

## SEVERE SCORPION ENVENOMATION IN BRAZIL. CLINICAL, LABORATORY AND ANATOMOPATHOLOGICAL ASPECTS.

Palmira CUPO (1), Mauro JURCA (2), Marisa M. AZEVEDO-MARQUES (2), João Samuel M. OLIVEIRA (3)  
& Sylvia E. IIERING (1)

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### SUMMARY

Scorpion stings in Brazil are important not only because of their incidence but also for their potential ability to induce severe, and often fatal, clinical situations, especially among children. In this report we present the clinical and laboratory data of 4 patients victims of scorpion stings by *T. serrulatus*, who developed heart failure and pulmonary edema, with 3 of them dying within 24 hours of the sting. Anatomopathologic study of these patients revealed diffuse areas of myocardiocytolysis in addition to pulmonary edema. The surviving child presented enzymatic, electrocardiographic and echocardiographic changes compatible with severe cardiac involvement, which were reversed within 5 days. These findings reinforce the need for continuous monitoring of patients with severe scorpion envenoming during the hours immediately following the sting.

**KEYWORDS:** Scorpions stings; *T. serrulatus*; Scorpion venom "cardiomyopathy".

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### INTRODUCTION

Scorpion envenomation in Brazil, as also in other parts of the world, represents a medical-sanitary problem of great importance for urban populations in certain regions because of its high incidence and its potential induction of serious, and often fatal, clinical pictures, especially among children. The severity of scorpion envenomation is related to the cardiorespiratory alterations it may provoke, with manifestations such as pulmonary edema and circulatory failure triggering death<sup>1-8, 14, 17, 21-23, 28-31, 33, 47</sup>.

It has been well established that the clinical manifestations observed in patients following *T. serrulatus*

envenomation are due to the action of neurotransmitters released by the autonomic nervous system and adrenal medulla in the various sectors of the organism<sup>19, 21, 27</sup>. However, the physiopathology of pulmonary edema and of cardiac failure has not been fully elucidated<sup>6, 7, 12, 22-24, 28-31, 33, 34, 36, 47, 49</sup>.

Despite the relative incidence in certain regions and the potential seriousness of scorpion envenomation, few studies are available about this phenomenon in Brazil, and over the last decade, they have been limited mainly to short communications, with description of isolated cases or epidemiologic data<sup>2-7, 14, 15, 17-19, 28-33, 39, 40</sup>.

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(1) Depto. de Puericultura e Pediatria da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (FMRP-USP). Ribeirão Preto, São Paulo, SP.

(2) Depto. de Clínica Médica da FMRP-USP. Ribeirão Preto, São Paulo, SP.

(3) Depto. de Patologia da FMRP-USP. Ribeirão Preto, São Paulo, SP.

Endereço para correspondência: Dra. Palmira Cupo, Depto. de Puericultura e Pediatria da FMRP-USP. CEP 14049-900 Ribeirão Preto, São Paulo, Brasil.

In the present report we describe the clinical and laboratory course of a patient with severe scorpion envenomation, as well as the clinical and the anatomopathological data of the 3 children who died, in order to discuss the physiopathology and the therapeutic approach to scorpion envenomation in the light of present knowledge.

## CASE REPORTS

### Patient 1

A 5-year and 1-month old girl from Batatais, SP, was stung by *T. serrulatus* in the right supraclavicular region. Intense local pain, muscle contracture and several vomiting episodes started soon after envenomation. The child was hospitalized in her town in a state of semi-torpor, with bradycardia, bradypnea, and blood pressure (BP) 180/120 mmHg, and was treated with two ampoules of scorpion antivenom (SAV) subcutaneously. There was an improvement of consciousness level, but with persistence of local pain and vomiting. Approximately 12 hours after the sting, the patient presented severe and sudden hypotension, was medicated with dopamine and sent to the Emergency Unit of the University Hospital of the Faculty of Medicine of Ribeirão Preto (EU-UHFM RP). Upon admission, she was conscious, with tachydyspnea, hypothermia (35.8°C), tachycardia (170/min), BP 60/0 mmHg, a filiform pulse, and bilateral moist rales, with persistence of vomiting of pinkish material. A chest X-ray was compatible with the presence of pulmonary edema, demonstrating enlargement of the heart. Despite the measures instituted, the patient suffered several cardiorespiratory arrests one hour after admission at our hospital. She was intubated

and ventilated and even an external pacemaker was applied. All of these measures, however, were unsuccessful and the child died 17 hours after envenomation.

