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Trypanosoma cruzi, the causal agent of Chagas disease: boundaries between wild and domestic cycles in Venezuela

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Trypanosoma cruzi the etiological agent of American Trypanosomiasis or Chagas disease (ChD) is transmitted by triatomines vectors between mammals including man. *T. cruzi* has existed for *circa* 150 Ma in the Americas and nearly 10 million people are currently infected. The overlap between wild and domestic ecotopes where *T. cruzi* circulates is increasing. Host–parasite interactions have been determined by infection patterns in these cycles, all under natural or laboratorial conditions. This mini-review describes specific parasite niches, such as plant communities or biological corridors between domestic and wild landscapes, in order to help identify risk factors for ChD and define the boundaries between wild and domestic transmission cycles, with an emphasis on research undertaken in Venezuela.

Keywords: *Trypanosoma cruzi*, domestic cycle, wild cycle, Chagas disease, Venezuela

INTRODUCTION

Parasites and their hosts form part of trophic webs and may be considered bioindicators of climate changes and anthropogenic impacts (1). American trypanosomiasis (AT) or Chagas disease (ChD) is a complex parasitosis caused by *Trypanosoma cruzi* (Kinetoplastida, Trypanosomatidae), which can be dispersed by enzootic or anthroponotic routes in trophic webs, which involve several mammals groups including human beings (**Figure 1**). So, this parasite affects currently, until 10 million people and as such can be considered a re-emerging public health problem especially in Venezuela (2, 3).

The *T. cruzi* life cycle begins when vectors (Hemiptera, Reduviidae, Triatominae) expel feces or urine with infective metacyclic trypomastigotes which then come into contact with mammals via intact mucous or skin abrasions. The trypomastigotes pass into the bloodstream and invade a wide range of tissues where they differentiate into amastigotes, epimastigote, and trypomastigotes once again. The latter are re-released into the bloodstream and can be imbibed by another or the same vector, which pass into the intestine and transform, once more, into metacyclic, performing a vectorial transmission (3).

Recent outbreaks of oral transmission in Brazil and other Latin American countries, including Venezuela, emphasize the importance of this alternative route in enzootic and zoonotic cycles (4).

Trypanosoma cruzi has been grouped into six discrete typing units (DTU): *T. cruzi* I (TcI) to *T. cruzi* VI (TcVI). The TcI–TcVI classification is, however, a relatively recent nomenclature and the associations of the different genotypes with particular hosts, ecotopes, or transmission cycles remains under debate (5).

Trypanosoma cruzi has existed in the Americas for *circa* 150 Ma and has been in contact with Amerindians for 15,000 years. The genome of this parasite in mummies from the American Pacific (7,500 BC to 1,500 AC) indicates a pre-Columbian origin thus breaking the myth of its establishment as a product of recent colonialism (6).

The host–parasite associations and risk factors associated with ChD is being described in recent studies of specific niches such as mammal caves, plant communities, and biological corridors between domestic and wild ecotopes, in order to widen the understanding of the boundaries between wild and domestic *T. cruzi* cycles in Venezuela.

VECTOR–PARASITE: PATTERNS OF WILD AND DOMESTIC *TRYPANOSOMA CRUZI* CYCLES

Triatomines are eclectic in their ecological niches: they are found from 42°N to 46°S and between 400 and 1200 m.a.s.l. (7). A total of 140 species are grouped into 8 tribes and 15 genera. *Triatoma maculata*, *Rhodnius prolixus*, and *Panstrongylus geniculatus* are the most important in Venezuela by their frequency of infection by *T. cruzi* and their association with domestic and peridomestic ecotopes in economically depressed rural areas (8).

Rhodnius prolixus in Venezuela, is predominantly intradomiciliary with a high-reproduction rates, a voracious blood intake and fast defecation time, all of which are attributes of a primary vector. In the wild, this triatomine is predominantly found in palms with synanthropic vertebrates providing the blood source (9, 10). *T. maculata* is found in palms, dry trees, wooden fences, and bird nests near human dwellings. Its domiciliation, in function to phenotypic and genotypic discrimination according to its ecotopes, guarantee the previous consideration about its presence a risk factor for parasite transmission in Brazil, Colombia, and Venezuela (11–13).

