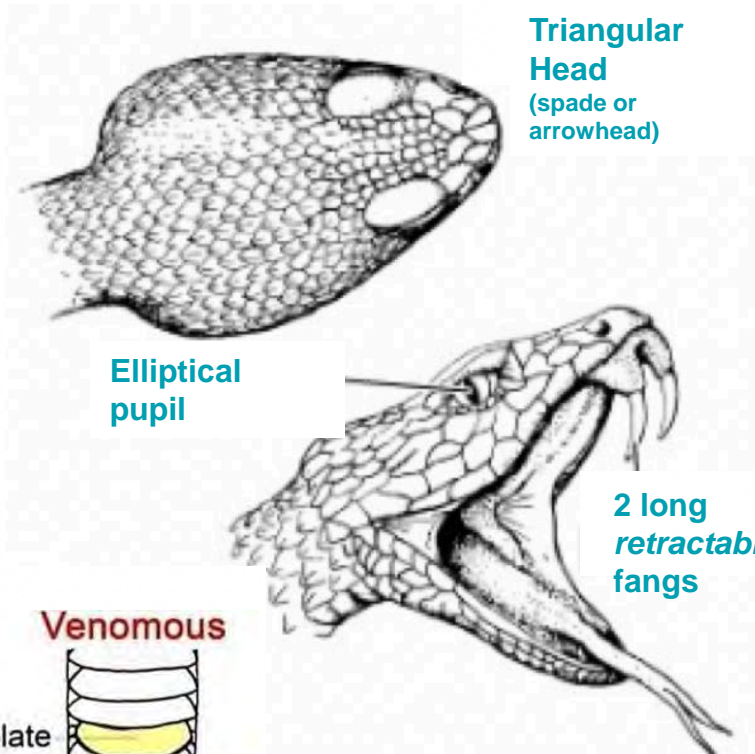
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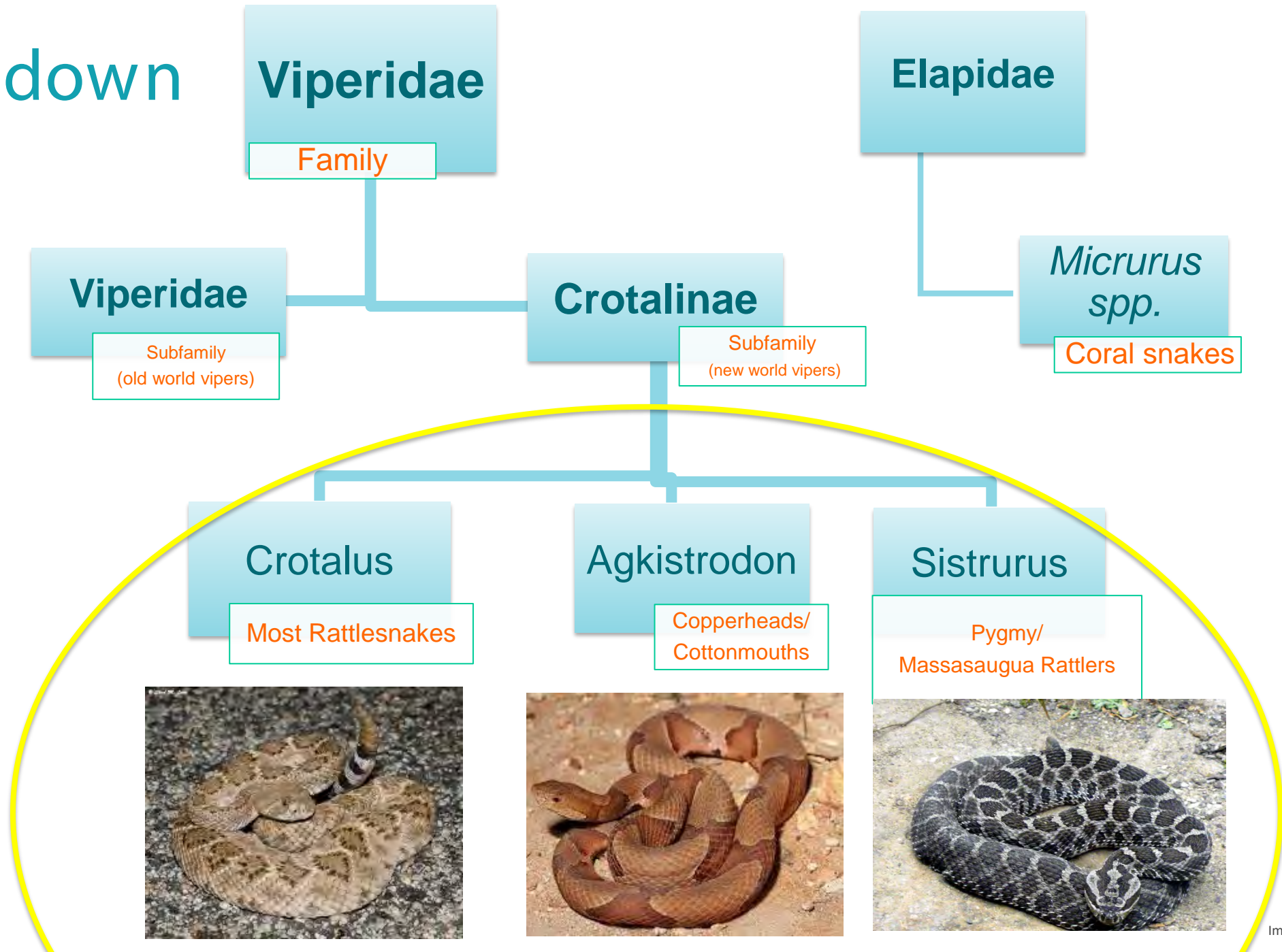


VENOMOUS vs. NON-VENOMOUS

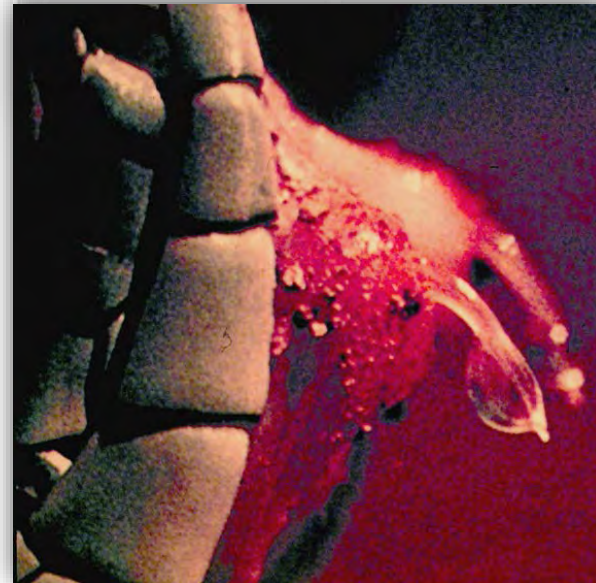
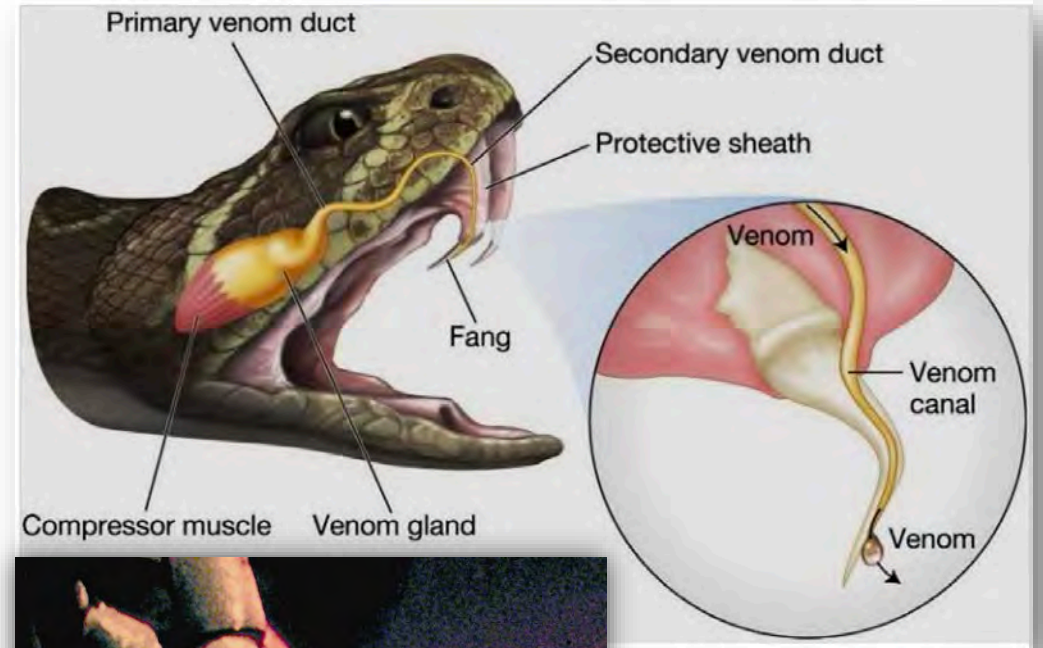
AKA: how to make a herpetologist cringe



Breakdown



Pit Vipers



Venomous Snakes of Oklahoma

NORTHERN COTTONMOUTH



WESTERN PYGMY RATTLESNAKE



COPPERHEAD



PRARIE RATTLESNAKE



WESTERN MASSASAUGA RATTLESNAKE



TIMBER RATTLESNAKE



WESTERN DIAMONDBACK RATTLESNAKE



COPPERHEAD

(*Agkistrodon contortrix*)

