

CHALLENGING NEGLECT OF TEGUMENTARY LEISHMANIASIS: HEALTH PROMOTION IN AN ENDEMIC AREA IN SOUTHERN BRAZIL

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ABSTRACT: This study aimed to verify the epidemiological profile of tegumentary leishmaniasis (TL) in an endemic area in Southern Brazil and to develop health education activities with the local population to prevent new cases. This was a prospective study conducted with residents of the Borba Gato district, Maringá-Paraná, from March 2018 to June 2023. A questionnaire was applied to the participants to investigate the previous knowledge about TL and exposure to risk factors. Laboratory tests were performed to actively search for new cases of TL in the neighborhood. A total of 61 patients underwent indirect immunofluorescence (IFI) examination. Eight of them had a history of the disease, of which three continued to have positive titers on the test (IFI > 40) even after years of treatment completion. A new case of the disease was confirmed during the development of the study and progressed to clinical cure following administration of meglumine antimoniate 20mg/kg/day. Distribution of educational leaflets and lecture cycles with the population and health professionals of the neighborhood were developed to elucidate them regarding the form of transmission and preventive measures against TL. Health surveillance actions are necessary to control TL in endemic areas and promote human and animal health.

KEYWORDS: Leishmaniasis; Epidemiological Monitoring; Primary Prevention; Health Promotion; Health Education.

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DESAFIANDO A NEGLIGÊNCIA DA LEISHMANIOSE TEGUMENTAR: PROMOÇÃO DA SAÚDE EM UMA ÁREA ENDÊMICA NO SUL DO BRASIL

RESUMO: Este estudo objetivou verificar o perfil epidemiológico da leishmaniose tegumentar (LT) em área endêmica no sul do Brasil e desenvolver atividades de educação em saúde com a população local para prevenir novos casos. Foi realizado um estudo prospectivo com moradores do bairro Borba Gato, Maringá-PR, de março de 2018 até junho de 2023. Um questionário foi aplicado aos participantes para investigar o conhecimento prévio sobre a LT e exposição aos fatores de risco. Foram realizados exames laboratoriais para buscar ativamente novos casos de LT no bairro. Um total de 61 pacientes foram submetidos ao exame de imunofluorescência indireta (IFI). Oito deles tinham histórico da doença, dos quais três continuaram com títulos positivos no teste (IFI >40) mesmo após anos de conclusão do tratamento. Um novo caso de LT foi confirmado durante o desenvolvimento do estudo e progrediu para cura clínica após administração de antimoniato de meglumina 20mg/kg/dia. Foram distribuídos panfletos educativos e realizados ciclos de palestras com a população e profissionais de saúde do bairro para esclarecê-los sobre a forma de transmissão e medidas preventivas contra a LT. Ações de vigilância em saúde são necessárias para controlar a LT em áreas endêmicas e promover a saúde humana e animal.

PALAVRAS-CHAVE: Leishmaniose; Monitoramento Epidemiológico; Prevenção Primária; Promoção da Saúde; Educação em Saúde.

DESAFIANDO LA DESATENCIÓN DE LA LEISHMANIASIS TEGUMENTARIA: PROMOCIÓN DE LA SALUD EN UNA ZONA ENDÉMICA DEL SUR DE BRASIL

RESUMEN: Este estudio tuvo como objetivo verificar el perfil epidemiológico de la leishmaniasis tegumentaria (LT) en un área endémica del sur de Brasil y desarrollar actividades de educación sanitaria con la población local para prevenir nuevos casos. Se realizó un estudio prospectivo con residentes del barrio Borba Gato, Maringá-PR, desde marzo de 2018 hasta junio de 2023. Se administró un cuestionario a los participantes para investigar el conocimiento previo sobre LT y la exposición a factores de riesgo. Se realizaron pruebas de laboratorio para buscar activamente nuevos casos de LT en el barrio. Un total de 61 pacientes se sometieron a una prueba de inmunofluorescencia indirecta (IFI). Ocho de ellos tenían antecedentes de la enfermedad, de los cuales tres siguieron presentando títulos positivos en la prueba (IFI > 40) incluso años después de finalizar el tratamiento. En el transcurso del estudio se confirmó un nuevo caso de LT, que evolucionó hacia la curación clínica tras la administración de antimoniato de meglumina 20mg/kg/día. Se distribuyeron folletos educativos y se impartieron charlas a la población y a los profesionales sanitarios del barrio para informarles sobre la forma de transmisión y las medidas preventivas frente al LT. Las acciones de vigilancia sanitaria son necesarias para controlar la LT en zonas endémicas y promover la salud humana y animal.

