ORIGINAL ARTICLE / ARTIGO ORIGINAL

Chagas disease transmission by consumption of game meat: systematic review

Transmissão da doença de Chagas por consumo de carne de caça: revisão sistemática

Luiz Henrique Conde Sangenis¹, Marco Antonio Prates Nielebock¹¹, Ceumara da Silva Santos¹¹, Mateus Curty Carriello da Silva¹¹, Glauber Motta Ribeiro Bento¹¹

ABSTRACT: *Objective:* To evaluate the influence of game meat consumption in Chagas disease (CD) transmission, the conditions under which it occurs and the frequency of reports in the literature. *Methods:* Through systematic review, databases PubMed, LILACS, MEDLINE, and SciELO were consulted, and articles written in Portuguese, English, and Spanish were included, with no limitation over publication date. We used the following descriptors: *oral, transmission, meat, wild animals, hunt, carnivory,* and *Chagas disease.* Articles that mentioned consumption of animal meat as a form of human transmission of CD were included. We used epidemiological, clinical, and laboratory evidence criteria to confirm cases. *Results:* Among the 298 articles identified, only six met the eligibility criteria. Only five episodes of oral transmission through wild animal meat or blood consumption were identified. However, in two of them, the possibility of vectorial transmission could not be ruled out. Most reports met the epidemiological, clinical, and laboratory evidence criteria established to support the transmission. *Conclusion:* Though CD transmission is uncommon, hunting and consumption of wild mammals that serve as *Trypanosoma cruzi* reservoirs should be discouraged in endemic countries in light of the risks inherent to these practices.

Keywords: Chagas disease. Trypanosoma cruzi. Transmission. Epidemiology. Meat. Wild animals.

¹Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz - Rio de Janeiro (RJ), Brazil.

"Universidade Estácio de Sá, Nova Friburgo Campus – Rio de Janeiro (RJ), Brazil.

Corresponding author: Luiz Henrique Conde Sangenis. Instituto Nacional de Infectologia Evandro Chagas. Avenida Brasil, 4365, Manguinhos, CEP: 21040-360, Rio de Janeiro, Brazil. E-mail: lhcsangenis@gmail.com

Conflict of interests: nothing to declare - Financial support: none.

RESUMO: *Objetivo*: Avaliar a influência do consumo de carne de caça na transmissão da doença de Chagas (DC), assim como as condições em que ela ocorre e a frequência de relatos na literatura. *Métodos*: Mediante revisão sistemática, foram consultadas as bases PubMed, LILACS, MEDLINE e SciELO, sendo incluídos artigos escritos em português, inglês e espanhol, sem limitação do ano de publicação. Os descritores utilizados foram: *oral, transmission, meat, wild animals, hunt, carnivory* e *Chagas disease*, sendo inseridos na análise os artigos que mencionavam o consumo de carne de animais como forma de transmissão humana da DC. Foram utilizados critérios de evidência epidemiológico, clínico e laboratorial. *Resultados*: Entre os 298 artigos identificados, apenas seis preencheram os critérios de elegibilidade. Foram identificados somente cinco episódios de transmissão oral por consumo de carne ou sangue de animais silvestres, porém em dois deles não foi possível afastar a possibilidade de transmissão vetorial. A maior parte dos relatos preencheu os critérios de evidência epidemiológico, clínico e laboratorial, estabelecidos para sustentar a transmissão. *Conclusão*: Apesar da transmissão de DC ser incomum, a caça e o consumo de mamíferos silvestres reservatórios devem ser desestimulados nos países endêmicos em função dos riscos inerentes a essas práticas.

Palavras-chave: Doença de Chagas. Trypanosoma cruzi. Transmissão. Epidemiologia. Carne. Animais silvestres.

