# "Venom Week"

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## *SCORPIONS*

### EFFICACY AND SAFETY OF F(AB)2 ANITVENOM FOR SCORPION ENVENOMATION

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**Abstract:** Systemic envenomation from scorpion sting is endemic in North America, from Arizona through southern Mexico. In the United States, approximately 200 people annually present for medical care of systemic neurotoxicity. Double-blind, placebo-controlled clinical trials in Arizona suggest that treatment with an F(ab)2 antivenom (Anascorp) may be safe and efficacious for management of scorpion neurotoxicity. Clinical trials of this investigational product are ongoing.

### THE GEOGRAPHIC DISTRIBUTIONS OF MEDICALLY IMPORTANT SPECIES OF THE GENUS *CENTRUROIDES MARX* (SCORPIONES, BUTHIDAE)

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**Abstract:** Ten species-level taxa of the genus *Centruroides* are considered responsible for the majority of scorpion stings which require medical attention in North America. In alphabetical order they are: *C. balsasensis*, *C. elegans*, *C. infamatus*, *C. limpidus*, *C. meisei*, *C. noxius*, *C. ornatus*, *C. sculpturatus*, *C. suffusus* and *C. tecomanus*. Approximately 6,500 museum specimens belonging to these 10 taxa were identified. A data base of 750 localities were geo-referenced (latitude-longitude coordinates). The known distribution of each taxon was mapped with the program ArcView. Subsequently, GARP (=Genetic Algorithm for Rule-set Prediction) was used to model the fundamental niche (abiotic component only) of each taxon, and maps were generated of their potential distributions. Some applications derived from this distributional information for current and future research opportunities are discussed.

### SCORPION ENVENOMATIONS IN SOUTHERN ARIZONA: A COSTING STUDY OF SCORPION STINGS

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**Objective:** The purpose of this study is to determine the direct monetary costs of scorpion envenomation events in the acute care setting for patients treated in a southern Arizona hospital.

**Methods:** A chart review analysis of documented treatment of scorpion envenomations at a university hospital was conducted to compile demographic, drug use, and resource utilization information. Patients were selected based on an ICD-9 code diagnosis of scorpion envenomation within the years 1993 to 2001.

**Results:** 103 patient charts were reviewed. The average length of stay was 1.21 days (range 0.5–6.5 days), the average age was 4.7 years (range 0.2–53 years old). Males comprised 54% of the patients, 51.9% Caucasian, 41.6% Hispanic, and 60.2% were from an urban setting. The average drug cost was $51.82 (SD = 53.22). The total average cost in the entire population was $6,764.54, (SD = $3,866.55). The average cost of rural versus urban was $7,535.74 and $6,254.55, respectively (p = 0.100). The average cost for male versus female was $6,949.64 and $6,520.90 (p = 0.581), and the average cost for the 0–3 years group was $6,721.10, the >3 years to 14 years group's average cost was $6,643.33, and the >14 years of age group's average cost was $8,578.42. None of the comparisons between age groups were statistically significant, with p values ranging from 0.274 to 0.922.

**Conclusion:** Although scorpion envenomations were costly, there were no statistically significant differences noted between any of the comparison groups. Transportation, including air transport in the rural setting, did not account for a significant change in cost. Many of the patients that were envenomated in the rural setting were seen at a regional hospital and then transported as necessary.

## CASE REPORT: VOMITING REQUIRING PROLONGED HOSPITALIZATION AFTER *CENTRUROIDES SCULPTURATUS* ENVENOMATION TREATED WITH ANASCORP®

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**Background:** Vomiting is an uncommon symptom of systemic envenomation by *C. sculpturatus*. It is also an uncommon side effect of both lorazepam and midazolam, common treatments for systemic scorpion envenomation.

**Case Report:** On June 27, 2007 a five-year-old male was treated in a facility in southern Arizona for systemic scorpion envenomation. His family reported that he was stung on the right foot at 14:45 (the high temperature for the day was 104°); the scorpion was seen. His presenting symptoms were nystagmus, thrashing and diaphoresis. Prior to treatment with Anascorp®, he was treated with midazolam and lorazepam. His baseline vitals at 18:00: temp, 38.1C, pulse 175, respirations 21, a blood pressure was not reported, weight 22 kg. He was treated with 3 vials at 18:05 and an additional 1 vial at 18:40. The antivenom is administered in 50 ml of normal saline; otherwise he did not have any fluid intake. Symptoms improved at 19:00 and resolved at 19:30. Per the protocol, he was watched for 30 minutes prior to discharge and during that time, was given water to drink. He vomited twice and the treating physician decided to observe him overnight. He was not given any medications other than fluids and he did not have any more episodes of vomiting. He was discharged the next morning.

**Discussion:** Anascorp® has been given to well over 300 children and adults in Arizona in clinical trials, Completed analysis of preliminary studies have indicated it to be a treatment with minimal associated adverse events. However, in the treatment year of July 1, 2006 through June 30, 2007, there have been two cases of vomiting that required a prolonged hospitalization; one is described above. In both cases, the investigator reported that the SAE was not related to Anascorp®. Noteworthy in the above case is the excessive heat for the day, presenting symptom of diaphoresis, mildly elevated temperature prior to treatment with antivenom, and treatment with two drugs with the potential to cause vomiting. Further research can clarify if post treatment episodes of vomiting are related to residual envenomation, dehydration, or concomitant medications, such as benzodiazepines, given prior to Anascorp®. This will facilitate the development of treatment guidelines that might prevent the need for prolonged hospitalization in those with post treatment vomiting.

# *SNAKEBITES, VENOMOUS*

## ENVENOMATIONS DUE TO PYGMY RATTLESNAKES IN OKLAHOMA: TREATMENT OPTIONS

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**Abstract:** The clinical course and treatment outcome associated with pygmy rattlesnake envenomation has not been well reported especially in the context of newer antivenom options. The size and relatively modest local tissue damage along with geographic overlap makes it common for the copperhead and pygmy rattlesnake to be considered as similar in presentation and outcome in our area. A retrospective chart review of 75 pit viper envenomations was undertaken for a cohort of patients admitted to a northeast Oklahoma hospital. Of the 75 patients, 32 identified the pit viper as a copperhead, 10 were pygmy rattlesnakes, 4 were "other" rattlesnakes and 28 unknown pit vipers. Foot and hand bites predominated and males were more than twice as likely to be the victim. Comparing the

copperheads and pygmy rattlesnakes, 1/32 of the copperhead bites had a platelet count of <100k on admission. 3/10 of the pygmy rattlesnakes had a low platelet count on admission but when subsequent labs were obtained 6/10 of the pygmy rattler bites fell below 100k during the hospitalization. Copperheads were treated with an average of 2.5 vials of antivenom (15/32 received no AV treatment), while pygmy rattlesnake bites received 10.6 vials on average. Of the pygmy bite patients treated with antivenom, 4 received equine derived polyvalent antivenom (average 4.7 vials) and 5 received ovine fab fragment antivenom (average 17.4 vials). 4/5 of the latter group had initial improvement but required retreatment after rebound. 2 of those patients ultimately received the horse derived antivenom. We conclude that copperhead envenomations received modest to no antivenom treatment. Pygmy rattlesnake bites are frequently associated with thrombocytopenia without other coagulopathy. Treatment with ovine fab antivenom required retreatment in 80% of cases with the most common reason being recurrence of thrombocytopenia. Despite the relatively small size of the reptile and modest appearance of the local tissue damage the average number of vials used clinically to treat pygmy rattlesnakes is relatively high compared to the copperhead. In our region it seems prudent to continue antivenom treatment of pygmy rattlesnakes after initial control to include subsequent doses at 6 hour intervals in order to avoid rebound symptoms. We plan to prospectively consider this approach.

## US SNAKEBITE MORTALITY, 1979–2005

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**Aim:** To examine the epidemiology of US snakebite fatalities for the period 1979–2005. Introduction: Death is a relatively rare outcome of snakebite in the USA, yet the circumstances and epidemiology of such events are poorly described. Given that this type of injury outcome offers an opportunity to understand the determinants of severe morbidity, we systematically assessed the available information concerning the epidemiology of US snakebite related mortality.

**Methods:** We searched the CDC Wonder database of vital statistics for detailed demographic and circumstantial information concerning snakebite related fatalities for the period 1/1/79–12/31/05. We also examined snakebite related journal articles cited in PubMed covering the same period. In addition we also used the National Poison Control (PCC) Annual Reports and Lexis Nexis newspaper database in order to find details concerning individual cases. Where available, additional information was also sourced from individual PCC's and clinicians.

**Results:** The CDC Wonder database documented 134 snakebite fatalities for the study period. Further investigation of other resources suggested that eight more deaths occurred during the same period. Over all, 80% (113/142) of the victims were male, 94% (133/142) were white and 52% (73/141) were individuals between 25–54 years-of-age. In absolute terms, the five states with the greatest mortality were Texas [with 15% of the national total], Georgia [13%], Florida [12%], Arizona [8%] and California [7%]. For 27 cases, we found some additional details: these cases were a good representation of the total group with very similar demographic ratios. Of these 27 cases, 70% (19) were either confirmed or likely to be various rattlesnakes and 15% (4) from exotic (non-US) snakes. Time from bite to death ranged from just minutes to 8 days of hospital treatment. Many cases involved alcohol use and delays or refusal of medical care. A significant number of the latter were individuals involved in snake-handling religious ceremonies. Treatment delays were especially apparent in cases of exotic snakebites where the victim would be reluctant to call for help in fear of losing their pet.

**Conclusions:** Snakebite fatalities tend to be more prevalent in more southerly and westerly states and involve alcohol use and delayed medical care in white males of middle age. Those involved in religious use of snakes and keeping exotic snakes are important high-risk groups. The rarity of fatal snakebites amongst females and non-whites suggests that targeted interventions to address high-risk groups and behaviour may reduce the burden of US snakebite mortality and severe morbidity.

