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Rombod Rahimian MPH , F. Mazda Shirazi MD, PhD ,  
Justin O. Schmidt PhD , Stephen A. Klotz MD

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## **Honeybee Stings in the Era of “Killer Bees”: Anaphylaxis and Toxic Envenomation**

**Rombod Rahimian, MPH,<sup>1</sup> F. Mazda Shirazi, MD, PhD,<sup>2</sup> Justin O. Schmidt, PhD,<sup>3</sup>**

**Stephen A. Klotz, MD<sup>4</sup>**

University of Arizona School of Medicine<sup>1</sup>; Department of Emergency Medicine<sup>2</sup>;  
Department of Entomology<sup>3</sup> and Department of Medicine<sup>4</sup> University of Arizona,  
Tucson, Arizona

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**Corresponding Author:** Stephen A. Klotz, [sklotz@u.arizona.edu](mailto:sklotz@u.arizona.edu); Division of Infectious Diseases, 1501 N. Campbell Ave., Tucson, AZ 85724

**Address Correspondence to:** MF Shirazi, Director, Arizona Poison and Drug Information Center; [mshirazi@aemrc.arizona.edu](mailto:mshirazi@aemrc.arizona.edu)

### **Clinical Significance**

- In the Southwest “killer bees” are the predominant feral honeybee and sting in mass.

- Bee stings due to feral “killer bees” result in anaphylaxis as well as toxic envenomation following massive stinging.
- Anaphylaxis occurs within minutes whereas, toxic envenomation from massive stinging may take hours to days to manifest.
- Medical responders need to recognize the risks of massive stinging that requires observing victims over several days.

### Abstract

**Background:** Twenty-six years after the arrival of “killer bees” in Arizona, the entire state with the exception of high elevations in the north is populated with this bee variety and 11 people have died at the scene of massive bee attacks.

**Methods.** Due to the aggressive behavior of these bees we studied bee stings reported to the Arizona Poison and Drug Information Center.

The center received 399 calls regarding 312 victims of bee stings from January 2017 through June 2019. Calls originated from private residences and emergency centers.

**Results.** Stings occurred at victims’ home residences in 272 (84.7%) of cases and 24 (7.5%) in public areas; 251 people suffered 1 sting; 42 individuals, 2-10 stings, 4 had 11-49 stings and 13 individuals had >50 stings (so-called massive stinging). Three individuals were admitted to intensive care units (ICU) and one 35-year old man died of anaphylaxis after one sting; moderate clinical effects occurred in 32 individuals including 6 admitted to non-ICU beds. Anaphylaxis occurred in 30 (9.6%) of individuals, 16 receiving 1 sting. Toxic effects, tachycardia, elevated creatinine and/or rhabdomyolysis occurred in 13 (4.2%) individuals.

**Conclusions.** In the past, individuals stung more than 50 times were beekeepers working with European honeybees whereas, in the current era, single as well as massive stings are due to feral “killer bees”. This change in epidemiology requires a new approach to sting

victims: those with massive stinging should be evaluated and observed for anaphylaxis and serial laboratory values obtained for days to detect the toxic effects of envenomation.

### Introduction

Africanized bees or “killer bees” (*Apis mellifera scutellata*) were first reported in the United States in Hidalgo, Texas in 1990, a small community located several miles north of the Rio Grande River. The ‘killer bees’ quickly made their way from Mexico into Arizona and New Mexico by 1993 and subsequently, California and Nevada.<sup>1</sup> Today, all wild honeybees in Arizona are “killer bees” with the exception of those in the high elevations of the northernmost part of the state where these bees cannot survive the winter months (JO Schmidt, personal observation). Geographic spread of this bee newcomer into the Southwest may have been assisted by the almost coincidental decline in feral and domestic honeybee populations from parasitic infections.<sup>2,3</sup> For example, colonies of feral European honeybees existed in Organ Pipe National Monument in southern Arizona in the 1980’s, but *Varroa* mites exterminated them by the 1990’s (JO Schmidt, personal observation).

Most residents of Arizona are aware of the presence of “killer bees” in their state and stinging incidents prompt phone calls to the Arizona Poison and Drug Information Center and visits to urgent care centers and emergency rooms. We report a 30-month experience with honeybee stings as well as coroner cases of lethal bee attacks in the state and attempt to determine if the presence of “killer bees” has changed the epidemiology and medical treatment of bee stings.

