Treatment of *C. sculpturatus* envenomation: F. Mazda Shirazi

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Distribution:

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Scorpions:

1. Out 16 families only two are of medical importance:

- Buthidae (~ 530 Species)
- Scorpionidae (~183 species)
- Hemiscorpinidae (~15 specie)

- ~2000 species
  - 25-50 species are dangerous to humans

https://animaldiversity.org/accounts/Scorpionidae/
Handbook of research on Global Environmental Changes & Human Health, Ed. K. Kahime, et.al.,Chapter 23, Climate Change Scorpion Ecology, and Environment, pp 460-474, 2019, IGI global, Hershey, Pennsylvania, USA

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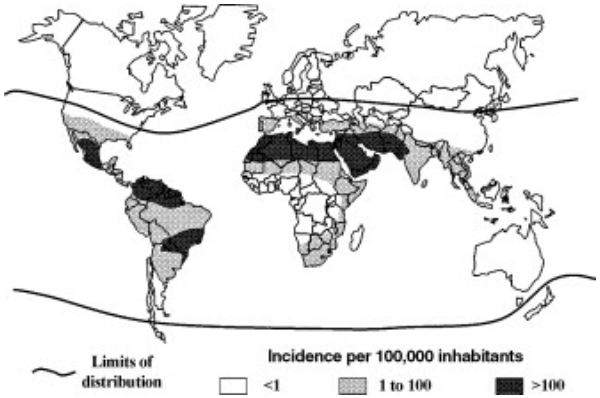
Distribution:



North Africa & Middle East:

- Androctonus, (cardiac toxicity)
- Buthus, (cardiac toxicity)
- Hottentotta, (cardiac toxicity)
- Leiurus, (neuro & cardiac toxicity)
- Parabuthus, (neuro-muscular toxicity)
- Hemiscorpius lepturus,* (cytotoxic, renal toxicity)

Sudan/India:

- Mesobuthus (cardiac toxicity)
- Hetrometrus swammerdami * (cardiac toxicity)

- South America:
  - Tityus (neuro-toxicity)

NorthAmerica:

- Centruroides (neuro-muscular toxicity)

Handbook of research on Global Environmental Changes & Human Health, Ed. K. Kahime, et.al.,Chapter 23, Climate Change Scorpion Ecology, and Environment, pp 460-474, 2019, IGI global, Hershey, Pennsylvania, USA.

