



TOXTALKS

A BULLETIN FOR HEALTHCARE PROFESSIONALS WHO MANAGE POISONED PATIENTS

Blue Ridge Poison Center

University of Virginia Health

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Battle of the Antivenoms: CroFab vs ANAVIP

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Introduction

According to the CDC, about 7,000-8,000 people per year in the US experience a venomous snakebite, or an “envenomation.” With appropriate medical care, the mortality rate is low with an estimated death rate of five people per year. This is not the case worldwide with over 130,000 deaths estimated yearly by the World Health Organization. The mainstay of treatment in the US for pit viper envenomation is with Crotalidae polyvalent immune Fab antivenom (brand name CroFab). However, a new antivenom, Crotalidae equine immune F(ab’)2 (brand name Anavip) is now available. Anavip has proposed advantages over CroFab due to a longer half-life but CroFab is still the most widely available in the region.

Background on venomous snakes in the US and Virginia

All native venomous snakes in the US belong to either the Viperidae subfamily Crotalinae or the Elapidae family. They are more commonly referred to as Elapids (the only native Elapidae is the coral snake) and Crotalids (pit vipers). CroFab and Anavip are not used for Elapid envenomation as that has its own antivenom. The following table lists the snakes native to Virginia and the snakes whose venom is used to make the two types of antivenoms.

Virginia snake envenomations

Envenomation by a Crotalid causes pain, local tissue swelling and ecchymosis. Copperhead and cottonmouth envenomations may need treatment with antivenom depending on the severity and location of symptoms. In the case of rattlesnakes, envenomation also causes thrombocytopenia, hypofibrinogenemia and coagulopathy. Coagulopathy induced by rattlesnake envenomations should always be treated with antivenom. The timber rattlesnake is notorious for causing severe thrombocytopenia that can rebound even after antivenom treatment. Thrombocytopenia may persist with or without treatment for 2-3 weeks.

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Table 1. A selection of venomous snake found in North America.

Family/subfamily	Genus	Species	Common name
Viperidae/Crotalinae	<i>Agkistrodon</i>	<i>contortrix</i>	Copperhead*
Viperidae/Crotalinae	<i>Agkistrodon</i>	<i>piscivorus</i>	Cottonmouth or water moccasin*/+
Viperidae/Crotalinae	<i>Crotalus</i>	<i>adamanteus</i>	Eastern diamondback rattlesnake+
Viperidae/Crotalinae	<i>Crotalus</i>	<i>atrox</i>	Western diamondback rattlesnake +
Viperidae/Crotalinae	<i>Crotalus</i>	<i>scutulatus</i>	Mojave rattlesnake+
Viperidae/Crotalinae	<i>Crotalus</i>	<i>horridus</i>	Timber rattlesnake*
Viperidae/Crotalinae	<i>Crotalus</i>	<i>horridus atricaudatus</i> (subspp)	Canebrake rattlesnake*
Viperidae/Crotalinae	<i>Crotalus</i>	<i>durissus</i>	South American rattlesnake++
Viperidae	<i>Bothrops</i>	<i>asper</i>	Terciopelo or fer-de-lance++

*Found in Virginia

+Used to make the antivenom CroFab

++Used to make the antivenom Anavip

CroFab vs ANAVIP

CroFab is the most widely available antivenom used in the treatment of North American Crotalid envenomations. In 2015, Anavip was FDA approved, but was not released for distribution until 2018. While CroFab is approved for all North American Crotalids (including copperheads), Anavip is only approved for North American rattlesnake envenomations. A comparison of the antivenom characteristics can be found in Table 2. Anavip is a F(ab')₂ fragment with two venom binding sites, compared to a CroFab which is a single Fab fragment with one venom binding site (see Figure 1). The F(ab')₂ confers a longer elimination half-life, and therefore is proposed to require less re-dosing than the single Fab antivenom. In the studies done comparing CroFab to Anavip, Anavip resulted in significantly lower rates of recurrent or late thrombocytopenia than CroFab. This is thought to be because the Anavip has a much longer half and can better combat the subacute phase of envenomation that can lead to rebound thrombocytopenia after an initial phase of recovery. The two antivenoms had similarly low rates of adverse reactions.

