

Recognizing and Reducing the Risks of Chagas Disease (American Trypanosomiasis) in Travelers

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Chagas disease, or American trypanosomiasis, is an arthropod-borne protozoan infectious disease endemic throughout most of the Americas, caused by the trypanosome, *Trypanosoma cruzi*, and transmitted to humans by reduviid, or kissing, bugs. Reduviid bugs (phylum: Insecta, order: Hemiptera, family: Reduviidae, subfamily: Triatominae) transmit several zoonotic strains of *T cruzi* among many mammalian reservoir hosts throughout the Americas. Chagas disease is most commonly transmitted to humans via *T cruzi*-infected reduviid bug defecations near bite wounds or exposed mucosal surfaces. Chagas disease may also be transmitted congenitally, by ingestion of *T cruzi*-infected reduviids or their feces, by blood product transfusions, and by organ transplants. Indeterminate and chronic infections may be reactivated by immunosuppression, particularly human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS), and by pregnancy. Characterized by an influenza-like illness acutely in adults, Chagas disease may result in chronic heart disease or gastrointestinal megasyndromes following a prolonged, indeterminate stage of subclinical infection.

In its 2003 World Health Report, the World Health Organization (WHO) noted that Chagas disease caused more deaths from parasitic disorders than from any other parasitic disease in Latin America and that *T cruzi* was responsible for the third

highest number of parasitic infections in the world following malaria and schistosomiasis.¹ Chagasic heart disease has become an increasingly common indication for heart transplantation in Latin America and the United States.^{2,3} Chagas disease has now occurred in three US recipients of heart, kidney, liver, and pancreas transplants from a single Central American immigrant donor and in two US recipients of heart transplants from *T cruzi*-infected donors (Figure 1).³⁻⁵ Chagas disease may pose increasing communicable disease risks to travelers in endemic regions of the Americas, including beachside resort regions and interior rural regions.

Materials and Methods

A MEDLINE search, from 1966 to 2007, of the world's salient scientific literature of case reports, case series, laboratory investigations, epidemiological investigations, and reviews was conducted to determine the changing epidemiology and outcomes of Chagas disease in the Americas. In addition, recognizable risk factors for Chagas disease were identified and recommendations to reduce such risks developed for travelers touring Chagas disease-endemic areas of the Americas.

The History, Disease Burden, and Epidemiology of Chagas Disease in the Americas

Dr Carlos Chagas first described Chagas disease in 1909, during the construction of a railroad system in northern Brazil.⁶ Chagas correctly identified the arthropod vectors of American trypanosomiasis as reduviid bugs and the zoonotic reservoirs as several warm-blooded mammalian vertebrates, including

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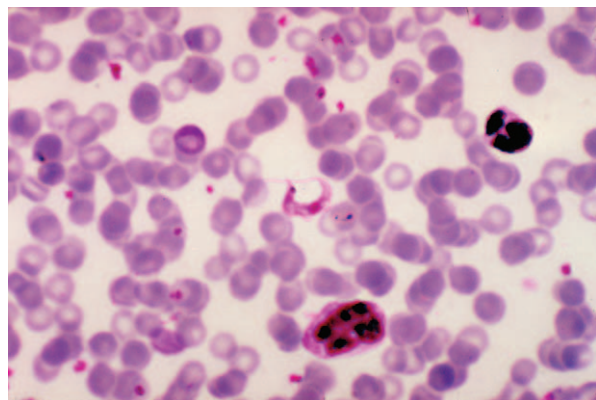


Figure 1 *Trypanosoma cruzi* metacyclic trypomastigote on a peripheral blood smear prepared with Giemsa staining technique. Source: US Centers for Disease Control and Prevention, Atlanta, GA, USA. Public Health Image Library ID #3014. Copyright permission not required.

domestic animals and humans.⁶ Chagas also observed infective-stage metacyclic trypomastigotes in the gastrointestinal tract and feces of reduviids and correctly described the two most common modes of transmission of metacyclic trypomastigotes to humans (Figure 1). Although transmission of Chagas disease may be congenital or acquired via blood product transfusions and organ transplants, transmission most commonly occurs through either reduviid fecal contamination of bite wound sites, often near the mouth (hence the vernacular name, “kissing” bugs, for reduviids), or transmucosally, often transconjunctivally, following periorbital defecation.

Zoonotic *T cruzi* infections of reduviid vectors and many wild animal reservoir hosts are now distributed widely across the Americas from 46° north latitude to 42° south latitude.⁶ This vast region of the Americas includes all the southern United States, all of Central America, and most of South America. There are nearly 20 million seropositive persons with Chagas disease in the Americas, and 90 million persons, or about one fifth of Latin America’s population, are at risk of *T cruzi* infection.^{6–8} Although acute Chagas disease is often subclinical, symptomatic Chagas disease will occur in 30% of infected individuals, or in about 5 million people, after an asymptomatic, seropositive, indeterminate stage lasting 10 to 30 years.^{6–8} Therefore, indeterminate or latent Chagas disease now exists in approximately 15 million persons, all infected with *T cruzi* and capable of transmitting arthropod-borne, blood transfusion, or tissue-borne infections. The WHO has estimated that Chagas disease causes 667,000 disability-adjusted life years annually in the

Americas.¹ There are now more than 100,000 seropositive people infected with *T cruzi* residing within the United States, and these numbers are anticipated to rise with increasing emigration from Latin America to the United States and with proposed legislation to grant amnesty and residency status to more than 12 million illegal Latin American immigrants, now living in the United States.¹

The sylvatic transmission cycle of *T cruzi* from mammalian reservoir hosts indirectly to humans occurs more often in endemic, interior rural areas of South America, such as Argentina, Brazil, Bolivia, Paraguay, Peru, Uruguay, and Venezuela, than in nonendemic areas of the urban Americas. Humans may be infected with *T cruzi* by disrupting the sylvatic cycle as infected reduviids invade rural households and even suburban households in recently deforested areas to breed and to nocturnally blood-feed on nearby humans. When domestic animals or pets become infected by ingesting or being victimized by infected reduviids, peridomestic living reduviids may subsequently transmit *T cruzi* between infected domestic animals and their human owners.

