Chapter 17

ACCIDENTS WITH VENOMOUS ANIMALS

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Accidents involving venomous animals such as snakes, scorpions, and spiders represent a significant public health problem, especially frequent in rural areas of tropical countries. These incidents result from the injection of toxic substances by animals, triggering severe reactions in the human body, with generally more severe impacts on children than adults, which is particularly alarming in the pediatric

context. While in Europe reporting these events is not mandatory, in Brazil they have been considered compulsory notifications since 2010, reflecting the seriousness and prevalence of the problem (Konstantyner *et al.*, 2022; Silva, Bernade, and Abreu, 2015; Paolino *et al.*, 2023).

The World Health Organization (WHO) included snakebite envenoming on the list of Neglected Tropical Diseases in 2009. In Brazil, the incidence rates of accidents with venomous animals have increased, except in the Southern region, where incidents are less frequent. Scorpions and snakes are the most common culprits, especially among individuals aged 10 to 19 years. However, approximately 90% of snake bites and spider bites do not have the animal's genus identified, which hinders investigation and appropriate treatment since each species requires specific management approaches due to their toxins (Konstantyner *et al.*, 2022; Silva, Bernade and Abreu, 2015; Amado *et al.*, 2021; Santana *et al.*, 2020).

In severe cases of envenomation by armed spiders, neurological and cardiac complications may occur due to the venom's toxicity to these systems. In scorpion envenomations, variables such as the type of venom, number of stings, and injected quantity can influence the outcome, potentially leading to complications like pulmonary edema or cardiac dysfunction. Regardless of the involved animal, early identification and proper patient management are crucial to increasing survival chances (Konstantyner *et al.*, 2022; Silva, Bernade and Abreu, 2015; Amado *et al.*, 2021; Santana *et al.*, 2020).

Studies indicate that the number of accidents with venomous animals is likely to increase in the future due to climate change, which will result in greater interaction between humans and these animals, altering the ecology and geographic distribution of species and consequently increasing the morbidity and mortality associated with these accidents (Paolino *et al.*, 2023).

The pediatric population is particularly vulnerable to these accidents due to their natural curiosity and lower capacity for self-protection, in addition to physiological differences that can intensify venom toxicity. Current trends indicate a growing demand for prevention policies, training of healthcare professionals for effective diagnosis and treatment, as well as educational campaigns targeted at at-risk communities to reduce the morbidity and mortality related to these accidents. Implementing prevention methods and effective public policies can mitigate this problem (Forrester *et al.*, 2018).

EPIDEMIOLOGY

Accidents involving venomous animals are frequent and continue to grow, representing a significant public health concern, especially in tropical countries like Brazil. From 2007 to 2019, 2,164,654 cases of venomous animal accidents were reported in Brazil (Tomaz, Soares, & Bonfada, 2023), of which 594,447 occurred among children and

adolescents, reflecting a 122.5% increase in the annual number of cases from 2007 to 2019 (Konstantyner *et al*., 2022). Among venomous animals, snakes, scorpions, and spiders are the most prevalent and lethal.

Snakes are responsible for approximately 29,000 cases per year and an average of 125 deaths, with Jararacas accounting for 86.23% of reported cases (Silva, Bernade and Abreu, 2015). In 2013, spider envenomations totaled 27,125 annual cases, with 36 resulting in death, while scorpion stings resulted in 69,036 cases, with 80 deaths (Silva, Bernade and Abreu, 2015).

Accidents with venomous animals vary according to age group, gender, geographic region, and involved species, with greater severity observed in children under 10 years old (Silva; Bernade and Abreu, 2015). In Brazil, 55% of victims in the pediatric range are between 10 and 19 years old, except in the Southern region, where the prevalence is higher in children aged 0 to 9 years. The Northeast region has the highest incidence, with 74.26% of cases in children aged 0 to 9 years and 82.44% in young people aged 10 to 19 years (Konstantyner *et al*., 2022).

There are significant variations in the species of venomous animals according to each region of Brazil. In the North, snakes predominate, responsible for 60% of local accidents, while in the South, there is a prevalence of spider envenomations, affecting 47.94% of children. In the Southeast, Midwest, and Northeast, scorpion stings are more common (Konstantyner *et al*., 2022).