## THE EFFICACY AND SAFETY OF CROFAB™ IN THE TREATMENT OF SEVERE CROTALINE SNAKE ENVENOMING

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**Background:** Traditionally, crotaline snakebite has been graded for clinical severity using major scales available, although no scoring system has ever been validated for clinical use. Currently, the only crotaline snake antivenom widely available in the United States,

Crotalidae Polyvalent Immune Fab (CroFab®, FabAV), is approved for mild and moderate envenoming by North American crotaline snakes. However, crotaline envenoming is a dynamic process during which all bites begin with few clinical effects, which then may worsen over time and ultimately achieving severe effects. This presentation documents the important components of clinical progression and presents data assessing the use of antivenoms in the treatment of severe envenoming.

**Methods:** A rigorous multicenter nationwide chart review of medical records of patients treated with FabAV in 17 U.S. hospitals was performed. Severity was defined as using a 6 point standardized scale, a modification of a previously validated research snakebite severity scale. Patients achieving a score >4 points were included. Initial control was determined by an expert panel using the predefined definition: halting of progressive swelling and pain, reversal of systemic effects and a trend toward normalization of coagulation parameters. Recurrence was defined as a worsening of coagulation parameters after IC had been achieved.

**Results:** Of 228 patients treated with FabAV, 28 (12%) met inclusion criteria. All patients were envenomated by a rattlesnake or unidentified snake in a rattlesnake endemic area. The mean severity score prior to FabAV was 5.3 points. All patients improved following initial FabAV infusion (median dose, 12 vials total): the severity score improved by a mean of 4.0 points. Coagulation recurrence was found in 7 of 11 patients with lab results 24 hours after initial control. No fasciotomies were performed and no deaths occurred.

**Discussion:** Severe envenomation was present in 12% of patients, all with suspected or confirmed RS bite. All patients improved after FabAV therapy; control of all venom effects with FabAV was achieved in most patients. All patients recovered. Coagulation recurrence was more common than in other post-marketing studies with rates of 8–22%, which included less severely envenomed patients.

## CLINICAL MANIFESTATIONS AND MANAGEMENT OF VIPER BITES IN AFRICA

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**Abstract:** Bites of Viperidae (Viperinae) represent the great majority of the snakebites occurring in sub-Saharan Africa. Those involve more than 500,000 viper envenomations leading to 20,000 deaths each year. Inflammatory syndromes are present in 86% of the envenomations, hemorrhagic syndromes in 48% and necrosis appear in 10% of the cases.

Severity of viper envenomations is considerably worsened by a) the delay of treatment, b) the lack of drugs, in particular antivenom and c) the insufficient training of health staff.

The development of new antivenom (Antivipmyn Africa®) effective, well tolerated, freeze-dried and cheap should constitute an essential tool leading to an improvement of the management of snakebites in Africa.

## CASE REPORT: RECURRENT HEMORRHAGE AFTER WESTERN DIAMONDBACK RATTLESNAKE ENVENOMATION TREATED WITH CROTALIDAE POLYVALENT IMMUNE FAB (OVINE)

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**Introduction:** Recurrent coagulopathy has been observed in patients after rattlesnake envenomation treated with the current updated dosage recommendations for Crotalidae Polyvalent Immune Fab (ovine) [FabAV]. While recurrent coagulopathy is well documented in the literature, clinically significant delayed sequelae have not been reported. We present a case of recurrent thrombocytopenia after western diamondback envenomation treated with FabAV, resulting in an extensive recurrent local hemorrhage.

**Case Report:** A 24 year-old male presented to our emergency department several hours after western diamondback envenomation. He sustained bites to both hands and the right flank by leaning over his pet "snake enclosure". On presentation, the patient was hypotensive, tachycardic and thrombocytopenic, with a platelet count of 17/nl. Antivenom therapy was initiated according to the current FabAV protocol. However, sixteen hours after completion of the recommended FabAV infusion, the patient experienced a recurrent thrombocytopenia with a dramatic seventeen point drop in hematocrit. The source of bleeding was clinically attributed to an expanding hematoma at the site of envenomation.

**Discussion:** FabAV has become the standard treatment for symptomatic crotalid envenomation. However, the pharmacokinetics of this drug predispose it to recurrent coagulopathies. While studies have shown persistent and recurrent coagulopathic derangements after FabAV therapy, no clinically significant sequelae have been reported. This report highlights the potential for recurrent local hemorrhagic complications following rattlesnake envenomation in a patient who likely received a very large venom load.

**Conclusions:** Recurrent coagulopathy following current dosing recommendations for FabAV therapy can result in clinically significant delayed hemorrhage, supporting the observation that extended repeat dosing may be necessary to adequately treat subjects of rattlesnake envenomation.

## TRENDS IN THE NEUTRALIZATION OF LOCAL TISSUE DAMAGE INDUCED BY VIPERID SNAKE VENOMS

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**Abstract:** Local tissue damage, i.e. myonecrosis, dermonecrosis, blistering, hemorrhage and edema, is one of the most serious consequences of envenomations by snakes of the family Viperidae, often resulting in permanent tissue loss and dysfunction. Antivenoms are of low efficacy in the neutralization of these effects, mainly owing to the very rapid development of the effects once venom is injected. Novel alternatives for confronting this serious consequence of snakebite envenomation must be based on a thorough understanding of the pathogenesis of the effects, of the toxins involved, and of the role that inflammation plays in this pathology. On the basis of this growing body of knowledge, it is proposed that the use of novel neutralizing molecules, both natural and synthetic, as well as of pharmacological interventions aimed at modulating the inflammatory response and at improving the process of tissue regeneration, may become adequate therapeutic avenues to ameliorate the impact of local tissue damage in these envenomations. The future scenario of viperid venom-induced local tissue damage will encompass a combination of rapid administration of antivenom, together with administration of toxin inhibitors and the modulation of inflammation and tissue regenerative responses.

## LOCAL TISSUE INJURIES IN VENOMOUS SNAKEBITE

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**Abstract:** Most local injury is likely caused by venom enzymes, whose injury is manifested because of their speed of action, difficulties in neutralization by antivenom, interference with vascular and nerve supply, and other factors. Accurate markers of local injury are difficult to measure and apply in both research and clinical settings. Swelling is almost always an accompanying feature. It may be extensive or limited and of variable timing and its relationship to injury, as well as the optimal marker measures (circumferential measurement? extent of proximal progression? ecchymoses? blister formation?) are not clear. Pain is also a common accompaniment to snakebite but its utility as a marker of injury, response to therapy, or outcome is also unclear. Tissue pressures may be indicative of swelling and, when measured in compartments or confined tissue spaces may indicate risk to vascular and nerve supply, but is limited in terms of the percentage of cases where it is a factor, and by questions regarding the meaning and management of specific pressure numbers. Subcutaneous necrosis, myonecrosis, and direct vascular injury are also likely to play a part in outcome. Serum or plasma markers of tissue injury, such as creatinine kinase, IL-6, IL-1β and TNF-α, or degradation products of extracellular matrix proteins (laminin, collagens, fibronectin) may have some utility in assessing the extent of tissue damage. Short and long-term functional assessments may be of use in both clinical and research settings. Consensus can be found regarding the general worsening of local effects by any measures that prolong venom time in the bite site area. Promising areas of management of local injury include the use of mass-action neutralization of venom components in the blood stream, lower molecular weight antivenom components, and administration of venom enzyme synthetic inhibitors of metalloproteinases and phospholipases.

## ELAPIDS AND COAGULOPATHY

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**Abstract:** Coagulopathy is a major effect of many snake venoms and is a particular problem in Australian elapids. The most common form is a venom induced consumption coagulopathy (VICC) which is due to procoagulant toxins in the venoms. VICC differs from disseminated intravascular coagulation, although it is being increasingly recognized that it may be associated with a thrombotic microangiopathy or the haemolytic uraemic syndrome/thrombotic thrombocytopenic purpura spectrum. There is ongoing controversy

about the treatment of VICC, the role of antivenom, the appropriate dose of antivenom, the time of recovery after antivenom and the role of factor replacement. Anticoagulant coagulopathy is much less common in elapid snake envenomation, is much less severe and responds well to antivenom.

## FAMOUS SNAKE BITES: FATAL MISTAKES OF FOUR AMERICAN HERPETOLOGISTS

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**Abstract:** Fatal mistakes can happen in many ways, but when they involve a venomous snake and a well-known herpetologist they tend to become "legend." A South African boomslang, an Arizona Mojave rattlesnake, an Indian cobra, and a Thai multi-banded krait are all species that are well respected by most herpetologists. The potential threat to human life by bites from any of these snake species, whether encountered in the wild or in a captive setting, should never underestimated. During the latter-half of the twentieth century and the initiation of the 3rd millennium, four illustrious American herpetologists lost their lives as a result of envenomation by one of these species. Academician Joseph B. Slowinski, Ph.D., prominent museum curator Dr. Karl P. Schmidt, Frederick A. Shannon, M.D., and the unconventional Grace Olive Wiley each made a momentary flaw in judgment that led to a fatal mistake. All were skilled with the handling of venomous snakes. Most history books lack mention of these seasoned herpetologists, yet their names are legend to amateur and professional herpetologists throughout the United States and world. In their own way the tragic ends to their lives contributed significantly to the historical knowledge of venomous snakebites and the potentially devastating medical consequences that can result from a momentary slip of thought. It would seem that there should be a strong and long-lasting message as a result of these unfortunate events; however, there is a reasonable probability that history will repeat itself in future decades.