In South America, the endemic region for vectoral and transfusional transmission of Chagas disease is often referred to as the Southern Cone and includes the following nations: Argentina, Bolivia, Brazil, Chile, Paraguay, and Uruguay. In 1991, the Ministers of Health of the Southern Cone nations met in Brasilia and initiated a subregional project sponsored by the Pan American Health Organization and called INCOSUR, for the Intergovernmental Commission of the Southern Cone for the Elimination of *Triatoma infestans* and the Interruption of Transfusional Transmission of American Trypanosomiasis. *Triatoma infestans* is the principal reduviid vector of Chagas disease throughout the Southern Cone.

Since its inception, INCOSUR has presided over remarkable achievements and successes in the control of Chagas disease in the Southern Cone including the interruption of vectoral and transfusional transmission in Uruguay by 1997, the interruption of vectoral transmission in four of the largest provinces in Argentina by 2001, the nearly complete interruption of vectoral transmission in Paraguay by 2002, and the interruption of vectoral transmission throughout Brazil by 2006. INCOSUR is now focusing its regional Chagas disease control activities in Bolivia, Paraguay, and the remaining endemic provinces of Argentina. Despite the administrative and political challenges to disease control in mountainous rural areas with remote access, particularly in Bolivia, further successes by INCOSUR in interrupting Chagas disease transmission are anticipated.

Trypanosomiasis, American (Chagas' disease)
(*Trypanosoma cruzi*)

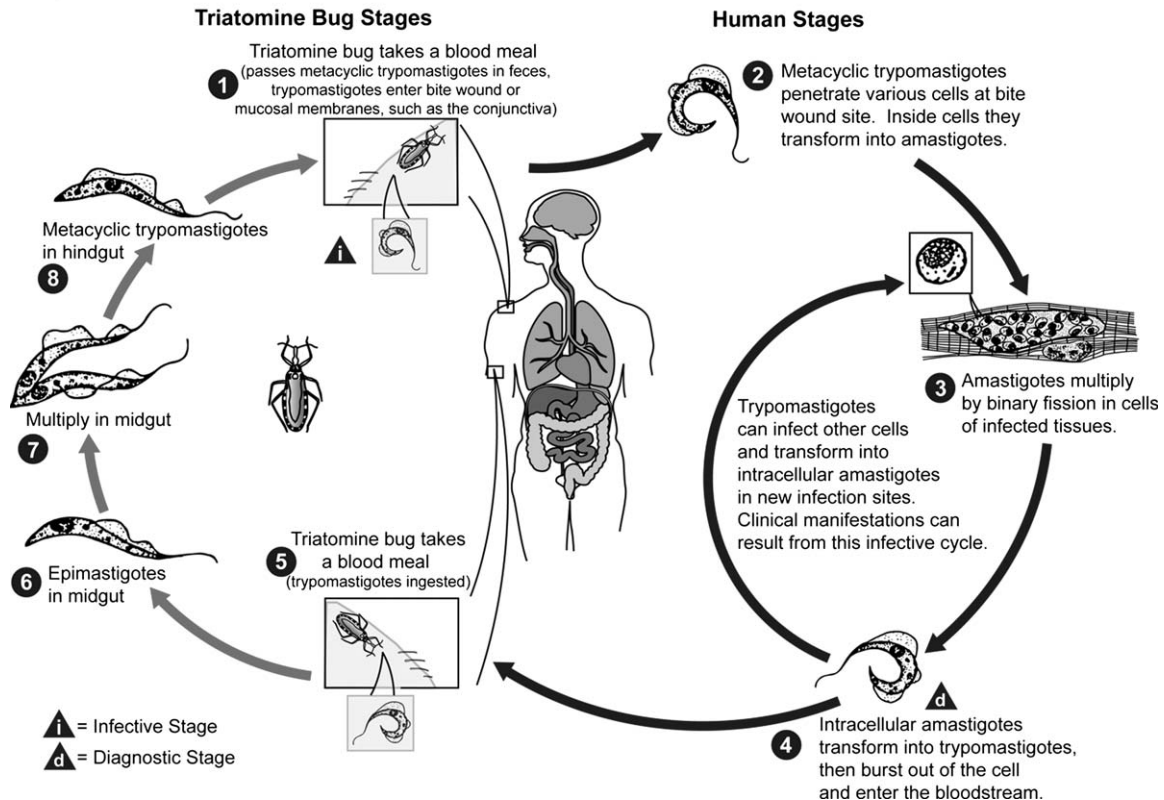


Figure 2 The life cycle of *Trypanosoma cruzi*, the causative agent of Chagas disease (American trypanosomiasis). Source: US Centers for Disease Control and Prevention, Atlanta, GA, USA. Public Health Image Library ID #3384. Copyright permission not required.

The Life Cycle of *T. cruzi*

The life cycle of *T. cruzi* in reduviid vectors and vertebrate hosts, including humans, is depicted in Figure 2.

Reduviid Vectors of Chagas Disease in the Americas

Among the more than 100 species of reduviids, the preferred vectors for Chagas disease in Latin America include reduviids from three genera: *Triatoma*, *Panstrongylus*, and *Rhodnius*.^{6,8} Each species of reduviid has its own unique feeding pattern, ecological niche, preferred wild animal reservoir, and geographic distribution. *Triatoma infestans* is the principal vector of Chagas disease in animals and in humans in Argentina, Bolivia, Brazil, Chile, Paraguay, Peru, and Uruguay. *Panstrongylus megistus* is an important vector in human transmission in northeastern Brazil. *Rhodnius prolixus* is a common vector in Columbia and Venezuela and throughout Central America. *Triatoma dimidiata* is a principal

vector in the natural transmission of Chagas disease in Mexico, especially in the Yucatán peninsula.⁶⁻⁹

In the United States, the principal reduviid vectors in the transmission of *T. cruzi* infections among wild and domestic animals are *Triatoma sanguisuga*, followed by *Triatoma lecticularia* and *Triatoma gerstaeckeri* (Figure 3).⁶⁻¹¹ The *T. cruzi* infection rate for reduviids in the United States as in Latin America is approximately 20%, ranging from reported *T. cruzi* seroprevalence rates for *T. sanguisuga* of 20% in Louisiana and the Yucatán to 60% in Georgia.⁶⁻¹⁴

Wild Animal Reservoirs of Chagas Disease in the Americas

The wild animal reservoirs of *T. cruzi* in the Americas are very varied and not species specific. In Latin America, the common animal reservoir hosts for *T. cruzi* include armadillos, capybaras, coatimundis, marsupials, monkeys, opossums, porcupines, raccoons, rodents, and sloths.^{6,8} In the United States, common wild animal reservoirs for *T. cruzi* include armadillos, opossums, raccoons, rodents, and squirrels.⁹⁻¹⁴



Figure 3 *Triatoma infestans* adult, dorsal view, a common vector for Chagas disease in the Americas. Source: US Centers for Disease Control and Prevention, Atlanta, Ga, USA. Public Health Image Library ID #6282. Copyright permission not required.

