

“Kissing Bugs”: Potential Disease Vectors and Cause of Anaphylaxis

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Physicians in the United States should familiarize themselves with “kissing bugs” endemic to their area of practice and appreciate the medical implications of their bites. Bite victims often seek advice from physicians about allergic reactions as well as the risk of contracting Chagas disease. Physicians are generally knowledgeable about the role of kissing bugs in the transmission of *Trypanosoma cruzi* in Latin America. However, they may be unaware of (1) severe allergic reactions to kissing bug salivary antigens, (2) the widespread occurrence of *T. cruzi* amongst vertebrate hosts of kissing bugs, and (3) the incidence of *T. cruzi* among kissing bugs (*T. cruzi* may infect >50% of sampled bugs). Despite the potential for Chagas disease transmission, the major concern regarding kissing bugs in the United States is anaphylactic reactions to their bites resulting in frequent emergency department visits, especially in areas of endemicity in the Southwest.

Exotic vector-borne diseases have emerged as public health threats due to increasing globalization and transfer of goods, along with travel and immigration. Chagas is a protozoan disease of particular importance in the United States, because ~300,000 Latin American immigrants may be infected [1]. The risk of infection by transfusion was of such great concern that screening for Chagas was instituted for the US blood supply in 2007 [2].

The most common mode of transmission in Latin American countries where Chagas is endemic is via an insect vector com-

monly known in the United States as the “kissing bug.” Kissing bugs belong to the family Reduviidae, subfamily Triatominae in the order Hemiptera, and are referred to as triatomines. Most members of this large family are predators on other insects, but kissing bugs are bloodsuckers on a wide variety of warm-blooded animals. There are 141 species of kissing bugs [3], of which 40 species and subspecies inhabit North America [4], and 12 species belonging to the genera *Triatoma* and *Paratriatoma* are found in the United States [5].

Chagas disease is caused by a protozoan hemoflagellate, *Trypanosoma cruzi*, which is ingested by the kissing bug when it feeds on the blood of infected mammals. The parasite is transmitted to humans via kissing bugs through contamination of mucous membranes or breaks in the skin with parasite-infected feces. After the initial introduction of the parasite, an incubation period of 7–15 days leads to the acute stage of the disease, which may last for several weeks [6]. Parasitemia is evident during this stage; in most cases, there are no symptoms, possibly because the inoculum is small [7]. When symptoms occur, the most recognizable is Romaña sign, which is said to be pathognomic of *T. cruzi* infection [8]. It consists of unilateral swelling of the eye at the site of the initial infection accompanied by localized lymphadenopathy. The acute stage of Chagas is followed by an indeterminate stage lasting ≥10 years. Serious symptoms of disease emerge 10–20 years later during the chronic stage, when 10%–40% of infected persons develop cardiovascular and gastrointestinal complications [6].

Fortunately, there is a low risk of transmission of Chagas disease to humans via kissing bugs in the United States, with only 6 autochthonous cases reported [9]. Possible reasons for this low incidence include delayed defecation after biting by the bugs [10–12], a preference for animal hosts other than humans, the essentially wild nature of kissing bug species native to the United States [13], and most importantly, housing conditions that are not conducive to bug colonization. Nevertheless, the disease is considered an emerging public health threat in Texas and other states because of the widespread prevalence of *T. cruzi* among sylvan and domestic mammals [14] and the immigration of people from areas of endemicity [15]. The role of global climate change and its effect upon the expanding North American distribution of *T. cruzi* is unknown. In addition to its most common mode of transmission (ie, by insect vector), other mechanisms of infection include blood transfusion and organ transplantation, congenital transmission [7], ingestion of contaminated comestibles such as palm fruit paste [16], and laboratory accidents [7].