INTRODUCTION

Chagas disease (CD) is an antropozoonosis endemic to the American continent which has the protozoan Trypanosoma cruzi (T. cruzi) as its etiological agent^{1,2}. The main form of transmission occurs by means of the contact of damaged skin and mucous membranes with feces contaminated by insect vectors of the subfamily Triatominae². The geographic scope of the endemy extends from Mexico, in North America, to Argentina in South America^{3,4}. In the last decades, several epidemiological changes have occurred owing to successful campaigns aimed at controlling vectorial and blood transfusion transmission in endemic countries, leading to a significant reduction of new cases^{2,4,5}. However, the occurrence of the disease in some South American countries such as Bolivia, Argentina, and Brazil still is high². A recent meta-analysis has estimated the prevalence of CD in Brazil at 2.4%, corresponding to 4.6 million infected individuals⁶. Furthermore, we observed an increase in the number of oral transmissions through the ingestion of food contaminated by triatomine infected by T. cruzi^{3,4,7}. In Brazil, dozens of outbreaks of acute CD have been documented between 1965 and 2013 due to ingestion of contaminated food. Most cases were related to the consumption of açaí juice and sugar cane juice8,9. Other South American countries such as Venezuela, Colombia, and the French Guiana have also documented outbreaks of acute CD related to food consumption¹⁰⁻¹². Oral transmission is nowadays one of the main forms of transmission of this disease in Brazil, particularly in the Amazon Region^{8,9}. The consumption of raw or poorly cooked wild animal meat infected with T. cruzi is mentioned as one of the forms of transmission, something that has been demonstrated in experimental animal studies^{3,13}. *T. cruzi* infection has been identified in over a hundred species of wild mammals, in addition to domestic species like dogs, cats, pigs, goats, guinea pigs, and rabbits^{2,3,14-17}.

Synanthropic and household mammals are an integral part of peridomestic T. cruzi cycles, representing a risk for human transmission of CD^{17-19} .

Native populations had the habit of consuming meat from hunting, and this was an important source of food when animal husbandry techniques were not yet known²⁰. In the American continent, wild animal meat was part of the diet of indigenous peoples and pre-Colombian civilizations²⁰⁻²². Paleoparasitology studies have found that CD is a very old disease in this continent. By means of polymerase chain reaction techniques, T. cruzi DNA was found in mummies of African and American primitive civilizations²³. The oldest infection by CD in the Americas was discovered in mummies of the Chinchorro people, who lived 9,000 years ago in the Atacama Desert region, in northern Chile^{22,23}. More evidence of CD was found in 4,000 years old mummies belonging to the primitive inhabitants of Chile and Peru, prior to the onset of the Inca civilization²². There is a great possibility that these primitive individuals acquired CD via the oral route, when consuming game meat^{22,23}. However, the possibility of vectorial transmission cannot be ruled out²². The Chinchorro people lived in caves inside rocks, and fishing and hunting were their main sources of food²². Little is known about the hosting of triatomines in such remote ages, and indeed this must have happened much later, after the emergence of animal husbandry and agriculture^{1,22,23}. Andean civilizations developed the raising of guinea pigs (Cavia sp), which may have contributed to bringing triatomines to the home environment²³. In addition, it is believed that the consumption of raw meat and blood of these animals in rituals and religious ceremonies was the main factor of emergence of CD in these civilizations^{22,23}. Indigenous peoples of the Chaco region in Argentina and Paraguay may also have acquired CD by consuming wild animal meat²⁴.

In Brazil, game meat was a natural source of food for several indigenous ethnic groups. Currently, it is still part of the intake of tribes that live in the Amazon Region^{25,26}. There is poor evidence that CD was a health problem for native Brazilians, and there is scant information on the hosting of triatomines in indigenous huts²⁵. Although there is proof of T. cruzi infection in primitive humans, it is believed that the disease has spread due to colonization, deforestation, and internal migrations that developed after the arrival of European colonizers^{1,23,25}. Although it is not yet very clear, it is likely that the few cases of CD found in native individuals occurred via the oral route — through consumption of meat infected with T. cruzi²⁵. Game meat consumption is common in Brazilian rural populations^{20,21}. However, wild animal meat consumption was appreciated even by the Portuguese court during their stay in Brazil in the 19th century²⁷. This habit may be a result of their contact with natives and Africans during the colonial period²⁰. Recent research conducted in rural areas of Rio de Janeiro shows that consumption of wild animal meat was reported by 78% of residents and in the 15 cases of CD classified as autochthonous¹⁸. Armadillo and opossum, known reservoirs of T. cruzi, were the most cited animals^{18,28}. Although hunting of wild animals was forbidden in Brazil in 1967, it still occurs in rural areas, and not only as a means of survival²⁹. This study aims at analyzing the influence of the consumption of game meat in human transmission of CD, under what conditions it takes place, the frequency of reports in the literature, and what evidence was used when confirming cases.