### Autopsy findings

**Brain:** intense cerebral edema with vascular congestion. **Heart:** overall dilation, pale cardiac muscle and opening of the pectineal muscles of both chambers revealed by sectioning. Coronaries free of obstructive processes. Interstitial edema with a moderate inflammatory infiltrate consisting of neutrophilic and some eosinophilic cells. Signs of leukodiapedesis with sparse focal myocytolysis and mild vacuolar degeneration of cardiac fibers (Fig. 1A). **Lungs:** tracheobronchial tree with a light pink foamy fluid. Both lungs showing an approximately 3-fold increase in size, hardened, elastic, with a smooth and bright surface. Sectioning showed a hard reddish parenchyma with friable areas, without crepitation. Microscopy revealed diffuse alveolar edema and hemorrhage and polymorphonuclear infiltrate (Fig. 2). **Liver:** diffuse vacuolar degeneration of the parenchyma. **Pancreas, Kidneys and Intestinal Tract:** no macroscopic abnormalities.

### Patient 2

A 4-year and 2-month old boy from Ribeirão Preto, SP was stung by a yellow scorpion in the sternal region and was admitted to the EU-UHFM RP 4 hours and 30 minutes after the accident. He presented intense pain immediately after the sting, with abundant and frequent vomiting. The initial examination revealed a dehydrated patient, alternating between a state of torpor and periods of agitation, at times establishing good contact, with tachydyspnea, bilateral myosis, cold extremities, fainter



Fig. 1 (A) Section of myocardium of patient 1 stained with phosphotungstic hematoxylin, showing dissolution of a myocardial cell with coagulative myocytolysis (arrow). Fiber dissociation due to edema and other cells with loss of striation, as well as an early process of myocytolysis can be observed. (B) Section of myocardium of patient 3 showing fiber dissolution due to edema and one cell with hialinized cytoplasm without nucleus (arrow) (hematoxylin-eosin) (x400).

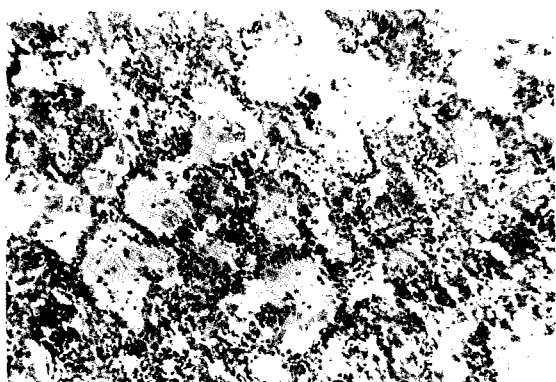


Fig. 2. Histologic picture of lung of patient 1 showing diffuse intraalveolar edema and hemorrhage and polymorphonuclear cell infiltrate (Hematoxylin and eosin) (x400).

and arrhythmic heart sounds at 60-80/bpm, with no peripheral pulse and with BP difficult to measure. Immediately after admission, the child received four intravenous SAV ampoules and parenteral hydration and was sent to the Intensive Care Unit (ICU). Some improvement in general condition occurred, but 7 hours after admission, he was still moaning, with cold extremities, agitated, dyspneic, with generalized lung rales, arrhythmic and tachycardiac heart sounds, with BP 30/0 mmHg and the liver was palpable 4 cm bellow the right costal margin. He was treated with digitalis, diuretics and dopamine, but suffered irreversible cardiac arrest 13 hours after envenomation.

