Health, science and development: the emergence of American cutaneous leishmaniasis as a medical and public health challenge in Amazonas state, Brazil

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Abstract

The history of the emergence of American cutaneous leishmaniasis in the Brazilian state of Amazonas since the 1970s is analyzed as an object of knowledge and a medical and public health challenge. An overview of the period is provided, including the public health measures and scientific studies undertaken in the context of the execution of large-scale regional developments pursued in the name of national integration by the federal government. The methodology uses documental analysis of laws, the scientific literature, research reports, epidemiological bulletins, and newspapers. The results show that American cutaneous leishmaniasis emerged as a major health problem in Amazonas in close association with the political, economic, and socioenvironmental changes seen in the period.

Keywords: American cutaneous leishmaniasis; history of leishmaniasis; leishmaniasis; public health policies; development projects.

Cláudio de Oliveira Peixoto[i]

[i] Health Administration Analyst, Leônidas and Maria Deane Institute/Fiocruz. Manaus – AM – Brazil

orcid.org/0000-0002-8518-9249

claudio.peixoto@fiocruz.br

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In July 1985, a 4-year-old boy, E.C.B., resident of Colônia Santo Antônio, Manaus, left the house to continue a life of pain. He was given another painful injection, one more after the two hundred he had already received to treat the ulcers on his body. His parents, Raimundo and Edmilza, had contracted the same disease months earlier, and accompanied their son on this daily "procession," which lasted around half an hour, come rain or shine, to a health clinic in Cidade Nova, Manaus. It was a long walk, around six kilometers.

Their shanty was home to eight other children and four adults. Nearby, almost every household had someone ill. These families, who came from rural parts of the state or from elsewhere in search of employment in retail, industry in the free trade zone of Manaus, the service sector, or the city's informal labor market, encountered a harsh reality: hunger, shortage of housing and disease.

The place where they lived was a plot of land that had no running water, no electricity, no sewers, and no waste collection. The same area was occupied by over seven hundred households. The residents of Colônia Santo Antônio had to draw water from wells or go to the stream some two kilometers away to get (relatively) clean water to drink, cook, wash, and do laundry.

The lack of resources meant many of the residents were inclined to venture into the nearby forest to hunt small rodents to eat. Even when they did this, they were aware of the risk of being bitten by the *tatuquira*, as they called the phlebotomine sandflies that transmitted the disease that swept through the community.

So it was for Paulo and Maria da Conceição. Everyone in their family had fallen ill. Their daughter, aged just 16 months, had already been given over thirty doses of the medicine in painful injections. Neither she nor the adults were able to rid themselves of that disease. It was common for people to suffer mild and even serious side effects from the substance injected. The older folk would take herbal and plant-based remedies. One such remedy involved taking the extract of *batata de onça*, a medicinal plant common in the region, making a paste from it and applying it to the sores. Another option was to ignite gunpowder on the lesioned skin in a vain attempt to "burn" off the disease.

Many of the locals remembered a former resident, Sandra, whose eight children, one of whom was just 6 months old, were deformed beyond recognition as the disease spread over their whole bodies. However, it normally presented in the form of one or more round sores that never healed. In some cases, nodules would appear or moist, open plaques, releasing copious quantities of fetid pus on their limbs or face. In other cases, it would affect their mucous membranes and gradually eat away the tissue within the nose and mouth.

While these people were coping with the illness, a doctor on television announced the state of emergency in Manaus to the Brazilian nation. In the small clinic in Cidade Nova, other doctors were treating the sick and attempting to control the epidemic. At the Institute of Tropical Medicine of the University of Amazonas and at the National Institute of Research of the Amazon (Instituto Nacional de Pesquisas da Amazônia, INPA), efforts were being made to identify the vectors and parasites responsible for the proliferation of those cases, new drugs for its treatment were being tested, and measures to mitigate the effects of the epidemic were being discussed.

Detached from the world of medical and scientific studies in the field of epidemiology and even the guidance passed down by the Department of Health, people like Paulo, Maria da Conceição, and Sandra were unaware that leishmaniasis was caused by a protozoan of the genus *Leishmania*. Even so, the doctors who went out into the field did their best to convince them not to go out into the forests and streams at dawn or dusk, because these were the times when the fly that transmitted it would go out to feed. But how could they not go to the stream if they had no running water? How could they not venture into the forest if that was their backyard? People could not understand why that disease had become such a major health hazard.

This narrative is based on information from scientific articles and news stories published in the mid-1980s (Surto..., 12 jul. 1985; Leishmaniasis..., 14 jul. 1985).

In the 1970s, Amazonas state became an important region for the study of different forms of leishmaniasis. Scientists were keen to identify the biology and distribution of different species of *Leishmania*, its cycles in the wild animals that served as its natural reservoirs, in the insects that were its vectors, and in its human hosts. They were also attentive to synergies between vectors, parasites, and the socioenvironmental impacts arising from territorial incursions into the Amazon.

American cutaneous leishmaniasis (ACL) was first identified as a health problem in the Amazon in the early twentieth century (Jogas Jr., 2014, p.19), but it was in the 1970s that it became a more serious and widespread issue and took on increasing importance in national and international scientific circles. The World Health Organization (WHO) today classifies it as one of the most neglected tropical diseases in the world because it affects the health and life of poor populations in developing countries and normally receives scant attention from the authorities and limited funding for research (Conceição-Silva, Alves, 2014, p.17).

There were outbreaks and epidemics of the disease in the state of Amazonas, Brazil, as the state capital, Manaus, grew and development projects were rolled out, causing huge socioenvironmental impacts. Together with malaria, ACL then became one of the most widespread endemics in the state, and began to draw the attention of researchers from Brazil and elsewhere with a background in medicine and biology, who started to do research at local institutions with increasingly close links to institutions from other parts of the country and the world.

This resulted in a considerable volume of studies about the epidemiology and pathogeny of cutaneous and mucocutaneous leishmaniasis, the taxonomy and biology of the species of protozoa that cause the disease, the phlebotomine sandflies that are its vectors, and the animal hosts of *Leishmanias*. These helped to project the Amazon region nationally and internationally in the ambit of tropical medicine, but it did not have such a great impact in the field of public health, insofar as it translated into relatively few practical prevention and control measures (OMS, 2010, p.XII).

