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# Massive Honey Bee Envenomation-Induced Rhabdomyolysis in an Adolescent

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## ABSTRACT

Massive envenomations by honey bees are capable of causing multiorgan dysfunction as a result of the direct toxic effects of the large venom load received. Although all varieties of honey bee have the potential for these attacks, the Africanized honey bee (*Apis mellifera scutellata*) is the most commonly implicated subspecies. In the United States, the Africanized strain is found primarily in the southwestern states and is known for its highly defensive behavior if disturbed. Mechanisms behind the multiorgan dysfunction produced by these mass envenomations are not clearly understood. We present a case of a 13-year-old male who was stung by ~700 honey bees and developed progressive upper-body swelling and systemic manifestations of mass envenomation including rhabdomyolysis, renal insufficiency, and a transient transaminase elevation.

**T**HE DANGERS OF Hymenoptera (wasps, bees, hornets, and yellow jackets) have long been known as a potential environmental hazard. An estimated 40 deaths occur in the United States each year, nearly all of which are the result of immunoglobulin E-mediated type I anaphylactic reactions from isolated stings.<sup>1</sup> Massive honey bee envenomations (>50 stings), in contrast, recently have become of greater concern in the United States with the northward migration of the highly defensive Africanized honey bee into the southwestern states over the last 15 years. Reports of these mass honey bee attacks on humans and pets abound in the lay press; however, scientific literature concerning the specific health effects and the mechanism of toxicity after massive envenomations remains relatively scarce. Here we report a case of massive honey bee envenomation in a young male that resulted in significant systemic toxicity.

## CASE REPORT

A 13-year-old, 55-kg male was attacked by a large number of honey bees while walking through a heavily wooded preserve in southern California in June 2004. Two companions, 1 of whom received an estimated 50 stings, described the child's face and upper torso as being hardly visible because of the large number of attacking bees. While continuing to be stung, he ran several hundred feet to a nearby house, where he was sprayed down with water from a garden hose by a local homeowner,

causing the remaining bees to disperse. Emergency medical services arrived minutes later and found the boy to have a pulse of 126 beats per minute, respirations of 26/minute, blood pressure of 96/palpable mm Hg, and pulse oximetry of 85% on room air. The child was placed on a nonrebreather face mask with immediate improvement in oxygenation. Pulmonary auscultation was remarkable for diffuse wheezing. He received nebulized albuterol and Atrovent treatments, 50 mg of oral diphenhydramine, and 0.3 mg of subcutaneous (1:1000) epinephrine en route to the emergency department. A local exterminator was called to the scene and destroyed the suspected hive within hours after the initial attack, with no bees surviving or collected for subspecies identification.

On arrival to the emergency department, an estimated 700 stings were noted primarily over the boy's head, arms, and upper torso. The imbedded stingers were removed shortly after arrival. No evidence of urti-

**Key Words:** environmental risk, renal failure, rhabdomyolysis, bee envenomation, Hymenoptera

**Abbreviations:** CPK, creatinine phosphokinase; IV, intravenous(ly)

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caria, pruritis, respiratory distress, airway compromise, or hypotension was appreciated during this emergency-department evaluation. He was given alprazolam 0.5 mg orally for agitation and discomfort. Other than localized irritation at the multiple sting sites, there were no physical-examination abnormalities appreciated. Given his benign appearance, normal vital signs, and improved comfort, he was discharged from the hospital with his parents after 4 hours of observation and given instructions to continue oral diphenhydramine for symptomatic relief.

Eight hours after the initial stinging episode, he began to experience diffuse pain, facial swelling, nausea, and multiple episodes of vomiting. Several dead honey bees were visualized in the vomitus. He returned to the emergency department approximately 4 hours later. Initial vital signs on return included a temperature of 100.4°C (rectally), pulse of 101 beats per minute, respirations of 20/minute, blood pressure of 106/64 mm Hg, and pulse oximetry of 98% on room air. He was evaluated by the medical toxicology service at this time and was noted to have a markedly edematous face with hundreds of erythematous, crusty, nonpurulent sting sites on his ears, nose, lips, scalp, and neck (Fig 1). Massive periorbital soft tissue swelling prevented corneal visualization. Diffuse tongue and soft palate swelling with multiple stings were noted in the oropharynx. There was no drooling or stridor. The skin on his chest, abdomen, and upper extremities revealed several hundred similar sting sites (Fig 2). Pulmonary examination revealed no rales, wheezing, or rhonchi. Cardiac and abdominal examinations were normal. Relatively few stings were noted on the lower extremities. He answered questions appropriately with muffled, slurred speech and showed no evidence of neurologic deficits.

