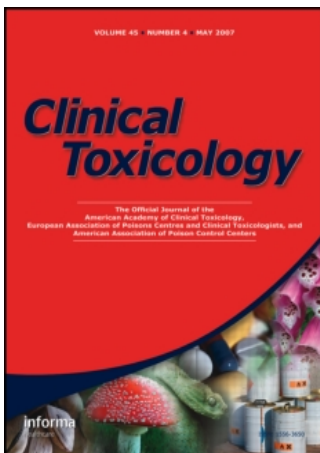


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Publisher: Informa Healthcare
Informa Ltd Registered in England and Wales Registered Number: 1072954
Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Clinical Toxicology

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597279>

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Steven C. Curry ^a, Michael V. Vance ^a, Patricia J. Ryan ^a, Donald B. Kunkel ^a, William T. Northey ^b

^a Central Arizona Regional Poison Management Center St Luke's Medical Center, Phoenix, Arizona

^b Department of Botany and Microbiology, Arizona State University, Tempe, Arizona

Online Publication Date: 01 May 1983

To cite this Article: Curry, Steven C., Vance, Michael V., Ryan, Patricia J., Kunkel, Donald B. and Northey, William T. (1983) 'Envenomation by the Scorpion *Centruroides Sculpturatus*', *Clinical Toxicology*, 21:4, 417 - 449

To link to this article: DOI: 10.3109/15563658308990433

URL: <http://dx.doi.org/10.3109/15563658308990433>

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ENVENOMATION BY THE SCORPION CENTRUROIDES SCULPTURATUS

Steven C. Curry, M.D.*

Michael V. Vance, M.D.*

Patricia J. Ryan, M.D.*

Donald B. Kunkel, M.D.*

William T. Northey, Ph. D.**

*Central Arizona Regional Poison Management Center
St. Luke's Medical Center
1800 East Van Buren Street
Phoenix, Arizona 85006

**Department of Botany and Microbiology
Arizona State University
Tempe, Arizona 85287

ABSTRACT

Envenomation by the scorpion *C. sculpturatus* can be life threatening. The action of the venom is to produce prolonged and excessive firing of neuronal axons which results in a wide variety of signs and symptoms. Records of 670 patients suffering from scorpion stings in central Arizona in 1982 were reviewed to characterize the clinical course of these patients. While adults appear to be stung more often than children, children are more likely

to develop a severe illness requiring intensive supportive care. The intravenous administration of specific C. sculpturatus antivenom results in resolution of serious signs and symptoms within minutes, with patients completely asymptomatic within 1 1/2 hours. The administration of antivenom is recommended as the treatment of choice for severe envenomations after the initiation of appropriate supportive care.

INTRODUCTION

Scorpions were among the first animals known to appear on land and even today pose a serious threat to life in many areas of the world. Fossils of creatures which appear similar to present day species have been found in rocks over 400 million years old (1).

Of the approximately 650 known living species, all of the dangerous scorpions are members of the family Buthidae (1). These arthropods are well adapted to life in desert or semiarid conditions, and indeed most of the species live in such an environment.

In the continental United States, the only scorpion whose sting is truly dangerous to humans is Centruroides sculpturatus. It will be the purpose of this article to discuss the clinical toxicology of this species.

C. SCULPTURATUS: DESCRIPTION AND HABITAT

The body of a scorpion consists of 3 main parts: the cephalothorax, abdomen, and the tail or postabdomen. From the cephalothorax arise 2 pairs of pedipalps to which are attached a pair of chelae or pincers. Continuous with the opposite end of the abdomen is the six-segmented tail. The last segment of the tail is termed a telson and contains the venom apparatus. In C. sculpturatus the venom apparatus consists of a pair of venom glands and a

sting. The glands are composed of 2 types of tall columnar cells. One type of cell is responsible for production of toxins while the other type of cell is engaged in mucous production. Both secretions make up the venom of C. sculpturatus (2).

C. sculpturatus (also known as C. exilicauda or the "bark scorpion") ranges in size from 13 to 75 millimeters, depending on the degree of maturity (2). Major morphologic characteristics that help to distinguish it from other scorpion species include the following: 1) the pincers are slender and about 6 times as long as the broadest part; 2) A small tubercle is located at the base of the sting (this may require a magnifying glass to see); 3) The proximal tail segment is rectangular rather than square shaped (See Figure I).

All scorpions spend light hours under cover and are active at night in warm temperatures. They lie quietly in their territory waiting to ambush unsuspecting prey such as insects or small lizards. The prey is captured with their pincers and then killed or paralyzed with stings from the tail which is thrust over their backs.

C. sculpturatus is rather unique in that it is a climbing species and never burrows (2). As the common name "bark scorpion" implies, this species prefers to be in or near trees, especially sycamore, mesquite, or cottonwood. They can also be found near palm trees.

Scorpions are not aggressive toward man and only sting when handled or threatened. In defending themselves they grasp their victims' flesh with their pincers and repeatedly sting the victim by thrusting their tail over their bodies.

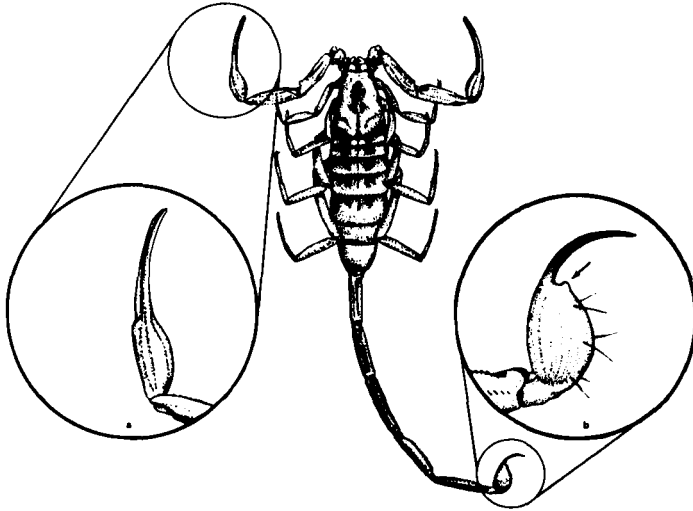


Figure 1. Bark scorpion, *Centruroides sculpturatus*; a) enlarged chela; b) enlarged vesicle showing tubercle below sting. Body length, including telson, 55 mm. Reprinted by permission from Ref. (2).