Recent studies show that the changes in the profile of ACL were related to the urbanization and industrialization of Amazonas. In the early 1900s, when rubber was a major export commodity for Brazil, ACL was spread in the wild and mostly affected the workers who went out into the forest. By the 1970s, outbreaks and epidemics were afflicting urban and peri-urban areas of Manaus and other towns and cities, changing the profile of this once rural disease. By then, Amazonas had become one of the states with the highest endemicity of the disease in Brazil and the world (Guerra et al., 2015, p.13).

In this article, I analyze the emergence of ACL as a public health and medical challenge in the context of the introduction of development projects in Amazonas state. I relate epidemiological data to the construction of the Manaus-Itacoatiara highway (AM-010) and the Manaus-Boa Vista highway (BR-174) in 1965 and 1978, respectively, as well as the development of mining in Pitinga (1982), the construction of the Balbina hydroelectric power plant (1988), the Coari-Manaus gas pipeline (2006), and the creation of the free trade zone of Manaus (1957). I particularly consider the studies on leishmaniasis conducted at the Institute of Tropical Medicine, founded in 1970, precursor of the Heitor Vieira Dourado Tropical Medicine Foundation (Fundação de Medicina Tropical Heitor Vieira Dourado), and at the National Research Institute of the Amazon (Instituto Nacional de Pesquisas da Amazônia, INPA), particularly the Leishmaniasis and Chagas Disease Laboratory, set up in 1975. The scientists from these two institutions feature in the production of knowledge about ACL and other diseases in the region.

Development projects and ACL in Amazonas

A considerable body of literature in the field of tropical medicine has related alterations in the profile of ACL transmission to economic and socioenvironmental changes in Brazil. Vale and Furtado (2005, p.424) note that it spread across practically the whole of Brazil as of the 1950s. This was when there began to be large-scale migrations from rural parts to the big cities and the southeast and northeast of the country underwent rapid urbanization, all driven by the construction of roads and highways.

Epidemics of cutaneous and visceral leishmaniasis broke out in different parts of northeastern Brazil in the early 1950s. Epidemiological studies were performed in conjunction with the use of DDT and other residual insecticides. These actions, in the wake of the anti-malaria campaigns, resulted in the decline of both forms of the disease. However, they subsequently grew and spread to other parts of the country (Vale, Furtado, 2005, p.424).

The economic situation in the late 1960s and early 1970s was propitious for investments in the Amazon. The civil-military government's development projects, under the motto "integrate to defy defeat," were designed to foster the recovery of the region's economy, the maintenance of the country's borders, the reduction of conflicts over land ownership and use in other parts of the country, the occupation of the Amazon, seen as a "demographic void," and the "overcoming of tensions that put in jeopardy some of the preconditions for the maintenance and expansion of capitalist accumulation in Brazil" (Seráfico, Seráfico, 2005, p.103).

The rise in the number of cases of infectious diseases in the region came about in the context of significant migratory flows stimulated by the federal government by major roadbuilding initiatives such as the Belém-Brasília highway (1958) and the trans-Amazonian highway (1970). Deforestation, an ecological factor that was a hallmark of this managed migration policy, had a big impact on the number of cases of malaria (Andrade, 2016, p.75). One important development was the free trade zone of Manaus.[1] Devised in 1957 and rolled out as of 1967, this new industrial and trade hub attracted great numbers of people from elsewhere in Amazonas and other states to Manaus in search of work and better living conditions (Schweickardt, Martins, 2017, p.28).

Along with these great migratory flows, the outbreaks of malaria and ACL in Amazonas have been attributed to the expansion of agriculture, mining, oil exploration, road building, hydropower generation, and the occupation of new urban areas as of the 1970s (Guerra et al., 2015, p.13). These projects intensified the movements of people and triggered a number of changes in the environment, with deforestation causing serious health issues, unprecedented ecological liabilities, and significant climatic alterations (Patz et al., 2000, p.1396; Paes, Barros, Toledo, 1997, p.II.3.7).

According to Araújo Filho (1981, p.187), deforestation gave rise to the migration of natural reservoirs of *Leishmania*, like marsupials, xenarthran mammals, and rodents, to other areas, forcing sandflies to feed on human blood. Studies in the last thirty years show that some species of sandflies adapted to peri-urban settings as a consequence of socioenvironmental changes (Brasil, 2017, p.9).

The impacts on the relationships between insect vectors, parasites, human hosts, and other reservoirs (wild and domestic) resulted in increased number of cases, of localized outbreaks and even epidemics of the disease (Barrett, Senra, 1989, p.256). The intensified flows of people in and out of the region also contributed to the spread of ACL to previously unaffected areas (Sousa, Pearson, 2009, p.916; Altamirano-Enciso et al., 2003, p.858).

Studies of this dynamic since then show that it is directly linked to changes wrought by regional development projects. Table 1 show the large-scale developments that shaped urbanization and industrialization processes and the epidemiology of ACL in Amazonas.

Table 1 – Main developments in the state of Amazonas that were important for mapping the American cutaneous leishmaniasis (1960-2015)

Year(s)	Project
1960-1970	Shift of the agricultural frontier from the central west region to the south of Amazonas state
1970-1980	Building of important highways in Amazonas: Manaus-Itacoatiara (AM-010), Manaus-BoaVista (BR-174), Manaus Porto Velho (BR-319), Trans-Amazonian (BR-320)
1967	Introduction of the Free Trade Zone of Manaus
1978	Mining in Pitinga
2006	Construction of Balbina hydroelectric power plant
2006	Construction of Coari-Manaus gas pipeline
2006	Discovery of new mineral reserves in Novo Aripuanã, Apuí, and Humaitá
1970-2015	Building of housing projects and land occupations in Manaus

Source: Peixoto (2017).

Although these new ventures and developments were implemented by governments of different political inclinations, they had one thing in common: they were and they continue to be excluding and predatory on the sociocultural and environmental diversity of the Brazilian Amazon. Furthermore, the new mode of occupation bore with it the scourge of infectious diseases that affected – and affect – the living conditions and health of the people in the Amazonian region.

From rivers to roads: the routes of leishmaniasis

At the beginning of the twentieth century, epidemics of cutaneous and mucosal ulcers broke out in the state of São Paulo during the construction of its railroad network. It was there, in 1909, that the etiological agent of leishmaniasis was identified in Brazil – in the worksites for the North-West of Brazil railroad, which connected the states of São Paulo and Mato Grosso (Pessoa, Barreto, 1944, p.31). The construction of railroads was designed to interconnect the country, expand its domestic market, and facilitate the export of agricultural and mining products. Tropical diseases like leishmaniasis and malaria had a strong impact on these and other infrastructure developments. Associated with modernization in the burgeoning republic and new synergies between biological and socioeconomic processes, they were the target of some relatively successful public health actions and spurred some important investigations in the field of tropical medicine (Benchimol, Silva, 2008, p.720).

