Forum: geographic spread and urbanization of visceral leishmaniasis in Brazil. Postscript: new challenges in the epidemiology of *Leishmania chagasi* infection

Fórum: expansão geográfica e urbanização da leishmaniose visceral no Brasil. Posfácio: novos desafios na epidemiologia da infecção por *Leishmania chagasi*

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Visceral leishmaniasis is a disease that reemerged in various locations in Brazil in the 1980s and spread to new areas, including the Southeast and Central-West of the country. Previously, visceral leishmaniasis was a disease that occurred in rural areas of the Northeast, mainly affecting children [1]. However, most cases of visceral leishmaniasis now come from periurban areas of cities in Northeast, Central-West, and Southeast Brazil [2,3,4].

The articles in this Forum [5,6,7,8] discuss key aspects related to the urbanization of visceral leishmaniasis in Brazil, including new approaches to deal with the disease and conditioning factors for the vector's capacity to transmit *Leishmania*. The complexity of vector and reservoir control is identified as a factor that hinders the management of visceral leishmaniasis in the country. The Forum proposes a new discussion and reassessment of current intervention measures. The latter focus on culling dogs infected with *Leishmania* and residual-action pesticide spraying, but these measures are normally implemented after human cases of visceral leishmaniasis have already been identified, often long after the occurrence of *Leishmania* infection, due mainly to its long incubation period [9,10]. Still, as commented in the article by Maia-Elkhoury et al. [5], the regularity of these intervention measures can have an impact with a reduction of up to 39% in *Leishmania* infection in humans, according to studies by the Brazilian Ministry of Health.

The peri-urbanization of visceral leishmaniasis in Belo Horizonte, presented by Oliveira et al. [6] as an example of this process in Brazil, was similar to that observed in the Northeast, with subsequent spread to other cities in the Southeast and Central-West. It is worrisome that these endemic areas have a high population density, thus placing the population at increased risk of infection.

Dogs have traditionally been considered the principal reservoirs of *Leishmania chagasi* in periurban areas [11]. Canine visceral leishmaniasis generally precedes human disease in these new areas [4]. This was demonstrated in the visceral leishmaniasis epidemic in Araçatuba, São Paulo State [12,13]. Studies in the State of Rio Grande do Norte show a 32.6% *Leishmania* infection rate in dogs in an endemic area on the outskirts of the State capital Natal, with a 30% six-month seroconversion rate in these animals. Asymptomatic *Leishmania* infection in humans is also high, with 24.6% of individuals presenting anti-*Leishmania* antibodies and 38.6% of these showing a positive delayed hypersensitivity skin test to *Leishmania* antigens [14].

The high asymptomatic *Leishmania* infection rate in humans, as observed in Rio Grande do Norte, shows that visceral leishmaniasis is only the lesser component in the process, and that asymptomatic infection is more frequent. The role of asymptomatic *Leishmania* infection in humans and canines has still not been fully

elucidated within the *Leishmania* transmission chain, and further studies are needed to better document and evaluate the impact of silent infection in maintaining the endemicity. This fact is a cause for concern, especially considering the endemization of visceral leishmaniasis in major peri-metropolitan areas of Brazil. Thus, studies are also needed to assess the role of asymptomatic *Leishmania* infection on blood and organ donations, since these procedures are currently widespread in cities that are endemic for visceral leishmaniasis and that present a high asymptomatic *Leishmania* infection rate. The development of post-transplantation visceral leishmaniasis has been documented in Europe, although the numbers are not high [15]. The magnitude of asymptomatic *Leishmania* infection in Brazil may also result in a change in the epidemiological profile of visceral leishmaniasis. Given the panorama presented here, one can predict that more cases of visceral leishmaniasis associated with immune suppression will occur, involving greater severity and more complex treatment management, as observed in Europe [16,17,18].

The control of dogs infected with *Leishmania* is difficult, as discussed in the article by Oliveira et al. [6]. When dogs are culled, they are promptly replaced with others, and the act of culling is controversial and not always readily accepted by the population [19]. It has been demonstrated in various places around the world [20] that cypermethrin-impregnated dog collars are effective repellants against the visceral leishmaniasis vector, but the strategy is costly given that only a small portion of the population can afford this control method.

Lutzomyia longipalpis is the principal vector for *L. chagasi* in Brazil and elsewhere in Latin America [21]. Rangel et al. [7] reviewed the conditioning factors for the vectorial competence of *Lu. longipalpis* in transmitting *L. chagasi* in Brazil and its adaptation to periurban areas. This vector has highly eclectic eating habits and adapts easily to peridomiciliary conditions [22,23]. *Lu. longipalpis* is most active from 7:00 to 11:00 PM [22], when most residents are normally inside or around their homes. These observations back the hypothesis that infections normally occur indoors or in the peridomicile. Meanwhile, we demonstrate that *Leishmania* infection in humans is found in all age brackets and equally in both sexes, although men develop visceral leishmaniasis more frequently than women [24], thus reinforcing the hypothesis that *Leishmania* infection occurs in the domestic environment.

The adaptation of *Leishmania* vectors to periurban areas and their spread to new areas in Latin America expand the endemic leishmaniasis regions, with increased risk of infection. *Leishmania* infection is now found in northern Argentina and Paraguay [25,26]. Visceral leishmaniasis control measures in other countries have also been associated with vector control. The use of residual DDT in India to control malaria vectors resulted in a significant decrease in cases of visceral leishmaniasis [27,28], indicating that effective vector control can be achieved. However, it is necessary to develop new insecticides and control the spraying areas with monitoring and evaluation of their efficacy, as discussed in the article by Costa [8].

Visceral leishmaniasis control also involves community education in risk areas, teaching measures to avoid producing areas that favor the development of phlebotomine sand files in backyards and in the vicinity of homes. The identification of spatial clusters of human and canine visceral leishmaniasis in Teresina, Piauí, led to the identification of focal areas at risk of *Leishmania* infection, thereby facilitating the definition of areas to undergo specific interventions [29,30]. However, the decentralization of epidemiological surveillance and visceral leishmaniasis control activities to the municipalities could be an additional complicating factor, due to deficiencies in infrastructure at the local level for dealing with the problem's complexity. On-going joint work between the Ministry of Health and the Brazilian scientific community can assist in the understanding and development of new strategies to deal with visceral leishmaniasis, including educational measures, especially considering that no anti-*Leishmania* vaccine will be available in the short term.

Contributors

All the authors contributed equally to the article.

Acknowledgements

The authors wish to thank Prof. Dulce Almeida (Department of Microbiology and Parasitology, Federal University in Rio Grande do Norte), for reviewing the manuscript.

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Submitted on 06/Mar/2008
Final version resubmitted on 12/Jun/2008
Approved on 16/Jun/2008