Coconut palms (*Coccus nucifera*) is a suitable triatominae ecotope in peridomicile environments in north-eastern Venezuela, as was corroborated by the presence of 242 *R. prolixus* and 144 *T.*

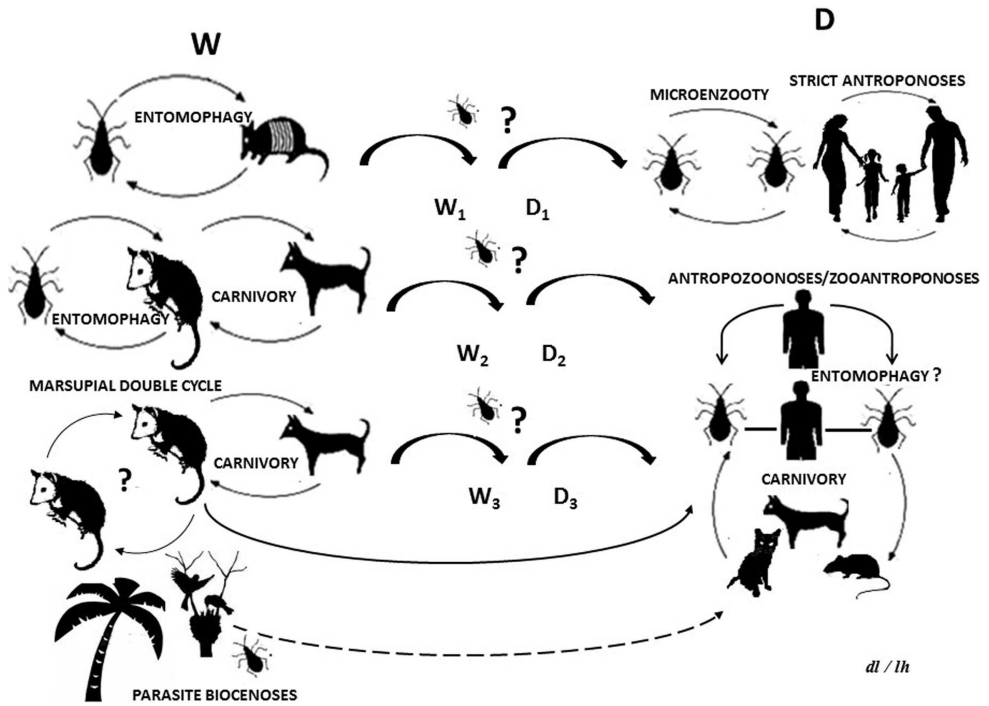

FIGURE 1 | Life cycle of *Trypanosoma cruzi*: (W) wild cycle with enzootic parasite circulation between wild and synanthropic mammals and other biotic components. (D) Domestic cycle with parasites circulating as a zooanthroponosis, anthropozoonosis, strict anthroponosis, or micro-enzooty. (W_n) Wild sub-cycles (D_n) domestic sub-cycles. Question marks indicate uncertainty as regards parasite circulation patterns or processes. The dotted line indicates a hypothetical route.

maculata adults in 14 coconut palms just 5 m away from human habitations. PCR amplification of the D7 divergent domain of the 24S rRNA genes; the non-transcribed spacer of mini-exon genes and the size-variable domain of the 18S rRNA genes confirmed that 98% of the *R. prolixus* and 70% of the *T. maculata* individuals were infected by *T. cruzi*–TcI. Exploration of coconut and its derivatives in industry and ethno-botany could pose a risk by exposing human beings to contaminated triatomines fluids (14).

Other triatomines vector species can acts as boundaries between wild and domestic environments. Examples are *Eratyrus mucronatus* and *Panstrongylus rufotuberculatus* found in palms, tree holes, and the dens of animal reservoirs, in Bolivia, Colombia, and Venezuela (15, 16). *P. rufotuberculatus* is a widely dispersed triatomine; in Venezuela could be monitored in peridomiciles in Anzoátegui state when wildlife fauna was affected or natural enemies were altered. Inoculation of the intestinal content of these insects in murine model, shown invasion of chondral tissue, brain, and kidney, revealing novel clinical aspects to be considered in relation to ChD (16).