### Methods

**Data Collection.** The Arizona Poison and Drug Information Center in Tucson (Pima County) receives calls from 14 of the 15 counties in Arizona and surrounding states concerning victims of bee and wasp stings; all data is stored in the ToxSentry database. We accessed ToxSentry for all reports pertaining to bee and wasp stings from January 2017 through June 2019. Calls were received by trained personnel who took a history and either, suggested on-site care of the bee sting or referred victims to a health care facility for further care. All sting victims were followed to resolution of the problem or discharge from medical care and follow up. Data collected regarding each sting incident included: age and sex of victim; whether the victim was pregnant; where the exposure occurred (residence, school, etc.); county where sting occurred and date; the clinical management site and the clinical effects of the exposure and therapy employed. Minor clinical effects included pain, swelling and erythema from stings; moderate clinical effects included patients referred for further health care; and major clinical effects were severe anaphylaxis or toxic effects requiring hospitalization within intensive care units (ICU).<sup>4</sup> Daily medical notes along with therapy and laboratory data were recorded. The Arizona Poison and Drug Information Center's standard practice is to advocate for hospital observation in individuals stung more than 50 times (FM Shirazi, personal observation).

**Definitons.** A two-fold definition of anaphylaxis adopted by the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network was used and included: 1) acute onset of illness in the skin, mucosa, or both including hives, pruritus, flushing, swollen lips-tongue-uvula in addition to either respiratory compromise, reduced blood pressure or end-organ dysfunction; and 2) Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): a.

Involvement of the skin-mucosal tissue; b. Respiratory compromise; c. Reduced blood pressure or associated symptoms; d. Persistent gastrointestinal symptoms. Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours).<sup>5</sup>

## Results

**When and where stings occurred.** During the study period of January 2017 through June 2019 399 calls were received regarding stings to 321 individuals, the majority, 312 or 97.2% were stung by honeybees and 9 people by wasps or unknown insects. There were 185 victims in 2017, 96 in 2018, and 40 sting victims in 2019. The majority of victims, 192 (59.8%), were stung in Pima County where Tucson is the county seat or Maricopa County where Phoenix is the county seat (36 or 11.2%); the remainder of sting victims came from 12 other Arizona counties (no calls were received from La Paz County) and 17 victims were from out of state. The majority of exposures, 244 (76%), occurred during the months of April through September with June having the most sting episodes, 62; May had 40 episodes. In colder months there were far fewer reports of stings, for example, 8 stings in January and 4 reported in December.

**Number of stings and exposure sites.** Most victims, 251 (83%), received 1 sting; 42 individuals received 2-10 stings and 17 people had more than 10 stings (number of stings was unknown in 11 individuals) (**Table 1**). The exposures occurred at various locations, but the majority of stings, 271 (84.4%), occurred at the victim's home residence; 24 (7.5%) occurred in public areas; 5 (1.5%) of victims were stung at their workplace; 2 (<1%) at school, 1 (<1%) in a vehicle, and 17 (5.3%) were stung at unknown locations.

**Demography of victims.** More females, 172 or 53.5% were stung than males, 144 or

46.5%; 5 females were pregnant and reported only minor consequences of the stings. The age of sting victims ranged from 6 months to 87 years of age, the average age being 31 years old.

**Clinical Effects.** There were 146 (45.5%) individuals followed by the APDIC and clinical outcomes recorded. One victim died from anaphylaxis resulting from 1 sting and 3 individuals were judged to have major effects requiring admission to the ICU. The victims in the ICUs received 1,120 and 300 stings (**Table 2**). There were 32 (10%) sting victims with moderate clinical consequences including 6 people admitted to a non-ICU hospital beds; the latter group had 35, 50, 200, 300 and 950 stings (the number of stings for one hospitalized victim was not recorded). Most sting victims, 243 or 75.7%, were managed on-site by APDIC personnel and not referred to health care facilities. The most commonly reported clinical effect was a puncture wound in 302 (94.1%) of victims with pain in 231 (72%), swelling or edema at the puncture site in 178 (55.4%) and erythema at the puncture site in 105 (32.7%) victims.