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Kissing bugs. Salivary antigens from North American kissing bug species cause allergic reactions in sensitized individuals [17–19]. The spectrum of allergic reactions to kissing bug bites encompasses local reactions (eg, angioedema at the bite site or elsewhere) to more systemic reactions, including mild to severe anaphylaxis. Most allergic reactions are to bites of *Triatoma rubida* in Arizona and *Triatoma protracta* in California (Figure 1). There is little or no antigenic cross-reactivity between salivary proteins from these 2 species [20]. Both species normally dwell among and feed upon wood rats, but during their annual flight dispersal, they sometimes enter homes and feed upon the occupants. In one community in southern California, 6.7% of the population was sensitized to *T. protracta* [21]. Anaphylactic reactions to *Triatoma* species in certain areas exceed those from bee stings and other Hymenoptera. Triatomines are widely distributed across the lower two-thirds of the United States, and several species are implicated in allergic reactions or autochthonous Chagas transmission (Table 1 and Figure 1). In addition to these 5 common species, reports of the allergic reactions have been attributed to a rarer species, *Triatoma rubrofasciata* [22].

Humans are encroaching on kissing bug habitats in the Southwest, especially in foothill locales in and around Tucson and Phoenix, Arizona, and San Diego, California. Adult bugs disperse from their winter abodes during a 4–6-week period in late spring and early summer. In late May and June in Tucson (when rainfall is at its lowest and temperatures rise to their summer peak), bugs can be attracted to “black lights” placed within the home ranges of the insects (see Figure 2). Shortly at or after dusk, adult male and female insects fly toward the lights, often alighting on the ground some distance from the lights and walking toward the light source where they are easily collected. Nymphs of kissing bugs are flightless and, therefore, are rarely, if ever, captured at black lights. The bugs are also attracted to houselights (as they are to black lights) in or around human domiciles and then enter the homes. These flights are

not likely for purposes of mating, because captured females often lay eggs within 1–2 days after capture. Hunger may be a motivating factor for dispersal flights, because the majority of *T. recurva* and *T. rubida* collected at black lights were in a “starved” condition [24]. June—shortly after they undergo dispersal flights—is when the largest number of human bites by triatomines is reported in Tucson (Figure 2).

Once in the home, bugs emerge at night to feed, orienting to olfactory and thermal cues emanating from a vertebrate host, including humans and domestic animals, such as dogs and, more rarely, cats [25–27]. Typically, human victims are bitten during sleep and often find engorged bugs in or around their bed. Triatomines feed for several minutes but, because of movement of the host, feeding may become interrupted and resumed in a nearby area, leaving a pattern of multiple clustered bites. Often insects defecate while feeding, and parasite-laden feces from infected bugs are the source of the *T. cruzi* inocula. The common name “kissing bug” is derived from their frequent habit of biting the victim’s face, an area usually uncovered at night. Variation occurs among species as to the presence or absence of pain associated with the bite, duration of feeding, and timing of defecation during the feeding.

Because of the serious health risks associated with kissing bugs, their control around the home in high-risk areas is recommended along with control of reservoir animals, such as rodents, armadillos, and possums. Homeowners living in high-risk areas should consult a pest management professional [28]. Rodent control typically consists of baiting, trapping, and habitat modification. In areas of the Southwest where pack rats are common, removal of available food, water, and unoccupied nests is an excellent control strategy [29].

Allergic reactions. Typically, the initial lesion from a kissing bug bite is a papule with a central punctum that arises over 24 h and is composed of a nonspecific lymphocytic infiltrate [30]. After receipt of additional bites, the reaction may “accelerate”—that is, there may be local to diffuse urticaria and

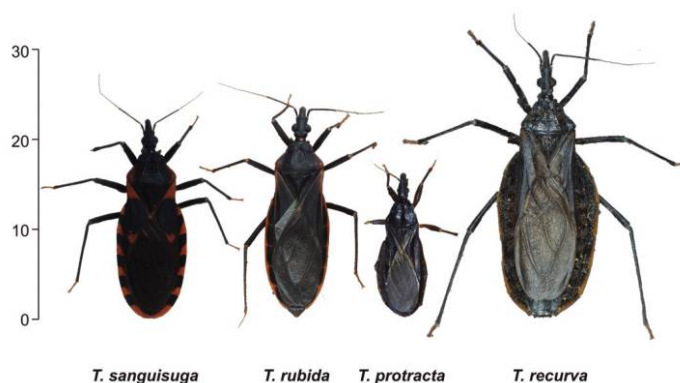


Figure 1. Adult stages of *Triatoma sanguisuga*, *Triatoma rubida*, *Triatoma protracta*, and *Triatoma recurva* “kissing bugs” involved in the case reports. Photos, with permission, are from H. Baquet (*T. sanguisuga*) and J. Cowles (other 3 species). Scale is in millimeters.