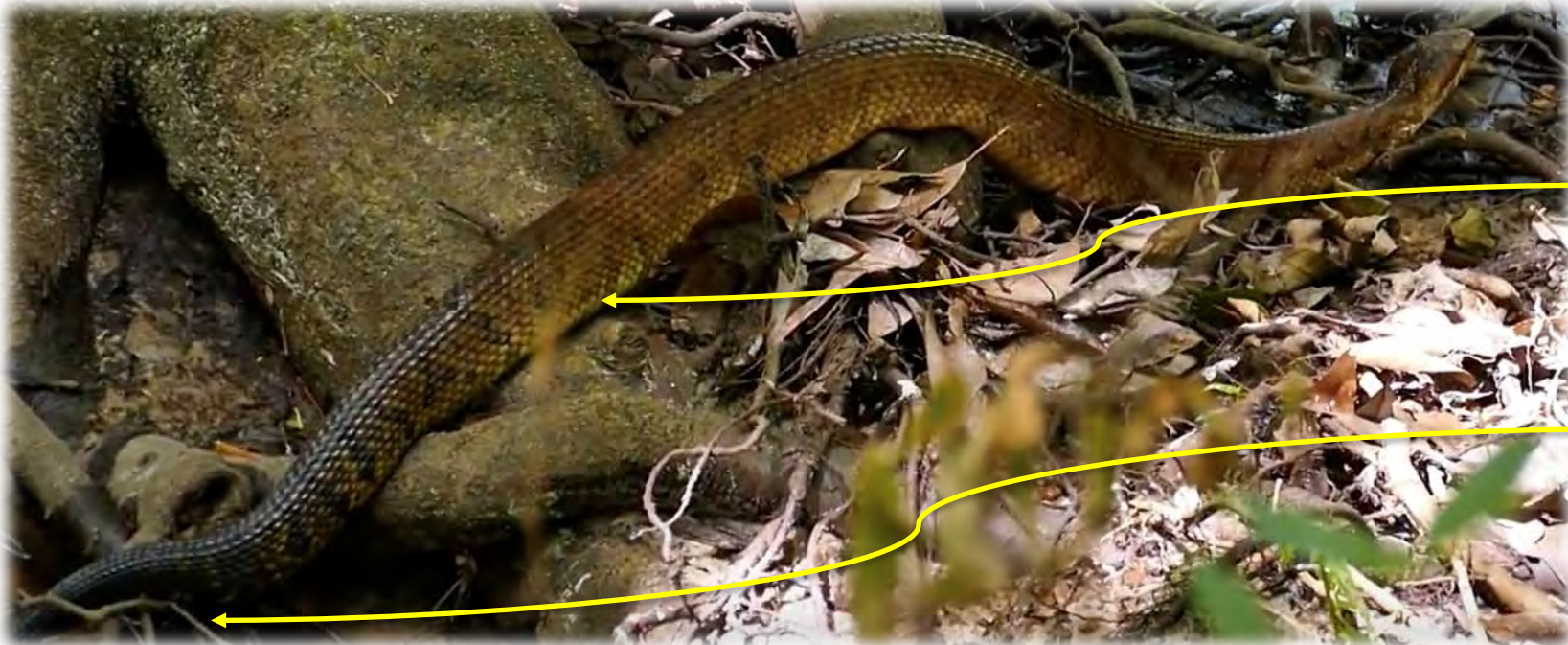
Narrow, often touching apices (Hourglass shape)



Image slide: Nancy Onisko, DO



Pattern of wide, triangular base



**BIG HUGE
FAT BODY**

**STUMPY
TAIL**

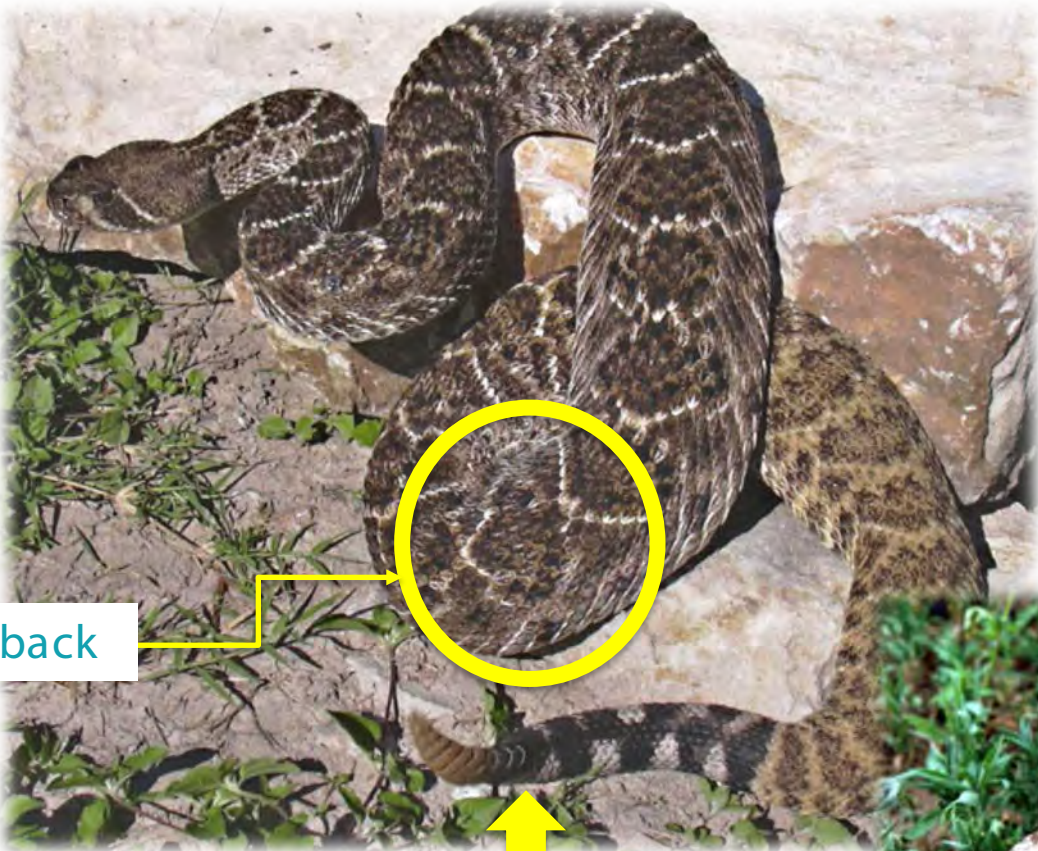
COTTONMOUTH

AKA WATER MOCCASIN
(*Agkistrodon piscivorus*)



