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Coagulation laboratory studies after rattlesnake bite- what you see may not be what your patients have!

By: Vance G. Nielsen, MD

Thousands of people throughout the Americas receive treatment annually for envenomation by rattlesnakes. Typical patient care consists of assessing the extent of tissue injury, administering antivenom, providing supportive care like pain relief, and performing various laboratory evaluations. Standard hemostatic tests include the activated partial thromboplastin time (aPTT), prothrombin time (PT), fibrinogen concentration, and platelet count. The results of these tests are used to diagnose envenomation initially, as well as to determine the need for additional antivenom. The severity of most signs and symptoms will typically trend alongside hemostatic test results. However, sometimes the severity of laboratory coagulopathy does not match with the clinical picture. “Incoagulable” laboratory results usually mean that a patient (not a rattlesnake bite) has a very high risk for spontaneously developing a life-threatening bleed, and standard treatment involves some form of blood transfusion. We see these incoagulable lab results routinely in rattlesnake bite patients, yet they almost never develop clinically important bleeding. Instead of a transfusion, we administer antivenom, after which the fibrinogen and platelet levels return to normal values at varying velocities. Eventually, stable coagulation is achieved and determined by normal laboratory test results without transfusing any blood products.

NEWSLETTER HIGHLIGHTS

Image 1: Arizona Black Rattlesnake (*Crotalus cerberus*)

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So, what happened? Did the antivenom somehow enhance fibrinogen synthesis? Were the platelets aggregated (stuck together) somewhere, and then rejoined the bloodstream after circulating venom was neutralized? I propose another reason for "bleeding test tubes" and minimally bleeding patients: calcium-independent, hemotoxic snake venom enzymes. This explanation was recently published [1], and the present article serves as a call to arms to seriously consider point-of-care (POC) technologies to assess coagulation in the setting of any potential rattlesnake envenomation.

A critical problem exists in medical research, where the basic science and clinical care worlds each have the knowledge to understand a problem but fail to sufficiently communicate with each other. For decades basic scientists have classified venom enzyme activities in various ways, including whether the enzyme requires calcium for activity. Similarly, providers managing envenomed patients have long used citrate anticoagulated (blue top) and EDTA (purple top) tubes to collect patient blood and prevent thrombin generation from human enzymes compromising test results. Samples are usually transported and processed in a laboratory remote from the emergency room or intensive care unit. A typical workflow of this process is depicted in figure 1.

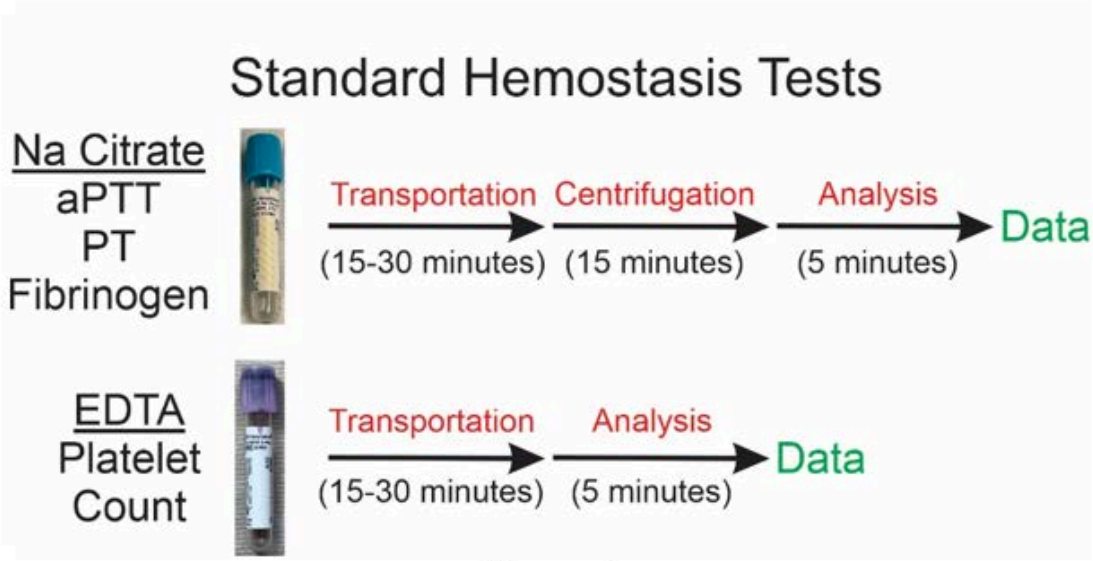

Figure 1

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When considered together, this diagnostic arrangement is fine for venom composed of calcium-dependent enzymes such as the Mojave rattlesnake (venom type B). The human and venom enzymes will both be inhibited in the standard blue and purple top tubes. However, both Western and Eastern diamondback rattlesnakes possess venom with calcium-independent fibrinogenolytic and thrombin-like enzymes, respectively. Thus, while the blood samples are being transported and further processed, the venom enzymes continue to degrade the blood sample, resulting in unmeasurable laboratory values that do not reflect the actual current clinical picture. In summary, considering the biochemical and clinical chemistry facts, it should not be a surprise that the administration of antivenom will attenuate or even prevent degradation of blood sample coagulation values, resulting in a “return” of platelet count and fibrinogen.