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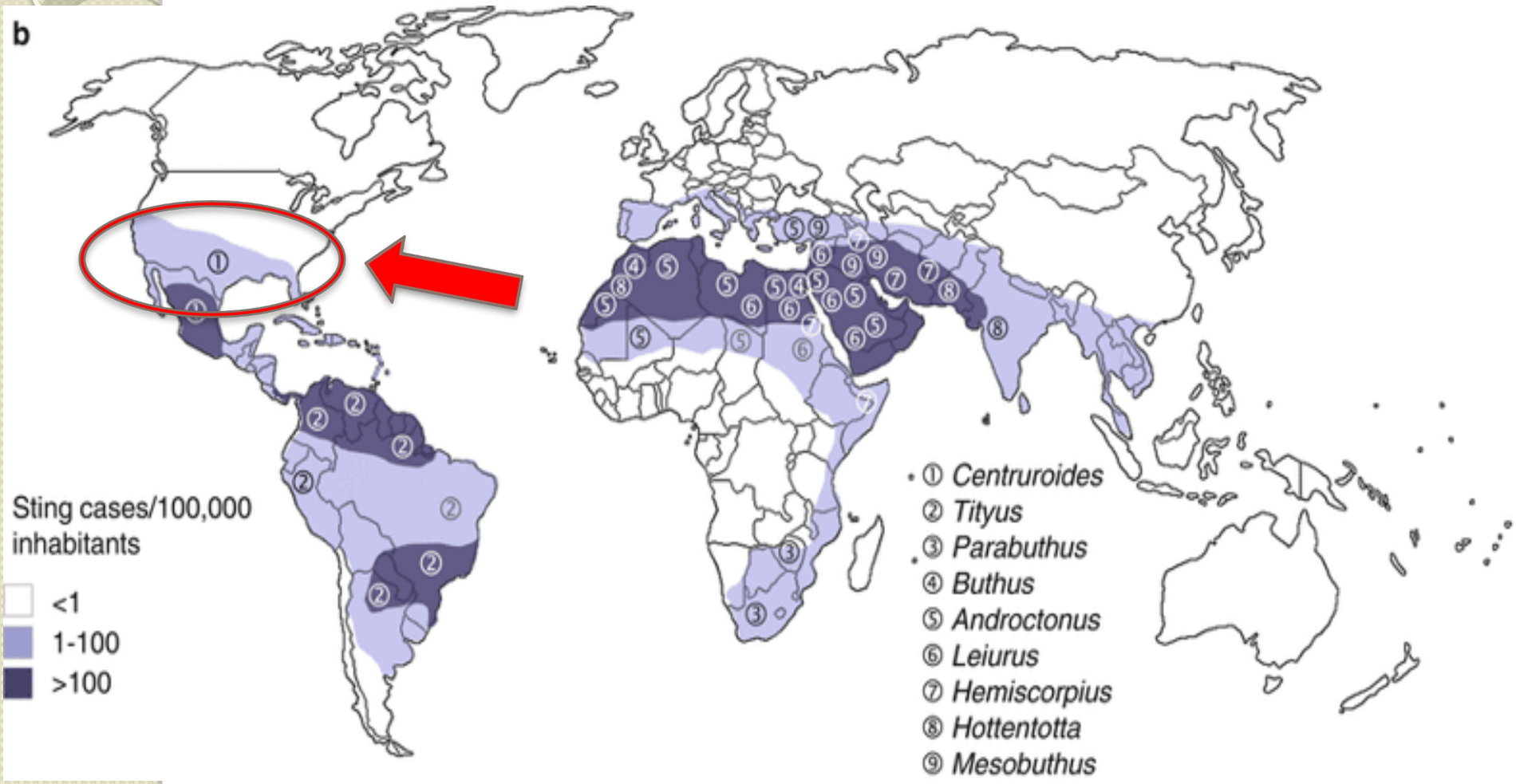
Envenoming density:



https://link.springer.com/referenceworkentry/10.1007%2F978-94-007-6416-3_36

Chippaux JP, Goyffon M. Epidemiology of scorpionism: a global appraisal. Acta Trop. 2008;107:71–9.

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By the Numbers:

- 2019; 9,765 Scorpion sting calls to the poison centers most from Arizona

- In home disease:
  - 33% in the bedroom
  - 24% in the living room
  - 6% in bathroom.

- 276 required antivenom 50% under age 6

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Scorpion Venom: almost 100% cause pain

- Toxic fraction: neurotoxins (polypeptides) specific for ion-channels (Na, K, Ca, Cl):
  - Alpha-type: specific for mammals Na-channels site 3 (membrane potential dependent affinity) →prolongation of action potential.
  - Beta-type: American scorpions, specific for mammals Na-channels (non-membrane potential dependent affinity) →activation at lower potential.

- Non-toxic fraction:
  - Mucopolysaccharides &
  - Enzymes (hyaluronidases & phospholipases),
  - Protease inhibitors,
  - Bioamine(histamine, serotonin)

Geoffrey K. Isbister & Himmataro Saluba Bawskar, Scorpion Envenomation, N. ENGL. J. MED. 371;5; July 31, 2014

P. Gopalakirishnakone, Ed. Scorpion Venoms, Chapter 2, Introduction to scorpion biology& ecology, Springer 2015

Jeffrey Brent et al. Critical Care Toxicology, Yona Amitai, pp22255-2267, Middle East and North African Scorpions, Springer 2017

