



Clinical consequences of toxic envenomations by Hymenoptera

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ABSTRACT

Many familiar Hymenoptera are brightly colored and can sting painfully—thus, their threat and clinical importance may be exaggerated. Most stinging insects only sting to defend themselves or their colonies from predators. The clinical nature of Hymenoptera envenomations contrasts that of other venomous animals, including other arthropods, primarily because allergic reaction, not direct intoxication, is the usual main concern. This review focuses mainly on the clinical features of direct toxicity to Hymenoptera envenomations, which can induce a high incidence of acute renal failure, liver failure, multiple organ failures, and death. Toxic mass envenomations by honeybees usually entail many hundreds or more stings per victim. In contrast to honeybee toxic envenomations, hornet sting envenomations can be clinically threatening with only 20–200 stings needed to cause kidney and other organ failures. Many lethal envenomations by honeybees occur in rural areas in the New World and Africa and are not recorded or documented. In contrast, deaths by hornets occur mainly to Asia. The most frequent and important envenomating taxa are honeybees, hornets, yellowjacket wasps, paper wasps, fire ants, and jack jumper ants. Occasional envenomating taxa include bumblebees, bullet ants, harvester ants, solitary wasps, solitary bees, and various ants of lesser clinical importance. Envenomations by Hymenoptera usually can be avoided if one considers that bees, wasps and ants “view” us as potential threats or predators, and that with information about the biology of stinging Hymenoptera, humans can minimize adverse incidents.

1. Introduction

The bees, aculeate wasps (true stinging wasps), and ants of the enormous insect order Hymenoptera conservatively number some 92,000 species and likely several times that number (Goulet and Huber, 1993). Those species that are known to sting human beings number under 200 and the most important species that commonly sting people number less than 100. Of these only honeybees, hornets (*Vespa*), and yellowjackets (*Vespula*) are able to kill people via direct toxic envenomation. Thus, by the author's estimates, only about 0.2% of hymenopteran species actually sting people, of which only less than 0.04% (*Vespa* = ~12 spp.; *Apis* = 7 spp.; *Vespula* = ~12 spp.) are capable of toxically killing a person by venom overload. The overall conclusion is that the vast majority of Hymenoptera are not a threat to human beings and are generally beneficial insects (Triplehorn and Johnson, 2005).

The human perception of potential harm by Hymenoptera is much stronger than the actual threat for several reasons. First, unlike scorpions, spiders and other venomous animals, many familiar Hymenoptera live in social colonies having many individuals who can actively fly and deliver numerous stings, thereby enhancing human fear. Second, stinging Hymenoptera are often aposematically brightly colored making them conspicuous and intimidating to predators and

humans. Third, many hymenopteran species are able to sting painfully. This combination of factors results in overall fear and apprehension. In reality, the threat to life and limb and clinical importance of stinging Hymenoptera is exaggerated. Often forgotten is the fact that most stinging insects sting only to defend themselves or their colonies from predators, though some ants, for example, fire ants (*Solenopsis* spp.) are exceptions that appear to sting for no obvious reason to an intruding person other than that one is intruding into their territory. Several taxa of ants deliver non-venomous, albeit sometimes painful, bites, especially formicine ants that also spray formic acid into the bite wound.

The clinical nature of Hymenoptera envenomations contrasts that of other venomous animals, including other arthropods, primarily because allergic reaction, not direct intoxication, is the usual main concern. This is a result of two factors: first, most Hymenoptera venoms are not highly toxic to humans or mammals, or the amounts of venom injected are small (Schmidt et al., 1980; Schmidt, 2014) and, second, repeated envenomations by Hymenoptera are more frequent than by other venomous animals. Repeated envenomations provide ideal conditions for the development of allergic responses. Copious literature on the aspects of clinical allergy to Hymenoptera envenomations is available (Freeman and Tracy, 2017) and allergy will only be briefly mentioned here. This review will focus on the clinical aspects of direct toxicity to Hymenoptera envenomations with presentations on the most frequent

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Table 1

Number of stings of representative Hymenoptera based on calculations that are predicted based on mice to deliver an acute LD₅₀ envenomation for a 70 kg person. (Species known to be responsible for fatalities due to toxic envenomation rather than allergic reactions are indicated in bold).

Taxon	Species	LD50 (mg/kg)	µg venom per insect	Lethal capacity ^a human	Stings for LD ₅₀ envenomation of a 70 kg
SOCIAL BEES					
Apidae	<i>Bombus sonorus</i> (bumblebee)	12	760	63	1105
	<i>Apis mellifera</i> (honeybee)	2.8	160	57	1225
SOCIAL WASPS					
Vespidae	<i>Vespa mandarinia</i> (giant hornet)	4.4	1420	323	220
	<i>Polistes arizonensis</i> (paper wasp)	2.0	170	85	820
	<i>Dolichovespula maculata</i> (baldfaced hornet)	6.1	300	49	1420
	<i>Vespula germanica</i> (yellowjacket)	2.9	130	44	1560
ANTS					
Formicidae	<i>Paraponera clavata</i> (bullet ant)	1.4	400	286	245
	<i>Pogonomyrmex maricopa</i> (harvester ant)	0.19	20	105	665
	<i>Myrmecia pilosula</i> (jumper ant)	5.7	33	5.8	12100
SOLITARY BEES AND WASPS					
Apidae	<i>Xylocopa californica</i> (carpenter bee)	14	420	30	2330
Pompilidae	<i>Pepsis grossa</i> (tarantula hawk wasp)	90	2500	28	2520
Mutillidae	<i>Dasymutilla klugii</i> (cow killer wasp)	70	420	6.0	11670
Sphecidae	<i>Sphecius grandis</i> (cicada killer wasp)	45	250	5.56	12600

