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ANIMAL BITES AND STINGS WITH ANAPHYLACTIC POTENTIAL

John H. Klotz, PHD,* Stephen A. Klotz, MD,† and Jacob L. Pinnas, MD†

*Department of Entomology, University of California, Riverside, Riverside, California and †Department of Medicine, University of Arizona School of Medicine, Tucson, Arizona

Reprint Address: John H. Klotz, PHD, Department of Entomology, University of California, Riverside, CA 92521

□ **Abstract—Anaphylaxis to animal bites and stings poses a significant medical risk of vascular or respiratory reactions that vary according to the patient's response and nature of the insult. Emergency Physicians frequently see patients who complain of an allergic reaction to an animal bite or sting. Although Hymenoptera stings, specifically those of wasps, bees, and hornets, account for the majority of these cases, other invertebrates and vertebrates are capable of causing allergic reactions and anaphylaxis. Many of the causative animals are quite unusual, and their bites and stings are not commonly appreciated as potential causes of anaphylaxis. We conducted a literature review to identify documented reports of anaphylaxis and anaphylactoid reactions to animal bites and stings. This summary is meant to heighten awareness of the diversity of animals that may cause anaphylaxis, hopefully leading to more rapid diagnosis and treatment of this dangerous condition. A diverse group of animals was found whose bites and stings cause anaphylaxis and anaphylactoid reactions. Some case summaries are presented. A potentially life-saving plan is to direct patients to proper follow-up care to prevent a future life-threatening reaction, including: prescribing epinephrine and antihistamines with proper instructions for their use; referral to an allergist to determine if skin testing, radioallergosorbent test, and immunotherapy are indicated; and reporting the case to state or local Poison Control Centers. In some cases it may be helpful to consult an entomologist or a pest control service for help in identification and elimination of certain offenders. © 2007 Elsevier Inc.**

□ **Keywords—anaphylaxis; anaphylactoid; systemic reactions; insect venoms; animal venoms; bites and stings**

INTRODUCTION

Historical Perspective and Definition

Anaphylaxis, meaning "without protection," was coined in the early 1900s by Richet, who, with Portier, discovered the phenomenon while conducting experiments on venom from the Portuguese man-of-war and sea anemone. They exposed dogs to small doses of venom and then, several weeks later, repeated the injection on these healthy dogs. Within seconds of the second injection the dogs became ill, and shortly thereafter, died. Richet and Portier proposed two factors that were necessary and sufficient to cause an anaphylactic reaction: "increased sensitivity to a poison after previous injection of the same poison, and an incubation period necessary for this state of increased sensitivity to develop" (1).

Modern definitions of anaphylaxis reflect our more advanced understanding of its physiological basis: an acute systemic allergic reaction occurring as a result of the release of chemical mediators after an immunologic reaction, typically IgE-mediated. Since its discovery, numerous causative agents in addition to venom have been implicated, including anaphylactic reactions to foods, medications, latex, vaccines, allergenic extracts, hormones, animal or human proteins, colorants, polysaccharides, and exercise (2). Insect sting allergies, however, are the only form of anaphy-

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laxis for which allergen-specific immunotherapy is currently available (3).

Clinically, anaphylactic or anaphylactoid (resembling anaphylaxis but mechanism unknown) reactions can take almost any form but most commonly present with urticaria and angioedema, followed by respiratory distress, dizziness, syncope, and shock. In some, death may occur (2,4). Gastrointestinal manifestations may accompany any of the above signs and symptoms. Toxic reactions may be caused by multiple stings, up to hundreds or thousands, and vary with the toxins introduced and the makeup and size of the individual. Therapy for anaphylaxis includes H_1 and H_2 antihistamines and epinephrine by injection, with steroids for the more persistent or refractory cases (5).

Hymenoptera stings are one of the most common causes of anaphylaxis (4). Anaphylactic reactions to bites and stings of other arthropods are less common, and even fewer have been reported for non-arthropod groups (6). Taken together, these organisms pose a significant medical risk.