In the Amazon in the early 1900s, information about leishmaniasis (known locally as "fierce wounds") was mostly associated with patients from rural hinterlands and rubber tapping zones who had been attracted to the big cities of Belém, Manaus, and Iquitos. The places they came from were virtually untouched by state actions and rarely accessible for observation by travelers and scholars. Yet by the 1960s and 1970s, the incidence of leishmaniasis in the Amazon had increased substantially, in association with the roadbuilding efforts designed to integrate the region to the rest of the country and assure a land route for the movement of natural products and goods from the free trade zone of Manaus to other markets.

Unlike other regions, in the Amazon the main routes of transportation and communication are the rivers. This makes them important for understanding processes of health and illness not only in socioeconomic and political terms, but also biologically, namely, their influence on the life cycles of pathogens, hosts, and vectors. The Amazon, Juruá, Purus, Madeira, Negro rivers, their tributaries, and the whole watershed with its streams, branches, and braids had and still have an influence not just on the political, social, and economic history of the Amazon, but, to a greater or lesser extent, the course of infectious diseases there.

According to Gonçalves (2008, p.79), the region's social, historical, and geographical configuration largely follows two patterns. The river-floodplain-forest pattern predominated until just after the middle of the twentieth century. It was marked by river-based organization, whereby the rivers were the point of reference for the sociocultural life, lifestyles, and identities of the river-dependent and indigenous peoples, and a forest-based extractivist economy based on the exploitation of forest products like rubber.

The second pattern – road-dry land-subsoil – has to do with the mode of economic development introduced around the 1970s, when the Amazon became an area of strategic interest to the nation, with the adoption of policies and measures designed to "incorporate territorial, scientific, and cultural frontiers" (Faulhaber, 2005, p.241). With this came a new mode of occupation for the region, marked the building of roads and highways, industrialization, and mining. This pattern began in the 1950s with Juscelino Kubitschek's developmentalist government and the building of the Belém-Brasília highway, followed by others built under subsequent governments (Gonçalves, 2008, p.79).

As of the 1960s, in the wake of these roadbuilding initiatives, the agricultural and ranching frontier pushed up from the central-west region to the south of Amazonas, causing huge environmental impacts in the municipalities of Lábrea, Novo Aripuanã, Humaitá, Boca do Acre, and Apuí. Another process that brought with it unplanned occupation, predatory exploitation of the riches of the land and subsoil, and led to large-scale deforestation and severe outbreaks of leishmaniasis was the introduction of agricultural colonization projects and gold mining (Guerra et al., 2015, p.15).

The migration and development policies in Amazonas thenceforth changed the patterns of land occupation, but this did not mean the rivers ceased to be an important point of reference. Their influence continued, but now in association with the activities that arose with the new roads and highways, such as the economic exploitation of the land and new human settlements along their trajectories, which influenced the outbreaks of leishmaniasis and other diseases.

At this time, INPA and the Tropical Disease Clinic developed some important entomological, biological, medical, and epidemiological investigations in the areas modified by these different developments. Djalma da Cunha Batista,[2] who ran INPA from 1959 to 1968, attributed the rise in the number of people afflicted by ACL to the settlements along the newly built roads and the disturbance of the habitats of the flies that transmit it – i.e., the destruction of their ecological cycle (Batista, 2007).

Importantly, according to the press, WHO statistics put the number of cases of cutaneous leishmaniasis in the Amazon at negligible levels – just 71 – between the 1940s and 1968. However, studies by the physician Mário Augusto Pinto de Moraes (1926-2016),[3] in Amazonas, and Domingos Barbosa Silva (1917-1996), a dermatologist with the Department of Pathology at the Federal University of Pará, indicated the existence of some 633 cases between 1954 and 1968. Another 266 cases were recorded by the parasitology section of the Evandro Chagas Institute (Instituto Evandro Chagas) in Pará (Fonseca, 19 jun. 1977, p.1). In other words, the disease was far more prevalent than the WHO estimated, but the species of parasites and the vectors responsible for its occurrence in the region were still not well known.

When rubber tapping was at its peak in the region, leishmaniasis and other parasitic diseases appeared primarily along the rivers and their tributaries. With the new pattern of land occupation, new routes were opened up by man and his diseases along land highways and byways. The main research institutions in the region set the challenge of studying the ecology of the vectors and the epidemiology of the main diseases along these routes. They collected data, insects, parasites, and vertebrates, provided health care, performed experiments, and conducted environmental impact studies to identify how changes to the environment were affecting health and biodiversity in these areas.

Roads, health, and science: revealing the ecology of the vectors and epidemiology of ACL in Amazonas

Two roadways were particularly important in shaping the epidemiology of cutaneous leishmaniasis in the region. The Manaus-Itacoatiara (now AM-010, originally AM-1) was the first highway in Amazonas state. Construction began in 1955 under the administration of President Plínio Ramos Coelho (1955-1959). It was completed ten years later, in 1965, under President Arthur Cézar Ferreira Reis.[4] Stretching 269 kilometers, it cut through a densely forested region rich in wood and teeming with biodiversity, with countless rivers and streams. The disease spread in the farming settlements that grew up there and among the servicemen who used the area for training (Guerra et al., 2003, p.588).

The Manaus-Boa Vista highway (BR-174) was part of the national roadbuilding plan devised when Juscelino Kubistchek (1956-1961) was president. It was finally completed in 1978. Built for the mines opened up in indigenous lands and for transporting cargos of nuts, rubber, and rosewood, it also became an export route for products from the free trade zone of Manaus to markets in the north, such as Venezuela. Built in the name of delivering the natural resources of the land and subsoil into the hands of international capital, it displaced and all but wiped out the Waimiri-Atoari people (Silva Filho, 2015, p.40).

In a replay of the tragedy wrought by European colonialization, diseases like measles, flu, smallpox, TB, and malaria struck down whole villages, introduced by the functionaries and workers recruited for the roadbuilding. The indigenous peoples, seen as obstacles standing in the way of the unfettered exploitation of the natural riches of the Amazon, were also targeted for contract killings and by the military (Rodrigues, 2013, p.239).