**Anaphylaxis and anaphylaxis-like reactions and venom effects.** Signs and symptoms of anaphylaxis occurred in a number of victims from one sting only as well as victims of massive stinging in which the toxic effects of envenomation may occur simultaneously with anaphylaxis. We therefore attempted to separate anaphylaxis from toxic responses to venom. Using the criteria of anaphylaxis adopted by the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network<sup>5</sup>, 6 patients met the first criterion for anaphylaxis and 24 met the second criterion for anaphylaxis for a total of 30 patients with anaphylaxis (9.6%). Nine patients received epinephrine therapy. The majority of patients (16) with anaphylaxis were stung once. The only fatality in the entire

study was a 35-year old male stung once who died of anaphylaxis. Upon admission he had CNS depression, hypotension, atrial fibrillation, acidosis, torsade de pointes, and asystole. The patient received antihistamines, IV fluids, vasopressors, sodium bicarbonate, steroids, intubation and ventilation, a hypothermia protocol, and cardiopulmonary resuscitation without success.

Many patients receiving 50 or more stings (**Table 3**), suffered both from anaphylactic symptoms including pain, vomiting, erythema, edema, hypotension, tachycardia as well as toxic effects of the venom such as tachycardia, increases in creatinine, rhabdomyolysis, or acidosis. Of the 13 victims of massive sting attacks, 6 victims were discharged home following evaluation and one left against medical advice and only 6 were hospitalized for observation and serial measurements of blood, renal function and cardiac monitoring as recommended by the APDIC.

**Therapy.** The most common therapy given sting victims was irrigation of the puncture site in 205 or 63.9% of victims (**Table 2**). This was followed by use of antihistamines in 129 or 40.2% of victims; 30 (9.3%) individuals received steroids; 19 (5.9%) individuals were administered intravenous fluids and 9 (2.8%) individuals received epinephrine.

**Lethal ‘killer bee’ attacks in Arizona.** Massive bee attacks resulting in death outside of a healthcare facility are treated as coroner’s cases and are not reported to the APDIC. We were able to find accounts of 11 lethal massive bee attacks in the state of Arizona (**Table 4**) since the arrival of “killer bees” in the state in 1993. Victims were predominately men engaged in outdoor work such as landscaping and operating a backhoe that disturbed colonies (**Figure 1, Left**) or men hiking or climbing. Climbers may find themselves

adjacent to a colony of honeybees hidden in the rocks (**Figure 2, Right**) and escaping an attacking swarm maybe impossible. Two men climbers fell to their deaths after being attacked by swarms of honeybees.

## Discussion

Treatment of bee sting victims in the United States preceding the arrival of Africanized bees was focused upon recognition and treatment of anaphylaxis.<sup>6</sup> Prior to the arrival of “killer bees” in the US in 1990, beekeepers were the sole victims of 50 or more stings.<sup>7</sup> In our study, 13 individuals (4.2%) over a 30-month period received >50 stings, mainly outside their home residence (**Table 3**) and displayed some features of toxic envenomation. All these victims survived, the only death in the study being due to anaphylaxis from 1 sting. Despite recommendations from medical toxicologists and the Arizona Poison and Drug Information Center in regard to evaluation and treatment of massive bee envenoming (>50 stings), 7/13 victims of massive stings were evaluated and sent home or left the emergency room against medical advice rather than admitted to the hospital for observation and serial monitoring of laboratory values over several days. Thus, insufficient time elapsed between the stinging incidents and when laboratory values were obtained since the toxic effects of venom occur hours to days after stinging.

However, immediate allergic phenomena were recognized and treated successfully. Thirty individuals (9.6%) among the 312 sting victims showed signs and symptoms of anaphylaxis. Appropriate and adequate use of blood pressure support, antihistamines, steroids and epinephrine were employed.<sup>6</sup> (see **Table 2**). It is estimated that 5% of the population suffer anaphylaxis during their lifetime and in a random sample of 1000

American adults it was found that 7.7% had a confirmed diagnosis of anaphylaxis with 19% of those due to insect stings (overwhelmingly, honeybees).<sup>8</sup> Jerschow reported 374 venom-related lethal anaphylactic deaths from 1999 to 2010 for an average of 34 per year in the US.<sup>9</sup> A more recent report claimed there were 1,109 deaths from hornet, wasp and bee stings in the US from 2000 through 2017 for an average of 62/year.<sup>10</sup> How these data compare with that of Jerschow<sup>9</sup> is not apparent. One cannot tell the impact of the new bee variety upon these data. It is an interesting irony that beekeepers who are stung on a daily or weekly basis tend not to suffer from anaphylaxis<sup>11</sup> and have high levels of blocking IgG antibodies that are believed to prevent IgE from expressing its activity. Self-therapy with epinephrine is an effective therapeutic modality for those with a history of anaphylaxis,<sup>12</sup> but it is not always instituted or instituted too late to help. The one death in our study was the victim of one bee sting and entered the hospital in irreversible shock from anaphylaxis. Victims of massive bee attacks treated for anaphylaxis successfully once may “slip” back into anaphylaxis a day or two later due to the large amount of venom injected, so-called biphasic anaphylaxis.<sup>13</sup>