## CORAL SNAKE ANTIVENOM: CLINICAL DIFFERENCES BETWEEN CASES RECEIVING IT AND THOSE THAT DID NOT

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**Background:** Current treatment guidelines recommend empiric administration of antivenin for US *Micrurus* species coral snake envenomations. Despite these recommendations, poison center data reveals that only about half of presumed coral snake bite victims ultimately receive antivenom. It is unclear what factors health care providers have used to determine whether to administer coral snake antivenom. We queried poison center databases to obtain clinical information from coral snake bite cases to determine if significant differences between the presenting signs and symptoms of patients receiving antivenom compared to those who did not.

**Methods:** Retrospective, observational study of victims with coral snakebites reported to seven poison centers in Texas and Florida from 2003 to 2005. All cases were reviewed for date, snake species, identification of the snake, patient age and gender, duration and characteristics of bite, body part bitten, wound presence, local effects (pain, swelling, paresthesia), systemic effects, hospital length of stay, and outcome. Absolute risk differences and odds ratios were calculated with 95% confidence intervals.

**Results:** Of the 109 victims, 51.4% received antivenom (AV) and 48.6% did not (NoAV). The AV victims were more likely to report the snake 'hung on' to the bite site (81.3% and 25.7%), have localized swelling (66.7% and 28.9%), have systemic effects (46.4% and 9.4%), and have severe clinical findings (32.1% and 5.7%). The time from bite to telephone call was shorter on average for the AV victims (91 minutes and 162 minutes). The AV victims had longer hospital lengths of stay (28.9 hours and 13.1 hours). There were no deaths in either group.

**Discussion:** In opposition to published recommendations, some providers chose not to administer antivenom to suspected coral snake envenomation victims. The differences between AV and NoAV cases suggest that the presence of systemic effects and/or severe clinical findings may play an important part in this decision. Although there is no literature to suggest snake 'hang time' and/or localized swelling correlates with patient morbidity or mortality, some providers may have used these to decide treatment. Many victims with only local symptoms did not receive antivenom and never developed systemic effects.

**Conclusion:** There were significant differences between patients that received antivenom and those that did not. It is unclear if these differences correlate with progression to systemic symptoms and/or the need for antivenom. More study is needed to determine optimal indications for the administration of coral snake antivenom.

## ASSOCIATION OF FIRST-AID, METHOD OF ARRIVAL, AND TIME TO PRESENTATION WITH THE AMOUNT OF ANTIVENOM REQUIRED AND THE CASE FATALITY RATE IN VENOMOUS SNAKEBITE IN BHARATPUR HOSPITAL, CHITWAN, NEPAL

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**Background:** Venomous snakebite in Nepal has a high case-fatality rate. Many people apply a tourniquet to the bitten extremity and either walk or bicycle to the hospital. Elapids include the Indian cobra (*Naja naja*) and the common krait (*Bungarus caeruleus*). Viperids include Russell's viper (*Vipera russellii*, the saw-scaled viper (*Echis carinatus*) and the green pit viper (*Trimeresurus albolabris*). Polyvalent, anti-snake antivenom (AV) is an expensive and limited resource.

**Objective:** To characterize the association of AV use and fatal outcomes with application of a tourniquet, mode of arrival, and time to presentation.

**Methods:** The study was carried out from April to July 2007 at Bharatpur Hospital, Nepal, which receives snakebite victims from 4 adjoining districts. Envenomed patients were studied consecutively using a pre-tested data collection instrument.

**Results:** There were 21 snakebite victims, 2 by viperids and 19 by elapids. The case fatality rate was 28.6%. The range of AV vials consumed by patients arriving alive was 10 to 94. No AV was given to viper bite patients. One victim was dead on arrival. The average number of AV vials given to 18 elapid envenomed patients was 40.4. More than half (52.4%) applied a tourniquet prior to arrival, but there was no association with the number of vials of AV given. Those who arrived at hospital ≥2 hours after envenoming received a significantly greater number of AV vials than those who arrived <2 hours (60 vs. 94 vials). Of those arriving on foot or by bicycle, the case fatality rate was 66.6%. Compared with patients who arrived by Ambulance, these patients also consumed a significantly greater number of AV vials.

**Discussion:** In Nepal, anti-snake antivenom is more effective in elapid envenomations if given early, prior to the development of neurotoxicity. Patients presenting ≥2 hours from envenomation required larger doses and had a higher case-fatality rate. Walking and/or riding a bicycle post-envenomation increased neurotoxicity, the number of AV vials administered, and the case-fatality rate. In the present study, slightly more than half applied a tourniquet, but this did not significantly change the need for antivenom or outcomes.

**Conclusions:** In elapid envenomings, the application of a tourniquet pre-hospital did not decrease the antivenom requirement; walking and bicycling as a means of transport to a hospital increased antivenom need and the case fatality rate; and early arrival at hospital (<2 hours) decreased the need for antivenom and increased survival.

## HEMORRHAGIC, FIBRINO(GENO)LYTIC, COAGULANT AND LETHAL ACTIVITIES OF VENOMS OF THE SOUTHERN PACIFIC RATTLESNAKES

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**Objective:** To study the intraspecific hemostatic and lethality variations of venoms from the Southern Pacific Rattlesnakes.

**Background:** *Crotalus oreganus helleri* snake venoms from southern California, show biochemical and hemostatic variations.

**Methods:** Fibrinogenolytic effects, procoagulant and fibrinolytic activities and ion exchange chromatography profiles were analyzed.

**Results:** Differences were observed in fibrinolytic activity: kallikrein-like amidolytic activity was highest in the *C. o. helleri* venom 058-806-546 found in Riverside, Co.; t-PA- like amidolytic activity was also high in this venom followed closely by *C. o. helleri* venoms 058-819-883 and 059-009-599 from San Bernardino and Riverside Co., respectively. *C. o. helleri* venom 058-359-257 from San Bernardino Co., showed the maximum fibrin lysis using fibrinogen with and without plasminogen. The highest hemorrhagic activity was seen in 058-359-257 and 058-893-793 venoms with a MHD of 2.5 μg, followed by venom 058-806-546 at 9 μg. The MHD of venoms 059-009-599 and 058-819-883 were not determined at concentrations up to 15 μg. The $LD_{50}$ for 058-359-257 and 058-893-793, both from San Bernardino Co, were ~5 mg/kg, while that of 059-009-599 and 058-819-883, from Riverside and San Bernardino Co. were 0.56 and 0.65 mg/kg, respectively. The $LD_{50}$ for venom 058-806-546 was 2.4 mg/kg, which represents venom containing both hemorrhagins and neurotoxins. Thrombin-like activity was highest in venom 059-009-599 at 118 IU thrombin/mg, while venom 058-359-257 had the lowest at 9.27. All venoms were able to clot human plasma and purified fibrinogen with the exception of venom

058-893-793. Venoms 058-893-793 and 058-359-257 had the most fractions with fibrinolytic activity followed by venom 058-806-546. Venom 059-009-599 contained no fractions with fibrinolytic activity, while 058-819-883 had only one with activity.

**Discussion/Conclusions:** These results represent the intraspecific hemostatic and lethality variations of venoms from similar geographical locations and could facilitate a better understanding of the clinical picture when humans are envenomated.

## COPPERHEAD ENVENOMATION: TO CROFAB™ OR NOT TO CROFAB™? THAT IS THE QUESTION

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**Background:** Coagulopathy, neurotoxicity and compartment syndrome are life and limb threatening effects of rattlesnake envenomation warranting crotaline Fab antivenom (CroFabTM) administration or polyvalent Wyeth antivenin. These serious effects are much less common with *Agkistrodon contortrix* (copperhead) bites. Tissue destruction (pain, edema, necrosis), however, is common with copperhead bites in our state and may cause significant loss of function and impaired activities. Local tissue effects may be delayed beyond 6 hours in copperhead envenomation leading to delay in recognition of more serious tissue damage and inappropriate triage to "non-significant envenomation". Early use of CroFab™ (within 6 hours) has been advocated. We believe antivenom use in copperhead envenomation is limited due to a misperceived disproportionate risk/benefit ratio.

**Methods:** We examined outcome severity (Grade I–IV Scoring Method) and use of antivenom for venomous snakebites reported to our center over a 6 year period. RPC staff graded snake envenomation based upon standard guidelines outlined in an internal resource manual. RPC staff categorized medical outcome according to AAPCC categories: "No effect", "Minor effect", "Moderate effect", and "Major effect". Cases were followed from the initial call until resolution of symptoms and signs were evident or, in the case of inpatients, the time of discharge.

**Statistics:** Comparisons were made between groups using Chi-square with Yate's correction factor.

**Results:** Of 596 venomous snakebites reported, 87.2% were copperhead, 8.5% rattlesnake and 4.3% cottonmouth. Tissue effects accounted for the majority of signs. Rattlesnake outcomes were 26% minor, 42% moderate and 8% major. There was no significant difference between groups with regard to pain, erythema, edema or ecchymosis. There was a significant difference ($\chi^2 = 31.425$; $p < 0.01$; OR =16.702, 95% CI 4.512 to 63.825) for nausea when comparing rattlesnakes to copperheads. Copperhead outcomes were 35.7% minor, 46.5% moderate and 2.7% major. There was no significant difference between groups ($\chi^2 = 0.221$; $p = 0.6381$) in categorization of severity. There was a significant difference in antivenin use between rattlesnakes and copperheads ($\chi^2 = 22.111$, $p < 0.01$ ), OR = 4.461 (95% CI = 2.243 to 8.835). In 49.2% (255/518) there were signs that might have benefited from antivenom therapy yet only 22.7% (58/255) were treated.

**Conclusions:** The outcome profile for both groups was similar, yet copperhead envenomation was undertreated compared to rattlesnakes. The superior risk/benefit profile for Fab crotaline antivenom makes it a viable treatment option in the management of tissue destruction from copperhead bites.

