Chagas disease is caused by *Trypanosoma cruzi*, a protozoal organism primarily transmitted by triatomine insect vectors, also known as “kissing bugs.” It is a zoonotic disease originally described by Brazilian physician Dr. Carlos Chagas in 1909 and is widespread in Latin America. Although triatomines and *T. cruzi* have long been endemic to the southern United States, awareness and identification of infected vectors and animals have recently increased throughout the United States. Canine Chagas disease can be acute or chronic and is predominantly characterized by inflammation and fibrosis of the heart, resulting in arrhythmias, myocardial dysfunction, heart failure, and sudden death, although many infected dogs are asymptomatic.

High densities of dogs in confined areas are associated with heat and carbon dioxide, which attract kissing bugs.

**TRIATOMINE VECTORS**

Triatomine insect vectors belong to the family Reduviidae, subfamily Triatominae (**FIGURE 1**). In the southern United States, 11 triatomine species are established; species regularly encountered by people and dogs include *Triatoma gerstaeckeri*, *Triatoma sanguisuga*, *Triatoma rubida*, and *Triatoma recurva* (**FIGURE 2**). In contrast to the domesticated species found in Central and South America, which live in human dwellings, many triatomines of the southern United States are considered to be sylvatic (associated with wildlife and natural habitats) and only occasionally drawn into the domestic and peridomestic environments. Colonization of homes by triatomines in the United States is often associated with rustic or dilapidated housing, or with the *T. recurva* species in Arizona.

Triatomine insects feed primarily on blood. They are generalist feeders and obtain blood meals from many hosts, predominantly vertebrates (e.g., wild/domestic mammals, birds, amphibians, reptiles, humans); they have also been shown to feed on invertebrates (e.g., crickets).

Infection prevalence of *T. cruzi* in triatomines ranges from approximately 20% to 70% depending on species, with an overall 54% infection prevalence reported.
across specimens from 17 states (predominantly Texas) submitted to a Kissing Bug Citizen Science program.\textsuperscript{3}

Risk factors for \textit{T. cruzi} infection include living in or traveling to an area with infected insect vectors.\textsuperscript{4} All dogs are at risk for infection; however, dogs with lifestyles that include outdoor work or housing can have increased risk of exposure.\textsuperscript{4-6} Dog kennels may be particularly suitable environments for the establishment of \textit{T. cruzi} transmission cycles. High densities of dogs in confined areas are associated with heat and carbon dioxide, which attract kissing bugs. For example, nearly 40% of triatomines collected by members of the public and submitted to a Kissing Bug Citizen Science program were collected from kennel environments.\textsuperscript{3}

Several insects appear similar to the kissing bug and cause confusion among the public and veterinary community (BOX 1). These “look-alike” insects do not feed on blood from humans or animals (although some are associated with painful bites) and pose no risk for the transmission of \textit{T. cruzi}.

\textbf{TRYPANOSOMA CRUZI}

\textbf{Life Cycle}

The morphologic forms of the \textit{T. cruzi} parasite include amastigotes, epimastigotes, and trypomastigotes. Amastigotes are found in mammalian host cells, and epimastigotes live in the hindgut of the triatomine insect. Both replicate by binary fission. Trypomastigotes are present in the bloodstream of mammalian hosts during acute infection and can be seen in blood smears (FIGURE 3). Infective trypomastigotes are also present in the hindgut and feces of the triatomine insect vector.
Transmission

The *T. cruzi* parasite is transmitted through the stercorarian (vector-fecal) route when a kissing bug excretes the parasite in its fecal material onto the host and the parasite enters through the bite wound, a break in the skin, or a mucous membrane. Although this method of transmission is inefficient, an epidemiologic setting with insects that colonize the home and feed night after night is a high-risk scenario for vector-fecal transmission to humans. Oral transmission can occur after consumption of fruit or juices contaminated with triatomine feces or through consumption of infected insects, as has been shown in experimental lab studies with raccoons. The relative importance of stercorarian versus oral transmission in dogs is unknown.

Nonvector routes of parasite transmission include transplacental and transmammary from infected mother to offspring (human, animal), blood transfusion (human), ingestion of an infected animal (human, animal), and rare laboratory accident (human). In pregnant women with antibodies to *T. cruzi*, the global rate of transmission is estimated to be 4.7%, while a corresponding estimate for veterinary congenital transmission is unknown.