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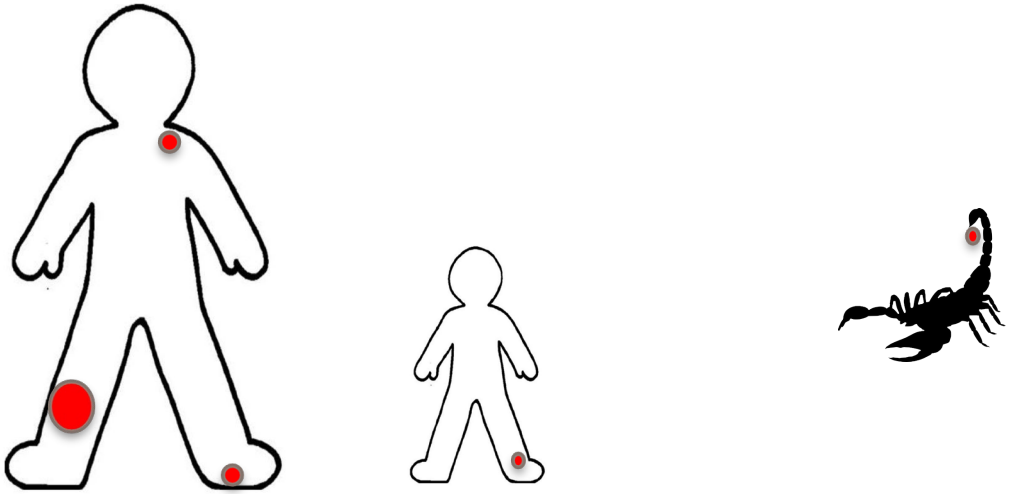
Determinant high risk symptomology:

1. Site of sting, upper thorax and neck
2. Age of the victim, < 5 yrs or elderly
3. Weight, <50 Kg
4. Amount of venom injected (# stings)
5. Health of the victim,



P. Gopalakirishnakone, Ed. Scorpion Venoms, Chapter 2, Introduction to scorpion biology& ecology, Springer 2015

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Symptomology 1:

1. Pain 80-85%
2. Restlessness,
3. Vomiting, Nausea 80-85%
4. Numbness,
5. Inflammation

* These may be local, moderate or severe without chronological order between them.

*Syndrome vs Graded symptomology?

Fatma El-Zahraa A. Abd El-Aziz et al, Toxicological and epidemiological studies of scorpion sting cases and morphological characterization of scorpions (*Leiurusquin questriatus* and *Androctonus crassicauda*) in Luxor, Egypt, Toxicology Reports 2019.
P. Gopalakirishnakone, Ed. Scorpion Venoms, Chapter 2, Introduction to scorpion biology& ecology, Springer 2015