PALABRAS CLAVE: Leishmaniasis; Monitoreo Epidemiológico; Prevención Primaria; Promoción de la Salud; Educación en Salud.



1. INTRODUCTION

Leishmaniasis represents a public health challenge due to the variety of parasites, reservoirs, and vectors involved in its transmission, presenting worldwide distribution and high endemicity in developing countries (aPAHO, 2023). Globally, leishmaniasis ranks among the ten most important neglected tropical diseases, with approximately 350 million people at risk of infection and more than 12 million people infected (aPAHO, 2023; bPAHO, 2023). In South America, Brazil is responsible for the highest incidence rates of tegumentary leishmaniasis (TL) (PAHO, 2022).

TL is transmitted by the inoculation of protozoa of the genus *Leishmania* into the host's skin during the blood meal of infected female sandflies (bPAHO, 2023). TL was initially considered wild animal zoonosis, which occasionally affected people in contact with forests. In recent decades, changes in the pattern of transmission of the disease have been observed, and cases of TL in rural areas and periurban regions have been reported (BRAZIL, 2017).

The Paraná state (PR) concentrates the largest number of cases of TL in the southern region of Brazil (MATTOS *et al.*, 2023). In the urban environment of some municipalities of the state there are remnant forest fragments of Atlantic Forest. The transmission of TL among residents near the environmental preservation areas indicates the probable existence in these places of vectors and wild animals that maintain the parasite cycle and the infection of man (ARRAES *et al.*, 2008).

The limited knowledge about the local patterns of TL transmission makes it difficult to control; therefore epidemiological surveillance activities are required to assess the social and environmental characteristics of endemic areas and thus elucidate the epidemiological profile of the disease. Furthermore, activities involving health education should be included in all services that carry out leishmaniasis surveillance and control actions in endemic areas to ensure prevention and health promotion of the population at risk of infection (BRAZIL, 2017).

Thus, we evaluated the epidemiological profile of TL in an endemic area for the disease at the Paraná state, southern Brazil, and also developed health education activities with the local population.



2. MATERIALS AND METHODS

2.1 Study design

This is a prospective epidemiological study conducted in the urban area of Maringá-PR between March 2018 and July 2019, with two patient health monitoring until June 2023. The city of Maringá is located in the Northwest region of the state of Paraná and is crossed by the Tropic of Capricorn. It has the geographical coordinates 23° 25' south latitude and 51° 57' west longitude, altitude of 596m, with an average annual rainfall of 1,500mm and relative humidity of 66% (^aMUNICIPALITY OF MARINGÁ, 2020). The study included residents of the Borba Gato district whose homes were located on the edge of the Conservation Unit Borba Gato Park (Figure 1). This park has an area of 76,540.37m² (^bMUNICIPALITY OF MARINGÁ, 2020) and is currently closed to the public due to reported cases of leishmaniasis in the region. It is home to wild animals, such as monkeys and possums. This study was approved by the Permanent Committee on Ethics in Research with Human Beings of the State University of Maringá under protocol number 2.609.591. The research was conducted after obtaining the Informed Consent Form (ICF) from each participant.



Figure 1: Study area - The marginal area of the Conservation Unit Borba Gato Park, Maringá, Paraná, Brazil.



2.2 Data collection

Individuals with and without a history of TL were invited to participate in this study during home visits. A semi-structured questionnaire was applied to investigate environmental and personal characteristics. Serum and lesion material samples were collected for laboratory diagnosis of TL. The home visits were carried out with the assistance of a Community Health Agent (CHA) during the opening hours of the Iguaçu Basic Health Unit of the public health system (Iguaçu BHU - Monday to Friday, 7 am to 5 pm), which is responsible for the primary health care of the neighborhood's population. After three attempts to contact the residents, those who were not found were excluded from the study.