## EASTERN CORAL SNAKE ENVENOMATION IN THE DOG

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**Abstract:** The main signs of Eastern Coral Snake envenomation in the dog include varying degrees of lower motor neuron weakness that can progress to causing respiratory paralysis requiring ventilator support. About 50% also show hemolysis with RBC morphological changes including spherocytosis and echinocytes. Survivial is generally good with intensive care with or without the use of antivenom (which is no longer available to veterinarians).

## EXOTIC ANTIVENOMS IN THE U.S.

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**Background:** There are over 50 bites per year by non-native species in the US, involving at least 77 different species over the past decade. 81% occurred at a private residence. These envenomations are unfamiliar to most healthcare providers, require significant

healthcare resources, have barriers to antivenom determination and acquisition, and have worse clinical outcomes and a higher case-fatality rate than native envenomations. **The Current "System":** With the vast majority of bites occurring in private collections, there is usually no knowledge of the snake's existence, no clinical familiarity of local practitioners in the management of these cases, and no prior preparations. Eventually, the regional poison center and/or a zoo become involved. The Online Antivenom Index is employed to determine and locate antivenom. If an appropriate antivenom is available at a US zoo, a request for compassionate release is made and antivenom is transported to the patient's location. Delays of 12–36 hours are not uncommon. Practitioners are usually ignorant of IRB and FDA reporting requirements for IND drugs which are thus rarely, if ever, completed. The zoos may not receive reimbursement for their provision of antivenom. Zoos obtain antivenoms for their employees' use and purchase antivenoms against only the snakes in their collections. They are under no legal obligation to provide them outside of their institutions. If no US zoo has a particular snake, the antivenom for it may not be in the US, although the snake may exist in private collections. If an antivenom is available, it may be located far from where the envenomation has occurred. Many antivenoms are only available in expired form. A recent study found that of 44 antivenoms listed by 53 AZA institutions, all lots of 18 types (41%) were expired. Even when unexpired stock is available, zoos may choose to send their expired stock. Antivenom acquisition, maintenance and replacement costs can be considerable, ranging up to tens of thousands of dollars for adequate amounts of a single antivenom. Finally, the typical shelf-life of biologics is three to five years. **A Strategic Exotic Antivenom System:** A strategic exotic antivenom system would begin with an analysis of what antivenoms are required and how they should be distributed, would have a clear, easy to use antivenom determination and location system, provide for rapid antivenom transport, would provide non-expired stock when available, for replacement of expired stock, a system of expert assistance, track antivenom use and clinical data, and be sustainable. A three-year HRSA Grant to establish such a system has just been obtained.

## NPDS-BASED CHARACTERIZATION OF NATIVE US ELAPID ENVENOMATIONS

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**Background:** Envenomations by the coral snake, the US's only native elapid, have not been systematically characterized with regard to demographic associations, clinical effects, managements, and outcomes, or in comparison with native viperids (rattlesnakes, copperheads and cottonmouths) and non-native elapids.

**Methods:** The National Poison Data System (NPDS) database from 2001–2005 was analyzed by descriptive and statistical measures. 111 cases coded as *Micrurus alleni* (a Central American elapid) were likely miscoded native envenomations and were included. 18 cases coded as other non-native *Micrurus* species were excluded. Chi-squared and Odds Ratios were determined where appropriate.

**Results:** There were 382 native US elapid envenomations over the 5 year period (average = 76 per year). Compared with native US viperid exposures, native elapid exposures: 1) Involved a significantly higher incidence of males; 2) were less likely to be managed in a non-healthcare setting, less likely to be treated and released and more likely to be admitted to an ICU; 3) had a greater likelihood for effects to be "None" or "Minor," but rates of serious outcomes did not differ (Major Effects 4%; Death 0%); 4) were less likely to produce local tissue injury and hematologic effects and more likely to produce neurologic effects; 5) had clinical effects of shorter duration; and 6) were more likely to receive antivenom, antihistamines and steroids, and less likely to receive antibiotics. Exposure site data, age distribution, and rates of endotracheal intubation and hypotension requiring pressors did not differ between snake classes (Table 1). Compared with non-native US elapid envenomations in the NPDS database, native elapids: 1) Had more "Minor" outcomes and fewer "Major" outcomes; 2) were less likely to be intubated; 3) had shorter durations of clinical effects; and 4) were more likely to receive antivenom (Table 2).

**Conclusions:** Significant differences exist between native US elapid and viperid envenomations, as well as between native and non-native elapids with regard to demographic associations, clinical effects, therapeutic interventions and outcomes. Rates of serious outcomes are similar between native elapid and viperid envenomations. Improvements to Poisindex's listing of coral snakes and to the NPDS data collection system would enhance the accuracy, completeness, and utility of the envenomation database.

## ASIAN ELAPIDS

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**Abstract:** There are three well-recognised clinical syndromes of Asian elapid envenoming: local envenoming of variable intensity with or without descending paralysis (cobras), descending paralysis with negligible local envenoming but abdominal pain and distinct epidemiological features (kraits) and descending paralysis with marked rhabdomyolysis (sea snakes). However, there are several puzzling and some newly described clinical features that deserve more attention from toxinological, pathophysiological and therapeutic

**Table 1: Native Elapids v. Native Viperids**

| | Native Elapids (%) | Native Viperids (%) | Significance |
|---|---|---|---|
| **Gender** | | | |
| Males | 81 | 71 | $p < 0.0001$; OR 0.5801; $CI_{95\%}$ 0.4455–0.7554 |
| **Treatment Site** | | | |
| Non-HCF | 5 | 13 | $p < 0.0001$; OR 0.3776; $CI_{95\%}$ 0.2403–0.5933 |
| Tx & released | 24 | 35 | $p = 0.0002$; OR 0.6430; $CI_{95\%}$ 0.5094–0.8116 |
| ICU Admit | 43 | 19 | $p < 0.0001$; OR 3.339; $CI_{95\%}$ 2.821–4.099 |
| **Clinical Effects** | | | |
| No Effects | 8 | 4 | $p < 0.0001$; OR 2.82; $CI_{95\%}$ 1.928–4.127 |
| Minor Effects | 48 | 19 | $p < 0.0001$; OR 1.727; $CI_{95\%}$ 1.411–2.115 |
| Major Effects | 4 | 4 | ns |
| Death | 0 | 0 | ns |
| **Treatment** | | | |
| Antivenom | 47 | 26 | $p < 0.0001$; OR 2.502; $CI_{95\%}$ 2.042–3.066 |
| Antihistamines | 9 | 5 | $p = 0.0002$; OR 1.999; $CI_{95\%}$ 1.391–2.871 |
| Steroids | 6 | 3 | $p = 0.0010$; OR 2.118; $CI_{95\%}$ 1.367–3.280 |
| Antibiotics | 3 | 12 | $p < 0.0001$; OR 0.2071; $CI_{95\%}$ 0.1104–0.3887 |

**Table 2: Native Elapids v. Non-native Elapids**

| | Native Elapids (%) | Non-native Elapids (%) | Significance |
|---|---|---|---|
| **Clinical Effects** | | | |
| Minor Effects | 48 | 19 | $p < 0.0001$; OR 4.084; $CI_{95\%}$ 2.772−6.017 |
| Major Effects | 5 | 10 | $p = 0.0105$; OR 0.4192; $CI_{95\%}$ 0.2189−0.8028 |
| **Treatment** | | | |
| Antivenom | 47 | 25 | $p < 0.0001$; OR 2.706; $CI_{95\%}$ 1.892−3.872 |
| Intubation | 1 | 9 | $p < 0.0001$; OR 0.1143; $CI_{95\%}$ 0.03855−0.3388 |

points of view. These include: the mechanism of pre-paralytic drowsiness, involvement of the autonomic nervous system, pupillary changes, mechanism of severe abdominal and generalised musculo-skeletal pain in krait envenoming, the occurrence of rhabdomyolysis in krait envenoming, the role, timing and efficacy of antivenom and ancillary pharmacological treatments (e.g. anticholinesterases) in the treatment of pre- and post- synaptic neurotoxicity and the role of antivenom against cobra-venom-induced local tissue necrosis. The greatest practical challenges posed by neurotoxic elapid envenoming in rural Asia are, first, reducing the risk of bites through community education, and second, preventing death from respiratory paralysis before bite victims reach a medical facility where they can be intubated and artificially ventilated.

## AUSTRALIAN ELAPIDS

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**Abstract:** Australia has a diverse and unique Elapid snake fauna which includes many small species of no medical significance, over 20 species of terrestrial dangerous snakes, including some of the most toxic species globally, and many sea snake species, the

latter considered to have evolved from the terrestrial fauna. Envenoming causes principally systemic rather than local problems, with all species producing one or more of the following; flaccid neurotoxic paralysis, myolysis, coagulopathy (procoagulant defibrination or anticoagulant), renal damage/failure (plus microangiopathic haemolytic anaemia in some cases). High quality retrieval and ICU services and ready availability of effective antivenom ensure annual death rates around 2–6 cases, out of an annual snakebite toll of around 1,000 cases. Management recommendations are in an era of change as ongoing prospective clinical research indicates major shifts in policy are possible.

## ARIZONA BLACK RATTLESNAKE ENVENOMATION

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**Background:** The Crotalidae family is responsible for 99% of venomous snakebites in the United States (1). The Arizona black rattlesnake was originally classified as a subspecies of the western rattlesnake (*Crotalus viridis cerberus*). In 2000 it was identified as a separate species using mitochondrial DNA analysis (2). The black rattlesnake is endogenous to Arizona and is found in mountainous regions of 5,000 to 9,150 feet (3). We present the first reported case of a *Crotalus viridis cerberus* envenomation successfully treated with CroFab® (Antivenin – Crotalidae).