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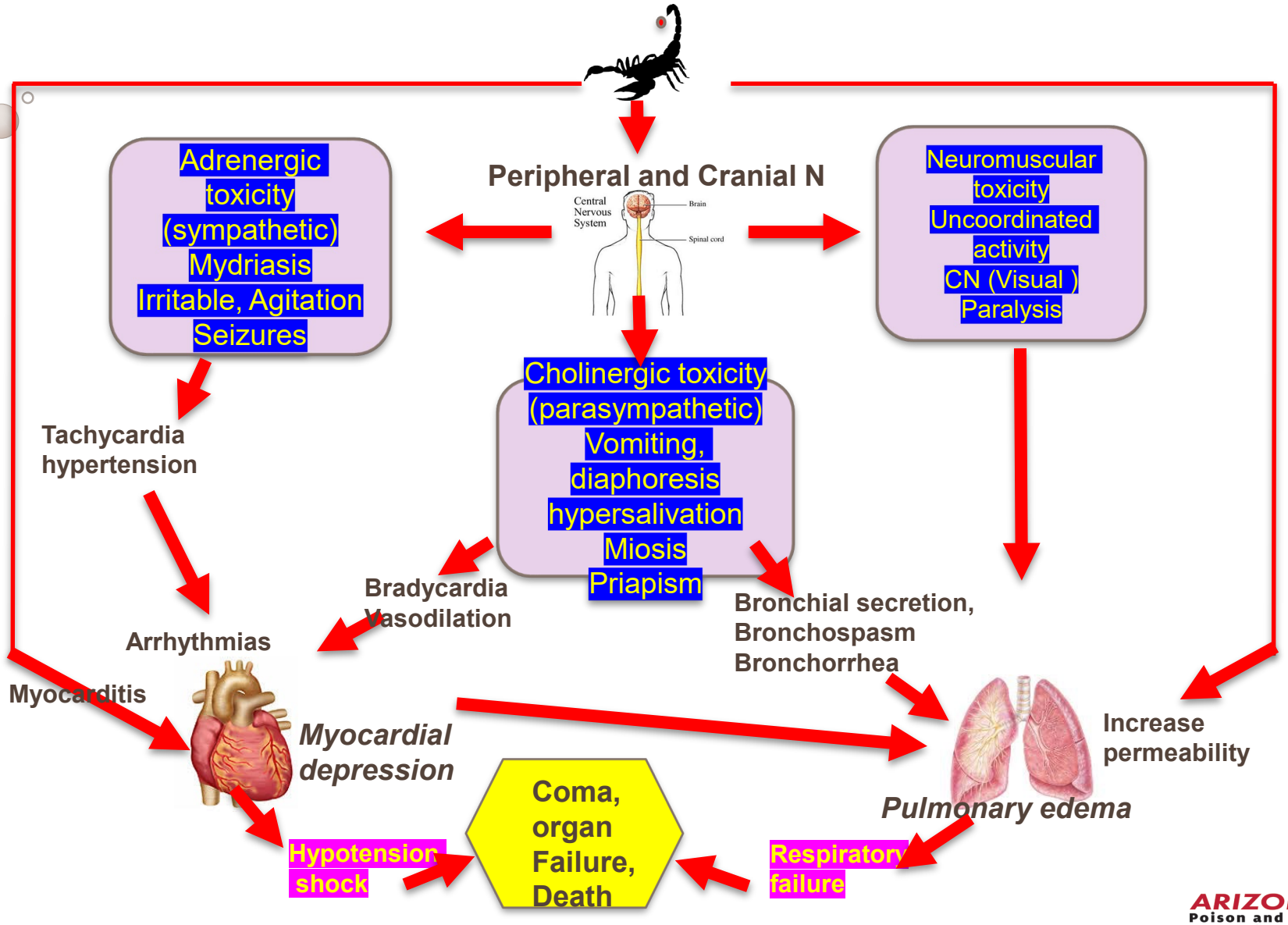
Scorpion venom pathologic effects:



Geoffrey K. Isbister & Himmataro Saluba Bawskar, Scorpion Envenomation, N. ENGL. J. MED. 371;5; July 31, 2014

