

Anaphylaxis and the Venomous Keeper:

What you need to know.

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That venomous snake handlers can develop hypersensitivities to snake venom is not a new revelation. Both L. M. Klauber and Findlay Russell, M.D. made reference to it in their writings; Klauber doing so in 1956. But within the venomous and medical communities alike, there is currently confusion as to how this process occurs and how to differentiate it from hypersensitivity to antivenom.

Key Words

Allergen: a substance that can produce a hypersensitive reaction in the body but is not necessarily harmful to everyone.

Antigen: a substance, usually a protein, that causes the formation of an antibody and reacts specifically with that antibody.

Histamine: An amine released by mast cells and basophils that promotes inflammation.

Immunoglobulin: any of 5 structurally and antigenically distinct antibodies present in the serum and external secretions of the body, including IgA, IgD, IgE, IgG, and IgM.

Shock: Inadequate perfusion of blood and oxygen to the tissues of the body.

In your lifetime, you will be exposed to thousands of foreign proteins. Some will be injected into your body in the form of an inoculation, or a wasp sting; some proteins will be inhaled as you pet your dog, sending his dander flying into the air. And some protein molecules are ingested, i.e., peanuts, shellfish, etc. By whatever method they enter your body, they are recognized by your immune system as being "foreign", that is, not part of your body. Once these foreign proteins have entered your body, they are called "antigens" and must be dealt with by your immune system.

Once an antigen has been identified by your immune system, an antibody is formed specifically for that antigen. Think of antibodies as the armed guards of your blood stream. These antibodies will be produced by your body to fight the foreign invasion and then their numbers will dissipate when they are no longer needed. At that point, memory cells that "remember" that particular antigen are embedded in the marrow of your bones. If that specific antigen ever shows up again, your body will call on those memory cells to begin producing antibodies to fight the designated antigen. This time it will only take three to four days. *[Incidentally, this is why Bill Haast has to inject himself weekly - to maintain a high number of active antibodies. If he stops, the antibodies will not be active in high enough numbers to counter-act a snakebite. And with a snakebite, he doesn't have time to wait for his memory cells to go into production.]*

When an antigen (that has been previously identified by your immune system) is spotted flowing through your blood stream, the antibodies attach themselves directly to the antigen, thereby marking the antigen for destruction. White blood cells, called "macrophages" then envelop or literally "eat" the antigen. This is how our body deals with all unwelcome intruders, and in reality, this process occurs in your body many times each day. *(Hopefully not with snake venom proteins though!)*

So what does all of this mean for venomous keepers? Well, snake venom is an organic soup, made up of many different proteins. And throughout your career as a professional or hobbyist, you are exposed to these proteins in one way or another. Whatever the source, your body recognized these proteins and your immune system responded, most likely a long time ago. As you read this, your memory cells stand ready to defend your body from attack. But unfortunately, there is a fine line between immunity and hypersensitivity.

Allergic Reactions and Anaphylaxis: What's the difference?

Most people are familiar with the words "allergic reaction" and "anaphylaxis", but few know the difference. An immune response between antibodies and antigens is a normal protective function of the body to guard against diseases or infections. However, when the immune system over reacts, or is "hypersensitive", an allergic reaction occurs. The antigen causing the allergic reaction is then referred to as an "allergen".

An allergic reaction is marked by an increased physiological response to an antigen after a previous exposure, beyond what is considered normal. There are then 4 levels of response that may occur: A type I response occurs when a substance called "immunoglobulin E" or IgE, reacts to the presence of the antigen. This may lead to symptoms of

hay fever or asthma, but possibly - anaphylaxis, *which I'll get to in a moment*. Type II and III reactions occur when immunoglobulins G or M combine with an antigen. These reactions may cause anything from local itching to widespread hives and other associated symptoms. Type IV reactions are caused by cells called T lymphocytes, and are usually quite delayed in onset, and generally not very severe.

Symptoms of an allergic reaction may be minor or severe, local or systemic. They may include local redness and itching, or itchy welts that appear over the whole body. The raised area that appears around a mosquito bite is an example of a local response. But I have personally seen severe allergic reactions that caused a person's face to swell to cartoonish proportions. However, this did not constitute anaphylaxis. So let's return to Type I reactions since they are potentially the most severe, and define anaphylaxis.

What is Anaphylaxis?