2.3 Laboratory diagnosis

Serum samples were used for the detection of IgG anti-*Leishmania* antibodies by indirect immunofluorescence (IFI) examination. Title ≥ 40 were considered significant (ARRAES *et al.*, 2008). When the IFI result was positive, the chemiluminescent microparticle immunoassay (CMIA) was performed using a serum sample for the differential diagnosis of Chagas disease (Architect ChagasTM, Abbott) (IBORRA-BENDICHO *et al.*, 2012). Scarification lesion samples were fixed on glass slides and stained with the Giemsa method for the direct parasite search (DP). The presence of *Leishmania* spp. amastigote forms was investigated using a common microscope (1000X). The polymerase chain reaction (PCR) was also performed to detect the parasite DNA in the lesion material (VENAZZI *et al.*, 2006).

2.4 Health education

Educational pamphlets were distributed to neighborhood residents during home visits and educational lectures were held with students at the Youth Center of Borba Gato district to clarify the mode of transmission of TL and preventive measures against the disease (video available at: https://youtu.be/-w3r9kzTtoU). A cycle of lectures was also held with the professionals of the Iguaçu BHU to update them about the number of TL cases in the Borba Gato district in recent years and advancements in the diagnosis and treatment of the disease.



2.5 Statistical analysis

The data obtained were organized in spreadsheets on Microsoft ExcelTM and statistically analyzed using Stata 9.1 and OpenEpi 3.01. The analysis of categorical variables was performed using Fischer's exact test. The odds ratio was calculated as a measure of association between the predictor variables and outcome. The confidence interval used in the tests was 95% (p<0.05).

3. RESULTS

3.1 Study area

The marginal area of the Conservation Unit Borba Gato Park selected for the research development comprised 93 houses. Of these, eleven were uninhabited (11.83%). Of the 82 houses visited by the researchers, three refused to participate in the survey (3.66%) and 34 were excluded after three attempted visits (41.46%). Of the 45 participating houses (54.88%), the average of residents of the houses was 2 ± 1.94 people/home. A total of 77 neighborhood residents answered the questionnaire and participated in health monitoring. Of these, 61 performed the IFI (79.22%) (Figure 2).



Figure 2: Study flow diagram. IFI: indirect immunofluorescence examination, DP: direct parasite search, PCR: polymerase chain reaction, TL: tegumentary leishmaniasis.

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3.2 Epidemiological profile of the studied population

Most of the patients who underwent serological examination were female (67.21%, n=41), with an average age of 49 ± 20.8 years, had a family income below 3 minimum wages/US\$247.00 (67.21%, n=41), and owned pets (83.81%, n=51) (Table 1). During the research development, two dogs (3.28%) with suspected lesions of TL in the muzzle and ear region were identified. The Zoonosis Control Center of the municipality was notified to investigate these cases.

Variables	Total		Odds ratio	<u> </u>	n
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Sex		, 0			
Male	20	32.79	Reference		
Female	41	67.21	1.85	0.34-10.07	0.704
Age					
0-19	6	9.84	Reference		
20-59	30	49.18	2.27	0.16-156	0.958
>60	25	40.98	1.27	0.06-97.58	1.000
Family income					
1-3 minimum wages	41	67.21	Reference		
>3 minimum wages	20	32.79	10.5	1.63-67.48	0.004*
Have Pets					
Yes	51	83.81	Reference		
No	10	16.39	1.57	0.27-9.14	0.633
Pets with lesion					
Yes	2	3.28	20.46	0.77-1662	0.076
No	59	96.72	Reference		
Schooling					
<8 years	51	83.61	Reference		
>8 years	10	16.39	1.57	0.27-9.14	0.633
Heard about TL					
Yes	53	86.89	Reference		
No	8	13.11	2.19	0.35-13.42	0.336
Know how to					
prevent					
Yes	23	37.70	Reference		
No	38	62.30	1.25	0.27-5.64	1.000
Uses insecticide					
Yes	56	91.80	1.47	0.11-99.14	1.000
No	5	8.20	Reference		
Uses insect repellent					
Yes	31	50.82	1.25	0.29-5.25	1.000
No	30	49.18	Reference		

Table 1: Epidemiological profile of residents of the Borba Gato district who underwent serological examination for TL.

CI 95%: 95% confidence interval, *p-value <0.05 was considered significant.

