Tropical dermatology: Venomous arthropods and human skin

Part II. Diplopoda, Chilopoda, and Arachnida

Vidal Haddad, Jr, MD, PhD,^a João Luiz Costa Cardoso, MD,^b Omar Lupi, MD, PhD,^c and Stephen K. Tyring, MD, PhD^d Botucatu, Manaus, and Rio de Janeiro, Brazil; and Houston, Texas

CME INSTRUCTIONS

The following is a journal-based CME activity presented by the American Academy of Dermatology and is made up of four phases:

- 1. Reading of the CME Information (delineated below)
- 2. Reading of the Source Article
- 3. Achievement of a 70% or higher on the online Case-based Post Test
- 4. Completion of the Journal CME Evaluation

CME INFORMATION AND DISCLOSURES

Statement of Need:

The American Academy of Dermatology bases its CME activities on the Academy's core curriculum, identified professional practice gaps, the educational needs which underlie these gaps, and emerging clinical research findings. Learners should reflect upon clinical and scientific information presented in the article and determine the need for further study.

Target Audience:

Dermatologists and others involved in the delivery of dermatologic care.

Accreditation

The American Academy of Dermatology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AMA PRA Credit Designation

The American Academy of Dermatology designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credits*TM. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

AAD Recognized Credit

This journal-based CME activity is recognized by the American Academy of Dermatology for 1 AAD Credit and may be used toward the American Academy of Dermatology's Continuing Medical Education Award.

Disclaimer:

The American Academy of Dermatology is not responsible for statements made by the author(s). Statements or opinions expressed in this activity reflect the views of the author(s) and do not reflect the official policy of the American Academy of Dermatology. The information provided in this CME activity is for continuing education purposes only and is not meant to substitute for the independent medical judgment of a healthcare provider relative to the diagnostic, management and treatment options of a specific patient's medical condition.

Disclosures

Editors

The editors involved with this CME activity and all content validation/peer reviewers of this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Authors

The authors of this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Planners

The planners involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s). The editorial and education staff involved with this journal-based CME activity have reported no relevant financial relationships with commercial interest(s).

Resolution of Conflicts of Interest

In accordance with the ACCME Standards for Commercial Support of CME, the American Academy of Dermatology has implemented mechanisms, prior to the planning and implementation of this Journal-based CME activity, to identify and mitigate conflicts of interest for all individuals in a position to control the content of this Journal-based CME activity.

Learning Objectives

After completing this learning activity, participants should be able to describe the cutaneous manifestations of infections by tremadoes and cestodes and identify appropriate therapy.

Date of release: September 2012

Expiration date: September 2013

© 2012 by the American Academy of Dermatology, Inc. http://dx.doi.org/10.1016/j.jaad.2012.05.028

Technical requirements:

American Academy of Dermatology:

- Supported browsers: FireFox (3 and higher), Google Chrome (5 and higher), Internet Explorer (7 and higher), Safari (5 and higher), Opera (10 and higher).
- JavaScript needs to be enabled.

Elsevier:

Technical Requirements

This website can be viewed on a PC or Mac. We recommend a minimum of:

- PC: Windows NT, Windows 2000, Windows ME, or Windows XP
- Mac: OS X
- 128MB RAM
- Processor speed of 500MHz or higher
- 800x600 color monitor
- Video or graphics card

Sound card and speakers

Provider Contact Information:

American Academy of Dermatology Phone: Toll-free: (866) 503-SKIN (7546); International: (847) 240-1280 Fax: (847) 240-1859

Mail: P.O. Box 4014; Schaumburg, IL 60168

Confidentiality Statement:

American Academy of Dermatology: POLICY ON PRIVACY AND CONFIDENTIALITY

Privacy Policy - The American Academy of Dermatology (the Academy) is committed to maintaining the privacy of the personal information of visitors to its sites. Our policies are designed to disclose the information collected and how it will be used. This policy applies solely to the information provided while visiting this website. The terms of the privacy policy do not govern personal information furnished through any means other than this website (such as by telephone or mail).