Table 1. Commonly Encountered Triatominae, Their Distribution in the United States, and Their Importance to Human Disease

<i>Triatoma</i> species	Range	Importance
<i>Triatoma gersteckeri</i>	New Mexico and Texas	Implicated in autochthonous Chagas disease; bite can cause allergic reaction
<i>Triatoma protracta</i>	California, north to Utah, and east to Texas	Implicated in autochthonous Chagas disease; bite can cause anaphylaxis
<i>Triatoma recurva</i>	Arizona	Bite can cause local reaction (this report)
<i>Triatoma rubida</i>	California to Texas	Bite can cause anaphylaxis
<i>Triatoma sanguisuga</i>	Arizona, north to Illinois, and east to North Carolina	Implicated in autochthonous Chagas disease; bite can cause anaphylaxis

even erythema multiforme [30]. Allergic reactions are either localized at the site of the bite with a substantial welt that itches intensely or are systemic with anaphylaxis [20]. Anaphylactic reactions can take many forms but most commonly manifest as hives (urticaria) or swelling (angioedema). One victim lost consciousness after a bite and, on another occasion, had a seizure [31].

Periorbital and conjunctival edema may accompany allergic reactions to agents contacting the eye, such as insect bites or stings, pollen, aspirin, or a foreign body. These may be confused with the Romaña sign, but the latter is typically more inflammatory, persistent, and unilateral. Usually, allergic swelling of the eye lasts hours to several days, whereas the Romaña sign is present for weeks. In areas where *T. cruzi* is endemic, parasite transmission merits inclusion in the differential diagnosis of the painless, swollen eye; however, the sign may occur after a bite even in the absence of *T. cruzi* transmission [32].

The following patient cases illustrate the broad panorama of disease involving kissing bugs in the United States.

Patient 1: Romaña sign. A 57-year-old woman awoke on 29 March 2008 and noticed an insect bite at the nasal side of her right eyebrow. She lived near coastal marshes in southern Louisiana, and she left the doors and windows open at night. The bite site developed a small papule that was pruritic. She also noticed 3 small papules on her right arm that were pruritic. That afternoon, she found a bug in her bed that was confirmed to be *T. sanguisuga* (Figure 1) in one of the author's laboratory (P.L.D.). The next day, her right eye swelled shut, a condition that persisted for several days. In addition, blisters appeared down the right side of her nose and forehead and lasted for 1 month. Her lesions became vesicular, and she was treated with oral prednisone and topical diphenhydramine. Tests were negative for Chagas disease (Table 2).

Patient 2: Romaña sign. A 37-year-old woman had numerous kissing bug bites in the 5 years that she resided in the foothills of Tucson. On 10 May 2008, several days after she had been bitten by a kissing bug, she awakened to find her left eye closed and a *T. rubida* insect (Figure 1) on her leg. She went to the emergency department, where she was informed that it was an allergic reaction. No bite site was identified near the

eye. She searched her home and found 12 kissing bugs. She called the Arizona Department of Health and the Centers for Disease Control and Prevention (CDC), who recommended that she undergo tests for Chagas disease. Three weeks after the bite, blood samples tested negative for Chagas disease (Table 2).