#### Autopsy findings

**Brain:** with signs of cerebral edema, and diffusely softened. **Lungs:** both increased in volume, with a wine coloration and increased consistency. Sectioning revealed that the parenchyma was quite congested, with the emission of a foamy red fluid upon compression. Pulmonary alveoli diffusely flooded by material at times appearing to be proteinaceous and amorphous and most intermingled with confluent erythrocytes, frequently forming focal points of massive hemorrhage which flooded the alveolar spaces. **Heart:** preserved morphology and increased volume, with enlarged right ventricle (RV) and increased wall thickness of left ventricle (LV). Pervious coronaries. No microscopic examination was performed. **Liver, Pancreas and Adrenals** were of normal macroscopic appearance. The gastrointestinal tract was normal, with the presence of *Ascaris lumbricoides*.

#### Patient 3

A 4-year and 3-month old girl from Barrinha, SP stung on the hand by *T. serrulatus*, presented severe

local pain after the sting, as well as nausea and profuse vomiting. After being taken to the hospital in her town, she was sent to EU-UHFMRP 1 hour and 30 minutes after envenomation. At admission she appeared prostrated, somnolent but conscious, presented vomiting, with profuse sialorrhoea and sudoresis, cold extremities, a cold sensation, regular heart rate at 160/min, BP 100/70 mmHg and tachydyspnea. Ten intravenous SAV ampoules were administered.

Approximately 3 hours and 30 minutes after the sting, the child maintained tachycardia and tachydyspnea, with flaring of the nostrils, sialorrhoea and crepitations rales in the base of the lungs, although with good peripheral perfusion and BP 120/80 mmHg. A chest X-ray revealed signs of pulmonary edema, with no enlargement of the heart. The child received diuretics and nasal oxygen, with a discrete improvement of the clinical picture and reduced rales. She continued with tachydyspnea, agitation, cold extremities, and satisfactory diuresis. Worsening of signs and symptoms occurred over the next few hours, with increased respiratory distress, sudoresis, a cold sensation, and hypotension. She then suffered a sudden seizure, with limb rigidity and cardiorespiratory arrest which could not be reversed, with death occurring 15 hours after envenomation.

Laboratory tests performed upon admission showed leukocytosis (WC = 30,500/ml), hypopotassemia (2.5 mEq/L), hyperglycemia (20 mmol/L) and glycosuria. Creatinekinase (CK) was 74 IU/L at admission, reaching 640 IU/L 12 hours after the sting, with the appearance of the CK-MB and CK-BB fractions. An increase in lactate dehydrogenase (LD) was also observed, with fraction LD1 > LD2. Two electrocardiograms (ECGs) taken 3 and 8 hours after the sting revealed diffuse repolarization changes, sinus tachycardia, and signs of subendocardial damage and ischemia in the inferior leads.

#### Autopsy findings

**Brain:** signs of cerebral edema and congestion. **Lungs:** increased volume, with intense alveolar edema and septal congestion. **Heart:** no macroscopic changes in myocardium, endocardium or valves. Some points of subepicardial hemorrhage were noted in the epicardium. Microscopy revealed myocytolysis and unstructured fibrillar cytoplasmic architecture turning into an amorphous eosinophilic mass (Fig. 1B). The ventricular lumen between the papillary muscles contained a

**Table 1**  
Laboratory tests performed on patient 4

Hours after Sting	CK < 80 U/L	CK-MB < 10 U/L	LD 120-240 U/L	LD1>LD2 "Fleep"	AST < 18 U/L	Amylase 16-108 U/L	White Cells 5-10000/ml	Glucose mmol/L	Potassium mEq/L
6	694	79	486	+	85	336	12400	16.55	2.3
9	773	76	642	+	101	305	8700	nm	nm
16	925	93	659	+	131	223	nm	6.60	3.7
24	816	57	792	+	131	132	nm	nm	nm
40	184	13	901	+	79	48	nm	nm	nm
64	36	6	578	+	23	39	nm	nm	nm
88	62	6	355	+	12	nf	nm	nm	nm

nm = not measured  
CK = Creatinequinase  
LD = Lactic Dehydrogenase  
AST = Aspartate aminotransferase

+ = present  
CK-MB = Creatinequinase isoenzyme  
LD1, LD2 = Lactic dehydrogenase isoenzymes

polymorphonuclear cell infiltrate. *Pancreas, Liver and Gastrointestinal Tract* showed no macroscopic alterations.