E-mail Addresses and Other Personal Information - Personal information such as postal and e-mail address may be used internally for maintaining member records, marketing purposes, and alerting customers or members of additional services available. Phone numbers may also be used by the Academy when questions about products or services ordered arise. The Academy will not reveal any information about an individual user to third parties except to comply with applicable laws or valid legal processes.

Cookies - A cookie is a small file stored on the site user's computer or Web server and is used to aid Web navigation. Session cookies are temporary files created when a user signs in on the website or uses the personalized features (such as keeping track of items in the shopping cart). Session cookies are removed when a user logs off or when the browser is closed. Persistent cookies are permanent files and must be deleted manually. Tracking or other information collected from persistent cookies or any session cookie is used strictly for the user's efficient navigation of the site.

Links - This site may contain links to other sites. The Academy is not responsible for the privacy practices or the content of such websites.

Children - This website is not designed or intended to attract children under the age of 13. The Academy does not collect personal information from anyone it knows is under the age of 13.

Elsevier: http://www.elsevier.com/wps/find/privacypolicy.cws_home/privacypolicy

Members of arthropod classes Chilopoda (centipedes), Diplopoda (millipedes), and Arachnida (spiders and scorpions) cause tissue injury via bites, stings, and/or a release of toxins. A few members of the Acari subclass of Arachnida (mites and ticks) can transmit a variety of infectious diseases, but this review will cover the noninfectious manifestations of these vectors. Dermatologists should be familiar with the injuries caused by these arthropods in order to initiate proper treatment and recommend effective preventative measures. (J Am Acad Dermatol 2012;67:347.e1-9.)

Key words: bite; centipede; envenomation; millipede; mite; scorpion; spider; sting; tick; tropical dermatology.

DIPLOPODA AND CHILOPODA Key points

- Centipedes have fangs that feature poison glands containing metalloproteases; the main symptom of injury is pain
- Millipedes have lateral glands, instead of fangs, which contain cyanide and quinones; the main sign of injury is hyperpigmentation

Centipedes and millipedes belong to the classes Chilopoda and Diplopoda, respectively. Most species of the first class are carnivorous and have a body made of flattened segments covered with chitin with a pair of legs on each segment. The first segment has 2 large tusks originating from the pair of legs, which act as organs of defense and also as a method to capture prey-these animals are able to inject poison from glands contained in the trunk. The venom contains several different enzymes, especially metalloproteases, that have myotoxic, cardiotoxic, and neurotoxic activities. The Scolopendra genus

CAPSULE SUMMARY

- Centipede bites cause pain and erythema via metalloproteases, which can be treated with cold compresses and analgesics.
- Millipede contact can result in erythema and hyperpigmentation via cyanide and quinones, which can be treated with topical alcohol.
- The brown recluse spider bite can produce extensive skin necrosis (ie, loxoscelism via sphingomyelinase D), which can be treated with antivenom and/or sulfones.
- Tarantula bites can cause pain via activation of capsaicin receptor, which can be treated with analgesics.
- Tarantula contact with body bristles can result in dermatitis and conjunctivitis via allergic reactions, which can be treated with topical corticosteroids and oral antihistamines.
- Scorpions stings can produce cutaneous necrosis, bullae, and multisystem failure, including death via tityustoxin, hemicalcin, and a complex mixture of basic proteins, which can be treated with local anesthetics, antiserum, and cardiopulmonary life support.
- Tick bites or burrowing mites can activate an immunoglobulin E—driven T_H2 response with erythema, edema, papules, and pruritus, which can be treated with topical corticosteroids and oral antihistamines.

reaches up to 25 inches long and causes the most serious injuries (Fig 1).¹⁻³

Millipedes are structurally similar to the Chilopoda but they do not have cephalic fangs and have 2 pairs of legs on each body segment (Fig 2). They have lateral glands in each segment that produce cyanide and quinones to repel predators. Occasionally, skin and mucous membrane lesions can be observed in humans.⁴

Injuries in humans caused by Chilopoda (centipedes) are observed sporadically, and pain is the main symptom, with mild erythema and edema at the site of injury (Fig 3). A few case reports have noted the onset of headache, malaise, anxiety, and dizziness. The injury is characterized by 2 points where there is penetration of the fangs. There are rare reports of human deaths caused by the bites of centipedes.^{1,5,6} Secondary infection is a major complicating factor in the envenomation.