Image slide: Nancy Onisko, DC

RATTLE SNAKES



Diamondback



CLASSIC Western Diamondback
BLACK/WHITE STRIPED TAIL



TIMBER RATTLER



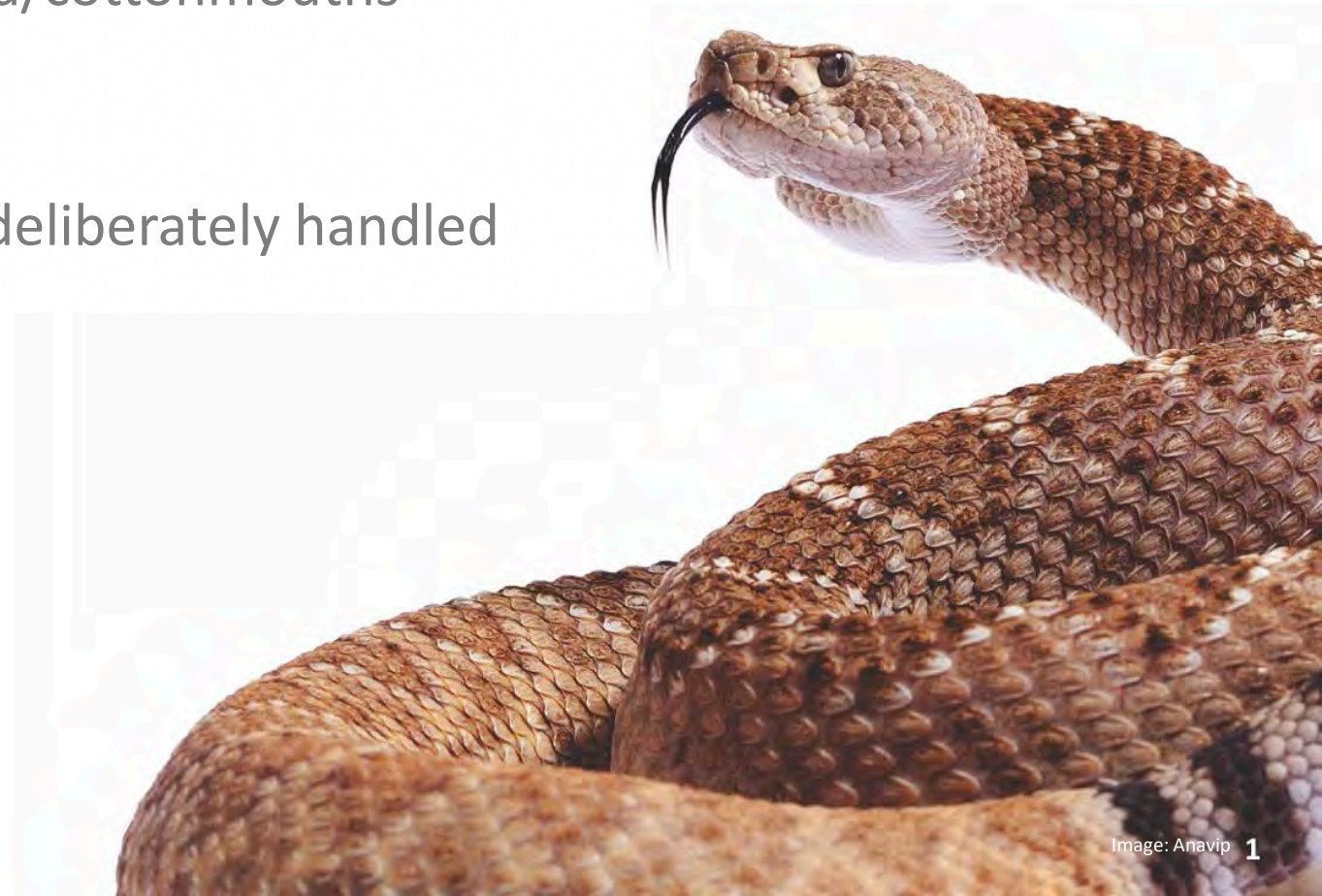
Image slide: Nancy Onisko, DO

Often w/ vertical brown stripe down the back and almost chevron pattern of stripes



BACKGROUND

- 5000+ bites from native venomous species reported to US Poison Centers.
- Majority from pit vipers
- 50% rattlesnakes, 50% copperhead/cottonmouths
- < 10 deaths/yr
- 75% male, 10-15% children
- > 50% occur when snake is being deliberately handled



Clinical Presentation of envenomation

- Highly variable depending on
 - Amt. and potency deposited (defensive vs predatory bite)
 - Location of bite
 - Pt. comorbidities
- Severity: Rattlesnake > Cottonmouth > Copperhead
- Sx onset c/b delayed 8-10 hrs

Once you see the envenomation progressing,

Do not dither!

- Don't delay taking action.
- Be decisive.
- If unsure what to do, call poison center.

- Think of snakebites like a fire:
 - If contained & treated, resources are saved & damage prevented.
 - If delayed, it consumes resources (antivenom) to extinguish and causes more damage.



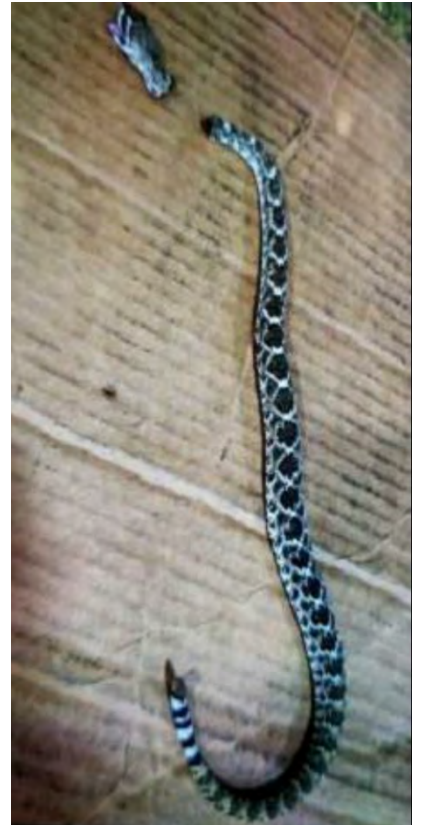
Snakes & medicine go way back...



So how do we guide treatment decisions?



Not like this...



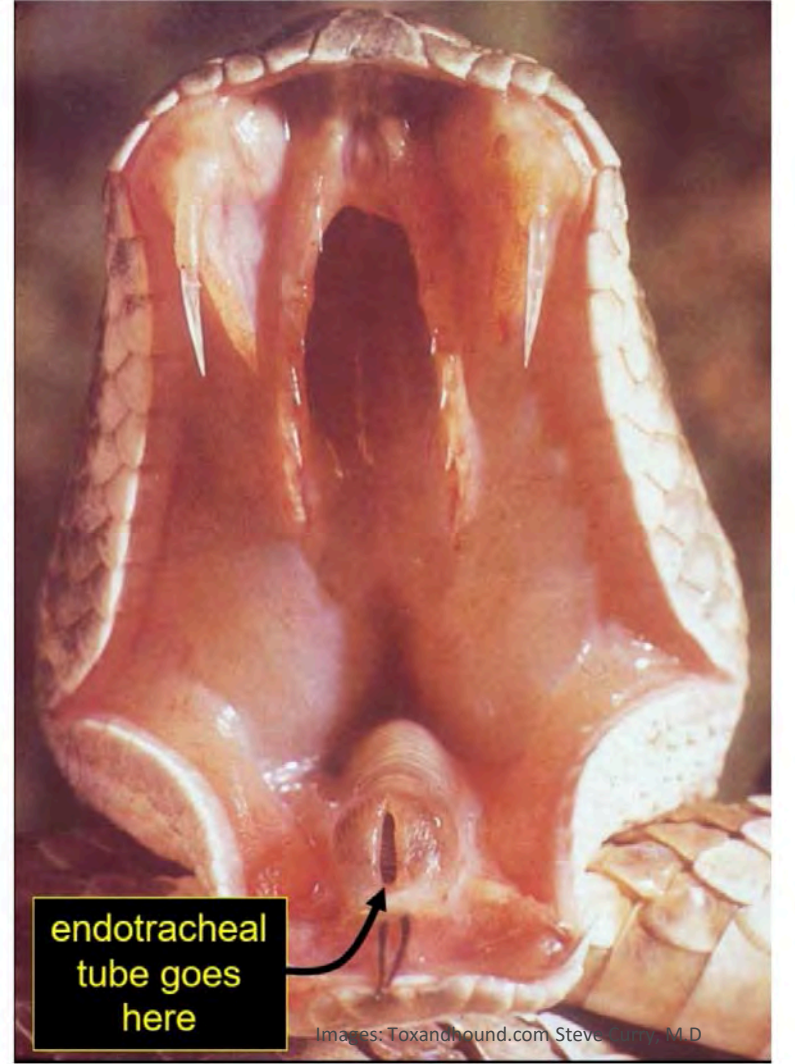
Don't waste time capturing or killing. Don't bring it to the hospital!



But if you need to resuscitate a rattlesnake...



Resuscitate the patient, not the snake



endotracheal tube goes here

Images: Toxandhound.com, Steve Curry, M.D.

Things to avoid...

- Pack wound in ice or apply heat.
- Stun gun or electric shock.
- Cut/Suck.
- Tourniquet (*call poison control before removing one*)
- NSAIDs
- Prophylactic antibiotics
- Prophylactic fasciotomy
- Routine use of blood products
- Steroids (except for allergic phenomena)



Complications in Part Due to Packing Extremity in Ice

Suction for Venomous Snakebite: A Study of “Mock Venom” Extraction in a Human Model

See related article, p. 187.

Michael B. Alberts, MD
Marc Shalit, MD
Fred LoGalbo, MD

From the Department of Emergency Medicine, University Medical Center, University of California, San Francisco–Fresno (Alberts, Shalit), and the Department of Radiology, Community Medical Center of Central California (LoGalbo), Fresno, CA.

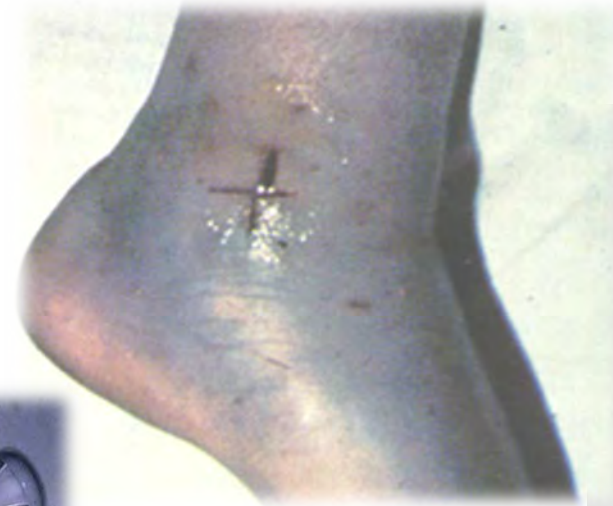
Study objective: We determine the percentage of mock venom recovered by a suction device (Sawyer Extractor pump) in a simulated snakebite in human volunteers.

Methods: A mock venom (1 mL normal saline solution, 5.0 mg albumin, 2.5 mg aggregated albumin) radioactively labeled with 1 mCi of technetium was injected with a curved 16-gauge hypodermic needle 1 cm into the right lateral lower leg of 8 supine male volunteers aged 28 to 51 years. The Sawyer Extractor pump was applied after a 3-minute delay, and the blood removed by suction was collected after an additional 15 minutes. A 1991 Siemens Diacam was used to take measurements of the radioactive counts extracted and those remaining in the leg and body.

Results: The “envenomation load,” as measured by mean radioactivity in the leg after injection, was 89,895 counts/min. The mean radioactivity found in the blood extracted in the 15 minutes of suction was 38.5 counts/min (95% confidence interval [CI] –33 to 110 counts/min), representing 0.04% of the envenomation load. The postextraction leg count was less than the envenomation load by 1,832 counts/min (95% CI –3,863 to 200 counts/min), representing a 2.0% decrease in the total body venom load.