Brazilian and foreign researchers were drawn to Amazonas and neighboring Pará to study the extraordinary diversity of phlebotomine sandflies and protozoa of the genus *Leishmania*. With a climate and environment propitious for their development, the region was unparalleled for the research of leishmaniasis, given that the anthropic changes happening along the roads, with new settlements, deforestation, and other environmental alterations, turned these and other diseases into a serious public health problem for the region.

By the early 1960s, the Second Division of Medical Research at INPA already had a program in place that aimed to identify the natural reservoirs of *Leishmania braziliensis*, the supposed agent of the ACL that was wreaking havoc in the Amazon. Zoologists and parasitologists examined wild mammals captured at a pilot station set up at kilometer 46 of the Manaus-Itacoatiara highway and undertook expeditions, some led by foreign researchers, to different parts of the state and areas of Roraima, Acre, and Rondônia. The species collected on these expeditions included phlebotomine sandflies, potential vectors of *Leishmania* (INPA, 1963, p.6).

The researchers of the Second Division were familiar with leishmaniasis and its vectors in Brazil and elsewhere. They knew how to capture the vectors using light traps and human bait, dissect them, isolate the parasites, macerate them in saline solution, and conduct experimental infection. They knew all the species that had been identified by Pifano[5] in Venezuela and Floch[6] in Guyana. Yet they were unsuccessful in their efforts to find flagellates from the life cycle of the disease in the insects and animals they captured.

At the Evandro Chagas Institute, in Pará, the British scientists Ralph Lainson and Jeffrey Jon Shaw set up a parasitology unit funded by the Wellcome Trust Foundation, in 1965. The main aim was to identify (through parasitology, entomology, and medical zoology) new species of *Leishmania* and their vectors and vertebrate hosts in the Brazilian Amazon. Their work, in collaboration with other Brazilian and British investigators, completely changed the way cutaneous leishmaniasis was understood. What they found was that the parasite populations, with their respective vectors and vertebrate hosts, were far more heterogeneous than previously believed[7] (Shaw, 2016, p.37; Lainson, 2010, p.14).

The quest for new species in Amazonas was triggered by the rise in the number of cases of the disease, first along the new highways. In the 1960s, at kilometer 65 of the AM-010, the Amazonas state government assigned an area of primary forest on dry land between the Puraquequara river and Rio Preto da Eva to the Brazilian army. There, they set up Base BL1 of the Jungle Warfare Training Center. This specialized unit became the heart of what came to be known as the "accursed quadrangle," not least because of the diseases that plagued the lives of the servicemen there. Two decades later, over 80% of the personnel on military training there were struck down by an outbreak of ACL (Pinheiro, Luz, Franco, 2008, p.166).

Most of the ACL patients were treated and studied in Manaus. The deterioration of this city's public health situation, especially of diseases that were traditionally the object of tropical medicine, prompted the creation of a small tropical disease clinic, which began to function precariously in 1970 in an annex of Hospital Getúlio Vargas, administrated by the state government through the Department of Health and Social Welfare (Barros, 12 set. 2016).

The initiative was spearheaded by Heitor Vieira Dourado (1938-2010) and Carlos Augusto Telles de Borborema (1939-2017), two professors from the Department of Health Sciences at the University of Amazonas, who enrolled 16 medical students from their institution for the initiative. The clinic was named after Dr. Luiz Montenegro and became a hospital in 1974. Four years later it became the Institute of Tropical Medicine and now goes by the name of Heitor Vieira Dourado Tropical Medicine Foundation (Fundação de Medicina Tropical Heitor Vieira Dourado, FMT-HVD). It is known internationally for its cutting edge research and treatment of different forms of leishmaniasis and other infectious and parasitic diseases (Barros, 12 set. 2016).

The tropical disease clinic was the material expression of a project that was initially isolated in the local medical context: to redress the lack of any research infrastructure for the tropical diseases that had become such a public health headache in the state. In this same setting, biomedical institutions and researchers from other regions of Brazil and abroad turned their sights to that other portion of the "tropics," the Amazon, attracted by the "raw material" it offered studies in tropical medicine.

The research at the clinic in those early years involved intense synergies between science and medical and health care for patients via the public health system. At the same time, the medical training and practice of its researchers overlapped with the interests of scholars and institutions from other parts of Brazil, and its physicians and scientists began to investigate, among other endemics, ACL in the worksites of the major developments rolled out during the civil-military regime in Manaus and other parts of the state.

In Amazonas, the traditional focus of interest of tropical medicine, malaria, was now joined by leishmaniasis, an endemic of growing magnitude, as well as filariasis, typhoid fever, hepatitis, sexually transmitted diseases, amebiasis and other worm infections, arboviruses and, later, AIDS. The increasing incidence of these diseases made their research even more pressing, not just for academic reasons, but to provide valuable insights for their prevention and control and the treatment of their victims.

The construction of a hospital specializing in tropical diseases was justified when it became clear the clinic could no longer cope with the numbers of people falling ill in the peri-urban parts of Manaus and elsewhere in the state. The transmission of cutaneous leishmaniasis was particularly high in Manaus. The research and healthcare infrastructurestructure devoted to infectious and parasitic diseases, the focus of INPA's work, had to be expanded.

Jorge Ramon Arias (1943-2014), a Panamanian naturalized in the United States with a PhD in entomology from the University of California, reached Amazonas state in 1974 to set up the Leishmaniasis and Chagas Disease Laboratory at INPA. Arias and the local entomologist Rui Alves de Freitas embarked on their studies in areas adjoining the AM-010 highway and in the forestland near the housing projects Parque 10 de Novembro and Parque das Laranjeiras, in Manaus. Taking the same approach as Lainson and Shaw, they researched the phlebotomine sandflies and the *Leishmania* species and how these variables translated into different clinical forms of ACL in human hosts (Arias, Freitas, 1978, p.387-395).

The sandfly specimens were collected using the human bait method or CDC light traps imported from the United States. From 1977 to 1982, the researchers at Arias's lab confirmed that *Lutzomyia umbratilis* was the main vector of *Leishmania (Viannia) guyanensis,* the principal causal agent of ACL in the Manaus region, northern Amazonas and Guyana. Meanwhile, *Leishmania (Viannia) braziliensis* was encountered south of the Amazon river, and *Leishmania (Leishmania) amazonensis* – responsible for the (rarer and more aggressive) diffuse cutaneous form of the disease – was encountered in both the north and the south of the state. This new classification was based on a review of the neotropical diseases studied in Brazil since 1965 and proposed by Lainson and Shaw in 1987, refuting the idea that had prevailed until the 1960s that all forms of ACL were caused by *L. braziliensis* (Lainson, 2010, p.14).