Millipedes do not have fangs, but their toxic fluids may be ejected and cause erythema and brown or

Funding sources: None.

From the Department of Dermatology of the Faculdade de Medicina de Botucatu at Univ Estadual Paulista,^a Vital Brazil Hospital, Instituto Butantan and Fundacao de Medicina Tropical do Amazonas,^b Manaus; Universidade Federal do Estado do Rio de Janeiro and Policlinica Geral do Rio de Janeiro,^c Immunology Section, Faculdade de Medicina, Universidade Federal do Rio

de Janeiro, Brazil; and the University of Texas Health Science ${\sf Center}^{\sf d}$ Houston, Texas.

Reprint requests: Stephen K. Tyring, MD, PhD, Center for Clinical Studies, University of Texas Health Science Center, 451 N Texas Ave, Houston, TX 77598. E-mail: styring@ccstexas.com. 0190-9622/\$36.00



Fig 1. Centipede. **A**, The *Scolopendra* genus (Chilopoda) reaches up to 25 inches long and can cause marked envenomation with severe pain. **B**, The fangs of the arthropod. Photograph courtesy of Vidal Haddad, Jr, MD.

black pigmentation in the affected skin (Fig 4).⁷ Injuries most often occur when victims put on their shoes, because millipedes often enter homes seeking dark places to take refuge. The pigmented lesions may persist for months.⁸

When the injury is caused by a centipede, there is spontaneous resolution without complications. The site should be washed with soap and water; cold compresses should be tried. Analgesics are essential for pain control (Table I).⁹

Millipedes cause acute inflammatory lesions without major repercussions. The immediate use of alcohol or ether on the site is encouraged, because it could dissolve toxins.⁴ Eye injuries should be washed, and the patient should be referred to an ophthalmologist, because severe envenomation can result in blindness.¹⁰

ARACHNIDA

Spiders

Key points

- Brown recluse spiders can cause extensive skin necrosis and acute renal failure via sphingomyelinase D; therapy is with antivenom (antivenin) and/or sulfones
- Tarantulas can release bristles resulting in dermatitis and conjunctivitis or can bite causing pain via activation of the capsaicin



Fig 2. Millipede. Diplopoda can cause lesions in humans with initial inflammation and marked pigmentation. Photograph courtesy of Vidal Haddad, Jr, MD.



Fig 3. Centipede. Envenomation by Chilopoda. Note the erythema and the small perforation. Photograph courtesy of Vidal Haddad, Jr, MD.

receptor; treatment includes the use of oral antihistamines and topical steroids

Spiders that cause major injuries in humans belong to the genus *Atrax* (the funnel web spider of Australia, of the Orthognata infraorder), genus *Phoneutria* (armadeira spider), genus *Latrodectus* (the black widow spider), and the genus *Loxosceles* (the brown recluse spider; Fig 5). The first 3 spiders cause serious injuries with a risk of death, but the toxins are primarily neurotoxic, and little or no change is noted in the skin of a local sting.¹⁻³

Brown recluse spiders, however, cause exuberant skin manifestations. These spiders live in dark and dusty places, such as garages and warehouses, being cosmopolitan (with the exception of cold places).¹⁻³ The venom is capable of causing extensive skin necrosis, and in about 5% of cases hemolysis can cause acute renal failure, especially by the action of sphingomyelinase D, an enzyme that destabilizes the vessel walls and membranes of red blood cells.^{11,12}

Loxosceles spiders are timid animals and run away when in danger, only biting when pressed against the victim's body or handled without care. The

