The Sugarcane Juice was Delicious, but...

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"The sugarcane juice was delicious, but the hangover, which only manifested itself fifteen days later, nearly killed me". This same thought must have crossed the mind of the 25 people (five of whom died) orally infected with *Trypanosoma cruzi* in Navegantes, Santa Catarina, early this year. Not long thereafter, 26 people were infected after drinking parasite-contaminated açaí juice in Igarapé da Fortaleza, Amapá state. Thus, in the first quarter of 2005 alone, 51 people developed acute Chagas disease (American trypanosomiasis). These events, which exposed an often neglected means of transmission, made the headlines in all major Brazilian newspapers and TV newscasts.

In the case of the Navegantes episode, public health agents found ten infected vectors in a palm tree located next to the kiosk where the sugarcane juice was sold, one infected vector inside the kiosk, and 33 vectors – only three of which were not infected – in the dense vegetation behind the kiosk. Nearby the agents also found a female opossum and four baby opossums, all infected.

The central and southern regions of Brazil have already been certified by the Pan American Health Organization as having vectorial transmission of *Trypanosoma cruzi* under control. However, the parasite has now reappeared and is causing acute cases of Chagas disease – now by means of oral contamination.

Microepidemics featuring high infectivity rates and some deaths were registered (Teutonia, RS; [1,2] Catolé do Rocha, PB; [3] Amazônia brasileira),[4-7] but the possibility of oral transmission is a long recognized fact. In 1921, trypomastigote bloodstream forms inoculated orally in animal models led to the development of the disease.[8] In 1933, metacyclic forms of the parasite found in feces of insect vectors inoculated orally in animal models also caused the disease.[9] Transmission among wild animals (predators and their infected preys)[10] was demonstrated in 1940. And in 1991, 26 acute cases caused by infected sugarcane juice were reported in Catolé do Rocha in the state of Paraíba following a family reunion at a farm in the region. [3] Since 1987 it is known that *Trypanosoma cruzi* can remain infectious for 24 hours in sugarcane juice[11].

One of the possibilities raised at that time was that some insects could have been ground in the course of the cane grinding process. Another hypothesis, an intriguing one, is that the sugarcane had been contaminated by secretions of wild animals, among them opossums.

A very interesting article was published in 1984 showing that in the same animal, opossum *Didelphis marsupialis*,[12] there are both a vertebrate and an invertebrate cycle. The authors found epimastigotes multiplying extracellularly and also metacyclic trypomastigotes - stages that correspond to the *Trypanosoma cruzi* life cycle in the intestinal lumen of the vector insect - in the lumen of the anal glands of this wild animal, inoculated subcutaneously with infected feces of triatomids. The presence of these forms of *Trypanosoma cruzi* in the lumen of the anal glands of the opossum requires a high degree of adaptation to the environment, yet may act as a reservoir from which the parasite can spread to other tissues through the bloodstream. It is also an effective protection against the immune response of the host that, in the opossum, is as effective as in other vertebrate hosts, including humans. In the vertebrate host, *Trypanosoma cruzi* multiplies intracellularly as amastigote, but in the insect, it multiplies extracellularly in the lumen of the digestive tract as epimastigote. The parasite does not replicate as trypomastigote, form that develops at the final phase of the vertebrate cycle and is used to invade new cells or remain in the bloodstream, infecting invertebrates. Also in the insect, the metacyclic trypomastigote form is the end product of the replication cycle, being the infectious form to the mammalian host.

Due to mammal's high body temperature, the mammalian environment is usually adverse to the replicating forms in insects. Epimastigotes are readily lysed or phagocytized and digested. But this does not occur with metaclycic trypomastigotes. The reason may be that the body temperature of opossums is lower than that of most similar mammals.

In Amazônia, the first three cases were registered in 1966, also associated with oral contamination. Up to 2001, 148 cases had been reported in the Brazilian Amazonia, 121 of which were acute infections, with five deaths. In Pará state alone, 71 cases were reported, including seventeen familial microepidemics, especially

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Received on 05/03/05 • Accepted on 05/04/05

through the ingestion of parasite-contaminated açaí juice. Açaí palm (*Euterpe oleracea*), together with bacaba palm (*Oenocarpus bacaba*) - the juice of which is also drunk in that region - and babaçu palm (*Orbignia martiana*) are known to harbor triatomids in northern Brazil. Curiously enough, in the thirteen acute cases reported in Abaetetuba (Pará), nearly half had normal electrocardiogram, a characteristic observed in field studies in other Brazilian regions.

Studies performed with rats and mice inoculated orally with *Trypanosoma cruzi*, obtained from blood of infected mice or infected feces from triatomid bugs, showed that the infection was more severe when secondary to oral inoculation of infected feces from triatomids, demonstrating that infection with metacyclic trypomastigotes is higher than with the bloodstream form.[14]

These forms have also been isolated from the urine of vectors fed repeatedly on highly-parasitemic mice.[15]

Another intriguing point is how effectively the gastric juice can act as a barrier. *Trypanosoma cruzi* can invade and replicate in the murine gastric mucosal epithelium, and some researchers believe this might aid in the development of a vaccine. [16]

It was also experimentally observed that circulating trypomastigotes cannot efficiently initiate infection from the mucous membrane, even with high inocula, unless in the presence of mucous membrane defects or periodontal disease; on the other hand, lower inocula metacyclic trypomastigote administered orally are highly infectious.[17]

Another interesting experiment was conducted on mice infected by gavage, as compared to intraperitoneal inoculation with Colombian and Peruvian strains of *Trypanosoma cruzi*. [18]

The Colombian strain showed similar high infectivity level by both routes, whereas the Peruvian strain showed high infectivity level by peritoneal route and low infectivity level when administered by gavage. In human beings, the effect of the strain during oral transmission has not yet been proven, but it is likely to be relevant as well. In the Icoaraci (Pará) and Catolé do Rocha (Parabaíba) episodes, strains found in the sylvatic cycle were isolated. The fact that these microepidemics occur near sylvatic ecotopes only corroborates the relationship with the parasite strain.

