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Geographical and Environmental Variables of Leishmaniasis Transmission

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1. Introduction

Leishmaniasis, an infectious disease is not contagious. It belongs to the group of tropical neglected diseases [1, 2] that are ignored as priority in terms of eradication. It is estimated to be the ninth largest cause of disease among infected individuals [3, 4] ; it can cause intense epidemics that are primarily associated with the nutritional and the migratory factors [5, 6].

Most likely leishmaniasis originated in East Africa, however, it has been reported in ancient Egypt and in Christian Nubian approximately 4,000 B.C. In fact, it appears that Egyptians got the disease in the trade, as Egyptian Nile Valley is not a niche to sand flies [7]. Currently it has been reported in more than 80 countries, primarily in the developing countries in 4 continents, reaching indices around 500,000 new cases/year, with relatively higher incidence in India, Bangladesh, Nepal, Sudan and Brazil; approximately 200 million people have been estimated to get the exposure to the risk of its transmission [8].

Protozoan *Leishmania*, a unicellular flagellate, is the root cause of the disease; the parasite is transmitted to humans via female sand flies and manifests into two main forms: visceral [LV], and tegumentary [LT], the later divides into cutaneous [LC] and mucocutaneous [LMC] sub forms [7] (figure 1). Leishmaniasis has different clinical forms depending on the parasite, immune responses of the infected individuals and additional still unknown factors. Indeed,

studies on leishmaniasis could be focused on both unknown and known factors to eradicate this disease.

The LV, also known as Kala-azar (Indian name), black fever or DumDum fever, is the most severe form of leishmaniasis (figure 1) caused by *Leishmania donovani* and *Leishmania infantum* (*Leishmania infantum chagasi*, a subspecies typical of Brazil), both protozoans belonging to the same family, *Trypanosomatidae*. These species have different geographical distribution: *Leishmania infantum* is typical of South America, Europe and Northern Africa, while *Leishmania donovani* is commonly found in Eastern Africa.

LV is a chronic and systemic disease characterized by anemia, mucosal ulcers, fever, hepatomegaly and splenomegaly, lymphadenopathy, pancytopenia, weight loss, weakness and, eventually death due to lack of treatment [9].

The most common form of leishmaniasis in the world is LC, it can progress to other forms and is caused by about 20 different species of *Leishmania*; it is known with various different names, such as Aleppo boil, Chiclero ulcer, Bauru's ulcer, Bay sore, Biskra button, Lahore sore, Oriental sore, Pian bois, Uta and leishmaniasis tropica.

LMC produces destructive and disfiguring lesions in the body, especially in the face (figure 1), they are primarily caused by *Leishmania braziliensis* and rarely by *Leishmania aethiopica*.

Regardless of the type of leishmaniasis this disease is transmitted through the bite of the female sand flies and the geographical distribution of this disease is directly associated with the habitat of its vector. Phlebotomine sand flies primarily inhabit hot and wet tropical regions with regular pluvial index [10], however, sometimes they also inhabit the dry and hot places; therefore, the environmental and geographical niches of this vector that are associated with its natural vertebrate hosts are determinants of the disease transmission.

The association of the vector with natural reservoir became a propitious factor towards keeping an endemic status for leishmaniasis. In fact, there are many natural reservoirs such as canine, avian (chicken), bovine, equine, caprine, ovine, swine and feline [11-14] ; all of them inhabit the same regions as Phlebotomine.



Figure 1. Clinical features of *cutaneous leishmaniasis* (left), and *mucocutaneous leishmaniasis* (right).

In addition, an important factor associated with leishmaniasis occurrence is the canine leishmaniasis (figure 2), a zoonosis that indirectly indicates the prevalence of this disease in humans at a specific site.

Indeed, leishmaniasis is associated with the tropical and the equatorial zones, poor sanitary conditions and surveillance in the areas where the parasites and the vectors are close to the reservoir and the humans, therefore, the most important point to understand the cause of epidemic and the transmission of the disease is the knowledge on the geographical and the environmental variables. Nevertheless, both these variables will be considered here into two categories: the worldwide and the regional.

In the geographic terms, the worldwide variables represent the geographic area where the vector has its niches and where the climate is favorable to its development. However, there are places and the environmental factors that are relatively propitious to the transmission of leishmaniasis than other factors such as higher population of the sand flies; these are considered as the regional variables that would be accountable for the frequency of the disease.