Patient 3: anaphylaxis. A 46-year-old female resident of the foothills of rural San Diego County had been bitten by kissing bugs over a 7-year period, and the reaction was itching at the site of the bite. In September 2008, she was bitten once again, awoke scratching her left leg, and discovered that her face was red. She became too weak to walk, diaphoretic, and short of breath. Emergency medical technician services took her to a hospital, where her anaphylaxis was diagnosed and treated successfully. An adult male *T. protracta* insect (Figure 1) was discovered in her home on her bed comforter (Table 2). The patient's daughter had been bitten as well and had a swollen tongue. She consulted an infectious diseases physician about the incident and was told that she need not worry about Chagas disease, because it was a "South American problem."

Patient 4: localized swellings. A 63-year-old woman resident of Bisbee, Arizona, was referred to clinic to test for Chagas disease. She estimated that she had been bitten by kissing bugs ~5 times each year for the past 22 years. After receiving a bite, the site swells to half-dollar size and itches intensely. She has no history of anaphylaxis or any accelerated allergic reaction to the bites. She brought *T. rubida* and *T. recurva* insects (Figure 1) to the clinic and stated that both had bitten her in the past (Table 2).

Patient 5: Chagas disease transmitted by organ transplantation. A 69-year-old woman underwent hemodialysis for 6 years while awaiting kidney transplantation. She was a resident of Ohio most of her life and moved to Tucson in 1992. In March 2001, she received a cadaveric kidney transplant. The donor was a 28-year-old man who had died in an accidental death in Atlanta, Georgia. He had emigrated from El Salvador 5 years earlier, and the donor's family filled out a questionnaire stating that he did not have Chagas disease. The patient received standard immunosuppression (corticosteroids, mycophenylate, and tacrolimus) after transplantation. The CDC