#### Patient 4

A 6-year old boy from Pirassununga, SP was stung by a yellow scorpion on the left foot, near a site containing wood and bricks. He complained of intense pain and was taken to the hospital 30 minutes after envenomation. He presented with tachypnea and vomiting, at first consisting of food and then of bloody material, with abundant sudoresis, abdominal pain, and headache. He first received two SAV ampoules i. v., followed by four ampoules of polyvalent ophidic antivenom due to uncertainty about the offending animal. Four hours after envenomation, he presented worsening of the respiratory pattern, with diffuse pulmonary rales and pinkish

oral and nasal secretion, with continuing bloody vomiting. The patient was transferred to EU-UHFMRP, where he arrived 5 hours and 30 minutes after the sting. He had tachydyspnea, with important intercostal retractions. He was pale, with cold extremities and generalized cold sudoresis, with petechiae on the face. Undetectable BP and faint arrhythmic heart sounds with filiform pulse and HR at 160/min were detected. He presented alternating periods of somnolence with agitation, poor peripheral perfusion, cyanotic lips and extremities, and pinkish nasal secretion. He received ten SAV ampoules i. v.

A chest X-ray revealed bilateral pulmonary infiltrates more accentuated over the right lung (Fig. 3). Diuretics, nasal oxygen, and limb tourniquets were used, and dopamine and dobutamine were started, with progressive improvement of pulmonary edema, peripheral perfusion and BP.

The child still presented several episodes of vomiting and abdominal pain, with tachydyspnea and tachycardia persisting for approximately 48 hours. Dopamine and dobutamine were maintained during the first 20 hours after admission. The sequential laboratory tests, ECG and the echocardiography (ECHO) data resembling myocardial injury pattern are presented in Tables 1 and 2 and in Fig. 4 and 5. The child had a satisfactory course and was discharged 7 days after the scorpion sting with normalization of ECGs, ECHO and of most of the laboratory tests.

## DISCUSSION

*T. serrulatus* is the scorpion of greatest medical interest in Brazil because of the dangerousness of its

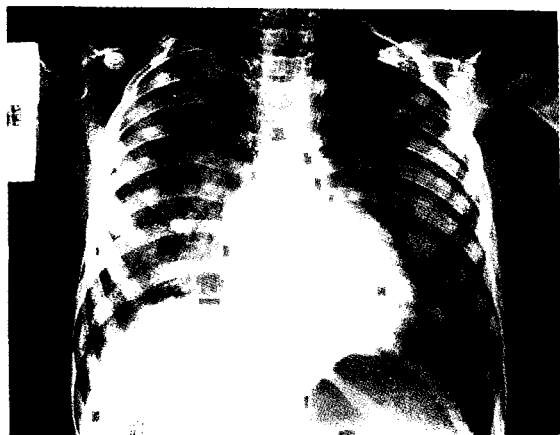


Fig. 3. Anteroposterior chest roentgenogram of patient 4, obtained 6 hours after sting by *T. serrulatus*, showing enlarged heart and bilateral lung edema more severe over the right lung, with air bronchograms.

sting, although severe and lethal cases have also been reported after envenomation by *T. bahiensis* and *T. stigmurus* 2-8, 13, 14, 17, 28-31, 33, 37, 39, 40, 46.