The incidence of accidents with venomous animals in populations composed of adolescents and children establishes an outstanding epidemiological and statistical scenario in the field of pediatric emergency and urgency, considering the vulnerability of this group. This population set exhibits unique epidemiological characteristics, with an exponentially growing trend of these accidents in the age range of 10 to 19 years in all regions of Brazil. Incidents with scorpions, snakes, and spiders stood out as the most prevalent in this clinical population analysis. Therefore, specialized medical attention is crucial in these situations, given the potential severity of the condition (Konstantyner *et al*., 2022).

Prevention initiatives for these accidents have shown potentially positive results, improving therapeutic approaches to these conditions. Early diagnosis associated with immediate treatment, observing the patient's clinical characteristics and knowledge of the epidemiological profile, are directly related to more favorable clinical outcomes. Thus, the importance of socio-educational actions directed at the population and effective public health policies is emphasized, aiming to reduce the potentially fatal outcomes of accidents with venomous animals in children and adolescents (Konstantyner *et al*., 2022).

Historically, accidents with venomous animals, such as snake bites, were treated with traditional remedies and rudimentary medical practices, resulting in high mortality rates. In the 19th and 20th centuries, advances in medicine, such as the development of specific antivenoms, revolutionized the management of these incidents (Forrester, Weiser,

& Forrester, 2018). In the 1980s, there was a significant increase in the documentation and research on snake bites, especially in the United States, where national databases were established to monitor these cases (Greene; Folt; Wyatt and Brandehoff, 2021). Today, the epidemiology of snake bites and other venomous animal accidents is well understood. Most bites occur in rural and suburban areas, with few deaths in the United States due to better access to medical care and the use of antivenoms. Rattlesnakes and copperheads are responsible for most envenomations, while bites from non-native snakes are rare and occur mainly in private collections and zoos (Forrester; Weiser and Forrester, 2018).

Between 2008 and 2015, there were 1,610 animal-related deaths in the U.S., with most caused by non-venomous animals. Deaths caused by hymenoptera (wasps, bees, and ants) remained stable, while mortality from snake bites is very low, with about 9,900 annual envenomations and a mortality rate of only 0.05% (Greene; Folt; Wyatt and Brandehoff, 2021).

Geographic location is one of the main risk factors, with rural and suburban areas near the natural habitat of these animals presenting a higher incidence of bites. Additionally, climatic conditions play a crucial role, with more incidents occurring in warmer months when people are more outdoors (Silva; Bernade and Abreu, 2015). Activities like camping, gardening, and farming increase the risk, as does handling venomous animals in controlled environments (Forrester; Weiser and Forrester, 2018). Limited access to medical care in remote areas exacerbates the consequences of these accidents, while a lack of education on prevention and first aid contributes to the severity of incidents. Alcohol or drug consumption can result in risky behaviors, increasing vulnerability (Greene, Folt, Wyatt and Brandehoff, 2021). Men and people of productive age are at greater risk due to higher occupational and recreational exposure, while children and the elderly are more vulnerable to severe complications (Konstantyner *et al.*, 2022).

DIAGNOSIS

Healthcare professionals often face challenges in accurately identifying snakes, as they are not experts in this field, which can lead to inadequate treatment of the victim. Given the acute nature of snakebite envenoming, it is crucial to quickly identify and administer the appropriate treatment, such as antivenom and ventilatory support. Although immunoassays and molecular tools exist to identify specific snake species, they are limited by high cost, need for specialized technicians, and low specificity, currently restricted to Australia and Papua New Guinea. Rapid diagnostic tests are in development, but their effectiveness in low- and middle-income countries remains uncertain. The syndromic approach is common in managing snakebite envenoming, aiding in species identification, though it also presents limitations (De Castañeda *et al.*, 2019).

A snakebite, whether from a venomous or non-venomous snake, triggers anxiety, fear, and other autonomic manifestations (e.g., nausea, vomiting, tachycardia, diarrhea,

diaphoresis), which can be difficult to distinguish from systemic envenoming symptoms. The severity of envenoming is categorized as minimal, moderate, or severe, based on local findings, systemic signs, coagulation tests, and laboratory results. The evaluation should prioritize the most severe symptoms, signs, or laboratory findings, given the potential rapid progression of envenoming from minimal to severe, requiring continuous reevaluation (Silva *et al*., 2017).