Conclusion: The Sawyer Extractor pump removed bloody fluid from our simulated snakebite wounds but removed virtually no mock venom, which suggests that suction is unlikely to be an effective treatment for reducing the total body venom burden after a venomous snakebite.

[*Ann Emerg Med.* 2004;43:181-186.]

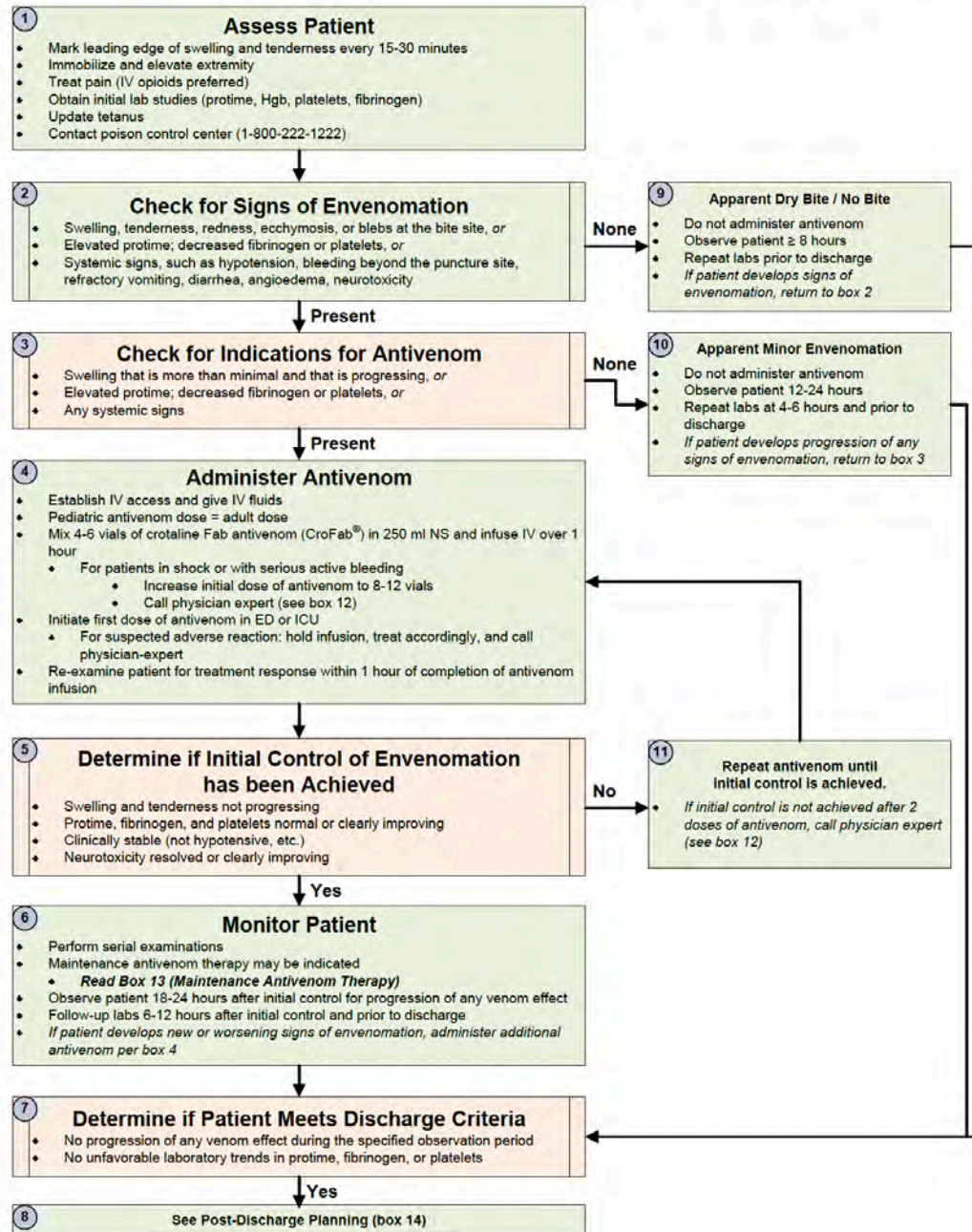


Removes virtually no venom

- **So now for a better guide to treatment...**

Emergency Department and Hospital Management of Pit Viper Snakebite

Includes: Rattlesnakes, Copperheads, and Cottonmouths (Water Moccasins)



NOTE: guidelines are being updated. Only CroFab is referenced in current chart, but we'll discuss AnaVip, too

CASE 1

28 yo male with no PMH presents to your ED 2.5 hrs after being bitten by a snake on the L foot. Other than a couple fang marks and some mild pain on the foot, the patient has no complaints.

He brings you a plastic container with the dead snake in it and wants to know if it's "poisonous" and if he's going to die.

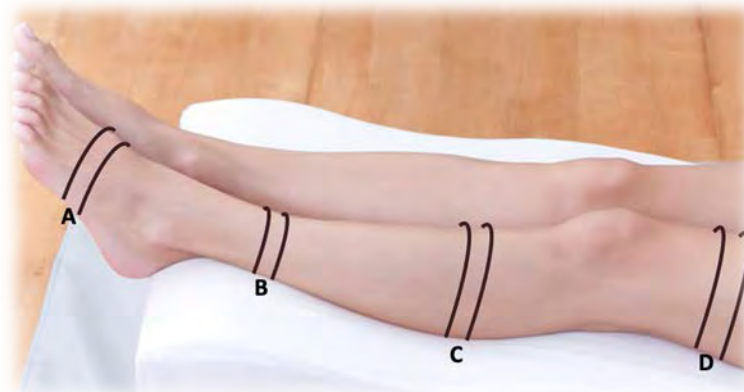


Management

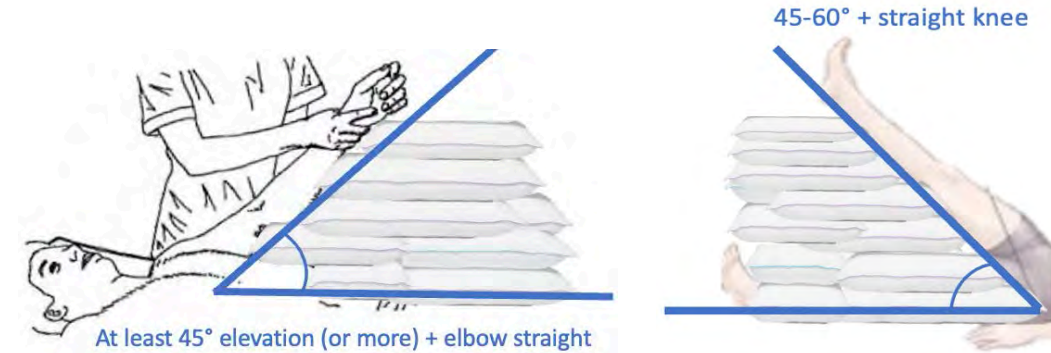
Assess Patient

- Mark leading edge q 15-30m
- Immobilize & elevate
- Treat pain with IV opioids, avoid NSAIDs
- Labs (PT, PTT, Hgb, platelets, fibrinogen) CK
 - Timing is critical
 - Very unlikely to be abnormal with copperhead, or minimal bite
- Update Tetanus
- Call poison control

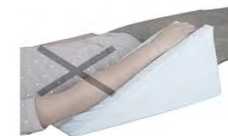
Measurement



Elevation



Inadequate:



Management



Signs of Envenomation

- Swelling, TTP, redness, ecchymosis, blebs at bite site, *or*
- \uparrow PT; \downarrow fibrinogen or platelets, *or*
- Systemic: hypotension, bleeding beyond bite site refractory vomiting, diarrhea, angioedema, neurotoxicity

NOTE: Systemic signs = very serious envenomation!



Management



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- Swelling, TTP, redness, ecchymosis, blebs at bite site, *or*
- \uparrow PT; \downarrow fibrinogen or platelets, *or*
- Systemic: hypotension, bleeding beyond bite site refractory vomiting, diarrhea, angioedema, neurotoxicity

NOTE: Systemic signs = very serious envenomation!



CASE 1

An hour after your initial evaluation, you reassess the patient. VSS. Patient is now c/o increased pain and you note swelling up to the mid calf and some mild ecchymosis.

- INR = 1.0/PT: 14.2
- FIBRINOGEN: 160 mg/dL (nml: 150-400 mg/dL)
- PLT: 135
- Hgb: 14

What's your next move, doctor?



Image slide: Nancy Orisko, DO



Management

Indications for Antivenom

- Swelling more than minimal **and progressing**, or
- \uparrow PT; \downarrow fibrinogen or platelets, or
- Any systemic signs
- Some panelists use:
 - Threshold of swelling crossing 1 major joint & approaching 2nd joint
 - Others treat minor hand envenomation more aggressively

Check for:

- **CV**: Hypotension, tachycardia, pallor, angioedema, myocardial necrosis.
- **Coagulation**: \downarrow fibrinogen, platelets. \uparrow PT, PTT, hemolysis, fibrin split products.
- **Other**: Rhabdo, sweating, lymphadenopathy, metallic taste, diarrhea, emesis/hematemesis.
- **Neuro**: cranial nerve palsies, generalized paralysis (Timber- Mojave Rattlesnake).

