

Review

Chagas' Disease as a Foodborne Illness

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MS 08-276: Received 12 June 2008/Accepted 3 October 2008

ABSTRACT

Various researchers have studied the importance of the oral transmission of Chagas' disease since the mid-20th century. Only in recent years, due to an outbreak that occurred in the Brazilian State of Santa Catarina in 2005 and to various outbreaks occurring during the last 3 years in the Brazilian Amazon basin, mainly associated with the consumption of Amazonian palm berry or açai (*Euterpe oleracea* Mart.) juice, has this transmission route aroused the attention of researchers. Nevertheless, reports published in the 1960s already indicated the possibility of Chagas' disease transmission via food in Brazil, mainly in the Amazonian region. Recently, in December 2007, an outbreak of Chagas' disease occurred in Caracas, Venezuela, related to ingestion of contaminated fruit juices. The objective of this article is to point out the importance of foodborne transmission in the etiology of Chagas' disease, on the basis of published research and Brazilian epidemiology data.

South American trypanosomiasis or Chagas' disease is an infectious disease whose etiological agent is the flagellate protozoan *Trypanosoma cruzi*. The researcher Carlos Chagas discovered it in 1908 in the village of Lassance, an inland town of the State of Minas Gerais, Brazil (30). The worldwide incidence of Chagas' disease is currently estimated at 200,000 cases per year. World Health Organization data indicate that between 5 and 6 million people are infected with the disease in Andean and Central American countries (45).

T. cruzi. The life cycle of the protozoan *T. cruzi* includes passage through two types of host. The intermediate host includes hematophagous hemipteran true bugs called triatomines, commonly known as *barbeiros* (barbers) in Brazil. The definitive host consists of mammals from various different classes, including humans. *T. cruzi* multiplies in the digestive tract of the insects, and the infectious form is eliminated in their feces. It generally circulates in the blood of the mammals and lodges in muscle and/or heart tissue (10).

The *T. cruzi* life cycle includes several stages: infective metacyclic trypomastigotes invade a definitive host (e.g., human) cell, lose their flagellum, and transform into amastigotes, which replicate by binary fission within the cytoplasm. The amastigotes will differentiate back into trypomastigotes and be released from the infected cell. These trypomastigotes can invade another cell and repeat the replicative process, or they may enter the circulatory system

and be taken up by a triatomine bug during feeding. Within the vector's midgut the parasite differentiates to an epimastigote and undergoes multiple rounds of binary fission. The epimastigotes stop dividing and differentiate back into metacyclic trypomastigotes in the hindgut (46).

Transmission. The transmission mechanisms of this disease in humans include transfusions, congenital factors, oral or buccogastric transmission, and principally, vector transmission. The last pathway occurs when infected bugs, mainly triatomines such as *Triatoma infestans*, which defecate on the skin, bite humans. When the individual scratches the location of the bite, the contaminated insect feces enter the blood stream.

Symptoms. Chagas' disease presents two distinct phases in humans. The first phase, called the acute or initial phase, is frequently asymptomatic or oligosymptomatic, mainly in adults, depending on the population affected. When present, the symptoms can include fever, edema, adenomegaly, hepatosplenomegaly, and myocarditis and/or meningoencephalitis. This phase is characterized by the presence of the protozoa in the patient's blood. The second or chronic phase is characterized by compromised heart and/or digestive systems of the patient, including cardiomyopathy, cardiac insufficiency, megaesophagus, megacolon, etc. In this phase the parasite cannot be directly detected in the host's blood. The existence of an indeterminate or latent phase in Chagas' disease is to be noted, in which no clinical symptoms of any importance can be discerned. The patient may remain in this condition for years, without reaching the chronic phase of the disease (10).

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Treatments. Treatment for Chagas' disease is indicated for the acute phase and recommended for chronic infection that was acquired less than 10 years previously. There are two drugs for treatment of the disease: benznidazole and nifurtimox. These drugs are moderately effective, achieving cure in 60% of cases in the acute phase, and can cause many adverse reactions in patients (e.g., hypersensitivity reactions, bone marrow depression, neuropathies, and agranulocytosis). Benznidazole is the most available and widely used drug but is not indicated for pregnant women (45).