^a Lethal capacity is the weight (g) of mammal that would receive a median lethal dose of venom if envenomed with all the venom from one insect.

envenomating taxa (Table 1, Fig. 1). Steps to avoid Hymenoptera envenomations will not be emphasized other than to highlight that most envenomations can be avoided if one considers how the bee, wasp or ant “views” us as potential threats or predators. By use of information about their biology and behaviour, humans can usually avoid coming into adverse contact with stinging Hymenoptera (Schmidt, 2016).

A major weakness in our knowledge concerning toxic envenomations by Hymenoptera is the paucity of information on the frequency of massive stinging events and toxic envenomations. This result is partly because most stinging events involving Hymenoptera are of minor medical importance and the stung individuals usually are not seen by medical providers, and partly because few governmental agencies collect detailed data on attack frequencies. One exemplary exception is reported by Chippaux (2015) for envenomations by animals in Brazil. Over a 12 year period 1,192,667 envenomations were recorded, of which 66,283 (5.6% of the total) were listed as “bees”. Other Hymenoptera were not listed and likely were inconsequential because Brazil has no hornets or yellowjacket wasps and envenomations by ants are infrequent and mostly minor. Of the bee attacks, 216 deaths, equivalent to a 0.3% mortality rate, were reported, most of which were due to allergic reactions.

2. Social bees

2.1. Honeybees (apidae: *Apis*)

Honeybees are an Old World genus of nine commonly recognized species (Michener, 2007) and numerous subspecies (Sheppard, 2015). All can sting and readily lose their sting apparatus embedded in the skin of stung humans and many vertebrate animals. The major toxic components of the venoms of the species are also similar (Hoffman and Schmidt, 2000; Baracchi et al., 2013). Eight of the species are limited to Asia and the Middle East and are generally of less clinical concern than the common “Western hive bee”, *Apis mellifera*, which includes Africanized honeybees. *Apis mellifera* which originally inhabited Africa, Europe, and parts of the Middle East; now because this species provided highly-sought-after honey, beeswax, and other hive products of interest, humans dispersed them throughout the world (Schmidt, 2016). All species of honeybees will attack if provoked sufficiently. Reports of toxic envenomations by species other than *A. mellifera* are rare. *Apis dorsata*, the giant honeybee, is noted for its uncommon, though ferocious, stinging attacks. Older references mainly discussed toxic envenomations in a general nature (Beard, 1963; Morse and Liago, 1969). More recent clinical reports of envenomations by *A. dorsata* describe

individuals who clinically experienced pain, nausea/vomiting, and renal, pulmonary, cardiac, liver and/or GI dysfunction (Budagoda et al., 2010; Islam et al., 2011; Witharana et al., 2015). The only clinical report of a toxic envenomation by the Asian hive bee, *Apis cerana*, is of an attack on a German shepherd dog that received 150 stings of unverified bee species in which the dog died after two days (Mughal et al., 2014).

Clinically-important toxic envenomations by honeybees require massive numbers of stings, often in the range of hundreds to thousands of stings—though fewer numbers of stings causing serious conditions have been reported—and some individuals have survived several thousand stings, or, in the case of an infant, several hundred stings (Table 2). One man in Africa survived 2243 stings (Murray, 1964). One of the problems with honeybee envenomations is that so many stings are delivered that too often the counts in the clinical setting are simply rough estimates.

Honeybee venom has a lethality to mice of 2.8 mg/kg and *A. mellifera* contains on average about 160 µg of venom/bee (Schmidt, 1995). If we use the lethal toxicity of honeybee venom to mice as a model to extrapolate toxicity we obtain an expected median lethality for a 20 kg child of 350 stings and a 70 kg adult of 1225 stings. Toxic envenomations most commonly affect blood and kidney functioning, but other organs as listed in Table 3 are frequently involved as will be further discussed under the heading of Africanized and African honeybees which are responsible for the majority of toxic stinging events.

2.2. African and africanized and honeybees (Apidae: *Apis mellifera* various subspecies found in Africa, and the New World hybrid of mostly *A. mellifera scutellata*)

Africanized honeybees are so named because they are a genetic mix of honeybees from Africa brought to Brazil in 1956, plus a minor genetic infusion from the local honeybee population originally brought in from Europe (Michener, 1975). African bees are those populations of bees present in Africa. Because the behavior of these two groups of bees is similar they will be categorized and discussed together and generally referred to simply as Africanized bees because the majority of clinical reports come from Latin America. The main differences between Africanized honeybees and those honeybees of European origin is behavioral; that is, Africanized bees are quick to arouse defensively and have a tendency to massively attack and sting when accidentally or intentionally provoked. European honeybee envenomations typically involve few stings and are mainly of concern in the respect of acute local pain at the sting site.