Other triatomine species is *P. geniculatus*, which has been associated to infection of rodents and marsupials in rural or domestic ecotopes. The loss of its natural niches has also promoted its avid penetration in human dwellings. This is particularly worrying as this insect has been imputed as parasite font in cases of oral transmission of ChD in Caracas, and other cities in Venezuela. The modification of reservoir niches by climate change or the human exploitation of landscapes favors its peridomestic and domestic colonization (8, 17, 18).

The recent report of K-DNA and satellite DNA of *T. cruzi* in the intestines of *P. geniculatus* from sites along the Orinoco River, near Amerindian settlements, was associated with records of this species in neighboring countries, which could constitute evidence of biological corridors of the parasite with potential impacts on indigenous populations (19).

RESERVOIR–PARASITE: THE INTERACTION OF WILD MAMMALS, HUMAN BEINGS, AND DOMESTIC ANIMALS

Up until now, 180 species have been identified as reservoirs included in Artiodactyla, Carnivora, Cingulata, Chiroptera, Didelphimorphia, Lagomorpha, Perissodactyla, Pilosa, Primates (including man), and Rodentia orders (18).

Trypanosoma cruzi is considered as euryxenic according to the range of reservoirs it inhabits and eurytopic as regards the different organs it infects. Alternative transmission routes have also been reported in order to fluctuations in reservoir subpopulations, which could explain the plasticity of this zoonosis and urban outbreaks. The parasite may be orally transmitted via ingestion of infected triatomines, contaminated food, blood, or viscera from reservoirs (18, 20).

Studies of the distribution patterns of *T. cruzi* genotypes should consider ecological peculiarities since that genetic diversity has on the outcome of zoonosis or human disease (20). *T cruzi* Z3 in the southern Amazon (*Trichomys* rodent–*T. cruzi* complex in Brazil)

and *T. cruzi* TcIII in the northern Amazon (*Dasypus–T. cruzi* complex in Venezuela) provide instances of the expansion of these wild genotypes into urban cycles (21, 22).

Particularly, *Dasypus novemcinctus* form part of an ancient enzootic *T. cruzi* cycle in the touristically important north-eastern region of Venezuela. These mammals act as TcIII reservoirs, as has been shown by the PCR amplification of the intergenic region of HSP60 genes for *T. cruzi* and the restriction digest of PCR products by *Eco*RV. The interaction of *Dasypus novemcinctus* with human beings, domestic animals, and peridomestic triatomines in this region, may be an important risk factor (22).

The ubiquity of *T. cruzi* in mammal reservoirs and its effect on host fitness represents an element that has been scarcely studied. Parasite isolates from *D. marsupialis*, *R. prolixus*, and *T. maculata* from rural and urban areas of Venezuela have yielded 10^5 flagellates/ml of blood in mice models, producing 80% mortality with neurological symptoms such as ataxia, paralysis, and sphincter relaxation. Alterations as meningo-encephalitis, edema of the neuropil and parasitism near vascular system could facilitate the hematological dispersion of the parasites. These neurological disorders could alter the behavior of mammals toward predators thus modifying parasite transmission in trophic web (23, 24).

CONCLUSION

Parasitism implicates energy movement among organisms, affecting the interactions and robustness of some trophic webs. *T. cruzi* is a clonal parasite with wild and domestic cycles, some author has proposed that vector–mammal interaction and saturation vector feeding rates, depend on mammal density when the vector/mammal ratio is low and vector density when this ratio is high (25). The number of infected mammals is conditioned by their relative abundance, which thus influences their availability as a blood source for triatomines.

New incursion of some vectors or mammals reservoirs species in *T. cruzi* life cycle, is important in the epidemiology of AT and ChD. The potential trophic web can include ingestion of insects, contaminated food, or host carnivorous behavior, which could be the primary route for *T. cruzi* transmission in some wild cycles (**Figure 1**). Synanthropic mammals and vectors are not excluded from this, thus, providing a way by which the wild and domestic cycles could be crossed (26–28).

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