Trypanosoma cruzi has been isolated from both reduviids and wild mammals, most commonly raccoons and armadillos, in most southern US states, including Alabama, Arkansas, Georgia, Florida, Louisiana, Oklahoma, South Carolina, Texas, and Virginia.^{10–14} All US authors have now concluded that wild mammals are being increasingly exposed to *T cruzi* in an expanding region of the southern and mid-Atlantic United States.^{10–16}

Domestic Animal Reservoirs of Chagas Disease in the Americas

In the endemic areas of Latin America, seroprevalence for *T cruzi* among many domestic animals and pets is high, reaching 80% in dogs; 60% in cats, guinea pigs, and rabbits; 19% in sheep, and 9% in goats.^{6–10} In the United States, the prevalence of *T cruzi* infections among domestic dogs, particularly

hunting dogs kenneled outdoors, remains significantly lower than in Latin America but is steadily increasing (J. Malone, personal communication, 2005–2006).^{15,16} In 1998, Meurs and colleagues reported their experiences in treating 11 domestic dogs with chagasic heart disease in Texas over a 10-year period, from 1987 to 1996.¹⁵ In 2000, Bradley and colleagues reported a seroprevalence of 3.6% ($n = 11$) in 301 domestic dogs tested for *T cruzi* antibodies in Oklahoma.¹⁶ Most ($n = 10$) of the seropositive dogs were hunting dogs that lived outside.¹⁶ Although *T cruzi* infections have been recognized in wild animals throughout the southern United States for some time, recent reports have documented that domestic animals, particularly outdoor-kenneled dogs, are becoming increasingly infected by reduviid vectors with wild animal strains of *T cruzi* (J. Malone, personal communication, 2005–2006).^{15,16}

Autochthonous Chagas Disease in the United States

Chagas disease in humans has now been reported in the nonendemic areas of the Americas and, specifically, in the United States, where most cases are imported from Latin America, but autochthonous cases are also increasing, with six cases now reported. The first autochthonous case of Chagas disease in the United States was reported in an infant in Corpus Christi, Texas, in 1955.¹⁷ The second autochthonous case in the United States was reported in a 56-year-old woman in California in 1984.¹⁸ Two more infant cases of Chagas disease were again reported from Texas in 1996, using postmortem polymerase chain reaction (PCR) analysis to confirm the diagnosis.¹⁹ The fifth case of autochthonous Chagas disease was reported from Tennessee, once again in an infant and using PCR to confirm the diagnosis.²⁰

In April 2007, Dorn and colleagues reported the sixth autochthonous case of *T cruzi* infection in a 74-year-old woman, without a relevant travel history to *T cruzi*-endemic regions of Latin America and residing in a heavily wooded area of New Orleans, Louisiana.²¹ Following household fumigation, extensive investigations of the index patient's residence and grounds produced 20 dead adult *T sanguisuga* reduviids and 1 live, second-stage *T sanguisuga* nymph in an armadillo burrow approximately 50 m away from the residence.²¹ More than half (56%) of the collected reduviids tested positive for *T cruzi* DNA by PCR.²¹ Trypanosomes consistent with *T cruzi* were observed in hemoculture performed at the Centers for

Disease Control and Prevention (CDC), Atlanta, GA, USA, and amplification of a *T cruzi*-specific RNA gene confirmed that the index patient's hemoculture was *T cruzi* positive.²¹

The Clinical Presentations of Chagas Disease

Although often asymptomatic and undetected in infants and adults, acute Chagas disease may be accompanied by a constellation of nonspecific, influenza-like symptoms including anorexia, fever, malaise, nausea, vomiting, and diarrhea. Neonates with congenital Chagas disease, children with acute Chagas disease, and adults with HIV/AIDS and acute or reactivated Chagas disease may develop fulminant symptoms with generalized lymphadenopathy, myocarditis, hepatosplenomegaly, meningoencephalitis, and high case fatality rates. A reactivation of acute Chagas disease with meningoencephalitis, or, less commonly, acute myocarditis, was recently described in *T cruzi*-seropositive patients who subsequently contracted HIV/AIDS.^{22,23} After an initial high parasitemia peaks on the 10th day of acute illness, symptoms resolve in 1 to 2 months and patients remain chronically infected with *T cruzi* for life.

Approximately one third of patients with indeterminate Chagas disease, characterized by low-to-no parasitemia and positive seroreactivity to *T cruzi* antigens, will develop chronic Chagas disease with chagasic heart disease, most commonly, gastrointestinal megasyndromes, or, rarely, both (approximately 2.5%).⁶⁻⁸ The perinatal transmission of Chagas disease may occur in 2% to 10% of women of childbearing age with indeterminate or chronic Chagas disease.^{24,25}

The pathogenesis of Chagas disease remains incompletely understood but requires the persistence of parasite antibodies in affected organs that appear to initiate a neurotropic autoimmune response. Autoimmune damage directed against autonomic nervous tissue epitopes in cardiac conduction tracts and gastrointestinal tract ganglia is now believed to be responsible for the unique pathological outcomes of chagasic heart disease and gastrointestinal megasyndromes. The clinical manifestations of Chagas disease are compared in Table 1.

The Diagnosis and Treatment of Chagas Disease

The major diagnostic laboratory methods for detecting *T cruzi* infections and their sensitivities and

utilities in the different stages of Chagas disease are presented in Table 2. The WHO recommends using at least two antigen detection tests to confirm a Chagas disease diagnosis: (1) a sensitive initial screening test, such as an enzyme-linked immunosorbent assay (ELISA), an indirect immunofluorescent antibody test (IFAT), or radioimmunoassay precipitation assay (RIPA); and (2) a subsequent, more specific confirmatory test, such as hemoculture or detection of amplified *T cruzi* DNA or RNA by PCR.^{1,8,29}