From May 1976 to April 1977, Arias and Freitas, failing to find *Leishmania (Viannia) guyanensis* flagellates in any sandfly specimens captured to the north of the Amazon river and failing to find any infection in them to the south of the river, put forward the hypothesis that the river acted as a natural barrier to the distribution of the vector/parasite/man cycles (Arias, Freitas, 1978, p.387). Knowledge of the spatial and ecological distribution of phlebotomine sandflies was at stake because of its importance in disease surveillance for leishmaniasis.

Studies run by INPA and the Institute of Tropical Medicine implicated several species of phlebotomine sandflies in the transmission of ACL in settlements adjacent to the AM-010 and BR-174 highways: *Luztomia anduzei, Luztomia whitmam*, and *Luztomia umbratilis*, the last of which was the main vector in the region and an extremely anthropophilic species associated with the transmission of *Leishmaniasis (V.) guyanensis*, which, as we have seen, occurred to the north of the Amazon river in recently colonized areas (Arias, Freitas, 1978, p.387).

In the late 1970s, the team at Arias's laboratory and the research done there diversified with the arrival of the wife-and-husband team Maricleide and Roberto Naiff, disciples of Lainson and Shaw at the Evandro Chagas Institute, and the subsequent hiring of the British entomologist Toby Vincent Barrett. After twelve years working at INPA, Arias left in 1986 to take up an invitation from the Pan-American Health Organization to work in Brasília and subsequently in Panama, Venezuela, and the USA, handing over the rudder at INPA to Barrett. Toby Barrett's arrival at the lab strengthened the work in the identification and taxonomy of species that was already done there.

At the Institute of Tropical Medicine, the physicians working with leishmaniasis were involved in providing healthcare for patients via the public health system. Official statistics indicated a rise in the incidence of the disease, but thus far little scientific work had been published about the outbreaks or the measures adopted for their control. This was a time when several large-scale hydropower plants were constructed in the Amazon – Tucuruí, in Pará (1985), Balbina, in Amazonas (1988), and Samuel, in Rondônia (1982) – while Manaus became increasingly industrialized. All of this resulted in the forced relocation of indigenous peoples and other traditional communities from their homelands and put at risk the region's biodiversity and the health of the workers and populations affected by these projects.

Pitinga and Balbina: development, ecological disaster, and leishmaniasis

The 1980s was marked by other projects designed to "develop" the region, which nonetheless ushered in profound socioenvironmental impacts and the proliferation of diseases. These included mining in Pitinga district (1982) and the construction of the Balbina hydropower plant (1988), both of which were on the route of the BR-174, in lands occupied by the Waimiri-Atroari peoples.

In 1979, 320km away from Manaus, the biggest multi-mineral mine in the world was discovered, prompting the construction of Vila Pitinga, the administrative headquarters and home to workers from the Taboca mining company, part of the Paranapanema group, acquired in 2008 by the Peruvian mining giant Minsur. In 1982, several minerals started being extracted from the mine, including tin, obtained mainly from cassiterite, as well as iron ore, niobium, and tantalum. The workers quickly succumbed to outbreaks of leishmaniasis and other endemic diseases (Rodrigues, 2013, p.170).

Like most of the state, Pitinga river valley has a hot, humid climate, with frequent rainfall almost all year round. It boasts a great diversity of mammals and insects, phlebotomine sandflies included. The area bought by the mining company was completely cleared of forest to make way for the workers' village, which was divided into four sectors, A, B, C, and D. There was also a church, clubs, a hotel, a shopping area, a kindergarten, a school, a restaurant, an airport, and a private hydroelectric power plant with the capacity to generate up to 250MW, which only increased the impact on the environment.

A hospital had to be built to cope with the number of workers and other residents who were taken ill. When the INPA and Institute of Tropical Medicine researchers got to the settlement, they examined the patient control records, beginning with the ones who had sores. They then tested them to find out whether they had a *Leishmania* infection. If diagnosed, they were referred for treatment. The aim of the studies was to understand better the epidemiology of the diseases that were spreading there. In the case of leishmaniasis, sandflies were captured and efforts were made to find their breeding grounds and assess the effectiveness of the control measures adopted by the mining company (Chagas et al., 2006, p.188).

Most of the cases of ACL registered at Vila Pitinga involved men who worked in direct contact with the forest. The disease control measures adopted consisted of fumigating with insecticide in the late afternoon and prohibiting the hunting of game and bathing or camping in the forest. These measures, along with health education, seem to have led to a decline in the incidence of the disease in the region (Chagas et al., 2006, p.191).

Still in the Waimiri-Atroari territory, the construction of Balbina hydropower plant on the Uatumã river, partially started up in 1988, resulted in the flooding of 2,360km^2 of forest. Not only was this one of Brazil's biggest ever environmental disasters, but it was instrumental in destroying the way of life of the Waimiri-Atroari peoples and other groupings who inhabited the region (Rodrigues, 2013, p.80).

As of 1981, Brazil's environmental legislation required environmental impact reports[8] to be approved before a permit could be issued for the construction of any hydroelectric development. This prompted the signing of agreements between INPA and the electricity utility Eletronorte, making funds available for scientific studies of the local vector fauna. New species of phlebotomine sandflies were identified and the effects of deforestation on the proliferation of leishmaniasis were analyzed (Araújo Filho, 1981, p.187).

A settlement was built at Balbina to house the approximately four thousand workers recruited to build the plant and their two thousand family members. It was split into two areas, called Waimiri and Atroari, in ironic homage to the ethnic group the plant was decimating. Field reports note that in 1987 an agreement was signed by the Ministry of Science and Technology, Eletrobras, and INPA for experiments using chemicals against the vectors, as well as the identification of species and mitigation of environmental impacts arising from the flooding of the land for the reservoir (INPA, 23 jan. 1988, p.1).

