CANINE LEISHMANIASIS: CURRENT SITUATION IN BRAZIL

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Epidemiological situation

The term leishmaniosis refers to infectious non-contagious diseases with clinical cutaneous or visceral signs, caused by trypanosomes protozoa of the genus *Leishmania* sp., that parasitise mammals' mononuclear phagocytic system cells.\(^1,2\)

The main *Leishmania* species in relation to the number of human cases in Brazil are *Leishmania* (Viannia) *braziliensis* and *Leishmania* (Viannia) *amazonensis*, etiologic agents of the American tegumentary leishmaniasis (ATL), and *Leishmania* (Leishmania) *infantum* chagasi that causes Visceral Leishmaniasis (VL).\(^2,3\)

In Brazil, dogs (*Canis familiaris*) have already been naturally infected by different species of *Leishmania*, such as *Leishmania* (Viannia) *braziliensis*\(^4\), *Leishmania* (L.) *chagasi infantum* and *Leishmania* (L.) *amazonensis*\(^5\).

Although it is considered the main domestic reservoir for VL from the epidemiological point of view, the role of the dog as a domestic reservoir for TL is controversial\(^7,8\), being considered an accidental host for the disease, according to the Ministry of Health, and with not recommendations for their control when infected\(^9\).

For a long time, VL was restricted in the North and North-East regions of Brazil and was considered a disease of rural areas.\(^1,2,9\)

In the 90s, the disease was urbanized and spread to other regions, catching special attention of the veterinarians and public health professionals due to its zoonotic nature, a significant increase in the number of human and canine cases and a high rate of human mortality\(^6,9\) (currently 7.8%).

Numerous aspects can explain this expansion and urbanization, and we can highlight the continuous migration of people to urban areas (due to economic, demographic, cultural and political reasons); inadequate hygiene and sanitation conditions; lack of awareness of the disease by health professionals; discontinuity of control measures; the presence of immunosuppressive diseases such as Acquired Immunodeficiency Syndrome - AIDS (currently 7.4% of co-infection rate); and the adaptation of the vector to these areas.\(^2,6,8,9,10\)

Figure 1 - Epidemiological situation in Brazil, SVS, 2015.
Since then, the transmission of the disease is being described in several municipalities, throughout the year, in the five regions of the country, in 22 federal units, and according to the epidemiological data from the Ministry of Health reported in 2015, with 54.9% of the cases concentrated at the north-east region; 20.1% in the south-east region; 16.7% in the northern region; 8.1% in the Midwest region and 0.2% in the southern region. Annual average of 3289 new human cases for VL. However, data are not updated frequently as it is not a notifiable disease in endemic areas and therefore the actual prevalence could be greater than the reported prevalence 11.

*Lutzomyia longipalpis* is the main vector involved in the dissemination and transmission of the VL. Recently, *Lutzomyia cruzi* was incriminated as vector in the State of Mato Grosso do Sul 8,9,10.

For TL, the main transmitters are phlebotomine from the *Nyssomyia intermedia* complex (*N. intermedia* in the coast and *N. neivai* in interior areas), associated with *N. whitmani* and *Migonemyia migonei* as potential secondary vector species 12.

**VL Control program proposed by the Ministry of Health**

The main strategies of the control program of leishmaniasis are the free diagnosis and the treatment of human patients with leishmanicidal drugs, with antimonates, amphotericin B and liposomal amphotericin B standing out; the vector control, mainly in areas of human and canine transmission, via the application of insecticides in shelters and kennels; health education, and in the case of VL, control of the canine reservoir with the euthanasia of seropositive and / or positive dogs to direct parasitological tests 3,9,10. Although it has been working for a long time, the Brazilian program is ineffective, since the number of disease cases is increasing in the various regions where there is parasite transmission, in addition to the already described territorial expansion 13.

Some authors describe that failures in effectiveness can be attributed to the often isolated actions; the long period between diagnosis and treatment or disposal of the reservoir dogs; low sensitivity of serological tests; partial access to the infected dog population; owner opposition to the elimination of the animal; high rate of replacement of the animals by their owners due to bonding factors 14; and the existence of other reservoirs 6,10,13,14.

The euthanasia of the dogs has proved to be an ineffective and expensive approach 13. Diagnosis in the private network is performed by clinicians via serology, ELISA and indirect immunofluorescence (IFA); rapid immunochromatographic tests; parasitological methods with aspiration cytology of lymph nodes and / or bone marrow; and molecular methods (by conventional polymerase chain reaction and / or real time) from skin, bone marrow and lymph nodes.

On the public network, a seroepidemiological survey is carried out annually in endemic regions. In 2011, the Surveillance and Control Program of the Visceral Leishmaniasis, in order to improve the speed, accuracy, and logistics of the diagnosis, recommended changing the Diagnostic Protocol, using the Dual Path Platform (DPP®) instead of the RIFI as screening test and using ELISA as confirmatory test 15. DPP® is a rapid test that uses recombinant antigen rk28. The presence of antibodies is indicative of infection and not cross reactivity with antigens of co-infections are reported 16.

**Individual and collective control measures**

For many years, the treatment of VL was banned in Brazil through an inter-ministerial ordinance thought to avoid the possibility of interference with the humane treatment and parasite resistance 1.

In 2016, Miltefosine was launched in the veterinary market with the exclusive indication for canine treatment Studies showed a clinical improvement in 94.2% of the treated animals; reduction of the parasite load through lymph node, bone marrow, and skin real-time PCR; and 50% reduction in the infectivity to the phlebotomines.

Currently, the protocol advocated by the practitioners consists in the use of the association of allopurinol with miltefosine, clinicopathological revaluations and miltefosine reinforcements every 4 to 6 months 17. As a measure for the protection dogs, the use of numerous repellents and insecticides is an option. 4% deltamethrin-impregnated dog collars, propoxur, flumethrin and imidacloprid, are products for individual protection and can also aid in the collective control, demonstrated in many already published studies 18.

Currently, municipal policies have adopted the use of 4% deltamethrin collars that are systematically distributed free of charge and to the population.
The use of repellent or insecticide collars or spot-on formulations as a way of treatment of the animal is a condition required to avoid the chances of reinfection and an aid in the control of the disease. Vaccination of the animals is not a measure of public health and is not recommended by the Ministry of health, but it is used individually by veterinary practitioners. The commercially available presents a recombinant A2 saponin-associated protein.

To start the vaccination protocol, the animal must be 4 months old and serologically or parasitologically negative. The primary course of vaccination consists of 3 doses, with an interval of 21 days between applications, and annual boosters.

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