Laboratory studies at the time of his returned emer-



**FIGURE 1**  
Multiple sting sites noted to the face, neck, and scalp with diffuse swelling 24 hours after envenomation.



**FIGURE 2**  
Chest and right upper arm 24 hours after envenomation, with localized swelling at the site of the multiple stings.

gency-department evaluation included sodium (135 mEq/L), potassium (4.0 mEq/L), chloride (99 mEq/L), bicarbonate (20 mEq/L), serum urea nitrogen (38 mg/dL), creatinine (3.1 mg/dL), creatinine phosphokinase (CPK) (32 520 ng/mL), white blood cell count (24 000/mm<sup>3</sup>), hemoglobin (13.6 g/dL), and platelets (245 000/mm<sup>3</sup>). Additional studies obtained on the day of admission included a troponin-I of 1.7 ng/mL (reference: <0.3 mg/mL), alanine aminotransferase of 132 IU/L, albumin of 3.9 g/dL, and urinalysis remarkable for 3+ protein, 3+ blood, 7 red blood cells per high-power field, and coarse granular casts. An electrocardiogram and chest radiographs showed no abnormalities. He was admitted to the hospital and treated initially with methylprednisolone 125 mg intravenously (IV), ranitidine 300 mg IV, and diphenhydramine 25 mg IV in addition to cefazolin 1 g IV for concerns with overlying skin infection. Morphine and lorazepam were administered for pain. He was given 2 liters of normal saline by intravenous bolus followed by continuous infusion at 200 mL/hour.

During the initial 24 hours of monitoring, his urine output was minimal (~300 mL) but eventually responded with aggressive hydration and intravenous furosemide, resulting in a large diuresis by the second hospital day. Generalized facial and thoracic swelling gradually improved over the course of the next several days, with the patient able to open his eyes without assistance by the third hospital day. There was a mild decrease in the hemoglobin to 10.8 g/dL and slight hyperbilirubinemia (measured total bilirubin: 1.5 mg/dL; indirect bilirubin: 0.2 mg/dL). Pain was controlled initially with IV morphine and lorazepam, eventually converted to oral opioid analgesics. Renal insufficiency from rhabdomyolysis improved rapidly after reaching a peak CPK level of 106 720 ng/mL at 48 hours after the stings (Fig 3). A transient elevation of hepatic transaminases

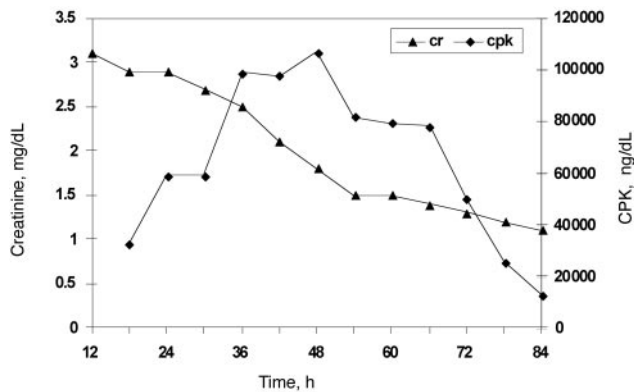


FIGURE 3  
CPK and creatinine (cr) plasma levels measured following the time from envenomation.

was evident with a peak alanine aminotransferase of 242 IU/L on the third hospital day before gradually returning to normal. In addition, he became and remained persistently hypoalbuminemic up to discharge, with an albumin nadir of 2.5 g/dL on hospital day 3. He continued to be treated with oral steroids, diphenhydramine, cimetidine, and antibiotics throughout his hospitalization.