In terms of use for Virginia snakes, Anavip may be of benefit in treating patients with timber rattlesnake envenomations who are at high risk for rebound thrombocytopenia and who have classically required robust repeat dosing of CroFab. While Anavip is not FDA approved for non-rattlesnake envenomations, patients with copperhead envenomations were included in studies of the newer antivenom. Most of the data about Anavip in comparison to CroFab is concerning its ability to treat the hematologic effects of rattlesnake envenomation, which are not seen with copperhead snakes. Based on the current literature, it is not clear how well Anavip works for the treatment the local pain and soft tissue swelling that is seen in isolation from copperhead envenomations. Future research into the use of Anavip vs CroFab specifically with common Virginia snakes like the copperhead and timber rattlesnake would be beneficial. Based on the predominance of copperheads in the region covered by the Blue Ridge Poison Center, and the lower risk of severe coagulopathy from the regional snakes, we do not recommend changes to hospital stocking of antivenom at this time.

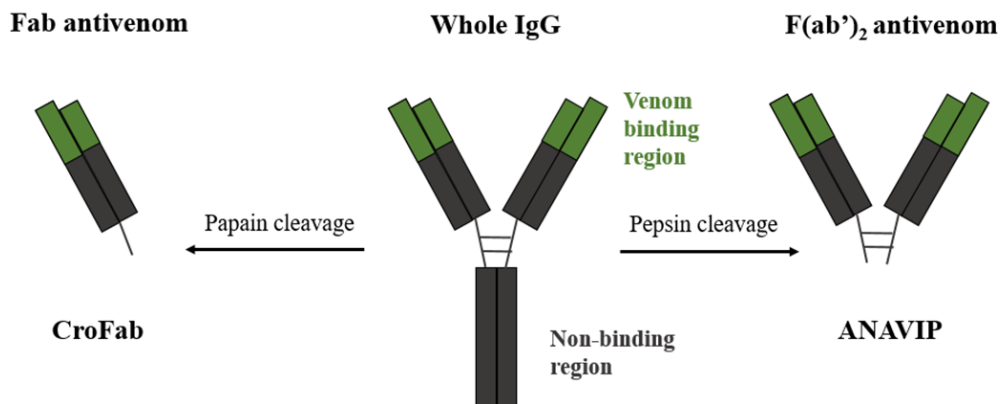
The experts at the Blue Ridge Poison Center are available for advice in treating envenomations or any poisoning exposure. Call 1-800-222-1222. Health care providers may also call the dedicated HCP hotline: 1-800-451-1428.

References available upon request.

Table 2. A comparison of Fab and F(ab')₂ antivenoms.

	CroFab (Crotalidae polyvalent immune Fab)	ANAVIP (Crotalidae equine immune F(ab')₂)
Manufacturer	BTG International	Instituto Bioclon
Fab fragments	Ovine derived Fab fragments One venom binding site	Equine derived F(ab') ₂ fragments Two venom binding sites
Snakes used in antivenom creation	Snakes found in the US: -Eastern diamondback rattlesnake (<i>C. adamanteus</i>) -Western diamondback rattlesnake (<i>C. atrox</i>) -Mojave rattlesnake (<i>C. scutulatus</i>) -Cottonmouth (<i>A. piscivorus</i>)	Snakes found in Mexico/Central America: -Terciopelo (<i>B. asper</i>) -South American rattlesnake (<i>C. durissus</i>)
Elimination half life	12-23 hours	5.5 days
Dosing	Initial: 4-6 vials Maintenance: 2 vials every 6 hours for 3 doses for all pts with coagulopathy, additional doses to control symptoms	Initial: 10 vials Maintenance: 4 vials only if needed to control symptoms
Relative contraindications	Allergy to: -Sheep -Pineapple -Papaya -Alpha gal	Allergy to: -Horses
Adverse effects	Allergic reaction Anaphylaxis Serum sickness	Allergic reaction Anaphylaxis Serum sickness

Figure 1. A visual representation of Fab vs F(ab')₂ fragments.



The Blue Ridge Poison Center receives funding from University of Virginia Health, the Virginia Department of Health, and the U.S. Health Resources Services Administration (HRSA). We are accredited by the American Association of Poison Control Centers. We've been proudly serving the Commonwealth since 1978.