NEWS FROM THE PIT

Arizona Poison and Drug Information Center

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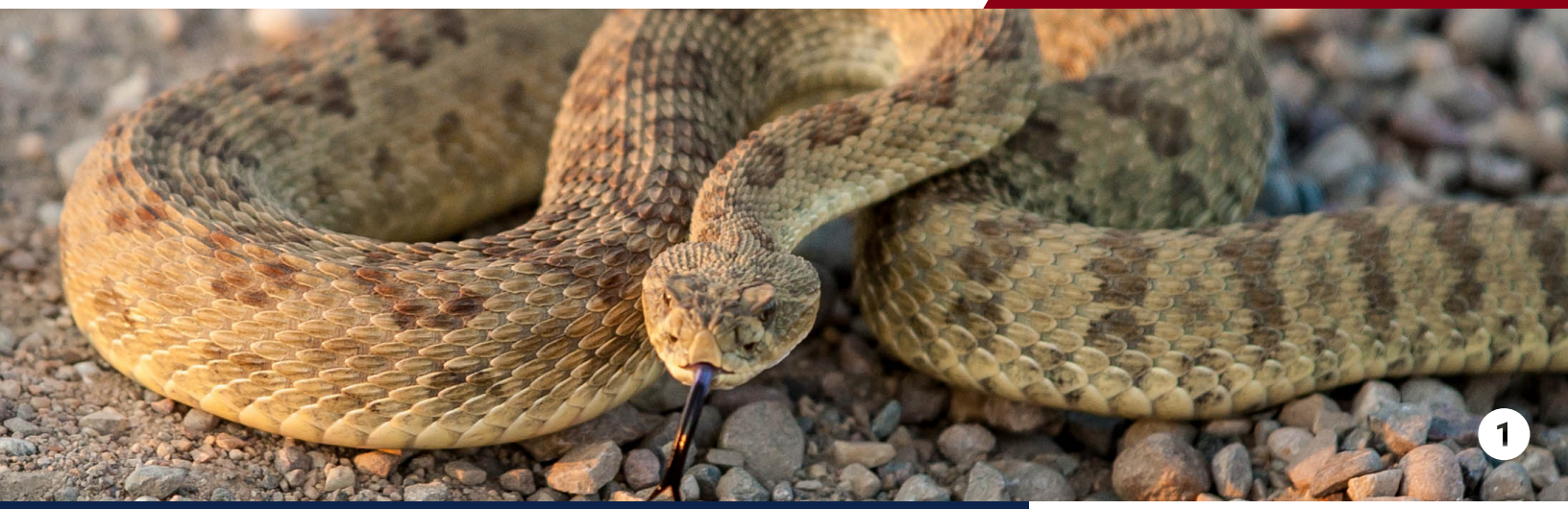

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Thromboelastography (TEG) and Snakebites

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Managing a rattle snake envenomation can prove to be difficult, considering all the different clinical effects we may see. The challenges can start with the history and diagnosis. Based on some preliminary AzPDIC research, around 20% of patients never see a snake, not even after they are bitten. This forces us to look for other ways to determine if a snakebite occurred, if it was a venomous snake, or was the patient simply pricked by a cactus thorn? Once a clinical diagnosis is made, it will ultimately determine whether antivenom is given.

Don't forget that antivenom works as a preventative treatment. Giving it after tissue damage has occurred is kind of like using the King's College Criteria to determine when NAC should be started for acetaminophen toxicity and is probably not in your patient's best interest. You know what else is not in their best interest? Getting a $100,000 hospital bill instead of a $1 band aid for a cactus poke. So, no pressure to arrive at the correct diagnosis as fast as possible, right? And it doesn't stop there. After you start antivenom, several other questions come up: How do you know the antivenom is working? When do you give more? What are you looking for to determine that the patient is safe to go home?

NEWSLETTER HIGHLIGHTS

Image 1: Prairie Rattlesnake, Crotalus viridis

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Thankfully, we don't always have to rely on a clinical diagnosis for envenomation. Useful objective markers can be obtained with conventional lab testing such as: complete blood counts (hemoglobin, hematocrit, platelets), prothrombin time, and fibrinogen levels. In the southwestern United States, about 60% of rattlesnake bites cause disturbances in platelet function or a depletion of available fibrinogen stores. Although obtaining platelet and fibrinogen levels can provide us with a quantitative analysis useful for diagnosis, they don't tell us anything about the patients bleeding risk. To do this, a global assessment of the coagulation process is needed, and this is where thromboelastography (TEG) may be of assistance.