C. sculpturatus is mainly found in Arizona where it has a state-wide distribution (3). Parts of Texas, New Mexico, northern Mexico, and small areas of California (4) also harbor colonies of the organism. Through our being consulted regarding a child who was critically ill from a scorpion sting, we recently became aware of C. sculpturatus inhabiting the area around the northern shore of Lake Mead in Nevada.

It is important to realize that stings from C. sculpturatus are not always limited to the above mentioned areas. Travelers and vacationers may unknowingly transport scorpions in personal belongings to other parts of the country where envenomation may then take place (5).

C. SCULPTURATUS VENOM

Chemical Characteristics

Many scorpion toxins can cause widespread effects including bleeding disorders (6), myocardial injury (7,8,-10), pulmonary edema (8,9), cardiovascular collapse, neurotoxicity (11), and pancreatitis (12). The effect of C. sculpturatus venom, however, appears to be mainly, if not entirely, neurotoxic. As the focus of this article is on the clinical aspects of C. sculpturatus envenomation, only a brief review of the composition and action of its venom will be presented.

C. sculpturatus venom is a complex chemical mixture composed of a large number of basic proteins of low molecular weight along with other small molecules. The venom is resistant to the action of proteolytic enzymes and is dependent upon intact disulfide bridges (13, 28). There are no enzymes which cause tissue destruction, and this is why there is usually no inflammatory response at the site of the sting.

At least 8 protein toxins of similar chemical characteristics have been isolated from C. sculpturatus venom (14). Those which have been analyzed are single chained proteins containing no more than 60 to 70 amino acids. There are several disulfide bridges in each chain which maintain the toxin in a compact and stable structure (15).

Normal Axonal Condition

Before discussing the biological action of the neurotoxins, a very simplified and brief review of axonal conduction will be presented.

Each nerve cell possesses an active sodium pump which moves Na^+ from inside the cell to the outside,

raising the relative concentration of positive charges on the outside of the cell membrane. The membrane also contains channels through which sodium ions may move into the cell, depending on whether the sodium channels are activated (permeable to sodium) or inactivated (impermeable to sodium). If sodium channels were not inactive while the neuron was at rest, Na^+ would quickly move into the cell because of the attraction of the relatively negative intracellular space, and because of the tendency to diffuse down a concentration gradient. However, because of the active sodium pump and because of the inactivated sodium channels, the neuron is able to maintain a resting membrane potential of about -90mv, the inside being relatively negative to the outside.

If a neuron is excited (e.g. by a neurotransmitter or pressure) sodium channels will become slightly activated, and a small inward current of Na^+ will develop, resulting in the membrane potential moving toward zero (becoming less negative as positive charges move intracellularly). This slight depolarization of the cell membrane causes further activation of sodium channels with a greater inward movement of Na^+ . This positive feedback cycle continues until there is a massive influx of Na^+ resulting in the production of a positive action potential. During the depolarization which produces the action potential, sodium channels are quickly inactivated. The resting membrane potential then returns to about -90mv as positively charged potassium ions move out of the cell to the extracellular space.

Action of Neurotoxins

The protein neurotoxins in C. sculpturatus venom

bind to sodium channels to cause incomplete sodium channel inactivation (14,16). These toxins can be divided into at least 2 main groups with regard to their effects on axonal membranes (14).

One group causes incomplete sodium channel inactivation during depolarization, resulting mainly in a widening of the action potential. These toxins have been termed "stabilizers" because of their ability to maintain the sodium channel in an ion conducting state (16).

The second group of toxins act to induce a slowly developing inward sodium current after membrane repolarization (following a depolarization). Their action results in the movement of the positive feedback system involving sodium channel activation and cell membrane depolarization to more negative membrane potentials (14). That is, there is more sodium channel activation at a given negative membrane potential than would be present in the absence of the toxin. This is also accompanied by a decrease in the height of the action potential, although it is usually still quite adequate for propagation down an axon.

The ability of the toxins to widen action potential and to enhance membrane depolarization by producing an inward Na^+ current at more negative membrane potentials causes or enhances repetitive firing of axons.

One might expect that the toxins from C. sculpturatus venom might also affect dendrites and muscle since all excitable membranes possess sodium channels and undergo depolarization with the propagation of an action potential. Indeed it has already been shown that one toxin of C. sculpturatus venom can stimulate chick muscle in vitro in the presence of neuromuscular blockade, indicating a

direct effect on muscle (17). However, most in vitro studies which best characterize the actions of the toxins have been done on axonal preparations, although future research may show important effects on excitable membranes other than axons.

The prolonged and excessive firing of axons induced by C. sculpturatus venom would be expected to produce excessive activity of the respectively innervated effector organ. For example, spontaneous and uncoordinated muscular activity would result from excessive presynaptic activity at the neuromuscular junction. Increased salivation would be expected because of stimulation of salivary glands by parasympathetic nerves. Catecholamine release from adrenergic nerve endings and from the adrenal medulla plays an important role in the pathogenesis of toxic effects seen with other scorpion species (7-10,18-22), but has an unclear role in C. sculpturatus envenomation. This will be discussed further under "Clinical Findings".