Chemical weapons were widely used in the war against the vectors. Dichlorodiphenyltrichloroethane (DDT), a powerful residual insecticide, was used to fight the vectors of malaria and other diseases, including the phlebotomine sandflies that transmitted cutaneous and visceral leishmaniasis (Nery-Guimarães, Bustamante, 1954, p.127). Encouraged by its apparent efficacy for public health and agriculture, international health authorities began to believe in the possibility of eradicating malaria in the short term, but studies revealed that the vectors developed resistance to the insecticide (Andrade, 2016, p.71). Even so, in Amazonas, DDT was widely used to fight the endemics in the 1970s and 1980s, especially against the vectors of malaria in the areas of influence of the trans-Amazonian highway, the BR-174 highway, and Balbina.

Between May 24 and June 22, 1988, when the Balbina reservoir was filled, a team went out into the region to study the local sandflies and experiment with the pyrethroid insecticide deltamethrin for their control. This was an alternative to the more toxic insecticides, especially DDT, whose efficacy declined as the insects that carried malaria and other diseases acquired resistance to it. A government public health department (Sucam) was responsible for executing the project, while the Institute of Tropical Medicine was in charge of caring for the patients. In 1987, around twenty cases of ACL were reported every month in Vila de Balbina (INPA, 23 jan. 1988, p.1).

The investigations incriminated *Luztomyia umbratilis* as the primary vector. The sandflies, with infection rates ranging from 10% to 30%, were found in large quantities around the houses and were infected by mammals that acted as natural reservoirs for *Leishmania*: the two-toed sloth, the anteater, and the opossum. As for the flies, the scientists collected them at the bases of trees using CDC light traps placed between one and 15 meters from the ground. As *L. umbratilis* showed no inclination to feed at night, they raised the hypothesis that people were attacked during daylight hours at the foot of the trees when they entered the forest. However, attracted by the artificial lighting in the houses, the insects would also attack the women and children around their homes because they were so close to the forest (INPA, 23 jan. 1988, p.2-4).

In response, a strip of forest around the houses in the Waimiri and Atroari zones of the settlement was fumigated with deltamethrin to reduce the intensity of transmission. In some areas, there was no significant reduction in the number of sandflies captured even after this was done, while in other areas there was. The scientists recommended continuing the study and providing health education in order to minimize the effects of transmission (INPA, 23 jan. 1988, p.5).

The cases from these areas drew the attention of the public health authorities and scientists keen to identify the *Leishmania* species and study the ecological and epidemiological aspects of the outbreaks in the region. However, it was in the capital of Amazonas, Manaus, that cutaneous leishmaniasis erupted as a public health crisis, forcing government officials to announce a public state of emergency.

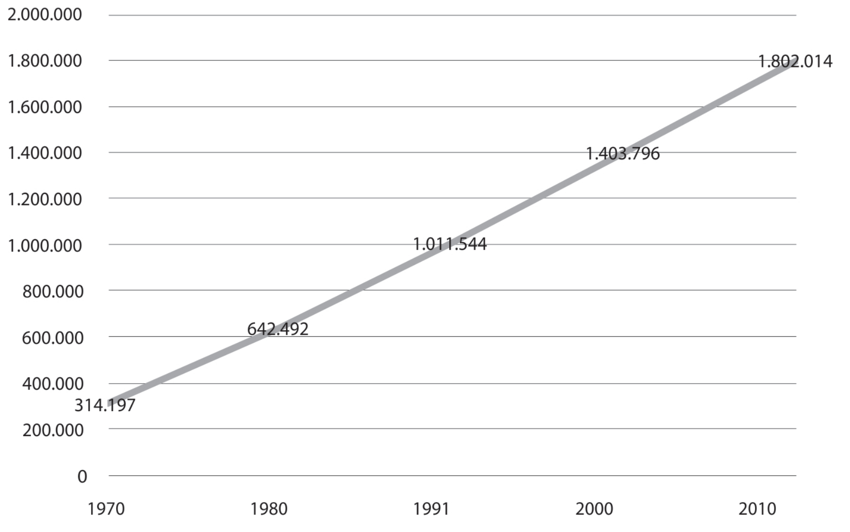
Leishmaniasis in Manaus, Rio Preto da Eva, and Coari

Manaus is a good example of how ecological and biological factors in association with socioeconomic conditions transformed ACL into a severe public health problem. Created by law n.3173, of June 6, 1957, the free trade zone of Manaus gave rise to profound urban transformations and a population boom in the city (Schweickardt, Martins, 2017, p.28).

The 1971 flood meant many families in the south of Amazonas lost their homes. This disaster, in conjunction with the allure of the free trade zone and the shortage of healthcare in the rest of the state, spurred increased migration to the state capital. In the second half of the year, malaria broke out on the banks of the Purus river, followed by the Solimões and the Negro. The families affected who went in search of healthcare in the big city swelled the ranks of those already moving there from other parts, settling in the outskirts of the city and taking with them malaria and leishmaniasis. It was not long before epidemics of these diseases occurred in these new districts and occupations in and around Manaus (Paes, Barros, Toledo, 1997, p.II.3.6).

As of the mid-1970s, multinationals started to move into Manaus, and the free trade zone became a strong magnet for people from the rural areas of Amazonas and neighboring states. As the population grew (Graphic 1), the ruling elites and the government destroyed huge swathes of forest to build new housing developments (Silva, 2011, p.521). Thus was the genesis, as of the 1960s, of the housing projects in the districts of Raiz, Flores, and Parque 10.

Graphic 1: Population growth in Manaus, 1970 to 2010



Source: IBGE (2010).

Leishmaniasis left a trail of destruction in Manaus. Heitor Vieira Dourado, director of the former tropical disease clinic, reported on the first great outbreak in the district of Coroado, in 1971, which affected almost five thousand people. Speaking to *Jornal do Brasil* newspaper in 1972, he said that cutaneous leishmaniasis, hepatitis D, and other forms of hepatitis on the Solimões river were the Amazon's most pressing public health challenges (Médico..., 24 fev. 1972).

Marcus Vinítius Guerra, a physician from the same institution, mentioned another great outbreak during the construction of the city's international airport in 1972. There, the workers were falling ill so often that it shook the paradigm then in vogue that malaria should only be looked for in patients presenting with fever. Accordingly, more attention was paid to the parasites themselves (Guerra, 1 jun. 2016).