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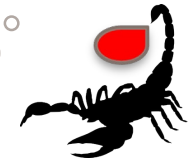
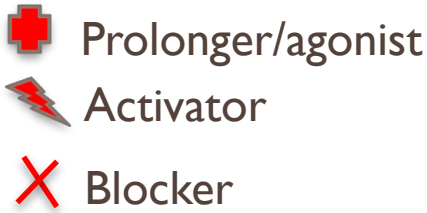
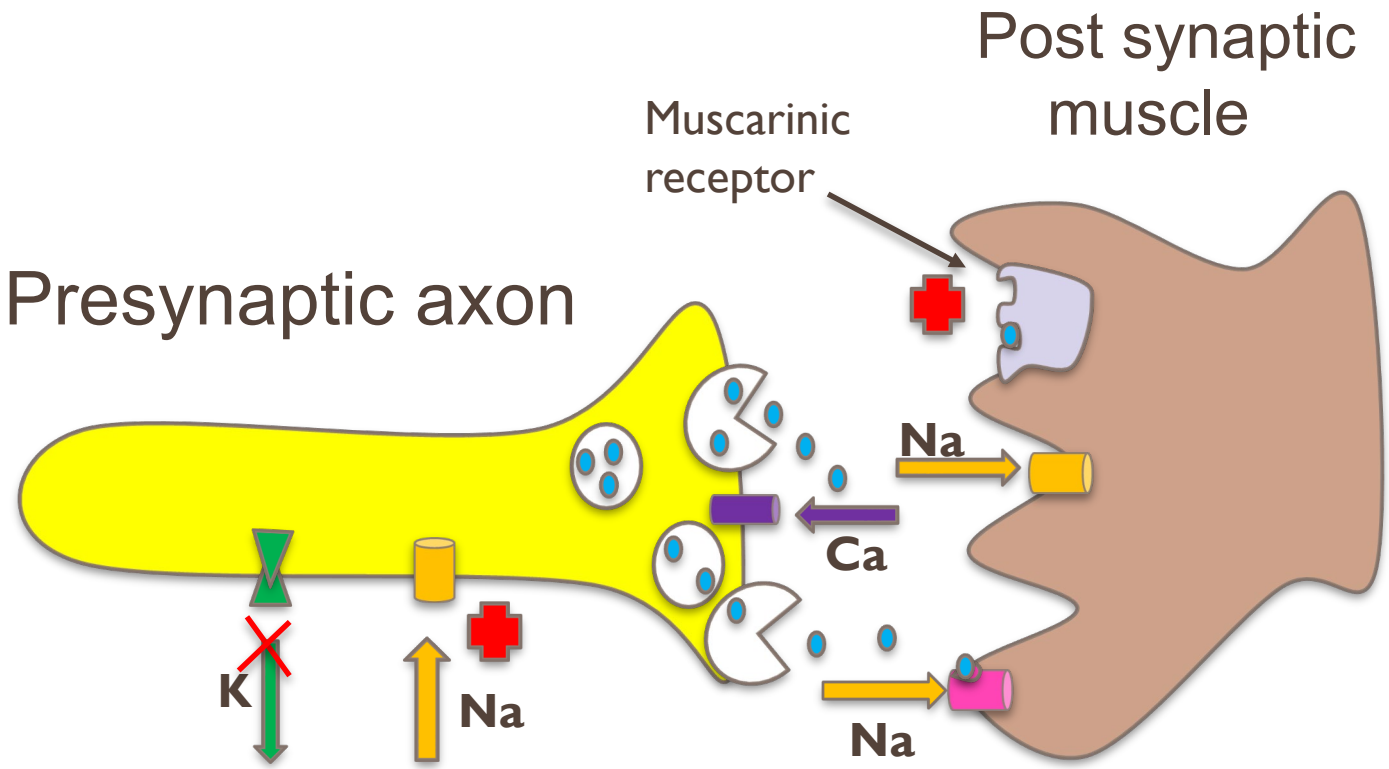
Site of action of scorpion venom:



Alpha toxin: Na Channel prolongers
Beta-toxin: Na Channel activators
Cn-11-toxin: Na Channel blockers
Short scorpion toxin: K channel Blockers
Other toxins: Muscarinic receptor agonist





Bryan G. Fry, et al.The Toxicogenomic Multiverse: Convergent Recruitment of Proteins Into Animal Venoms, Annu. Rev. Geom. Human Genet. 2009. 10: 483-511
http://www.venomdoc.com/new-page-2

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Syndrome vs Gradation

Grade	Description
I	Localized pain and/or paresthesias at the site of envenomation
II	Pain and/or paraesthesias remote from site of envenomation
III	Either cranial nerve or neuromuscular dysfunction
	Cranial nerve dysfunction: tongue fasiculations, hypersalivation, slurred speech or opsoclonus
	Neuromuscular dysfunction: involuntary shaking and jerking of the extremities
IV	Both cranial nerve and neuromuscular dysfunction

Adapted from grading system outlined in Curry et al. [8]

Syndrome:

1: Minimal localized pain and paresthesia
2: Symptoms that spread to the whole extremity
3: Mild nystagmus, involuntary movements, fasciculations, hypersalivation
4: Altered mental status, marked neurological symptoms, salivation, seizure like activity, uncontrollable jerking