Other Components of Venom

In addition to the neurotoxins, other molecules have been isolated from C. sculpturatus venom. A fraction of venom which lacks neurotoxicity has been shown to stimulate aggregation of dog platelets in vitro (24). Bleeding disorders have not been reported in those stung by C. sculpturatus, making the significance of this observation unclear. An inhibitor of angiotensin-converting enzyme has been isolated; however, the role this inhibitor plays remains uncertain (23).

CLINICAL FINDINGS

Brief Review of Findings

In our experience, the great majority of scorpion

stings are to extremities. After the sting there is the immediate onset of a painful tingling or burning sensation. There is no visual evidence of envenomation and this lack of any inflammation at the site of the sting strongly leads one to suspect envenomation by C. sculpturatus in our area. The site is usually very hyperesthetic, and tapping over the site of the sting produces severe pain (positive "tap test"). Over minutes to several hours the paresthesias and hyperesthesia may travel up the extremity and even become generalized. Complaints of a "thick tongue" and "trouble swallowing" in the absence of objective motor abnormalities are not unusual findings. Frequent rubbing of the nose, and sometimes the eyes and ears, can be seen in both children and adults, while infants may present with unexplained crying.

In more severe cases variable cranial nerve and somatic motor abnormalities develop. Cranial nerve dysfunction is characterized by roving and/or rotatory eye movements, blurred vision, fasciculations of the tongue, and loss of control of pharyngeal muscles with resultant stridor and occasional respiratory arrest. Excessive drooling is sometimes seen in children and is probably a combination of excessive salivary secretion along with difficulty in swallowing. Excessive somatic neuromuscular activity presents initially as uncontrollable jerking of the extremities, or as what appears to be restlessness, with the victim unable to lie still. This then may progress to chaotic thrashing about. Severe cases of excessive neuromuscular hyperactivity may be mistaken for centrally mediated seizure activity. However, in the absence of hypoxemia or exhaustion, the victim often appears to remain awake and alert the entire time.

Vomiting can be seen in children. Frothy sputum (increased salivation?) and wheezing have been noted and have confused the clinical picture in some patients (25).

As mentioned earlier, the role of catecholamine release has not been well defined in C. sculpturatus envenomation. A "sympathetic storm" may contribute to the restlessness that patients exhibit; however, the severe thrashing about that may develop is much more than would be expected from increased adrenergic activity alone. The hypertension, tachycardia, and hyperthermia that can be seen may also be due in part to adrenergic hyperactivity. No doubt the neuromuscular hyperactivity and the increased metabolic demand required of such also contributes to the pathogenesis of these findings.

In recent years no known deaths have been reported from C. sculpturatus stings. However, at one time C. sculpturatus was reported as being the primary killer among Arizona's venomous animals. Between 1931 and 1940 there were over 40 deaths attributed to envenomation by this scorpion, mainly involving children and infants (3). Since deaths can be prevented today with good supportive care, it can be assumed that the loss of upper airway and respiratory muscle control contributed greatly to patient demise. No doubt, the metabolic acidosis and hyperthermia from excessive muscular activity, along with occasional cases of aspiration also were, in part, responsible for patient morbidity and mortality.

Grade of Envenomation

At our center we grade C. sculpturatus envenomations I through IV, depending on their severity (Table I). Grade I envenomations have only local pain and/or paresthe-

TABLE I
GRADES OF ENVENOMATION

GRADE	DESCRIPTION
I	LOCAL PAIN AND/OR PARESTHESIAS AT SITE OF ENVENOMATION
II	PAIN AND/OR PARESTHESIAS REMOTE FROM THE SITE OF THE STING IN ADDITION TO LOCAL FINDINGS
III	<i>EITHER CRANIAL NERVE OR SOMATIC SKELETAL NEUROMUSCULAR DYSFUNCTION</i> 1) cranial nerve dysfunction: blurred vision, wandering eye movements, hypersalivation, trouble swallowing, tongue fasciculation, problems with upper airway, slurred speech 2) somatic skeletal neuromuscular dysfunction: jerking of extremity(s), restlessness, severe involuntary shaking and jerking which may be mistaken for a seizure disorder
IV	<i>BOTH CRANIAL NERVE AND SOMATIC SKELETAL NEUROMUSCULAR DYSFUNCTION</i>

sias. The "tap test" is almost always positive. Grade II envenomations, in addition to local findings, have pain and/or paresthesias remote from the site of the sting (e.g. paresthesias moving up an extremity, perioral "numbness"). Those patients with Grade III envenomations have one of the following: 1) cranial nerve dysfunction; 2) somatic neuromuscular dysfunction resulting in skeletal muscle hyperactivity. In this grading system, somatic skeletal neuromuscular dysfunction or "neuromuscular hyperactivity" is defined as involuntary increased activity in skeletal muscles other than those innervated by cranial nerves. Most Grade III patients have cranial nerve dysfunction, as it is unusual to see a patient with skeletal neuromuscular hyperactivity who does not also exhibit signs of cranial nerve dysfunction. Grade IV envenomations produce findings of both components of Grade III.

A REVIEW AND DISCUSSION OF 673 SCORPION STINGS IN CENTRAL ARIZONA

Between January 1 and December 30, 1982, the Central

Arizona Regional Poison Management Center received 707 phone calls concerning scorpion stings. Over 600 of these patients were managed at home. The rest were referred to a hospital, or had previously sought medical care. Nursing personnel at the poison center made followup calls for 24 hours to check on patients' symptoms until patients were no longer symptomatic, no longer desired followup calls, or until they could no longer be contacted. All information was recorded on poison information forms.

All poison information forms, and any other medical records made available to the authors, were reviewed in order to determine patient age, grade of envenomation, and location of the sting(s). In addition, the time of onset of symptoms, treatment, and duration of symptoms were noted when possible. Thirty-four patients were excluded because patient age and/or grade of envenomation could not be determined, the scorpion was identified as not being C. sculpturatus, or clinical symptoms and signs (swelling and erythema at the site of the sting in Grade I envenomations) were not characteristic of C. sculpturatus envenomations.