EXPERIMENTALLY INDUCED ORAL TRANSMISSION OF CHAGAS' DISEASE

The role of the oral route in transmission of *T. cruzi* is not a recent idea. The importance of this infection pathway has long been known in the case of susceptible omnivorous or insectivorous animals, which feed on vector insects and infected animal reservoirs. Various episodes and studies have provided evidence for this fact (12, 38).

Some researchers have put forth the possibility that Carlos Chagas, in his first study carried out with Oswaldo Cruz, played an important role in the first case of oral transmission of Chagas' disease. Marmosets (*Callitrix penicillata*) were placed in cages together with insects infected by the parasite and also acquired the parasite. It is now known that transmission to these animals by insect bites is rare, and at the time of the experiment no entrance points were found on the animals; thus, the hypothesis of ingestion of the insects by the marmosets cannot be discarded (9, 12).

According to Coura (9), the experimental demonstration of the transmission of Chagas' disease via the oral route, using sanguineous protozoa, was first carried out by Nattan-Larrier in 1921. A series of experiments by Carlos Diaz Ungria et al. in Venezuela between 1960 and 1980 demonstrated the infection of dogs, hamsters, and other rodents via the oral route by *T. cruzi* (12). An experiment carried out by researchers in Goiás, Brazil, demonstrated the development of Chagas' disease in mice that fed on mouse blood infected with *T. cruzi* cells (41).

In Brazil, Ezequiel Dias, who observed armadillos feeding on the insect *Panstrongylus megistus* in his laboratory, made the first reference to this transmission mode. This researcher also confirmed the importance of the transmission of the protozoa to cats that fed on infected insects and mice (28). The infection of mice with Chagas' disease due to the ingestion of wild animal meat can also be verified (Storino and Jörg, 1994, cited by Coura (9)).

Jansen and Deane (17) noted the importance of the opossum (*Didelphis marsupialis*) as a reservoir and transmitter of *T. cruzi*: mice were infected when they fed on foods contaminated with excrement from this mammal.

Calvo-Méndez et al. (5) carried out an experiment aiming to prove infection by *T. cruzi* from the ingestion of contaminated foods. They showed that drinking water, pasteurized milk, raw and cooked minced beef, fresh cheese, and cooked rice, when inoculated with the feces of the insect *Triatoma pallidipennis* containing *T. cruzi*, were capable of infecting mice orally with Chagas' disease. There

was variation in efficiency with respect to infective capacity according to the food used, milk being shown to be the most effective medium for transmitting the protozoa. Brazilian scientists also demonstrated the infection of mice with Chagas' disease by ingestion of foods contaminated with *T. cruzi*: sugar cane juice (7, 8) and Amazonian palm berry juice (3, 13).

ORAL TRANSMISSION OF ACD IN HUMANS

The latest acute Chagas' disease (ACD) outbreak transmitted orally occurred in a municipal school in Chacao (metropolitan Caracas, Venezuela). One hundred twenty-eight positive cases were confirmed, with one death, and the most probable source of infection was prepared fruit juice. Visits to the household where the fresh fruit juice was prepared every day (which is located outside Chacao) revealed that there were many triatomine bugs in its surroundings. This is the largest outbreak of Chagas' disease transmitted orally (16, 29).

Routes. There are various ways of acquiring Chagas' disease orally, which include the ingestion of infected mother's milk; of raw or undercooked meat from infected animals; of foods contaminated with infected triatomines and/or their feces; of foods contaminated with anal gland secretions of marsupials; and of the triatomines themselves. Brener (4) even reported a case of Chagas' disease due to the ingestion of flagellates when pipetting an acellular culture medium containing the protozoa.

Mazza et al. (22) reported the first case of transmitting Chagas' disease to humans via the mother's milk, and various other authors subsequently provided experimental evidence for the presence of *T. cruzi* in the milk of animals infected by the parasite (14).