In the environmental terms, the worldwide variables indicate the global climate and the associated landscape; however, the anthropomorphic factors and the climate peculiarities in a specific region represent the regional variables.

This chapter will present the worldwide and the regional aspects of geographical and environmental variables associated with leishmaniasis transmission.



Figure 2. A photographic representation of a dog displaying clinical symptoms of canine leishmaniasis.

2. Materials and methods

The goal of this chapter is to collect the information from an extensive literature using the followings electronic databases: MEDLINE, Plos, PubMed, LILACS, CAPES periodic, Open Journal System, Scielo and Google Academic. The descriptors used were: *leishmaniasis*, *leishmaniasis visceral*, *leishmaniasis cutaneous*, *leishmaniasis mucocutaneous*, *Phlebotomine*, *the sand flies*, *the geographical aspects of leishmaniasis* and *the environmental aspects of leishmaniasis*.

2.1. Inclusion criteria

Indexed papers published in the last 20 years; classic indexed papers on more ancient and severe areas. Some textbooks have also been used to elaborate this chapter.

2.2. Exclusion criteria

Papers that did not mention the main ideas used in this chapter and the texts with the same contents as the most recent papers used here.

3. Geographical variables

3.1. Worldwide variables

In the terms of biosphere, geographical variables of leishmaniasis transmission are associated with tropical zone as well as hot and the wet climates with regular pluvial index [10]. The countries that are underdeveloped as well as the developing countries show the highest incidence of leishmaniasis transmission (figures 3 and 4).

Indeed, both human LV and LC follow the geographical distribution of the insect vector (see [15]); it is found globally between tropics but has also been detected in some regions with relatively rigorous winter such as in France [16], Portugal, Russia and China [3].

Based on the information available since past ten years, in Africa, the data on reported cases of LV are sparse and the reported cases in sub-Saharan African region are scarce (table 1); Nigeria had just one reported case within this period [3]. However, in Eastern African countries, LV is endemic and the reported cases have increased above predicted expectation in the last 20 years [9]. The countries with the most infections are Sudan [17, 18], Ethiopia [2, 9], South Sudan [3], Somalia, Uganda, Kenya [9] and Eritrea [3] (table 1, figures 3 and 4).

As for LC, Sub-Saharan region (figures 3 and 4) showed elevated number of the reported cases than cases for LV, i.e., 154 cases of LC in comparison to 1 case of LV; whereas the countries with higher number of LC cases are Cameroon and Nigeria respectively. In Eastern Africa, interestingly, Eritrea is the country with the lowest cases of LV and the highest cases of LC, while other countries in this region have no reported cases in the past ten years (table 1). In general, in African subcontinent, the number of reported cases of LV is much higher than those of LC, i.e., 8,571 of LV in comparison to 204 of LC.