Age Distribution

Table II shows the age distribution of all 673 patients included in the study. Examination shows that the majority of victims were greater than 20 years of age. Still, a significant number (about 15%) were children under 11 years. It is unlikely that this age distribution accurately reflects the population of people stung by scorpions in central Arizona. Parents may be more likely to call the poison center because of concern over their children, while adult victims may not call unless they

TABLE II
AGE DISTRIBUTION OF
673 PATIENTS STUNG BY SCORPIONS

AGE (YRS)				
0-5 # (%)	6-10 # (%)	11-20 # (%)	21+ # (%)	TOTAL
58 (8.6)	42 (6.2)	117 (17.4)	456 (67.8)	673 (100)

TABLE III
GRADE OF ENVENOMATION OF
673 PATIENTS STUNG BY SCORPIONS

GRADE					
NO SYMPTOMS # (%)	I # (%)	II # (%)	III # (%)	IV # (%)	TOTAL # (%)
45 (6.7)	515 (76.5)	61 (9.1)	32 (4.7)	20 (3.0)	673 (100)

are very symptomatic. Thus, the true proportion of envenomations to children under 11 years of age may be less than 15%.

Grading of Symptoms

The grade of symptoms was also able to be determined from all 673 charts that were reviewed. Table III demonstrates that a total of 83.2% of patients had no symptoms, or had symptoms typical of Grade I. The percentage of patients with Grades II, III, and IV progressively decreased, with values of 9.1%, 4.7%, and 3.0% respectively, making serious envenomations much less common. It must be noted that while only C. sculpturatus is capable of producing symptoms of Grades II, III, or IV, there are several scorpion species in Arizona that can produce symptoms of Grade I envenomations. In fact, in the majority of cases of Grade I envenomations, the scorpion was not identified by an expert. However, C. sculpturatus is

more likely to be inhabiting a populated area in Central Arizona than other scorpion species.

Some patients who had no symptoms had a questionable history of being stung. For example, a scorpion may have been found on or near a child, but the child appeared completely asymptomatic and was too young to give a history. Therefore, the number of patients who are asymptomatic after a sting may be over-represented. No doubt, some asymptomatic patients also may have been stung by a scorpion species other than C. sculpturatus.

Table IV compares age with grade of envenomation. In children under the age of 5 it was often difficult to determine whether a child should be classified Grade I or II since the criteria for these grades are entirely subjective. Therefore, Grades I and II were combined in this age group.

In the 6-10, 11-20, and 21 and older age groups, Grade I envenomations were by far the most common, accounting for 69%, 84.6% and 79.2% respectively. In the 0-5 age group, Grades I and II combined made up 50% of the patients as compared to 73.8% in the 6-10 group, 94% in the 11-20 group, and 89.1% in the 21 and older group. 17.3% of children in the 0-5 group and 14.3% of those in the 6-10 group developed Grade IV signs and symptoms. This is in sharp contrast to the 11-20 age group where there were no Grade IV patients. Thus, of all patients greater than 10 years of age, only 4 patients (0.7%) suffered from Grade IV envenomations as compared to 16% of all those 10 years old and younger.

The difference between those under 11 and those 11 and older may be even greater than these figures indicate.

TABLE IV
GRADE OF ENVENOMATION vs AGE
IN 673 PATIENTS STUNG BY SCORPIONS

GRADE	AGE (YRS)			
	0-5 # (%)	6-10 # (%)	11-20 # (%)	21+ # (%)
NO SYMPTOMS	14 (24.1)	4 (9.5)	5 (4.3)	22 (4.8)
I	29 (50)	29 (69)	99 (84.6)	361 (79.2)
II		2 (4.8)	11 (9.4)	45 (9.9)
III	5 (8.6)	1 (2.4)	2 (1.7)	24 (5.2)
IV	10 (17.3)	6 (14.3)	0 (0)	4 (0.9)
TOTAL	58 (100)	42 (100)	117 (100)	456 (100)

The percentage of Grade IV patients in the youngest age group might be under-represented as compared to the general population because of the possibility that many asymptomatic patients were never stung (discussed earlier). If all of these patients could be eliminated, the Grade IV patients would make up a larger fraction of the total age group. Using similar reasoning, the percentage of adults who develop Grade IV symptoms may be even lower due to the fact that adults may not frequently call the poison center if suffering from only minor symptoms.

The finding that children are usually more severely affected than adults agrees with observations by previous authors. Stahnke noted that symptoms are invariably more pronounced in children (3). Rimsza *et. al.* reviewed hospital charts for 24 patients seen in four large hospitals in 1978 who suffered from scorpion stings (25). Forty percent were less than four years old, and 80% were less than 10. Since more symptomatic patients would be expected

to seek medical care, it is noteworthy that most of their patients were children. Rimsza also noted that of 10 patients older than 10 years of age, none developed restlessness, while 85% (12/14) below the age of ten did (25). In attempting to grade those patients, it can be said that if all ten patients older than ten years of age had cranial nerve findings, the highest grade they could have been was Grade III, again indicating that Grade IV envenomations in patients greater than ten years old are uncommon. The finding of Rimsza and colleagues that 85% of the patients less than ten years old were restless, and thus probably Grade IV (in our experience it is unusual to see skeletal neuromuscular hyperactivity without cranial nerve findings) is higher than our data indicates. Their study group was not representative of all people stung by scorpions, however, in that their study group was composed of patients who had already decided to seek medical care, and were, therefore, more likely to be seriously ill.

