



The Superiority Of F(ab')₂ Compared To FabAV Or Vice Versa?

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High-Yield Med Reviews

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Disclosures

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*The relevant financial relationship listed for this individual has been mitigated

By the end of this lecture, pharmacists will be able to...

1. Describe the important differences *between* antivenom products.
2. Debate whether **Copperheads** should be considered in a different category to other pit vipers for the purposes of antivenom treatment and outcome measurement.
3. Critique the definition of “**initial control.**”

Question 1

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Question 2

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Question 3

Dr. Emmanuel is a critical care physician consulting you on a snake bite patient admitted to the ICU. The patient in question was admitted yesterday and received a complete course of FabAV, however, the erythema, edema, and pain of the extremity where the envenomation occurred and was present at FabAV initiation has not been resolved, but is no longer progressing. Which of the following is the most appropriate recommendation at this time?

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Crofab

Crotalidae polyvalent immune Fab (Ovine) (FabAV)

Vs.

Anavip

Crotalidae equine immune F(ab')₂ (F(ab')₂)

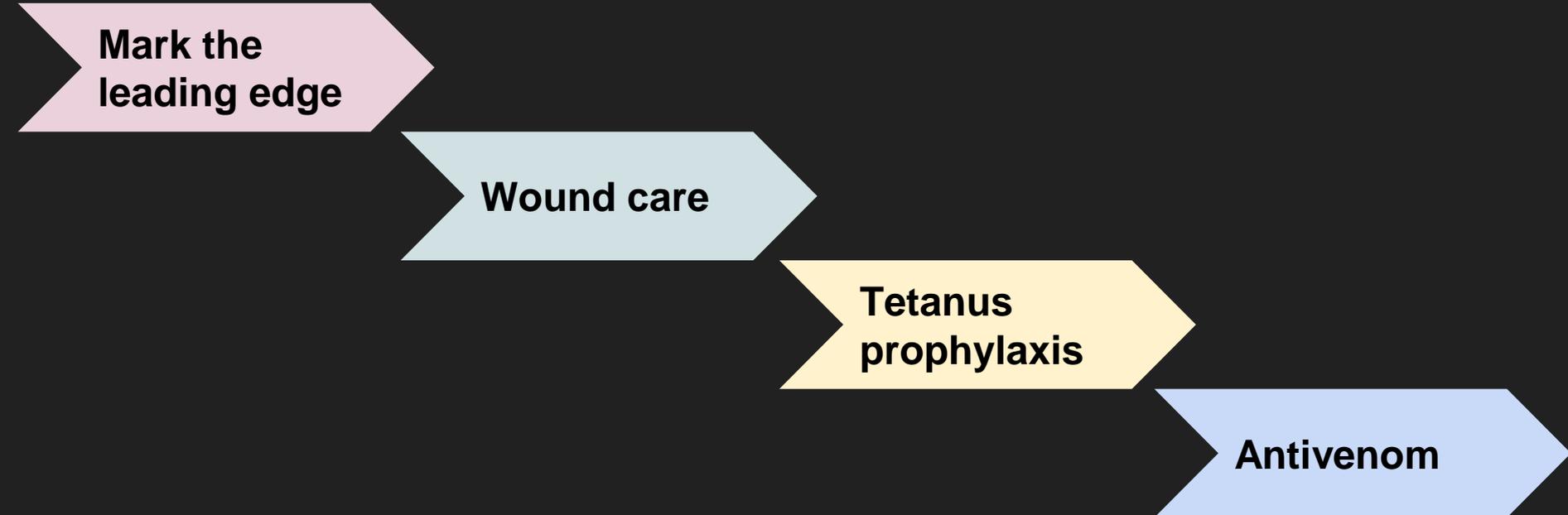
Rapid ED Care

**Mark the
leading edge**

Wound care

**Tetanus
prophylaxis**

Antivenom

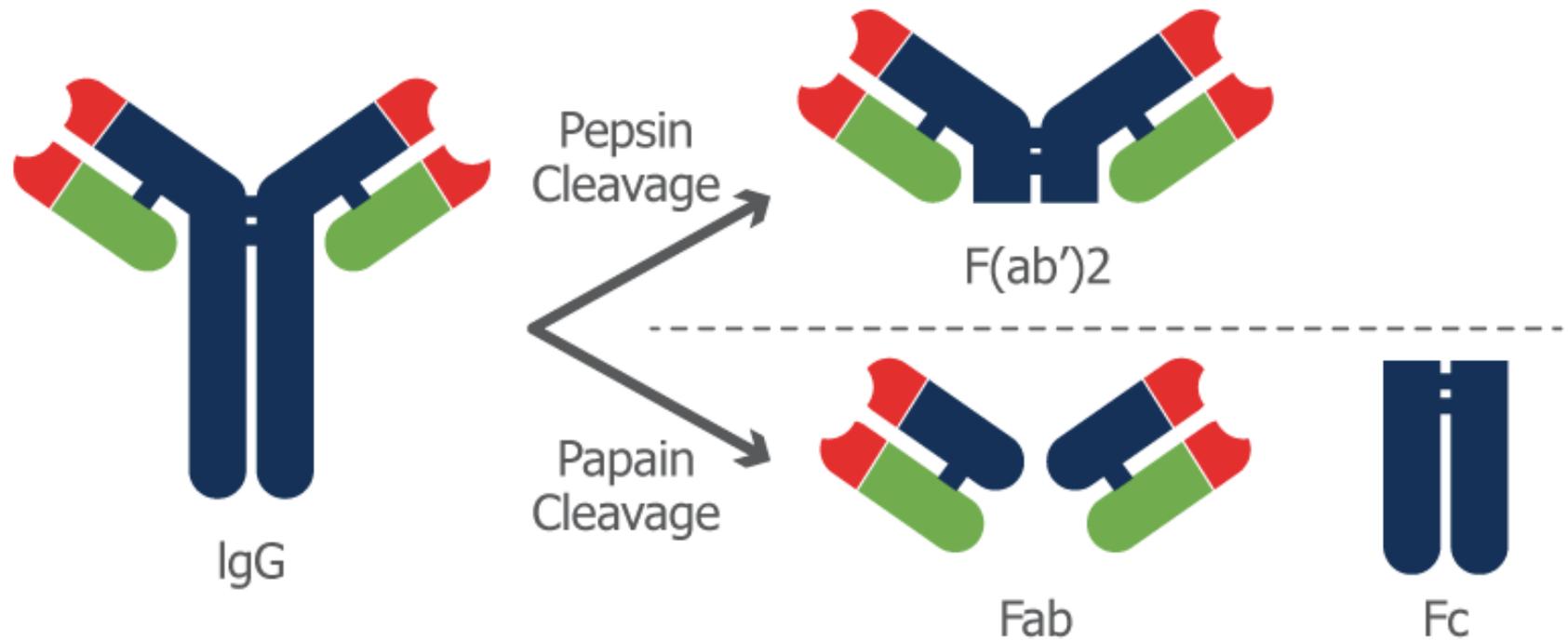


Infectious Disease → Venom

ABX spectrum (***Snake species covered by AV***)

Sensitivity/MIC (***Venom component specificity***)

