



## CLINICAL TOXINOLOGY SPECIAL SECTION

## COMMENTARY

## Navigating the Partly Charted Seas of Clinical Toxinology

Frequently credited as the founder of toxicology, Paracelsus (1493-1541) famously observed,

“Alle Ding’ sind Gift, und nichts ohn’ Gift; allein die Dosis macht, daß ein Ding kein Giftist” (“All things are poison and nothing is without poison, only the dose permits something not to be poisonous”). With keen insight, this early Renaissance medical practitioner/astrologer thereby identified the commonly thin line that can define tolerance, toxicity, or medical benefit of a given substance. The central concept of “dose makes the poison” assumes direct relevance in clinical toxinology which is concerned with the human and veterinary medical effects of injected or inoculated animal venoms or ingested/absorbed poisons/toxins from animals, plants, fungi, and microorganisms. The quantity of venom injected into a person by a spider or snake, as well as the amount of toxic compound present in the seeds, stems, fruit, or leaves of an ingested plant or bioconcentrated toxic mollusc have central importance in the clinical evolution and medical management of the presenting envenomed or poisoned patient. These characteristics of venomous and poisonous lifeforms have compelled scientific debate and pertinent investigation; do venomous snakes meter the quantity of venom delivered in a given strike? Do blue-ringed octopuses (*Hapalochlaena* spp, Octopodidae) and the rough-skinned newt (*Taricha granulosa*, Salamandridae) synthesize tetrodotoxin, the powerful antagonist of several subtypes of Na<sub>v</sub> channels, or is it produced from endosymbiosis by an assortment of facultative bacterial taxa? To some observers, the first impression of such questions may suggest that the answers would primarily constitute “knowledge for knowledge’s sake.” However, these phenomena are more often applicable for our sake than commonly acknowledged.

Unfortunately, diagnosis and management of patients affected by these “natural toxins,” constituting the practice of “clinical toxinology,” is sometimes viewed as “different.” This is commonly because of the need to comprehend the biology of the etiological agents, the living complex organisms, that contribute to the presenting patient’s disease. However, the general basis for

this needed understanding does not substantially differ from medical parasitology or most infectious diseases, although it may be more complex when considering the organisms, their venoms or poisons, and their myriad effects on human beings from diverse backgrounds and cultures.

While certainly substantial, the global significance of envenoming and poisoning remains imprecise. Annually, toxin-induced disease undoubtedly affects millions of people, and the most important form of envenoming, snakebite envenoming, predominantly impacts rural and semi-rural populations in economically-challenged nations. Thus, it constitutes a serious public health hazard among these communities that often lack the resources necessary to provide evidence-based management sufficient to achieve favorable outcomes in many seriously envenomed patients. Therefore, the global impact of snakebite envenoming also tragically highlights one of a number of prominent inequities posed by the burden of mortality and morbidity borne by economically disadvantaged populations.

In common with other scientific disciplines, the advent of “omics,” single cell technologies, and other innovations have advanced toxinology research. However, in comparison with many other avenues of biomedical investigation, support is minimal and scarce. This is also clinically relevant; eg, RNA polymerase II transcription inhibition is a well-acknowledged mechanism of  $\alpha$ -amanitin toxicity in poisoning by some of the medically important “death angel” mushrooms (*Amanita* spp, Amanitaceae). However, other pathophysiological mechanisms may contribute to the fulminant hepatotoxicity that follows serious poisoning by these species, and investigation of these is highly desirable.

Not surprisingly, clinical diagnosis and some interventions for the envenomed or poisoned patient can lack a high-powered evidence-base and/or may be controversial. For example, vinegar, as well as hot- or cold-water immersion, have all been recommended as effective first aid for stings from cnidarians such as cubozoans and hydrozoans (the former seeking to inactivate non-discharged nematocysts adherent to the

victim's skin, the latter primarily as analgesia); however, these have been mainly tested with limited, low-powered observational trials. Likewise, the efficacy of some antivenoms such as those used for severe envenoming by widow spiders (*Latrodectus* spp, Therididae) and some medically important scorpions, has been questioned by some investigators, while others firmly support their effectiveness. Several of these sometimes hotly debated issues in clinical toxinology can serve as a reminder that in reality evidence-based medicine is often an *unequal* ratio of composite observed beneficial interventions and outcomes, considered recommendations from formal trials (when available), and patient expectations.

In this issue, several groups of investigators provide contributions that address some important concerns in clinical toxinology. For example: Rongzhi Liu and colleagues report on the outcome of using hybrid blood purification for life-threatening mass wasp stings in Sichuan Province, China; R.M.M.K. Namal Rathnayaka and colleagues describe using therapeutic plasma exchange, a notably controversial intervention, for management of severe complications (eg, acute kidney injury and thrombotic microangiopathy) following hump-nosed viper

(*Hypnale* spp Viperidae, Crotalinae) envenoming in Sri Lanka (there is no antivenom available for treating bites by these pit vipers); and a random controlled trial conducted by Kasım Turgut and associates compares the clinical efficacy of several analgesics for pediatric patients with painful scorpion envenoming in southeastern Turkey.

Hopefully, further documentation of investigations and considered approaches to clinical management will provide improved outcomes for patients affected by venomous and poisonous animals, plants, and fungi, whether in an austere or urban locale. These contributions are reminders that seeking the best benefit and outcome for the envenomed or poisoned patient does not differ at all from the approach to any other distressed human being presenting for medical care: "The good physician treats the disease; the great physician treats the patient who has the disease" (William Osler, 1849-1919).

Scott A. Weinstein, MSc, PhD, MD, MBBS, FAAFP  
*Senior Editor, Toxinology*

© 2022 Wilderness Medical Society. Published by Elsevier Inc.  
All rights reserved.

<https://doi.org/10.1016/j.wem.2022.10.003>