The presence of parasites in the gastric and esophageal mucosa is not always detected in these experimental studies;[16] in some of them, such as in the study mentioned above, there is only an inflammatory infiltrate.

Another concern regarding oral transmission is the consumption of raw or undercooked game meat by some populations in the rural areas of Brazil, especially by indigenous peoples.[19]

To this day we are still dealing with the same disease that our eminent fellow brazilian physician Dr. Carlos Chagas described so clearly a hundred years ago. And we, a century later, are still incapable of halting its transmission by means that depend merely on practicing basic principles of food preparation hygiene. What would Carlos Chagas think of us, already in the 21st century and still dealing with this same problem? Maybe now that *Trypanosoma cruzi* has moved from the brazilian hinterland to the beautiful white sand beaches frequented by Brazilians in the higher income brackets, Chagas disease will gain visibility and the population as a whole will demand its definitive control, as has been the case with other infectious diseases more regularly featured in the media. It must be kept in mind that measures as simple as the use of insecticides virtually eliminate the possibility of new infections in risk areas. The subject definitely provides food for thought.

References

1. Nery-Guimarães F, Silva NN, Clausell DT et al. Um surto epidêmico de doença de Chagas de provável transmissão digestiva, ocorrida em Teutônia (Estrela-Rio Grande do Sul). Hospital (Rio de Janeiro) 1968; 73: 1767-804.
2. Neves da Silva N, Clausell DT, Nólibos H et al. Surto epidêmico de doença de Chagas com provável contaminação oral. Rev Inst Med Trop São Paulo 1968; 10: 265-76.
3. Shikanai-Yasuda MA, Marcondes CB, Guedes LA et al. Possible oral transmission of acute Chagas' disease in Brazil. Rev Inst Med Trop São Paulo 1991; 33: 351-7.
4. Crescente JA, Valente SAS, Valente VC et al. Ocorrência de 4 casos agudos de doença de Chagas na vila de Icoaraci-PA. Rev Soc Bras Med Trop 1992; 25(supl. I): 29.
5. Valente SAS, Valente VC, Fraiha Neto H. Transmissão da doença de Chagas: como estamos? Considerações sobre a epidemiologia e transmissão da doença de Chagas na Amazônia Brasileira. Rev Soc Bras Med Trop 1999; 25(supl .2): 51-5.
6. Valente VC, Valente SAS, Pinto AYN. Perfil parasitológico e sorológico em microepidemia familiar de doença de Chagas em Abaetetuba, Estado do Pará. Rev Soc Bras Med Trop 2001a; 34: 20-1.
7. Valente SAS, Pimentel, OS, Valente VC et al. Microepidemia familiar de doença de Chagas em Santarém. Primeiro registro no oeste do Pará. Rev Soc Bras Med Trop 2001;34(supl I):19-20.
8. Nattan-Larrier L. Infections à Trypanosomes et voies de penetration des virus, Bull Soc Path Exot 1921; 14: 537-42.
9. Kofoid CA, Donat E. Experimental infection with *Trypanosoma cruzi* from the intestine of cone-nose bug *Triatoma protracta*. Proc Soc Exp Biol Med (NY) 1933; 30: 489-91.
10. Dias E. Serviço de estudos de grandes endemias. Transmissão do *" Schizotrypanum cruzi"* entre vertebrados, por via digestiva. Brasil Med 1940; 54: 775.
11. Soares VA, Dias JCP, Marsden PD, et al. Sobrevivência do *T cruzi* em caldo de cana: resultados preliminares. Rev Soc Bras Med Trop 1987; 20(supl 2): 38.
12. Deane MP, Lenzi HL, Jansen A. *Trypanosoma cruzi:* vertebrate and invertebrate cycles in the same mammal host, the opossum *Didelphis marsupialis*. Mem Inst Oswaldo Cruz, Rio de Janeiro 1984; 79: 513-5.
13. Pinto AYN, Harada GS, Valente VC et al. Acometimento cardíaco em pacientes com doença de Chagas aguda em microepidemia familiar,

em Abaetetuba, na Amazônia Brasileira. Rev Soc Bras Med Trop 2001; 34: 413-9.

14. Calvo Mendez ML, Nogueda Torres B, Alejandre Aguilar R. The oral route: an access port for *Trypanosoma cruzi*. Rev Latinoam Microbiol 1992; 34: 39-42.
15. Kirchhoff LV, Hoft DF. Immunization and challenge of mice with insect-derived metacyclic trypomastigotes of *Trypanosoma cruzi*. Parasite Immunol 1990; 12; 65-74.
16. Hoft DF, Farrar PL, Kratz-Owens K et al. Gastric invasion by *Trypanosoma cruzi* and induction of protective mucosal immune responses. Infect Immun 1996; 64: 3800-10
17. Hoft DF. Differential mucosal infectivity of different life stages of *Trypanosoma cruzi* . Am J Trop Med Hyg 1996; 55: 360-4.
18. Camandaroba EL, Pinheiro Lima CM, Andrade S. Oral transmission of Chagas' disease: importance of *Trypanosoma cruzi* biodeme in the intragastric experimental infection. Rev Inst Med Trop São Paulo 2002; 44: 97-103.
19. Prata A. Clinical and epidemiological aspects of Chagas' disease. Lancet Infect Dis 2001; 1: 92-100.