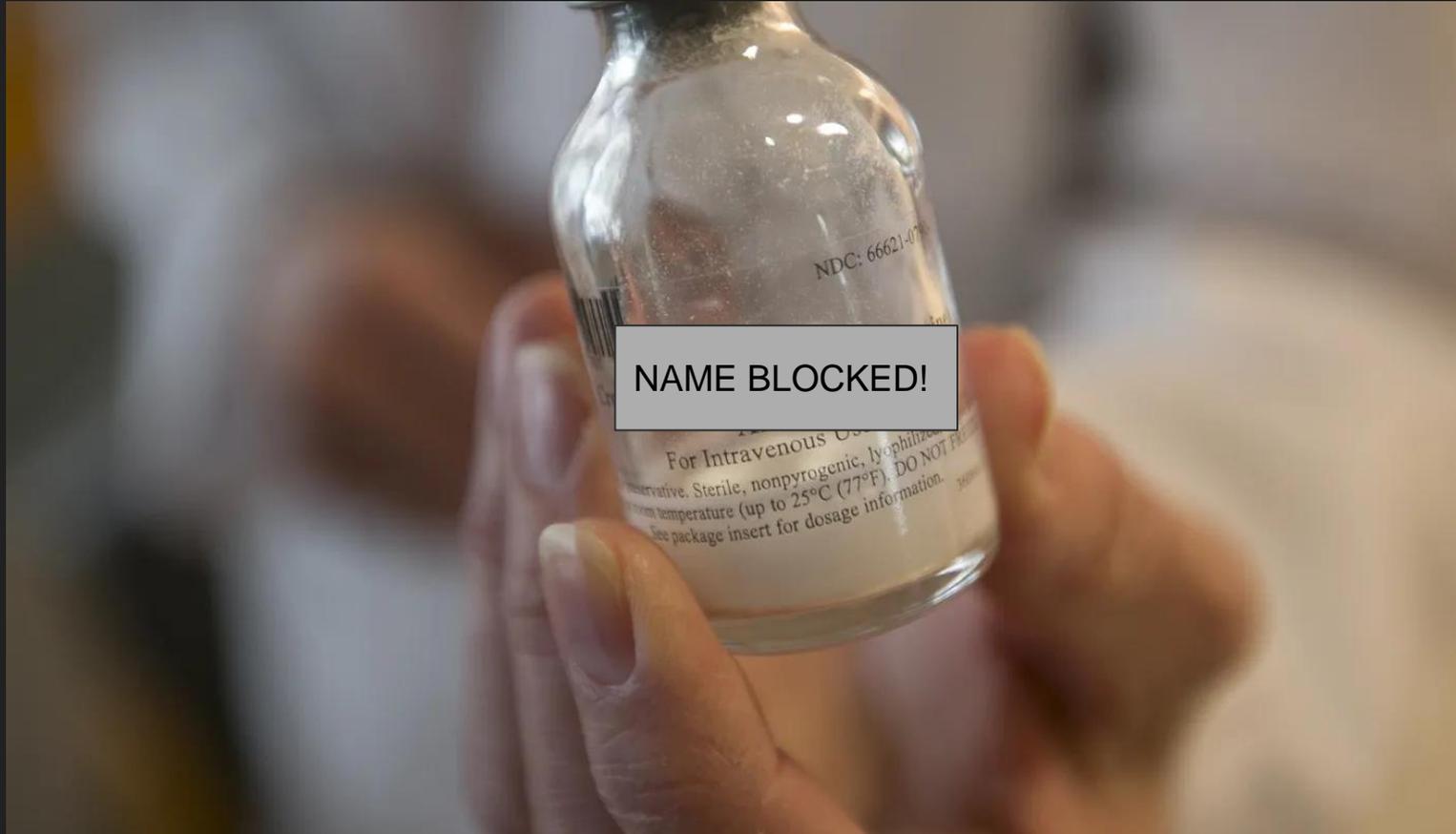
Clinical outcomes (***Initial control***)



Antivenom	Snake venom components	FDA approved indication	Dosing
FabAV	<i>C. adamanteus</i> <i>C. atrox</i> <i>C. scutulatus scutulatus</i> <i>A. piscivorus</i>	Management of adult and pediatric patients with North American crotalid envenomations (eg, <i>Crotalus</i> , <i>Sistrurus</i> , and <i>Agkistrodon</i> [including <i>A. contortrix</i>])	Initial dose: 4-12 vials. Repeat initial dose every 2 hours until IC achieved Maintenance: 2 vials every 6 hours for 3 doses
F(ab')₂	<i>B. asper</i> <i>C. durissus</i>	Management of adult and pediatric patients with North American rattlesnake envenomation (eg, <i>Crotalus</i> , <i>Sistrurus</i> , and <i>Agkistrodon</i> [including <i>A. contortrix</i>])	Initial dose: 10 vials. Repeat the initial dose as needed every hour until IC achieved Maintenance: 4 vials as needed during the 18-hour observation period

IC - Initial Control

Reconstitution - F(ab')₂



Reconstitution - FabAV



20-25 mL of NS

1



2



3



So Why Are We Not All Using F(ab')₂?