NOTE: Systemic signs = very serious envenomation!



Management

Administer Antivenom

Pop-Quiz: What's the pediatric dose?

- Pediatric dose = adult dose
 - Initiate first dose
 - Suspected adverse reaction: hold/slow infusion
 - treat accordingly
 - call poison control
 - Re-examine for treatment response within 1 hour of completing AV infusion
-
- Ask about Papaya allergy (CroFab)
 - Consider asking about allergy to red meat
 - Watch for anaphylactoid reaction during infusion



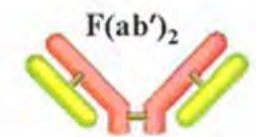
CROFab®
Fab



ANAVIP®
F(ab')₂



Papain

Pepsin



Contains	Mercury previously	Cresol currently
Protein/vial	up to 1,000 mg	200 mg
Serum		
Indications	N. American Crotalid adult & pediatric	N. American Crotalid adult & pediatric
Composition	Native to US <i>Crotalus atrox</i> <i>Crotalus adamanteus</i> <i>Crotalus scutulatus</i> <i>Agkistrodon piscivorus</i>	Not native to US <i>Bothrops asper</i> <i>Crotalus durissus</i>

CROFab®
Fab

ANAVIP
F(ab')₂

Storage



Reconstitution



Dosing

Load: 4-12 vials (typically 4-6)
Repeat as needed to achieve initial control

Maintenance: 2 vials Q6H x 3 doses
PRN: 2 vials

Load: 10 vials
Repeat as needed to achieve initial control

Maintenance: None
PRN: 4 vials

CROFab[®] Fab

ANAVIP[®] F(ab')₂

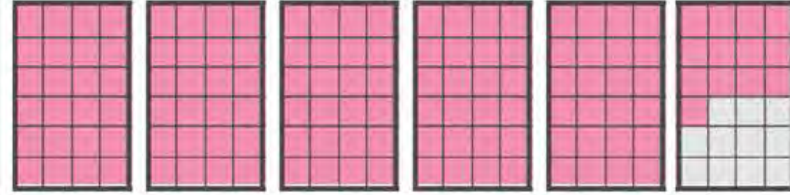
T_{1/2}

15h (12-23h)

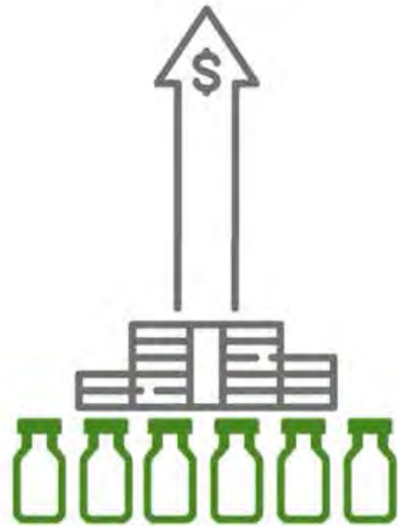
■ = 1h



133h (5.5 days)



Cost



\$3,316 /vial
6 vials \$19,896
12 vials: \$39,792



\$1,120 /vial
10 vials: \$11,200

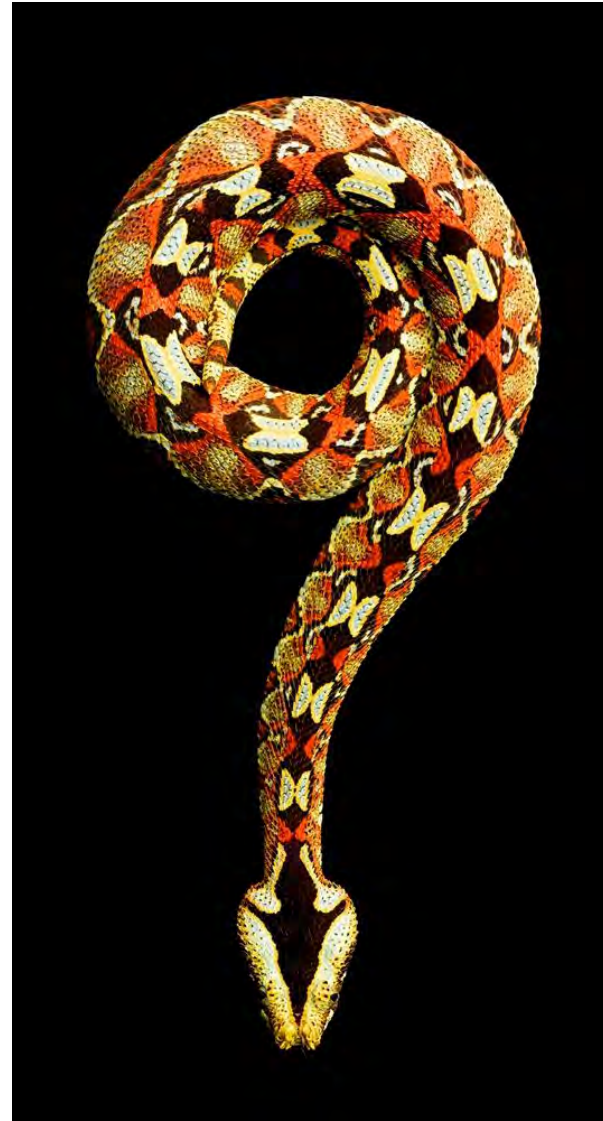
Average cost billed pt for 1 vial of CroFab: \$12,500

Boyer, L. The American Journal of Medicine, Vol 128, No 12, December 2015

CASE 1 Continued

An hour after AV infusion, the swelling stopped progressing. VSS. Labs WNL

- “Your initial loading dose of 6 vials of Crofab is in now doctor.” Do you want more?
- How many loading doses should you give?
- Should you give maintenance doses?
- What could happen if you don't?



Management

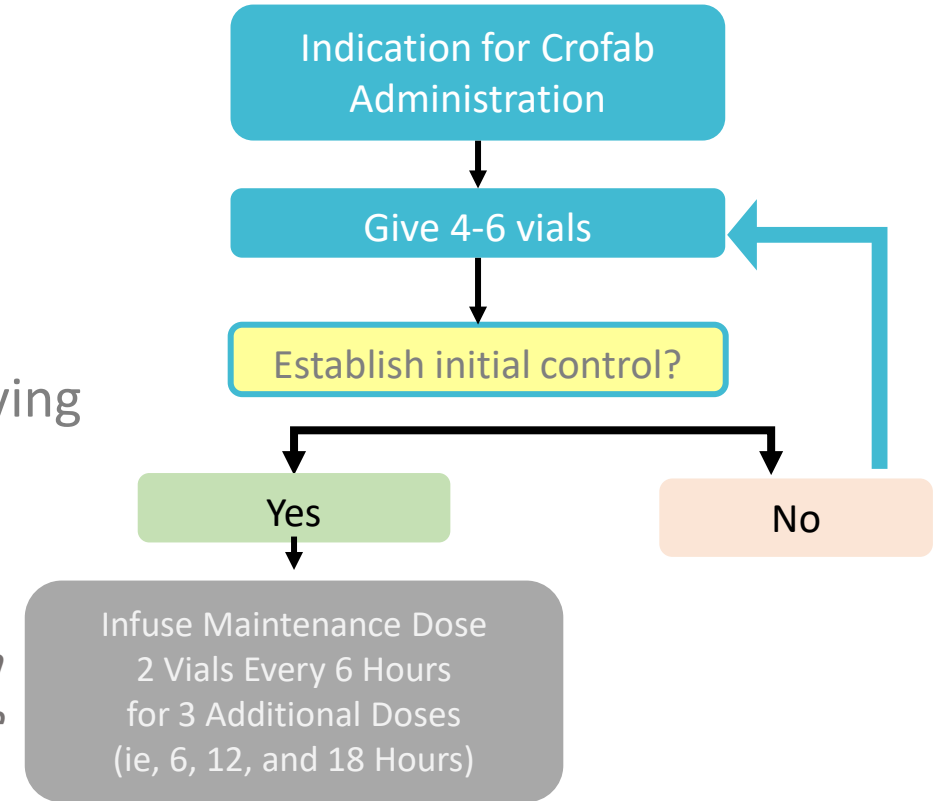
Initial Control Achieved?

- Swelling more than minimal and progressing, or
- Swelling and tenderness not progressing
- PT, PTT, fibrinogen, and platelets normal or clearly improving
- Clinically stable (not hypotensive, etc.)
- Neurotoxicity resolved or clearly improving

Monitor Patient

- Serial exams
- Maintenance antivenom therapy may be indicated
 - (Not really needed in copperheads)
- Observe 18-24h after initial control for progression of any venom effect
- Follow-up labs 6-12 hours after initial control and prior to discharge
- If patient develops new or worsening signs of envenomation, administer additional antivenom per box 4

Brief note on maintenance



Associate the term “Maintenance” with Crofab (not Anavip)

- Maintenance may not be indicated in certain situations, such as
 - Minor envenomation
 - Facilities where close observation by a physician- expert is available.