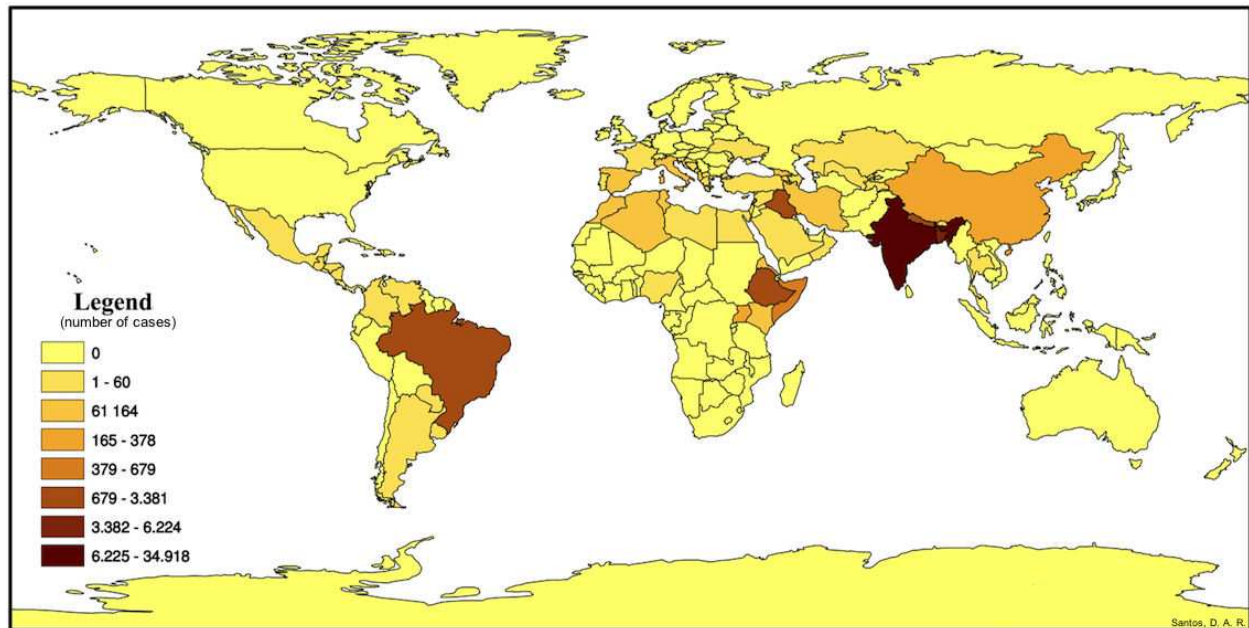


Figure 3. World LV distribution in the last 10 years.

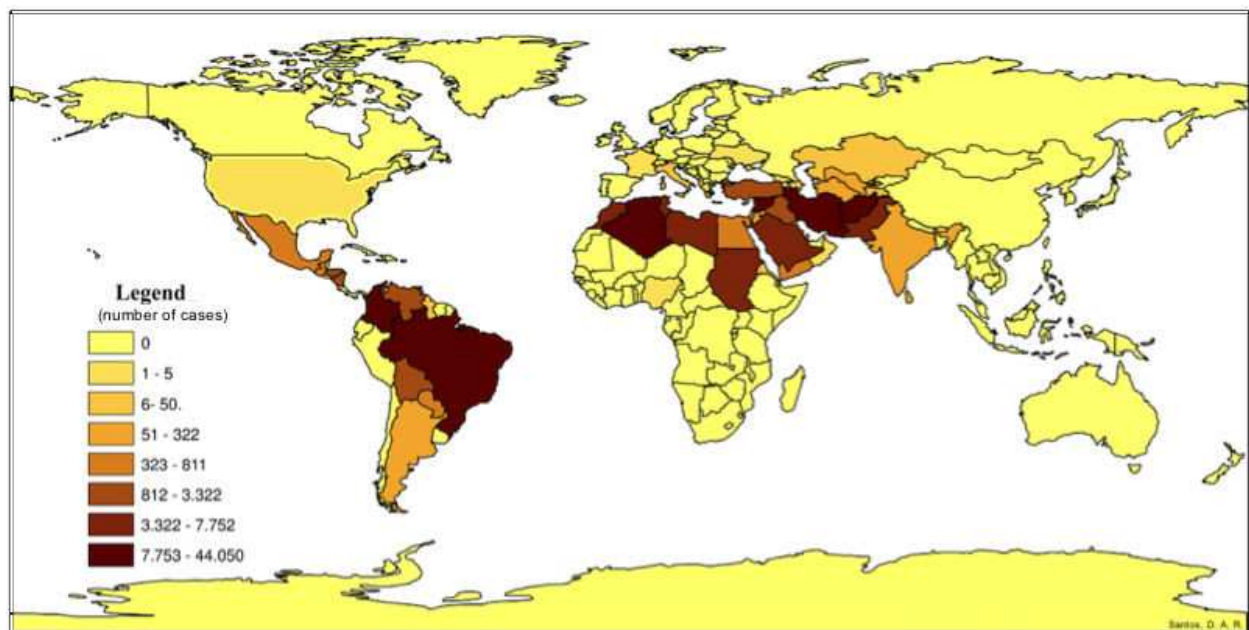


Figure 4. World LC distribution in the last 10 years.

Reported cases in Africa		
	Visceral leishmaniasis	Cutaneous leishmaniasis
<i>Sub-Saharan African region</i>		
Cameroon	0	55
Cote d'Ivoire	0	1
Ghana	0	27
Mali	0	58
Nigeria	1	5
Senegal	0	8
Total	1	154
<i>Eastern African region</i>		
Eritrea	100	50
Ethiopia	1860	0
Kenya	145	0
Somalia	679	0
Sudan	3742	0
South Sudan	1756	0
Uganda	288	0
Total	8570	50

Table 1. Geographical distribution of LV and LC in Africa based on reference [3].