Anaphylaxis is an extremely severe allergic reaction that is mediated by a molecule called IgE, and IgE molecules are attached to cells called "mast cells". Mast cells contain a substance called histamine, which you might recognize from the word "antihistamine". When an antigen crosses paths with IgE and mast cells, this substance called histamine is released. Now, histamine in low doses is not all that bad, but it is annoying. It's that stuff that makes your nose swell shut when you have a cold, and your chigger bites itch like the devil. The problem with histamine is that during anaphylaxis it is released in massive quantities. And histamine causes the walls of the vascular system to become "leaky", thereby allowing the fluids in the blood to escape the vascular system. Think of it in this way: the pipes that run through the walls of your house containing water develop some leaks. And the water escapes into spaces outside the pipes, causing the sheetrock walls to swell. If enough water were lost this way, what would happen to the water pressure at the faucet? It would drop right? Well, think of anaphylaxis as the pipes in your walls springing a thousand leaks all at once.

The rapid drop in blood pressure is actually what is called "relative hypovolemia". [*Hypovolemia means "low blood volume".*] The blood is still inside of the body, but it's not in the right place. That's why the tongue, face, neck and lips swell during an allergic reaction or anaphylaxis. The fluid causing the swelling is being drawn from the reservoir of the circulatory system. And the fluid will only stop leaking from the blood vessels when the pressure outside of the vessel walls is equal to the inside pressure. [*When the blood pressure is too low to perfuse the tissues of the body, the body is in the state known as "shock". And in this case, anaphylactic shock.*]

In response to the dropping blood pressure, the heart begins to beat faster to try to maintain an adequate pressure (to perfuse the brain), and in the process uses up more oxygen. Meanwhile the airways are swelling, making breathing increasingly difficult. At the same time, the smooth muscle fibers that line the airways are also contracting as part of the immune response. The immune system becomes the body's worst enemy!

What if I've never been bitten, *thereby developing venom antibodies* -- Do I still need to worry?

The answer to this question unfortunately is yes. And here are the reasons. Even though you haven't had snake venom proteins injected directly into your body, you have probably been exposed to the venom through snake handling, or even just day to day cleaning of your cages. The easiest way to develop an allergy is through exposure via the nose. This method of delivery allows for repeated exposure and the immune system seems to be geared towards it (hence hay fever). For the venom allergies this particularly holds true.

Co-author of this article, Dr. Bryan G. Fry, has developed severe allergies to numerous genera of snake simply from working around the venom. In three cases, he went into anaphylactic shock following his very first envenomation by a species. Any keeper therefore, can develop an allergy simply from being exposed to the dried venom in a cage. With most species this may not be a problem, but it is a problem with spitting cobras or species that are very generous in their venom delivery, such as king cobras, rattlesnakes, etc. They may leave copious amounts of venom (*especially from a molecular perspective*) on a food item, which then spreads the venom over the rest of the cage as it either runs until dead, or the snake drags it as it eats. A snake may also strike cage glass, or even tools that we handle. The venom then dries and can be blown around in the air as we clean or work around a cage.

Something else to consider is what is known as "cross reactivity". What this means is that there may be components that make up one snake's venom, that are also found in another snake's venom. If you have an antibody for that specific venom/ protein molecule, then it doesn't matter what the source is, you can still have a reaction to that antigen. To give you an idea about how many venom components are shared within the snake world, it only takes the combined venoms of 4 species to make the antivenin "Crofab", which covers every species of rattlesnake, cottonmouth and copperhead in North America (*although with varying degrees of effectiveness depending on the species involved*).

Why are so many people allergic to antivenom if they've never been exposed to horse blood?

Even though most people have never been exposed to horse blood, up to 75% of people that receive Wyeth Antivenin Crotalidae Polyvalent, a horse blood product, have some type of allergic reaction. How could this be? Well, how many people have ever ridden a horse? Or had their photo taken on a pony when they were 5? Plenty.

The immunoglobulins from the horse are (*in the undigested form*) shaped like a Y. The parts that bind to the antigen are the V parts of the Y shape. The I part (of the Y shape) contains sequences that identify the source of protein. This is the area that screams "horse!" and is what the immune system reacts to. To give another example, in many autoimmune diseases, the person's immune system is unable to recognize that the I part of the Y in their own proteins, is part of their body. Instead, their immune system starts attacking it's own proteins thinking that it's foreign. This is also why the better antivenoms are just the V (Fab2 antivenoms) or the \ and / (Fab antivenoms) and are consequently much less allergenic. These antivenoms, such as CroFab, thus are fabulous (sorry for the pun).

So, people can be allergic to horse blood products simply from being around horses and inhaling their dander/horse proteins, thereby developing a sensitivity to sequences that are similar to the I region of the Y that makes up the antibody IgE and other antibodies. Does the same apply for snake dander? Well, no. The components we are exposed to on a horse's skin include horse antibodies, but the inside of a venom gland in a snake is actually a distinct molecular entity from the rest of the snake. For the most part the proteins share little or no homology with anything else found in the snake.