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Approximately 85% of the study participants had attended school for less than 8 years (83.61%, n=51) and reported having heard about TL due to the disease's history in the neighborhood. Despite the frequent use of insecticide (91.80%, n=56) and insect repellent (50.82%, n=31), the majority of them reported not being aware of preventive measures against TL (62.30 %, n=38) (Table 1). Selective waste collection in the neighborhood occurs three times a week.

Eight participants in the study had a history of TL (13.11%) and a new case of the disease (1.89%) was confirmed in the neighborhood during the prospective study (case 3) (Figure 2). Out of the nine patients, seven were women (77,78%), and eight were between 20 and 59 years old (88,89%). The patients reported that they had not traveled to TL endemic regions in the months preceding the onset of lesions, suggesting their residence as the probable place of infection. All patients achieved clinical cure after treatment with 20 mg/kg/day of meglumine antimoniate. However, three of them continued to show positive titers on the IFI examination, even after several years of treatment (cases 1, 2 and 4). One of the study participants, despite not having a history of TL, presented an IFI titer higher than 40 (case 5).

3.3 Clinical cases

3.3.1 Case 1

M.R.T.P, woman, 51 years old, reported being diagnosed with TL in 2004, along with her husband. She mentioned that several of her neighbors were also diagnosed with TL between 2003 and 2004. She has completed high school and has a family income of less than 3 minimum wages, working as a manicure in the neighborhood for several years. She resides on the outskirts of the woods and owns more than 10 pets, including dogs, cats, birds, and chickens.

At the time of the patient's diagnosis, the Zoonosis Control Center of the municipality identified a suspected TL lesion on one of her dogs. With the owner's authorization, the animal was euthanized as a preventive measure against new cases of the disease among family members and neighborhood residents. During the study, another suspected TL lesion was found on one of her dogs. The Zoonosis Control Center was once again contacted to investigate the case.

M.R.T.P. mentioned that she became aware of TL only after her own diagnosis. Since then, she has been using insect repellent and insecticide, and she has mosquito nets



on the doors and windows of her residence. The patient had a clinical cure, without new skin lesions since the treatment. However, her serological test still showed a positive result (IFI = 40) even after 15 years of TL treatment. The patient has no history of Chagas disease.

3.3.2 Cases 2 and 3 (family cases)

N.A.O.F, woman, 24 years old, domiciled on the edge of the woods and earns more than three minimum wages. She went to the neighborhood BHU in 2016 with a leg wound that was difficult to heal. The patient reported that her father had been diagnosed with leishmaniasis years ago. Due to the similarity between her lesion and her family member's wound, she suspected she had the same illness. Faced with the long wait for medical appointments and laboratory examinations at the BHU, the patient opted to seek medical attention in the private sector.

The diagnosis of leishmaniasis was confirmed by laboratory tests (IFI = 80 and DP positive). The patient underwent a cardiac function evaluation through an electrocardiogram (ECG) prior to starting the treatment, which showed no relevant cardiac abnormalities. N.A.O.F. underwent treatment by administering 20 mg/kg/day of meglumine antimoniate (60 ampoules) for 20 days. The healing of the lesion began approximately one month after the last dose of medication (Figure 3). Another ECG was performed, revealing no significant changes. Despite having no new lesions, the patient's serological examination remained positive (IFI = 40) three years after completing the treatment. The patient has no history of Chagas disease.



Figure 3: Evolution of skin lesion of patient N.A.O.F, diagnosed with TL and treated with 20 mg/kg/day of meglumine antimoniate (60 ampoules) for 20 days.



Her sister, F.A.S.O.C., 28 years old, domiciled at the same address, contacted the researchers during the course of the study after noticing the appearance of a wound similar to that of N.A.O.F. The patient was referred for medical appointment, and laboratory tests were performed to diagnose TL. The results of the tests were positive (IFI = 320, DP positive and PCR positive). The patient evolved to clinical cure after undergoing conventional treatment for the disease. Serology for leishmaniasis was performed again six months after the completion of the medication, yielding negative results.

N.A.O.F. and F.A.S.O.C. have four dogs in their residence, all of which show no lesions. The patients report that they started using insecticide at home after the diagnosis of leishmaniasis, although they do not always remember to use repellent. The patients were followed by the researchers for five years. In 2023, they were contacted again, and no reactivation of the lesion was observed.