Location of Sting

Of the 673 charts that were reviewed, the site of the sting(s) was recorded in 555 patients. Table V breaks these patients down to the site of the sting and grade of the envenomation. Records in 9 of the 20 Grade IV patients did not indicate the site of the sting, and in infants, this was often not even known at the time of initial presentation. A review of Table V shows that the great majority of stings were divided fairly equally among upper and lower extremities. When examining Grades I, II, and III, no particular site seemed to predispose one to a particular grade of envenomation. The lack of information

TABLE V
LOCATION AND GRADE OF ENVENOMATION
IN 555 PATIENTS STUNG BY SCORPIONS

LOCATION*	GRADE OF ENVENOMATION			
	1 # (%)	2 # (%)	3 # (%)	4 # (%)
U	205 (44.5)	26 (43.3)	12 (52.2)	1 (9.1)
L	217 (47.1)	29 (48.3)	10 (43.5)	10 (90.9)
T	31 (6.7)	4 (6.7)	1 (4.3)	0 (0)
H	7 (1.5)	1 (1.7)	0 (0)	0 (0)
F	1 (0.2)	0 (0)	0 (0)	0 (0)
TOTAL	461 (100)	60 (100)	23 (100)	11 (100)

*L = Lower Extremity
U = Upper Extremity
T = Trunk
H = Head
F = Face

regarding sites of envenomation in almost 1/2 of the Grade IV patients makes it difficult to evaluate this small group. Of the 11 Grade IV patients where the site of envenomation was known, 10 were stung on the lower extremity.

Onset of Symptoms

In all cases the onset of local pain and/or paresthesias (Grade I) was immediate. The rapidity of progression to higher grades of envenomation was not predictable, but always occurred in less than five hours. Newborns and infants sometimes presented with Grade IV signs and symptoms within 15-30 minutes of being stung.

Treatment and Duration of Symptoms: Grade I and II Patients

Symptomatic relief of Grade I and II envenomations was provided by analgesics and by the local application

of ice to the site of the sting. The application of a cold compress was not done to prevent absorption of the venom so much as to provide relief of local pain. Out of 576 Grade I and II patients, only 48 were seen at a medical facility for reasons other than to receive a tetanus toxoid injection. Many of these patients were not in severe pain but simply required reassurance. Also, our poison center staff routinely referred infants to hospitals for observation because of their increased risk of developing a severe illness, and many infants only developed minor symptoms. Finally, an unknown number of these patients may have been stung by a species of scorpion other than C. sculpturatus (discussed earlier).

The local application of ice and use of analgesics appears to have helped most patients in that only one of the 576 Grade I and II patients required admission to a hospital for control of severe pain.

Of the 576 Grade I and II envenomations reviewed, 433 records (75%) contained adequate information to determine the duration of symptoms. This data is presented in both Table VI and Figure II. All patients were well or had only minimal symptoms 24 hours after envenomation, and followup calls were not made after this time.

Examination of Table VI and Figure II reveals that, generally, younger Grade I and II patients became asymptomatic sooner than adults and older children. A total of 37/50 (74%) children aged 0-10 had resolution of symptoms by four hours while only 93/382 (24.3%) of those older than 10 were well within four hours. In fact, 69.2% of the 0-5 group and 58.4% of the 6-10 group were well within two hours as compared to 17.5% and 18.5% in the 11-20 and 21+ age groups respectively.

TABLE VI
DURATION OF SYMPTOMS IN 432 PATIENTS
WITH GRADE I AND II SCORPION ENVENOMATIONS

DURATION OF SYMPTOMS (HRS)	AGE OF GRADE I AND II PATIENTS (YRS)			
	0-5 # (%)	6-10 # (%)	11-20 # (%)	21+ # (%)
0-2	18 (69.2)	14 (58.4)	14 (17.5)	56 (18.5)
3-4	3 (11.6)	2 (8.3)	5 (6.3)	18 (6.0)
5-8	3 (11.6)	2 (8.3)	9 (11.2)	36 (11.9)
9-16	1 (3.8)	2 (8.3)	13 (16.3)	49 (16.2)
17-24	1 (3.8)	3 (12.5)	18 (22.5)	71 (23.5)
24	0 (0)	1 (4.2)	21 (26.2)	72 (23.9)
TOTAL	26 (100)	24 (100)	80 (100)	302 (100)

Only 1/26 patients in the 0-5 group had symptoms lasting between 17 and 24 hours, and no patient had symptoms for over 24 hours. In contrast, 89/382 (23.3%) of those older than ten required between 17 and 24 hours to become asymptomatic, and 93/382 (24.3%) had symptoms for over 24 hours. The 6-10 age group was intermediate with 3/24 (12.5%) requiring 17-24 hours to become well, and 1/24 (4.2%) remaining symptomatic for over 24 hours.

How long symptoms persisted after 24 hours could not be determined in this study. However, in the personal experience of the authors and of Stahnke (3), mild paresthesias, numbness, and pain may persist from several days to two weeks. Our data indicate that these patients are usually older ten years of age.