The ingestion of food contaminated with infected triatomines and/or feces (with *T. cruzi* in metacyclic forms) is considered to be the most important route involved in Brazilian foodborne outbreaks. However, the presence of metacyclic forms of *T. cruzi* in anal gland secretions of the opossum (*Didelphis marsupialis*), an animal with wild and peri-urban habits, cannot be overlooked as an element favoring the possibility of oral transmission (41). This could explain some outbreaks that occurred in Brazil (17, 37, 39).

Aufderheide et al. (1) studied 283 naturally (spontaneously) mummified bodies from coastal sites located in southern Peru and northern Chile and demonstrated a Chagas' disease prevalence rate of about 41% over the past 9,000 years. They considered that oral transmission might have occurred by ingestion of infected, uncooked meat, such as that of guinea pigs (*Cavia porcellus*). In Argentina it is known that one case of Chagas' disease occurred by ingestion of wild animal meat (12).

Symptoms. In the majority of cases, when transmitted orally, Chagas' disease manifests itself in the acute form. As mentioned earlier, ACD is characterized by the presence of large numbers of the protozoan in the patient's bloodstream. Due to its high mortality rate, especially in children under 2 years of age and in the elderly and immunocom-

promised populations, notification of the occurrence of this disease is compulsory in Brazil.

One of the main symptoms is a moderate, prolonged high temperature (7 to 30 days) that persists despite the administration of common temperature-reducing medication. The patient may show asthenia, loss of color, adenopathy, and local and generalized edemas. Hepato- and splenomegaly can also occur, as well as signs of acute myocarditis and in rare cases meningoencephalitis (31).

In foodborne ACD outbreaks that occurred in Brazil (Teutônia, Rio Grande do Sul, in 1965 and Catolé do Rocha, Paraíba, in 1986), the patients were incorrectly diagnosed first as having typhoid and subsequently as presenting cases of acute toxoplasmosis. Laboratory examinations failed to confirm either suspicion but instead indicated the presence of *T. cruzi* in the patients' blood (38).

The ACD symptoms are worse when the parasite itself is ingested due to its greater infectivity when ingested via the oral route and its ability to penetrate the mucous membrane. The causes of this increased infectivity are still unknown. It is known that the particular strain of the protozoan directly influences the clinical evolution of the patient (6). In an outbreak in the State of Santa Catarina, Brazil, the endoscopic examinations of the acute-phase patients showed ulcerated lesions in the intestinal mucous membrane when the parasite was present. Thus, when ingested, the protozoa are capable of penetrating the esophageal, gastric, and/or intestinal mucous membranes, causing local ulceration as well as invading the host organism (12).

BRAZIL'S EPIDEMIOLOGICAL DATA

In mid-March 2005, a large-scale outbreak of ACD was reported to be associated with the consumption of sugarcane juice from a kiosk on the Brazilian Motorway BR-101 in the municipality of Navegantes in the State of Santa Catarina. On this occasion 25 cases of the disease were confirmed, and 3 of them led to death (31).

Two main hypotheses were formulated to explain the contamination of the sugarcane juice by the protozoa. The first hypothesis involved the grinding of the sugarcane together with triatomine insects infected by the protozoa. The second hypothesis involved the contamination of the sugarcane by the feces of wild animals, such as the opossum, that are hosts of *T. cruzi*. The following findings corroborated these hypotheses: 10 infected vectors were found in a palm tree near the kiosk, and 30 infected vectors were found in the dense wild forestland behind it. One infected vector (*Triatoma tibiamaculata*) was found in the kiosk, and finally an infected female opossum was found with four infected babies (15).

On 31 March of the same year, a report from the Evandro Chagas Institute (Pará [PA], Brazil) confirmed the cause of an outbreak of an acute-fever-producing disease in Igarapé da Fortaleza in the city of Santana (Amapá, Brazil), which had occurred in December 2004, as being ACD. Twenty-seven cases of the disease were confirmed in this outbreak, and the common point between them was the consumption of açai juice from the same sales outlet (32).