Unlike the diagnostic laboratory methods for Chagas disease, drug treatment choices for Chagas disease are limited; not uniformly available; hampered by significant adverse effects; and work best only in the earliest stages of acute or reactivation Chagas disease, that are often undetected. Both nifurtimox (Lampit[®] or Bayer 2502, Bayer AG, Leverkusen, Germany) and benznidazole (Rochagan[®] or Radanil[®], F. Hoffman-La Roche, Ltd, Basel, Switzerland and Roche US, Nutley, NJ, USA) are effective in clearing parasitemias in the earliest stages of acute and, possibly, reactivated Chagas disease, but neither drug is approved for use in the United States by the Food and Drug Administration. Only nifurtimox is available in the United States from the CDC by special request (CDC Drug Service, 404-639-3670). In 1995, oral nifurtimox was successfully used to prevent acute reactivation of chagasic cardiomyopathy in two patients undergoing orthotopic heart transplantation for chagasic heart disease.³⁰ Pharmacotherapy with either benznidazole or nifurtimox is now recommended in all acute cases and reactivated cases of symptomatic Chagas disease, especially in children, adolescents, and all immunocompromised persons.^{26,30}

Although there is a current trial of chemotherapy in indeterminate Chagas disease with nifurtimox, many authorities recommend no drug treatment for indeterminate disease and supportive treatment only for chronic disease.³⁰ Congestive heart failure, dysrhythmias, and heart blocks in chagasic heart disease are managed in standard regimens with angiotensin-converting enzyme inhibitors, antiarrhythmics, and pacemakers. Beta-blockers and digitalis are relatively contraindicated in chagasic heart disease due to their potential for precipitating intracardiac conduction disturbances. Beta-blockers are contraindicated in patients with progressive dilated cardiomyopathy with increasing risks of congestive heart failure and left ventricular aneurysm. Refractory heart failure and nonresectable, apical left ventricular aneurysm are

Table 1 Clinical manifestations of Chagas disease

Clinical features	Acute stage	Indeterminate stage	Chronic stage
Parasitemia	High.	Low.	Low.
Constitutional symptoms	Nonspecific, flulike symptoms; high fever possible.	Asymptomatic.	Chest pain, dizziness, dyspnea, edema, palpitations, syncopal episodes.
Cardiac	Acute myocarditis.	No cardiac or electrocardiographic manifestations of Chagas disease.	ECG abnormalities present (>50%): conduction blocks, sick sinus syndrome, multifocal PVCs. Pathognomonic ECG abnormalities may include right bundle branch block, left anterior fascicular block, complete heart block, cardiomegaly, with CHF, apical left ventricular aneurysm with mural thrombus.
Gastrointestinal	Diarrhea, vomiting, and rarely hepatosplenomegaly.	No gastrointestinal manifestations of Chagas disease.	None to symptomatic achalasia and chronic constipation. Megasyndromes may include megaesophagus with achalasia, megacolon with intermittent obstruction and painful abdominal distension.
Neurologic	Meningoencephalitis in neonates with congenital Chagas disease and HIV/AIDS patients.	No neurologic manifestations of Chagas disease.	Rarely meningoencephalitis, especially in HIV/AIDS.
Immunologic	Generalized lymphadenopathy, seropositive.	Seropositive. In the indeterminate stage of Chagas disease, only the positive serologic tests for Chagas disease indicate the presence of <i>T cruzi</i> infection.	Seropositive.
Miscellaneous	Inoculation chagoma, Romana's sign.	Not applicable.	Not applicable.

CHF = congestive heart failure; ECG = electrocardiogram; HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome; PVCs = premature ventricular contractions.

becoming increasingly common indications for heart transplantation in chagasic heart disease throughout the Americas.^{3,31} Gastrointestinal megasyndromes are most effectively managed with conservative medical treatment and surgical resection of dilated, functionally aganglionic segments of the colon and esophagus.

Because no new proprietary drugs are currently under research and development for Chagas disease and because some strains of *T cruzi* are either moderately or naturally resistant (*Colombiana*) to both benznidazole and nifurtimox, Araujo and colleagues have recently tested combinations of benznidazole with either ofloxacin or ketoconazole in treating *T cruzi*-infected mice.³¹ The authors reported some success with the benznidazole-ketoconazole combination in eradicating parasitemias in mice infected with moderately resistant *T cruzi* strains and recom-

mended further investigations of the potentially synergistic combination of azoles in infected animal models and humans.³¹

Although there has been little impetus to develop a Chagas disease vaccine, the molecular characterization of the *T cruzi* genome could lead to a number of advances in the primary prevention and treatment of Chagas disease. Such advances would be welcomed worldwide and might include the development of (1) attenuated live or inactivated vaccines for humans and domestic animals using epitopes from less virulent strains, such as R36; (2) altruistic *T cruzi* vaccines for domestic and wild animals that target the epimastigotes in the gastrointestinal tracts of triatomines; and (3) new molecularly designed, receptor-targeted chemotherapeutics for acute and chronic Chagas disease, and, perhaps, other trypanosomal diseases, such as

Table 2 Diagnostic methods and their utilities (+/-) in the different stages of Chagas disease^{4-6,8,19-21,25-28}

Diagnostic methods	Acute Chagas disease	Indeterminate Chagas disease	Chronic Chagas disease
Direct detection methods			
Centrifugation blood culture	+	-	-
<i>Trypanosoma cruzi</i> DNA by PCR	+	+	+
Direct light microscopy	+	-	-
Thick and thin blood smears	+	-	-
Xenodiagnosis by laboratory-raised reduviid bugs	+	+	+
Indirect (serologic) detection methods			
Enzyme-linked immunosorbent assay	- (IgG)	+	+
Radioimmunoassay precipitation assay	-	+	+
Indirect immunofluorescent antibody staining	+	+	+
Complement fixation (Machado-Guerreiro test, no longer in general diagnostic laboratory use)	-	+/-	+/-
Hemagglutination	-	+	+

(+) = very useful and recommended for laboratory diagnosis in this stage of Chagas disease; (-) = not as useful and not recommended for laboratory diagnosis in this stage of Chagas disease; Ig = immunoglobulin; PCR = polymerase chain reaction.

those caused by the African trypanosomes, *Tbrucei gambiense* and *Tbrucei rhodesiense*.

