

# NEWS FROM THE PIT

Arizona Poison and Drug Information Center



## *Bothrops lanceolatus*

The snake that literally gives you a heart attack

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It's finally that time. The time you look forward to all year. The time you are finally able to get away from your job and just relax. You know the time I mean—Vacation Time.

For many of us, our dream vacation is a tropical island getaway. A few perfect days of sunny skies, warm weather, cold drinks, and outdoor activities without a care in the world other than deciding where to get our next meal.

On one Caribbean Island however, a carefree day in the sun can quickly take a deadly turn.

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**A history of fear surrounds the Martinican lancehead and its potent venom.**



## A Stroke of Bad Luck

One sunny day in 2008, a 74-year-old man was outside gardening when he was bitten by a snake on his left elbow. Initially there was swelling of the arm, and he applied a local remedy to the wound instead of going to the hospital. He was found unresponsive by his family two days after the snakebite occurred and was taken to the hospital. He received antivenom in the hospital, however, this did nothing to improve his condition. Unfortunately, multiple cerebral infarcts were shown on magnetic resonance imaging. Additionally, his electrocardiogram and troponin level revealed that he had suffered a myocardial infarction as well. Despite treatment in the intensive care unit, the patient ultimately developed heart failure and died six days later.

Now I know what you're thinking: "That man was elderly; he probably had undiagnosed vascular disease and risk factors for ischemic events. That stuff would never happen to a young healthy person like me!" Unfortunately, you would be incorrect—thromboembolism resulting in death happens in young and old victims alike. Sadly, the man described in this case report is just one example of the potentially deadly effects caused by the venom of *Bothrops lanceolatus*—the lancehead viper of Martinique. *B. lanceolatus* is the only snake indigenous to Martinique, one of the Windward Islands in the Lesser Antilles archipelago of the eastern Caribbean Sea.

The densely populated island covers 436 square miles and is home to over 364,000 people as of 2019. A history of fear surrounds the Martinican lancehead and its potent venom. There are 20-30 reported snakebites in Martinique every year. That might not sound like many bites, however for an island population heavily reliant on jobs from tourism and agriculture, the morbidity and mortality this snake causes are significant. Up to 40% of patients who do not receive antivenom treatment suffer thrombotic complications, and up to 25% die or have life-changing sequelae, such as permanent paralysis from cerebral infarction or heart failure from myocardial infarction. These sequelae are in sharp contrast to the injuries from venomous snakes found on the American continents.



## A Snake of a Different Color

Despite being closely related genetically, the venom effects of mainland American pit vipers are opposite those of the *B. lanceolatus*. As you probably remember from a prior issue of News from the Pit, pit vipers like the rattlesnakes, copperheads, and cottonmouths of North America are known for their potential to cause bleeding (not clotting) complications. With mainland pit viper envenomation, it is common to see markers of impaired clotting such as thrombocytopenia, as well as decreased fibrinogen with elevated prothrombin time (PT) and activated partial thromboplastin time (aPTT). While significant bleeding is considered uncommon, blood clots by comparison are extremely rare.

In Arizona, we have treated over 2,000 pit viper envenomations since 2009, and around 100 of those patients experienced more than just minor bite site bleeding; however that bleeding was considered clinically significant in only about 1/3 of cases. Among the same 2,000 envenomated patients, only 5 patients developed a complication related to blood clotting. In Martinique and the neighboring island of St. Lucia, *Bothrops* envenomation causes the same initial presentation of tissue injury and even thrombocytopenia that we see with rattlesnakes; however, it is more likely to cause elevated fibrinogen levels and minimally or unchanged PT and aPTT, and within 48 hours the envenomated patient is highly likely to develop clotting of both small and large vessels.

In our current News from the Pit series focusing on venom and hemostasis, we have covered that we expect to see thrombocytopenia and hypofibrinogenemia with rattlesnake envenomation, and that the hypofibrinogenemia was the result of thrombin-like enzymes in venom. These thrombin-like enzymes consume fibrinogen to make fibrin, but the fibrin that forms is not the same as normal fibrin and ends up being rapidly degraded. In fact, snake venom is so effective at consuming fibrinogen without causing a clot that the drug Arvin, which is derived from the venom of the Malaysian pit viper, has been studied for decades as an anti-clotting treatment via a mechanism termed “therapeutic defibrination.”