In most cases, a scorpion sting provokes only local pain ranging in intensity from mild to severe, almost unbearable, and accompanied or not by paresthesia and

**Table 2**  
Echocardiographic data obtained in patient 4

Time after Sting	Movement			L V		Enlarged Heart Chambers	Mitral Regurgitation
	IVS	PLVW	RV	FS (>26%)	EF (>0.58)		
20 hs	Hypo +++	Hypo +++	Hypo +++	12	0.31	LV/LA	+ / + +
5 days	N	N	N	35	0.72	LA	+
7 days	N	N	N	43	0.82	LA	-

IVS = Interventricular Septum  
FS = Fractional Shortening  
Hypo = Hipokinetic  
+ = Present  
- = Absent

PLVW = Posterior Left Ventricular Wall  
EF = Ejection Fraction  
LV = Left Ventricle  
LA = Left Atrium  
N = Normal

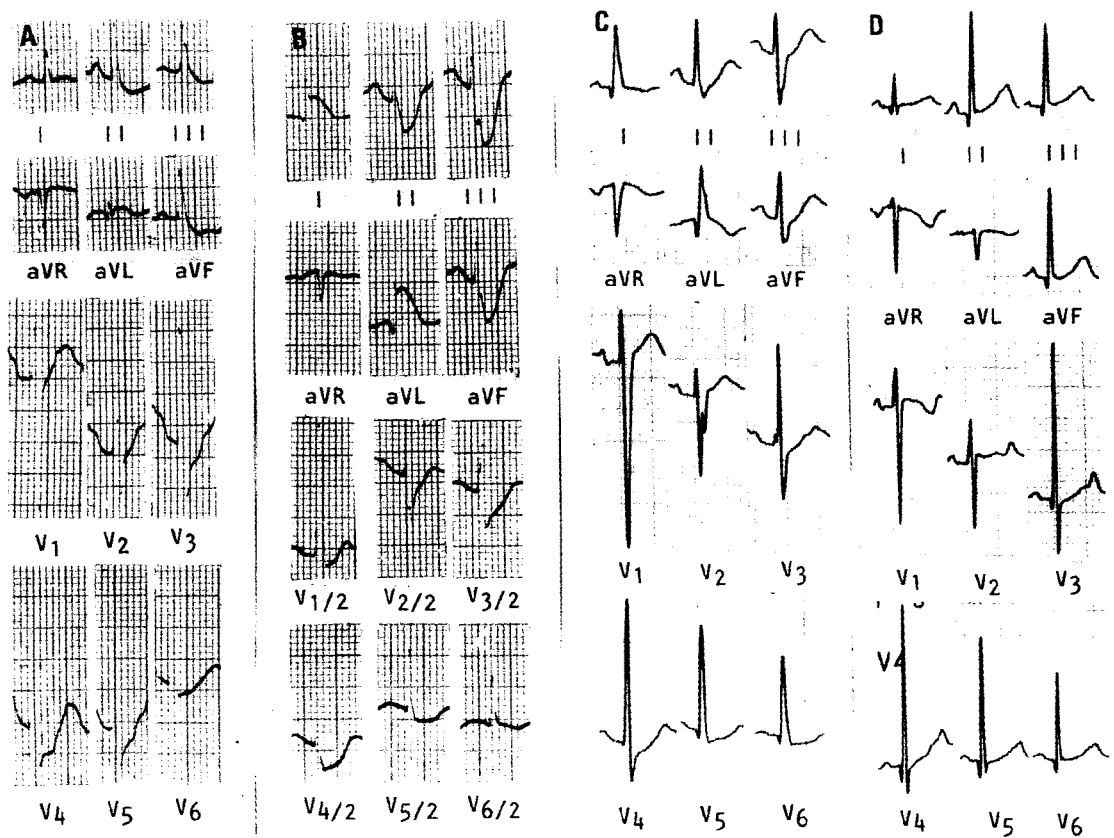


Fig. 4. ECGs from patient 4. (A) Taken 6 hours after sting, showing sinus tachycardia (rate:150/min), ST segment depression in leads II, III, aVF and V3-6 and mild ST segment elevation in aVL. (B) Taken 12 hours after sting, with persistence of sinus tachycardia (rate:160/min), ST segment depression in leads II, III, aVF, V1-5, elevation of ST segment in leads I and aVL resembling an acute myocardial pattern. (C) Taken 2 days after the sting, showing sinus tachycardia (rate:120/min), enlarged QRS complexes, left axis deviation compatible with a left anterior hemiblock. Important regression of the ST segment changes. (D) Taken 5 days after sting, showing sinus rhythm (rate:104/min) and regression of ST changes.