Typical symptoms of toxic envenomations by honeybee stings are

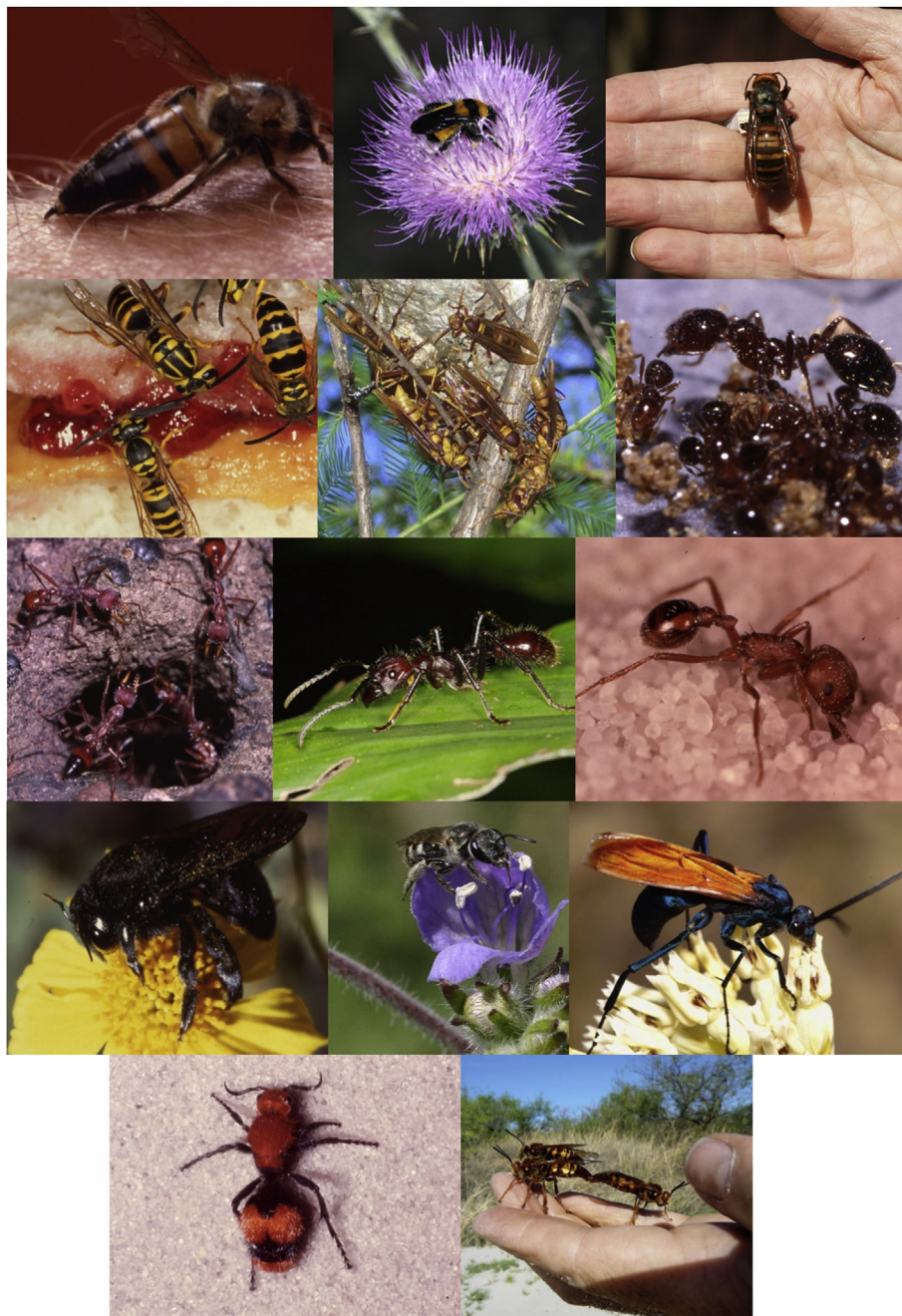


Fig. 1. Representative stinging insects. From top left across, then down: honeybee (*Apis mellifera*); bumblebee (*Bombus sonorus*); hornet (*Vespa mandarinia*); yellowjackets (*Vespula maculifrons* & *V. squamosa*); paper wasps (*Polistes carnifex*); fire ants (*Solenopsis invicta*); bulldog ants (*Myrmecia gulosa*); bullet ant (*Paraponera clavata*); harvester ant (*Pogonomyrmex maricopa*); carpenter bee (*Xylocopa californica*); sweat bee (*Halictus* sp.); tarantula hawk (*Pepsis* sp.); velvet ant (*Dasymutilla occidentalis*); cicada killer wasps (*Sphecius convallis*).

listed in Table 3. All envenomations, no matter how trivial, produce instantaneous local pain at the sting site. This is followed by a whitish wheal immediately surrounding the sting puncture site, which in turn is surrounded by a reddish flare (Fig. 2). The symptoms usually resolve in a few minutes and no further complications are noted. In some cases individuals will develop large local reactions in which the skin and tissue around the sting site becomes swollen and may remain swollen for several days to a week. These reactions differ from, and are not related to, the familiar allergic reactions experienced by 1–4% of the population and that constitute the main health concern from one or a few of stings (Freeman and Tracy, 2017).