**Case Report:** A 45-year-old male presented to a community ED after being envenomation of his right middle finger by an Arizona black rattlesnake. With in 1hour of envenomation his physical exam revealed local erythema, pain, swelling to right upper arm, and muscle fasciculations of right arm and leg. His blood pressure was 151/107. All other vital signs were normal. He had no other signs of systemic effects. Initial chemistries were normal, the CBC showed a leukocytosis (WBC 14,800/mm3), INR 1.1, platelet count 369,000/mm3, fibrinogen 294. The patient received tetanus prophylaxis, IV fluids, pain control, and was transferred to a tertiary care facility. Two and a half hours post bite, the patient's local symptoms progressed to his anterior chest wall with evident fasiculations. The regional poison control center was consulted and a 6 vial loading dose of CroFab® was started, followed by a maintenance dose of 2 vials every 6 hours for 3 doses. Repeat labs 4 hours post loading dose revealed normal chemistries, WBC decreased to 10,800/mm3, INR 0.97, PTT 37, CK 37 U/L. On hospital day 3, the patient remained stable, was relieved of pain, showed no progression of edema; final lab values showed WBC 9,600/mm3, INR 0.91, platelets 294,000/mm3, PT 9.7, CK 35 U/L and the patient was discharged. One week post discharge he was re-evaluated. The swelling had improved, the wound was healing, repeat CBC and coagulation studies were normal.

**Conclusion:** The Arizona black rattlesnake, *Crotalus viridis cerberus*, is a newly identified species. This envenomated patient showed only rapidly progressing local symptoms and fasciculations. His signs and symptoms responded well to CroFab administration and he had no apparent hematological effects or long-term systemic sequela.

## SYSTEMIC EFFECTS AFTER COPPERHEAD ENVENOMATION

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**Background:** 45,000 snakebites occur annually in the United States, 8,000 of which are from venomous snakes. The Crotalidae family account for 99 percent of these snakebites and approximately 13% are copperhead envenomations. Copperheads are considered to be the least toxic, often causing local tissue injury and swelling rather than systemic toxicity. This case presents a positively identified Copperhead envenomation victim who developed systemic and hematologic effects.

**Case Report:** A 45year old, male with a history of aortic valve replacement on warfarin (noncompliant), presented to a tertiary care center's emergency department immediately following a snakebite. The snake was positively identified by an attending medical toxicologist as a Copperhead. On initial presentation the patient had decreased alertness, lethargy, hypoglycemia, diaphoresis, tachycardia, tachypnea, bronchospasm and hypotension. Two sets of two puncture marks were found over the dorsum of the patient's right foot with a hemorrhagic bleb and surrounding erythema and edema. Initial labs: platelets 368 $\times$ 10e9/L, hemoglobin 19.8 g/L, PTT 33 sec, PT 47.8 sec and INR 4.4. The patient was admitted to the ICU, given a loading dose of 6 vials of Crofab, steroids, antihistamines, and IVF. The patient's anaphylactic type symptoms resolved. Approximately 16 hours post envenomation the patient became more coagulopathic (INR 7.4, FSP $>$20mcg/ml and fibrinogen 307 mg/dl). On hospital day two the INR was 8.2, PT 95.7 sec, PTT 57 sec, fibrinogen 280 mg/dl, FSP $<$5, and platelets 198 $\times$10e9/L with no active bleeding. The patient received a repeat loading dose of 4 vials of Crofab and scheduled maintenance dosing of 2 vials every six hours times three doses. 2 units of FFP were administered, but not recommended. Post FFP and Crofab infusion the INR decreased to 1.3, platelets 142 $\times$10e9/L and hemglobin 11.1 g/L. The patient was transferred to the floor and began re-anticoagulation. He was discharged on hospital day eight.

**Conclusion:** Systemic toxicity has been reported with Copperhead envenomations but is extremely rare. This patient appeared to have an anaphylactic reaction, systemic effects, and hematological effects to copperhead venom. The coagulopathy may have been confounded by warfarin, but the elevation of PT, PTT, fibrin split products and evidence of platelet consumption are suggestive of effects from Copperhead venom.

## *SPIDERS*

### LOXOSCELES GRETA, A NEW SPECIES FROM CASAS VIEJAS, SINALOA STATE, MEXICO (ARANEAE, SIICARIDAE)

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**Abstract:** *Loxosceles (Siicaridae*) species diversity is of interest for understanding their diversification history and because their venoms are medically important. In the most recent revision of North American Loxosceles Gertsch and Ennik (1983) cataloged ~50 species with 39 described in Mexico. In the last 4 years, Instituto Bioclon, has been developing an antivenom for Loxosceles spider bites. The goal is for this antivenom to be effective for treatments of bites of all members of this genus. To facilitate this work Octolab, arachnid venom provider of Instituto Bioclon, has extensively collected Loxosceles with an effort to fully understand species diversity in Mexico. In the process of this work we have found at least two populations that are sufficiently distinct from described taxa to warrant new species status. Here we describe one of these based on examination of 3 adult males and 5 adult females from Sinaloa State in North western México. We propose the name *Loxosceles greta* after Dr. Greta Binford, a researcher of world *Loxosceles*. This species is similar to *Loxosceles alamosa* (Gertsch,1958) if we compare the epigyna but the receptacles are closer in *Loxosceles greta* and at the base of them are sharp pointed . Each receptacle present long irregular finger-like lobe arising from the middle and this flanked by one or more smaller irregular lobes. The male palpi have a curved embolus with any irregularity.

### A MOLECULAR PERSPECTIVE ON THE EVOLUTION AND DIVERSITY OF BLACK WIDOW SPIDERS AND THEIR POTENT VENOM NEUROTOXINS

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**Abstract:** The venom of black widow spiders (genus *Latrodectus*) contains a powerful neurotoxin that triggers mass release of transmitters from vertebrate neurosecretory cells and causes severe envenomation in humans. In addition to this vertebrate neurotoxin (alpha-latrotoxin), *Latrodectus* venom contains additional toxins that share similar molecular features but selectively affect invertebrates. Together, these toxins are considered functionally distinct members of a single gene family. At the molecular level, the diversity and distribution of this gene family has only been thoroughly characterized in a single Eurasian species, though biochemical and clinical data suggest that latrotoxins occur in other members of the *Latrodectus* genus (31 described species) and related genera. Here, we review the diversity and phylogenetic history of the spider genus *Latrodectus*, as inferred from genetic markers. In order to further investigate latrotoxin diversity, we have determined sequences of the alpha-latrotoxin gene from multiple *Latrodectus* species. Protein sequences inferred from our data differ by many non-conservative amino acid substitutions, suggesting they may also exhibit significant functional differences in vertebrate toxicity. We interpret this interspecific genetic variation in light of previous literature reporting variation in vertebrate toxicity across *Latrodectus* and related species and consider its evolutionary significance.

### THE REDBACK SPIDER ANTIVENOM EVALUATION STUDY

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**Objectives:** There is ongoing controversy regarding the appropriate route of administration of redback spider (RBS) antivenom. We aimed to compare the effectiveness of intravenous (IV) versus intramuscular (IM) RBS antivenom.

**Methods:** This was a double dummy placebo randomised controlled trial of IV versus IM RBS antivenom in 126 patients with moderate to severe RBS envenoming. The primary outcome was a clinically important reduction in pain as measured by the visual analog scale two hours after antivenom. Secondary outcomes were a reduction in systemic effects, clinically significant reduction in pain at 24 hours, use of further antivenom doses of antivenom and use of analgesics. Primary analysis was by intention to treat using a fully Bayesian approach. A clinically significant absolute difference in treatment effect was defined as 20% corresponding to a number needed to treat of five, based on a survey of emergency physicians.

**Results:** Sixty four patients received IV antivenom and 62 IM antivenom. The two groups had similar baseline features except those receiving IV antivenom were slightly older. Two hours after one or two vials of antivenom, 63% (40/64) of the IV group had clinically improved pain versus 53% (33/62) treated with IM antivenom [+9%; 95% Credible interval (CrI): −8% to +26%]. The probability that the difference between treatments was greater than zero was 85%, but the probability that it was greater than 20% was only 11%. Systemic effects occurred in 44% of patients, and following IV antivenom 58% had improved systemic effects compared to 67% receiving IM. Fewer patients receiving IV antivenom (23%) required further antivenom compared to IM (39%) [−15%; 95%CrI: −30% to +1%], and 85% receiving IV antivenom had clinically improved pain at 24 hours versus 73% receiving IM, [+13%; 95%CrI: −2% to +27%]. There were no significant differences in analgesic administration in hospital (36% vs. 33%) or after discharge (44% vs. 50%).

**Conclusions:** There was not a clinically significant difference between the IV and IM route of administration of RBS antivenom in reducing pain.

## PRIAPISM ASSOCIATED WITH *LATRODECTUS MACTANS* ENVENOMATION

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**Introduction:** Black widow spider (*Latrodectus Mactans*) envenomations commonly produce pain and hypertension. Other symptoms include muscle spasms, nausea, vomiting, sweating, tachycardia, restlessness, and facies lactrodectismica. Rarely, *L. Mactans* has caused priapism. We report a case of black widow envenomation-induced priapism in a 7 year old boy.

**Case Report:** A 7 year old boy was bitten on the left elbow by a "black shiny spider with an orange bottom." Thirty minutes after the bite he became agitated, diaphoretic, and had total body pain. Symptoms continued at home overnight and he was taken to an emergency department nearly 15 hours after the bite occurred. The patient's initial vital signs were blood pressure (BP) 128/77, pulse 105, respirations 20, afebrile and a pain score of 10/10. The patient was crying in pain. There was no lesion on the left elbow and no priapism. He was treated with calcium gluconate, lorazepam, and morphine intravenously, plus oral acetaminophen with codeine. Six hours after hospital arrival, the admitting physician noticed priapism. Due to lack of pediatric specialists, the patient was transferred to our pediatric tertiary care hospital. On arrival 23 hours post-envenomation he was intermittently crying, diaphoretic about the nose and upper lip, had a tense abdomen, mild eyelid edema, and priapism. Pain and hypertension (maximum 150/110) persisted, despite repeated doses of fentanyl. One vial of *L. Mactans* antivenom (Merck & Co., Inc.) was administered resulting in reduction of blood pressure from 149/104 to 114/61 within two hours and gradual penile detumescence over seven hours after the start of antivenom infusion. A pediatric urologist evaluated the patient verifying resolution of priapism.