Massive sting attacks were not unknown in the past, but were due to accidents involving beekeepers working with domesticated European honeybees.<sup>7</sup> Now massive stinging originates from feral colonies of “killer bees” and involves people engaged in outdoor activities such as climbing, hiking, and working outside with machinery or merely walking outside their homes (**Table 3**). Adult individuals receiving 50-200 stings are at risk for renal failure; those with 200-500 stings often suffer from multi-organ failure and individuals with >500 stings the situation is life-threatening and death can occur.<sup>14</sup> Honeybee venom is mainly composed of melittin, apamin, mast cell

degranulating peptide, phospholipase, hyaluronidase, histamine, dopamine and norepinephrine.<sup>15</sup> Melittin is probably the largest constituent by weight and the component of honeybee venom responsible for myocardial, kidney and other organ injury.<sup>16</sup> But the quantity of stings sustained from “killer bees,” not the quality of the venom is responsible for the adverse effects.<sup>17</sup> For example, the average amount of venom in a “killer bee” venom sac is 94  $\mu\text{g}$  *versus* an average of 147  $\mu\text{g}$  of venom in a European honeybee venom sac.<sup>18</sup> However, “killer bee” venom contains more phospholipase A<sub>2</sub> than venom of European bees and it is the most allergenic component of bee venom.<sup>15</sup> Variation in responses to the stings by individuals in our study could be explained by the variation in venom that occurs within different colonies of “killer bees.”<sup>15</sup> For example, one individual in our study was stung 35 times (by definition not massive stinging), but suffered from rhabdomyolysis and coagulopathy.

Not every Arizonan appreciates the potential danger of these insects. The man killed by a massive bee attack in Yuma, Arizona was attempting to remove a bee colony from a couch in his back yard. Rock climbers in the state are at particular risk and should be warned of the peril of scaling or rappelling mountains in Arizona (**Table 4**). Fear of “killer bees” did change public perception at least in regard to the potential to harm their pets.<sup>19</sup> A feature of Africanized bee behavior increasing the risk for massive attacks is once a colony is disturbed it takes an average of 28.2 minutes to “settle down” as opposed to European bees that “settle” on average, within 2.9 minutes (AC Stort in Michener<sup>7</sup>). “Killer bees” despite their name, possess favorable characteristics for bee husbandry such as increased reproduction, swarming behavior and foraging activity, and resistance to diseases and parasites.<sup>7</sup>

The clinical signs, symptoms and laboratory derangements following massive bee envenomation may be a manifestation of anaphylaxis (hypotension, nausea, vomiting, tachycardia) occurring early in the course of envenomation or due to direct venom toxicity, e.g., myocardial and other muscle injury, renal failure, thrombocytopenia and coagulopathy observed hours to days later. Our study contained examples of both allergic and toxic effects of bee stings. Anaphylaxis was addressed successfully by healthcare workers and victims alike. However, less than half the victims (6/13) suffering 50 or more stings were managed according to expert advice. Swarms of attacking bees target and penetrate the nasal cavity, bronchial tree (requiring bronchoscopic removal), esophagus, stomach, external ear canal and burrow under the eyelids (MF Shirazi personal observation, multiple patients) and these attacks may require hospitalization not only for observation, but removal of bees from the body. Physicians and other healthcare workers are generally unfamiliar with the systemic toxicity from envenomation due to massive numbers of honeybee stings and entrance of bees into body cavities. Education of healthcare workers is needed to address this deficiency.

### Figure Legends

**Figure 1; Left.** Swarm of honeybees in a Blue Palo Verde tree in Tucson, Arizona. This swarm is pausing in these branches and will move on to discover a new colony site with better protection. These swarms can be a hazard in residential areas if they are disturbed.

**Figure 1; Right.** A colony recently destroyed by mites in a rock crevice on the side of a wash in Tucson, Arizona. Dead bees lie in the dirt below numerous combs filled with honey within the crevice. The location of this colony was particularly a risk for dogs and other small mammals investigating the site.

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**Figure 1; Left.** Swarm of honeybees in a Blue Palo Verde tree in Tucson, Arizona. This swarm is pausing in these branches and will move on to discover a new colony site with better protection. These swarms can be a hazard in residential areas if they are disturbed.