Perhaps you are asking yourself, “Why do bites from these snakes cause different clinical effects?” It likely comes down partially to differences in the composition of their venom. Viper venom is made up of many different proteins that lead to the constellation of signs and symptoms we see when treating envenomation. Multiple studies looking at venom composition between and among pit viper species have shown that the relative composition of a snake’s venom—how much of a certain type of protein compared to other types of protein—causes the varying spectrum of effects we see in envenomated individuals.

# A Snake of a Different Color

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In other words, each snake's unique venom "recipe" is a little different, and this causes some patients to have more swelling and tissue damage, whereas some may have more bleeding, or occasionally clotting, and some even manifest neurotoxicity. This may be consistent with yet another clinical difference between North American rattlesnakes and the vipers of Central America: bites from *Bothrops* species are notorious for causing significant local tissue damage. There has been an assumption that this additional tissue damage is related to prolonged time to antivenom administration.

In North America, time to antivenom is usually under a couple of hours for patients seeking healthcare. Studies from Central America report times far greater, sometimes with mean time to antivenom measured in days. While the "time is tissue" mentality is important, it may not be the entire explanation for the differences in local tissue injury. Perhaps different cytotoxins are present, or perhaps the snakes in Martinique are simply better able to get cytotoxins into the vasculature due to different "spreading factors" than other snake venoms.

It would be convenient to assume that the species that cause clots—*B. lanceolatus* and its St. Lucian relative, *B. caribbaeus*—simply have different venom compositions than their mainland *Bothrops* relatives, but this is not necessarily the case. If all *Bothrops* species actually have relatively similar venom compositions, then what is it about the island snakes that causes clots?

It is possible that a prothrombotic protein unique to *B. lanceolatus* and *B. caribbaeus* venom has not yet been identified, but there may be an alternative explanation. An autopsy was performed on the man who died of multiple infarctions in the beginning of this article. The authors of the case report propose that, rather than a procoagulant venom protein, it was actually damage to (and subsequent activation of) the vascular endothelium that led to this patient's deadly thromboemboli. Specifically, they liken the histopathological effects to the thrombotic angiopathy seen in patients with thrombotic thrombocytopenia, hemolytic uremic syndrome, and other conditions.



*If all Bothrops species actually have relatively similar venom compositions, then what is it about the island snakes that causes clots?*

# Better Living Through Chemistry

An equine-derived antivenom specific to *B. lanceolatus* became available in 1993, and its use has led to greatly reduced morbidity and mortality, largely from prevention of blood clots. This effect most benefits patients who are treated early—up to about six hours after being bitten. Patients may still develop blood clots despite antivenom treatment, but this is more common if they present late to a healthcare facility. Clot prevention with early antivenom is the best intervention, as evidence shows that prophylaxis and treatment with commonly used anticoagulants and fibrinolytics is ineffective.

## Looking A(lance)head

There is evidence that the population of this unique snake species has declined drastically since the middle of the 20th century. From 1970 to 2002, the government of Martinique supported an eradication program and would pay \$20 USD per snake killed. Twelve thousand snakes were killed the first year of the program, and that number declined by 97% over the next 32 years, with 386 snakes killed in 2002. Some experts attribute the steep decrease in snake killing to fewer sightings of the snake in the wild, indicating an overall decrease in population. With the end of the eradication program in 2002, there is no longer a monetary incentive to kill the snakes, and there has been a concomitant decrease in snake hunting by humans.

Nevertheless, the Martinican lancehead population remains threatened by local residents' fear of snakes, as well as loss of habitat caused by human encroachment. There will always be some danger associated with pit viper envenomation; however, the availability of antivenom specific to *B. lanceolatus* greatly reduces the risk of death and long-term physical impairment, and the risk of human harm must be balanced with the risk of losing the species altogether. *B. lanceolatus* is only found on the island of Martinique, and *B. carribaeus* is only found on St. Lucia. Venomous snakes play an integral role in the health of many ecosystems, as they help to control the rodent population. Additionally, many venoms are being investigated for their role in developing new pharmaceuticals. Maybe one day these unique snakes' venom will be used not to harm people but to help them, if we do not lose the snakes to extinction first.



**The Martinican lancehead population remains threatened.**