METHODS

Literature Review

This article summarizes the various cases that have been reported of anaphylactic and anaphylactic-like reactions to animal bites and stings. A MEDLINE search was conducted to find these reports employing a keyword search with OVID, using the following terms: anaphylaxis, anaphylactoid, systemic reactions, insect venoms, and animal venoms. The search was limited to articles in English from 1966–2005. Secondary sources of information on anaphylaxis were identified from references in these articles and also were included in this review.

The cases of anaphylaxis are categorized taxonomically by the offending organisms in Tables 1 and 2. Also shown is evidence for an IgE-mediated basis: i.e., (+) in vivo skin test, or (+) in vitro RAST (radioallergosorbent test) reactivity, and the pertinent references. Case presentations that to date lack evidence for IgE-mediated reactivity are listed as anaphylactic-like in Table 3. Some cases are not covered in the text but are listed in the

Table 1. Anaphylactic Reactions to Insect Bites and Stings

Scientific Nomenclature (Common Name)*	Evidence for IgE Mediation†		
	In Vivo Tests	In Vitro Tests	References
Phylum: Arthropoda			
Class: Insecta			
Order: Hymenoptera			
Family: Vespidae			
Genus: *Vespula* (ground-nesting yellowjackets)	+	+	8–12
Dolichovespula (aerial-nesting yellowjackets)	+	+	11,12
Vespa (hornets)	+	+	8,23
Polistes (paper wasps)	+	+	19,20
Family: Apidae			
Genus: *Apis* (honey bees)	+	+	11,13,14
Bombus (bumble bees)	+	+	24
Family: Formicidae			
Genus: *Solenopsis* (fire ants)	+	+	16,17
Pogonomyrmex (harvester ants)	+	+	21,22
Tetramorium	+		31
Myrmecia (bulldog ants)	+	+	32–35
Pachycondyla (Chinese needle and Samsum ants)	+	+	37–41
Formica (wood ants)	+	+	43
Order: Hemiptera			
Family: Reduviidae			
Genus: *Triatoma* (kissing bugs)	+	+	44–46
Order: Diptera			
Family: Tabanidae			
Genus: *Chrysops* (deer flies)	+	+	52,54
Family: Simuliidae (black flies)	+	+	48
Culicidae (mosquitoes)	+		55
Muscidae			
Genus: *Glossina* (tsetse flies)		+	60
Order: Lepidoptera			
Family: Notodontidae			
Genus: *Thaumetopoea* (pine processionary caterpillars)	+	+	62–64

* Common names in parentheses were reported to induce the reaction.
† Empty spaces indicate no evidence for IgE mediation.

Table 2. Anaphylactic Reactions to Bites and Stings of Invertebrates (Non-insect) and Vertebrates

Scientific Nomenclature (Common Name)*	Evidence for IgE Mediation†		
	In Vivo Tests	In Vitro Tests	References
Phylum: Arthropoda			
Class: Arachnida			
Order: Acari			
Family: Ixodidae			
Genus: *Ixodes holocyclus* (Australian paralysis ticks)	+	+	67
Ixodes pacificus (western black-legged ticks)		+	69,70
Ixodes ricinus		+	72
Rhiphicephalus		+	71
Family: Argasidae			
Genus: *Argas* (pigeon ticks)	+	+	73,74
Order: Scorpiones			
Genus: *Centruroides* (common striped scorpions)	+	+	77,78
Phylum: Cnidaria			
Class: Scyphozoa			
Genus: *Chrysaora* (sea nettles)		+	87,88
Phylum: Chordata			
Class: Reptilia			
Order: Squamata			
Family: Viperidae			
Genus: *Crotalus* (rattlesnakes)	+		93
Vipera (vipers)	+	+	94,95
Family: Elapidae			
Genus: *Hemachatus* (rinkhals)		+	100
Class: Mammalia			
Order: Rodentia			
Family: Muridae			
Genus: *Rattus* (rats)	+	+	106,107
Mus (mice)	+	+	107,109
Gerbillus (gerbils)	+		110
Phodopus (hamsters)	+	+	111,113

* Common names in parentheses were reported to induce the reaction.
† Empty spaces indicate no evidence for IgE mediation.

tables along with references numbered according to their taxonomic category. Common toxic reactions that do not resemble anaphylaxis are not included in this review (e.g., spider envenomations).