Moderate envenomations of about 50–200 stings per adult and correspondingly fewer for children will include: anxiety, nausea and

vomiting, abdominal pain or diarrhea, tachycardia often with hypertension, and renal failure (McKenna and Brown, 2017). More serious honeybee envenomations involving 200 to 500 stings per adult often induce multi-organ failures that typically worsen over two or more days. These symptoms involve blood (hemolysis), muscles (rhabdomyolysis), kidneys (acute renal failure), liver damage, lung damage (pulmonary congestion), and gastrointestinal tract failure. Serious life-threatening envenomations of over 500 stings per adult often cause total kidney failure (Mejia et al., 1986; França et al., 1994; Betten et al., 2006; Mejia-Vélez, 2010), liver failure (França et al., 1994; Kolecki, 1999; Diaz-Sanchez et al., 1998), disseminated intravascular coagulation (França et al., 1994; Kolecki, 1999; Mitchell, 2006), and death (Table 2). Kidney failure frequently appears 2–9 days after the stinging

Table 2

Summary of outcomes of humans stung by more than 1000 honeybees with noteworthy cases involving fewer stings.

Number of stings	Age (years)	Notes	Fate	Reference
125	66M	metastatic cancer	died	Kolecki, 1999
200	3M	returned home day 21	lived	de Azevedo et al., 2006
200 +	2M		lived	Kini et al., 1994
400 +	8M		died	França et al., 1994
700	73 F		died	McKenna, 2003
800	9M	32 days in hospital	lived	Bresolin et al., 2002
800 +	13M		died	França et al., 1994
Av = 900	> 60	of 43 cases	7 died	Mejia-Velez, 2010
~1000	88 F	intestinal ischemia	died	Mitchell, 2006
1000 +	15M		died	Daisley, 1998
1000 +	31M		lived	Humblet et al., 1982
1000 +	47M		lived	Mejia et al., 1986
1000 +	62M		lived	Mejia et al., 1986
1000 +	64M		died	França et al., 1994
1000 +	74M		died	Mejia et al., 1986
1000 +	77M		lived	Mejia et al., 1986
1000 +	78M		lived	Patrick et al., 1987
1000 +	80M		lived	Mejia et al., 1986
1200 +	52M		lived	Beccari et al., 1992
1200 +	85M		died	Beck, 1935, p 85
1500	50 F		lived	McKenna, 2003
2000	19M		lived	Nag et al., 2015
2000 +	30M		lived	Diaz-Sanchez et al., 1998
2243	30M		lived	Murray, 1964
5–6000	77M	85 kg weight	died	Moret et al., 1983

Table 3

Common clinical symptoms of honeybee envenomations. Modified from McKenna and Brown (2017).

Mild envenomation (< 1 sting/kg)
Short-term local pain
Cutaneous symptoms
Moderate envenomation (1–4 stings/kg)
(Those for mild envenomation), plus:
Anxiety
Nausea/vomiting
Abdominal pain/diarrhea
Tachycardia
Hypertension
Renal function compromised
High envenomation (4–9 stings/kg)
(Those for moderate envenomation), plus:
Multiple organ systems affected; worsening over 48–96 h
GI tract
Cardiovascular
Hematologic
Acute renal failure
Hepatic damage
Pulmonary
Very high envenomation (> 9 stings/kg)
(Those for high envenomation), plus:
Altered mental state/unconscious
Acute toxic death ^a

^a Estimated LD₅₀ is 19 stings/kg body weight (Schmidt, 1992).

event, often after the patient has been discharged. Those who survive kidney failure commonly are hospitalized for many days to several weeks before kidney function returns sufficiently for release (Diaz-Sanchez et al., 1998; Kolecki, 1999; Gabriel et al., 2004; Nag et al., 2015; Jimoh et al., 2016). In addition to these clinical manifestations of massive honeybee envenomation, a variety of unusual symptoms have been noted, including, pancreatitis, cardiac compromise, and

convulsions (França et al., 1994; Daisley, 1998; de Azevedo et al., 2006; Akolly et al., 2016). Individuals at particular risk of serious consequences from toxic envenomations are individuals over 60 years of age, small children, and those with known or unknown underlying medical conditions (McKenna and Brown, 2017). At present no antivenom for bee stings is available for clinical use, though efforts are ongoing to develop a treatment (Barbosa et al., 2017).