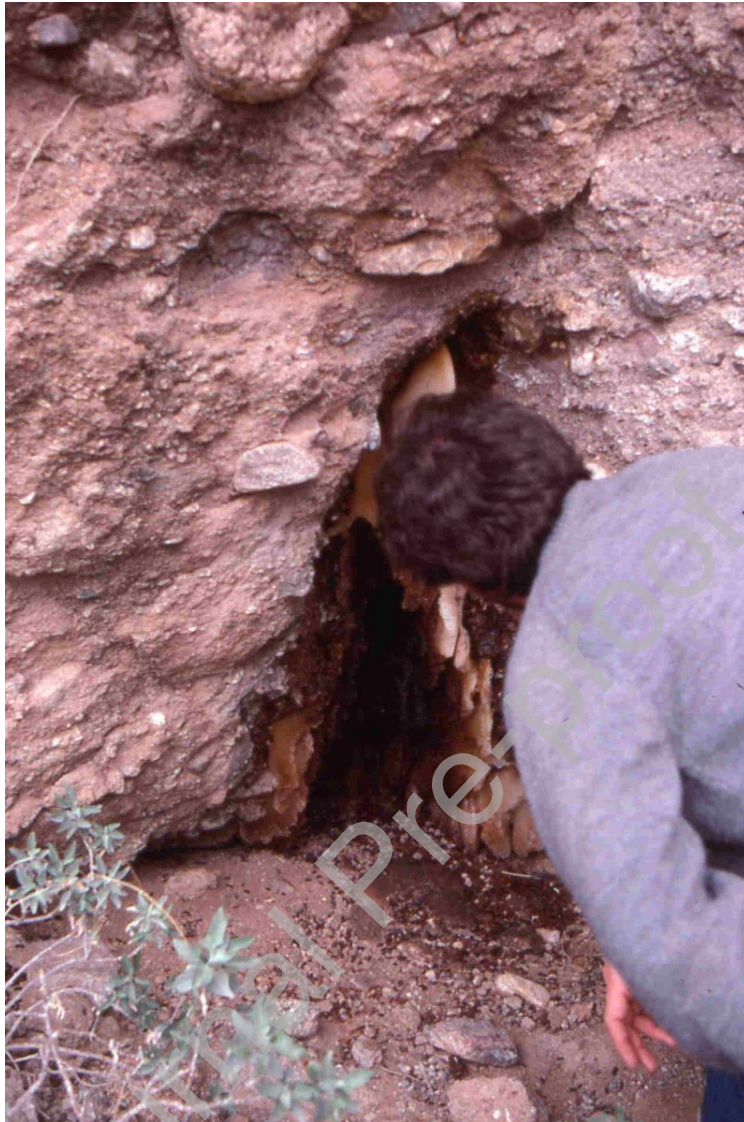


**Figure 1; Right.** A colony recently destroyed by mites in a rock crevice on the side of a wash in Tucson, Arizona. Dead bees lie in the dirt below numerous combs filled with honey within the crevice. The location of this colony was particularly a risk for dogs and other small mammals investigating the site.

| Number of Stings | *Number of Victims/Percent |
|------------------|----------------------------|
| 1 sting          | 251 (81%)                  |
| 2-10 stings      | 42                         |
| 11-49 stings     | 4                          |
| 50-100 stings**  | 7                          |
| 101-500 stings** | 5                          |
| >501 stings**    | 1 (950 stings)             |

**Table 1. Number of honeybee stings/person during January 2017 through June 2019 reported to the Arizona Poison and Drug Information Center.** There were 321 individuals stung, 312 by honeybees; 9 individuals were stung by insects other than honeybees; \*11 reports did not specify the number of stings;\*\* massive sting victims.

| Outcome of sting                           | Individuals (Number of Stings)                                                 |
|--------------------------------------------|--------------------------------------------------------------------------------|
| Death                                      | 1 (1 sting)                                                                    |
| Major effect, Poisoning Severity Score*    | 3 in ICU (1, 120, 300 stings)                                                  |
| Moderate effect, Poisoning Severity Score* | 32<br>(6 hospitalized with 35, 50, 200, 300, 950 stings; number unknown for 1) |
| Minor effect, Poisoning Severity Score*    | 110                                                                            |
| Not followed (managed on-site)**           | 140                                                                            |
| Unable to follow and unknown               | 35                                                                             |
| Therapy                                    | ***Number (%) received therapy                                                 |
| Irrigate and wash puncture site            | 205 (63.9%)                                                                    |
| Antihistamines therapy                     | 129 (40.2%)                                                                    |
| Steroid therapy                            | 30 (9.3%)                                                                      |
| Intravenous fluid                          | 19 (5.9%)                                                                      |
| Vasopressors (epinephrine)                 | 9 (2.8%)                                                                       |