RESULTS AND DISCUSSION

Anaphylactic and Anaphylactic-like Reactions to Insects (Tables 1 and 3)

Hymenoptera (bees, wasps, and ants). Of the invertebrates, insects, particularly Hymenoptera, most commonly cause anaphylaxis. In stinging bees, wasps, and ants, the ovipositor of females has been modified into a stinger. This venom delivery system is a powerful defense against vertebrates, which, in the case of humans, may be life-threatening when the individual is sensitized to allergens in the venom.

About 1% of children and 3% of adults are reported to have had systemic allergic reactions, but these may be underestimates due to inadequate data (7). The species most responsible for these allergic reactions in the United States are yellowjackets (*Vespula* and *Dolichovespula*) and honey bees (*Apis*), followed by fire ants (*Solenopsis*) and paper wasps (*Polistes*) (8–20). Harvester ants (*Pogonomyrmex*), the introduced European hornet (*Vespa crabro*), bumble bees (*Bombus*), and sweat bees (Halictids) are of lesser importance (21–26).

Ant stings, an emerging problem. Ants are not generally appreciated as causes of anaphylaxis, but a growing number of species in North America and on other continents are being reported as causes of this medical emergency. The following case describes an anaphylactic reaction to a sting from a rough harvester ant, *Pogonomyrmex rugosus* (27).

Case summary 1. A 41-year-old man was brought to the University Medical Center Emergency Department in Tucson, Arizona by ambulance in September of 2003. He stated that he had painful ant "bites" to his groin and that he was short of breath and dizzy. The blood pressure was 89/64 mm Hg, pulse 112 beats/min, and respiratory rate 22 breaths/min. There was

Table 3. Anaphylactic-like Reactions* to Bites and Stings of Invertebrates and Vertebrates

Scientific Nomenclature (Common Name)†	References
Phylum: Arthropoda	
Class: Insecta	
Order: Hymenoptera	
Family: Halictidae (sweat bees) Formicidae	25
Genus: *Pseudomyrmex* (twig ants)	30
Hypoponera	30
Rhytidoponera (greenhead ants)	36
Odontomachus (trap-jaw ants)	42
Order: Hemiptera	
Family: Cimicidae	
Genus: *Cimex* (bedbugs)	49
Order: Diptera	
Family: Ceratopogonidae	
Genus: *Culicoides* (punkies)	48
Family: Rhagionidae	
Genus: *Symphoromyia* (snipe flies)	58
Family: Therevidae	
Genus: *Thereva* (stiletto flies)	59
Order: Lepidoptera	
Family: Anthelidae	
Genus: *Chelepteryx* (white-stemmed gum moths)	61
Family: Megalopygidae	
Genus: *Megalopyge* (puss caterpillars)	66
Class: Chilopoda (centipedes)	82
Phylum: Cnidaria	
Class: Hydrozoa	
Genus: *Physalia* (Portuguese man-of-wars)	89
Millepora (fire corals)	91
Class: Cubozoa	
Genus: *Carybdea* (Hawaiian box jellies)	90
Phylum: Chordata	
Class: Reptilia	
Order: Squamata	
Family: Viperidae	
Genus: *Bothrops* (lance-headed vipers)	98
Family: Elapidae	
Genus: *Notechis* (tigersnakes)	101
Family: Helodermatidae	
Genus: *Heloderma* (Gila monster & Mexican beaded lizards)	102–104
Class: Mammalia	
Order: Primates	
Genus: *Nycticebus* (slow lorises)	114

* Mechanism unknown (may or may not be IgE-mediated).
† Common names in parentheses were reported to induce the reaction.

periorbital and perioral edema with cyanosis of the lips, severe wheezing bilaterally, and marked erythema of the right groin and scrotum. Symptoms resolved within 4 h after treatment with epinephrine, diphenhydramine, and steroids. At the time, an extremely tender and enlarged lymph node was present in the right groin along with a 1-cm red papule, and piloerection of the surrounding hairs that are characteristic of *Pogonomyrmex* stings. A nest of *P. rugosus* was present under the edge of the sidewalk where the patient had been sitting.