**Discussion:** *L. Mactans* envenomations are fairly uncommon. Opioids and benzodiazepines are often adequate to control symptoms. Priapism is a rare complication of these bites. Two cases are reported in the medical literature, both reporting resolution with antivenom. The mechanism of priapism is postulated to arise through overstimulation of the parasympathetic nervous system causing smooth muscle relaxation in conjunction with decreased penile venous outflow due to acetylcholine release at the neuromuscular junction.

**Conclusion:** We report a case of black widow envenomation resulting in priapism. While antivenom resulted in a rapid reversal of pain and hypertension, priapism took many hours to resolve.

## AUSTRALIAN SPIDERS

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**Abstract:** Australia is home to a huge array of spiders, including the most dangerous species globally, the funnel web spiders. Spiderbite is both common and a common concern for the Australian population, representing one of the most frequent reasons to contact a poisons information centre or medical call centre. However, most bites are minor, with just two groups causing nearly all medically significant cases; funnel web spiders and red back spiders. Red back spiders are widow spiders, common throughout much of urban and rural Australia, causing thousands of bites each year, with around 1,000 + cases receiving antivenom. If used in sufficient

dose antivenom appears effective at relieving symptoms, greatly shortens hospitalisation and period of suffering, with adverse effects uncommon and controllable. Recommended doses have recently increased. Funnel web spider bites are uncommon but potentially lethal, unless treated with specific antivenom, which is highly effective.

## *VENOMOUS ANIMALS, OTHER*

### INTRACRANIAL HEMORRHAGE FOLLOWING STINGRAY ENVENOMATION IN A CHILD WITH UNDIAGNOSED CEREBRAL AVM

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**Background:** Stingray envenomations are common and usually minor, although they can be very painful. Severe and even fatal events are associated with penetrating trauma from the stingray's barb. We present a case of intracranial hemorrhage following stingray envenomation in a child with an undiagnosed cerebral arterial-vascular malformation (AVM). Case: An 8 year-old boy was wading in shallow ocean water in Mexico when he was barbed on the dorsum of the left foot by a stingray. He immediately cried and complained of extreme pain. He was treated at a nearby first-aid facility with intradermal lidocaine and local wound care. Within 2 hours he developed vomiting and severe headache, and 90 minutes later suffered a generalized seizure followed by apnea. He received BVM-assisted ventilations, chest compressions, IV steroids and diazepam at an ED in Mexico. Spontaneous respirations returned, he was rushed to a US border hospital and then flown to Phoenix Childrens Hospital for management of the presumed effects of stingray envenomation. On arrival, approximately 8 hours after the envenomation, he was sitting up, confused and vomiting. HR was 89, RR 18, BP 122/65 and oxygen saturation 100% on 2L of oxygen by nasal cannula. There was an angular, 5 mm puncture wound over the dorsum of the left foot with edema distal to the wound. 1 hour after arrival to the ED he developed a disconjugate gaze and left-sided mydriasis. CT of the brain revealed parenchymal hemorrhage in the posterior left frontal and parietal lobes, a cystic mass anterior to the hemorrhage and midline shift to the right. An MRA confirmed the presence of a vascular malformation. The patient was intubated, sedated and treated for increased intracranial pressure. On hospital day 2 he was placed on cefazolin but did not demonstrate signs of wound infection. He was extubated on day 3 with good neurological function. Conclusion: Stingray venom does not produce neurological toxicity in humans but can cause pain out of proportion to the degree of traumatic injury. It's possible that severe pain created a hyperadrenergic state, causing an undiagnosed AVM to bleed and consequent seizure. Seizures and cranial nerve findings in the setting of stingray envenomation require a full neurological work-up, including CT to rule out intracranial hemorrhage.

### LESSER KNOWN VENOMOUS CREATURES: INTERESTING CASES

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**Background:** In 2006 approximately 20% of the cases reported to the Arizona Poison and Drug Information Center involved an envenomation. These included 2,729 scorpion stings, 378 spider bites and 204 snakebites. The center is occasionally called upon to consult on cases involving some of the lesser known venomous creatures. Here we present two such cases: a patient bitten by *Heloderma suspectum* and a patient bitten by *Micruroides euryxanthus*.

**Case 1:** A 35 year-old male, amateur herpetologist was bitten on his right hand while handling a *Heloderma suspectum* (Gila monster). The Gila monster remained attached to the patient for 42 seconds. The patient became nauseated, light headed, dizzy and defecated approximately 2 minutes after disengaging the Gila monster. The patient was transported to the emergency department via private vehicle. Soon after his arrival he experience facial and tongue swelling. The patient was treated with epinephrine, dopamine, steroids, and H1 and H2 blockers. Mild edema at the bite site progressed proximally over the next 18 hours, at which time the patient was extubated and discharged.

**Case 2:** A 40 year-old male was bitten on his left hand between the second and third digit while handing a *Micruroides euryxanthus* (coral) snake. The patient was referred to the emergency department. There were two puncture wounds and minor swelling at the bite site. A fang was removed from one of the puncture wounds. The patient described numbness at the bite site, some facial numbness, and a metallic taste in his mouth. The patient was admitted for observation and discharged 13 hours later without complications.

## ARE KILLER BEES KILLERS? A CASE SERIES OF MASSIVE AFRICANIZED BEE ENVENOMATION

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**Background:** "Killer bees" (Africanized honey bees) have been established in the southern US for over 17 years. The incidence of multiple bee stings has been on the rise. The patients at the extremes of age have been proposed to be at highest risk of organ failure and death.

**Case Reports:** Here we describe three cases of massive bee envenomation, two of which were in geriatric patients. All patients were documented to have over 100 stings, with the highest one being a case of an 83 year old envenomated by over 400 Africanized honey bees (AB). All patients seemed to do well with supportive medical care, and were discharged from the hospital after 3–6 days of observation. The two geriatric patients were given epinephrine in the field and both had an increase in their Troponin I levels. It was not clear if this rise in Troponin I was an effect of epinephrine itself or a direct effect of the bee venom. Both geriatric patients were observed the longest in their Troponin I, and were released without any sequelae. Except for cases of anaphylaxis, we believe that these three cases show that supportive care is sufficient for patients with massive bee envenomation (over 100 stings).

**Discussion:** Bee venom contains melittin, phospholipase A, histamine, degranulating peptides, and hyaluronidase. The $LD_{50}$ for AB is similar to the $LD_{50}$ reported for the European honey bee. It is the defensive nature of AB that results in a greater number of stings, and consequently a greater venom load potentially resulting in failure of various organ systems. This fact has been reported by Franca et al, with regard to both proximal tubule and cardiac toxicity. Immediate and delayed toxicity including heart failure, rhabdomyolysis, thrombocytopenia, hemolysis, and renal failure have all been reported with Africanized honey bee envenomations. However, there seems to be some anecdotal evidence that envenomations of more than 500 stings may be fatal, and associated with delayed toxicity. Many of the reports of death associated with "killer bees" in the general media are sensationalized or exaggerated.

**Conclusions:** We theorize that many of the immediate deaths by the Africanized bee attacks are associated with anaphylaxis or angioedema and not necessarily related to multisystem organ failure.

# *VENOMS/ANTIVENOMS*

## WHAT CAN PREY TELL US ABOUT ENVENOMATION?

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**Abstract:** Snake venoms have been a topic of research since the late 18th century. Much information is available on venom toxins and their mechanisms of toxicity in humans and animal models. There is also a well-developed literature on treatment for envenomation. However, investigation of innate resistance to snake venoms in prey species is relatively recent. General patterns of venom resistance revealed from an ecological and evolutionary perspective on the extant literature, as well as current gaps in this knowledge base, are presented. Research on California ground squirrel (*Spermophilus beecheyi)* and rock squirrel (*Spermophilus variegatus*) resistance to rattlesnake venom is presented as an example of how a comparative approach can provide insight into the coevolution of snakes and prey. Leads into promising areas of research with likely future clinical significance are also explored.

## COMPARATIVE ACTION OF SPECIFIC FAB AND FAB'$_2$ ANTIBODIES TO PHARMACOKINETICS OF VIPER AND SCORPION VENOMS DURING ENVENOMATIONS

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**Background:** Antivenom immunotherapy is the unique specific treatment of envenomations. Although widely used and medically accepted, it is still empirically administered. Its improvement requires accurate criteria to assess when this treatment has to be used or not. It also requires accurate guidelines to improve the efficacy and the safety of this treatment. In particular, little information is available concerning the relative efficacy of monovalent (Fab) and divalent (Fab'$_2$) antibodies to remove venom toxins in antivenom treatments.

**Methods:** ELISA tests were set up to follow the venom toxins in patients' blood during envenomations and pharmacokinetics were followed in experimentally envenomed rabbits, in the absence of, or after antivenom therapy with Fab or Fab'$_2$. In a first step,

ELISAs were used in parallel with clinical grading of viper and scorpion envenomations. In both cases, a good correlation was observed between venom levels in the blood and clinical symptoms. In a second step, we examined the venom kinetics, in the absence of, and after antivenom administration. Investigations were carried out in the case of envenomations by viper (*V. aspis*) in France and by scorpion (*A. a. garzonii*) in Tunisia and (*C. l. limpidus*) in Mexico. The relative efficacy of specific Fab and $Fab'_2$ antibodies was also tested.