12 When to Call a Physician-Expert

Direct consultation with a physician-expert is recommended in certain high-risk clinical situations:

- **Life-threatening envenomation**
 - Shock
 - Serious active bleeding
 - Facial or airway swelling
- **Hard to control envenomation**
 - Envenomation that requires more than 2 doses of antivenom for initial control
- **Recurrence or delayed-onset of venom effects**
 - Worsening swelling or abnormal labs (protime, fibrinogen, platelets, or hemoglobin) on follow-up visits
- **Allergic reactions to antivenom**
- **If transfusion is considered**
- **Uncommon clinical situations**
 - Bites to the head and neck
 - Rhabdomyolysis
 - Suspected compartment syndrome
 - Venom-induced hives and angioedema
- **Complicated wound issues**

If no local expert is available, a physician-expert can be reached through a certified poison center (1-800-222-1222) or the antivenom manufacturer's line (1-877-377-3784).

15 Treatments to Avoid in Pit Viper Snakebite

- Cutting and/or suctioning of the wound
- Ice
- NSAIDs
- Prophylactic antibiotics
- Prophylactic fasciotomy
- Routine use of blood products
- Shock therapy (electricity)
- Steroids (except for allergic phenomena)
- Tourniquets

16 Notes:

- All treatment recommendations in this algorithm refer to crotalidae polyvalent immune Fab (ovine) (CroFab®).
- This worksheet represents general advice from a panel of US snakebite experts convened in May, 2010. No algorithm can anticipate all clinical situations. Other valid approaches exist, and deviations from this worksheet based on individual patient needs, local resources, local treatment guidelines, and patient preferences are expected. This document is not intended to represent a standard of care. For more information, please see the accompanying manuscript, available at www.biomedcentral.com.

13 Maintenance Antivenom Therapy

- Maintenance therapy is additional antivenom given after initial control to prevent recurrence of limb swelling
 - Maintenance therapy is 2 vials of antivenom Q6H x 3 (given 6, 12, and 18 hours after initial control)
- Maintenance therapy may not be indicated in certain situations, such as
 - Minor envenomations
 - Facilities where close observation by a physician-expert is available.
- Follow local protocol or contact a poison center or physician-expert for advice.

14 Post-Discharge Planning

- Instruct patient to return for
 - Worsening swelling that is not relieved by elevation
 - Abnormal bleeding (gums, easy bruising, melena, etc.)
- Instruct patient where to seek care if symptoms of serum sickness (fever, rash, muscle/joint pains) develop
- Bleeding precautions (no contact sports, elective surgery or dental work, etc.) for 2 weeks in patients with
 - Rattlesnake envenomation
 - Abnormal protime, fibrinogen, or platelet count at any time
- Follow-up visits:
 - Antivenom not given:
 - PRN only
 - Antivenom given:
 - Copperhead victims: PRN only
 - Other snakes: Follow up with labs (protime, fibrinogen, platelets, hemoglobin) twice (2-3 days and 5-7 days), then PRN

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And now for something strange...

Case 2

22:30

60 y/o ♂ with snake bite to left outer ankle

- Promptly called 911

22:45

EMS

- BP 77/54 mmHg → 500ml NS

23:00

ED:

- Arrives “tachycardic & hypotensive” (values not recorded)
- Tongue & facial swelling → Epi, solumedrol, diphenhydramine
- Hypotension → Sudden PEA arrest for 8 minutes → ROSC
- IVF x 2 L, epi, levo, vaso gtt

Poison center informed of case:

60 y/o ♂ with snake bite to left outer ankle

PMH: HTN & BPH

Home RX: Amlodipine tamsulosin finasteride

Exam:

- “Foot does not have much swelling”
- “2 clear punctures, no swelling or bruising”
- Good pulses and cap refill
- Blood in mouth and oozing from IV line



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- Facial or airway swelling
- Hard to control envenomation
- Envenomation requiring >2 doses AV for initial control
- Recurrence or delayed-onset venom effects
- Worsening swelling or abnormal labs on follow-up visits
- Allergic reactions to antivenom
- If transfusion considered
- Uncommon situations
 - Bites to the head and neck
 - Rhabdomyolysis
 - Suspected compartment syndrome
 - Venom-induced hives and angioedema
 - Complicated wound issues

Use 10—12 vials in cardiac arrest

Case 2

Labs and AV Timeline

	AV 1-12	AV 13-24	AV 25-36	AV 37-42	AV 43-60	Maintenance AV 61-66				Bolus AV 67-72		Bolus AV 67-72						
TIME	+1h	+4h	+8h	+12h	Day 1	Day 2	Day 3	Day 4	Day 5	TIME	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12
WBC x10 ⁹ /L	34	35.3	17.8	24	25.63	9.7	12.86	17.39	25.04	WBC x10 ⁹ /L	25.04				21.81			
Platelets x x10 ⁹ /L	333	215	51	108	159	32	31	31	36	Platelets x x10 ⁹ /L	36		187	186	195	180	186	
PT Sec	15.4	>120	>120	>120	19.5	20	11.4	10.7	10.8	PT Sec	10.8	10.9	12	11.3	12.8	10.9	11.3	12.8
INR	Unable to calculate	Unable to calculate	Unable to calculate	Unable to calculate	1.7	1.8	1.0	0.9	0.9	INR	0.9	1.0	1.1	1	1.1	1	1	1.1
PTT Sec	>250	>250	43	43.1	43.1	38.7	28.9	25.5	25.3	PTT Sec	25.3	25.7	38.5	28.2	26.6	25.7	28.2	26.6
Fibrinogen mg/dL	1200	60	<35	67	99	546	883	850	735	Fibrinogen mg/dL	735	1046	958	883	1135	1046	883	1135
Exam	Shock, bleeding from mouth	Shock, oozing from IV	Shock, oozing from IV	Shock, oozing from IV	Oozing from IV	No UOP		Oozing from IV	No UOP	Exam	No UOP	No bleeding				No UOP	No UOP	No UOP
Cr mg/dL	1.2	2.0	3.5	4.1	4.2	4.4	3.7	2.5	6.8	Cr mg/dL	6.8				3.6	5.3	3.6	6.1
Other						CRRT	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn	Other	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn	Vanc Zosyn
								Platelets infused	CRRT		CRRT					CRRT	CRRT	CRRT

Case 2

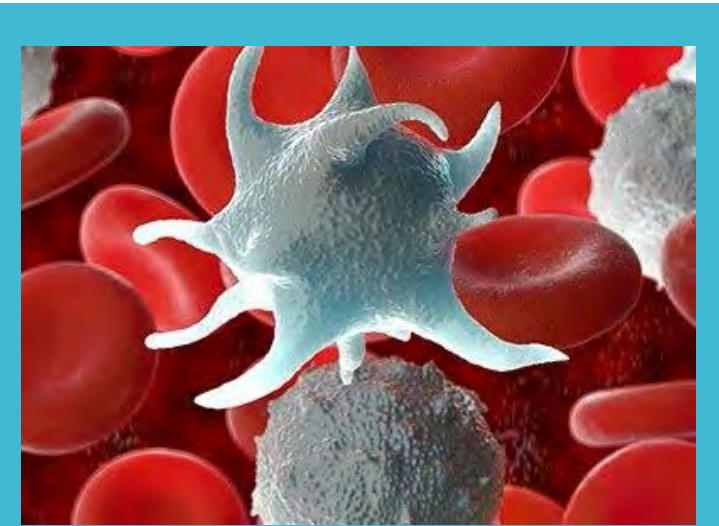
ICU and Hospital Course

- 60-year-old ♂, rattle snake bite Left ankle
- Anaphylactoid → rapid collapse
- Intubated, sedated for 13 days
- 72 vials AV for shock and VIC
- Dialysis for fluid overloaded

- Fever up to 105°F
- ARDS
- C-diff positive → intra-abdominal abscess
- Bleeding from the mouth and IV sites

- DNR → Family withdrew care
 - Died on Day #13



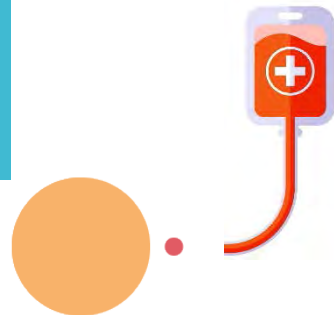


Hematologic Effects



Images: Toxandhound.com Steve Curry, M.D

- Immeasurable, or low fibrinogen, $PT > 100s$, and platelet counts lower than 30,000K can be encountered after rattlesnake envenomation.
- Such abnormal results *alone* should *not* prompt blood product infusion in absence of clinically significant bleeding.
- Circulating venom is still present, and will inactivate transfused components.
- The mainstay of treatment of crotaline envenomation-induced coagulopathy and thrombocytopenia is antivenom, *not blood products*.



Additional Topics of Interest:

Tox and Hound – Fellow Friday

Rapid Collapse and Anaphylactoid Reactions from Rattlesnake Bites

by Steve Curry, M.D.