Case summary 2. A 3-month-old baby in Phoenix, Arizona died in 2003 as a result of an anaphylactic reaction to stings by southern fire ants, *Solenopsis xyloni*, that had invaded the home and were found covering the child in her crib. She was in respiratory distress and taken by helicopter to a local hospital where she died. She received hundreds of stings, but may have been sensitized by an earlier sting that went unnoticed. A positive postmortem RAST result to imported fire ants, *Solenopsis invicta* (there is almost total cross-reactivity among venoms within the genus *Solenopsis*), and elevated serum tryptase level helped to confirm that it was an anaphylactic reaction (28).

Management of Hymenoptera stings. In the United States, at least 30–40 people die each year from Hymenoptera stings, many of whom have no prior history of allergic reactions (29). Allergic reactions to Hymenoptera stings are more common in men and can occur in any age group, but are often more severe in adults over age 30 years. Treatment of Hymenoptera sensitivity should include prevention of stings and immediate treatment of reactions when they occur, proper identification of the offending insect, and immunotherapy with venom preparation when available (5). Epinephrine and $H_1 + H_2$ antihistamines may be life-saving when administered early during an anaphylactic reaction. For Hymenoptera, skin testing and RAST are available for several venom preparations (5). Immunotherapy, when indicated, may prevent fatalities in sensitized patients.

Due to the specificity of an allergic reaction to a particular allergen, it is worthwhile to attempt to identify the offending insect, or refer the patient to have a record of the insect genus or species that induced the reaction. For the more common causes of sting allergy, such as yellowjackets, honeybees, and imported fire ants, immunotherapy prescribed by an allergist may be available. It involves repeated injections of increasing doses of venom extracts, but in the case of imported fire ants, whole body extracts have been used successfully.

Unfortunately, for less common causes of sting allergy, commercial extracts are not available. Nevertheless, hypersensitive individuals should carry an epinephrine kit (EpiPen or Twinject) and antihistamines so that they can administer an injection of epinephrine at the first sign of anaphylaxis.

Hemiptera (bugs). Anaphylactic reactions to saliva from the bites of kissing bugs (*Triatoma protracta* and *T. rubida*) are species-specific (44–46). Although the geographic range of these two species overlap, *T. rubida* is more common in Arizona and *T. protracta* in California. There is little or no antigenic cross-reactivity between these species. Their bite is painless, usually occurs dur-

ing sleep, and is more common in adults. For most people the bite is harmless, but for those who are sensitized it can cause a life-threatening reaction.

Case summary 3. A 45-year-old woman in southern Arizona has had four severe reactions to an insect bite, and found the insect, which was identified as a kissing bug, in bed each time. She did not feel the bites, but noticed her heart rate increasing, and then felt hot. In two instances she lost consciousness and in one she had a seizure (47). Kissing bug victims are typically bitten while sleeping, and often find the engorged bug in their beds. Usually there are multiple bites that are clustered on areas of the body not covered, such as the arms, shoulders, neck, and face. There are two types of allergic reactions: localized intensely pruritic urticaria at the site of the bite, or anaphylaxis. Severe reactions require immediate treatment, so persons at risk should keep a kit containing medications close at hand in their bedroom.

Other than kissing bugs, anaphylactic reactions to biting insects are relatively uncommon (48). An anaphylactic-like reaction to a bedbug bite was reported 50 years ago (49). The common bedbug, *Cimex lectularius*, is a cosmopolitan species that is most frequently found in northern temperate regions. Over the last few years there has been an increasing incidence of bedbug infestations in the United States (50). Bedbugs have piercing-sucking mouthparts; one stylet carries saliva into the wound while the other imbibes blood.

Diptera (flies). There are reports of anaphylactic and anaphylactic-like reactions to bites from horse flies and deer flies (Tabanidae), black flies (Simuliidae), and mosquitoes (Culicidae) (48,51–55). About 350 species of tabanids and 165 species of simulids inhabit North America, and some are vicious biters (56). Female tabanids and simulids are blood-suckers like mosquitoes. Mosquito bites often induce large local reactions but surprisingly few cases of anaphylaxis (57).

