2023 Faculty Research Proposal for UAMS College of Pharmacy Summer Student Research Fellowship

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FACULTY INFORMATION:

NAME: Click or tap here to enter text.
DEPARTMENT: ☒Pharmacy Practice
☐Pharmaceutical Sciences

LOCATION: Arkansas Poison and Drug Information Center

PROJECT INFORMATION:

TITLE: Functional Outcomes Following Copperhead Snakebite Treated with Low-Dose Crotaline Fab Antivenom

LOCATION OF THE PROJECT: Arkansas Poison and Drug Information Center

BRIEF DESCRIPTION OF THE PROJECT OR SPECIFIC AIMS:

This is a prospective observational study examining outcomes in patients envenomated by copperhead snakes and treated with Crotaline Polyvalent Immune Fab (CroFab®).

Envenomations from copperhead snakes (*Agkistrodon contortrix*) are generally recognized as being relatively more benign, requiring less antivenom and shorter duration of hospitalization than other North American pit vipers (1). Clinical effects are primarily limited to soft tissue swelling, and they do not cause coagulopathy (2) as with some other species. While antivenom (Crotaline Polyvalent Immune Fab, CroFab®) improves functional recovery early after copperhead snake envenomation, patients approach full or near-full recovery by 28 days (3,4) regardless of antivenom administration.

CroFab® remains an expensive antidote, with wholesale acquisition cost of $1,484.51 per vial at UAMS. Currently, The FDA package label recommends a starting dose of four to six vials of CroFab® followed by scheduled maintenance dosing. However, as-needed dosing of CroFab® after initial antivenom load has been shown to provide similar functional outcomes to scheduled maintenance dosing while reducing antivenom use (5).

Given the relatively more benign course of copperhead envenomations, trend towards full recovery irrespective of antivenom use, and limited utility of scheduled maintenance dosing, it has been the practice pattern of the Arkansas Poison Center to consider using two-vial loading dose for initial management as opposed to a four-vial loading dose. The antidote is re-dosed as needed should the patient fail to achieve symptom control with initial management. However, re-dosing is often not indicated. We wish to compare the outcomes of patients who received two vials versus four vials initial loading dose, with the hypothesis that those treated with lower-dose CroFab have similar short and long-term outcomes.

The Arkansas Poison Center receives more than 100 calls per year regarding snake envenomations, with the majority of those being copperhead snakes. The results of this study

would hold dramatic implications for snakebite management, not only for medication associated costs, but for minimum antidote stocking considerations in more resource-limited settings. We hope that the findings of this prospective study might justify a larger, multi-state trial to more carefully study this question.

STUDENT'S RESPONSIBILITIES/DUTIES FOR THE PROPOSED PROJECT:
Primary responsibilities include: data collection (patient callback), functional outcome scoring, training Specialists in Poison Information (SPI), interim data analysis. In advance of the summer research component, the selected participant will be given the opportunity, if desired, to assist in drafting the IRB and development of the more granular aspects of the study design. This is not a required component for participation in the summer research experience.

ESTIMATED TIME FOR PROJECT COMPLETION: __12____ weeks (≥10 weeks required). Study will run 52 weeks, but 12 weeks required for full-time data collection during high-volume summer months.

DOES THE WORK INVOLVE ANIMAL RESEARCH? ☐YES
☒NO

ORAL/POSTER PRESENTATION OPPORTUNITY:
ACMT Annual Scientific Meeting: 3/2024
North American Congress of Clinical Toxicology (NACCT): 9/2024

MANUSCRIPT SUBMISSION:
We will encourage manuscript submission to one of the following target journals: *Clinical Toxicology (Phila)*, *Journal of Medical Toxicology, Annals of Emergency Medicine,* or *Toxicology Communications.* Alternative journals will be considered.

REFERENCES:
1. Ruha AM, Kleinschmidt KC, Greene S, Spyres MB, Brent J, Wax P, Padilla-Jones A, Campleman S; ToxIC Snakebite Study Group. The Epidemiology, Clinical Course, and Management of Snakebites in the North American Snakebite Registry. J Med Toxicol. 2017 Dec;13(4):309-320. doi: 10.1007/s13181-017-0633-5. Epub 2017 Oct 3. PMID: 28975491; PMCID: PMC5711762.
2. Ali AJ, Horwitz DA, Mullins ME. Lack of coagulopathy after copperhead snakebites. Ann Emerg Med. 2015 Apr;65(4):404-9. doi: 10.1016/j.annemergmed.2014.08.006. Epub 2014 Sep 6. PMID: 25199611.
2. Gerardo CJ, Quackenbush E, Lewis B, Rose SR, Greene S, Toschlog EA, Charlton NP, Mullins ME, Schwartz R, Denning D, Sharma K, Kleinschmidt K, Bush SP, Ryan S, Gasior M, Anderson VE, Lavonas EJ. The Efficacy of Crotalidae Polyvalent Immune Fab (Ovine) Antivenom Versus Placebo Plus Optional Rescue Therapy on Recovery From Copperhead Snake Envenomation: A Randomized, Double-Blind, Placebo-Controlled, Clinical Trial. Ann Emerg Med. 2017 Aug;70(2):233-244.e3. doi: 10.1016/j.annemergmed.2017.04.034. Epub 2017 Jun 13. PMID: 28601268.
3. Anderson VE, Gerardo CJ, Rapp-Olsson M, Bush SP, Mullins ME, Greene S, Toschlog EA, Quackenbush E, Rose SR, Schwartz RB, Charlton NP, Lewis B, Kleinschmidt KC, Sharma K, Lavonas EJ. Early administration of

Fab antivenom resulted in faster limb recovery in copperhead snake envenomation patients. Clin Toxicol (Phila). 2019 Jan;57(1):25-30. doi: 10.1080/15563650.2018.1491982. Epub 2018 Sep 3. PMID: 30175628.
4. Gerardo CJ, Quackenbush E, Lewis B, Rose SR, Greene S, Toschlog EA, Charlton NP, Mullins ME, Schwartz R, Denning D, Sharma K, Kleinschmidt K, Bush SP, Ryan S, Gasior M, Anderson VE, Lavonas EJ. The Efficacy of Crotalidae Polyvalent Immune Fab (Ovine) Antivenom Versus Placebo Plus Optional Rescue Therapy on Recovery From Copperhead Snake Envenomation: A Randomized, Double-Blind, Placebo-Controlled, Clinical Trial. Ann Emerg Med. 2017 Aug;70(2):233-244.e3. doi: 10.1016/j.annemergmed.2017.04.034. Epub 2017 Jun 13. PMID: 28601268.
5. Spyres MB, Skolnik AB, Moore EC, Gerkin RD, Padilla-Jones A, Ruha AM. Comparison of Antivenom Dosing Strategies for Rattlesnake Envenomation. Crit Care Med. 2018 Jun;46(6):e540-e544. doi: 10.1097/CCM.0000000000003079. PMID: 29521714.