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When Poison Is the Remedy

Chemicals found in the venom of Brazilian vipers have revolutionized how we treat hypertension, heart failure and kidney disease.

By Jennie Erin Smith
Aug. 30, 2016 7:09 pm ET

Bill Haast began injecting himself with minute quantities of cobra venom in 1948 under the well-founded if risky premise that if horses could develop antibodies to venom toxins through gradual exposure, so could he. Priming his immune system—making his body manufacture its own antivenom, in effect—may have kept Haast safe while he handled cobras and rattlesnakes in front of tourists for nearly 40 years as director of the Miami Serpentarium: He survived more than 170 bites on the job. Even after retiring, he received regular injections of venomous cocktails, suspecting that the health benefits of venomwent beyond the adaptive immunity it could confer. Haast died in 2011, six months past his 100th birthday.

Scientists have been able to isolate useful components of snake venom for a while. In the 1970s, researchers at E.R. Squibb & Sons (now Bristol-Myers Squibb) identified a peptide in the venom of a Brazilian viper that influences the dilation of blood vessels and the reabsorption of water by the kidneys. They synthesized the peptide, and the resulting drug was Captopril, the first in a class of agents called angiotensin-converting enzyme, or ACE, inhibitors.

Used widely in hypertension, heart failure and kidney disease, ACE inhibitors may be the most important medicines to come from venom research, but over the past 20 years a plethora of new possibilities have emerged, thanks to what molecular biologist Christie Wilcox calls "venomics." As Ms. Wilcox explains in "Venomous," a vibrant tour through this exciting field, venomics uses advanced molecular techniques to study the structure and function of venom components alongside gene sequencing, which sheds light on how the components evolved, among other things. The upshot, Ms. Wilcox writes, is that "we have come to know venomous animals far more intimately than at any point in history, and we have learned that their biochemical prowess is far more impressive than we ever imagined."

For five years the author studied lionfish, the extravagant spiny reef fish

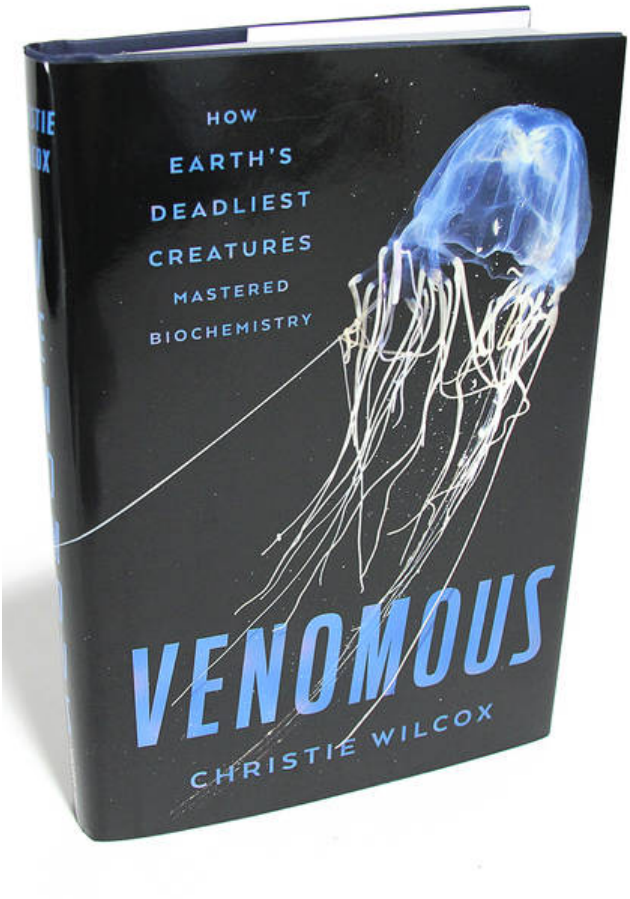

PHOTO: WSJ

VENOMOUS

By Christie Wilcox
Scientific American/FSG, 236 pages, $26

that fascinate divers in the Pacific Ocean (and now those in the Atlantic, where the fish have become invasive). Lionfish, like their cousins the stonefish and scorpionfish, have spines covered in venomous tissues that leach toxins into a victim's flesh. This prompts the release and spread of the neurotransmitter acetylcholine, resulting in "radiating agony," Ms. Wilcox writes. There's no real damage occurring—the venom is a fast-acting neurotoxic blend meant to defend, not kill—but it can be bad enough to send a human victim into shock.

Genetic work on lionfish, scorpionfish and stonefish has revealed them to be less closely related to one another than to some nonvenomous fish in the same order. The harmless species retained the genes for venom-making, Ms. Wilcox found, but produced less of it or none: They'd lost it over time. Why?

Venom, Ms. Wilcox surmises, might have been what got their common

ancestor through the bad old days. Sixty-six million years ago, “when oceans were dominated by vicious sharks, giant marine reptiles, and other big, toothy species,” an extra shot of defense helped, she writes. But venom is expensive for any animal to produce, metabolically speaking. Descendants of those Cretaceous fish, hit with mutations that diminished their venom production, enjoyed as much reproductive success—or more—without it.

Researchers studying reptiles found a parallel phenomenon. Even so-called harmless snakes and lizards may produce trace amounts of venom proteins or mild venoms but have found other ways to do business: constricting their prey instead of poisoning it, for example, or becoming vegetarian.

How venom arose in the first place is more mysterious. Random duplications in immune-system genes are thought to be responsible, Ms. Wilcox writes. Venom has evolved independently across different animal groups, though they recruit many of the same proteins to make it. Research into the natural history of venom offers new ways of understanding the selective forces that keep venom in play and how some species have co-evolved to resist it. Honey badgers, for example, have built-in immunity to cobra neurotoxins thanks to modified receptors in their muscle cells.

The more venom toxins are identified, in species as diverse as rattlesnakes, komodo dragons, box jellyfish, jewel wasps or, for that matter, mammals like the platypus, the broader the catalog of chemicals to study. Ms. Wilcox says that at least 300,000 toxic peptides await to be discovered among the venomous marine snails alone. While venoms are often broadly classed as hemotoxic (targeting blood cells) or neurotoxic (affecting the nervous system), the activity of each component is much more specific, and specificity “is gold when it comes to pharmaceuticals.” One toxin might act as an enzyme, Ms. Wilcox writes, chopping up molecules in cells, while another competes with body compounds for receptors. Drugs from chemicals found in cone snails and Gila monsters have been approved to treat pain and hyperglycemia, respectively. The pipeline of venom-derived treatments, which is long and diverse, includes a stonefish toxin with immunosuppressant activity and a spider peptide that causes erections.

Some venom research remains focused, as it should be, on treating human victims of envenomation. Snakebites kill tens of thousands of people a year, often in gruesome ways, Ms. Wilcox reminds us. Research into the handful of mammals with innate defenses offers the potential for new avenues of treatment, while a community of venom “self-injectors,” most of them snake keepers upholding Bill Haast’s tradition, may have something to contribute as well. One Danish group is studying them, Ms. Wilcox writes, to learn whether quality antivenom can be derived from human blood. The author, not the type to take gratuitous risks, reveals that she has only been envenomated by a sea urchin, fighting burning pain and nausea as she yanked the offending spines from her fingers. An hour later she was fine.

Ms. Smith is the author of “Stolen World: A Tale of Reptiles, Smugglers and Skulduggery.”

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