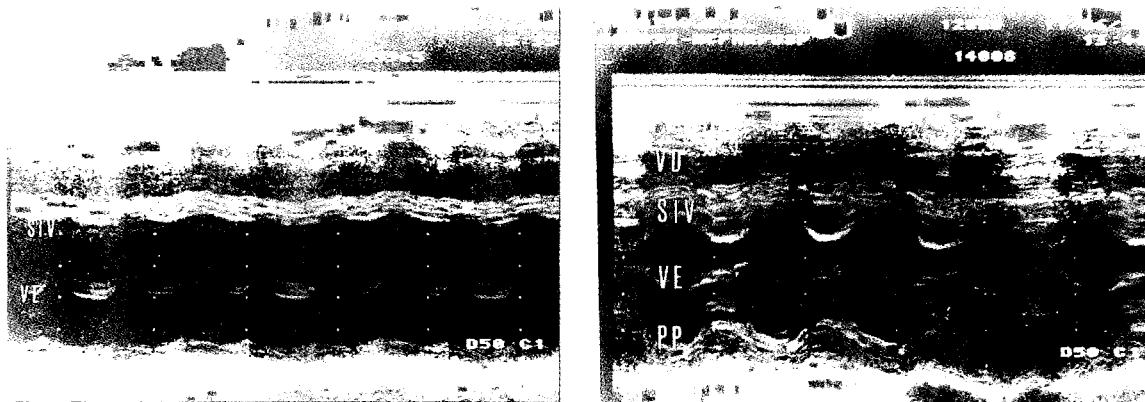


Fig. 5. M-mode echocardiograms recorded in patient 4 at the level of the ventricles. A. 18 hours after sting by *T. serrulatus* showing severe hypokinesia of interventricular septum (SIV) and of the left ventricular posterior wall (PP). B. Return to a normal pattern 7 days after the sting.

irradiation. Some signs and symptoms associated with local pain may also appear, such as nausea and occasional vomiting, tachycardia and some agitation, characterizing a mild case (Table 3).

The frequency and intensity of vomiting is a quite sensitive premonitory sign of the severity of envenomation. It should be pointed out that the severity of clinical picture is defined in most cases during the first two hours after the sting.

In severe envenomation, which occurs mainly in children the picture is much polymorphic and often dramatic, with important alterations of the cardio-respiratory systems, leading to circulatory failure, pulmonary edema, and death (Table 3), as we could see in our patients.

Until a few years ago, evidence of heart damage in human scorpion envenomation was restricted to changes in ECG, with a pattern similar to that of myocardial infarction or myocarditis<sup>21-23, 28, 29, 31, 33, 35, 41, 44, 45</sup>, to the increase in CK-MB and LD1 isoenzymes<sup>28, 29, 31, 44, 45</sup>, to the detection of myoglobin in patient serum and urine samples<sup>28, 29</sup>, and to the few autopsy data available for victims of scorpion envenomation<sup>8, 22, 23, 30, 43</sup>.

Echocardiographic changes were first reported in 1988 in Jerusalem, supporting the occurrence of myocardial damage in scorpion envenomation<sup>12</sup>. In the same year, ECHO alterations after severe *T. serrulatus* envenomation were also documented in Brazil<sup>29</sup>. An important reduction of interventricular septum motility and mitral regurgitation were observed in two children which disappeared within 5 to 7 days. New cases have

been described since then, not only in Brazil<sup>4-7, 31, 33, 39</sup> but also in other countries<sup>1, 26, 36, 42</sup>.

As to the dreaded complication of scorpion envenomation, i. e., pulmonary edema, its pathophysiology has been accepted as being of multifactorial origin. Cardiac-failure caused by left ventricular dysfunction or by hemodynamic disorders resulting from an increase preload or afterload or from severe arrhythmias<sup>1, 4-7, 12, 22-24, 29, 31, 33, 35, 36, 39, 41, 42, 47, 49</sup> and/or from increased pulmonary vascular permeability triggered by the release of chemical mediators in the lung<sup>6, 7, 19, 34, 40, 42</sup> have been the major mechanisms involved.