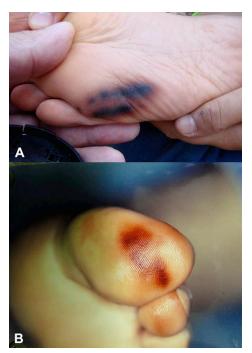


Fig 4. Millipede. **A** and **B**, Classic late hyperpigmentation after the crushing of a millipede in a shoe. Photograph courtesy of Vidal Haddad, Jr, MD.

manifestations begin with a burning sensation or can even be painless. About 6 hours later, an ischemic area is clearly delineated with cyanotic, pale, and erythematous variations of color in the affected area—a characteristic sign known as a marble plaque (Fig 6). During this period, it is possible to observe blisters with a hemorrhagic content, and the injury is very painful because of local ischemia. The plaque evolves to frank necrosis in about 1 week, and an eschar remains firmly attached for up to 3 weeks (Fig 7). At this stage, there is no more pain. When the eschar finally falls off, a large and deep ulcer can be seen, typically with a granular base and elevated edges. In this phase, confusion with other ulcers is common, especially with cutaneous leishmaniasis (Fig 8). The ulcer healing is slow and resolves after months.^{13,14}

The differential diagnosis of necrotic araneism depends on the phase of the injury: in the initial envenomation, the differential diagnosis includes cellulitis, erysipelas, and necrotizing fasciitis. In the necrotic phase, there may be confusion with skin necrosis caused by other animals (eg, snakes), drugs, and bacteria. At the ulcer stage, it is necessary to differentiate from other chronic ulcers, such as mucocutaneous leishmaniasis, paracoccidioidomycosis, sporotrichosis, cutaneous tuberculosis, and cutaneous squamous cell carcinoma. Histopathology allows for the correct diagnosis, because in cutaneous loxoscelism there is fibrosis and neovascularization; these alterations are not found in granulomatous processes. $^{15}\,$

Treatment of cutaneous loxoscelism also depends on the phase of the injury: early diagnosis allows for the reduction of the clinical manifestations by use of antivenom against the toxins of the spider, but it is not used in all countries. An alternative is to use sulfone (100-300 mg daily) to prevent the diapedesis of neutrophils to the point of ischemia and reduce necrosis. Corticosteroid use is controversial. In later stages with large ulcers, it is possible to use skin grafts for repair.¹⁶⁻¹⁹

Some Theraphosidae spiders (tarantulas) can liberate body bristles (especially of the abdomen) and cause an irritant dermatitis and conjunctivitis in humans.^{20,21} Tarantula bites can cause pain via activation of the capsaicin receptor.²² These injuries are common in persons that have contact with the spiders (eg, biologists). The lesions are highly pruriginous, but can be treated with topical corticosteroids and oral antihistamines (Figs 9 and 10).²³

Scorpions

Key points

- Most scorpion stings cause cardiac arrhythmias and acute pulmonary edema without significant skin changes; the venom of *Tityus serrulatus*, containing tityustoxin, is the most potent
- The sting of *Hemiscorpius lepturus*, found in Iraq and Afghanistan, can result in extensive skin necrosis and neurotoxic symptoms caused by hemicalcin
- All severe stings should be treated with antiscorpion serum; anesthetics without vasoconstrictors can be used for local pain

Scorpions are dangerous animals that are present in all tropical and temperate regions and can cause death in children and debilitated individuals⁴ (Fig 11). Their venom causes intense stimulation of the autonomic nervous system, resulting in cardiac arrhythmias and acute pulmonary edema. In the majority of the scorpions' stings, there are no significant skin manifestations⁴ (Fig 12). Some species, however, can cause necrotic and purpuric plaques that can ulcerate or form bullae (Fig 13).