In 1978, Marcus Luiz Barroso Barros and Marcilene Gomes Paes, physicians from the Institute of Tropical Medicine, treated hundreds of patients with leishmaniasis in a small outpatient clinic set up in the district of São José Operário, an area of primary forest in the outskirts of the city, cleared by the government and given over for house building. Together with Marcus Vinítius Guerra, Nelson Antunes de Araújo Filho, and the entomologist Nelson Fé, they formed the institute's leishmaniasis unit. In the mid-1980s they were joined by the physician Jorge Augusto de Oliveira Guerra and other medical doctors and students. According to the epidemiological bulletins, leishmaniasis was second only to malaria in the number of cases (Barros, 12 set. 2016).

That year, while the peripheries of Manaus grew apace, the government set about building a new sector of the Cidade Nova housing project, adding over ten thousand new homes, which were gradually occupied as of 1981. The land where they were built had been completely deforested. Because it was so near the forest, with an abundance of vectors, and because basic infrastructure and amenities were lacking, like waste collection and running water, it witnessed serious outbreaks of the disease (Andrade, 1998, p.35). According to the local press, at the height of this epidemic some three hundred people were treated per day (Surto..., 12 jul. 1985).

Studies done at the time showed that ACL often affected the workers and residents who lived or worked near the forest. It presented mainly in the form of skin lesions (individual or multiple) that were flat and round, had clearly defined edges, with an incubation period that ranged from two weeks to several months. Less often, it would also present in mucous membranes (Paes, Barros, Toledo, 1997, p.II.3.5). There was a popular belief that the extract of a type of tuber (*Zamia ulei*), known as *batata de onça*, would treat these "fierce wounds." In 1988, scientists from INPA attempted to prove the efficacy of this Amazonian plant in the treatment of the disease. However, a study on hamsters showed that "unlike the hoped-for leishmanicide action, the experimental results indicated extremely dangerous activity" (Silva et al., 1988, p.212).

Treatment with antimonials was painful and potentially toxic. Today, the pentavalent form of meglumine antimoniate (glucantime) is the primary treatment, and pentamidine and anphotericin B are used in cases that do not respond to antimonials (Rath et al., 2003, p.551-554). The Institute of Tropical Medicine tested new drugs for its treatment and did much of the clinical care, while INPA built up its knowledge about the species of medical interest. An INPA entomologist, Rui Alves Freitas, took part in tests for one of the alternative treatments developed at the institute, taking rifampicin[9] after catching leishmaniasis caused by *L. (V.) guyanensis* during fieldwork. However, its therapeutic effect proved inferior to that provided by the antimonial (Freitas, 18 maio 2017). In the 1980s, the epidemic raised the number of cases to over one thousand a year.

In Amazonas, 3,464 cases of cutaneous leishmaniasis were recorded in 1985, dropping to 1,641 in 1986. In 1987 and 1988, similar numbers were recorded: 2,528 and 2,532 (Guerra et al., 2015, p.13). Over half of these cases were treated at the Institute of Tropical Medicine. Most of the patients came from Cidade Nova, Colônia Santo Antônio, and adjacent areas. Most cases occurred in unregulated occupations known as "squats" and plots of land in different parts of the city: São José, Tancredo Neves, Cidade de Deus, and elsewhere. Deforestation coupled with extremely limited sanitation, propitious biological conditions, and contact with insect vectors and vertebrate hoses infected with *Leishmania* gave rise to severe outbreaks of ACL (Barrett, Senra, 1989, p.255).

By the late 1990s and early 2000s, when urban development brought the rise in cases under control, INPA and the Institute of Tropical Medicine engaged in studies to elucidate the relationship between the epidemiology of leishmaniasis, vegetation dynamics, and climatic factors, in particular rainfall and density of phlebotomine sandflies. In the metropolitan area of Manaus (Careiro da Várzea, Iranduba, Itacoatiara, Manacapuru, Novo Airão, Presidente Figueiredo, and Rio Preto da Eva), where most of the state's cases of ACL were reported (Maciel, 2013, p.17), it was found that the outbreaks varied according to rainfall patterns. From November to June, the risk was higher, diminishing in the period from July to October, when the waters were low (Carvalho, 2011, p.55).

Similarly, in studies conducted as of 2001 in Rio Preto da Eva, the municipality with the second highest number of cases, where INPA set up an important partnership with Hospital Thomé de Medeiros Raposo and Manoel Rumão primary healthcare unit, it was found that climatic and social factors were instrumental in the emergence of cases, especially in patients from the settlements along the AM-010. On weekly visits, the scientists would collect sandflies and material from lesions in search of the species of vectors and parasites. Investigations conducted between 2005 and 2012 led to the identification of phlebotomine sandflies related to infection by *L. (V.) guyanensis*, responsible for over 80% of cases in that area, and cases related to *Leishmania (V.) naiffi*, and *Leishmania (L.) amazonensis* were identified (Figueira et al., 2014, p.173; Naiff Jr., 2009, p.103).

Similar studies were done by scientists from the Federal University of Amazonas at an oil exploration plant in the microregion of the middle Solimões river, in the Urucu region, Coari municipality, some 650km away from Manaus. In 1986, when the company announced the discovery of a large natural gas reserve, the construction of a gas pipeline became the target of much controversy because of the socioenvironmental and economic implications of the project. The idea was to supply Manaus, already the country's second biggest industrial hub.

The scientists found that the conditions in the biome meant there was a great diversity of *Leishmania* species, including the ones that caused leishmaniasis in man. Parallel to the studies done by the university, in August 2003, Luís Gomes, Liliane Nery, Francimeire Gomes, Rui Freitas, and Antônia Franco, from INPA, began a survey of the phlebotomines in the area of influence of the Urucu-Coari-Manaus gas pipeline. They managed to identify 25 species from eight sub-genera and four groups, of which *Lutzomyia umbratilis* was the most abundant (Gomes et al., 2009, p.234).

In 2006, when the construction of the pipeline began, outbreaks of the disease jeopardized the work. The workers contracted it when they came into contact with infected phlebotomines as they penetrated the dense forest to do the geophysical surveys, environmental impact studies, geotechnical and seismic surveys, and drill boreholes. In Coari, leishmaniasis was classified as an occupational illness because of the transmission pattern linked to the natural disease cycle (Alecrim et al., 2014, p.76). When the construction work ceased in the region, its incidence declined.

In Amazonas, ACL has affected children, youth, adults, and old people of both sexes, especially those who inhabit and work near forested areas. Major development projects cause environmental imbalances and result in human/vector contact in areas of risk and consequently outbreaks. Leishmaniasis has therefore been included in the agendas of the health services and institutions in Manaus and has mobilized an increasing number of physicians, public health specialists, and other scientists in a bid to study, provide medical care, and, to a far lesser extent, provide preventive and educational measures for the residents.