2.3. Bumblebees (*Apidae: Bombus*)

Bumblebees comprise a huge number of species, somewhere in the range of 250 species worldwide, most of which live in the cold and temperate regions of the northern hemisphere (Williams, 1998). Their colonies are small compared to honeybees and often contain only 20 to 500 individuals. Unlike honeybees that have a year-round lifecycle and can be responsible for stinging incidents anytime the ambient temperature rises above about 10°, bumblebee colonies begin in the spring with a single queen who builds the nest, forages, and raises her first batch of young workers. During this time stings are rare and mainly the result of somebody stepping barefooted on a foraging bumblebee on a flower. After the workers emerge, they take over most colony activities including foraging and defending the colony. Humans are stung by bumblebees mainly during the summer and autumn. Clinical symptoms of bumblebee stings are similar to those of honeybee stings with the exceptions that bumblebees do not lose their stinger in the victim and usually only 1 to 5 bumblebee stings are received during an incident. Consequently, no reports of toxic envenomations are present in the literature; something not surprising given that for a theoretical toxic death to occur, around 1100 stings per adult human would be predicted (Table 1), a number exceeding the number of bees in a bumblebee colony. A minor medical concern with bumblebee envenomations is the rare occurrence of allergic reactions (de Groot, 2006) and to date no deaths have been recorded.

3. Other bees

3.1. Sweat bees (*Halictidae*)

Sweat bees are small solitary bees numbering some 4387 described species (Danforth et al., 2006) in the family Halictidae that have a worldwide distribution (Michener, 2007). Their name derives from the habit of some species of landing on human skin to imbibe sweat secretions. Clinical problems arise when people inadvertently pinch the bee or trap it between clothes and the skin. In response the bee stings, delivering a short lasting sharp minor pain that is much less severe than the pain caused by a honeybee or common wasp sting. No toxic or fatal envenomations have been reported—not a surprising fact given that the bees are solitary and therefore cannot recruit other individuals for a defensive stinging attack. Thus, only single stings occur at a time. Sweat bees are clinical problem only in the respect that their stings can sometimes induce an allergic reaction (Pence et al., 1991).

3.2. Carpenter bees (*Apidae: Xylocopa*)

Carpenter bees are large, generally black solitary bees in the genus *Xylocopa* that contains 500 species distributed throughout most of the world including both tropical and temperate regions (Minckley, 1998). Most species nest in wood which often brings them in close contact with people who commonly use wood for structures and fences. Being solitary, carpenter bees do not attack human beings, though they sometimes appear intimidating when male bees will fly inquisitively near humans in attempts to ascertain if the human intruder is a competitor or threat within their mating territory. This threat is totally harmless, given that male Hymenoptera, including carpenter bees, lack the stinger (a modified ovipositor). A person can be stung if a female bee is grabbed and held or in the unlikely event when one is driving or riding



Fig. 2. Local sting reactions. Left is from the honeybee (*Apis mellifera*); right is from a tarantula hawk (*Pepsis* sp.).

outdoors that a bee becomes stuck between loose clothes and the skin. In this case, the bee will sting in self-defense. A carpenter bee sting is roughly as painful as a honeybee sting, though generally produces fewer and less intense local sting site reactions. It is also sharper with a less intense burning sensation than a honeybee sting. No known toxic envenomations are reported for the simple reason that these bees are solitary and only one bee sting occurs at a time. In principle allergic reactions could occur but to date only one has been confirmed (Kularatne et al., 2016).

4. Social wasps (Vespidae)

The terminology for social wasps is confusing in both common usage and in clinical literature. In much of the world the word “wasp” refers to any member of the subfamily Vespinae, including the genera *Vespa*, *Dolichovespa*, and *Vespula*. Some authors even lump into the term “wasp” the paper wasps (*Polistes*) and related genera. In Mandarin Chinese the terminology becomes even more general with the common name combining hornets (*Vespa*) and bumblebees (*Bombus*) together. This unfortunate naming causes confusion in the clinical literature where the term wasp is often used in a general sense without designating the scientific name to indicate the true identity of the offending species. This is important because the clinical situation often differs dramatically between the consequences of stings by true hornets in the genus *Vespa* and stings of *Vespula* or *Dolichovespula*, commonly referred to as yellowjackets or aerial yellowjackets in North America. In this review wasps in the genera *Vespula* and *Dolichovespula* will be called yellowjackets, wasps in the genus *Vespa* will be called hornets, wasps in the genus *Polistes* and related genera will be called paper wasps.

4.1. Hornets (*Vespa*)

Hornets are native to Asia, the Middle East, the Mediterranean, and Europe. One species, *Vespa crabro*, has also been introduced into eastern North America (Ross and Matthews, 1991). The most frequently reported offending species of hornets involved in mass stinging events are *Vespa affinis*, and to a lesser extent *V. orientalis* and *V. tropica*, with other species occasionally noted. Reasons are partly that these species tend to

nest near people, to be more defensive, to have large nest populations, and are more abundant and widely distributed than most other species of *Vespa*. In many cases the offending species is not identified even to the genus and the reader must surmise from the clinical symptoms and geographical location of the event the approximate identity. Nevertheless, in terms of clinical observations, no meaningful differences in envenomations between the different species of hornets are apparent. Also of interest is the observation that hornet stings often cause eroded, ulcerated pits to develop at the sting locations in the skin, something not observed in the case of yellowjacket, paper wasp, or honeybee stings (Yanagawa et al., 2007).