Treatment and Duration of Symptoms: Grades III and IV Patients

Patients with Grade III envenomations may vary widely

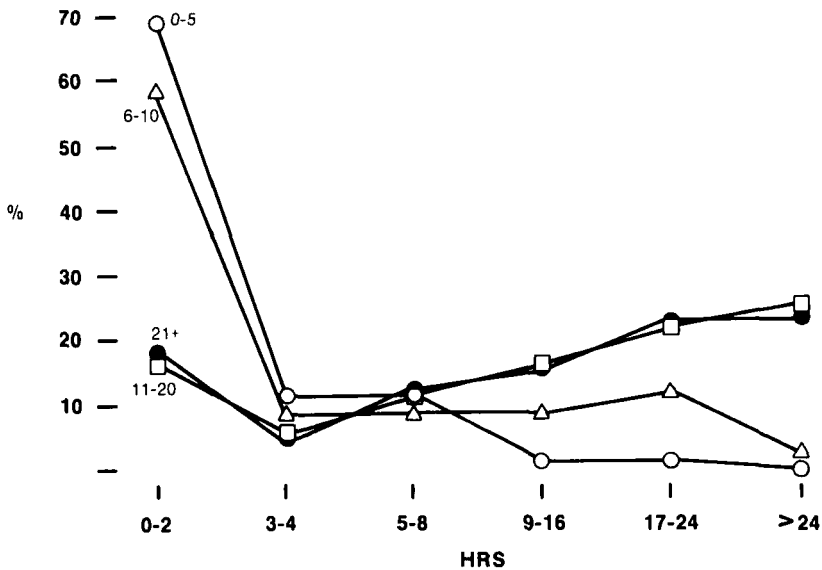


FIGURE II DURATION OF SYMPTOMS IN 432 PATIENTS WITH GRADE I AND II SCORPION ENVENOMATIONS

in the severity of their illness. A Grade III patient may only suffer from minor tongue fasciculations and generalized paresthesias, and recover at home with symptomatic care. Another Grade III patient may have severe cranial nerve dysfunction with hypersalivation and poor control of the upper airway. However, in our experience, it would be unusual for the latter patient not to have some increased neuromuscular activity, thus fulfilling the criteria of Grade IV.

Grade IV patients are almost always very ill. The uncommon patient who suffers from mildly abnormal eye movements and isolated minor jerking of an envenomated extremity may also do well with symptomatic care. However, the critically ill patient who is thrashing around on the

bed, hypersalivating, and stridorous is in immediate danger of losing his or her life.

Corticosteroids, antihistamines, and calcium have all been administered in attempts to reverse severe symptoms and alter the natural course of the envenomations. When looking at the mechanism of action of the scorpion neurotoxins, there is no rational basis for their use, and they have never been found to be effective.

For many years large doses of barbiturates have been recommended and used to control the severe neuromuscular activity seen in patients suffering from severe envenomations (3,26). However, repeated doses may be required, and the patient may need hours to recover from the central nervous system depression induced by the barbiturate. Also, the danger of sedating a patient who already has poor airway and/or marginal respiratory muscle control may obviously have disastrous consequences.

In recent years, the administration of intravenous Centruroides sculpturatus specific antivenom has been found to be very effective by physicians acquainted with its use. However, 15-30 minutes may be required for reversal of severe neurological symptoms (discussed below).

Therefore, supportive care with control of the airway, when needed, is of highest priority. Endotracheal intubation may be required and should not be delayed in those having respiratory difficulty. Indeed, the lack of deaths from scorpion envenomations in recent years is most likely due to good supportive care that was not available previously.

After instituting supportive care, patients who do not receive antivenom frequently need to be admitted to

an intensive care unit for continued therapy. Advocates of barbiturates would then sedate the patient carefully, as needed to maintain good respiratory control and limit excessive neuromuscular activity.

The clinical course of severely ill patients treated with barbiturates could not be adequately characterized in our study because all but 2 of the Grade IV patients received antivenom, with rapid reversal of severe signs and symptoms (discussed below). Rimsza *et. al.* provide the only good source of literature that describes the clinical course of patients treated with barbiturates (25). As noted earlier, all of their patients over ten years of age could be no higher than Grade III, while 12/14 (85%) of those under ten were probably Grade IV. Eleven of the 12 patients who were probably Grade IV received phenobarbital (Rimsza, personal communication). They noted that all patients more than ten years of age were symptom free by ten hours, while all patients less than three were symptomatic for more than ten hours. The duration of symptoms, generally, was inversely related to patient age. These authors concluded it was unfortunate that past literature suggested high doses of phenobarbital in that the complications noted in their patients (two respiratory arrests and four with prolonged lethargy) were related to the use of high dose barbiturates. They found no evidence that phenobarbital shortened the duration of symptoms and suggested that sedatives be used cautiously.

Because barbiturates have been associated with complications and have not shortened the duration of illness, some physicians carefully restrain the child and

provide respiratory support. Little or no attempt is made to pharmacologically decrease excessive skeletal neuromuscular activity.

The clinical course of patients treated with antivenom therapy has not been well described in the literature even though scorpion antivenom has a relatively long history. In the 1930's antivenom produced from horses was imported from Mexico into Arizona, but physicians were dissatisfied with its effects. Dr. Herbert Stahnke of Arizona State University subsequently developed both rabbit and cat serum scorpion antivenom for human use. Since 1965, goats have been the source of antivenom, and it is presently manufactured by the Antivenom Production Laboratory at Arizona State University in Tempe, Arizona, under the direction of Dr. William Northey. An application is being made to the Food and Drug Administration for the use of scorpion antivenom as an investigational new drug.

We have found that 1-2 vials (each vial is 5cc when reconstituted) given intravenously over 15-30 minutes reverses severe neurological symptoms within minutes following infusion. Complete resolution of minor cranial nerve and skeletal neuromuscular abnormalities may take up to 1 1/2 hours. In our experience, intramuscular administration of antivenom has little or no effect and cannot be recommended.

We examined all 673 patient records in our study to determine the clinical course of Grade III and Grade IV patients. Of the 52 Grade III and IV envenomations, 25/32 Grade III patient records, and 16/20 Grade IV patient records contained adequate information to deter-

mine the treatment rendered. The result of treatment with regard to cranial nerve and skeletal neuromuscular abnormalities could also be determined in most of these patients. All patients who received antivenom received a single dose of 1-2 vials (5-10cc) given intravenously over 15-30 minutes with one exception (described below). All patients were skin tested by intradermal injection of goat serum prior to administration of antivenom.

Grade III

Table VII shows that all but four Grade III patients were over 18 years of age, with three patients less than five and one patient age nine.