In Asian subcontinent from the Middle East to Central Asia, significant LV prevalence was only found in Iraq with more than 1,000 reported cases; in China, Georgia and Iran the reported cases ranged at little over 100. In this Asian region, the reported cases of LC are much higher than those of LV, i.e., 61,015 of LC in comparison to 2,497 of LV. As regards to LC, more than 1,000 cases were reported in Iran, Afghanistan, Pakistan, Saudi Arabia and Iraq; and in Yemen and Uzbekistan the number of reported cases was over 100 (table 2) (figures 4 and 5).

In Indian subcontinent [3, 20] and in Southwestern Asia [3, 21], there are more than 1,000 reported LV cases in countries like India, Bangladesh and Nepal; in this same territory LC cases higher than 100 in number have only been reported in Sri Lanka and India. The reported total LV cases are higher than LC cases in Indian Subcontinent and in Southeastern Asia, i.e., 42,623 of LV in comparison to 478 of LC (table 2, figures 4 and 5).

In Asia, overall number of the reported LC cases is higher than those of LV cases, i.e., 61,493 of LC while 45,120 of LV.

Reported cases in Asia		
	Visceral leishmaniasis	Cutaneous leishmaniasis
<i>Middle East to Central Asia</i>		
Afghanistan	0	22620
Armenia	7	0
Azerbaijan	28	17
China	378	0
Georgia	164	5
Iran	149	24630
Iraq	1711	1655
Kazakhstan	1	15
Oman	1	5
Pakistan	0	7752
Saudi Arabia	34	3445
Tajikistan	15	25
Turkmenistan	0	99
Ukraine	2	2
Uzbekistan	7	142
Yemen	0	603
Total	2497	61015
<i>Indian Subcontinent and Southeastern Asia</i>		
Bangladesh	6224	0
Bhutan	2	0
India	34918	156
Nepal	1477	0
Sri Lanka	0	322
Thailand	2	0
Total	42623	478

Table 2. Geographical distribution of LV and LC in Asia based on reference [3].

In the Mediterranean region, countries with more than 100 reported LV cases are Morocco, Italy, Spain, Albania and Algeria; for LC, the countries with more than 1,000 reported cases are Algeria, Syria, Tunisia, Libya, Morocco and Turkey (table 3, figures 3 and 4). Israel, Egypt, Jordan and Palestine are on lower tier of LC prevalence, in these countries, over 100 LC cases have been reported (table 3, figures 3 and 4). Thus in this region, overall number of the reported

LC cases is much higher than LV cases, i.e., 85,886 of LC in comparison to 874 of LV in the last ten years.

Reported cases in the Mediterranean region		
	Visceral leishmaniasis	Cutaneous leishmaniasis
Albania	114	6
Algeria	111	44050
Bosnia and Herzegovina	2	0
Bulgaria	7	0
Croatia	5	2
Cyprus	2	1
Egypt	1	471
France	18	2
Greece	42	3
Israel	2	579
Italy	134	49
Jordan	0	227
Libya	3	3540
Macedonia	7	0
Malta	2	0
Montenegro	3	0
Morocco	152	3430
Palestine	5	218
Portugal	15	0
Spain	117	0
Syria	14	22882
Tunisia	89	7631
Turkey	29	2465
Total	874	85556

Table 3. Geographical distribution of LV and LC in the Mediterranean region based on reference [3].

In Latina America, the number of LV cases have increased in northern Argentina [22], in areas bordering Brazil and Paraguay, in Colombia [23], in Venezuela [24] as well as in North America [25] ; recently one case has been recorded in Uruguay as well [19] (table 4).

Brazil is the only country in the Americas with over 1,000 reported cases of LV, in other countries the reported cases of LV are lower than 100 (table 4). In contrast, LC is relatively widespread with 10 countries that have over 1,000 reported cases, these are Brazil, Colombia, Peru, Nicaragua, Bolivia, Venezuela, Panama, Ecuador, Costa Rica and Honduras in descending order of prevalence. Additionally, 5 countries show over 100 reported cases, they are Mexico, Guatemala, Paraguay, Argentina and French Guyana respectively (table 4).

