New snakebite treatment makes major advance

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A University of Arizona researcher developing a therapy to prevent or delay the dangerous results of rattlesnake and other venomous snakebites in humans has shown that a combination of carbon monoxide and iron

inhibits snake venom's effects for up to an hour in animals, a major advance in bringing the treatment to market.

Snake venom is hemotoxic—destructive to the ability of blood to clot—and can cause the destruction of fibrinogen, an essential protein that enables blood to clot and stop excessive bleeding. Snake venom enzymes also can cause abnormally fast clotting, which can lead to heart attack, stroke and damage to the body's organs. Both reactions are inhibited by the therapy.

Vance G. Nielsen, MD, professor and vice chair for research in the UA Department of Anesthesiology at the UA College of Medicine - Tucson, has confirmed that, if given soon enough after a snake bite, the carbon monoxide-iron-based therapy directly can inhibit snake venom's ability to block blood clotting in laboratory animals for as long as an hour. Dr. Nielsen also demonstrated for the first time in the test tube that the therapy blocks snake venom's ability to cause abrupt clotting. The findings recently were published in the journals *Basic & Clinical Pharmacology & Toxicology* and the *Journal of Thrombosis and Thrombolysis*.

Time is of the essence following exposure to rattlesnake venom because without fibrinogen, blood does not clot and the risk of internal bleeding increases, resulting in serious health consequences such as blood entering the brain or intestines. In addition, abnormally fast clotting in the blood vessels can deplete clotting factors and cause excessive bleeding or the clots can block blood vessels, causing lethal loss of blood flow to tissue.

Dr. Nielsen has found that the therapy works against the venom of more than three dozen species of snakes throughout the world.

"The excitement is that we have proven that carbon monoxide has the ability to directly inhibit essentially all hemotoxic venom enzymes in the

test tube and that it blocks the effects of the Western Diamondback rattlesnake's venom in animals. The effects on coagulation of some of the deadliest snake venoms in the world—South American, North American and even African, such the cobra's—can be delayed by a treatment that could be delivered with a device much like an EpiPen used for allergic reactions," said Dr. Nielsen, who is working toward developing the treatment to work in humans.

To further advance the research, Dr. Nielsen is seeking commercial backing and is working with Tech Launch Arizona, the UA office that commercializes inventions stemming from university research, to protect the intellectual property of the treatment and strategize ways to get it into the hands of health professionals.

He also is collaborating with toxicologist Leslie Boyer, MD, founding director of the UA VIPER Institute and professor of pathology and pediatrician, who develops antivenom treatments for snakebite and scorpion stings. Dr. Boyer also is a member of the UA BIO5 Institute.

"Our aim is to bring to market a therapy that is safe for humans and animals, has a long shelf life, is readily available and can be stocked in ambulances, or even first-aid kits for campers or hikers, to save lives," said Dr. Nielsen.

More information: Vance G. Nielsen et al, Characterization of the Rabbit as an In Vitro and In Vivo Model to Assess the Effects of Fibrinogenolytic Activity of Snake Venom on Coagulation, *Basic & Clinical Pharmacology & Toxicology* (2017). DOI: 10.1111/bcpt.12848

Vance G. Nielsen. Effects of purified human fibrinogen modified with carbon monoxide and iron on coagulation in rabbits injected with Crotalus atrox venom, *Journal of Thrombosis and Thrombolysis* (2017). DOI: 10.1007/s11239-017-1549-2

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