Clearing up a misconception.

There is also an area of confusion that must be dealt with in regards to venom and antivenom hypersensitivity. In a television documentary about an antivenom production facility in South America, a worker was bitten by a juvenile *Bothrops jararaca*. The worker was subsequently taken to the hospital, where the doctor refused to administer antivenom. The doctor's reason for this was that since he was a "snake handler", he may be hypersensitive to the antivenom because it might have snake venom in it. And since he had already been injected with snake venom, he didn't want to make it worse. This is fallacious reasoning.

The antivenom is comprised of animal blood products, specifically horse blood sera, not snake venom. Let me repeat - there are no active venom components in the antivenom, just antibodies that are

designated to destroy venom molecules (*which the bitten individual certainly could have put to good use.*) Allergic reactions to antivenom are from the horse proteins that are part of the venom antibody.

I'm a venomous snake handler. So what should I do?

The first thing you need to do, is recognize that there is a distinct possibility that your next trip to the snakeroom could very well be an anaphylaxis inducing emergency - if you are bitten of course. And anaphylaxis is much more likely to kill you before the snake's venom has a chance to do its work.

A few years ago in a Transvaal Snake Park in South Africa, a snake handler died after an Egyptian cobra bit him on the left wrist during a public demonstration. The handler, Paul St. John Olsen, 25, reported the incident immediately but soon after lost consciousness. Within 10 minutes of the bite, paramedics and even a doctor were on the scene. But despite the rapid administration of an antivenin and attempts to resuscitate him, his condition continued to deteriorate. He was rushed to a hospital by ambulance, where ER staff continued attempts to resuscitate him for several hours. But he died without ever regaining consciousness. His death was later attributed to anaphylaxis.

When emergency personnel arrive at the scene of a snakebite, their adrenaline will be pumping and unfortunately, their mind will be racing - wondering what to do. Most EMS personnel know very little about snakebite. Signs and symptoms of anaphylaxis may in their minds be blurred with what they think snake venom is supposed do to a human body. This is why it is VERY important that you have protocols already written up, ready to go to the hospital with you - in the event that you are unable to speak. I have a single sheet of paper that reads: "*Venomous snake handlers may have allergic reactions to snake venom. Watch for Anaphylaxis!*" It's the first page of my bite protocol, stored in a folder on the wall of my snakeroom.

Also, talk with your personal physician about this potential medical emergency. Show him/ her this article and ask for an Epi-Pen or Anakit prescription. And if you are envenomated, watch for signs of anaphylaxis and treat yourself if necessary. Epinephrine (*a.k.a. adrenaline*), and antihistamines such as Benadryl, reverse the symptoms of anaphylaxis, and work best if given early. An Epi-Pen however is only a temporary fix. In my experience, symptoms may return full force within 20 minutes of an epinephrine injection. This means that you should hastily activate 911 if you ever have any symptoms of an allergic reaction, whether you treat yourself or not.

As a general deterrent, Bryan recommends wearing a good particulate filter mask and latex gloves when cleaning cages. The white surgical masks are useless, since they are designed to keep substances from coming out of the mouth and onto a patient rather than preventing airborne particulates from entering the mouth. The only masks that work well enough, are the rubber ones that filter all of the air entering the lungs.

Conclusion

It would be impossible for us to tell you whether or not you will be able to distinguish the signs and symptoms of anaphylaxis from the actual effects of a snake's venom. The reason is elementary - it depends on which species you are bitten by, and there are entirely too many to cover in this article. If you are bitten by a snake and feel as though you are having an allergic or anaphylactic reaction based on what you have read here, it probably won't hurt you to use an Epi Pen - even if you really aren't having an anaphylactic reaction. But you should immediately expect for your heart rate to increase dramatically - up to around 160+ bpm. The best bet is to talk this scenario over with your personal physician.

Anaphylaxis has been likened to a train sitting on a mountain top -- quite simple to stop at the top just by blocking the wheels, but almost impossible when it's running away and halfway down the mountain. We have all heard of people dying from allergic reactions to bee stings, and I've even seen it first hand. The last patient that I saw with anaphylaxis died even though she arrived at the ER 15 minutes after of the onset of her symptoms! And she was only stung by a bee. Think about the amount of venom that a snake injects compared to a bee! It is this tremendous volume of foreign proteins suddenly introduced into your body that could activate anaphylaxis. And the truth is, there's no sure fire method of determining if and when anaphylaxis will occur.

Now that you know it's a possibility, we hope you take the necessary precautions to both avoid and prepare for it. But better yet, avoid it altogether by not getting bitten! Be safe and enjoy the hobby.