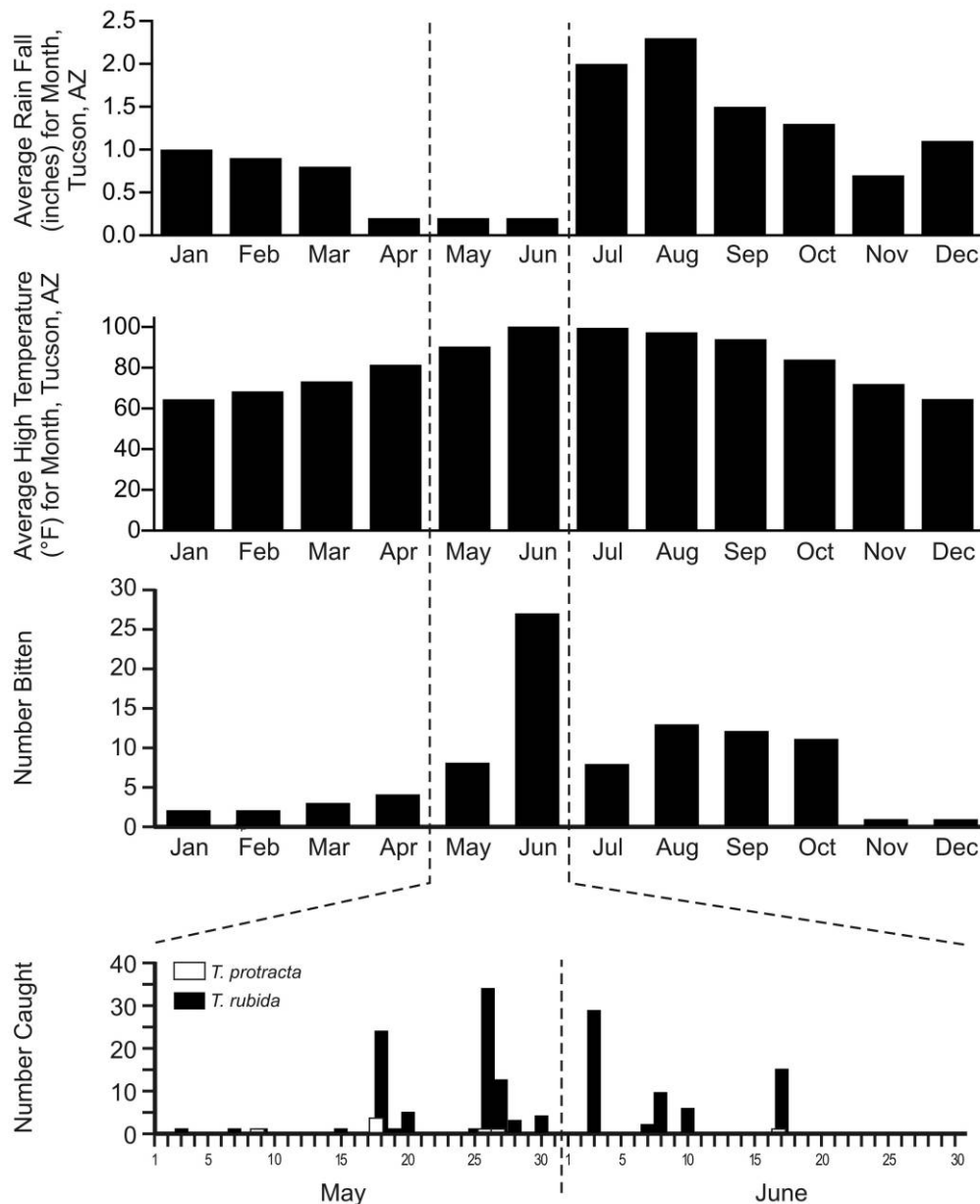


Figure 2. Seasonal behavior of *Triatoma* species in the Tucson, Arizona, foothills. A, Plot of mean monthly rainfall in Tucson and surrounding environs [23]. B, Plot of mean monthly high temperature for the same local [23]. C, Number of individuals reporting to Tucson Poison Control Center that they were bitten by kissing bugs (data from 2003). D, Plot of capture of *Triatoma* species at “black lights” in the Arizona-Sonora Desert Museum in May and June 2009.

informed physicians that 2 other recipients of tissue from the donor acquired *T. cruzi* infection. Ninety days after transplantation, the patient became ill with night sweats and experienced a 4-kg weight loss. One hundred twenty days after transplantation, physicians were notified that blood culture yielded *T. cruzi*. The patient received nifurtimox and shows no sign of relapse of Chagas disease to date (Table 2).

Comments on patient cases. Patients 1 and 2 presented

with a swollen eye arising shortly after they had received kissing bug bites. In both cases, the swollen eye was taken to be evidence of the Romaña sign that, in areas of Latin America, is considered pathognomic of Chagas disease. Neither patient was infected with *T. cruzi*. Allergic reactions, such as a swollen eye, are common, and these reactions should not be considered conclusive evidence of Chagas disease, particularly in the United States. However, the Romaña sign and infection followed direct

Table 2. Summary of Patient Cases

Patient	Age, years	Sex	Residency of patient	Complaint	Trypanosoma cruzi test result			Triatomine involved
					Serological test	PCR	Blood culture	
1	57	F	Orleans Parish, Louisiana	Romaña' sign	Negative	Negative	Negative	<i>Triatoma sanguisuga</i>
2	37	F	Tucson, Arizona	Romaña sign	Negative	Negative	Negative	<i>Triatoma rubida</i>
3	46	F	San Diego County, California	Anaphylaxis	ND	ND	ND	<i>Triatoma protracta</i>
4	63	F	Bisbee, Arizona	Local swelling after bites	Negative	ND	ND	<i>Triatoma recurva</i> and <i>T. rubida</i>
5	69	F	Tucson, Arizona	Kidney transplantation	Negative	Negative	Positive	Unknown

NOTE. ND, not done; PCR, polymerase chain reaction.

inoculation of feces from infected kissing bugs captured in the United States into the conjunctivum of a healthy prisoner [33]. In areas where Chagas disease is endemic, allergic reactions to kissing bug bites are common to all species that transmit the disease [34]. Conversely, the Romaña sign may occur without transmission of *T. cruzi*. Lumbreras et al [32] allowed 3 human subjects to be bitten by uninfected *Rhodnius prolixus* repeatedly on the arm over several months and then allowed the bugs to bite the subjects on the upper eyelid. Classic Romaña sign developed and lasted for weeks. Moreover, in a recent outbreak of Chagas disease after ingestion of contaminated palm fruit, 100% of the patients manifested facial edema in the absence of any bite [16].