Final considerations

It was in the 1970s that cutaneous leishmaniasis emerged as a major health issue in the Amazon. It did so in direct association with economic and political changes which caused profound socioenvironmental, urban, and demographic transformations. One important contributory factor to this was the migratory flow triggered by the creation of the free trade zone of Manaus in 1967 and other large-scale development projects in subsequent decades.

There is a certain similarity between the outbreaks seen in São Paulo in the early twentieth century, during the construction of a railroad, and these more recent outbreaks, also associated with the construction of large government-sponsored developments in the Amazon. In both cases, the cutaneous and mucocutaneous leishmaniasis epidemics were linked to the presence of humans in forests and with extensive deforestation for large-scale developments.

The intense flows of people, the uncontrolled occupation of the peripheries of Manaus, the movement of workers to the state to build the BR-174 and AM-010 highways and to work in the mines in Pitinga and on the construction of Balbina were all propitious for the incidence of leishmaniasis. In Manaus, these migrant jobseekers encountered a dire reality, like the one experienced by the residents of Colônia Santo Antônio narrated at the beginning of this article. Without even basic sanitation, drinking water, or public services, including healthcare, these populations were already facing extremely precarious living conditions when they were afflicted by violent outbreaks of leishmaniasis and malaria.

Brazil's economic policies in the 1960s and 1970s, driven by industrialization, the modernizing of farming practices, and urban development, ushered in a road-dry land-subsoil pattern of development that prevails to this day. Its cornerstones are big infrastructure projects, agribusiness, mining, and predatory logging, irrespective of the environmental costs. This model has wrought extremely rapid changes on ecosystems, which have been threatened by the appropriation of their natural resources, not to mention increased inequalities related to the well-being and health of the population and the emergence of leishmaniasis and other parasitic diseases.

Besides the transformations it brings to the environment – its fauna, flora, and mineral resources – this model has changed the sociocultural and economic way of life of river-dependent and indigenous communities. As their health and sanitation have been degraded, these groups have become increasingly vulnerable to epidemics of infectious parasitic diseases.

Repeated, refractory outbreaks of leishmaniasis are just one indicator that the current economic development model has more than run its course. The precarious living conditions of the vulnerable populations whose workforce keeps the cogs of this predatory, capital-concentrating model spinning are met by a health system that is overloaded and public policy responses that prove ineffectual.

Cutaneous leishmaniasis emerged in this context as a medical and public health challenge along with the emergence and consolidation of what is now Heitor Vieira Dourado Tropical Medicine Foundation and INPI. At these two institutions, great synergy between science and public medical/health care can be observed, but little headway has been made in terms of the treatment, prevention, and control of the leishmaniasis that still afflicts populations living in rural Amazonas state and the peripheries of Manaus.

This same contradiction can be seen throughout Brazil. Although in recent decades great strides have been taken in understanding various aspects of different forms of leishmaniasis, very little has been done in the way of government action to apply this knowledge to effectively control and reduce the cases of the endemic.

The important work of scientists at the institutions from Amazonas engaged in the study of leishmaniasis has been instrumental in building a body of knowledge about this disease and ways to combat it. The processes and facts reported here indicate the urgent need for more sustainable, equitable, and ecologically sound policies and programs to be planned, discussed, and evaluated for the social, economic, and public health development of the Amazon and Brazil.

NOTES

[1] The free trade zone of Manaus was devised by a group of politicians and intellectuals from Amazonas, based on the Asian model, and formalized by means of Act 3.173, of June 6, 1957, as a free economic zone. Implemented ten years later by the military government through decree 288, of February 28, 1967, it offered businesses tax incentives for thirty years for the purpose of developing an industrial, trade, and farming hub in the Amazon.

[2] Djalma da Cunha Batista – physician, writer, president of the Amazonian Academy of Letters and of INPA – was a hybrid researcher who transited between the scientific and literary worlds. He studied salmonellosis in the 1950s and was keenly interested in tropical medicine.

[3] Mário Augusto Pinto de Moraes was a physician and the first director of the Faculty of Medicine at the University of Amazonas, in 1965. He served as director of the Second Division of Medical Research at INPA (1957-1970), where he coordinated the first project designed to study cutaneous leishmaniasis in Amazonas.

[4] Arthur César Ferreira Reis (1906-1993) was a politician and historian from Amazonas. A staunch nationalist and leading political player in the Amazonian scene, he was the first superintendent of the Amazon Development Department (Sudam), formerly the Department of the Plan for the Economic Development of the Amazon (SPVEA); director of INPA (1956-1958), and governor of the state of Amazonas from June 24, 1964, to January 31, 1967.

[5] Félix Pifano Capdevielle (1912-2003), a Venezuelan physician and researcher, published over 250 works on tropical medicine, especially Chagas disease, cutaneous leishmaniasis, malaria, schistosomiasis, and arboviruses.

[6] Hervé Alexandre Floch (1908-1996) was a physician, biologist, and director of the Pasteur Institute in Guyana and in Guadalupe. He identified *L. tropica guyanensis* as the organism responsible for cutaneous leishmaniasis (*pian-bois*) in Guyana.

[7] The classification of the species of the genus *Leishmania* is hampered by the great morphological similarity between them. Initially, they were identified by the clinical presentation of the diseases,

although epidemiological data on the vectors and reservoirs suggested that the parasite populations were extremely heterogeneous. Based on extrinsic criteria, such as the parasite's behavior in a culture and in a hamster, Lainson and Shaw combined the species into three groups: *Leishmania braziliensis*, *Leishmania mexicana*, and *Leishmania donovani*. In 1987 they reviewed this classification into two sub-genera, *Viannia* and *Leishmania*, based on clinical and epidemiological characteristics, as well as biological, biochemical, and molecular aspects of the parasites.

[8] Environmental impact studies and environmental impact reports are multidisciplinary technical documents designed to enable a broad, comprehensive evaluation of the significant environmental impacts of a major development and indicate corresponding mitigatory measures.

[9] An antibiotic that inhibits the multiplication of bacteria sensitive to this medication; especially used in the treatment of Hansen's disease (*Mycobacterium leprae*) and tuberculosis (*Mycobacterium tuberculosis*).

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