An interesting aspect in the Americas is the inclusion of the United States in the world scenario with 42 reported cases of LC [25].

The overall number of the reported cases of LC is much higher than those of LV, i.e., 66,983 of LC in comparison to only 3,668 of LV in the American subcontinent.

Specifically in Brazil, and mostly in other developing countries, leishmaniasis was restricted to rural areas; however, currently the disease has advanced to other regions and has reached urban peripheries [26-28]. This demonstrates that the urbanization process is one of the major factors for the scattering of leishmaniasis.

Reported cases in America		
	Visceral leishmaniasis	Cutaneous leishmaniasis
Argentina	8	261
Bolivia	0	2647
Brazil	3481	26008
Colombia	60	17420
Costa Rica	0	1249
Ecuador	0	1724
French Guyana	0	233
Guatemala	15	684
Guyana	0	16
Honduras	6	1159
Mexico	7	811
Nicaragua	3	3222
Panama	0	2188
Paraguay	48	431
Peru	0	6405
Suriname	0	3
Venezuela	40	2480
Uruguay	1	0
United States	0	42
Total	3668	66983

Table 4. Geographical distribution of LV and LC in the Americas, based on references [3], [19] and [25].

The geographical distribution of leishmaniasis in the world appears to be changing, firstly, the variation of global climate [25, 29] could be increasing the area of Phlebotomine niches; and secondly, the globalization of economy increases the migration of the people among countries thereby increasing the contact of people with Phlebotomine niche where leishmaniasis is either incipient or non-existent. The former hypothesis could be explained by the growing economy in BRIC countries, such as Brazil, Russia, India and China; among these India and Brazil are endemic to leishmaniasis.

Nowadays, the geographical distribution of leishmaniasis is similar for LC and LV in the continents; however, differences exist among the countries. Indeed, approximately 57% of countries studied here showed both LC and LV. Nevertheless, in the last ten years the number of the reported LV cases in the world is approximately 58,413 with 77.2% in Asia. In contrast, the number of the reported LC cases in the world is approximately 214,082 with almost 40% of those in the Mediterranean region.

In fact, the reported LC cases are much higher than those reported for LV. A possible explanation for this scenario is the number of LC parasites, there are over 20 parasites causing LC whereas only just few parasites cause LV. Although there are only few sand fly species that are vectors for both LV and LC, both conditions have the same kind of reservoir hosts [30].

The above problems that have emerged from studying the worldwide geographical distribution must be resolved with the collaborative prevention measures by the countries where leishmaniasis is endemic; such cumulative force would lead to the global solutions to eradicate this disease.

3.2. Regional variables

Regional variables represent areas of the countries where the probability of existence of leishmaniasis has increased. In fact, there are internal regions in different countries such as the rural zone and the urban periphery where the incidence of leishmaniasis has increased (figure 6). A plausible explanation for such increase is the higher density of Phlebotomine and natural reservoir hosts of the parasites inhabiting these areas; these areas in the developing countries are infused with poverty where people live and work close to the forests or the woodlands.

In the developing countries, leishmaniasis was a rural disease, however, it was found to be associated with the growing urbanization. This disease began to develop in the urban periphery in Brazil and it was noted around 1970s [31]. A probable explanation of such spreading is the internal migration of the people from the rural zone to the urban areas [30].

People that arrive from the rural zones to the urban areas usually have limited and scant financial resources and therefore, they inhabit the periphery of the towns that are regions with the woodland and the forest remnants; they are basically inter tropical zones. Such city periphery is a risk zone for the dissemination of leishmaniasis since here the contact among humans, Phlebotomine and their hosts is maximized. Indeed, some reservoir hosts are used as the pets and others are raised in peridomestic areas to feed these people.

This regional geographical distribution of leishmaniasis incidence must be analyzed by public health agencies to identify and verify the risk zone for leishmaniasis. Additional studies are also required to identify all the causative factors; specifically the data on Phlebotomine niches, presence of natural reservoir hosts of *Leishmania* and the sanitary quality of the habitat for the people are of utmost importance.