There are 6 families of scorpions, but almost all scorpions dangerous to humans are in the Buthidae family.²⁴ The most common genus in this family in the United States is *Centruroides* spp.²⁵ The most scorpion stings reported in humans are from the Tityinae subfamily of Buthidae, which is found in Brazil and Venezuela. The venom of *Tityus serrulatus* is the most potent and results from

Arthropod class	Injurious components in venom/ mechanism of injury	Signs and symptoms	Management
Chilopoda (centipedes)	Metalloproteases (bite)	Erythema, edema, and pain	Wash site, cold compresses, and analgesics
Diplopoda (millipedes)	Cyanide and quinones (contact)	Erythema, pigmentation, and blindness	Wash site and topical alcohol
Arachnida (spiders)	Brown recluse— sphingomyelinase D (bite); tarantula—activation of capsaicin receptor (bite), allergic response (contact)	Brown recluse—ischemia, marble plaque, bullae, necrosis, eschar, and ulcer; tarantula—dermatitis, conjunctivitis, pain, and pruritus	Brown recluse—antivenom and sulfone; tarantula—topical corticosteroids and oral antihistamines
Arachnida (scorpions)	Tityustoxin, hemicalcin, and a complex mixture of basic proteins (sting)	Erythema, purpura, bullae, necrosis, ulcers, pain, nausea, vomiting, coughing, wheezing, heart failure, pulmonary edema, tremors, shock, and death	Local anesthetics, antiserum, and cardiopulmonary life support
Arachnida (mites and ticks)	Antigen activation of immunoglobulin E—driven T _H 2 response (contact)	Erythema, edema, papules, pruritus, and secondary bacterial infection	Topical corticosteroids, oral antihistamines, and antibiotics for infections

Table I. Management of injuries from Diplopoda, Chilopoda, and Arachnida



Fig 5. Brown recluse spider. *Loxosceles reclusa*, one of the species of brown recluse spider. Photographs courtesy of Vidal Haddad, Jr, MD.

tityustoxin. This toxin binds to voltage-dependent sodium and potassium ion channels, causing sialor-rhea, lacrimation, and rhinorrhea.²⁶

There are many reports of scorpion stings in American troops stationed in Iraq and Afghanistan.²⁷ The scorpion reported to produce the most cutaneous injury in this region is *Hemiscorpius lepturus*. The sting of this scorpion can produce erythema, purpura, bullae, necrosis, and ulcers (Fig 13).²⁸ A novel toxin from *H lepturus* is hemicalcin, which is active on ryanodine-sensitive calcium channels and produces neurotoxic symptoms.²⁹

Scorpion venom is a complex mixture of basic proteins of low molecular weight with small amounts of amino acids and salts, without hemolytic, protease, cholinesterase, or phospholipase activities or the consumption of fibrinogen. The site of the sting is sometimes detected with difficulty, and only mild edema and erythema can be observed with or



Fig 6. A and **B**, The marble plaque: a characteristic sign of the ischemia and necrosis caused by the envenomation by *Loxosceles* spiders. Photograph courtesy of Vidal Haddad, Jr, MD.

without sweating and horripilation. In addition, there may be nausea, vomiting, and colic type abdominal pain along with rhinorrhea, coughing, sneezing, and wheezing. Additional changes can occur, such as tachycardia or bradycardia (alternate or not), hypo- or hypertension, arrhythmias, chest tightness, heart failure, acute pulmonary edema, and



Fig 7. Brown recluse spider. An eschar is the second step in the development of the typical envenomation by *Loxosceles*. Photograph courtesy of Vidal Haddad, Jr, MD.



Fig 8. Brown recluse spider. A deep ulcer with infiltrated edges is the final evolution of the brown spider envenomation. This ulcer can be confused with granulomatous and neoplastic diseases. Photograph courtesy of Vidal Haddad, Jr, MD.



Fig 9. Tarantulas (Theraphosidae) are large spiders that can be dangerous, but the majority of the species do not cause envenomation. They can liberate bristles of the abdomen, which cause dermatitis in humans. Photograph courtesy of Vidal Haddad, Jr, MD.

shock, the latter being the most severe manifestations of scorpion sting.³⁰ Envenomation can cause tremors, psychomotor agitation, and myoclonus.



Fig 10. Tarantula dermatitis. These are the hands of a biologist who works in research on Theraphosidae spiders and who presented with erythematous and pruritic papules caused bristles on the skin. Photograph courtesy of Vidal Haddad, Jr, MD.