Let's take a closer look at...

- **Cost** comparison
- **Copperhead** vs Rattlesnake envenomations
- **“Initial Control”**

Cost Comparison

FabAV: \$3,316/vial (AWP) = **\$39,000 to 165,000**

F(ab')₂: \$1,120/vial (AWP) = **\$11,200**

(Definitely differs based on your hospitals purchasing agreements)

More F(ab')₂ Than Anticipated?

FabAV: 15.7 (+/- 2.6) vials = \$52,061.2 +/- 8,621.6

F(ab')₂: 35.3 (+/- 12.1) vials = \$39,536 +/- 13,552

F(ab')₂ VS FabAV: Head to Head

Multicenter, prospective, randomized, blinded, placebo-controlled

N= 123 with signs and symptoms of a pit viper bite, including

A. contortrix

Group 1: F(ab')₂-F(ab')₂

Group 2: F(ab')₂-placebo

Group 3: FabAV-FabAV

F(ab')₂ VS FabAV: Heat to Head

Occurrence of coagulopathy between the end of maintenance dosing and study day 8 (+/- 1 day)

- **F(ab')₂/F(ab')₂**: 4 patients (10.3%)
 - **F(ab')₂/placebo**: 2 patients (5.3%)
 - **FabAV/FabAV**: 11 patients (29.7%)
- p < 0.05**

n=21 attributed to **Copperheads...**

F(ab')₂/F(ab')₂ = 6, F(ab')₂/placebo = 7, FabAV/FabAV = 8

Post Hoc Analysis

Copperhead patient subgroup (**F(ab')₂AV** groups combined vs. **FabAV** group)

N = 21 Copperhead envenomations (**13** vs **8**)

Primary outcome - number of repeat doses required for ***initial control***

F(ab')₂AV - 1/13 (8%)

FabAV - 2/8 (25%)

No significant difference (95% CI -18, 57)

Initial Control: We Have A Problem

	FabAV PI and Evidence	F(ab') ₂ vs FabAV Study
Local Effects	No further progression of local effects	Leading edge of local injury was not progressing more than 1 inch per hour
Systemic Effects	Systemic effects are resolved or clearly improving	Not mentioned in study
Coagulation Abnormalities	Coagulation parameters normalized or are trending towards normal	Platelet count, serum fibrinogen level, prothrombin time (PT), and partial thromboplastin time (PTT) were either normal or returning toward normal.

