Coagulopathy: The Most Important Thing We Still Don't Know About Snakebite

Eric J. Lavonas, MD Rocky Mountain Poison and Drug Center–Denver Health, Denver, Colorado

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In this issue of *Western Journal of Emergency Medicine*, Moriarty et al present a thoughtfully analyzed case series of patients with crotaline snake envenomation.[1] They seek to answer a common and important question: Can we define a group of pit viper victims who are at low risk for hematologic venom effects (fibrinogen degradation and/or platelet destruction) and spare these patients the time and expense of serial laboratory testing? Because their institution in Mississippi sees a large number of rattlesnake and *Agkistrodon* victims, Moriarty and colleagues are well positioned to address this question.

The answer, notwithstanding the limitations of this paper, is no.

We know that bites inflicted by *Agkistrodon* snakes, and particularly copperheads, are generally less severe than rattlesnake bites. Previous studies suggest that only 10% to 20% of copperhead victims develop coagulopathy or thrombocytopenia at any time in their clinical course, compared with 50% or more of rattlesnake victims.[2,3] Physicians treating copperhead victims often order relatively few blood tests; in many cases, this can be considered standard care.[4] Similarly, it has long been observed that early hematologic venom effects strongly predict the late hematologic effects.[5] As a result, it seems like patients who have completely normal early labs are at low risk for developing coagulopathy and thrombocytopenia later. More recent studies have refuted this observation, at least in rattlesnake envenomation.[3] It is not clear who can forgo testing.

These are not academic arguments. Snakebite is a blue-collar disease. Medical bills are the leading cause of personal bankruptcy; despite the recent housing crisis, this proportion is actually increasing.[6] The costs of prolonged hospitalization and serial laboratory testing, transportation, and missed work are a real concern for our patients. In low-risk situations, practicing medicine with no regard for cost is disrespectful and harmful.

In their very nicely conducted multivariate analysis, Moriarity et al seem to have disproven the notion that any patient is safe from the risk of hematologic venom effects. Neither copperhead victim status nor low initial severity nor any other combination of initial factors they evaluated proved sufficiently sensitive to define a group of patients at low risk of hematologic venom effects. This is particularly striking because their observations ended at the time of hospital discharge. Had results of postdischarge lab testing been available for their study, Moriarity et al's results would have been even more convincing.

A crucial piece of this puzzle remains missing. Nearly 13 years after the first focused evaluation of late hematologic venom effects in the Fab-antivenom era, our understanding of the relationship between abnormal laboratory values and the risk of bleeding is weak and driven by anecdote.[5] To date, 4 case reports of late-onset, medically significant bleeding have been published.[7–10] At least 1 additional case has been litigated to conclusion.[11] Though very worrisome, these cases must be considered in context. Data from the National Electronic Injury Surveillance System–All Injuries Program show that more than 8,000 patients are treated in US emergency departments for crotaline snakebite each year.[12] In a multicenter case series of crotaline victims, only 1 of 209 antivenom-treated patients was reported to have delayed onset of medically significant bleeding.[10] None of the 42 patients in the Fab antivenom premarketing trials had major bleeding.[13,14] Two large cohort studies from Phoenix found no cases of delayed bleeding among 94 patients, most of whom had coagulopathy, thrombocytopenia, or both.[3,15] None of Moriarity et al's 131 patients experienced bleeding, and most of the laboratory abnormalities they evaluated posed only a minimal risk of bleeding.[1]

How many snakebite patients must we test or treat with additional antivenom to prevent 1 case of serious bleeding? Fortunately (for our patients), these cases are so infrequent that the issue is nearly impossible to study. As a result, there is currently no evidence-supported standard of care for surveillance laboratory testing. Substantial controversy exists

about what we should do with clinically occult hematologic venom effects once we find them. Moriarity et al tried to help us out of this morass, at least for putative low-risk patients, and found that even in this group there are no easy answers.

Address for Correspondence: Eric J. Lavonas, MD, Rocky Mountain Poison and Drug Center–Denver Health, 777 Bannock St, Denver, CO 80204. E-mail: eric.lavonas@rmpdc.org.

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