Prevalence

Prevalence of *T. cruzi* infection among dogs ranges depending on canine population and type of serologic test used. For example, antibodies against *T. cruzi* were detected in 18% and 7% of shelter dogs in Texas and Louisiana, respectively. In a study of dogs housed in kennels in central Texas where triatomines were abundant, seroprevalence exceeded 50%.

**CHAGAS DISEASE**

Distribution

Chagas disease is prevalent in Latin America and is increasingly recognized in the United States. In areas where triatomines are established, infections may be acquired from local vectors. However, Chagas disease is not geographically confined to regions where triatomines live, so human medical and veterinary providers may encounter patients with Chagas disease outside traditionally endemic environments. Travel and relocation of animals have the potential to redistribute infected dogs; for example, in one study, government working dogs that provide security and border protection in northern states tested positive for
T. cruzi, likely reflecting infections acquired when the dogs trained in southern states. Consequently, Chagas disease should be considered in the differential diagnosis for unexplained arrhythmias and myocardial dysfunction in dogs with unknown origin or travel history or known travel to endemic regions.

Clinical Presentation
The progression of Chagas disease in dogs is similar to that in humans. Inflammation, fibrosis, and cellular damage are caused by trypomastigotes invading host cells to become pseudocysts of intracellular amastigotes. Inflammation is more pronounced in the acute stage, developing into fibrosis in the chronic stage, at which point amastigotes are much less likely to be identified. While the heart is the organ primarily affected in dogs, parasites can be found in many other tissues (e.g., liver, kidney, spleen, brain, skeletal muscle, lymph node). Information about progression of disease in naturally infected dogs is expanding with continued study. Acute disease develops within approximately 21 days of infection, followed by an indeterminate, asymptomatic phase that can progress into chronic disease. In experimental T. cruzi infections, dogs developed chronic disease 8 to 36 months after inoculation. Dogs with acute and chronic disease often remain undiagnosed and are asymptomatic or have only mild clinical signs such as fever, lethargy, lymph node enlargement, and organomegaly (spleen, liver). Cardiac abnormalities develop in both acute and chronic disease, with damage resulting in arrhythmias, conduction abnormalities, heart enlargement, myocardial dysfunction, heart failure, and sudden death. Clinical signs include weakness, lethargy, collapse, and signs of congestive heart failure (e.g., abdominal distention, respiratory difficulty). Physical examination findings support the presence of heart disease, characterized most often as tachycardia/bradycardia, weak or irregular pulses, murmur, dyspnea, and ascites.

Diagnosis
Chagas disease is a diagnostic differential for dogs with arrhythmias, myocardial dysfunction, and congestive heart failure. It can present with findings similar to those of dilated cardiomyopathy (idiopathic, nutritional deficiency), arrhythmogenic right ventricular cardiomyopathy, other forms of infectious myocarditis, and congenital tricuspid valve dysplasia. The index of suspicion for Chagas disease increases in dogs from an endemic location or that have originated from, traveled to, or are currently living in an area where Chagas disease has been reported. Testing should be considered for dogs with a mother, littermate, or housemate (dog or cat) that has tested positive for T. cruzi infection. As there is no gold standard test, the sensitivity and specificity of the available tests are unknown.

Microscopy
Identification of trypomastigotes on a buffy coat or whole blood smear (FIGURE 3) can enable a positive diagnosis of an acute infection when serologic test results are negative early in the disease process. Trypomastigotes and amastigotes can be identified during thorough microscopic examination of needle aspirates of enlarged lymph nodes or, more often, on histopathologic sections of the heart (FIGURE 4) or other organs (e.g., spleen, liver, kidney, lymph node, diaphragm). Domestic cats are increasingly recognized as infected and potentially clinically affected hosts.
Serology

Indirect fluorescent antibody testing, currently available at the Texas A&M Veterinary Medical Diagnostic Laboratory, is the most accessible test for *T. cruzi* infection in dogs. It confirms exposure to the parasite, often indicating current infection because infections are thought to be lifelong.\(^\text{23}\) A correlation between titer result and clinical disease has not been established. False negatives are possible during an acute infection within the first month of exposure, and cross-reactivity with *Leishmania* is possible. In human medicine, diagnosis of Chagas disease is a challenge, and multiple independent testing platforms are commonly used to look for consensus in results.\(^\text{17}\) Rapid tests that detect antibodies to *T. cruzi* for the diagnosis of Chagas disease in humans are not currently approved for clinical use in animals.