Following these episodes, the oral transmission of Cha-

gas' disease started garnering more coverage in the media and in scientific publications. As examples, one can state the news divulged in the newspaper "Folha de São Paulo" with the title "Açaí infected 26 with Chagas' disease in AP" (26) and the article published in the *International Journal of Cardiology*, entitled "The oral transmission of Chagas' disease: an acute form of infection responsible for regional outbreaks" (2). In addition, scientific data involving food, which had been little divulged previously, came to the forefront, as well as much questioning concerning the exact mode of foodborne disease transmission and its prevention (12, 19, 20, 23).

Silva et al. (39) published the first scientific report of an orally transmitted outbreak of Chagas' disease in Brazil. This occurred in the district of Teutônia, municipality of Estrela (Rio Grande do Sul), in the year 1965, and it involved 17 people, of whom 6 died. The people all fell sick practically on the same day and presented the clinical symptoms of acute myocarditis. All of the cases attended the local Agricultural College (workers, students, or lecturers), and all ate there. A serological and entomological study was carried out. No triatomines were isolated on the grounds of the college, but an opossum (*Didelphis marsupialis*) infected by *T. cruzi* was found. Thus, the hypothesis raised for the occurrence of this ACD via oral outbreak was contamination of the food by excrement of an animal reservoir such as an opossum.

A second outbreak of ACD with food etiology was identified in Catolé do Rocha (Paraíba) in 1986. In this outbreak 26 people became sick, of whom 2 died, after taking part in festivities on the Aroeira farm (37). The meal had consisted of beef and lamb barbecue, a stew containing sheep entrails, cooked pork, salad, and sugarcane juice. Preliminary epidemiological studies indicated the possible contamination of the food and/or utensils by infected excrement from the mammal *Didelphis albiventris* (commonly known as the white-eared opossum, *saruê* or *mucura*), a common species in the area surrounding the farm and showing a high rate of infection.

Contamination of the sugarcane juice by triatomines and/or their feces seemed improbable, since the population density of these insects appeared to be low, as did their level of infection by parasites, requiring a large number of them to contaminate all the sugarcane juice consumed (21, 38). On the other hand, preliminary studies of the survival of *T. cruzi* in sugarcane juice corroborated the possibility of this having been the transmitting vehicle in this case of ACD in Paraíba (25, 40).

In the 1960s, the researchers Shaw, Lainson, and Fraiha (36) raised the possibility of the foodborne transmission of Chagas' disease in Belém do Pará, PA, Brazil. Four people from a single family were involved, and three of them were in the acute phase of the disease when diagnosed. Since then there have been many reports and records of oral infection with Chagas' disease in the Brazilian Amazon basin.

Between 1982 and 2001, 28 family microepidemics of Chagas' disease possibly associated with oral transmission were reported in the Brazilian Amazon basin, involving a

total of 149 people. In one of these microepidemics, in Mazagão (Amapá), the transmission mechanism was traced to ingestion of açai juice infected with the feces of wild triatomines. Açai juice was prepared at night, and the insects attracted to the electric lights fell into the juice being prepared in the machine and were ground up with the fruit pulp (42, 43).

Pinto et al. (24) reported the occurrence of a family microepidemic of acute trypanosomiasis probably transmitted orally, involving 12 people, of whom 2 died, in the municipality of Igarapé-Miri (PA) in July 2002. In 2004, an additional family microepidemic of ACD occurred in the city of Belém (PA), involving three people, and the contamination was suspected to have been via the oral route (44).

In 2006, 94 cases of ACD were reported in northern and northeastern Brazilian states, transmitted orally, with 6 cases leading to death, and all were associated with the consumption of açai or sugarcane juices (34). In the district of Mojuí dos Campos in the municipality of Santarém (PA), 17 cases of ACD were confirmed, with one death, infection probably being caused by the ingestion of bacaba (*Oenocarpus bacaba*) or white açai juice (33).