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Sign & Symptoms	Scorpion	
Pain	++++ (unable to assess in a child)	
Tachycardia	++++	82%
HTN	++++ ((unable to assess in a child)	49%
Pulse-ox low	++	18%
Fever	++	28%
Involuntary movement/ Hyperactivity	++++	100%
Nystagmus rotary/ Opsoclonus	++++(open the eyelids and check)	96%
Hyperesthesia/ Paranesthesia	++	
Fasciculation	+++	
Sweating	++++	11%
Flaccid paralysis	No	
Secretions hypersalivation	++++	82%
Dysphagia/ dysarthria	++++	
Respiratory, stridor Pulse-ox low Difficulty (PEEP)	++++	17-33%

J Med Toxicol. 2012 Sep; 8(3): 258–262. PMCID: PMC3550169
Published online 2012 May 5. doi: 10.1007/s13181-012-0233-3 PMID: 22562239

Clinical Course of Bark Scorpion Envenomation Managed Without Antivenom

Ayrn O'Connor[B] and Anne-Michelle Ruha

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Duration:

Table 2. Clinical Signs of Neurotoxic Effects, Cumulative Midazolam Dose, Venom Levels, and Adverse Events.*

Variable	Antivenom (N=8)	Placebo (N=7)	P Value
Any sign of neurotoxic effects — no. (%)†			
At baseline	8 (100)	7 (100)	
At 1 hour	4 (50)	7 (100)	0.08
At 2 hours	1 (12)	6 (86)	0.01
At 4 hours	0 (0)	6 (86)	0.001
Abnormal eye movements — no. (%)‡			
At baseline	8 (100)	7 (100)	
At 1 hour	2 (25)	6 (86)	
At 2 hours	1 (12)	5 (71)	
At 4 hours	0 (0)	4 (57)	
Limb thrashing — no. (%)§			
At baseline	8 (100)	7 (100)	
At 1 hour	3 (38)	5 (71)	
At 2 hours	2 (25)	6 (86)	
At 4 hours	0 (0)	4 (57)	
Respiratory compromise — no. (%)			
At baseline	2 (25)	1 (14)	
At 1 hour	1 (12)	1 (14)	
At 2 hours	0 (0)	0 (0)	
At 4 hours	0 (0)	0 (0)	

Boyer et al N. ENGL J Med, May 14, 2009

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Treatment

- Home care
  - Ice
  - Analgesics
- HCF
  - Supportive care
  - Benzodiazepines
  - Opioids
  - Airway management

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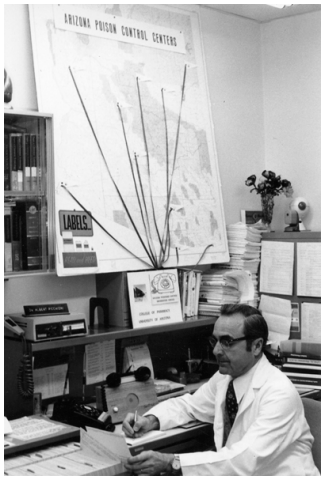
Antivenom:

Albert Picchioni



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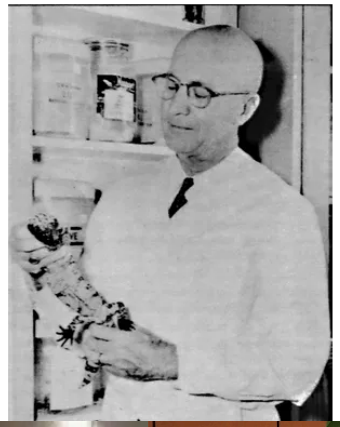
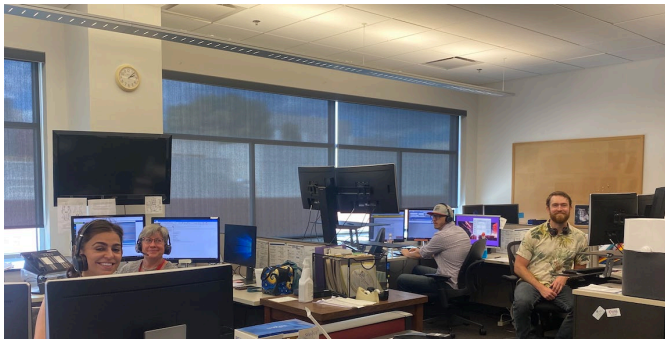
Herbert Stahnke