Polymerase Chain Reaction Testing

Polymerase chain reaction (PCR) testing is used to detect parasite DNA in blood and tissue.\(^\text{25}\) Antemortem testing of blood samples can detect circulating trypomastigotes more likely to be present in acute infections, but test results are limited by the amount of circulating organism present. In chronic disease, PCR results are limited by the low probability that a dog has circulating trypomastigotes. For these reasons, a negative PCR result should not be interpreted to indicate that the host is uninfected and alone is of limited utility as a test of cure. Postmortem PCR testing can be useful to confirm the presence of the organism in tissue samples (e.g., cardiac tissue).

Medical Tests for Heart Disease

Diagnostic tests for heart disease include electrocardiography (ECG), echocardiography, and cardiac troponin I. Screening for heart disease in asymptomatic dogs provides information about heart function and arrhythmias that may be clinically silent but increase the risk of clinical signs and sudden death. In dogs with *T. cruzi* infection, ECG abnormalities vary widely based on the location and extent of myocardial damage and resultant inflammation and fibrosis but include changes to the ECG complex, conduction disturbances (atrioventricular block, bundle branch block), and both brady- and tachyarrhythmias.\(^\text{3,20,21,24}\) Infected dogs are more likely to have ventricular arrhythmias and combinations of ECG abnormalities.\(^\text{4}\) An ambulatory ECG (Holter monitor) recording can detect arrhythmias not present during physical examination.\(^\text{4}\)

A recent study using Holter monitoring of serologically positive and negative working dogs along the Texas-Mexico border showed that 78% of positive dogs and 11% of negative dogs had ECG abnormalities, most commonly supraventricular and ventricular arrhythmias and atioventricular block.\(^\text{22}\)

Echocardiographic abnormalities include enlargement of all 4 heart chambers and ventricular systolic dysfunction. Elevations in cardiac troponin I, a nonspecific indicator of myocardial damage, are reported in dogs infected with *T. cruzi*.\(^\text{4,22}\)

Treatment

Antiprotozoal treatment protocols are not well established in dogs. Prospective studies that include risk-benefit assessment and further investigation into optimal timing and dose of medications are needed to help improve the long-term clinical course of Chagas disease. Anti-trypanosomal medications (e.g., benznidazole, nifurtimox, itraconazole) used specifically to treat *T. cruzi* infection may show promise but do not currently have consistently proven efficacy for curing Chagas disease in dogs or preventing the chronic fibrosis and progressive myocardial dysfunction that develops in dogs or humans.\(^\text{17,26}\) These medications have been associated with temporary suppression of parasitemia and have a range of side effects.\(^\text{17}\) Additionally, treatment response in dogs may be *T. cruzi* strain dependent.\(^\text{26}\)
Benznidazole treatment in humans and dogs has shown variable clinical benefit and a high possibility of adverse effects, and the medication is not readily available for dogs in the United States.\textsuperscript{17,26} The combined use of itraconazole and the antiarrhythmic medication amiodarone has been described in the treatment of serologically positive dogs.\textsuperscript{27}

Although complex, additional prospective investigation to determine therapeutic protocols, evaluate adverse effects, and establish diagnostic test strategies to assess potential cure and clinical response in symptomatic and asymptomatic naturally infected dogs would be useful.

Medical therapy is tailored to the clinical abnormalities identified in an individual dog, which are most often related to the heart. These include antiarrhythmics for tachyarrhythmias, pacemaker implantation for bradyarrhythmias, positive inotropic therapy with myocardial dysfunction, and diuretic therapy for heart failure.\textsuperscript{20} Symptomatic chronic disease requires long-term management.