Fig 11. Scorpions are dangerous animals that cause severe envenomation in humans (especially in children). This specimen is a *Tityius serrulatus*, a Brazilian (devil) yellow scorpion. Photograph courtesy of Vidal Haddad, Jr, MD.

Severe injuries present with systemic manifestations that are quite obvious and intense. Profuse and frequent vomiting is one symptom, and the intensity and frequency of vomiting is a sensitive premonitory sign of the severity of poisoning. Other symptoms include widespread and abundant sweating. Patients typically complain of cold, goose flesh, pallor, severe agitation alternating with drowsiness, hypothermia, tachycardia or bradycardia, extrasystole, hypertension, hyperpnea, tremors, and muscle spasms. There may be progression to cardiocirculatory and pulmonary edema, which are frequent causes of death. Treatment includes neutralizing the circulating toxin as quickly as possible, combating the symptoms of envenomation, and supporting the vital conditions of the patient.³¹ Local pain can be combated with anesthetics without vasoconstrictors, lidocaine 2% or bupivacaine 0.5% injected into the sting site, or in the form of regional blocking. The recommended dose is 3 to 4 mL for adults and 1 to 2 mL in children and



Fig 12. Scorpion sting. The site of a scorpion sting usually shows no important skin alterations. There is only a mild local inflammation. Photograph courtesy of João Luiz Costa Cardoso, MD.



Fig 13. Bullae from the sting of a scorpion (*Hemiscorpius lepturus*) in an American soldier in Iraq. Photograph courtesy of John Paul Trafeli, MD, and James W. Steger, MD, Department of Dermatology, Naval Medical Center, San Diego, CA.

may be repeated up to 3 times at intervals of 30 to 60 minutes.

Antiscorpion serum is indicated in all severe cases.³¹⁻³³ In 2011, the FDA approved the first treatment specifically for scorpion stings, ie, *Centruroides* (Scorpion) Immune F(ab')2 Injection (trade name, Anascorp, Rare Disease Therapeutics, Inc, Franklin, TN). The most feared complications of scorpion injuries are cardiac arrhythmias, shock, and pulmonary edema that can sometimes lead to death, even with proper medication and acute care—especially in children.

Ticks and mites

Key points

- The "comet" sign is classic for tick or mite bites; pruritus may result from hypersensitivity or foreign body reactions
- An immunoglobulin E-driven T_H2 response to mites can manifest as pruritic papules;



Fig 14. A tick on human skin looking for a place to start its blood meal. Photograph courtesy of Vidal Haddad, Jr, MD.



Fig 15. The "comet" sign. Ticks spread themselves after they obtain victims by hiding in low shrubs. Photograph courtesy of João Luiz Costa Cardoso, MD.

mite infestations can be treated with topical permethrin and/or oral ivermectin

Some arthropods that cause skin lesions are commonly mistaken for venomous animals. Ticks (Arachnida class, Acari subclass, and Ixodida order) can be a vector for agents of a variety of diseases, including Rocky Mountain spotted fever, Colorado tick fever, tick paralysis, tularemia, tick-borne relapsing fever, babesiosis, ehrlichiosis, and Lyme disease¹⁻³ (Fig 14). They also can provoke severe local reactions through hypersensitivity and by foreign body reactions precipitated by the persistence of fragments of mouthparts at the bite. These reactions are extremely pruritic and become infected easily in predisposed individuals because of intense erythema and edema. There is a classic sign of tick's (or mite's) or their nymph's bites (ie, the "comet" sign, where many bites spread from initial points in the distal areas of the ankles and legs, with a cone distribution (Fig 15).³⁴ This occurs by the ascending movement of 1 or more ticks.

Mites are also members of the Acari subclass and include vectors of various infectious diseases, such as scrub typhus and rickettsialpox. The most common cutaneous manifestations of mites, such as chiggers, scabies, and demodex, are pruritic papules caused by an immunoglobulin E-driven T_H2 response and which are seen worldwide.³⁵ Mite infestations may be treated with topical agents, mainly 5% permethrin or oral ivermectin.³⁶ Although scabies is more prevalent, more frequently associated with secondary staphylococcal and streptococcal infections,³⁷ and often more severe in tropical parts of the world, the cutaneous manifestations are very similar to those seen in temperate countries and therefore will not be discussed in this review.