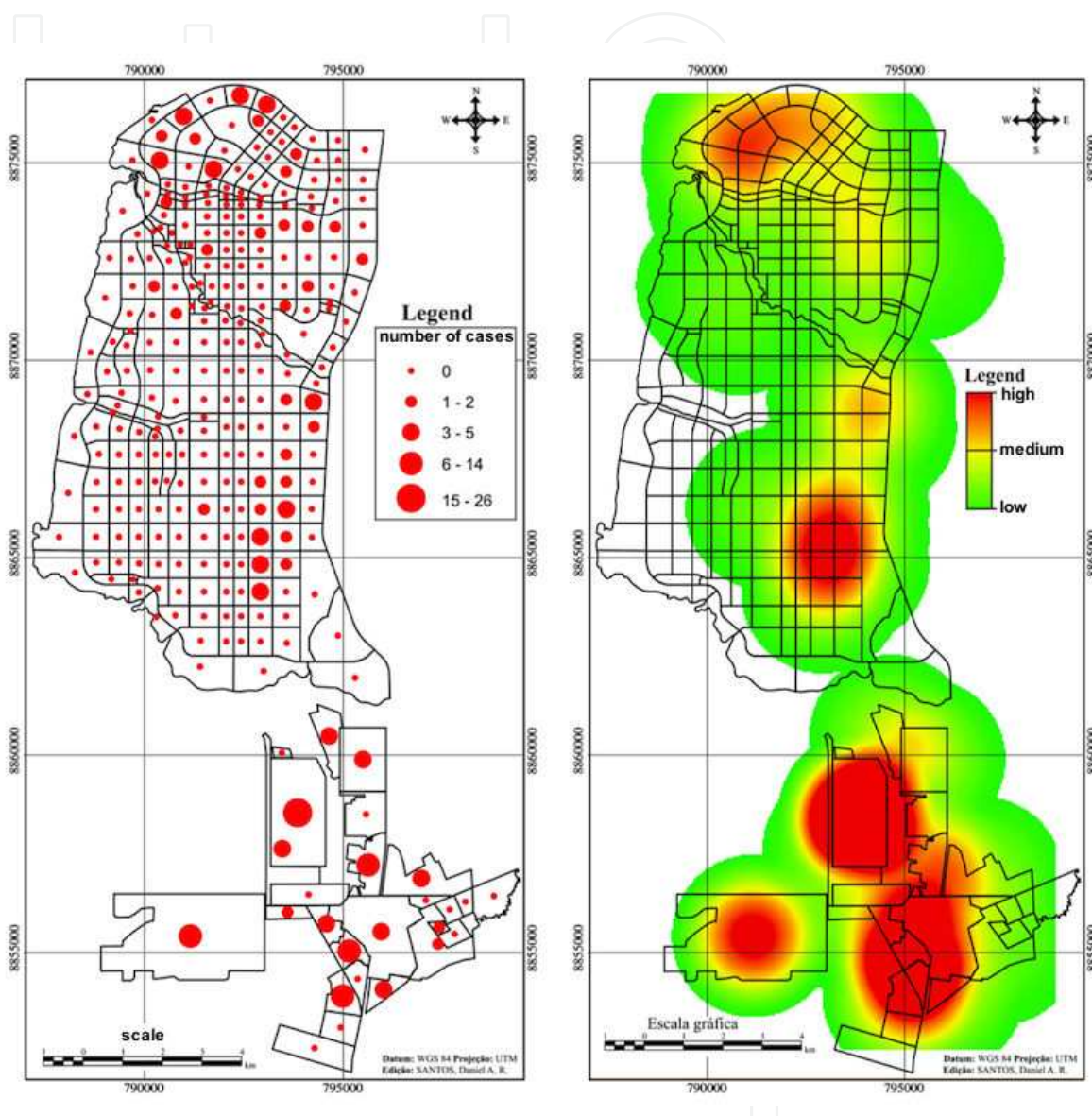


Figure 5. The map of city of Palmas, northern Brazil, is shown. On the left the dots represent reported cases for leishmaniasis in this municipality from 2007 to 2012. The Kernel map of the same locality is demonstrated on the right, where darker/stronger color indicates the higher number of cases. The bigger dots (left) and the dark color distribution (right) are present in periphery of the town, that is closest to the forest.

Briefly, the geographical areas of leishmaniasis dissemination are the rural zones and the urban peripheries.