Prevention
Vector control is an important part of managing disease transmission. Kissing bug habitats include wooded areas, brush piles, nests, and porches.\textsuperscript{1} The insects are most active at night, are attracted to lights, and can invade homes and kennels. Vector control can include turning off outdoor lights, cleaning up brush and woodpiles that serve as breeding areas for insects, housing animals inside, and using insecticides. Kissing bug control can be difficult in kennels, particularly in recently developed areas where kennels are surrounded by natural habitats with associated wildlife.

Improving public awareness for dog owners and medical professionals is an important step in infection prevention, vector control, and identification of infected animals. Because of its zoonotic potential, it is important for personnel handling blood and tissue of infected animals to take appropriate safety precautions.

CONCLUSION
Although the insects that transmit \textit{T. cruzi} are primarily reported in the southern half of the United States and across Latin America, any dog with vector contact can be infected, including dogs that live in northern states and have a travel history. Infected animals can be asymptomatic or develop a range of cardiac complications, including sudden death or chronic disease. Because of the challenges in diagnosis and lack of well-established antiparasitic treatments, Chagas disease is an active area of scientific study. TVP

References

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Mirataz™ (mirtazapine transdermal ointment)

For topical application in cats only. Not for oral or ophthalmic use.

CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

Before using this product, please consult the product insert, a summary of which follows:

INDICATION: Mirataz™ is indicated for the management of weight loss in cats. Do not use on cats with diabetes mellitus.

DOSAGE AND ADMINISTRATION: Apply a 1-inch ribbon of ointment approximately 2 mg/d to the inner pinna of each ear of the cat once daily for 14 days. Wear disposable gloves when applying Mirataz™. Do not administer daily application of Mirataz™ between the left and right inner pinna of the ears. See Product Insert for complete dosing and administration information.

CONTRAINDICATIONS: Mirataz™ is contraindicated in cats with a known hypersensitivity to mirtazapine or to any of the excipients. Mirataz™ should not be given in combination, or within 14 days before, or after treatment with MAO-A (e.g., selegiline hydrochloride (D-Deprenyl), amitriptyline), as there may be an increased risk of serotonin syndrome.

HUMAN WARNINGS: Not for human use. Keep out of reach of children. Wear disposable gloves when handling or applying Mirataz™ to prevent accidental topical exposure. Do not administer orally or to the eye. Use with caution in cats with hepatic disease. Mirtazapine may cause elevated serum hepatic enzymes (e.g., AST, ALT). Use with caution in cats with kidney disease. Kidney disease may cause reduced clearance of mirtazapine which may result in higher drug exposure. Upon discontinuation of Mirataz™, it is important to monitor the cat’s food intake. Food intake may lessen after discontinuation of mirtazapine. If food intake diminishes dramatically (>50%) for several days, or if the cat stops eating for more than 48 hours, reevaluate the cat. Mirataz™ has not been evaluated in cats <2 kg or less than 6 months of age. The safe use of Mirataz™ has not been evaluated in cats that are intended for breeding, pregnant or lactating.

PRECAUTIONS: Do not induce vomiting unless told to do so by the poison control center or veterinarian. Do not induce vomiting if the cat has ingested Mirataz™. If the cat ingests Mirataz™, call a veterinarian or poison control center immediately. Although not expected to be toxic, mirtazapine has the potential to cause reduced clearance of mirtazapine, which may result in higher drug exposure. Upon discontinuation of Mirataz™, it is important to monitor the cat’s food intake. Food intake may lessen after discontinuation of mirtazapine. If food intake diminishes dramatically (>50%) for several days, or if the cat stops eating for more than 48 hours, reevaluate the cat. Mirataz™ has not been evaluated in cats <2 kg or less than 6 months of age. The safe use of Mirataz™ has not been evaluated in cats that are intended for breeding, pregnant or lactating.

ADVERSE REACTIONS: In a randomized, double-masked, vehicle-controlled field study to assess the effectiveness and safety of mirtazapine transdermal ointment in cats, 115 cats treated with Mirataz™ and 115 cats treated with vehicle control were evaluated for safety. The vehicle control was an ointment containing the same inert ingredients without mirtazapine. The cats were randomized to treatment groups in a 1:1 ratio and were evaluated for safety. The most common adverse reactions observed during field studies were lethargy, behavioral changes, discomfort, and chemical odor. The most common adverse reactions observed during field studies were lethargy, behavioral changes, discomfort, and chemical odor.

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