Although a few members of the Acari subclass of arthropods transmit infectious diseases, the majority of Diplopoda, Chilopoda, and Arachnida cause tissue injury via release of toxins or by burrowing into the skin. It is important for dermatologists to be familiar with these arthropods and the injuries they cause in order to initiate proper therapy and to advise the patient on effective prevention.

REFERENCES

- 1. Undheim EA, King GF. On the venom system of centipedes (Chilopoda), a neglected group of venomous animals. Toxicon 2011;57:512-24.
- 2. Goddard J. Arthropods of medical importance. Boca Raton (FL): CRC Press; 1993. p. 480.
- Cardoso JLC, Wen FH, França FOS, Malaque CMS, Haddad V Jr. Animais peçonhentos no Brasil: identificação, clínica e terapêutica (Venomous animals in Brazil: biology, clinic and therapeutic). São Paulo: Editora Roca; 2008. p. 288.
- Haddad V Jr, Cardoso JLC. Acidentes provocados por Millepede com manifestações dermatológicas: relatos de doiscasos. An Bras Dermatol 2000;75:471-4.
- 5. Malta MB, Lira MS, Soares SL, Rocha GC, Knysak L, Martins R, et al. Toxic activities of Brazilian centipede venoms. Toxicon 2008;52:255-63.
- Yildiz A, Biceroglu S, Yakut N, Bilir C, Akdemir R, Akilli A. Acute myocardial infarction in a young man caused by centipede sting. Emerg Med J 2006;23:e30.
- De Capitani EM, Vieira RJ, Bucaretchi F, Fernandes LC, Toledo AS, Camargo AC. Human accidents involving *Rhinocricus spp.*, a common millipede genus observed in urban areas of Brazil. Clin Toxicol (Phila) 2011;49:187-90.
- Lima CA, Cardoso JL, Magela A, Oliveira FG, Talhari S, Haddad V Jr. Exogenous pigmentation in toes feigning ischemia of the extremities: a diagnostic challenge brought by arthropods of the Diplopoda class ("millipedes"). An Bras Dermatol 2010;85: 391-2.
- Chaou CH, Chen CK, Chen JC, Chiu TF, Lin CC. Comparisons of ice packs, hot water immersion and analgesia injection for the treatment of centipede envenomations in Taiwan. Clin Toxicol (Phila) 2009;47:659-62.