In geographical and regional terms the best way to start the fight against this disease, is the construction of a risk map for each municipality where leishmaniasis is endemic; it will indicate

the points where the eradication effort should be focused. Such approach would include the elimination of Phlebotomine along with the complete removal and killing of the natural reservoir hosts of *Leishmania* from the population. We shall not address these specific problems in this chapter, however, georeferencing studies using adequate maps such as Kernel maps (figure 5), utilizing the new technologies for geographical representation along with spatial analysis of databases [32] appear to be the principle strategies to combat leishmaniasis.

Leishmaniasis is a complex multi-systemic disease [33], and therefore, it requires multidisciplinary team effort of public health agencies working together with the health professionals and the scientists to generate the most positive results towards its eradication.

Specifically as regards to the topic of this chapter, the monitoring of the reported cases from the data is an important tool on the geographical variables to control leishmaniasis since it may spread by the internal migration of the people to endemic areas and increasing its incidence due to elevated person-to-person transmission in the crowded living conditions [32].

The analysis of the geographical region is the first step to monitor leishmaniasis, however, majority of causes for endemic outbreak are associated with the natural environment as well as man-made factors such as the human migration, the deforestation, the urbanization and the malnutrition [34].

4. Environmental variables

4.1. World variables

It is a well-established fact that the maintenance of LV is related to the environmental variables favoring the presence of both the vectors and the vertebrate hosts at the same site [24], and it can occur also for LC.

It is known that the geographical distribution of leishmaniasis follows the distribution of sand fly niches, this fact is observed worldwide and in the regional analyses. However, the distribution of the sand flies is dependent on the environmental variables such as the temperature, the vegetation, and the humidity.

Indeed, the geographical variables are directly associated with the environmental variables in the biosphere and are inter-dependent. The geographical distribution of leishmaniasis generally occurs in the tropical and the equatorial regions, where warm and rainy weather prevails [10, 35, 36] favoring Phlebotomine reproduction [37, 38].

In fact, the analysis of the planet temperature map compared to the maps of reported cases of leishmaniasis (figures 4 and 5) demonstrates that these regions are parallel (figure 7).

In general, leishmaniasis is primarily present in the tropics, however, its incidence is increasing in other areas as well, and most likely this increase is associated with the global climate changes [25].

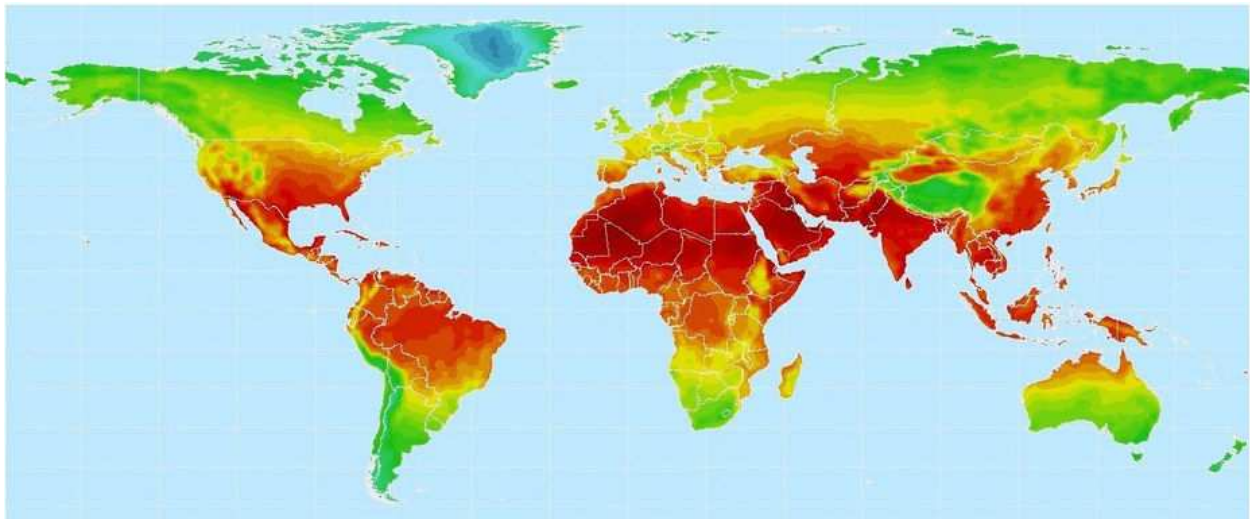


Figure 6. World temperature map where darker colors indicate higher temperatures

The world climate changes are implicated with physical consequences [21] as well as with the alterations of the vector niches and the reservoir species for the infectious diseases [21, 25].

