

## Scorpion Envenomation to Therapeutics

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The March 1969 issue of *Indian Pediatrics* included interesting research papers on scorpion envenomation, mass measles vaccination, intellectual disability (then mental retardation), poisoning, septic meningitis, and tubercular meningitis. We selected the study of physiological effects of scorpion envenomation for the present review as it is a common medical emergency in coastal and rural areas of India with case fatality being higher in children than adults. The study presents landmark research in establishing cardiac and behavioral changes after scorpion envenomation, which now form the basis of its treatment strategy.

### THE PAST

The study [1] was an animal experiment conducted in Andhra Pradesh, which was home to two types of poisonous scorpions (small, red *Buthus amarus* and large, black *Palamneus-gravimonus*). The scorpion venom was initially thought to be only neurotoxic as it was associated with severe local pain followed by brainstem involvement and death. The authors aimed to establish the cardiovascular effects of the poison as signs of myocarditis were observed in children who succumbed to scorpion sting. The authors experimentally extracted the poison from scorpions and injected it intravenously in fifteen anesthetized dogs and three rabbits, and intraperitoneally in three rats in varying concentrations. Two dogs succumbed after high-dose poison (>200 µg) administration with fatal ECG changes within two and half hours. The surviving dogs showed initial rise in blood pressure (by 50-60 mmHg by 5th minute) followed by a gradual decline that was associated with respiratory depression. Sinus tachycardia was seen in clinically asymptomatic dogs after 48-72 hours who had received less dose (35-100 µg) of poison. Higher dose of poison was associated with sinus tachycardia followed by sinus bradycardia, and later with ventricular

extrasystoles and changes of toxic myocarditis. The rabbits and rats developed marked prostration, dilatation of pupils, salivation and urination. A dose-dependent response was established.



*Historical background and past knowledge:* Scorpions are known to be one of the deadliest and poisonous species on Earth, mentioned even in ancient Indian vedas – Rig Veda and Atharva Veda. Scorpions have also been mentioned in the history of Middle-East, Indus valley civilization and Egyptian civilization. The deadly, fetish and vengeful attributes of the arthropod were notable in early ancient Egypt where rulers were known as ‘Scorpion King’ – later also filmed as movie series. Idols of scorpion goddesses are worshipped in eastern and southern parts of India.

Scorpions thrive well in dry climates globally and are classified as old and new world scorpion belonging to Eastern and Western hemisphere, respectively. There are about 86 species of scorpion in India out of which the *Buthidae* family is the most lethal. One of the earliest case report of scorpion bite from India dates back to 1926, manifesting as generalized pain, shock and pulmonary edema [2]. This case received local wound care and a concoction of whisky, intradermal caffeine and atropine along with supportive general measures. Numerous medicinal plants have been used since ancient times for their anti-inflammatory, anti-pruritic and analgesic properties in Eastern Asia. There are few reports of immunotherapy being practiced in ancient times. An ancient researcher from Iran practiced self-injection of small quantities of scorpion poison to induce tolerance. Scorpions were placed in sesame oil, which was topically applied to sting site as an antidote.

### THE PRESENT

Toxicology has evolved from mere recognition and management of scorpion bites to better understanding of

venom composition and its chemical use. The scorpion venom has been extensively studied for its varied chemical properties. The composition of scorpion toxin is water, salts, lipids, proteins, nucleotides, biogenic amines, enzymes and peptides. The toxin acts on voltage gated ion (sodium, potassium and calcium) channels to function as neurotoxin, cardiotoxin, nephrotoxin, hemolytic toxin and as enzymes [3]. The sodium channel toxins (alpha toxins) cause prolonged depolarization with neuronal excitation and are the most deleterious to mammals. The inactivation of sodium channels results release of catecholamine with an autonomic storm seen as sweating, salivation, cardiovascular instability, arrhythmias and increased respiratory secretions [4]. Death usually occurs from pulmonary edema, myocardial injury or lethal arrhythmias as was shown in the reviewed study [1]. The potassium channel toxins play role in T-cell mediated autoimmune diseases. Approximately 1,50,000 polypeptides in venoms from different scorpion species have been discovered. Scorpion venom has now been exploited for medicinal use as antibacterial, antifungal, anticancer agent, and against multi-drug resistant microorganisms or superbugs [3]. The immunological role of similar peptides contained in venom extracts is evolving with continued research.

The lethality of venom is dependent upon scorpion species, dose (as was also concluded in present study) and host response to sting. The main treatment approach in scorpion sting includes pain relief and first aid, cardiovascular support and antivenom administration. Pain due to local neurotoxicity is usually severe and its relief has been central to the management of scorpion sting. Various agents like topical lidocaine, paracetamol infusion and ice compresses have been used. The use of systemic steroids, antihistaminics or calcium-channel blockers has not shown any clinical benefit [4]. Cardiotoxicity is a hallmark of scorpion sting as was also reported by the reviewed paper for the first time from India [1]. Prazosin, a selective  $\alpha$ -1 adrenergic blocker is the pharmacological antidote, and is recommended for alleviating cardiovascular and autonomic symptoms of scorpion sting. Use of prazosin is associated with decreased incidence of massive pulmonary edema which has improved survival in affected children [5]. Scorpion

antivenom has been found efficacious for new world scorpion envenomation but not for old world scorpions that inhabit India. A recent meta-analysis reported similar rate of clinical recovery between antivenom and placebo groups [6]. Data on 53 patients from India reported prazosin to be superior than antivenom in clinical recovery and survival [7]. A combination therapy of antivenom with prazosin hastened recovery than use of prazosin alone [8]. Abnormal echocardiography at admission may predict the need for a second dose of antivenom in Indian children after scorpion bites [9]. Recent developments in immunotherapy are underway with use of avian antisera and less toxic adjuvants [10].

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