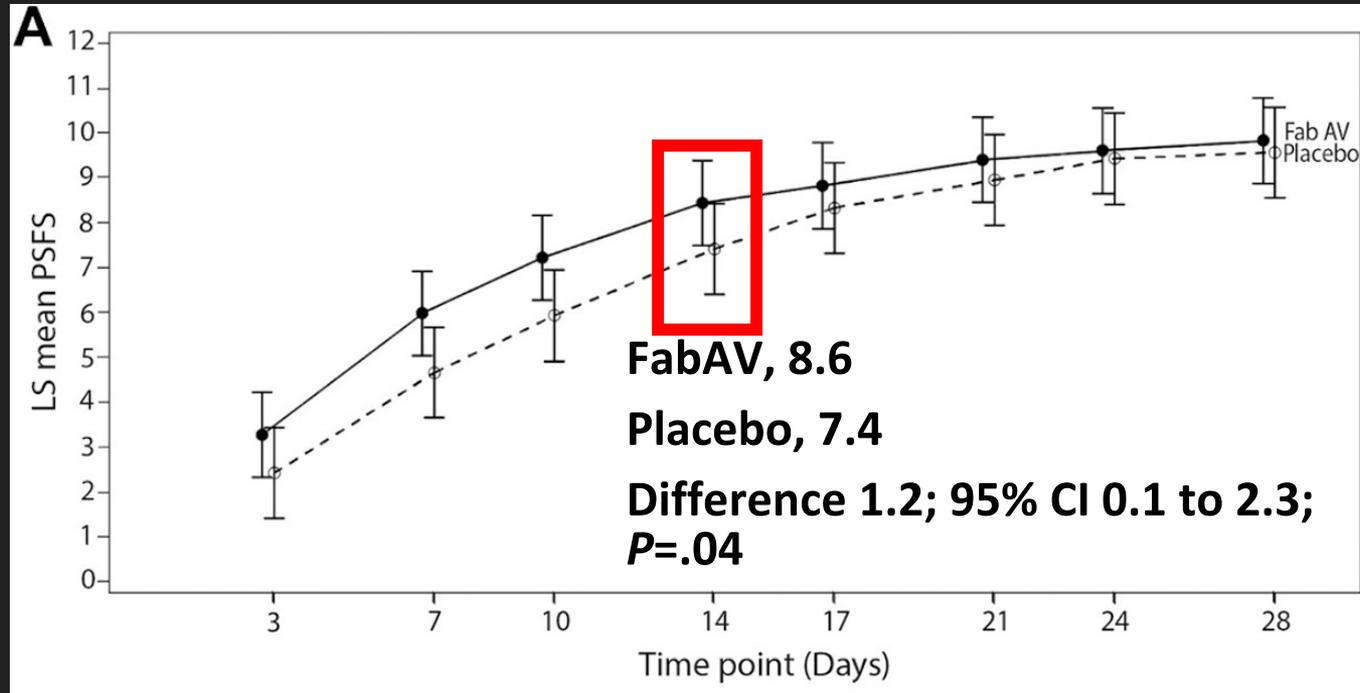
FabAV vs **Placebo** in Copperhead Envenomations

FabAV group received **6 vials** as initial treatment, repeated once if needed to halt progression of venom effects

- Maintenance dose of 2 vials of FabAV at 6, 12, and 18 hours

Placebo - visually identical normal saline solution

Primary Outcome



Envenomations,
N=75

Snake Bite Severity
Score Protocol, n=30

Standard care,
n=45

FabAV vials used (mean):
2.5 vials, 95% CI 1.1–3.9

p=0.007

FabAV vials used (mean):
4.7 vials, 95% CI 3.5–5.9

\$6,632 / dose

Why Not Give Less F(ab')₂?

Venom	LD50	R ²	F(ab') ₂ ED50	FabAV ED50	Ratio
C.s.scutulatus	0.47	0.99	140.5 (11)	24 (4)	6.7
C.adamanteus	1.84	1	34.9 (1)	70 (6)	0.67
C.atrox	5.1	1	295 (14)	310 (14)	0.95
A.c.contortrix	5.2	0.92	331.6 (15)	93.7 (9)	3.5
A.c.laticinctus	6.8	1	293 (13)	140.5 (11)	2.1

LD50 is the concentration of venom (mg/kg body weight) required to kill 50% of the BALB/c mice injected iv with 0.2 ml of the various snake venoms. LD50 was calculated using the LD50 calculator on the NTRC's homepage at <http://ntri.tamuk.edu/cgi-bin/ld50/ld50>. ED50 is expressed as mg of antivenom/kg of mouse body weight; ED50 values were determined against 3 × LD50 of venoms.

A dramatic landscape featuring a Y-shaped road that splits into two paths, leading into a vast field of golden-brown crops. The sky is filled with large, dark, textured clouds, creating a moody and atmospheric scene. The overall color palette is dark and desaturated, with the golden tones of the field providing a focal point.

Low Dose FabAV

F(ab')₂ Pioneer

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F(ab')₂ made with cleavage using pepsin

FabAV cleaved with pepsin then papain

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Treat the VENOM, not the patient

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Treatment goal for Copperhead envenomation is to halt the progression of tissue injury, improving time to functional recovery



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