**Results:** After intramuscular injection of viper venom, the resorption of the venom followed a complex process: it was fast during the first 24 hr then occurred at a slower rate over the subsequent 72 hr, resulting in a long half-life of elimination (36 hr). On the other hand, the absorption of scorpion toxins was very fast and complete and its half-life of elimination was short (2 hr).

**Discussion/Conclusions:** It appeared that detoxification process is explained by a redistribution of the venom from the extra vascular compartment to the vascular one, where the antibodies sequester it. Indeed, intravenous injection is the most effective route for antivenom administration. In viper envenomations, it was shown that $Fab'_2$ were more efficient than Fab because of more appropriate pharmacokinetic parameters. On the other hand, in scorpion envenomations, differences in Fab and $Fab'_2$ antibobies efficacy were not so pronounced, because of the fast elimination of the scorpion toxins, compared to the viper ones. These experimental studies provide an experimental model to optimize antivenom therapy.

## IMMUNOCHEMICAL CHARACTERIZATION OF *MICRURUS LATICOLLARIS* CORAL SNAKE VENOM

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**Abstract:** *Micrurus laticollaris* coral snake venom can produce rabbit serum titles higher than 300,000 with no capacity to neutrlize homologous venom. Horse specific antivenom shows neutralizing potency of 0.552 mg/ml with serum title of 108,000. We report advances in the study of the biochemical characterization of venom and immunochemical differences between horse and rabbit antiserum in order to explain why rabbit should produce high antibody titles with no neutralizing capacities.

## EVOLUTION OF AN ARSENAL: DIVERSIFICATION OF THE REPTILE VENOM SYSTEM

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**Abstract:** Despite the importance of venom as a key innovation underlying the evolution of Toxicofera reptiles (Anguimorpha + Iguania lizards and Serpentes, very little is known about venom system structural diversification, toxin recruitment event timings or toxin molecular evolution. We employed a multidisciplinary approach to examine the diversification of the reptile venom system and associated toxins across the full-range of the ~200 million year old Toxicofera clade. Analysis of cDNA libraries revealed complex venom transcriptomes comprising multiple toxin types. High levels of sequence diversity were observed in the transcripts for most toxin types and included mutations in the structural and functional residues, changes in cysteine spacing, and major deletions, indicative of neofunctionalisations. Morphological analysis comprising gross dissection, histology and magnetic resonance imaging also demonstrated extensive modification of the venom system architecture. Further a reduction in the size and complexity of the venom system was observed in species in which constriction has been secondarily evolved as the preferred method of prey capture or dietary preference has switched from live-prey to eggs or to slugs/snails. Investigation of the timing of toxin recruitment events indicates that the evolution of advanced venom systems in three front-fanged snake lineages are associated with recruitment of new toxin types or explosive diversification of existing toxin types. These results support the role of venom as a key evolutionary innovation in the diversification of Toxicofera reptiles and identify a potential role for venom toxins as lead compounds for drug design and development.

## THE MOLECULAR BASIS FOR CROSS-REACTIVITIES OF THE SNAKE VENOM DETECTION KITS

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**Background:** The Snake Venom Detection Kit (sVDK) is of major medical importance in Australia, yet it has never been rigorously characterised in terms of its sensitivity and specificity, especially when it comes to reports of false negative and false

positive results. We investigated reactions and cross-reactions of five venoms the sVDK is directed against and a number of purified toxins.

**Results:** Surprisingly, snakes showing the closest evolutionary relationships demonstrated the lowest level of cross-reactivity between groups. This was, instead, far more evident between snakes that are extraordinarily evolutionary separated. These snakes: *Pseudechis australis* (Mulga), *Acanthophis antarcticus* (Common death adder) and *Notechis scutatus* (Common tiger), in fact displayed more false positive results. Examination of individual toxin groups showed Phospholipase A2s (PLA2s) to tend to react strongly and display considerable cross-reactivity across groups while the three finger toxins (3FTx) reacted poorly in all but the death adder (*Acanthophis*) well. The hook effect was evident for all venoms, particularly the *Oxyuranus scutellatus* (Coastal taipan).

**Conclusions:** The results of this study show considerable variation in toxin detection, with implications in further development of venom detection, both in Australia and other countries.

## CONFRONTING THE PROBLEM OF SNAKEBITE ENVENOMATION IN CENTRAL AMERICA: A SUCCESSFUL ENDOGENOUS EFFORT BASED ON SCIENCE, TECHNOLOGY AND INSTITUTIONAL COMMITMENT

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**Abstract:** Snakebite envenomation represents a serious public health hazard in Central America, with about 5000 cases occurring every year. A long-term project developed in Costa Rica, aimed at generating scientific knowledge on the biochemical and toxicological profiles of snake venoms, together with technological research for the adaptation and development of technologies for the production of safe and effective antivenoms, has succeeded in generating a body of knowledge on snakes and their venoms, as well as a sustainable production of antivenom for the whole region. The project initially succeeded in the solution of this health problem in Costa Rica and, in the last decade, has been successfully extended to the rest of Central American countries. Along this process, a thorough assessment of antivenom efficacy and safety has been performed, at both preclinical and clinical levels. These scientific and technological efforts have come together with a significant institutional development of the public health sector in Costa Rica, together with permanent educational programs directed to health workers, to convey the basic elements of snakebite envenomation therapy; these efforts have greatly improved the management of snakebites in the region. Simultaneously, a successful preventive campaign to reduce the impact of this pathology has taken place in Central America. Further efforts have to be undertaken to further extend the benefits of this multifaceted approach and to focus on regions and social sectors that still remain out of reach of these public health initiatives.

## ANAPHYLAXIS FOLLOWING REEXPOSURE TO CROFAB™

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**Background:** Review of the literature does not reveal any cases of hypersensitivity reactions on delayed re-challenge to CroFab™. We report a case of hypersensitivity to CroFab™ in a patient previously treated without complications.

**Case Report:** A 55 yo man sustained a bite to the left 5th digit from a *Crotalus polystictus* at 12:00 pm. He was triaged at a local hospital at 12:58pm where initial vital signs were T: 98.7, BP 143/94, HR 86, R 20, room air O2 sat. 98%. He had no systemic symptoms; however, pain and swelling of the left upper extremity were noted. His past medical history was significant for previous rattlesnake envenomation in 2001 treated with CroFab™ without complication. The patient received 1L of NS, morphine and ondansetron and was noted to have stable vital signs. An infusion of CroFab™, 6 vials in 250ml, was started at 14:15 at an initial rate of 25ml/hr for 10 minutes. At 14:25 the rate was increased to 250ml/hr. At 14:35, the patient was diaphoretic and nauseated with a BP of 81/32 and a HR of 41. CroFab™ infusion was stopped and 500ml NS were given and BP improved to 100/39; at 14:45 CroFab™ was restarted at half the initial infusion rate. Hypotension recurred within five minutes, requiring an additional NS bolus. The CroFab™ infusion was continued and at 15:30 his BP was 106/58, HR 61. Five minutes later, the patient developed diffuse urticaria without bronchospasm or change in BP or HR. The CroFab™ infusion was discontinued, with 180ml of 250ml having been infused; diphenhydramine 50mg IV, famotidine 20mg IV, and methylprednisolone 125mg IV were given. An epinephrine gtt at 1mcg/min was started. On arrival to our facility, the patient was on an epinephrine gtt at 2 mcg/min, BP was 134/64, HR 94 and urticaria was persistent but improved. Left upper extremity edema was stable, no coagulopathy or thrombocytopenia developed and no further CroFab™ was administered. The patient was discharged on day 2 and seen 3 days later with improved symptoms and normal labs.

**Conclusion:** We present a case of 55 yo man with a history of prior uncomplicated treatment with CroFab™ who developed hypotension, urticaria, diaphoresis and nausea upon re-exposure to CroFab™. To our knowledge this is the first reported case of hypersensitivity syndrome in a patient sensitized to CroFab™ by prior administration.

## SERUM SICKNESS FOLLOWING ANASCORP® TREATMENT

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**Background:** Anascorp®, a $F(ab')_2$ antivenom derived from horses immunized with venom from *Centruroides* scorpions, is currently undergoing evaluation by the FDA for treatment of envenomation by *Centruroides sculpturatus*. Fab fragment antivenins are less immunogenic than Fc-based products, but they can still cause hypersensitivity reactions, particularly if there are residual Fc domains remaining in the final product after enzymatic digestion and purification. To date, there has been no report of serum sickness with Anascorp®: We present a case of a 6-month-old who presented with a bilateral, urticarial rash 7 days after receipt of 5 vials of antivenin.

**Case Report:** A 6 month boy old presented to our emergency department with a rash that had appeared suddenly that morning. Seven days prior he had received treatment with 5 vials of Anascorp® antivenin for treatment of a Grade IV scorpion sting without adverse effect. He had had some runny yellow stools $\times 24$ hours, but had no history of fever, vomiting, cough, or ill contacts. Exam revealed a marked maculopapular rash in his axilla and on his thighs with sparing of palms, soles, mucous membranes, oral cavity, face, back and trunk. The lesions blanched easily and appeared typical of that we have regularly encountered with serum sickness from Wyeth Crotalidae polyvalent antivenom. The child was otherwise well-appearing, interactive and playful with an age-appropriate neurological exam. A UA was negative for blood or protein. He was treated in the emergency department with dexamethasone, 4 mg, IV and was given a prescription for a two-week tapering dose of oral dexamethasone. The family declined antihistamine therapy. After the two week steroid taper, the rash had completely cleared.