**Table 2. Outcome and therapy of hymenopteran stings.\*:** Poisoning Severity Score<sup>4</sup> ; \*\*:Call was made to Arizona Poison and Drug Information Center and the sting victim was managed and discharged from care by trained personnel. \*\*\*: N=321 individuals stung; 9 stung by wasps had minor effects of the sting.

| Age | Stings | Site   | Vomit-<br>ing | Tachy-<br>cardia | Hyper-<br>tension | Hypo-<br>tension | LFTs | Creati-<br>nine | Acidosis | Tropo-<br>nin<br>/CK-MB | Coagu-<br>lopathy | Rhabdo-<br>myolysis | Com-<br>ment             |
|-----|--------|--------|---------------|------------------|-------------------|------------------|------|-----------------|----------|-------------------------|-------------------|---------------------|--------------------------|
| 71  | 950    | Home   |               | x                | x                 |                  |      |                 |          | x                       | x                 | x                   | Non-<br>ICU,<br>diarrhea |
| 51  | 300    | Home   |               | x                |                   | x                |      | x               | x        |                         | x                 |                     | Non-<br>ICU              |
| 75  | 300    | Home   |               | x                | x                 |                  |      | x               | x        | x                       |                   |                     | Non-<br>ICU              |
| 84  | 250    | Home   | x             | x                |                   |                  | x    |                 |          | x                       |                   |                     | non-<br>ICU              |
| 81  | 140    | Home   |               | x                |                   |                  |      |                 |          |                         |                   |                     | Home                     |
| 71  | 120    | Home   |               | x                | x                 |                  |      | x               | x        |                         |                   |                     | ICU                      |
| 49  | 100    | Public |               | x                |                   |                  |      |                 |          |                         |                   |                     | AMA                      |
| 33  | 100    | Public | x             |                  |                   |                  |      |                 |          |                         |                   |                     | Home                     |
| 54  | 100    | Public |               | x                |                   | x                |      |                 |          |                         |                   |                     | Home                     |
| 52  | 100    | ?      |               |                  |                   |                  |      |                 |          |                         |                   |                     | Home                     |
| 57  | 100    | Home   | x             |                  |                   | x                |      |                 |          |                         |                   |                     | Home,<br>ataxia          |
| 50  | 100    | Work   |               |                  |                   |                  |      |                 |          |                         |                   |                     | Home                     |
| 68  | 50     | Public | x             | x                |                   |                  |      |                 |          |                         |                   |                     | Non-<br>ICU              |

**Table 3. Toxic effects of massive stinging (>50).** Site: denotes where stinging occurred (home residence, public space, or workplace); x: presence of symptom, sign, elevated laboratory value or pathologic states; LFTs: elevated liver function tests; Comment: other finding; where in hospital cared for (Intensive Care Unit [ICU] or non-ICU hospital bed; Home or left the hospital against medical advice (AMA)).

| Date           | Gender/age | Where in Arizona | Activity when attacked; Reference              |
|----------------|------------|------------------|------------------------------------------------|
| October 1995   | Female/88  | Apache Junction  | Outside home; 1000 stings <sup>20</sup>        |
| 2004           | Male       | Phoenix          | Climbing; fell to death <sup>20</sup>          |
| September 2011 | Male/65    | Yavapai          | Working on home <sup>20</sup>                  |
| October 2012   | Male/19    | Tucson           | Climbing; fell to death <sup>20</sup>          |
| May 2013       | Male       | Tucson           | Climbing; 1,700 stings <sup>20</sup>           |
| October 2014   | Male/32    | Douglas          | Gardening <sup>20</sup>                        |
| May 2016       | Male/23    | Apache Junction  | Hiking; 1000 stings <sup>21</sup>              |
| July 2017      | Male       | Yavapai          | Working on road; using backhoe <sup>22</sup>   |
| August 2017    | Male       | Wickenburg       | Landscaping; using backhoe <sup>23</sup>       |
| April 2019     | Male/51    | Yuma             | Trying to remove bees from couch <sup>24</sup> |
| August 2019    | Male/73    | Cochise          | Cleaning up scraps along a road <sup>25</sup>  |

**Table 4. Lethal massive bee attacks in Arizona since 1993.** All were coroner cases since victims died at the scene of attack.