Autopsy findings related to cardiovascular pathology in fatal cases are scarce. Pulmonary edema with diffuse areas of hemorrhagic pneumonitis, left ventricular dilation and microscopically unchanged myocardium were observed in a 6-year old child<sup>22</sup>. Subendocardial hemorrhage in 2 of 7 fatal cases, one of them containing a mural thrombus in the LV, and pulmonary edema in all cases were described by REDDY et al<sup>43</sup>.

In a latter series of 7 victims of scorpion envenomation, GUERON & YARON<sup>23</sup> observed degenerative changes of cardiac fibers, focal necrosis, interstitial edema and increased cellularity involving lymphocytes and monocytes, with a predominant involvement of papillary muscles and subendocardial areas. In the lungs, the findings were compatible with pulmonary edema and diffuse areas of pulmonary hemorrhage.

In Brazil, BARROS<sup>8</sup> reported the autopsy findings for 2 children in 1938, with the detection of pulmonary

Table 3  
Classification and Treatment of Scorpion Envenomation (\*)

Classification	Clinical Manifestations	Treatment	
		Symptomatic	Specific
Mild	Presence of only a local painful picture. At times, tachycardia and agitation linked to pain	Pain relief	-
Moderate	In addition to local pain, some systemic manifestations as agitation, sudoresis, sialorrhea, tachycardia, tachypnea, arterial hypertension, all of mild intensity. Nausea and some vomiting may occur.	Same as above	SAV (**) is indicated for children younger than 7 years (2-4 ampoules i. v.)
Severe	Symptoms essentially characterized by changes in cardiac and respiratory rhythm accompanied by nausea, abundant and frequent vomiting, profuse and cold sudoresis, sialorrhea, tearing, arterial hypertension, agitation alternating with somnolence, tremors. It may progress to cardiac failure, pulmonary edema and shock.	Same as above. Relief of vomiting ICU care	SAV (**) (5-10 ampoules i. v.)

All patients should be kept under observation, in a hospital setting during the first 6 to 12 hours after the sting, even in benign cases, especially when children are involved.

(\*) Adapted from Manual de Vigilância Epidemiológica - Acidentes por Animais Peçonhentos. (Reference 38).

(\*\*) SAV = Scorpion antivenom (or antiarachnid serum).

edema and dilation of cardiac chambers, with the presence of clots upon macroscopic examination.

Macroscopic and microscopic findings compatible with a noncardiogenic acute pulmonary edema were recently described in a boy bitten by *T. serrulatus*<sup>7</sup>. This patient needed mechanical ventilatory support with 100% oxygen and although necrosis of the cardiac cells was not evident, he also presented cardiac involvement, as indicated by the enzyme pattern and by ECG and ECHO data.

The data obtained here for patients 1 and 3 whose hearts were submitted to anatomopathological examination are similar to those reported by GUERON & YARON<sup>23</sup>, with isolated focal myocytolysis and countless contraction bands (Fig. 1A and 1B). The lesions were more intense in patient 1, with a mononuclear infiltrate close to the areas of myocytolysis. Pulmonary edema was observed in all 3 patients.

The pathogenesis of "scorpionic cardiomyopathy" has been attributed to the adrenergic effects triggered by the venom and/or the toxic effect of the venom on cardiac fibers<sup>19, 21-24, 27, 30, 36, 41, 44, 45, 50</sup>.

The histopathological cardiac findings described for the fatal cases are similar to those observed in patients who died with pheochromocytoma or to those ex-

perimentally induced by scorpion venom or by injection of high doses of catecholamines<sup>23, 25</sup>. These, by their positive inotropic effect, may lead to a greater oxygen demand, with relative hypoxia and possible necrosis, a fact that would justify the enzymatic and ECG data obtained.