Hornets can be truly dangerous and massive hornet envenomations are often clinical emergencies that all-too-frequently become life-and-death situations. The number of stings necessary for massive envenomations is small compared to the numbers necessary for honeybee or yellowjacket toxic envenomations, in part because hornets are much larger than honeybees or yellowjackets and apparently deliver more venom in a sting (Table 1; Schmidt et al., 1986). When dealing with massive hornet envenomations the first and almost universal concern is protecting the kidneys. As few as a dozen to less than 100 stings can send a person into an acute renal failure, a difficult clinical situation often requiring long-term hospitalization. Frequent clinical observations and massive envenomations by hornets are listed in Table 4, and, in addition to kidney failure (Chugh et al., 1976; Das and Mukherjee, 2008; Vikrant et al., 2005; Wiwanitkit, 2005; Xuan et al., 2010; Xie et al., 2013; Liu et al., 2016), often involves failure of the liver (Kularatne et al., 2003; Vikrant et al., 2005; Xie et al., 2013; Liu et al., 2016), muscle (Korman et al., 1990; Xuan et al., 2010; Xie et al., 2013; Yamazaki et al., 2014), lungs (Wiwanitkit, 2005; Kularatne et al., 2014), heart (Kularatne et al., 2003; 2014; Lin et al., 2011; Liu et al., 2016), central nervous system (Korman et al., 1990; Wiwanitkit, 2005), G.I. tract (Vikrant et al., 2005; Yamazaki et al., 2014), and pancreas (Kularatne et al., 2003). Death resulting from as few as 17–200 stings is all too frequent, often after prolonged hospitalizations and in spite of rigorous treatment (Table 5). Initial localized or general pain and or nausea/vomiting are common reasons stung individuals present at clinics. These symptoms are frequently only initial reactions that diminish, leaving periods of feeling mostly well-being, only to be

Table 4
Common clinical symptoms of hornet (*Vespa* spp.) envenomations.

Mild envenomation (< 0.5 stings/kg)
Short-term local pain
Cutaneous symptoms
Erosion pit at sting site
Moderate/high envenomation (0.5–2 stings/kg)
(Those for mild envenomation), plus:
Anxiety
Nausea/vomiting
Abdominal pain/diarrhea
Acute renal failure
Tachycardia
Hypertension
Very high envenomation (> 2 stings/kg)
(Those for moderate/high envenomation), plus:
Multiple organ systems affected; worsening within 2–9 days
Acute renal failure
Hepatic damage
Muscle (rhabdomyolysis)
Pulmonary
Cardiovascular
Central nervous system
GI tract
Pancreas
Altered mental state/unconscious
Acute toxic death ^a

^a Estimated LD₅₀ is 3.2 stings/kg body weight for *Vespa mandarinia* (from Table 1).

followed hours or days later by serious failure of organ systems. Individuals older than 60 years of age or younger children are greatest risk of toxic hornet envenomations.

4.2. Common yellowjacket wasps (*Vespula* and *Dolichovespula*)

Yellowjackets are primarily found in temperate regions of the northern hemisphere with several species have been introduced into other parts of the world including Australia, New Zealand, South Africa, Chile, and Hawaii. Yellowjackets live in colonies with numbers up to 3000 individuals. Their lifecycle begins in the spring when overwintering queens forage and build a nest underground, in vegetation/sides of human structures, or within the walls of human buildings (Ross and Matthews, 1991). Stinging events at the early “queen-stage” of the

lifecycle in which only the queen and a few small workers are present are rare. As more workers are reared, the population rapidly increases to a peak in summer to the autumn. At this time stinging incidents become frequent. Yellowjackets also have recruitment alarm pheromones that alert nest mates to come to the defense of the colony. As a result, human and other intruders often receive many stings. Toxic envenomations only occur when the number of stings is large, often in the range of 50 or more stings for an adult human. Confirmed human direct toxic death is almost unknown (Gädeke et al., 1977), though severe cardiac or central nervous system effects, and even death, have been noted in patients receiving relatively few stings (Day, 1962; Levine, 1976; Rowe et al., 1979; Volders et al., 2012). These patient responses were almost certainly immunologically based, rather than the result of massive toxic challenge. Several studies report young children who have survived several hundred yellowjackets stings (James and Walker, 1952; Levick and Braitberg, 1996; West et al., 2011). The most noteworthy clinical observation with toxic yellowjacket envenomation is renal failure (James and Walker, 1952; Gädeke et al., 1977).

4.3. Paper wasps and other paper-nesting wasps (*Polistes* and others)

Paper wasps can deliver locally-painful stings, but rarely more than one or two at a time. Fortunately most paper wasp nests contain only a dozen to 100 or so individual wasps with the result that massive envenomations are absent from the literature. Envenomations by paper wasps usually require concern only about allergic reactions and consoling patients who present with cutaneous pain and inflammation. Fortunately allergic reactions to paper wasp stings are not as frequent as reactions to yellowjackets stings and allergic deaths are rare (Witharana et al., 2015).