Findlay E. Russell

John Sullivan

specialists



Leslie Boyer

Contents lists available at SciVerse ScienceDirect

Toxicon

journal homepage: www.elsevier.com/locate/toxicon

ELSEVIER

Review

History of scorpion antivenom: One Arizonan's view☆

Leslie Boyer*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antivenom for Critically Ill Children with Neurotoxicity from Scorpion Stings

Leslie V. Boyer, M.D., Andreas A. Theodorou, M.D., Robert A. Berg, M.D., and Joanne Mallie, R.N., for the Arizona Envenomation Investigators,* Ariana Chávez-Méndez, B.S., Walter García-Ubbelohde, M.D., Stephen Hardiman, Ph.D., and Alejandro Alagón, M.D., Ph.D.

Jude McNally

RDT

RARE DISEASE THERAPEUTICS, INC.

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Treatment:

Antivenom

- Centruroides (Scorpion) Immune $F(ab')_2$ (Equine)
- Initial dose 3 vials
- Additional vial q30-60 minutes if needed
- Average number of vials in the study to resolution 4.2 Vails

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Antivenom: "Anascorp"

- It is produced with the use of scorpions from several southern Mexican species in the same genus as the Arizona variety (C. limpidus limpidus, C.l. tecomanus, C. noxius, and C. suffusus suffusus).
- scorpion-specific F(ab')2 antivenom (Anascorp, Centruroides [scorpion] immune F(ab)2 intravenous [equine]
- 3 vials in 50mls NS as fast as possible (10 min)
- May repeat 1-2 vials 30-60 min after initial bolus

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Symptomology 1:

- Venom distributes form injection site to tissue in 15 minutes.

- Venom concentration is high:

Early : Cardiac overactivity: HTN, Tachycardia

- Site if injection,
- Serum,
- Liver,
- Heart

Late: (hours) Cardiac depression: Hypotension

- Lungs,
- Spleen,
- Pancreas

P. Gopalakirishnakone, Ed. Scorpion Venoms, Chapter 2, Introduction to scorpion biology& ecology, Springer 2015.

Bessalem etal. Bio Distribution of venom of Androctonus, Elsivier; 2002.

Avinash Agrawal, et al.,Scorpion bite, a sting to the heart!, Indian J. Crit. Care Med v. 19(4)2015April

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Lab abnormalities:

- ↑ ALT, AST, ALP, LDH, CK, Trop
- ↑ ,WBC, Transient Glucose, Hyperlipidemia, Angiotensin, Cortisol, K, glucagon
- ↓ Insulin
- EKG depressed or elevated ST, Q waves in I & aVL; Prolonged QTC, Peaked T waves

P. Gopalakirishnakone, Ed. Scorpion Venoms, Chapter 2, Introduction to scorpion biology& ecology, Springer 2015.

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Therapies:

Grade	Clinical Effects	Treatment
1	Local effects only	Analgesia, local anesthesia
2	Autonomic excitation	Antivenom, prazosin
	Agitation and anxiety	Benzodiazepines
3	Pulmonary edema	Admission to intensive care unit, noninvasive or mechanical ventilation, antivenom
	Hypotension and cardiogenic shock	Antivenom, dobutamine
	Severe neuromuscular excitation (associated with *Centruroides* species)	Antivenom, benzodiazepines
4	Multiorgan failure, including coma, seizures, and end-organ damage caused by hypotension	Supportive care, mechanical ventilation, inotropes (e.g., dobutamine), benzodiazepines