Banner – University Medical Center Phoenix

University of Arizona College of Medicine – Phoenix, Phoenix, AZ

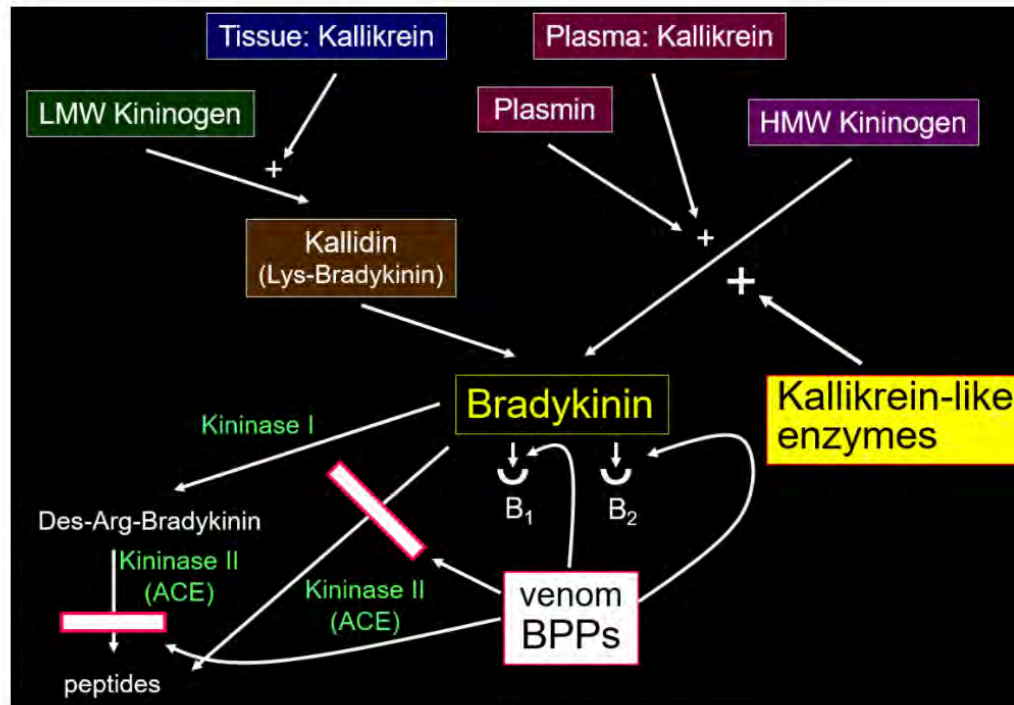


Fig. 23

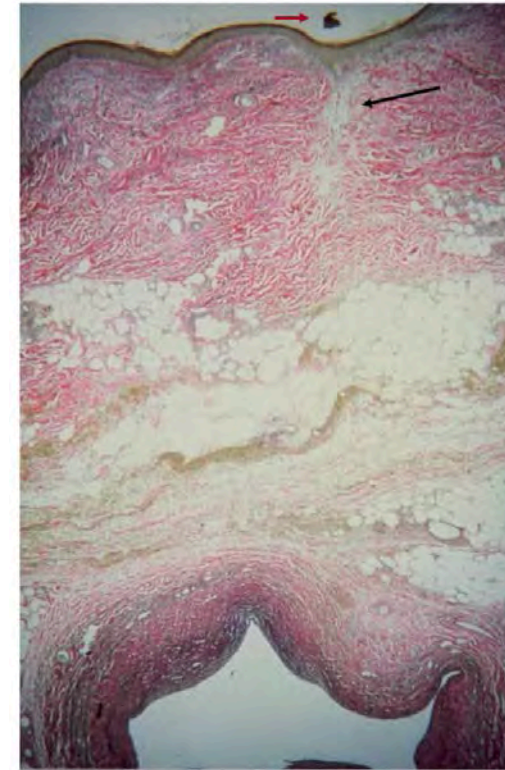


Fig. 19

Additional Topics of Interest:

Alpha-gal



Alpha-gal (galactose- α -1,3-galactose) is a sugar molecule found in most mammals.



Alpha-gal is **not** found in fish, reptiles, birds, or people.



Alpha-gal can be found in meat (pork, beef, rabbit, lamb, venison, etc.) and products made from mammals (including gelatin, cow's milk, and milk products).

Additional Topics of Interest:

RESEARCH & DISCOVERY

Meet the Doc Who Discovered the Infamous Red Meat Allergy Spread by Ticks



- Also called: Red meat allergy, Tick bite meat allergy
- Serious, potentially life-threatening allergic reaction.
- Not caused by an infection.
- Sx occur after people eat red meat or are exposed to other products containing alpha-gal.



Dr. Thomas Platts-Mills is head of UVA's Division of Allergy and Clinical Immunology and known around the world for several key discoveries. (Photo by Sanjay Suchak, University Communications)

AGS reactions can include:

- Hives or itchy rash
 - Nausea or vomiting
 - Heartburn or indigestion
 - Diarrhea
 - Cough, shortness of breath, or difficulty breathing
 - Drop in blood pressure
 - Swelling of the lips, throat, tongue, or eye lids
 - Dizziness or faintness
 - Severe stomach pain
-
- Symptoms commonly appear 2-6 hours after eating meat or dairy products, or after exposure to products containing alpha-gal (for example, gelatin-coated medications).
-
- AGS reactions can be different from person-to-person.
 - Can range from mild to severe or even life-threatening.
-
- May not have allergic reaction after every alpha-gal exposure.



Fischer J. • Eberlein B. • Hilger C. • Eyer F. • Eyerich S. • Ollert M. • et al.
Alpha-gal is a possible target of IgE-mediated reactivity to antivenom.
Allergy. 2017; **72**: 764-771

Rizer J. • Brill K. • Charlton N. • King J.
Acute hypersensitivity reaction to Crotalidae polyvalent immune Fab (CroFab) as initial presentation of galactose-alpha-1,3-galactose (alpha-gal) allergy.
Clin Toxicol (Phila). 2017; **55**: 668-669

α -Gal on Crotalidae-polyvalent Fab antivenom (CroFab): Investigating the relevance to immediate hypersensitivity reactions

[Matthew Straesser, MD,^{a,*}](#) [Behnam Keshavargz, PhD,^{a,*}](#) [Larry Borish, MD,^{a,b}](#) [Dilawar Khokhar, MD,^a](#) [Angela Holian, PharmD, BCPS,^c](#) [Nathan Charlton, MD,^c](#) [Thomas A.E. Platts-Millis, MD, PhD,^a](#) and [Jeffrey M. Wilson, MD, PhD^a](#)

Measurement of the oligosaccharide galactose- α -1,3-galactose (α -gal) in pit viper antivenom

Aled Griffiths,¹ Jami N Johnson,^{2,3} Suzanne Ward,² Christon Hill,² Ellen Dentten,¹ Olivia Bradbury-Williams¹

¹Protherics UK Ltd, Blaenwaun, Ffostrasol, UK; ²BTG Specialty Pharmaceuticals, West Conshohocken, PA, USA; ³University of Oklahoma College of Pharmacy, Oklahoma City, OK, USA

Figure 2. Electropherogram of α -gal in ovine Fab and equine F(ab')₂

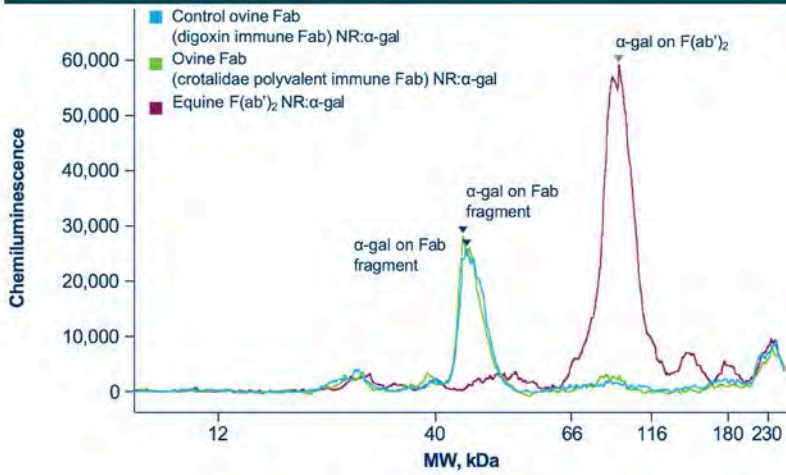
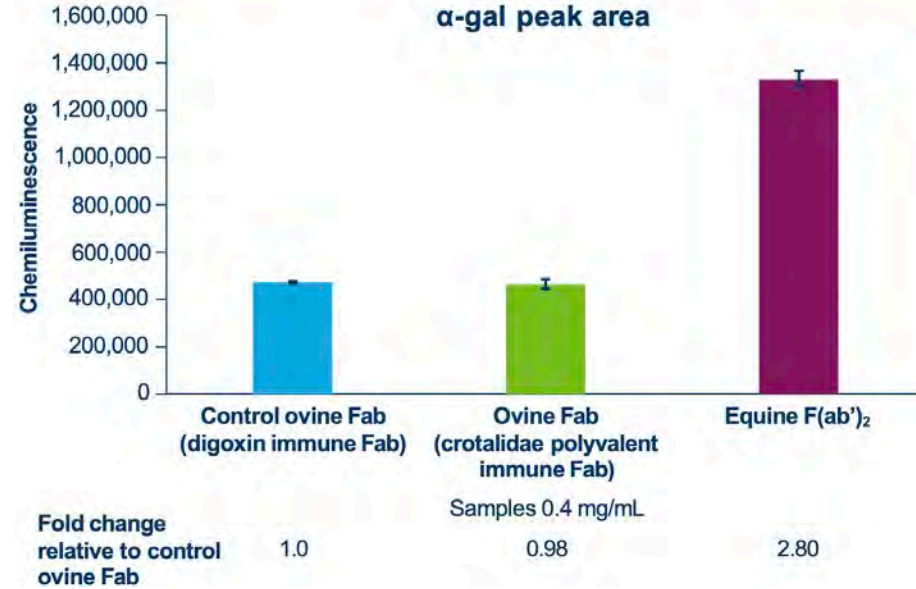


Figure 3. Sample α -gal peak area under the curve for control ovine Fab, ovine Fab, and equine F(ab')₂



CONCLUSIONS

- Analysis by western blot established that there is α -gal present in both ovine Fab and equine F(ab')₂ antivenoms.
- Analysis using the Protein Simple Jess system confirmed these findings and showed that the relative amount of α -gal in equine F(ab')₂ appeared to be three times that in the ovine Fab product.