METHODS

The collection of scientific publications for reviewing was conducted by two researchers between May and June 2015. Databases PubMed, LILACS, MEDLINE, and SciELO were consulted, and articles written in Portuguese, English, and Spanish were included, with no limitation over publication date. Initially, the Descritores em Ciências da Saúde (DeCS) database of the Biblioteca Virtual em Saúde was used for looking up descriptors in both Portuguese and English. In all databases consulted, the following descriptors were used: oral, transmission, and Chagas disease. The terms meat, wild animals and Chagas disease; hunt, meat and Chagas disease; carnivory and Chagas disease were also used in all bases, but only returned three articles.

An initial selection was made by reading titles and abstracts of the articles selected. All articles that mentioned the consumption of animal meat as a form of human transmission of CD were selected for analysis. Subsequently, all articles meeting the eligibility criteria were read in their entirety, and we selected those that met the inclusion criteria. As an additional selection strategy, the bibliographical references mentioned by the articles selected were also consulted. Articles that reported cases of CD related to oral transmission through consumption of meat were selected for review. For each eligible article, the evidence criteria used for detecting transmission were analyzed. Three evidence criteria were established:

- 1. epidemiology criterion: meat consumption was reported;
- 2. clinical criterion: CD signs and symptoms were reported;
- 3. laboratory criterion: positive parasitological, serological or pathological exams were reported. Articles which referred only to the oral transmission of *T. cruzi* infection in animals were excluded.

The selection process was performed independently by two examiners, and disagreements were discussed between both until a consensus was reached. As this is a literature review, there was no need to submit it for approval by the Ethics Committee.

RESULTS

Figure 1 shows the flowchart illustrating the selection of articles for review. 298 articles were identified through database querying: 117 in the PubMed database; 88 in MEDLINE; 52 in LILACS; 37 in SciELO, and 4 articles from other sources. After the exclusion of 45 duplicate articles, 253 were selected for screening. Most articles were excluded from analysis, as they did not address oral transmission of CD through meat consumption. Among the 233 articles excluded, 122 only discussed oral transmission by means of the consumption of drinks contaminated by *T. cruzi* (acaí, sugar cane juice, guava juice, and bacaba juice); 48 articles were excluded as they were limited to other forms of CD

transmission; 45 articles did not specify the type of food; and 18 of them dealt with oral transmission between animals.

After surveying articles' titles and abstracts, 20 of them were selected for thorough reading. In this stage, 14 other articles were excluded because they did not report human CD infection through meat consumption. Only six articles met the inclusion criteria for this review. Table 1 describes the articles selected for review. Location, timeframe,

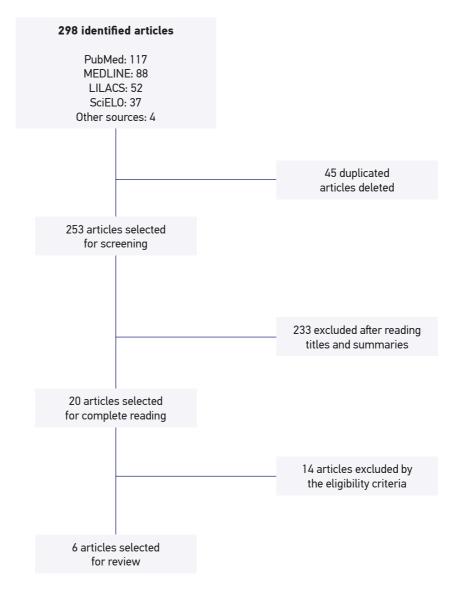


Figure 1. A flowchart illustrating the article selection process carried out in this systematic review on the oral transmission of Chagas disease related to consumption of game meat.

number of individuals infected, animal species involved, and evidence criteria utilized for confirming transmission were outlined for each study. Three of the articles were related to the same episodes of infection. Only five episodes of oral CD transmission via consumption of wild animal meat were identified. In addition to oral transmission, the possibility of vectorial transmission could not be ruled out in two articles. One of the articles also considered the possibility of transmission through contact with the animal body while preparing it for consumption.

DISCUSSION

Only six articles met the selection criteria for this systematic review^{18,30-34}. Three publications discussed the same infection episodes in Argentina, both involving children who had consumed raw or poorly cooked wild animal meat or blood³⁰⁻³². These three

Table 1. Description of the articles reporting cases of Chagas disease through meat consumption and assessment of the criteria of evidence used by each to detect transmission.

