NEWS FROM THE PIT

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The Things We Do For Blood

Management of Bleeding in Rattlesnake Envenomations

By Tyler Hoelscher, MD

A few years ago, I gave a talk to an OB/GYN residency program about management of rattlesnake bites. After I described the disruption to the body's ability to clot blood (coagulopathy) caused by rattlesnake venom, one of the senior physicians in the audience asked me, "If the patient is low on clotting factors and platelets, why not just transfuse them?". This is a very reasonable question; after all, that OB/GYN had treated many patients with massive bleeding after giving birth who developed coagulopathies and were treated by doing just that: replacing the lost blood products. Unfortunately for us, coagulopathies caused by rattlesnake bites are a different beast altogether.

Remember that blood clotting involves complex systems of proteins and platelets working together to form a blood clot capable of stopping a bleed. These systems happen to be the bane of medical students preparing for board exams across the world. There are many ways to disrupt these systems to create coagulopathies, so intelligent scientists have found ways of replacing clotting proteins and platelets. This is almost always done via transfusion of blood products. At modern-day blood banks whole blood is rarely transfused. Rather, when a physician needs to transfuse a patient, they will ask for the individual blood component their patient needs. This comes down to four things: packed red blood cells (PRBCs), fresh frozen plasma (FFP), platelets, and cryoprecipitate. PRBCs and platelets are pretty straightforward, but understanding the role of FFP and cryoprecipitate is just as important. Plasma is the complex mixture of water, salts, and proteins that forms the substrate of your blood. Among these plasma proteins are our clotting factors. After plasma is frozen into FFP, it is warmed by several degrees, and then spun in a centrifuge to collect the largest proteins that precipitate out of solution. This is our cryoprecipitate. There are several components to cryoprecipitate but the most relevant part for today is fibrinogen, the protein that is cleaved into fibrin to form a clot.

NEWSLETTER HIGHLIGHTS

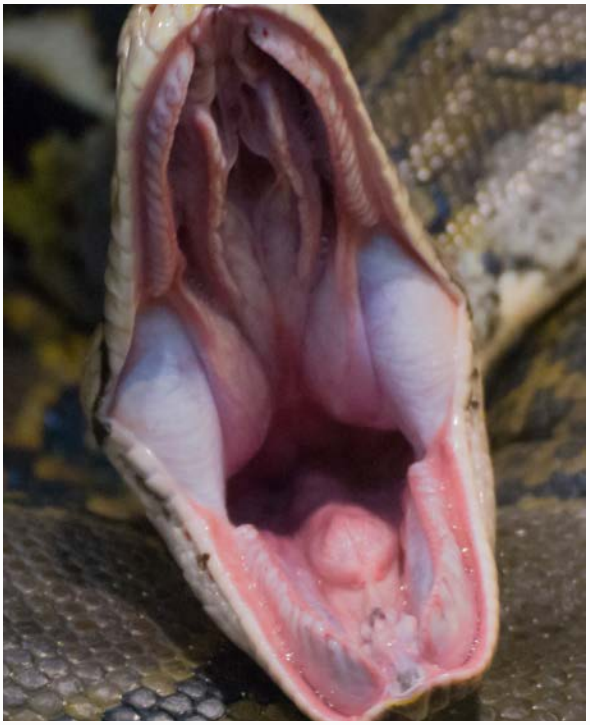
The Things We Do For Blood

Continued from page 1

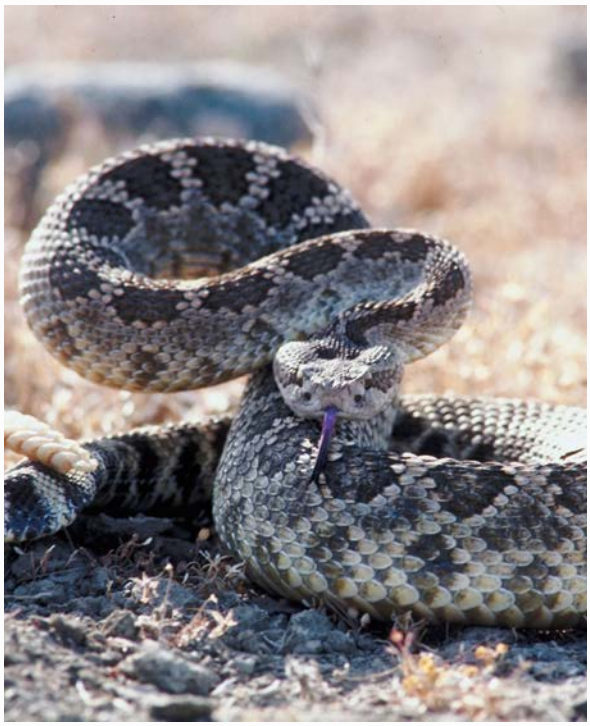
So, when I told that OB/GYN that rattlesnake-envenomated patients depleted their platelets and fibrinogen, his natural response was to suggest that we replace them. Trauma patients and patients bleeding after childbirth often become coagulopathic, similar to what is seen in rattlesnake envenomations, and require massive transfusions of whole blood, including PRBCs, FFP, platelets, and cryoprecipitate. Eventually these patients are unable to clot until they are given more clotting factors and platelets, so his suggestion was completely reasonable.