5. Solitary wasps of minor potential concern

5.1. Tarantula hawks (*Pompilidae*: *Pepsis*, *Hemipepsis*, and others)

Tarantula hawks and other large spider wasps within the hymenopteran family Pompilidae present an intimidating image with their large black or iridescent purplish bodies highlighted with brilliant orange or jet-black wings. These huge wasps usually engender fear and respect, and for good reason: their stings share with bullet ants the distinction of being the most painful of hymenopteran stings with a

Table 5
Summary of outcomes of humans receiving multiple stings by hornets.

Number of stings	Age (years)	Notes	Fate	Reference
17	62M		died	Yanagawa et al., 2007
20+	adult M	lived 8 h	died	Scragg and Szent-Ivany, 1965
20+	8 F	lived 40 h	died	Hoh et al., 1966
25	7M	lived 7 d	died	Vikrant et al., 2005
25	4 F	lived 24 h	died	Hoh et al., 1966
29	67 F	lived < 1 d; diabetic	died	Badiadka et al., 2017
30–40	78M		died	Yanagawa et al., 2007
40	46 F	lived 9 h	died	Kularatne et al., 2014
50	74M		died	Yanagawa et al., 2007
50–60	57M	lived 2 d	died	Kularatne et al., 2003
70	71M		died	Yanagawa et al., 2007
78	80M		died	Yanagawa et al., 2007
100	55 F		died	Yanagawa et al., 2007
109	3M	dialysis for 3 weeks	lived	Borochowitz and Hardoff, 1982
120	4 F	lived 18 h	died	Korman et al., 1990
130	48M	lived 32 h	died	Kularatne et al., 2014
150	55M	lived 8 d	died	Das and Mukherjee, 2008
180	19M		lived	Shilkin et al., 1972
180–200	25 F	28 d in hospital	lived	Ullah et al., 2016
250	33M	lived 9 d	died	Shilkin et al., 1972
Av = 50–70	adults	n = 62; 6 of 7 > 50 stings	7 died	Xuan et al., 2010
< 10–200	0.3–87	n = 1091; Hubei, China	48 died	Xie et al., 2013
> 10	18–78	n = 79; Shaanxi, China	4 died	Liu et al., 2016

rating of 4 on the insect sting pain scale, a scale rating the painfulness of hymenopteran stings and ranging from a low of 1 to a maximum of 4 (Schmidt, 2016). Fortunately, these solitary wasps have no colonies or nests to defend and, thus, are timid and unaggressive. They never intentionally attack humans or animals, reserving the sting for paralyzing tarantulas and other large spiders and, when necessary, as a personal defense when they are held or trapped against the body of a person. Although their stings are exceedingly excruciatingly painful, the pain lasts only a few minutes and causes almost no local inflammation or other signs of envenomation (Schmidt, 2004; Fig. 2). No dangerous clinical envenomations have been reported, other than mention of extreme patient anxiety or local pain.

5.2. Velvet ants (*Mutillidae*)

Velvet ants, sometimes called cow killers in North America because of the exceedingly painful stings they can deliver, comprise a large family, the Mutillidae, of more than 6000 species distributed worldwide in all environments except the most cold or isolated parts of the world. Velvet ant females are actually wingless solitary wasps (males have wings and can usually fly) which, when grasped or held, can deliver intensely painful stings. Fortunately, the stings are of low toxicity to mammals and present no clinical danger other than strong emotional reactions to the pain on the part of the patient (Schmidt, 2016). No allergic reactions to their stings have been reported.

5.3. Sphecids and other solitary wasps (*Sphecidae* and other families)

Sphecids wasps are among a large group of about 8000 solitary wasps (Goulet and Huber, 1993) in the Spheciformes, and they, plus a variety of other families of solitary wasps are sometimes large and conspicuous. Notable among these are the cicada killer wasps (*Sphecus* spp.) that superficially resemble enormous yellowjackets. Although frightening to some people, none of these wasps will sting unless held or restrained against the body. Their stings are very mild compared to the social wasps and no clinical problems relating to toxic envenomation have been reported.

6. Ants (*Formicidae*)

6.1. Fire ants (*Solenopsis*)

Fire ants consist of 60 or so species of small, darkish ants that live in large colonies containing upwards of several hundred thousand individuals. They originated in the New World and several species, particularly *Solenopsis invicta* and *S. geminata*, are invasive tramp species that have been transported through commerce to many parts of the world (Tschinkel, 2006). The stings of some fire ant species, including *S. invicta*, but not *S. geminata* or other North American “native” species, will produce small white-topped pustules at the sting sites. These pustules form after a day or two and resolve within several days. They are sterile and present no risk other than possible secondary infection subsequently to patient scratching (deShazo et al., 1990).