Lepidoptera (moths and butterflies). The term "lepidopterism" refers to the generalized ill effects that can result from contact with moths and butterflies (61). In northwestern Spain, 40% of 30 patients diagnosed with occupational urticaria suffered anaphylactic reactions to urticating hairs of the pine processionary caterpillar (*Thaumetopoea pityocampa*) (62). The hairs, which can be airborne, penetrate the skin and release a toxic substance (63,64). The caterpillars are gregarious and live in large silken nests at the tips of pine branches. They feed at night and form long lines with hundreds of individuals following a lead caterpillar both to and from the nest (65).

From 1955–1959 in Texas, there were 43 reported cases of stings by the puss caterpillar, *Megalopyge opercularis*. Most were localized reactions and a few were anaphylactic-like reactions (66).

Anaphylactic and Anaphylactic-like Reactions to Invertebrates Other Than Insects (Tables 2 and 3)

Arachnids

Ticks. There are two families of ticks: the Ixodidae or hard ticks and the Argasidae or soft ticks. All ticks are blood-sucking, both males and females. They are major vectors of various pathogens, and the toxins of some species can cause paralysis. Much less common are allergic reactions to tick bites. For example, allergic reactions to tick bites of the Australian paralysis tick, *Ixodes holocyclus*, make up about 0.7% of the total allergic reactions to arthropod stings and bites in Queensland, Australia (67,68).

In other parts of the world, there are fewer reported cases of anaphylactic reactions to tick bites, including the black-legged tick, *Ixodes pacificus*, a species that is widely distributed in western North America; and two other cases in western Europe, one involving a species of *Rhiphicephalus*, and the other *Ixodes ricinus* (69–72).

More common in Europe are anaphylactic reactions to bites of the pigeon tick, *Argas reflexus*, a soft tick that is a temporary parasite of wild and domesticated pigeons (73,74). When pigeons are unavailable these ticks often migrate into homes and feed on the occupants who, if sensitized, may have anaphylactic reactions to their bites.

Scorpions. Thousands of people are stung by scorpions each year. For example, in Arizona, excluding Maricopa County (the greater Phoenix area), there were 4655 scorpion stings reported over a 2-year period (2002–2004) (27). Fatalities are rare but have occurred. Five deaths from scorpion stings were recorded in the United States from 1950–1954, one of which appeared to be an anaphylactic-like reaction (75). In Arizona, death from an anaphylactic-like reaction was reported in 2001, the first fatality from a scorpion sting in that state in 36 years (76).

The common striped scorpion, *Centruroides vittatus*, is the most frequently encountered species in the United States, and anaphylactic reactions to their stings have been reported (77). Their venom has been reported to cross-react antigenically with whole body extract of imported fire ants, *Solenopsis invicta* (78). The high incidence of sensitization to fire ant stings in endemic areas (17% in one study) poses a risk to stings by the striped scorpion, whose geographic range overlaps that of imported fire ants (78,79).

A sting by a sculptured scorpion, *C. exilacauda*, commonly called the bark scorpion, has caused an anaphy-

lactic reaction (80). This species is mainly found in Arizona, and is the deadliest in the United States (81).

Additional Non-insect Invertebrates

Chilopoda (centipedes). Centipedes are multi-segmented, flat-bodied arthropods. On the first body segment behind the head they have a pair of venomous claws that they use for subduing prey and defense. Some species can inflict painful bites, but serious complications are rare (82). However, there has been one reported fatality and one reported anaphylactic-like reaction (82). In the case of the anaphylactic-like reaction, the individual was bitten on his little finger and shortly thereafter went into shock. He was treated with epinephrine and antihistamines in an Emergency Department and recovered.

Cnidaria (coelenterates). An encounter with a Portuguese man-of-war, *Physalia physalis*, can potentially result in several million stings (83). Most envenomations by Cnidaria cause local reactions, but fatalities due to anaphylactic-like or toxic reactions have occurred (84,85). A single nematocyst sting is sufficient to induce anaphylaxis (86). In vitro tests with serum of patients allergic to venom of the sea nettle, *Chrysaora quinquecirrha*, a common Cnidaria in Chesapeake Bay, showed cross-reactivity with venom of the Portuguese man-of-war (87,88). A surfer off the southern coast of Florida was treated for an anaphylactic-like reaction to stings by the Portuguese man-of-war (89). These colonial hydrozoans are almost worldwide in distribution, inhabiting both tropical and temperate seas.