**Conclusion:** We report the first case of serum sickness after Anascorp® administration in the United States.

## HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) AND DIFFERENTIAL IN-GEL ELECTROPHORESIS (DIGE) ANALYSIS OF SNAKE VENOMS

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**Abstract:** High performance liquid chromatography (HPLC) and differential in-gel electrophoresis (DIGE) are being developed as analytical techniques to study the variability of venom components in snake venoms. One-dimensional HPLC methods using $C_{18}$ reversed phase columns have been developed to give optimal separations of rattlesnake venoms. Commercial samples of pooled, lyophilized venoms from Mojave, Western and Prairie rattlesnakes have been analyzed and show striking differences. Our goal is to study the variation in venom samples between, for example, commercial and fresh venoms, variation between individual snakes of the same species, between old and young snakes or between wild caught and captive snakes. Differential in-gel electrophoresis (DIGE) is a two-dimensional electrophoretic technique used to separate large numbers of proteins components in biological samples. We are exploring the potential of DIGE to identify individual venom components in envenomated serum samples. Potential applications include: measurement of the time-course of clearance of individual venom components from serum, identification of venom components associated with serum sickness, and the identification of the species of snake responsible for the bite.

## IMPROVING CROFAB™ RECONSTITUTION TIMES

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**Study objective:** To determine whether filling CroFab™ vials to the top (25 cc) and hand rolling decreases the amount of time required to completely reconstitute CroFab™.

**Methods:** The package insert of CroFab™ recommends dilution with 10 mL of sterile water for injection (SWI), followed by gentle rolling. Three sets of five vials each were reconstituted with 10 mL SWI and compared to three sets of 5 vials each that were reconstituted with 25 mL of SWI. Each set of five vials was then either left undisturbed, agitated with the Baxter agitator, or rolled by hand.

All activities were performed at room temperature utilizing a standard timer. The time to complete dissolution of each of the vials was recorded. Groups were compared using a Mann-Whitney U test, with a two-tailed $p < 0.05$ chosen to represent statistical significance.

**Results:** Reconstitution with 10 mL of SWI undisturbed at room temperature dissolved in an average of 33.6 minutes (range 27 to 57 minutes) compared to reconstitution with 25 mL of SWI undisturbed at room temperature dissolving in average of 17.2 minutes (range 5.8 to 26 minutes) [$p < 0.008$]. Reconstitution with 10 mL SWI, gently agitated by Baxter agitator, required an average of 26.4 minutes (range 13.5 to 43 minutes) compared to 11.6 minutes (range 8.2 to 13.2 minutes) for CroFab™ reconstituted with 25 ml SWI that was gently agitated on the Baxter agitator [$p < 0.008$]. Reconstitution with 10 mL SWI, gently hand-rolled dissolved at an average of 4.5 minutes (range 3 to 6.8 minutes) compared to reconstitution with 25ml SWI hand-rolled that dissolved in an average of 1.1 minutes (range 0.92 to 1.3 minutes) [$p < 0.008$]. Less foaming was observed in vials reconstituted with 25 mL SWI regardless of agitation technique.

**Conclusion:** In this study of CroFab™ dissolution, the method with the shortest dissolution time consisted of adding 25 mL SWI and hand-rolling the vial. Addition of 25 mL SWI consistently decreased dissolution time compared with its 10 mL counterpart.

## WORLD ANTIVENOM SHORTAGE

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**Abstract:** There is a major global public health crisis resulting from the shortage of antivenoms for the treatment of envenoming by snakes and scorpions. These neglected diseases affect millions of people annually, especially in the rural tropics. Children and young agricultural workers are particularly affected. Antivenoms remain the only specific antidotes, but these essential drugs are often unavailable or unaffordable in the countries where they are most needed. The crisis in antivenom manufacture, distribution and correct use is most critical and urgent in sub-Saharan Africa. The number of antivenom manufacturers supplying this region has decreased while remaining production is inadequate and threatened commercially and politically. Current antivenom production provides only 1% of what is needed. The price of one vial of antivenom ranges between US$50 and US$150, often representing a high proportion of the annual income of a rural worker. The average dose of antivenom for complete treatment is usually at least 3 vials which, together with other drugs and equipment, makes the total cost of treating one envenomed patient in Africa about US$200. Most antivenoms imported to Africa from India are ineffective for the treatment of envenoming by African snakes because they are raised against inappropriate venoms (e.g. Indian cobra, Russell's viper and Indian saw-scaled viper). This situation, together with the poor development of health facilities and training of doctors, nurses and dispensers responsible for treating snake bites, has deterred many bite victims from seeking medical treatment and has driven them to seek help from traditional healers. This combination of factors has created a self-perpetuating vicious cycle that must be interrupted and corrected as a matter of urgency.

## DEVELOPING A TOXINOLOGY TOOLKIT FOR THE DEVELOPING WORLD

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**Introduction:** The global burden of snakebite is greatest in the world's poorest tropical countries. We have been working in this arena to develop a new approach to snakebite management and associated resource use aimed at improving both local systems and infrastructure and the individual prognoses of envenomed patients.

**Methods:** As part of a major study of snakebite in Papua New Guinea we are combining the use of zoogeographical, ecological, epidemiological, clinical, economic, and GIS studies with public and medical education to both resolve unanswered questions, and to develop local capacity for managing snakebite and improving clinical outcomes. Specific approaches are being developed for (1) epidemiological surveillance and reporting, (2) mapping and GIS analysis, (3) efficient pursuit of clinical investigations, (4) resolution of taxonomic questions, (5) improved resource management and distribution, (6) medical and community education, and (7) improving clinical outcomes.

**Results:** In Papua New Guinea our approach has lead to the establishment of a new plan for addressing the snakebite burden. A new National Snakebite & Antivenom Unit will use epidemiological, GIS and zoogeographic data in combination with mandatory reporting of snakebite cases by health service providers, locally initiated clinical studies, and the phased introduction of EIA-based

venom immunotype identification to better manage expensive antivenom supplies; ensuring needs-based distribution, stock accountability and cost minimization. Coordinated programmes of public education and nationwide training of health workers and medical professionals have also been implemented.

**Discussion:** Although clinical and epidemiological studies add significantly to our overall knowledge, they rarely produce lasting practical benefits for the countries in which they take place. Our approach combines this essential quest for knowledge with the creation of a functional legacy: improved local skills, resources and systems which can sustainably reduce morbidity, mortality and financial costs. We believe that offering this approach to others in the so-called 'under-developed' world may enable them to reap similar rewards.

## *ZOO AND REGIONAL REPTILE MANAGEMENT*

### HANDS-ON OR HANDS-OFF? MANIPULATION OF VENOMOUS REPTILES

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**Abstract:** Many people work with venomous reptiles, both in the field and in captivity. Researchers generally have some understanding of the risks involved in working with these animals but might not have a full appreciation of the consequences of a venomous bite. Most venomous snakes have the ability to inflict temporary injury, permanent disfigurement, or death. Surveys indicate that academic researchers are more likely than zoo personnel to be bitten by venomous animals. Results from these surveys will be summarized. Additionally, information regarding manipulation of venomous animals will be explored, including the equipment, techniques, training, protocols and the appropriateness of hands-on vs. hands-off approaches to work with venomous animals. We will offer up-to-date information allowing session attendees to make more informed choices regarding work with venomous animals, in the hope that it may reduce the likelihood of illegitimate envenomations in these settings.

### TRANSLOCATION OF VENOMOUS REPTILES IN PIMA COUNTY, ARIZONA: ADVICE AND CONSENT OR DISSENT?

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**Abstract:** People of North America have more information about snakes available to them than ever before. Yet, a majority of Americans remain largely ignorant about snake biology and ophidiophobia still ranks as one of the top phobias worldwide. Even many enlightened people are uncomfortable with snakes and lizards, especially venomous ones. Though these people may not advocate killing the animals outright, most people do not wish to share their land with these animals. Every year, in the U.S., Canada and elsewhere, thousands of well-intentioned people request to have snakes removed from their property. In Pima County Arizona, surrounding the city of Tucson, fire department rescue companies are the most common agencies asked to perform this service. For decades, little thought was given to what affect these translocations had on the animals, the populations that they originated from, or those that they were introduced to. Due to the outcry from snake conservationists, reptile translocation has been criticized heavily. In 1998, the authors—in conjunction with a local herpetological society and the Arizona Game and Fish Department—developed a new, more biologically sound protocol for one of the local fire departments. In 2000, Drexel Heights Fire Department adopted this protocol and the authors began a training program for department personnel. In 2003, the Drexel Heights Fire Department became the first fire department in the State of Arizona to be granted legal authority from the Arizona Game and Fish Department to translocate reptiles. Subsequently, other fire departments have adopted this new protocol and several of them have received training from the authors. Here we describe the situation in southern Arizona, how venomous animals have been handled in this area and the authors' experience with development and implementation of snake translocation protocols.

### MEXICAN RATTLESNAKES: PORTRAIT OF A BIOLOGICAL AND CULTURAL ICON

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**Abstract:** Mexico has the largest number of dangerously venomous snakes in the New World. The most charismatic and medically important are the rattlesnakes. Because 28 of the 32 presently recognized species of rattlesnake occur in Mexico, the country is

considered the center of diversification. Rattlesnakes are a mythical and historical symbol of Mexico as evidenced by Mesoamerican archaeology and the Mexican coat of arms. Ironically, Mexican rattlesnakes have faced a long-term conflict with human activities and settlements. Today, they are subject to constant persecution and killing. These increased interactions with humans have led to a high rate of bites attributed to rattlesnakes. The statistics of bite frequency show that most accidents occur in rural areas, although urban accidents due to habitat invasion and captive rattlesnake manipulation are increasing. Despite their historical importance and governmental protection, most rattlesnake species are declining in numbers throughout Mexico because of habitat destruction and the illegal pet trade. There is thus the need of further conservation mechanisms to protect rattlesnakes. Among the recent conservation efforts is the creation of a committee focused on the study and conservation of these snakes in Mexico.