In those not treated with antivenom, no child had cranial nerve or neuromuscular hyperactivity for over nine hours. In the adult patients who did not receive antivenom, cranial nerve or neuromuscular abnormalities resolved in 12 hours or less in all 10 cases in which this could be determined. 7/10 (70%) of these adults had resolution of cranial nerve or neuromuscular abnormalities by six hours. In contrast to the children not treated with antivenom, residual pain and/or paresthesias were common beyond 24 hours in adults. Of the patients that did not receive antivenom, only one patient was hospitalized. 11/17 (64.7%) were managed completely at home and were not seen at a medical facility.

A direct comparison between the group of Grade III patients that received antivenom and those that did not is difficult in that this was not a prospective randomized study. In fact, the patients that received antivenom were probably more ill since all sought care at a medical facility in contrast to only 1/3 (35.3%) of

TABLE VII
CLINICAL COURSE OF GRADE III PATIENTS

NO ANTIVENOM GIVEN						RECEIVED ANTIVENOM							
PATIENT #	AGE (YRS)	DURATION OF CRANIAL NERVE OR NEURO-MUSCULAR AB-NORMALITIES (HRS)	DURATION OF PAIN AND/OR PARESTHESIAS (HRS)	HOSPITAL ADMISSION	REASON FOR ADMISSION	PATIENT #	AGE (YRS)	DURATION OF CRANIAL NERVE OR NEURO-MUSCULAR AB-NORMALITIES BEFORE ANTI- VENOM (HRS)	DURATION OF CRANIAL NERVE OR NEURO-MUSCULAR AB-NORMALITIES AFTER ANTI- VENOM (HRS)	TOTAL DURATION OF CRANIAL NERVE OR NEURO-MUSCULAR AB-NORMALITIES (HRS)	DURATION OF PAIN AND/OR PARESTHESIAS (HRS)	HOSPITAL ADMISSION AFTER ANTIVENOM	REASON FOR ADMISSION
1	2	9	0	NO		18	9	2	$\frac{3}{4}$	2 $\frac{1}{2}$	0	NO	
2	4	8	24	NO		19	19	$\frac{1}{4}$	$\frac{1}{4}$	1	?	YES	OBSV
3	4	>8	?	YES	OBSV	20	ADULT	5	$\frac{1}{4}$	5 $\frac{1}{4}$	?	NO	
4	ADULT	4	24	NO		21	ADULT	8	<1 $\frac{1}{2}$	<9 $\frac{1}{2}$	20	NO	
5	ADULT	?	30	NO		22	ADULT	11	<1	<12	>24	NO	
6	ADULT	?	>24	NO		23	ADULT	2	1	3	?	YES	ETHANOL INTOXICATION
7	ADULT	?	6	NO		24	ADULT	7	$\frac{3}{4}$	7 $\frac{1}{4}$	?	NO	
8	ADULT	?	>24	NO		25	ADULT	3	<1	<4	?	NO	
9	ADULT	3	7	NO									
10	ADULT	2	>24	NO									
11	ADULT	2	>24	NO									
12	ADULT	10	>24	NO									
13	ADULT	12	24	NO									
14	ADULT	5	>24	NO									
15	ADULT	12	>24	NO									
16	ADULT	1	24	NO									
17	ADULT	6	9	NO									

those not given antivenom. It is also likely that physicians administered antivenom to only the more symptomatic patients. All patients who received antivenom, however, had resolution of cranial nerve or neuromuscular abnormalities within one hour after receiving an intravenous dose, regardless as to how long they had been symptomatic. In the two adult patient records where information was available, residual paresthesias still persisted. In this group of patients who were probably more ill than those who did not receive antivenom, only two were hospitalized, and one of these was for ethanol intoxication.

Grade IV

Only two Grade IV patients did not receive antivenom (Table VIII). Both required hospitalization, and both received phenobarbital for sedation. The two year old child was symptomatic for nine hours, and the four year old for ten hours. Neither patient complained of persistent pain or paresthesias. The duration of symptoms does not differ markedly from similar patients reported by Rimsza et. al. (25).

All but three patients who received antivenom were less than 11 years of age, as one would expect since Grade IV envenomations are unusual in adults. 12/14 (85.7%) had resolution of all cranial nerve and skeletal neuromuscular abnormalities within one hour of administration of antivenom. Patient number 12 received antivenom slowly over 1 1/2 hours because of a questionably positive skin test to goat serum. By the end of the infusion she was asymptomatic, but 1 1/2 hours was considered as the time required to improve since we did not want to

