NEWS FROM THE PIT

Arizona Poison and Drug Information Center

ARIZONA Poison and Drug Information Center
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Two Antivenoms, One Goal

Understanding CroFab and ANAVIP for rattlesnake bites

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There are two antivenoms for pit viper bites in the US: CroFab and ANAVIP. Both can stop venom from causing more harm and additional injury. They differ in how they are made, how long they last, and how they are given.

What does antivenom do?

Rattlesnake venom is a mixture of proteins that can damage tissue, affect blood clotting, lower blood pressure, and sometimes affect the nervous system. Antivenom contains purified antibody pieces that attach to venom toxins. Think of those pieces as specially shaped “catchers” that bind free venom so it can no longer reach new targets.

Antivenom is best at stopping damage from progressing. It cannot instantly erase tissue injury that has already occurred, which is one reason prompt medical evaluation matters.

NEWSLETTER HIGHLIGHTS

Image 1: Banded Rock Rattlesnake

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Same goal, different design

CroFab and ANAVIP are made in a similar way. Small amounts of snake venom are given to healthy animals. The animals make antibodies against the venom. The antibodies are then cleaned, cut into smaller pieces, and made into medicine.

CroFab

- Made from sheep antibodies.
- Each antibody is separated into smaller, single binding fragments called Fab fragments.

ANAVIP

- Made from horse antibodies.
- Two binding fragments remain linked together, creating the larger F(ab')2 fragment.

The shape of each product can affect how long it stays in the blood. CroFab has smaller pieces that leave sooner. ANAVIP has larger pieces that stay longer. This may help ANAVIP catch venom that enters the blood later. Still, one product is not always better for every person.

Why do the products act differently?

One arm or two linked arms

A full antibody looks like the letter Y. The two tips grab a target. CroFab has one separate tip, called Fab. ANAVIP keeps both tips linked, called F(ab')2. Both products remove the long stem, called Fc. The stem is not needed to grab venom. CroFab's small pieces can move into tissue. The kidneys remove them from the blood sooner. ANAVIP's larger pieces stay in the blood longer. The CroFab label lists a half-life of about 12 to 23 hours. Half-life is the time for the amount in the blood to drop by half. The ANAVIP label lists a mean half-life of 133 hours, or about 5.5 days. These numbers came from two small and different studies. They are not a fair head-to-head test.

Different snake venoms are used

CroFab comes from sheep. The sheep are given venom from four snakes: Western diamondback, Eastern diamondback, Mojave rattlesnake, and cottonmouth. Each antibody group is cleaned. The four groups are then mixed.

ANAVIP comes from horses. The horses are given venom from two snakes: the terciopelo and Central American rattlesnake. These snakes live farther south. Their venom has many of the same targets as U.S. pit viper venom. So the antibodies can also grab venom from U.S. snakes. ANAVIP is tested against seven kinds of venom.

Key idea: A drug does not need venom from every snake it treats. Many snake venoms share the same targets. The antibodies can grab these shared targets. Much of this proof comes from animal tests, not people.

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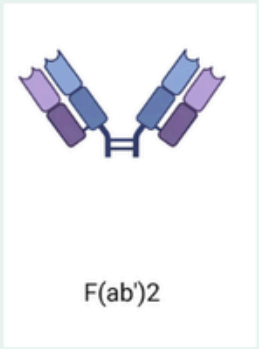
How the antibodies are cut

Where the cut is made matters

Both products start with full antibodies. An enzyme acts like a pair of tiny scissors. It cuts off the Fc stem. The tips that grab venom are left. The place of the cut decides if the two tips split apart or stay linked.

Step	CroFab	ANAVIP
Enzyme and cut	Papain cuts above the hinge. The two arms split apart. The Fc stem is removed.	Pepsin cuts below the hinge. The Fc stem is removed. The two arms stay linked.
Final product	Single Fab pieces from sheep. Four groups are cleaned and mixed.  Fab	Linked F(ab')2 pieces from horses.  F(ab')2

Allergy risks are different

Considerations	CroFab	ANAVIP
Animal source	Sheep-derived proteins	Proteins from horses. A horse-protein allergy raises the risk of a severe reaction.
Manufacturing-related	Papain is used to make CroFab. Tell the team about allergy to papain, papaya, chymopapain, or bromelain.	Pepsin is used to make ANAVIP. Tiny amounts of pepsin and cresol may stay in it. Cresol may cause pain at the IV site or muscle aches.

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Why might the hospital use one product instead of the other?

The medical team considers the patient's symptoms, laboratory results, allergy history, the species likely involved, the hospital's treatment pathway, and which antivenom is immediately available. Poison center specialists and medical toxicologists often help guide these decisions.

A clinical trial found fewer late clotting abnormalities with the longer-lasting F(ab')2 product than with Fab treatment. Even so, studies do not prove that one antivenom is superior in every situation. Both products can control North American pit viper envenomation, and both require careful monitoring.

Common question and misconceptions

The snake does not need to be captured for treatment. Clinicians treat the patient's symptoms and test results, not the photograph or the snake's size. A small or young rattlesnake can still cause important envenomation, while a large snake may deliver little venom. Likewise, early mild swelling does not guarantee that the bite will remain mild. Antivenom is not automatically given after every bite. If examinations and laboratory results remain normal during an appropriate observation period, treatment may not be necessary. When venom effects are progressing, however, delaying indicated antivenom can allow more injury to occur.

IF A RATTLESNAKE BITE OCCURS

- **Call 911.** Do not wait for symptoms to appear.
- **Move away from the snake.** Do not try to catch, kill, or photograph it up close.
- **Keep the person calm and still.** Remove rings, watches, and tight clothing near the bite before swelling worsens.
- **Do not cut, suction, ice, or apply a tourniquet.** These measures do not remove venom and may increase injury.
- **Go to a hospital.** Antivenom decisions require repeated examinations and laboratory testing.

The bottom line

CroFab and ANAVIP take slightly different routes to the same goal: neutralizing circulating venom and preventing further injury. CroFab uses smaller sheep-derived Fab fragments and a scheduled maintenance plan. ANAVIP uses longer-lasting horse-derived F(ab')2 fragments and an observation-and-redosing plan after control. The right product is the one the treating team can give promptly and monitor appropriately for that patient.

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Sources and further reading

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