3.3.3 Case 4

J.R.R., woman, 86 years old, semiliterate, retired, was diagnosed with TL in 2006 (IFI = 320, DP positive) and underwent the conventional treatment for the disease. She achieved clinical cure and did not develop new lesions. The patient reported using insecticide at home since her initial diagnosis. However, she only started using repellent after contracting the disease. She had a dog that showed no signs of skin lesions. During the study's follow-up examination, she tested positive for leishmaniasis in serology. However, further investigation was conducted due to the patient's mention of a history of Chagas disease, chronic bowel problems, and difficulty in swallowing. The differential diagnosis confirmed Chagas disease (ELISA ≥ 1.00 S/CO), and she was referred for medical follow-up at Iguaçu BHU.

3.3.4 Case 5

W. B. O., man, 82 years old, retired, reported no personal history of leishmaniasis but was aware of the disease because one of his friends had it during his youth. Being aware of the prevalence of the disease in the neighborhood, he developed a habit of using insecticide at home, maintaining a well-organized yard, and taking care of his two cats' health. During the health monitoring activity, his IFI result was 40. He reported a history of Chagas disease, which was confirmed by laboratory examination. The patient shows



no signs of skin or mucosal lesions. The IFI result demonstrates a cross-reactivity with antibodies produced due to *Trypanossoma cruzi* infection.

3.4 Educational activities with the community

During home visits, the researchers explained to the residents of the neighborhood the forms of transmission of TL, the clinical manifestations of the disease, and the main preventive measures against TL for humans and domestic animals. Educational pamphlets were distributed to residents at the end of the study with the information discussed during home visits.

The health education activity in the Youth Center of Borba Gato district involved 15 children between 7 and 12 years old, 17 teenagers between 13 and 20 years old and 11 educators. The activities with children and adolescents were elaborated according to the age and the educational level of the participants. For children, an illustrative plush of the parasite *Leishmania* and the insect vector were made, in addition to the presentation of the disease in comic book format. For the adolescents, an expository lecture was held that allowed the dialogue and discussion about the need for improvements in the neighborhood to prevent new cases of the disease in the area, especially the periodic cleaning of the surroundings of the woods by the town hall, awareness of residents about the proper disposal of waste produced by households and use of repellent collars by domestic animals residing in the perimeter of the woods.

The lecture cycle held at Iguaçu BHU involved 28 professionals, including ten CHAs, five nurses, three nursing technicians, three operating assistants, two nutritionists, one doctor, one speech therapist, one physical educator, one social worker, and one nursing teacher. For the professionals of the Iguaçu BHU, a dynamic lecture was given with case presentations, demonstration of the parasite under a microscope and discussion about the role of health professionals in the prevention, rapid diagnosis, and treatment of this pathology.

4. DISCUSSION

In this study of epidemiological surveillance of TL in an endemic urban area, it was possible to detect a case of the disease close to the remaining Atlantic Forest. Monitoring endemic areas for TL allows the development of prevention and health promotion strategies tailored to their specificities. Health education activities empower



individuals to understand their role as health promoters. When the population is aware of the neighborhood's health history, they take the first step towards disease control.

The first outbreak of TL in the Borba Gato district was recorded in September 2003, with 9 cases of the disease detected in the region. The entomology team of the 15th Regional Health of Paraná state confirmed the presence of the vector in the native forest of the Borba Gato Park, concluding that the reported cases were autochthonous (CARFAN *et al.*, 2004). Despite the development of disease control measures with the local population at the time of the outbreak, new cases of TL among neighborhood residents and dogs with asymptomatic infection continued to be detected (ARRAES *et al.*, 2008; CARFAN *et al.*, 2004; PITTNER *et al.*, 2009), reflecting the need for continued health surveillance in the endemic area. In our study, approximately 15 years after the first outbreak of TL in the neighborhood, we observed the persistence of the disease in the region.

