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CONCURRENT SESSION ABSTRACTS

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4. Repurposing DMPS, a metal chelator, as a rapid field intervention for treating hemotoxic snakebite

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Snakebite kills up to 138,000 people annually and ~400,000 are left with permanent disabilities. Envenomings by saw-scaled vipers (Viperidae: *Echis*) are responsible for high incidences of snakebite mortality and morbidity in Africa and Asia, and bites are characterized by systemic hemorrhage and coagulopathy. Antivenom, the only currently available specific treatment for snakebite, has poor specificity, low affordability for the affected impoverished populations, and must be administered in clinical settings due to its intravenous delivery and high rates of adverse reactions. Moreover, delays in accessing these healthcare facilities result in poorer outcomes for many snakebite victims. Here, we investigated the value of small molecule inhibitors, specifically metal chelators, as novel snakebite therapeutics. We show that these licensed, safe and affordable repurposed medicines effectively neutralize saw-scaled viper venoms *in vitro* and *in vivo*. Among the tested candidates, dimercaprol (British anti-Lewisite) and its derivative 2,3-dimercapto-1-propanesulfonic acid (DMPS), were found to effectively antagonize the procoagulant activity of Zn-dependent snake venom metalloproteinases from a variety of saw-scaled viper venoms. Both chelators prevented lethality in murine preclinical models of envenoming when the drug was delivered intravenously in conjunction with *Echis ocellatus* venom. Critically, DMPS significantly prolonged survival in envenomed mice when drug administration was delayed until after venom delivery. As DMPS is available as an oral therapeutic, we also investigated whether oral administration could delay or rescue lethality. Venom-induced lethality was partially prevented when the drug was given orally after venom administration, and was completely abolished when the clinical scenario of venom, immediate oral drug administration, and delayed antivenom treatment was tested. Thus, DMPS shows great promise as a novel therapeutic for treating snakebite envenomings caused by venoms rich in metalloproteinases. Its early oral administration may prove to be a valuable community-based intervention for the treatment of envenomings caused by many hemotoxic snake species.