Articles selected for review	Location/ timeframe of transmission	Individual Infected	Animals involved	Evidence criteria used		
				Epidemiological	Clinical	Laboratory
Amato- Neto et al., Toso et al. e Valente et al. ^{30-32*}	Argentinian Chaco / 1936	Child	<i>Dasypus</i> sp	Yes	Yes	No
	Argentina / 1962	12-Year-old child	Dasyprocta sp, Lagostomus sp	Yes	Yes	Yes
Carvalho et al. ³³	São Paulo, Brazil / from the 1920s to the 1980s	8 adults aged between 23 and 60 years**	Dasypus sp, Cuniculus paca, Pecari tajacu, Didelphis sp, Mazama sp, Callithrix sp, Allouatta sp, Cebus sp	Yes	No	Yes
Forattini et al. ³⁴	São Paulo, Brazil / 1979	9-year-old child***	<i>Dasypus</i> sp	Yes	Yes	Yes
Sangenis et al. ¹⁸	Rio de Janeiro, Brazil / from the 1930s to the 1990s	14 adults and 1 adolescent**	Didelphis sp, Dasypus sp, Cuniculus paca, Cavia sp	Yes	Yes	Yes

^{*}These three articles discussed the same cases; **there was a possibility of vector transmission; ***the possibility of infection through manipulation of the animal carcass during cooking was also considered.

articles also reported episodes cited in other bibliographical sources³⁰⁻³². The earliest oral transmission case took place in the Argentinian Chaco, in 1936, when a child fell ill after ingesting a drink made of herbs and armadillo blood that had been prescribed by a healer³⁰⁻³². Later, in 1962, another episode was reported in Argentina, in this case involving a 12-year-old child who died 20 days after ingesting poorly cooked wild rodent meat due to heart failure caused by acute myocarditis. The clinical suspicion was confirmed by the autopsy, which showed lesions that are characteristic of acute chagasic infections in the heart and the mesenteric ganglion³¹. Nearly all the reports in the six articles selected met the three evidence criteria used to confirm the cases (epidemiological, clinical, and laboratory findings)18,30-34. In two of the studies, it was not possible to rule out the possibility of vectorial transmission. However, such studies were performed in regions known for sporadic wild triatomine infestation and where game meat consumption was common, namely the southern coast of São Paulo and the state of Rio de Janeiro^{18,33}. Another article reported CD infection by a child from Cananéia, a coastal city in the south coast of São Paulo³⁴. In this case, the possibility of transmission through contact with dead armadillos (Dasypus sp) carcasses during cooking was also considered. The child showed signs and symptoms typical of the acute phase of CD, and there was also parasitological and serological laboratory confirmation. However, none of the typical signs of vector infection were detected, increasing the possibility of transmission via the oral route. The child was treated with benznidazole and recovered satisfactorily³⁴.

With the exception of cases taking place in the Argentinian Chaco or in Argentina, all remaining reports occurred in regions where vector transmission was not considered relevant (i.e. the São Paulo coastal area and rural Rio de Janeiro)^{18,33,34}. Two of these articles addressed studies developed in these states^{18,33}. These cross-sectional descriptive studies aimed at defining the prevalence of CD, in addition to investigating risk factors for exposure, such as the presence of triatomines in the home environment and the consumption of game meat^{18,33}.

Given that the consumption of game meat is common among rural populations in Brazil^{18,29}, it is possible that the transmission of the disease through this method is much more frequent than has been documented. As household triatomine infestation is the most significant factor for the occurrence of transmissions in a given region^{1,2}, this criterion may have obscured cases in which oral transmissions were the method of infection. Given the reduction in new cases involving transmissions caused by vectors and blood transfusions, it is likely that the new epidemiological scenario observed in Latin America in recent decades will reveal more cases of transmissions considered unusual, such as oral transmission by food consumption^{3,4}. Recent reports already serve as an indication of this process, detailing cases of oral transmission in Brazil, Colombia, Venezuela, and the French Guyana⁷⁻¹². However, ingestion of drinks contaminated with triatomines or triatomine feces remains the main cause of oral transmissions⁸⁻¹⁰. Biological and physicochemical studies indicate that the *T. cruzi* is eliminated after cooking in temperatures above 45°C, which constitutes an effective prophylactic measure¹³.

CONCLUSION

The few evidences of CD transmission through the consumption of meat from animals infected with *T. cruzi*, as indicated by this literature review, suggests that CD transmission through this method is rare. However, hunting, carcass handling, and consumption of wild mammals that serve as *T. cruzi* reservoirs, common practices in rural Brazil and Latin America must always be considered as possible causes for the transmission of the disease, particularly when no other suspicion factors are present. Educational measures aimed at discouraging hunting and consumption of wild animal reservoirs of *T. cruzi* should be adopted in endemic countries in light of the risks of CD transmission that are inherent in these practices.