Geoffrey K. Isbister & Himmataro Saluba Bawskar, Scorpion Envenomation, N. ENGL. J. MED. 371;5; July 31, 2014

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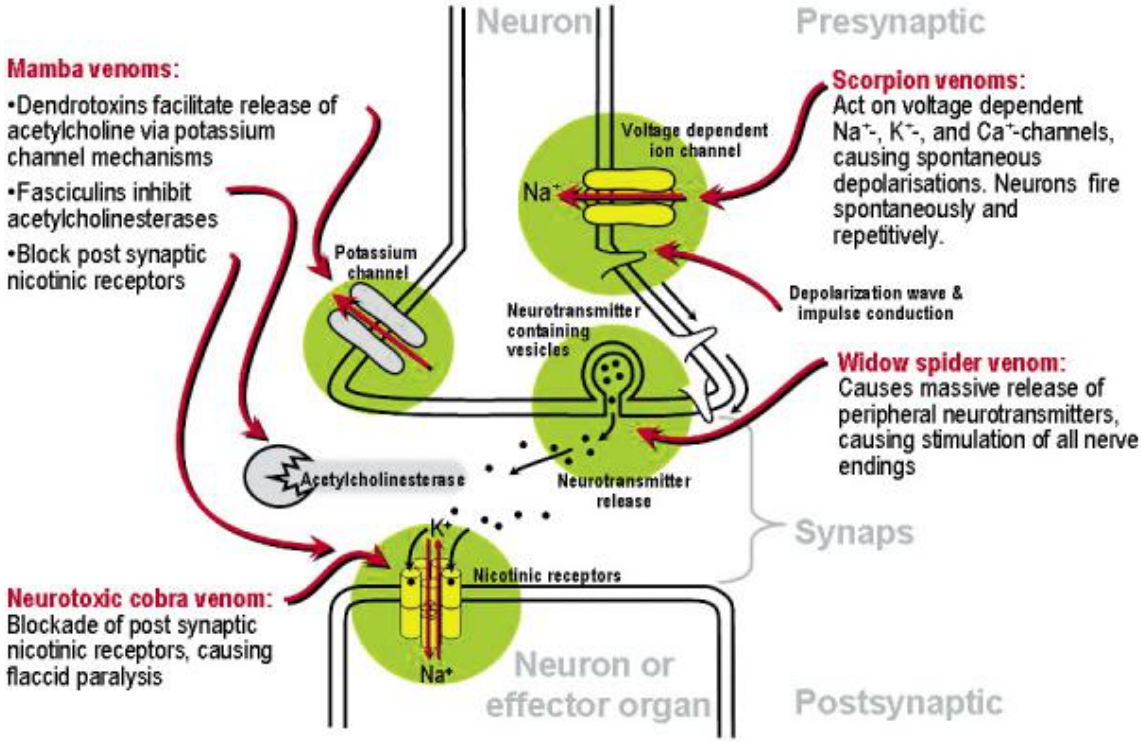
Mechanisms of action of neurotoxic venoms on the peripheral nervous system



Gert Muller, Scorpion sting in southern Africa: diagnosis and management

Distinguishing Scorpion from snake & spider envenoming:

Sign & Symptoms	Scorpion	Spider	Snake
Pain	++++	+	++
Involuntary movement	++++	-	+++
Dysphagia/ dysarthria	++++	+	-
Hyperesthesia/ Paranesthesia	+	++++	-
Fasciculation	++++	++	+
Hyperactivity	++++	++	-
Flaccid paralysis	-	-	++++
Sweating/ hypersalivation	++++	- (@bite)	++
Ptosis/ ophthalmoplegia	++	-	++++

Gert Muller, Scorpion sting in southern Africa: diagnosis and management
SA Journal of CPD CME,Vol.30 , No 10 ,2012.
http://www.cmej.org.za/index.php/cmej/article/view/2545/2580.

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Conclusion

- Patients treated with antivenom exhibited a rapid resolution of symptoms without immediate or delayed hypersensitivity reactions. We recommend broadened availability of antivenom at sites where it is most needed.

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