Loxoscelism, triggered by bites from Loxosceles spiders, requires diagnostic precision through the collection and identification of the spider. Only 23.3% of reported cases are confirmed by identification or immunoassay (ELISA), with most being presumed. The local and systemic symptoms of loxoscelism are not specific and can be confused with other conditions. In cases where the spider is not collected, the diagnosis is probable, supported by clinical manifestations. Understanding the disease course is crucial for presumptive diagnoses where the spider is not observed. Geography also influences, with misreports of loxoscelism in areas without documented presence of the spiders (Lopes, Squaiella-Baptistão and Marques and Tambourgi, 2020).

Laboratory tests complement the diagnosis of loxoscelism, such as hematologic, hemostatic, and biochemical tests, excluding other conditions and monitoring the disease. Besides ELISA, Coombs tests, cultures, and imaging exams are used to assess systemic and local complications. Urinalysis is crucial to detect complications like severe intravascular hemolysis. Cutaneous-hemolytic loxoscelism is monitored by the evolution of skin and adjacent tissue lesions, guiding appropriate treatment (Lopes; Squaiella-Baptistão; Marques and Tambourgi, 2020).

Scorpions also represent a serious public health problem related to accidents involving venomous animals. In Brazil, four species of the Tityus genus are responsible for most envenomations: *T. serrulatus, T. stigmurus, T. bahiensis,* and *T. obscurus*. In the Brazilian Amazon, where these species are prevalent, their toxins are extremely potent. The *Tityus* genus comprises 27 species, distributed in four subgenera, six of which are associated with human envenomations: *T. bastosi, T. silvestris, T. apicans, T. matthieseni, T. metuendus*, and *T. obscurus*. Although these species are mainly found in forest environments, they occasionally invade domestic areas, especially *T. metuendus*. There is a predominance of adult males causing envenomations, probably due to more intense activity in search of food and partners, while females tend to remain sheltered during pregnancy or lactation periods (Gomes *et al*., 2020).

Most envenomations occur in men of all age groups, with a particular prevalence among those aged 40 to 49 years, often affecting the feet and hands. Clinical data include venom classification, local and systemic signs and symptoms, antivenom use, the number of vials administered, and complementary laboratory tests. Stings are classified as: 1. Dry, without local or systemic manifestations; 2. Class I: only local manifestations; 3. Class II: non-severe systemic manifestations; 4. Class III: life-threatening manifestations. The

most common local and systemic symptoms include nausea (9.3%), myoclonus (8.6%), occasional vomiting (7.3%), lethargy (6.0%), tachycardia (4.6%), and tachypnea (4.6%). The most frequent local manifestations include pain (84.1%), paresthesia (34.4%), mild edema (25.8%), and hyperemia (21.9%). Severe symptoms include dyspnea, hypotension, profuse vomiting, and seizures, indicating severity. The analysis revealed that clinical manifestations are similar among patients stung by different species of scorpions. Patients envenomed by T. apicans often present piloerection and myoclonus, described by patients as a "sensation of electric shock" throughout the body (Gomes *et al.*, 2020).

TREATMENT

Studies highlight the urgency of prompt and effective management to increase survival and reduce complications in cases of envenomation by venomous animal bites, as evidenced by more than 5.4 million snakebite cases globally, resulting in nearly 138,000 deaths and 400,000 sequelae (Pucca *et al.*, 2020). The diversity of therapeutic approaches reflects the lack of a universally accepted standard, requiring the continuous development of effective, accessible, and low-cost treatments (Fry, 2018). Proper management depends on a multidisciplinary approach and consideration of epidemiology, ranging from supportive therapies like saline solution, antivenom, and systemic steroids to surgical interventions like fasciotomy and dermatotomy in severe cases, as well as dermatological management to prevent cutaneous necrosis complications (Di Nicola *et al.*, 2021). This study will address the importance of precise care, management strategies, and new therapies, exploring their risks and benefits.

Studies highlight the urgency of prompt and effective management to increase survival and reduce complications in cases of envenomation by venomous animal bites, as evidenced by more than 5.4 million snakebite cases globally, resulting in nearly 138,000 deaths and 400,000 sequelae (Pucca *et al.*, 2020). In the prehospital environment, it is crucial to follow WHO (2016) recommendations to remove tight objects around the bite area, reassure the victim to avoid movements that may accelerate venom spread, immobilize the affected area, and apply a moderate compression bandage. Analgesics like acetaminophen are administered according to specific dosage guidelines for local pain relief, while measures to prevent complications like vomiting are also essential. Immediate transport to a healthcare facility capable of administering antivenom and other care is recommended (Fry, 2018).