We observed a greater number of TL cases among women, although most epidemiological studies indicate a higher frequency of TL among men, relating their work and leisure activities with greater exposure to risk factors for leishmaniasis (BRAZIL, 2017; DETONI *et al.*, 2019; GOMES *et al.*, 2022; URSINE *et al.*, 2021). They lived on the margins of the Borba Gato Park and reported spending several hours performing domestic activities, which suggests a probable risk of domiciliary or peridomiciliary transmission among residents near the conservation unit. Most of the patients diagnosed with TL were between 20 and 59 years old, a finding consistent with the literature (GOMES *et al.*, 2022; PINTO *et al.*, 2020; URSINE *et al.*, 2021).

Individuals with a family income above 3 minimum wages were more likely to be diagnosed with leishmaniasis compared to those who were less economically favored, despite the study conducted by Cruz (2015) indicating that higher family incomes represent a protective factor against TL. We investigated the possible factors associated with our findings. In our study, we observed that some patients reported resorting to private healthcare services when they experienced difficulties in promptly diagnosing the disease through the public health system (cases 2 and 3). Patients with precarious financial conditions depend on the public health system for the diagnosis and treatment of diseases. When this system fails, the investigation of the clinical case may be interrupted. Faced with this situation, patients with better financial conditions turn to private healthcare services. These findings emphasize the necessity of continuous training



for primary healthcare professionals to quickly identify cases and provide appropriate treatment to patients residing in endemic areas (BRAZIL, 2017).

Approximately 84% of the total participants had pets, demonstrating that a large number of animals are at risk for *Leishmania* infection. In TL, the role of domestic dogs in maintaining the parasite cycle has not yet been fully clarified (BRAZIL, 2019; RATZLAFF, 2023; RESENDE *et al.*, 2021). Although our study did not show statistical significance for the relationship between domestic animals and the risk of TL to humans, we noticed that patients diagnosed with the disease had or resided near pets with suspected skin lesions. Based on literature data (RESENDE *et al.*, 2021; URSINE *et al.*, 2021; VALERO *et al.*, 2020) and this observation, we believe that infected domestic animals may represent a risk to the health of the population as they attract sand flies to the household.

This study reinforced the importance of maintaining epidemiological surveillance of endemic areas for TL and monitoring the health of the local population. Individuals previously diagnosed with leishmaniasis may continue to have elevated serological titers even years after treatment completion, as demonstrated in clinical cases. Patients who have had inadequate treatment or no health follow-up after spontaneous healing of the wound can progress to the clinical mucosal form, profoundly affecting their quality of life (BRAZIL, 2017; COLAÇA, 2018; FIGUEIREDO JÚNIOR *et al.*, 2020).

The differential diagnosis between leishmaniasis and Chagas disease is essential, as cross-reactions in serological tests may occur (BARCELOS *et al.*, 2021; CORDOVA R. *et al.*, 2020), as observed in our study (Cases 4 and 5). Both diseases are caused by trypanosomatid protozoa but require distinct therapeutic approaches (SCARIOT *et al.*, 2022), making accurate diagnosis critical to avoid inappropriate treatments that could worsen the clinical condition.

Approximately 80% of the participants were included in the serological investigation. The sample was not randomly selected, since our intention was to return to the streets where there were cases of disease in the past and to limit our area to the edge of the woods based on the insect's flight capacity (SANTOS *et al.*, 2018; TONELLI, 2021). However, we suggest that upcoming health surveillance and educational activities cover the entire population of the district, since residents of the neighborhood may attend the risk area even if they do not reside in the marginal area of the conservation unit.



Our study strengthened The Plan of Action of Leishmaniasis in the Americas 2017-2022 proposed by the Pan American Health Organization (PAHO), that aims to reduce morbidity and mortality in endemic regions by strengthening diagnosis, treatment, prevention, surveillance and control (PAHO, 2021). The Brazilian Ministry of Health (MS) emphasizes the importance of education activities to achieve this goal, with the effective involvement of multidisciplinary and multi-institutional teams, for an articulated work in the different service delivery units (BRAZIL, 2017; BRAZIL, 2023).

5. CONCLUSION

We conclude that health surveillance actions are necessary to control TL in endemic areas. Health education activities with the local population reinforces the principle of co-responsibility. The development of training courses for primary health care professionals is important for reducing morbidity and mortality from leishmaniasis, as proposed by the Plan of Action on Leishmaniasis in the Americas 2017-2022.

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