In 2007, 25 cases of ACD were confirmed in Coari (Amazonas), related to the consumption of açai juice from a single establishment in the city (35). In all, 88 cases of ACD were reported in the Amazon region from January to October 2007, with four deaths. Of these, 79 cases were transmitted orally, and the food most frequently involved was açai palm juice (34). Up to June 2008, 10 cases of ACD were reported in the state of PA (18).

There are two main pathways for contamination of açai by infected insects. In the first, the insects are attracted by the light on the inside of the machine used to grind the açai and are thus ground together with the fruit. In the second pathway, the contamination of açai pulp is due to a lack of hygiene in the harvesting, transport, and/or processing of the fruits. The *T. cruzi*-infected insects are transported to the processing machine together with the fruits, in baskets or sacks (43).

Figure 1 presents a map of Brazil highlighting the regions involved in the episodes of oral transmission of ACD presented in this review. It also highlights the Brazilian Amazonian region, the region registering the majority of the orally transmitted ACD cases, with epidemiological studies indicating the ingestion of contaminated açai juice as the cause.

The occurrence of ACD outbreaks associated mainly with the consumption of açai juice has generated considerable confusion in the media and has resulted in sensationalist coverage, with the presentation of few concrete, scientific data, as exemplified by one report in a newspaper with the title of "Açai claims 1 victim of Chagas' disease every 4 days in the Amazon region" (27).

FINAL CONSIDERATIONS

There is no doubt that in countries where it is endemic, Chagas' disease should now be considered to be a food-borne disease. A particular risk factor for oral transmission

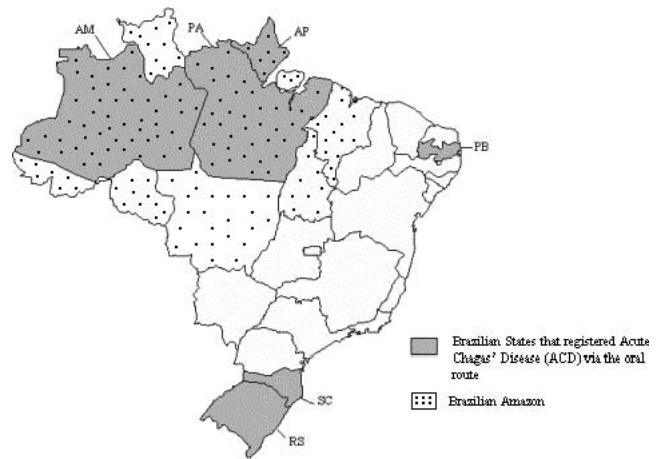


FIGURE 1. Map of Brazil highlighting the states involved in episodes of ACD transmitted via oral route: Amapá (AP), Amazonas (AM), Pará (PA), Paraíba (PB), Rio Grande do Sul (RS), and Santa Catarina (SC).

in the Brazilian Amazon has been identified as açai juice presses illuminated at night and open to contamination by light-attracted infected triatomine bugs (11).

However, there are many potential sources of food contamination, and not only açai juice must be considered as a high-risk food. Other high-risk foods can be raw meat from infected wild mammals carrying pseudocysts and blood form trypomastigotes and any *in natura* fruit juices prepared under unsanitary food-handling practices. The contamination of juices by *T. cruzi* can occur mainly when whole triatomine bugs or triatomine feces (containing highly infective metacyclic trypomastigotes) and/or anal gland secretions of infected opossums (*D. marsupialis*) (which are occasionally known to harbor metacyclic forms more typically seen in the insect vector) contaminate fruits under inadequate harvest, transport, storage, and manufacturing conditions.

Thus, efforts should be concentrated on preventing the contamination of these high-risk foods (e.g., vegetable beverages) by implementing standardized operational procedures, integrated pest management, good manufacturing practices, and eventually hazard analysis and critical control points. In addition there is a need to develop a methodology to detect *T. cruzi* directly in the foods and also the implementation of technology to ensure the safety of food contaminated by the protozoa (e.g., pasteurization of fruit pulps and juices).

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