Let's talk about rattlesnake venom again. Remember, venom is a complex mixture of proteins and other molecules that cause many harmful effects on their target, and hemotoxicity is one of them. Rattlesnake venom enzymatically causes the inappropriate activation of the clotting cascade and platelets to form a myriad of useless tiny clots throughout the victim's bloodstream. Then when your platelets and fibrinogen have been spent making these tiny clots, you don't have enough fibrinogen or platelets left to stop a bleed! Unfortunately, the enzymes in the snake venom are not used up in this process, so they can keep on tearing away at your platelets and fibrinogen unchecked.

Let's say we then take this person who is written up in the Annals of Emergency Medicine in 1991, who was bitten by a Western Diamondback rattlesnake (Crotalus Atrox). He was found to have dangerously low platelets (thrombocytopenia), of 1,000/ul (normally ≥ 150,000/ul). He was transfused 10 units (!) of platelets and his platelet count improved back to 17,000, which is still very low. The next day his platelets were checked again, and they were right back down to 1,000! A similar situation happened to a man bitten by a Massasauga (Sistrurus catenatus) documented in the same paper. After discharge he was found to have dramatically low fibrinogen levels - less than 50 mg/dl (normally ≥ 150,000 mg/dl). He was transfused 15 units of cryoprecipitate, and the next day his fibrinogen levels were unchanged.



What about when bleeding is in a place you can't see?



Is antivenom the miracle cure for all rattlesnake envenomations?

The Things We Do For Blood

Continued from page 2

One unfortunate situation we must face in medicine is resource management, and unfortunately our blood products are always somewhat limited. When platelets and cryoprecipitate do not seem to help, and we don't have much of them to spend, it looks like we should not be routinely using them for rattlesnake bite patients.

In both cases from this article the patients then went on to have full recoveries, but it still leaves us with the question, what are we seeing here? Why didn't those blood products work? Well, the rattlesnake venom was left in the body and continued to destroy platelets and clotting factors regardless of how much they were replaced in both patients. How then, do we stop this? Antivenom!

Antivenom consists of antibody proteins capable of binding and inactivating the venom causing the coagulopathy in the first place. In envenomated, coagulopathic patients we have seen demonstrated time and time again how efficaciously antivenom halts the coagulopathy associated with rattlesnake envenomation. Now keep in mind that I said it halts the coagulopathy, not reverses it. Those platelets and clotting proteins the venom destroyed are still just as useless as before, but with the venom neutralized, your liver and bone marrow can get back to work on replacing those.

Now, does that mean that antivenom is the miracle cure for all rattlesnake envenomations? Absolutely not. Keep in mind that if a patient is bleeding to death after a rattlesnake bite, their cause of death will be blood loss. No matter how much antivenom I give a patient, their heart can't beat if there's no blood to pump. What does this look like practically? In most cases of significant envenomation there is no bleeding. Those patients get antivenom and that's all. The patients should avoid things that might trigger bleeding, like elective surgeries, contact sports, and dental procedures, but more than likely they won't develop any significant hemorrhage.

The Things We Do For Blood

Continued from page 3

Next up is the patient who is sick, very anemic, but not actively bleeding. They may have had some type of bleeding that has since stopped, or they may be a dialysis patient who is just anemic all the time. These patients get antivenom, and may get a transfusion of PRBCs to stabilize them. The last thing you want is a patient who is already anemic, to start bleeding.

Lastly is the real nightmare, the envenomated patient who is sick, unstable, and actively bleeding. In these cases the source of bleeding should be located, but for many of these patients the source of the bleeding cannot be controlled. Remember, snakebitten patients often bleed from mucosa, like the intestines or bladder, or into their own tissues, so you can't exactly put a band-aid on them. For these patients, treatment should include everything, PRBCs (to "fill up the tank" if you will), antivenom (to bind the active venom), FFP, platelets, and cryoprecipitate. Just like a trauma patient, we want to give whole blood, every component that is fractionated. Didn't I just say that replacing platelets and clotting factors didn't work? Yes! However, if your patient is coagulopathic and actively bleeding, they will probably bleed to death before their body is able to replace the spent clotting components. Remember that antivenom doesn't reverse your coagulopathy, it only stops it. Will you use a lot of expensive blood products? Yes, but if your patient needs them, give them.

Now, what have we seen here at the AzPDIC? Of the last 2,000 hospitalized rattlesnake envenomation patients we have received calls on, 35 of them were sick enough to truly require transfusions, although other patients have received transfusions that they arguably did not need. Thankfully, these cases are very rare. Patients treated with antivenom alone are definitely the norm.

So, remember, snake venom causes coagulopathy by unnecessarily activating your own clotting mechanisms until they are depleted, and transfusing components will not help until you've inactivated the snake venom with antivenom. If your snakebite patient is coagulopathic, what they need is antivenom. If your snakebite patient is bleeding out, what they need is still antivenom, but don't let your patient bleed to death in the meantime, be ready with some blood.

Lastly, if you're the one taking care of this patient, don't be afraid to ask for help. A toxicologist is only ever a phone call away at 1-800-222-1222. In the next letter I'll discuss another challenge for toxicologists: managing rattlesnake patients who are prescribed anticoagulants.

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