TABLE VIII
CLINICAL COURSE OF GRADE IV PATIENTS

NO ANTIVENOM GIVEN							RECEIVED ANTIVENOM										COMMENTS
PATIENT #	AGE (YRS)	DURATION OF CRANIAL NERVE AND MUSCULAR SYMPTOMS (HRS)	DURATION OF PAIN AND OR PARALYSIS (HRS)	HOSPITAL ADMISSION	REACTION TO ADMISSION	PHENOBARBITAL USED	PATIENT #	AGE (YRS)	DURATION OF CRANIAL NERVE AND MUSCULAR SYMPTOMS BEFORE ANTIVENOM (HRS)	DURATION OF CRANIAL NERVE AND MUSCULAR SYMPTOMS AFTER ANTIVENOM (HRS)	TOTAL DURATION OF CRANIAL NERVE AND MUSCULAR SYMPTOMS (HRS)	HOSPITAL ADMISSION BEFORE ANTIVENOM GIVEN	HOSPITAL ADMISSION AFTER ANTIVENOM GIVEN	REASON FOR ADMISSION AFTER ANTIVENOM GIVEN	DURATION OF PAIN AND OR PARALYSIS (HRS)		
1	2	9	7	YES	SUPPORTIVE CARE	YES	3	23 (8 MO)	4		4		NO	YES	OBSV	?	NO OTHER TREATMENT
2	4	10	7	YES	SUPPORTIVE CARE	YES	4	?	8		8		NO	YES	OBSV	?	NO OTHER TREATMENT
							5	4	2	1	3	NO	YES	OBSV	?	NO OTHER TREATMENT	
							6	4	1	1	2	NO	YES	OBSV	0	ADMITTED BECAUSE OF LETHARGY FROM PHENOBARBITAL GIVEN BEFORE ANTIVENOM	
							7	4	1	1	2	NO	NO	-	3	NO OTHER TREATMENT	
							8	5	2	1	3	NO	NO	-	0	NO OTHER TREATMENT	
							9	7	4	1	5	NO	NO	-	0	NO OTHER TREATMENT	
							10	7	9	1	10	NO	YES	OBSV	?	NO OTHER TREATMENT	
							11	9	4	?	5	YES	-	-	0	30 mg PHENOBARBITAL GIVEN BEFORE ANTIVENOM WITHOUT EFFECT	
							12	10	3	1	5	NO	YES	OBSV	?	ANTIVENOM INFUSED SLOWLY BECAUSE OF POSITIVE SKIN TEST	
							13	10	1	1	2	NO	NO	-	20	15 mg PHENOBARBITAL GIVEN BEFORE ANTIVENOM WITHOUT EFFECT	
							14	39	11	?	11	NO	YES	OBSV	?	NO OTHER TREATMENT	
							15	46	1	1	1	NO	NO	-	12	NO OTHER TREATMENT	
							16	60	4	?	4	NO	NO	-	12	NO OTHER TREATMENT	

underestimate the duration of symptoms. Generally, a marked decrease in skeletal neuromuscular activity and serious cranial nerve dysfunction was noted during, or within 10-15 minutes after the administration of the antivenom. Over the next 15-45 minutes all eye findings, tongue fasciculations, and minor skeletal muscle hyperactivity would gradually disappear. Only 7/14 (50%) of the patients who received antivenom were admitted to the hospital. Patient number 6 was admitted only because of CNS depression induced by phenobarbital administered before antivenom was given. The other six patients all were admitted for observation. Five of these six patients remained completely asymptomatic and required no further treatment or supportive care. Patient number 12 redeveloped mild muscular twitching 3 1/2 hours after resolution of her original symptoms. This quickly disappeared after another vial of antivenom was given.

Because of the small number of patients who did not receive antivenom, it is difficult to compare the two groups of Grade IV patients. However, the clinical course of Grade IV patients treated with antivenom is quite different from the 12 probable Grade IV patients reported by Rimsza et al (25), and from the two patients in our study that did not receive antivenom. All of these patients required admission to the hospital, usually to an intensive care unit. Eleven patients in Rimsza's report, and both patients in ours were treated with barbiturates, and six suffered complications including respiratory arrest and prolonged lethargy. In contrast, all of the Grade IV patients treated with antivenom were asymptomatic within 1 1/2 hours after antivenom admini-

stration, with major symptoms generally gone in 15-30 minutes. Only 50% were hospitalized, and all of these but one remained asymptomatic.

Patients number 6, 11 and 12 received phenobarbital without satisfactory results. All three then responded well to the administration of antivenom.

Just as in Grade III patients, the antivenom did not seem to effect local pain or paresthesias in adult patients. Records indicate that 2 children definitely had persistent pain and/or paresthesias.

Safety of Antivenom

Of all the patients who received antivenom, the only adverse effect was a single urticarial lesion that developed during administration in the patient who had a questionably positive skin test. This rapidly cleared with epinephrine, and in fact, another dose of antivenom was administered 3 1/2 hours later with no adverse effects. The authors have personally treated over 30 patients with goat serum scorpion antivenom and have never seen a case of serum sickness. In contrast, 70-80% of the rattlesnake bite victims we treat with horse serum crotalid polyvalent antivenom develop serum sickness in 3-10 days. One may argue that larger amounts of horse serum are given to snake bite victims, and indeed, the small volume of goat serum required for a satisfactory response may in part be responsible for the lack of serum sickness seen in patients treated with scorpion antivenom. However, Russell reported the administration of crotalid antivenom prepared in goats to five snake bite victims who demonstrated hypersensitivity to horse serum (27). No patient suffered adverse effects during

administration, and interestingly, no patient developed signs or symptoms of serum sickness.

The administration of C. sculpturatus antivenom, then, resulted in dramatic reversal of severe signs and symptoms; all patients were asymptomatic within 1 1/2 hours. Patients who received C. sculpturatus antivenom did not need prolonged supportive care in a critical care unit, and in fact, were frequently discharged home from an emergency department. The goat serum product appears safe, and even when used in doses larger than those used in the treatment of scorpion envenomations, has not been associated with serum sickness. For these reasons the authors feel that after the initiation of supportive care in the emergency department, C. sculpturatus antivenom is the treatment of choice for severe envenomations.

CONCLUSIONS

Envenomation by the scorpion C. sculpturatus still poses a threat to life in some parts of the United States. Mild signs and symptoms consisting of local pain and/or paresthesias characterize the illness in most patients. Long-lasting pain and/or paresthesias are more common in those age 11 and older and appear unaffected by any form of treatment. Severe signs and symptoms can develop in any age group, but those age 10 and younger make up the great majority of these patients. Institution of prompt, supportive care with special attention to the airway is essential in managing those suffering from a severe envenomation. Treatment of severe envenomations with high doses of barbiturates has been associated with complications and does not shorten the duration of the

illness. In contrast, the intravenous administration of goat serum C. sculpturatus antivenom results in dramatic reversal of severe symptoms, with all patients asymptomatic within 1 1/2 hours and with only one patient in this review having a minor relapse of symptoms. The administration of C. sculpturatus antivenom appears safe and is recommended as the treatment of choice for severe envenomations after appropriate supportive care has been instituted. A multi-center prospective study of treatment of C. sculpturatus stings is recommended.

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