- 10. Hudson BJ, Parsons GA. Giant millipede "burns" and the eye. Trans R Soc Trop Med Hyg 1997;91:183-5.
- 11. Tavares FL, Peichoto ME, Rangel Dde M, Barbaro KC, Cirillo MC, Santoro ML, et al. Loxosceles gaucho spider venom and its sphingomyelinase fraction trigger the main functions of human and rabbit platelets. Hum Exp Toxicol 2011;30: 1567-74.
- Lee S, Lynch KR. Brown recluse spider (*Loxosceles reclusa*) venom phospholipase D (PLD) generates lysophosphatidic acid (LPA). Biochem J 2005;391:317-23.
- Pernet C, Dandurand M, Meunier L, Stoebner PE. Necrotic arachnidism in the south of France: two clinical cases of loxoscelism. Ann Dermatol Venereol 2010;137:808-12.
- 14. Manriquez JJ, Silva S. Cutaneous and visceral loxoscelism: a systematic review. Rev Chilena Infectol 2009;26:420-32.
- Robb CW, Hayes BB, Boyd AS. Generalized vasculitic exanthema following *Loxosceles reclusa* envenomation. J Cutan Pathol 2007;34:513-4.
- de Roodt AR, Estevez-Ramirez J, Litwin S, Magana P, Olvera A, Alagon A. Toxicity of two North American Loxosceles (brown recluse spiders) venoms and their neutralization by antivenoms. Clin Toxicol (Phila) 2007;45:678-87.
- 17. Elston DM, Miller SD, Young RJ 3rd, Eggers J, McGlasson D, Schmidt WH, et al. Comparison of colchicines, dapsone, triamcinolone, and diphenhydramine therapy for the treatment of brown recluse spider envenomation: a double-blind, controlled study in a rabbit model. Arch Dermatol 2005;141: 595-7.
- Hobbs GD, Anderson AR, Greene TJ, Yealy DM. Comparison of hyperbaric oxygen and dapsone therapy for Loxosceles envenomation. Acad Emerg Med 1996;3:758-61.
- Tambourgi DV, Goncalves-de-Andrade RM, van den Berg CW. Loxoscelism: from basic research to the proposal of new therapies. Toxicon 2010;56:1113-9.
- 20. Ratcliffe BC. A case of tarantula-induced papular dermatitis. J Med Entomol 1977;13:745-7.
- 21. Rutzen AR, Weiss JS, Kachadoorian H. Tatantula hair ophthalmia nodosa. Am J Ophthalmol 1993;116:381-2.
- Siemens J, Zhou S, Piskorowski R, Nikai T, Lumpkin EA, Basbaum AL, et al. Spider toxins activate the capsaicin receptor to produce inflammatory pain. Nature 2006;444: 208-12.
- 23. Hered RW, Spaulding AG, Sanitato JJ, Wander AH. Ophthalmia nodosa caused by tarantula hairs. Ophthalmology 1988;95: 166-9.
- Mesquita MB, Moraes-Santos T, Moraes MF. Centrally injected tityustoxin produces the systemic manifestations observed in severe scorpion poisoning. Toxicol Appl Pharmacol 2003;187: 58-66.
- 25. Forrester MB, Stanley SK. Epidemiology of scorpion envenomations in Texas. Vet Hum Toxicol 2004;46:219-21.
- Rogowski RS, Krueger BK, Collins JH, Blaustein MP. Tityustoxin K alpha blocks voltage-gated noninactivating K+ channels and unblocks inactivating K+ channels blocked by alpha-dendrotoxin in synaptosomes. Proc Natl Acad Sci USA 1994;91:1475-9.
- 27. Shiau DT, Sanders JW, Putnam SD, Buff A, Beasley W, Tribble DR, et al. Self-reported incidence of snake, spider and scorpion encounters among deployed U.S. military in Iraq and Afghanistan. Mil Med 2007;172:1099-102.
- Radmanesh M. Cutaneous manifestations of the *Hemiscorpius lepturus* sting: a clinical study. Int J Dermatol 1998;37: 500-7.
- 29. Shahbazzadeh D, Srairi-Abid N, Feng W, Ram N, Borchani L, Ronjat M, et al. Hemicalcin, a new toxin from the Iranian

scorpion Hemiscorpius lepturus which is active on ryanodinesensitive Ca^{2+} channels. Biochem J 2007;404:89-96.

- 30. Rahav RG, Weiis T. Scorpion sting-induced pulmonary edema: scintigraphic evidence of cardiac dysfunction. Chest 1990;97: 1478-80.
- Hiller K, Jarrod MM, Franke HA, Degan J, Boyer LV, Fox FM. Scorpion antivenom administered by alternative infusions. Ann Emerg Med 2010;56:309-10.
- 32. Brown N, Landon J. Antivenom: the most cost-effective treatment in the world? Toxicon 2010;55:1405-7.
- 33. Tuuri RE, Reynolds S. Scorpion envenomation and antivenom therapy. Pediatr Emerg Care 2011;27:667-72.
- Bellido-Blasco JB, Arnedo-Pena A, Valcuende F. Comet sign (and other) in Pyemotes dermatitis. Emerg Infect Dis 2009;15:503-5.
- 35. Walton SF. The immunology of susceptibility and resistance to scabies. Parasite Immunol 2010;32:532-40.
- 36. Monsel G, Chosidow O. Management of scabies. Skin Therapy Lett 2012;17:1-4.
- 37. Mahe A. Bacterial skin infections in a tropical environment. Curr Opin Infect Dis 2001;14:123-6.