Fire ants constitute a major source of sting venom allergy and anaphylaxis, including allergic deaths, and are of serious medical concern for that reason in most places where they are common (Freeman and Tracy, 2017). Other than a few deaths secondary to mass stinging events by fire ants coming indoors and attacking elderly bedridden individuals in long-term care facilities or immobile infants (Rupp and deShazo, 2006; More et al., 2008), no toxic envenomation deaths have been reported. The most extreme reported case of a healthy adult being massively envenomated by fire ants involved a middle-aged man who received over 5000 stings and was clinically hospitalized overnight before being discharged the next morning with no major medical consequences (Smith and Smith, 1971).

6.2. Jumper and bulldog ants (*Myrmecia*)

Jumper and bulldog ants consist of about a hundred species of large 1–2 cm long ants found in Australia, plus one species in New Caledonia (Ogata and Taylor, 1991). Their venom chemistry and allergenicity have been extensively investigated. Perhaps counter-intuitively the jumper ants, though smaller than bulldog ants, are the main cause of allergic reactions in Australia (Brown et al., 2014). Both jumper and bulldog ants are quick, agile ants with highly acute vision and a readiness to sting. Stings are painful and their venoms are highly toxic to mammals. Nevertheless, no massive envenomations or toxic deaths have been reported in the literature. This is likely because the number of ants in a colony is relatively small in comparison to honeybees, and the ants are much smaller than hornets; thus, the number of stings required for a life-threatening envenomation is too large to cause toxic deaths (Table 1).

6.3. Bullet ants (*Paraponera clavata*)

Bullet ants, also called tucandeiras and an assortment of other local names in South and Central America, are a monotypic species in their own monotypic subfamily of ants. They are distributed in the New World Atlantic moist forests from Nicaragua to Paraguay and live in large colonies of up to 3000 individuals. They are enormous, robust ants (second in size only to the giant ants in the genus *Dinoponera*) and attain 18–22 mm in length. Bullet ants have gained recent notoriety for their use by several human cultures in the Amazon that incorporate their stings as a part of puberty rites for boys in the community (<http://www.youtube.com/watch?v=XwvIF09srUw>; Lang, 1914). If ever there were to be a stinging insect to test one's mettle for pain and toughness to become a man, this is the species. Bullet ant stings are debilitatingly and excruciatingly painful, with the pain lasting between 12 and 36 h before finally receding and leaving little sign that the individual was envenomated (Schmidt, 2016). The venom is highly toxic to mammals (Table 1); nevertheless no clinically-dangerous envenomations have been reported in the literature. The lack of literature reports of either toxic envenomations or allergic reactions may, in large part, be because these stings are so painful that individuals go to extreme effort to prevent multiple or subsequent stings.

6.4. Harvester ants (*Pogonomyrmex*)

Harvester ants in the genus *Pogonomyrmex* are prominent members of many arid and semi-arid regions in the New World that have warm or hot summers. Colonies of the various species can range in numbers of individuals from around 100 to about 20,000. Their stings produce intense, long-lasting pain that often endures 4–8 h. Their venom is exceedingly toxic to mammals and induces several symptoms indicative of neurotoxicity including piloerection and localized sweating around the sting site (Schmidt, 2016). No clinically important toxic envenomations have been reported, though allergic reactions have been known and investigated for a number of years (Pinna et al., 1977). That no known clinically-important toxic envenomations have been reported is likely a consequence of the ants being conspicuous, generally unaggressive, and delivering highly painful stings, a combination that makes multiple stings or repeated stings rare.

6.5. Ants of minor concern (little fire ants [*Wasmannia auropunctata*], European fire ant [*Myrmica rubra*], asian needle ants [*Brachyponera chinensis*], and Samsum ants [*Bothroponera senaarensis*])

All of these ants are of minor medical importance and are of concern mainly because of their mildly painful stings, tendency to sting people, and record of causing allergic reactions and medically minor pathologies. Little fire ants are perhaps the clinically most important of the group with their stings causing ocular damage both in humans and

animals (Rosselli and Wetterer, 2017). They are a tiny tramp species of ant that has been transported to many tropical areas around the world where they cause agricultural and stinging problems, though they are not confirmed to produce allergic reactions. European fire ants are an invasive tramp species originally from Europe that was introduced into Northeastern North America and have since spread. Their stings are mildly painful and the ants are mostly disliked for their nuisance value. Allergic reactions are likely, though there is a paucity of reports (Grodén et al., 2005). Asian needle ants are indigenous to eastern Asia and are notably problematic in Korea and nearby areas because their stings can induce allergic reactions (Jeong et al., 2016). They became introduced into the Appalachian region of eastern USA where they are now established. Their sharp, low pain-intensity stings have been reported to induce allergic reactions among the inhabitants of the ants' new homes (Nedler et al., 2006). Samsun ants live in Africa and the Middle East where they may present a problem with venom allergy in stung individuals (Al Anazi et al., 2009). These small black approximately 5-mm-long ants sting remarkably painfully for their size and produce large colonies of several thousand individuals. To date, no clinically important toxic envenomations have been reported for any of these species.

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