ACKNOWLEDGMENTS

This study was carried out with the help of the Laboratory of Clinical Research in Chagas Disease of the Instituto Nacional de Infectologia, Fundação Oswaldo Cruz and Universidade Estácio de Sá in Rio de Janeiro, and was part the "Pesquisa e Produtividade" university extension project.

REFERENCES

- Coura JR. Chagas disease: what is known and what is need – A background article. Mem Inst Oswaldo Cruz 2007; 102(1): 113-22.
- Rassi A Jr, Rassi A, Marin-Neto JA. Chagas disease. Lancet 2010; 375(9723): 1388-402.
- Coura JR. The main sceneries of Chagas disease transmission. The vectors, blood and oral transmissions – a comprehensive review. Mem Inst Oswaldo Cruz 2015; 110(3): 277-82.
- Moncayo A, Silveira AC. Current epidemiological trends for Chagas disease in Latin America and future challenges in epidemiology, surveillance and health policy. Mem Inst Oswaldo Cruz 2009; 104(1): 17-30.
- Dias JC, Silveira AC, Schofield CJ. The impact of Chagas disease control in Latin America – a review. Mem Inst Oswaldo Cruz 2002; 97(5): 603-12.
- Martins-Melo FR, Ramos Jr AN, Alencar CH, Heukelbach J. Prevalence of Chagas disease in Brazil: a systematic review and meta-analysis. Acta Trop 2014; 130: 167–74.
- Organização Pan-Americana da Saúde. Doença de Chagas – Guia para vigilância, prevenção, controle e manejo clínico da doença de Chagas aguda transmitida por alimentos. Série de Manuais Técnicos 12. Rio de Janeiro; 2009.

- Shikanai-Yasuda MA, Carvalho NB. Oral transmission of Chagas disease. Clin Infect Dis 2012; 54(6): 845-52.
- Magalhães-Santos IF. Transmissão oral da Doença de Chagas: breve revisão. Rev Ciênc Méd Biol 2014; 13(2): 226-35.
- Rueda K, Trujillo JE, Carranza JC, Vallejo GA. Transmisión oral de *Trypanosoma cruzi*: una nueva situación epidemiológica de la enfermedad de Chagas en Colombia y otros países suramericanos. Biomédica 2014; 34(4): 631-41.
- 11. Noya BA, Díaz-Bello Z, Colmenares C, Ruiz-Guevara R, Mauriello L, Muñoz-Calderón A, et al. Update on oral Chagas disease outbreaks in Venezuela: epidemiological, clinical and diagnostic approaches. Mem Inst Oswaldo Cruz 2015; 110(3): 377-86.
- Blanchet D, Brenière SF, Schijman AG, Bisio M, Simon S, Véron V, et al. First report of a family outbreak of Chagas disease in French Guiana and posttreatment follow-up. Infect Genet Evol 2014; 28: 245-50.
- Dias JC. Notas sobre o *Trypanosoma cruzi* e suas características bio-ecológicas, como agente de enfermidades transmitidas por alimentos. Rev Soc Bras Med Trop 2006; 39(4): 370-5.