The patient was discharged home on the sixth hospital day with minimal pain and significantly decreased facial and upper-body swelling. No evidence of delayed hypersensitivity reaction such as urticaria, bronchospasm, joint swelling, or arthralgias occurred. Facial and scalp swelling gradually resolved, and he was reported by his father to be back to his normal appearance with no evidence of scarring or edema 2 months after his hospitalization. No follow-up laboratory studies after hospital discharge were available.

## DISCUSSION

Unlike immune-mediated anaphylactic reaction, toxicity from massive honey bee envenomations occurs from the direct toxic effects of the large volume of injected venom. Honey bee venom is a complex mixture of >20 identified enzymes, peptides, and active amines. Melittin, the primary pain-inducing compound, makes up ~50% by weight of the total venom and functions with phospholipase A<sub>2</sub> as a cytolytic agent, resulting in direct tissue damage such as hemolysis and rhabdomyolysis.<sup>2,3</sup> The roles of other major components including hyaluronidase acid, phosphatase, lysophospholipase, bradykinin, dopamine, and apamin are less well characterized. Honey bee venom contains small amounts of histamine (0.7–1.6%) in addition to mast cell degranulating peptides that cause additional endogenous histamine release, which contributes to localized inflammation and improved venom absorption.<sup>2</sup>

Immediate effects after multiple stings include localized pain, swelling, and erythema at individual sting sites. Stings to the eyes can result in corneal edema and ulceration.<sup>4</sup> When bees are swallowed, life-threatening

pharyngeal edema and respiratory obstruction may occur.<sup>5</sup> Early systemic symptoms after large-volume envenomation include fatigue, dizziness, nausea, vomiting, and diarrhea. Within 24 hours, hemolysis, hemoglobinuria, rhabdomyolysis, and hepatic transaminase enzyme elevations may develop. Subendocardial damage and cardiac enzyme elevations in human case reports and animal studies may result from direct venom effects in the absence of anaphylaxis and hypotension.<sup>6,7</sup> Renal insufficiency and electrolyte abnormalities such as hyperkalemia may occur secondary to rhabdomyolysis, hemolysis, and acute tubular necrosis.<sup>4,8–11</sup> Nonanaphylactic responses to multiple stings often will be apparent within the first several hours; however, severe systemic signs and symptoms have been delayed for up to 24 hours or more.<sup>12</sup> This seems consistent with our patient, who remained relatively asymptomatic during the initial 6 hours after envenomation until later onset of vomiting and progressive upper-body swelling. Although this individual's early hypoxia and pulmonary findings suggest a near-immediate histamine-mediated response, the subsequent multiorgan involvement in this hemodynamically stable individual seems consistent with the effects of direct venom toxicity.

Death from mass envenomation occurs rarely, primarily in individuals with >500 to 1000 stings; however, as few as 150 stings were implicated in 1 elderly man's death.<sup>13</sup> Survival with aggressive supportive care has been reported after >2000 stings.<sup>9</sup> It has been estimated that systemic toxicity may occur with a minimum of 50 stings in adults. A minimum number of stings to cause systemic toxicity in children is less clearly defined. Mass envenomations are rare occurrences in children despite the possibility of greater risk, given the inability of the very young to escape attacking honey bees, their decreased body mass/venom ratio, and the propensity of young people to provoke an active hive.<sup>11</sup> Renal failure requiring temporary dialysis and skin grafting for necrotic scalp lesions were needed for a 4-year-old who sustained >1000 stings in rural central Africa. Franca et al<sup>11</sup> reported 2 Brazilian youths, ages 8 and 13, who sustained 400 and 800 stings, respectively. Both displayed a significant hepatic transaminase elevation and leukocytosis, with the 13-year-old developing rhabdomyolysis, progressive renal failure requiring dialysis, and eventual death from complications related to the massive envenomation. A thorough review of the popular and scientific literature revealed no cases of massive envenomation in the pediatric population in the United States that culminated in death.