A solution to prevent a malalignment of clinical hemostasis and laboratory results is to minimize “needle to activation” time. Analogous to “fang to needle” time in the case of antivenom administration, it is proposed to minimize the time of blood collection from an envenomed patient to activation of the sample in a device to provide the hemostatic assessment. In the case of viscoelastic methods such as thrombelastography, blood can be obtained and the sample placed into a cup and activated within minutes to immediately generate data as displayed in figure 2.

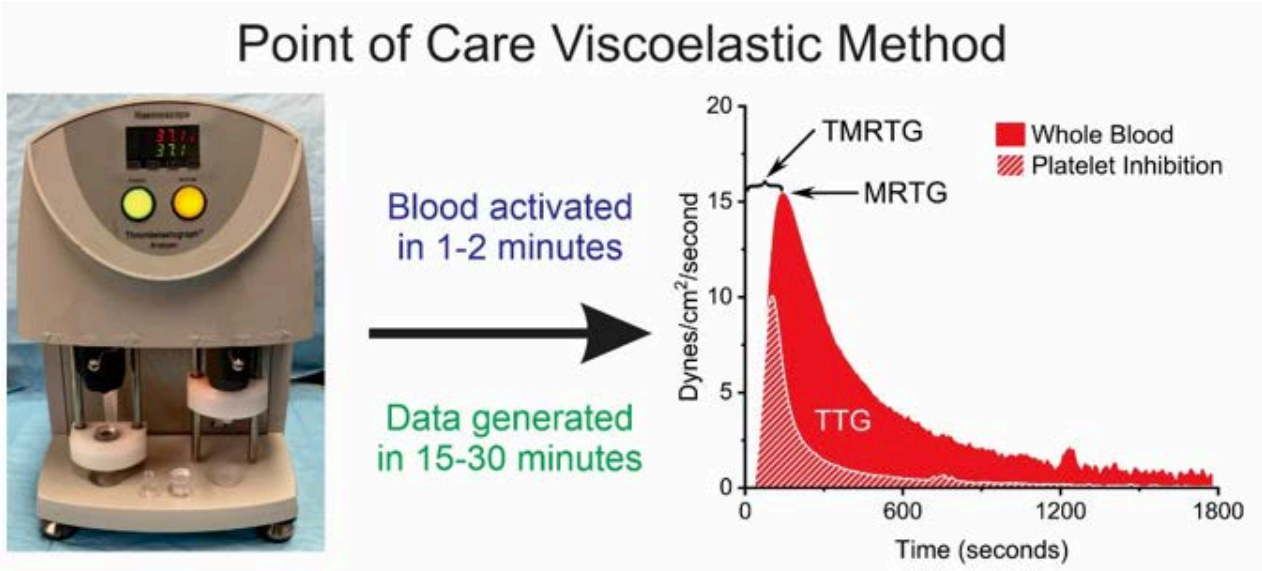

Figure 2

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Clearly not all emergency rooms or hospitals that treat rattlesnake bite victims have viscoelastic devices, and I am not advocating that. However, there are several POC devices that are available that could be maintained and transported anywhere in the hospital where envenomed patients are treated. A list of such devices is found in table 1.

Table 1

POC Device	Data	Manufacturer
PC100	Platelet Count	2M Engineering
qLabs FIB	Fibrinogen	Stago
Hemochron® Signature Elite	PT, aPTT	Werfen
ROTEM *sigma*	Viscoelastic	Werfen
TEG® 6s	Viscoelastic	Haemonetics Inc.

In conclusion, by diminishing the “needle to activation” time with POC methods of hemostatic evaluation, it is likely that the malalignment between the clinical picture and laboratory values of rattlesnake envenomed patients can be resolved. Any uncertainty of the species of rattlesnake or uncertainty of the presence of calcium-independent venom enzymes is diminished by the elimination of transportation/processing time with POC devices. Lastly, do not mistake this article as the final word on the matter. I strongly encourage the readership to compare standard hemostatic test and POC test generated results and draw their own conclusions on what sort of data they would want to decide how to treat their patients and administer antivenom.

1. Nielsen VG. Rattlesnake Roundup: Point-of-Care Thrombelastographic Methods Define the Molecular Impacts on Coagulation of Crotalus Venom Toxins In Vitro and In Vivo. Toxins, 2025;17:87.