- Jansen AM, Xavier SC, Roque AL. The multiple and complex and changeable scenarios of the *Trypanosoma* cruzi transmission cycle in the sylvatic environment. Acta Trop 2015; 151: 1-15.
- 15. Organización Panamericana de la Salud. Zoonosis y Enfermedades Transmisibles Comunes al Hombre y a los Animales. Parasitosis, volumen III. Publicación Científica y Técnica nº 580. Washington; 2003.
- Salazar-Schettino PM, Bucio MI, Cabrera M, Bautista J. First case of natural infection in pigs. Review of Trypanosoma cruzi reservoirs in Mexico. Mem Inst Oswaldo Cruz 1997; 92(4): 499-502.
- Montenegro VM, Jimenez M, Dias JC, Zeledon R. Chagas disease in dogs from endemic areas of Costa Rica. Mem Inst Oswaldo Cruz 2002; 97(4): 491-4.
- Sangenis LH, Saraiva RM, Georg I, Castro L, Santos Lima V, Roque AL, et al. Autochthonous transmission of Chagas disease in Rio de Janeiro State, Brazil: a clinical and eco-epidemiological study. BMC Infect Dis 2015; 15: 4.
- Lima MM, Sarquis O, Oliveira TG, Gomes TF, Coutinho C, Daflon-Teixeira NF, et al. Investigation of Chagas disease in four periurban areas in northeastern Brazil: epidemiologic survey in man, vectors, non-human hosts and reservoirs. Trans R Soc Trop Med Hyg 2012; 106(3): 143-9.
- Recine E, Radaelli P. Alimentação e cultura. Departamento de Nutrição, Universidade de Brasília. Secretaria de Políticas de Saúde: Ministério da Saúde. [acesso em 20 jul. 2015]. Disponível em: http://bvsms. saude.gov.br/bvs/publicacoes/alimentacao_cultura. pdf
- Ribeiro CS, Corção M. O consumo de carne no Brasil: entre valores sócios culturais e nutricionais. Demetra 2013; 8(3):415-38.
- Orellana-Halkyer N, Arriaza-Torres B. Enfermedad de Chagas en poblaciones prehistóricas del norte de Chile. Rev Chil Hist Nat 2010; 83(4): 531-41.
- Araújo A, Jansen AM, Reinhard K, Ferreira LF.
 Paleoparasitology of Chagas disease a review. Mem Inst Oswaldo Cruz 2009; 104(1): 9-16.
- 24. Basombrio MA, Segovia A, Peralta Ramos M, Esteban E, Stumpf R, Jurgensen P, et al. Endemic *Trypanosoma cruzi* infection in Indian populations of the Gran Chaco territory of South America: performance of diagnostic assays and epidemiological features. Ann Trop Med Parasitol 1999; 93(1): 41-8.

- Gurgel CB, Magdalena CV, Prioli LF. A Tripanossomíase Americana antes de Carlos Chagas. Cad Saúde Col 2009; 17(4): 827-39.
- Silva RJ, Garavello ME. Alterações nas estratégias de subsistência: o caso dos índios brasileiros xavantes.
 Segurança Alimentar e Nutricional 2009; 16(1): 32-48.
- 27. Gomes L. 1808 Como uma rainha louca, um príncipe medroso e uma corte corrupta enganaram Napoleão e mudaram a História de Portugal e do Brasil. São Paulo: Planeta do Brasil; 2007.
- 28. Yeo M, Acosta N, Llewellyn M, Sánchez H, Adamson S, Miles GA, et al. Origins of Chagas disease: *Didelphis* species are natural hosts of *Trypanosoma cruzi* I and armadillos hosts of *Trypanosoma cruzi* II, including hybrids. Int J Parasitol 2005; 35(2): 225-33.
- 29. Sampaio DT. A caça ilegal de animais silvestres na Mata Atlântica, Baixada Litorânea do estado do Rio de Janeiro, Brasil: eficiência de proteção de reservas biológicas e triangulação do perfil da caça. Tese [Doutorado em Ecologia e Recursos Naturais] – Centro de Biociências e Biotecnologia: Universidade Estadual do Norte Fluminense; 2011.
- Amato Neto V, Chieffi PP, Nisida IV, Umezawa ES, Sabino EC, Ruocco RM, et al. Prevenção referente às modalidades alternativas de transmissão do *Trypanosoma cruzi*. Rev Med 2000; 79(1): 12-26.
- Toso MA, Vial UF, Galanti N. Transmisión de la enfermedad de Chagas por vía oral. Rev Med Chil 2011; 139(2): 258-66.
- 32. Organización Panamericana de la Salud / Organización Mundial de la Salud Epidemiologia e transmissão oral da doença de Chagas na Amazônia Brasileira. In: Valente SA, Valente VC, Pinto AY. Informe de la consulta técnica en epidemiología, prevención y manejo de la transmisión de la enfermedad de Chagas como enfermedad transmitida por alimentos (ETA). Rio de Janeiro: OPS/OMS; 2006. p. 21-26.
- 33. Carvalho ME, Silva RA, Barata JM, Domingos MF, Ciaravolo RM, Zacharias F. Soroepidemiologia da tripanosomíase americana na região do litoral sul, São Paulo. Rev Saúde Pública 2003; 37(1): 49-58.
- 34. Forattini OP, Silva EO, Barata JM, Boainain E. Nota sobre caso autóctone de tripanossomíase americana no litoral sul do Estado de São Paulo, Brasil. Rev Saúde Pública 1980; 14(1): 143-9.

Received on: 11/18/2015 Final version presented on: 09/05/2016 Accepted on: 09/08/2016