In the hospital environment, evaluating tetanus immunization and other immunizations is a priority (Fry, 2018; Di Nicola *et al.*, 2021). Specific treatment involves administering antivenom, composed of essential polyclonal antibodies to neutralize the venom and prevent irreversible organ damage (Pucca *et al.*, 2019). The decision to administer antivenom should be quick and careful, especially in the presence of systemic envenomation signs or severe and progressive local symptoms, due to potential adverse side effects. Early

antivenom administration, preferably within 1 to 2 hours after the bite, is crucial to optimize its efficacy. The intravenous route is preferred due to its higher bioavailability, allowing the antivenom to reach up to 85% of the venom inoculation site within 2 hours. Dosage varies, generally administering 1 to 2 vials, although there is controversy over the ideal dosage, administration frequency, and treatment duration. Children require dosing based on the amount of venom injected, with specific guidelines still under debate (Le Geyt *et al*., 2021).

Local symptom management involves careful clinical evaluation of vesicles and blisters to monitor the extent of underlying necrosis. Cleaning and immobilizing the affected area are essential, using solutions like hydrogen peroxide, known for its effectiveness in dissolving venom. Compartmental pressure should be regularly monitored to detect early complications. Patients should be kept under continuous observation in the healthcare unit, with periodic laboratory and clinical investigations, including coagulation tests, complete blood count, urinalysis, liver function, blood glucose, and renal function within the first 24 hours, along with constant physical and vital monitoring. Discharge can be considered for patients who respond well to treatment and show clinical improvement, with recommendations for post-discharge follow-up and periodic reevaluation (Nelson *et al*., 2019; Di Nicola *et al*., 2021).

There are various antivenoms available, each with unique tissue penetration and body clearance characteristics (Fry, 2018). Monovalent antivenom is preferred when the snake species is identified, allowing more targeted treatment, while polyvalent antivenom is more widely used due to its effectiveness against multiple species. For complications like ulcers or cutaneous necrosis, adequate washing followed by debridement when necessary is recommended, with regular dermatological follow-up to avoid additional complications (Mercuri *et al*., 2018, 2020). Broad-spectrum antibiotic prophylaxis is indicated in cases of acute infection or high risk of secondary infections. Options include amoxicillin, cephalosporins, azithromycin, metronidazole, trimethoprim + sulfamethoxazole (Di Nicola *et al*., 2021). Fasciotomy is not recommended without evidence of critical compartmental pressure increase (Fry, 2018; Hamza *et al*., 2021).

New approaches are being explored to improve the distribution and implementation of therapies for snakebites. Animal studies have shown potential reversal of symptoms like coagulopathy and neurotoxicity with therapeutic agents like marimastat and varespladib, though their effectiveness in humans still needs confirmation. Current antivenom distribution strategies include the “hub-and-spoke” model, where rural facilities are connected to central hospitals in urban areas, ensuring rapid access to antivenoms and specialized support (Hamza *et al*., 2021).

Innovative approaches are being explored to improve the safety and efficacy of antivenoms. The continuous reassessment method (CRM) of 3 + 3 dose escalation has been successfully used to introduce antivenoms, although it has received criticism and suggestions for modifications. Recently, an adaptive design based on the Bayesian model

was developed, more efficient and flexible, using sequential patient data to continuously optimize the ideal, safe, and effective antivenom dose, as demonstrated in the treatment of Russell's viper envenoming. These advances are expected to lead to the development of more effective antivenoms against a wide variety of snake species, such as the idealized pan-African polyvalent antivenom. Improvements in production, implementation of Good Manufacturing Practices (GMP), and the introduction of WHO's antivenom prequalification program are fundamental strategies to increase the safety, efficacy, and accessibility of these products globally (Hamza *et al*., 2021).

With advances in recombinant DNA technology, there is a significant opportunity to develop new antidotes based on recombinant antibodies and antibody fragments (Laustsen *et al*., 2020). Human antibodies and their fragments, expressed by recombination, have shown efficacy in neutralizing snake venom toxins. Compared to animal-derived antibodies, human antibodies are less immunogenic for human receptors. Mixtures of monoclonal antibodies, targeted to neutralizing epitopes of clinically relevant toxins, have the potential to be optimized in terms of efficacy, batch-to-batch production consistency, and possibly reduced manufacturing cost (Hamza *et al*., 2021).

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