Threats to the Safety of the Human Blood and Transplant Organ Supplies Posed by Chagas Disease in the Americas

Transfusion- and transplant-related Chagas disease result from a combination of behavioral and demographic factors including rural to urban population movements in Latin America, massive immigration from Latin America to US cities, insufficient national blood and transplantable organ and tissue supplies, and insufficient blood and organ donor screening for *T cruzi* infection both in Latin America and in the United States.^{2,3,31-36} Depending on the volume of *T cruzi*-infected blood transfused, 12% to 44% of recipients of infected blood will become infected.³³ Because cardiac surgery patients often require multiple blood transfusions, their risks of acquiring Chagas disease, often manifesting as acute chagasic heart disease, especially in immunosuppressed heart transplant recipients, are significantly increased.^{2-6,30} Patients with HIV/AIDS are also at greater risks of acquiring Chagas disease from *T cruzi*-infected blood transfusions and, as noted, often present acutely with meningoencephalitis or chagasic cardiomyopathy.^{22,23}

Chagas disease is endemic throughout Mexico, and a recent seroprevalence study in five blood banks in Mexico determined that the overall prevalence of seropositive blood donors was 0.75%, or 1

in 133 donors.³⁴ Nearly half (44%) of the surviving recipients of blood products from *T cruzi*-infected Mexican donors were, in turn, infected with *T cruzi*.³⁴ The authors concluded that transfusion-transmitted *T cruzi* infections were occurring in increasing numbers in Mexico and recommended the mandatory screening of all donated blood products for *T cruzi* antibodies, as in many other Latin American countries.³⁴

Chagas disease is endemic in many regions of Latin America, such as the Yucatán peninsula of Mexico, a popular tourist destination.^{9,35} In the Yucatán, *T cruzi* seroprevalence rates of 11% to 18% and 5.6% have been reported in the general population and in blood donors, respectively.³⁵ Chagas disease is also endemic in the poor coastal communities of northeast Brazil, where 60% of persons aged 20 years and older tested seropositive for *T cruzi* infections.³⁶

Previous chemical methods to sterilize donated blood for transfusion in Chagas disease-endemic regions of Latin America, such as adding gentian violet to blood units, proved unacceptable due to purplish skin staining in transfusion recipients. Although newer methods of chemical sterilization are being investigated, universal blood donor screening both for Chagas disease risk factors and for serologic evidence of *T cruzi* infections is preferred over chemical sterilization for prevention of both transfusion- and transplant-related Chagas disease.

By 1999, 100% of blood donors were being serologically screened for *T cruzi* antibodies in the

following Latin American countries: Argentina, Colombia, Ecuador, El Salvador, Honduras, Paraguay, Uruguay, and Venezuela.^{37,38} Blood donor screening for *T cruzi* infection remains inconsistent in Bolivia, Chile, Mexico, and Nicaragua.^{37,38} The probability of receiving a *T cruzi*-infected blood transfusion will, therefore, vary by country.^{37,38} Schmunis has calculated the probabilities of transmitting *T cruzi* via infected blood transfusions, assuming a 20% infection rate, to be 219 per 10,000 units transfused in Bolivia, 24 of 10,000 units transfused in Colombia, 17 of 10,000 units transfused in El Salvador, and 2 to 12 per 10,000 units transfused in the remaining countries of Latin America.^{37,38}

In 1996, Galel and Kirchoff studied 18 California blood centers and reported a prevalence rate of 1 per 340 blood donors at high risk for transmitting *T cruzi* through donated blood.² High risk factors included living in endemic areas of Latin America for more than 1 year, living in thatched roof homes with mud walls, having a history of Chagas disease, and receiving blood transfusions in endemic countries.² Of the 17,521 donors studied, 0.33% had at least one risk factor for Chagas disease, and six donors even gave a history of Chagas disease.¹ In 1997, Leiby and colleagues performed a comprehensive seroprevalence study of nearly 300,000 blood donors in two American Red Cross donor center regions (Los Angeles and Miami).²⁷ *Trypanosoma cruzi* antibodies were confirmed in 34 donors, all of whom shared the same risk factor for Chagas disease, namely, birth or prolonged residence, or both in a *T cruzi*-endemic area.²⁷

In 2002, Leiby and colleagues queried more than 1 million blood donors in Los Angeles and Miami between 1994 and 1998 for the presence of risk factors for Chagas disease.³⁹ All positive risk factor respondents were then screened serologically by ELISA for *T cruzi* antibodies.³⁹ RIPA-confirmed seropositive donor prevalence was 1 in 7,500 in blood donors from Los Angeles, and 1 in 9,000 in Miami blood donors.³⁹ The authors concluded that significant numbers of confirmed *T cruzi*-seropositive blood donors contributed to the US blood supply, especially in Los Angeles and Miami.³⁹

Reports of organ transplant-transmitted Chagas disease in Latin America, particularly following kidney transplants, began in the 1980s and have continued.⁴⁰⁻⁴⁴ In 2002, the CDC reported the first cluster of three cases of *T cruzi* infection in recipients of four solid organs from a single immigrant donor from Central America (Figure 1).³ Of the three organ recipients with transplant-transmitted Chagas disease, all were treated with nifurtimox,

two organ recipients died within months of their organ transplants, and only one kidney recipient survived.³ The recipient of a kidney and pancreas transplant died of acute myocarditis, and the liver transplant recipient died of hepatorenal failure.³

In July 2006, the CDC reported the fourth and fifth cases of acute Chagas disease in heart transplant patients.⁴ In both cases, the heart transplant recipients were readmitted to Los Angeles County hospitals within 1 month of discharge with symptoms of anorexia, fever, and fatigue, suggestive of acute organ transplant rejection.⁴ In both cases, peripheral blood smears revealed *T cruzi* trypomastigotes (Figure 1).⁴ The organ recipients were seronegative for *T cruzi* antibodies but positive for *T cruzi* DNA by PCR.⁴ The patients had no birth country or travel risk factors for Chagas disease but had received multiple blood transfusions.⁴ In each case, all available blood donors tested seronegative for *T cruzi* antibodies, but both heart donors had significant risk factors for Chagas disease, either travel to or birth in Chagas disease-endemic areas of Latin America, and both donors were seropositive for *T cruzi* antibodies by RIPA.⁴

Recognizing the Risks of Chagas Disease in Travelers

A recognition of the sylvatic, periurban, and urban transmission cycles of Chagas disease will assist travel medicine physicians in advising their patients how best to avoid the risks of *T cruzi* infections while touring endemic areas. In the sylvatic cycle, preferred reduviid vectors throughout the Americas become infected with *T cruzi* as either nymphs (the five juvenile stages or instars) or adults during rainy seasons by feeding on many nonspecific wild animal hosts. As humans begin to deforest and develop rural areas for agriculture, ranching, and housing, infected reduviids are attracted to more stable, peridomestic environments.²⁸ These peridomestic environments are well populated with warm-blooded hosts, such as domestic animals in coops and pens, pet animals, and humans in poorly insulated homes.²⁸ In the poorer, rural areas of Central and South America, household dwellings are often characterized by thatched roofs of palmetto or palm fronds, the natural tree canopy homes for reduviids, and porous walls of logs and sticks.^{28,45} These walls are either left open for ventilation or loosely mortared with combinations of thatch, mud, *sillar* (compounded volcanic ash and water), or volcanic basalt.^{28,45} During the day, reduviid adults and nymphs, or instars, sleep in thatched roofs, wall

cracks, mortar pores, and crawl spaces of rural households.^{8,28,46} At nighttime, adult reduviids gently parachute or glide down, from roof crevices; and breeding adults and nymphs crawl out of their floor and wall cracks into domestic animal pens and household bedrooms to blood-feed on animal and human hosts.