In the United States, anaphylaxis is the most feared complication of a kissing bug bite (such as occurred with patient 3). Anaphylaxis caused by biting insects in the United States is most often due to kissing bugs [35]. Persons at risk should keep a kit (Epipen; Dey Pharma) close at hand in their bedroom [36]. There is currently no immune desensitization available for *Triatoma* bite allergies. Patient 4 reacted to bites with localized swelling only, even after years of exposure to *Triatoma* salivary antigens.

Patient 5 obviously had no history of *Triatoma* bites yet had Chagas disease. The laboratory diagnosis of Chagas disease is enhanced by appreciating where in the disease process the patient is. For example, during acute infection, the parasite may be observed microscopically on blood smears and polymerase chain reaction (PCR) may be useful [37]. For patient 5, examination of blood specimens at the time of onset of illness would likely have yielded positive results. The parasite was eventually cultured from blood samples, but the sensitivity of culture is unknown. Established infection is best detected by enzyme-linked immunosorbent assay (ELISA) and confirmed with another test with high specificity (radioimmuno-precipitation assay) [38]. In the United States, the Ortho *T. cruzi* ELISA Test System has been approved by the US Food and Drug Administration for donor screening and testing and is performed by Quest Diagnostics [23].

***T. cruzi* infected bugs in the United States.** Although the

risk of vector transmission of Chagas disease is extremely low in the United States, the possibility should be considered, given the high rate of *T. cruzi*-infected kissing bugs in some areas. For example, infection rates for *T. protracta* collected in central and southern Arizona were 26.3% [39], 33.1% in Griffin Park in Los Angeles [40], and 47.4% in San Diego County [41]. In more recent surveys, 1 of 4 *T. protracta* collected in the Tucson area harbored *T. cruzi*, and 4 of 20 collected in San Diego County were positive, for an overall rate of infection of 21% [12]. Fifty-six percent of *T. sanguisuga* insects collected at the site of the most recent autochthonous human case of Chagas disease were positive for *T. cruzi* [9].

In preliminary studies, bugs captured in the foothills of Tucson were found to contain human blood, whereas cow, rodent, chicken, and human DNA was found in bugs collected in Escondido, California. DNA was extracted from the rectum [42] of bugs and PCR performed to detect vertebrate DNA. Vertebrate DNA was found in 6 bugs; 3 bugs had been feeding on humans, 1 on rodents, 1 on chicken, and 1 on a cow [43]. Thus, sylvatic *Triatoma* clearly feed on humans as well as other vertebrates in the United States. The *Triatoma* species demonstrate feeding preferences [25], but where humans fall in the scale of preferred hosts of *T. protracta* and *T. rubida* is unknown.

Conclusions. Although physicians are aware of the hazard of kissing bugs as vectors of Chagas disease in Latin America, they may not appreciate, that in some geographical areas of the United States, a sizable percentage of the kissing bug population (depending upon the species, perhaps >50%) may harbor *T. cruzi*. Furthermore, the small vertebrate hosts (domestic and wild) that these bugs feed upon (and who feed upon the bugs) can provide a large reservoir of *T. cruzi*. Autochthonous cases of Chagas disease transmitted by kissing bugs are extremely rare in the United States. This is likely due to improved housing and the markedly different behaviors of the US kissing bug species as compared to those in Latin America. Many of the latter are more domesticated species; for example, *T. infestans* found in South America lives out its life cycle in the homes (ie, colonizes homes) and, therefore, is much more likely to transmit the parasite. However, North American kissing bugs

commonly feed on humans and are the most common cause of anaphylactic reactions among biting insects [31, 35]. Indeed, the Romaña sign, classically considered pathognomic of Chagas, is easily confused with allergic reactions to kissing bug salivary antigens. Physicians need to become more sophisticated in their understanding of kissing bugs and their role in clinical disease, both allergic reactions and Chagas, as this once “Latin American” disease emerges in the U.S.

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