Cubozoans, also known as box jellyfish due to the square-shaped bell when viewed from above, possess the most potent marine venom. Toxic reactions to their sting can cause extensive morbidity and pain, and in more severe cases, Irukandji syndrome, with muscle cramping, back spasm, and tremors (90). In a survey of 113 envenomated patients in Hawaii that was conducted over a 5-year period during the season when the box jellyfish, *Carybdea alata*, and Portuguese man-of-war are common on coastal beaches, 11 patients had suffered anaphylactic-like reactions, and 6 an Irukandji-like syndrome. The majority had local reactions (90).

Anaphylactic and Anaphylactic-like Reactions to Vertebrates (Tables 2 and 3)

Reptiles

Snakes. Anaphylactic and anaphylactic-like reactions to vertebrate bites are rare. Due to the systemic toxicity of reptile venoms, it is clinically difficult to differentiate an anaphylactic (IgE-mediated) from an anaphylactoid (non-IgE-mediated) reaction (92). Most of the evidence for anaphylactic reactions is derived from snake fanciers and handlers who have been repeatedly bitten, such as by rattlesnakes (*Crotalus*) and European vipers (*Vipera*) (93,94). A case of anaphylactic shock with vipers involved a man bitten for the second time by *Vipera aspis* while hiking in the Alps (95). Both genera belong to the family Viperidae, which is characterized by hinged hollow fangs that fold back against the roof of the mouth when it is closed. Anaphylactic-like reactions also have been reported for people bitten more than once by rattlesnakes and lance-headed vipers, *Bothrops moojeni* (96–98). In addition, there are reports of anaphylactic-like reactions to rattlesnakes that appeared to be first-time envenomations (99).

Lizards. Anaphylactic-like reactions to bites from lizards have been reported for two poisonous species in the family Helodermatidae: the Mexican beaded lizard, *Heloderma horridum* and the Gila monster, *Heloderma suspectum* (102–104). Beaded lizards, which are larger than Gila monsters, live along the west coast of Mexico from southern Sonora to Chiapas, and in southern Guatemala (105). The Gila monster lives primarily in the Sonoran Desert (105).

The venom of heloderms is produced in a pair of glands located in the lower jaw (vs. the venom glands in poisonous snakes that are located in the upper jaw). Heloderms have a strong bite with a vise-like grip. The venom travels through ducts to long, recurved teeth, which are grooved, where it then moves by capillary action to enter the tissues of the victim (105).

Mammals

Rodents. Anaphylactic reactions to bites by laboratory animals are extremely rare, but have been reported for rats (Rattus) and mice (Mus) based on in vivo and in vitro tests with their urine, dander, and serum (106,107). Although tests with saliva were not done in these cases, it has been shown with RAST that these other animal products have shared antigen(s) with saliva (108).

Animal handlers and pet owners often get nipped or bitten, sometimes innocuous incidents that they may not recall. A child bitten by a pet mouse had an anaphylactic reaction, and pet gerbils (*Gerbillus*) and hamsters (*Phodopus*) also have been reported to cause anaphylactic reactions to their bites (109–113).

Primates. The Sunda slow loris, *Nycticebus coucang*, is a nocturnal, tree-dwelling primate from Southeast Asia. It is sometimes kept as a pet, and has been reported to

cause anaphylactic-like reactions to its bite. In one case the victim died (114). A major allergen, Fel d 1, has been isolated from their saliva, and is similar to the major allergen in the saliva of domestic cats (115). In the slow loris, the allergen is produced by the brachial organ located on the flexor surface of the arm, and may be picked up in the saliva when the gland is licked during grooming (115).

CONCLUSIONS

This article summarizes the reported cases of animal-induced anaphylactic and anaphylactic-like reactions to bites and stings. The diversity of causative organisms spans the animal kingdom. However, the list of animals represents only reported cases, and may be only a fraction of the actual cases. Many more cases go unreported or are lumped together as venomous bites and stings without specifying the offending organism. The American Association of Poison Control Centers does not have comparative frequencies on all these animals because many were reported in journal articles and not to Poison Control Centers or local or state health departments.

As more cases are reported, the list of animals will inevitably grow to include more species. Additional research will ultimately determine whether some anaphylactic-like reactions may be found to be true anaphylactic reactions.

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