Clinical and laboratory findings similar to those observed in human scorpion envenomation have been described in a previously healthy patient who received an accidental high dose of adrenaline<sup>20</sup>. The patient became hypotensive, required mechanical ventilation and, paradoxically, exogenous catecholamines to maintain the perfusion pressure of vital organs. All alterations were reversed on the tenth day.

Although a direct effect of scorpion venom on cardiac fibers cannot be excluded<sup>41, 44, 45, 50</sup>, the evidence obtained thus far suggests that only the massive release of adrenaline could be the major factor responsible for the pathogenesis of the "reversible cardiomyopathy" of human scorpion envenomation.

On the basis of the clinical course data of our patients, it can be seen that after the administration of SAV, which only neutralized the circulating toxin, there was a general improvement of patient conditions. However, the cardiorespiratory changes due to the pharmacologic effects of the toxin already absorbed

persisted for varying periods of time, with the 4 patients developing shock and pulmonary edema. Thus, continuous and systematic monitoring of these patients is needed, even after the use of SAV, for the early detection of signs of heart failure, secondary to severe systolic dysfunction that may occur.

### TREATMENT

The treatment of scorpion stings is based on: 1) the relief of the signs and symptoms of envenomation, 2) neutralization of circulating venom, and 3) supporting the vital functions of the patient (Table 3).

Scorpion antivenom, whose objective is to neutralize the circulating toxin is formally indicated in all SEVERE envenomations and in MODERATE cases, only in patients younger than 7 years (Table 3)<sup>15, 32, 38</sup> and should always be given intravenously<sup>5, 6, 15, 16, 18, 32, 38</sup>.

Although there is controversy in the literature about the use of SAV in scorpion envenomation<sup>9-11, 25, 48</sup> also because some countries do not even procedure this antivenom, in Brazil there was a consense that SAV has a considerable beneficial effect, with a clear improvement of general patient condition occurring after its administration<sup>3, 8, 14, 15, 18, 19, 33, 37, 46</sup>, although the changes in cardiorespiratory rhythm persist for variable periods of time<sup>3, 14, 18, 33</sup>. Because of these changes, all affected patients should be kept under close observation until there is a sustained improvement.

Alpha blockers, vasodilators and calcium channel inhibitors have been recommended for patients with severe arterial hypertension, with good results<sup>9-11, 19, 25, 47, 48</sup>. In our patients, elevated pressure levels occurred immediately after the sting and were of transient nature, disappearing spontaneously.

The use of atropine is indicated only for patients with severe bradycardia or total atrioventricular block, since its use may precipitate the onset of pulmonary edema<sup>3, 11, 19</sup>.

In the presence of congestive heart failure and/or pulmonary edema, supportive treatment should be provided, with diuretics, alternately applied tourniquets, oxygen by nasal tube, and ventilatory support in the more severe cases<sup>2, 3, 14, 15, 18, 19, 31, 33, 38, 40, 47</sup>.

Exogenous catecholamines are indicated for pa-

tients who developed hypotension and shock not associated with hypovolemia<sup>3, 33, 47</sup>.

### RESUMO

#### Escorpionismo grave no Brasil. Aspectos clínicos, laboratoriais e anatomopatológicos.

Os acidentes escorpiônicos no Brasil, assumem grande importância não só pela sua incidência como pela sua potencialidade em induzir quadros clínicos graves, muitas vezes fatais, principalmente em crianças. Apresentamos neste relato os dados clínicos e laboratoriais de 4 pacientes vítimas de escorpionismo, causado pelo *T. serrulatus*, que evoluíram com falência cardíaca e edema pulmonar, sendo que 3 foram a óbito dentro das primeiras 24 horas após acidente. O estudo anatomo-patológico desses pacientes revelou áreas de miocardiocitólise, além do edema pulmonar. Na criança que sobreviveu foram detectadas alterações enzimáticas, eletro e ecocardiográficas compatíveis com grave comprometimento cardíaco, reversíveis dentro de 5 dias. Tais achados reafirmam a necessidade de monitorização contínua no paciente com escorpionismo grave, nas horas subsequentes ao envenenamento.

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