Measurement of the oligosaccharide galactose- α -1,3-galactose (α -gal) in pit viper antivenom

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BACKGROUND

- α -gal syndrome (a reaction to the oligosaccharide α -gal) is a newly reported food allergy with regional distribution most pronounced in the Southeastern US.^{1,2}
- While the pathophysiology is still being elucidated, it is thought that α -gal is introduced to the immune system via saliva following a tick bite, leading to the development of IgE antibodies against α -gal.²
- The presence of α -gal in mammalian products and certain drugs has been known to cause an allergic reaction in patients with α -gal syndrome.³
- Previously published work concluded that α -gal was detected in the ovine-derived Fab antivenom crotalidae polyvalent immune Fab (ovine).⁴

OBJECTIVE

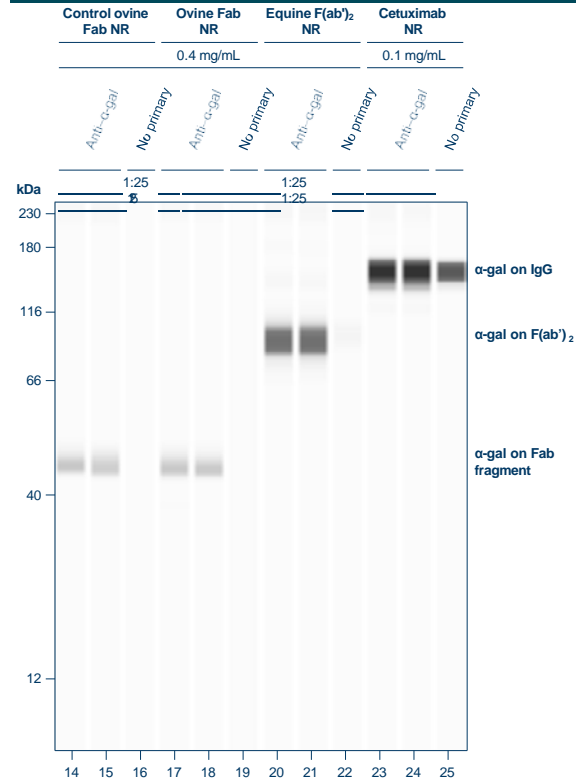
- To confirm the previous finding that α -gal is detected in crotalidae polyvalent immune Fab (ovine) and determine qualitative α -gal levels in both ovine Fab antivenom and the equine-derived F(ab')₂ antivenom crotalidae immune F(ab')₂ (equine).

METHODS

- Ovine Fab antivenom, a control ovine Fab, and equine F(ab')₂ antivenom at a concentration of 1 mg/mL were run in duplicate alongside cetuximab (a well-known commercial monoclonal antibody known to carry α -gal) at 1 mg/mL and 0.25 mg/mL using western blot analysis.
 - Western blot analyses were undertaken using a mouse antibody (clone M86) specific to α -gal.
- Confirmatory analyses were performed using the Protein Simple Jess western blot system, which automates protein separation and immunodetection workflow via capillary-based separation.
 - For the analyses using the Protein Simple Jess western blot system, the ovine Fab and equine F(ab')₂ samples were diluted to 0.4 mg/mL, and cetuximab to 0.1 mg/mL, based on expected signal response.
- Chemiluminescence detection and resulting electropherograms were generated allowing for direct comparison of α -gal response detected in each sample.

RESULTS

Figure 1. Protein Simple Jess western blot analysis of control ovine Fab, ovine Fab, equine F(ab')₂, and cetuximab



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Figure 2. Electropherogram of α -gal in ovine Fab and equine F(ab')₂

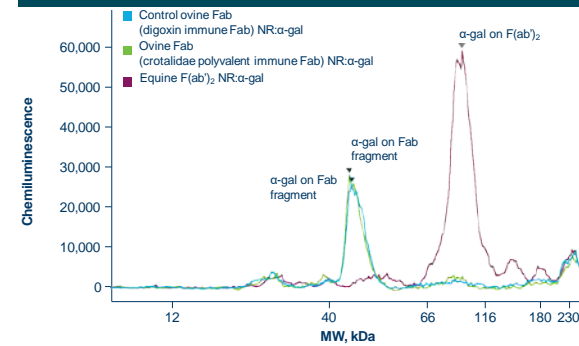
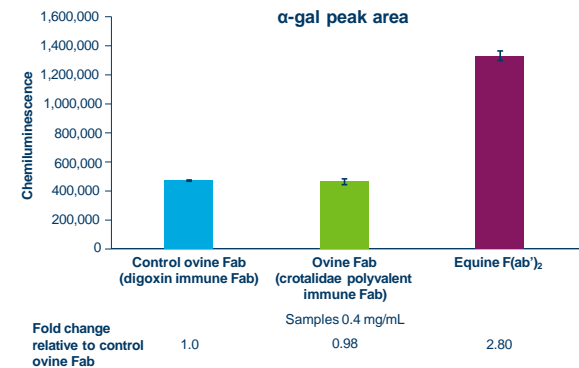


Figure 3. Sample α -gal peak area under the curve for control ovine Fab, ovine Fab, and equine F(ab')₂



Detection and relative quantification of α -gal

- Western blot analysis established that α -gal was present in ovine Fab, equine F(ab')₂, and cetuximab.
- Figure 1** shows results of the Protein Simple Jess western blot analysis.
- Peak areas calculated from electrophoresis analysis (**Figure 2**) were 467,648 for ovine Fab and 1,333,762 for equine F(ab')₂.
- Analysis conducted using the Protein Simple Jess western blot system confirmed the results of a previous western blot analysis, showing that the level of α -gal present in ovine Fab was three-fold lower than the level observed in the equine F(ab')₂ product (**Figure 3**).

CONCLUSIONS

- Analysis by western blot established that there is α -gal present in both ovine Fab and equine F(ab')₂ antivenoms.
- Analysis using the Protein Simple Jess system confirmed these findings and showed that the relative amount of α -gal in equine F(ab')₂ appeared to be three times that in the ovine Fab product.

Abbreviations

α -gal, galactose- α -1,3-galactose; Fab, fragment antigen-binding; IgE, immunoglobulin E; IgG, immunoglobulin G; MW, molecular weight; NR, normalized ratio.

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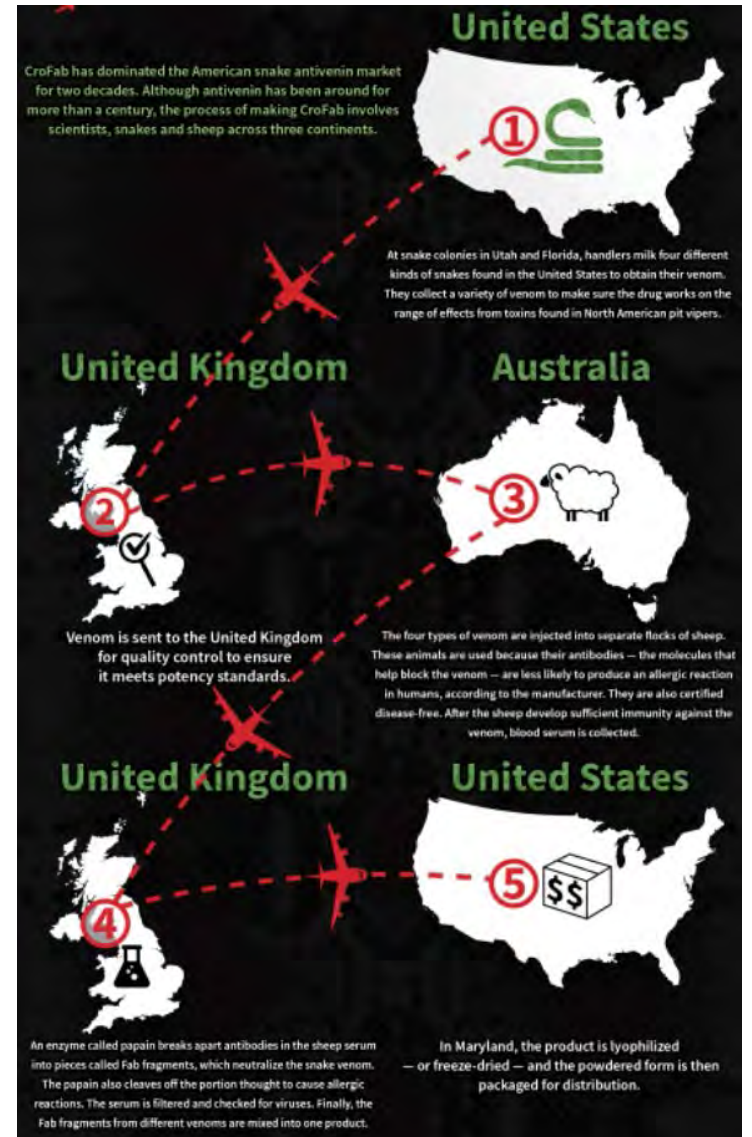
Acknowledgments

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Disclosures of interest

AG, ED, and OGW are employees of Protherics UK Ltd. JNJ, SW, and CH are employees of BTG Specialty Pharmaceuticals.

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