In 2004, Dumonteil and Goubrière reported on their experiences constructing a risk map for the natural transmission of Chagas disease in the Yucatán peninsula of Mexico, using geographic information systems to design predictive models of reduviid abundance (*T dimidiata*) and infection rates.⁹ Models were subsequently compared to insect counts from entomologic surveys and to microscopic examinations of reduviid feces for *T cruzi* trypomastigotes.⁹ As a result of their studies, the authors were able to accurately predict and confirm the following findings: (1) greater numbers of *T dimidiata* in warmer and drier climates of the Yucatán, including coastal tourist areas; (2) higher reduviid infection rates in areas with lower temperatures and higher precipitation rates, specifically rain forests; and (3) greater reduviid abundance in areas of “perturbed” vegetation, defined in their study as agricultural fields and pastures.⁹

Because the coasts, colonial cities, offshore islands, and Mayan ruins in perturbed forested areas of the Yucatán peninsula are among the most scenic and popular destinations for ancient historians, archeologists, ecotourists, and cruise line passengers, the significance of the study of Dumonteil and Goubrière is that the highest risk regions for Chagas disease are in areas most frequently visited throughout the year by travelers, specifically the northern regions of the states of Campeche and Yucatán.⁹ Travelers and their consulting physicians must recognize the changing nature of the ecology of Chagas disease and take appropriate steps to reduce the travel-associated risks of Chagas disease in all the *T cruzi*-endemic regions of the Americas, which are now being extended to higher altitudes and expanded by widening latitudes by global warming and other anthropogenic activities.^{9,33,35}

Unlike the sylvatic and rural, peridomestic ecology of Chagas disease in the Americas, the periurban and urban ecology of Chagas disease has not been as well studied and mapped. Recent investigations have demonstrated preferred domestic animal vectors and their enclosures for urban *T cruzi*-infected reduviids. In their entomologic survey of 347 households and domestic animal enclosures in Arequipa, Peru, a city of 850,000 in the arid, Andean highlands of southern Peru, Levy and colleagues

reported the following unique characteristics of an urban cycle of *T cruzi* infections among the most common Chagas disease vector in the region, *T infestans*.⁴⁵ First, household reduviid infestations were common in the high population density, low-income community of Guadalupe, perched on a hillside overlooking Arequipa.⁴⁵ Of the 347 households surveyed, reduviids were present in 194 (52%) households, and *T cruzi*-infected reduviids were found in 72 (19.3%) households.⁴⁵ Second, side yard guinea pig pens were more likely than other domestic animal enclosures to be infested with reduviids and harbored significantly more reduviids than other animal enclosures.⁴⁵ Guinea pigs and chickens remain stable sources of protein in South America and are often kept initially as pets, in pens and coops, or allowed to free roam.⁴⁵⁻⁴⁷ Cecere and colleagues previously noted that chickens were associated with increased reduviid densities and *T cruzi* infections, especially in rural areas.⁴⁶ Although domestic chickens do support and maintain reduviid densities, chickens are immune to *T cruzi* infections.^{28,46} Third, stacked brick and adobe animal enclosures were more likely to be infested with reduviids than wire mesh enclosures.⁴⁶ Fourth, only fully stuccoed and corrugated metal-roofed homes were fully protected from reduviid infestation.⁴⁶

Reducing the Risks of Chagas Disease in Travelers

Travelers may be at risk of interrupting the sylvatic and peridomestic transmission cycles of *T cruzi* infections by choosing to sleep outside pyrethroid-impregnated, insect-netted beds or hammocks in thatched roofed beachfront cabanas (*palapas*), or hunting or fishing lodges that have not been adequately insulated, mortared or stuccoed, and treated with pyrethroid-containing insecticides. As noted, reduviid bites occur at nighttime and are either painless, possibly from combinations of salivary local anesthetics and anticoagulants, or associated with pruritus. The localized pruritus only serves to induce rubbing and scratching by groggy victims, effectively dispersing infective trypomastigotes across bite-damaged epidermal surfaces or adjacent mucoepidermal junctions. Cabanas and lodges that provide accommodations in rural or isolated settings for large numbers of tourists are also perfect accommodations for reduviid families, who will both blood-feed and breed while hiding in such dwellings, some of which may be very comfortable and elegant. Finally, if such structures have layers of roof palm frond thatching, or are situated

against or atop hillsides or volcanic lava flows, reduviids will burrow deeply during the daytime in cracks and crevices in roofs, subfloors, and soil-filled foundations, safe from superficially sprayed insecticides.^{28,45–48}

Trypanosoma cruzi-infected reduviids have been frequently observed to infest palm trees and sugarcane fields in South America, especially in Ecuador and Brazil.⁴⁸ Several home-brewed popular cold drinks and alcoholic beverages are made with unpasteurized juices, fruits, or oils from palms and sugarcane and sold by street and beachside vendors in South America, particularly in Ecuador and Brazil.⁴⁸ Such local delights may be contaminated with *T cruzi*-infected reduviid or with unnoticed infected reduviid nymphs. Outbreaks of acute Chagas disease have now been reported following the consumption of such popular local brews, even in beachside resort areas. All travelers to *T cruzi*-endemic areas are encouraged to drink only bottled, boiled, or pasteurized beverages, and to avoid all local brews, especially those made from local palm trees and sugarcane. In addition, travelers should avoid chewing on unwashed sugarcane stems or palm hearts and avoid using unwashed sugarcane stems as swizzle sticks for beverages.