Our patient's venom-induced rhabdomyolysis and rapid onset of renal insufficiency are noteworthy with the CPK elevation of 106 720 ng/mL, representing the highest level reported after mass honey bee envenomation. Skeletal muscle biopsies after similar envenomations have demonstrated changes consistent with the

prominent inflammatory reaction expected in rhabdomyolysis.<sup>14</sup> Both hemolysis and a direct acting nephrotoxic component of honey bee venom have been proposed as alternative mechanisms for acute tubular necrosis after mass envenomation.<sup>4,8,15</sup> In severe cases, often involving a considerable delay in treatment, anuria and electrolyte abnormalities may develop, requiring temporary hemodialysis followed by eventual improvement in renal function.<sup>16</sup> Early intervention and aggressive hydration during the first 12 hours likely prevented this patient from developing worsened renal dysfunction. This option may not be readily available in certain areas of the world such as rural Africa, in which large envenomations occur more commonly. The presence of hypoalbuminemia, proteinuria, and edema in this patient are suggestive of nephrotic syndrome, as has been previously described after bee stings.<sup>17</sup> A 24-hour urinary protein collection was not performed in this case, so it is uncertain whether massive bee envenomation-induced nephrotic syndrome had developed.

Given the highly defensive behavior and recent entomological evaluation of honey bees in southern California, the likelihood of this attack being from a hive of Africanized honey bees seems plausible. The Africanized honey bee subspecies entered the United States in 1991, >30 years after an accidental release of the Africanized strain in 1957 from a Brazilian laboratory and subsequent northward migration throughout Latin America.<sup>18</sup> Since that time, these Africanized species' descendents have moved into parts of California, Nevada, Arizona, New Mexico, Texas, Oklahoma, and Alabama. Although the Africanized honey bee is morphologically similar and possesses near identical venom to the "native" European honey bee, in general, the Africanized honey bee possesses a more aggressive attacking and stinging behavior when threatened.<sup>18</sup> Reports exist of Africanized honey bees pursuing individuals up to one fourth of a mile.<sup>19</sup> Differentiation of honey bee subspecies requires appropriate collection techniques and mitochondrial DNA testing that were not performed before this hive's extermination.<sup>17</sup> Massive bee envenomations by other honey bee subspecies are less common but have been described in regions such as England, India, and Hawaii, where Africanized bees are nonendemic.<sup>20-22</sup>

Appropriate management of nonallergic massive honey bee envenomations relies on aggressive supportive care, because no commercially available antivenom exists. Stinger removal may improve cosmetic appearance and patient comfort; however, near-complete release of venom from the honey bee venom sac occurs within 1 minute after the actual sting, making immediate removal of stingers at hospital presentation less urgent than thought previously.<sup>23</sup> Presentations consistent with massive histamine release should be managed, similar to typical anaphylactic reactions, with antihistamines, steroids, epinephrine, and airway support as

needed. Maintaining adequate urine output should be instituted with aggressive hydration to reduce the likelihood of rhabdomyolysis-induced renal insufficiency. Prolonged treatment with steroids and antihistamines, although frequently administered as was done in our patient's case, would be expected to provide little benefit, because the venom effects do not seem to be immune-mediated. Corticosteroid administration, however, may offer some benefit should evidence of bee sting-induced nephrotic syndrome develop.<sup>15</sup> Antibiotics should be considered in the setting of overlying skin infections that may occur at multiple sting sites.

Laboratory abnormalities and signs of progressive toxicity may not be apparent in the initial few hours after envenomation, which makes prolonged monitoring imperative. Although this adolescent made a complete and full recovery, delayed toxicity resulting in eventual death has occurred in other cases of Hymenoptera envenomation in children who were discharged prematurely and showed no initial signs of overt toxicity after short observation periods.<sup>24</sup> Given the potential for delayed toxicity and limited experience with mass honey bee envenomation, we believe that >50 honey bee stings in an adult or 1 sting per kg in a child warrants extended observation up to 24 hours after envenomation, with close monitoring of serum chemistries and CPK levels. Individuals with progressive symptoms or laboratory abnormalities should be admitted for additional observation and supportive care.

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Arenson KW. *New York Times*. November 2005

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