Snake venom is a cocktail formed from dozens of various toxins, each with unique clinical effects. Thrombin-like enzymes are commonly found in Arizona rattlesnake venoms. These enzymes act like thrombin, converting prothrombin into thrombin, eventually cleaving fibrinogen into fibrin. This process is essential to form a stabilized blood clot to achieve hemostasis. However, thrombin-like enzymes do a subpar job creating a stabilized fibrin mesh: a key component to a robust blood clot. The fibrin meshwork created by these imposters generate weak blood clots that can be rapidly degraded, which will eventually result in venom induced consumptive coagulopathy. Once this process begins, fibrinogen stores start to become depleted, eventually resulting in hypofibrinogenemia. If you are waiting to see a drop in fibrinogen levels to confirm rattlesnake envenomation, then you are also letting all other venom effects go unchecked during that time. It seems less than ideal to sit and watch your patient deteriorate until it reaches the point that it becomes severe enough that you give antivenom, which again is a preventative antidote at best.

Let's discuss how TEG can aid in assessing and treating rattlesnake envenomated patients. The Functional Fibrinogen* assay available with the TEG hemostasis analyzer evaluates fibrinogen's contribution to overall blood clot strength (CFF-MA*). This fibrinogen test is a qualitative assessment of fibrinogen function, and not just a measurement of circulating fibrinogen. It is hypothesized that if the thrombin-like enzymes are creating subpar clots (low/weak MA), TEG would proactively identify this process as it is occurring, and not after the damage has been done. TEG also evaluates for the presence of hyperfibrinolysis (LY30*). If the patient was to experience abnormal clot degradation, the TEG would reveal an elevated LY30. The goal is for TEG to provide utility in assessing for fibrinogen depletion before complete defibrination occurs.

While the thrombin-like enzymes are busy depleting fibrinogen stores, the platelets are also experiencing disruption to their normal processes. Rattlesnake venom can bind to the PAR1, PAR4, and GP1bα platelet receptors. It is well established that these platelet receptors all play an important role in platelet adhesion, activation, and aggregation during the clotting process. When the venom adheres to these receptor sites, the effects are believed to be irreversible. This indicates that platelets can no longer adhere/activate/aggregate on their own due to the venom, and results in the inhibition of normal platelet function.

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*Please refer to the May newsletter for the article that describes TEG in detail.

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Obtaining quantitative platelet levels can determine if thrombocytopenia is present but fails to convey information regarding how well the platelets are working to build a clot. TEG Platelet Mapping can specifically target the adenosine diphosphate (ADP) and arachidonic acid (AA) pathways to determine how well the platelets can activate at both the ADP and TxA2 platelet receptor site.

A retrospective chart review from Banner University Medical Center, Phoenix, reviewed twelve envenomated patients who had obtained a TEG during care (Kang, 2019). It was identified that patients can demonstrate TEG-ADP inhibition independent of hypofibrinogenemia or thrombocytopenia. However, all patients with hypofibrinogenemia also showed TEG-ADP inhibition. One patient in the study had TEG-ADP inhibition that preceded a drop in platelet count, which speaks to the proactive treatment approach TEG can offer. No significant TEG-AA inhibition was noted, except in one patient who had taken aspirin prior to the test. In one patient with serial TEGs available, it was discovered that CroFab successfully reversed the TEG-ADP platelet inhibition. TEG identified fibrinolysis (elevated LY30*) in seven of the twelve patients. Ultimately, the chart review determined that fibrinogen concentration and platelet count alone were not sufficient tools to ascertain the severity of hemotoxicity with regards to bleeding risk. However, identifying TEG-ADP platelet inhibition may be an early means of diagnosing envenomation, as well as determining the need for additional antivenom.

Presently, the usage of TEG to treat snake bites is not widespread, and additional studies are needed. In a perfect world, TEG would be able to quickly establish if there was a coagulopathy present well before any conventional tests would detect an abnormality. TEG may also be useful when diagnosing dry bites, which could save patients hours of time sitting in the ER, or potentially even spare someone from receiving costly antivenom for a cactus poke. If a bite was confirmed, TEG could also aid the clinician in determining the degree of severity of the coagulopathy by looking at both fibrinogen and platelet function. And finally, TEG results could be trended over time to determine efficacy of the antivenom and timing for safe discharge from the hospital. There is still a lot to uncover when it comes to managing rattlesnake envenomations with TEG, but one may argue that a functional assessment is necessary to fully understand what is occurring in these situations.

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Disclaimer: Allison is the TEG Clinical Specialist in Arizona and the lead author of this newsletter. The intent of this newsletter is to shed light on the utility of TEG in rattlesnake bite patients. The information presented in this newsletter represents the personal interpretation and opinions of the available literature by the authors, and in no way reflects the opinions of HAEMONETICS®. Anyone seeking additional information is welcome to email Allison through the Send a letter or question to the editor. on the main page.

References:

Kang, A. M., & Fisher, E. S. (2019). Thromboelastography with platelet studies (TEG® with PlateletMapping®) after Rattlesnake Envenomation in the southwestern United States demonstrates inhibition of ADP-induced platelet activation as well as clot lysis. Journal of Medical Toxicology, 16(1), 24–32. https://doi.org/10.1007/s13181-019-00729-8