For travelers, the significance of recent urban transmission studies of Chagas disease, such as the one by Levy and colleagues in 2006, is simply that all major metropolitan areas in Latin America from Mexico City to Rio de Janeiro are surrounded with densely packed, low-income communities of former rural residents and their domestic animals, such as chickens, guinea pigs, cats, and dogs.⁴⁵ The inhabitants of these communities seek employment opportunities in cities and contribute their blood products and organs to local transfusion and transplantable organ stocks. Reduviids live alongside humans and animal hosts in both undeveloped rural and highly developed periurban settings; can survive for months without feeding, safely insulated from insecticides in poorly constructed animal enclosures and human dwellings; and can easily fly (adults) or walk (nymphs) to new feeding areas filled with warm-blooded hosts.^{28,45–47} Thus, reduviids are hardy and ubiquitous vectors of Chagas disease among wild and domestic animals and humans in a variety of transmission cycles, from dense rain forests to Andean highlands to packed cities and beaches. When staying in accommodations in Chagas disease-endemic areas that are not fully sealed with stuccoed walls and metal, shingled, or tiled roofs, travelers should consider further protecting themselves from reduviids with topical applications

of diethyltoluamide-containing insect repellants and pyrethroid-impregnated mosquito nets, fully covering sleeping beds and hammocks.

Travelers who may require blood transfusions or organ transplants in Chagas disease-endemic areas should inquire as to donor risk factors and serologic screening of donated blood and organs for *T cruzi* infections. In the past, donated blood products in Chagas disease-endemic areas were treated with gentian violet, which effectively cleared the parasitemias and risks of transfusion-transmitted disease within 24 hours. However, this practice has now been abandoned in favor of serologic screening due to the permanent and unacceptable bluish skin discoloration of gentian violet-treated transfusion recipients.

The differential diagnosis of any acute febrile illness in Chagas disease-endemic areas should include Chagas disease as well as malaria. The early detection of acute Chagas disease will require direct microscopic examination of the peripheral blood smear for trypomastigotes and serologic screening for *T cruzi* antibodies by ELISA, RIPA, or IFAT and later confirmation of *T cruzi* DNA or RNA antigens by PCR (Table 1; Figure 1).

The Prevention of Chagas Disease in Travelers

Because there is no vaccine to prevent Chagas disease and current chemotherapy is limited to two drugs, most efficacious only in the earliest stages of acute or reactivated *T cruzi* infections, the best preventive strategies for Chagas disease in travelers to the Americas should be directed at (1) the education of travelers to *T cruzi*-endemic areas of the Americas in the transmission risks of Chagas disease and (2) a recommendation for sleeping under pyrethroid-impregnated insect nets, especially when staying overnight in thatched and mud-walled huts or unmortared cabins.

Conclusions

Travel medicine physicians should now be concerned about the potential for autochthonous Chagas disease transmission by American reduviid bugs, with distribution zones expanded by global warming; the threats to local blood and transplantable organ supplies from mass population movements of *T cruzi*-infected donors; and the increasing susceptibility to Chagas disease by travelers, especially travelers immunocompromised by advancing ages and chronic diseases, to the *T cruzi*-endemic regions of the

Americas. Because the coasts, colonial cities, and ancient archeological ruins of Latin America are both Chagas disease endemic and among the most scenic and popular tourist destinations, travelers and their consulting physicians must recognize the changing ecology of and behavioral risk factors for Chagas disease and take appropriate steps to reduce the travel-associated risks of Chagas disease in *T. cruzi*-endemic regions throughout the Americas.

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The author states that he has no conflicts of interest.

References

- Control of Chagas disease: second report of the WHO expert committee. Technical report series 905. Geneva, Switzerland: World Health Organization, 2003.
- Galel SA, Kirchhoff LV. Risk factors for *Trypanosoma cruzi* in California blood donors. *Transfusion* 1996; 36:227–231.
- Leiby DA, Rentas FJ, Nelson KE, et al. Evidence of *Trypanosoma cruzi* infection (Chagas disease) among patients undergoing cardiac surgery. *Circulation* 2000; 102:2978–2982.
- Chagas disease after organ transplantation—United States, 2001. *MMWR* 2002; 51:210–212.
- Chagas disease after organ transplantation—Los Angeles, California, 2006. *MMWR* 2006; 55:798–800.
- Cetron MS. Chagas disease. In: Jong EC, McMullen R, eds. *The travel and tropical medicine handbook*. 2nd Ed. Philadelphia: W.B. Saunders Company, 1995:270–281.
- Rassi AJr, Rassi SG, Rassi A. Sudden death in Chagas disease. *Arq Bras Cardiol* 2001; 76:75–96.
- Peters W, Gilles HM. *Tropical medicine and parasitology*. 4th Ed. London: Mosby-Wolfe, 1997: 42–47.
- Dumontel E, Goubrière S. Predicting *Triatoma dimidiata* abundance and infection rate: a risk map for natural transmission of Chagas disease in the Yucatán peninsula of Mexico. *Am J Trop Med Hyg* 2004; 70:514–519.
- Pung OJ, Banks CW, Jones DN, Krissinger MW. *Trypanosoma cruzi* in wild raccoons, opossums, and triatomine bugs in southeast Georgia, USA. *J Parasitol* 1995; 81:324–326.
- Yaeger RG. The prevalence of *T. cruzi* infection in armadillos collected at a site near New Orleans, Louisiana. *Am J Trop Med Hyg* 1998; 38:323–326.
- Yabsley MJ, Noblet GP. Seroprevalence of *Trypanosoma cruzi* in raccoons from South Carolina and Georgia. *J Wildlife Dis* 2002; 38:75–83.
- Yabsley MJ, Noblet GP. Biological and molecular characterization of a raccoon isolate of *Trypanosoma cruzi* from South Carolina. *J Parasitol* 2002; 88:1273–1276.
- Hancock K, Zatac AM, Pung OJ, et al. Prevalence of antibodies to *Trypanosoma cruzi* in raccoons (*Procyon lotor*) from an urban area of northern Virginia. *J Parasitol* 2005; 91:470–472.
- Meurs KM, Anthony MA, Slater M, Miller MW. Chronic *Trypanosoma cruzi* infection in dogs: 11 cases (1987–1996). *J Am Vet Assoc* 1998; 213:497–500.
- Bradley KK, Bergman DK, Woods JP, et al. Prevalence of American trypanosomiasis (Chagas disease) among dogs in Oklahoma. *J Am Vet Assoc* 2000; 217:1853–1857.
- Woody NC, Woody HB. American trypanosomiasis (Chagas disease): first indigenous case in the United States. *J Am Med Assoc* 1955; 159:676–677.
- Schiffler RJ, Mansur GP, Navin TR, Limpakarnjanarat K. Indigenous Chagas disease (American trypanosomiasis) in California. *J Am Med Assoc* 1984; 251:2983–2984.
- Ochs DE, Hnilica VS, Moser DR, et al. Autochthonous acute chagasic myocarditis by polymerase chain reaction amplification of a species-specific DNA sequence of *Trypanosoma cruzi*. *Am J Trop Med Hyg* 1996; 54:526–529.
- Herwalt BL, Grijalva MJ, Newsome AL, et al. Use of polymerase chain reaction to diagnose the fifth reported case of autochthonous transmission of *Trypanosoma cruzi*, in Tennessee. *J Infect Dis* 2000; 181:395–399.
- Dorn P, Perniciaro L, Yabsley M, et al. Autochthonous transmission of *Trypanosoma cruzi*, Louisiana. *Emerg Infect Dis* 2007; 13:605–607.
- Vaidian AK, Weiss LM, Tanowitz HB. Chagas disease and AIDS. *Kinetoplastid Biol Dis* 2004; 13:1–6.
- Rivera J, Hillis LD, Levine BD. Reactivation of cardiac Chagas disease in acquired immune deficiency syndrome. *Am J Cardiol* 2004; 94:1102–1103.
- Gilson GJ, Harner KA, Abrams J, et al. Chagas disease in pregnancy. *Obstet Gynecol* 1995; 86:646–647.
- DiPentima MC, Hwang LY, Skeeter CM, Edwards MS. Prevalence of antibody to *Trypanosoma cruzi* in pregnant Hispanic women in Houston. *Clin Infect Dis* 1999; 28:1281–1285.
- Flores-Chavez M, Bosseno MF, Bastrenta B, et al. Polymerase chain reaction detection and serologic follow-up after treatment with benznidazole in Bolivian children infected with a natural mixture of *Trypanosoma cruzi* I and II. *Am J Trop Med Hyg* 2006; 75:497–501.

27. Leiby DA, Read EJ, Lenes BA, et al. Seroepidemiology of *Trypanosoma cruzi*, etiologic agent of Chagas disease, in US blood donors. *J Infect Dis* 1997; 176:1947–1952.
28. Marsden PD. American trypanosomiasis. In: Cook GC, ed. *Manson's tropical diseases*. 20th Ed. London: W.B. Saunders Company Ltd 1997: 1197–1212.
29. Coronado X, Zulantay I, Albrecht H, et al. Variation in *Trypanosoma cruzi* clonal composition detected in blood patients and xenodiagnosis triatomines: implications for molecular epidemiology of Chile. *Am J Trop Med Hyg* 2006; 74:1008–1012.
30. Blanche C, Aleksie I, Takkenberg JJ, et al. Heart transplantation for Chagas cardiomyopathy. *Ann Thorac Surg* 1995; 60:1406–1408.
31. Araújo MSS, Martins-Filho OA, Pereira MES, Brener Z. A combination of benzimidazole and ketoconazole enhances efficacy of chemotherapy of experimental Chagas disease. *J Antimicrob Chemotherapy* 2000; 45:819–824.
32. Rassi A Jr, Rassi A, Little WC, et al. Development and validation of a risk score for predicting death in Chagas heart disease. *N Engl J Med* 2006; 355:799–808.
33. Maguire JH. Chagas disease—can we stop the deaths? *N Engl J Med* 2006; 355:760–761.
34. Kirchhoff LV, Paredes P, Lomeli-Guerrero A, et al. Transfusion-associated Chagas disease (American trypanosomiasis) in Mexico: implications for transfusion medicine in the United States. *Transfusion* 2006; 46:298–304.
35. Dumonteil E. Update on Chagas disease in Mexico. *Salud Publica Mex* 1999; 41:322–327.
36. Maguire JH, Hoff R, Sherlock I, et al. Cardiac morbidity and mortality due to Chagas disease: prospective echocardiographic study of a Brazilian community. *Circulation* 1987; 75:1140–1145.
37. Schmunis GA. Risk of Chagas disease through transfusions in the Americas. *Medicina (B Aires)* 1999; 59:125–134.
38. Schmunis GA. Prevention of transfusional *Trypanosoma cruzi* infection in Latin America. *Mem Inst Oswaldo Cruz* 1999; 94:93–101.
39. Leiby DA, Herron RM Jr, Read EJ, et al. *Trypanosoma cruzi* in Los Angeles and Miami blood donors: impact of evolving donor demographics on seroprevalence and implications for transfusion transmission. *Transfusion* 2002; 42:549–555.
40. Riarte A, Luna C, Sabatiello R, et al. Chagas disease in patients with kidney transplants: 7 years of experience, 1989–1996. *Clin Infect Dis* 1999; 29:561–567.
41. Ferraz AS, Figueiredo JFC. Transmission of Chagas disease through transplanted kidney: occurrence of the acute form of the disease in two recipients from the same donor. *Rev Inst Med Trop Sao Paulo* 1993; 35:461–463.
42. deFaria JB, Alves G. Transmission of Chagas disease through cadaveric renal transplantation. *Transplantation* 1993; 56:1583–1584.
43. Vazquez MC, Riarte A, Pattin M, Lauricella M. Chagas disease can be transmitted through kidney transplantation. *Transplant Proc* 1996; 25:3259–3260.
44. Vazquez MC, Sabbatiello R, Schiavelli R, et al. Chagas disease and transplantation. *Transplant Proc* 1996; 28:3301–3303.
45. Levy MZ, Bowman NM, Kawai V, et al. Periurban *Trypanosoma cruzi*-infected *Triatoma infestans*, Arequipa, Peru. *Emerg Inf Dis* 2006; 12:1345–1352.
46. Cecere MC, Gürtler RE, Canale D, et al. The role of the peridomiciliary area in the elimination of *Triatoma infestans* from rural Argentine communities. *Rev Panam Salud Publica* 1997; 1:273–279.
47. Cecere MC, Gürtler RE, Chuit R, Cohen JE. Effects of chickens on the prevalence of infestation and population density of *Triatoma infestans* in rural houses of northwest Argentina. *Bull World Health Organ* 1990; 68:737–746.
48. Abad-Franch F, Palomeque FS, Aguilar HM, Miles MA. Field ecology of sylvatic *Rhodnius* populations (Heteroptera, Triatominae): risk factors for palm tree infestation in western Ecuador. *Trop Med Intl Health* 2005; 10:1258–1266.