According to Gonzalez *et al* [25], leishmaniasis is expanding to northern United States from Mexico and Texas, where it is considered autochthonous, primarily due to the increase in the niches of the sandflies associated with the reservoir hosts to *Leishmania*; however, other associated reasons could be dog importation [30] and the increase in human migration and/or travel in the recent years.

The movement of people occurs from countries where leishmaniasis is endemic to countries where climate is temperate. The people move from the temperate areas to the tropical and the equatorial climates, particularly for the holidays, sometimes they carry their dogs and other pets [30].

Climate is not the only factor associated with the vector niches, the vegetation also has some impact. In fact, in some regions, the climate indicates the existence of certain kind of vegetation, i.e., it is usual to think of the tropical forest in the tropical climate and the equatorial forest in the equatorial climate, however, it is possible to find desert, savanna, Cerrado (Brazilian savanna) and Atlantic forest in the same regions where the tropical and the equatorial climates prevail.

Phlebotomine prefers the forest areas, but, interestingly, it can also be found in open and urban areas [35].

In summary, the world environmental variables linked to Phlebotomine niche exist mainly in Latina America and some parts of Africa and Asia. The hot and the wet climates are associated with the forest and the woodlands areas; however, some species prefer open and the dry areas. In all these regions, it is possible to find some kind of host to *Leishmania*, nevertheless, the density of sand flies in some areas depends on the regional environmental variables.

4.2. Regional variables

In terms of the geographical and the regional variables, the main factor for the scattering leishmaniasis is the presence of Phlebotomine in the specific areas. In fact, since sandflies breed in soil or litter, they are dependent on the availability of water and the dampness. In addition, their small size enables them to live in various different microhabitats [36], however, an in-depth analysis detailing the breeding sites of sand flies and their larval development remains scarce [15].

Nevertheless, the peri-urban areas are important risk factors for leishmaniasis transmission since they maintain the niches for Phlebotomine and natural reservoir hosts. Indeed, some studies have demonstrated the increase of known natural reservoir hosts including *Galus domesticus* [39] and the pigs [40] in such areas.

In relation to the local environment, the urban periphery is frequently inhabited by poor populations, they are forced to live far from downtown and these habitats grow as the people arrive there from the rural areas. This is a common case in the poor and developing countries. Such lesser-developed areas are comprised of the forests or the woodlands and become a favorable place to increase contact of sandflies with the people as well as domestic and wild reservoir hosts of leishmaniasis.

At the same time, this population has limited access to basic sanitation and sewage treatment, and therefore, it generates exclusionary urbanization [41].

In fact, the deforestation linked to unplanned urbanization seems to be the cause of peak incidence of leishmaniasis in some regions [32]. Urbanization parameters associated with the growing cities and the deforestation areas generate ecological changes [41] that could modify the forest flora; this in turn generates trunks of dead trees thereby increasing the amount of decomposed organic material as well as the microorganisms on the ground that positively affect Phlebotomine cycle [38, 42-45].

These findings justify that in the peri-urban areas there is increase in number of the infected people carrying leishmaniasis and other infectious diseases that are dependent on the vector transmission, the people in those areas get higher exposure to vectors and reservoir hosts.

The reservoir hosts to *Leishmania* are the rodents, the marsupials, the monkeys, wild canines [30], the domestic dogs, chickens, the cattle, the equine, the caprine, the bovine, the swine and the feline species [11-14, 30], they all inhabit the areas populated with the sand flies.

Indeed, the presence of the swine species in the peridomicile is an important risk of the contamination [40], and the contamination has also been found associated with the presence of chickens as wild predators that are potential wild reservoirs hosts of *Leishmania* and feed on them, thereby intensifying the parasite cycle to the human and the canine populations [39].

The life cycle of *Leishmania* is mainly associated with the ecological factors in the rural or the peridomicile areas that harbor the sand fly niches and the reservoir hosts with human habitation (figure 7).

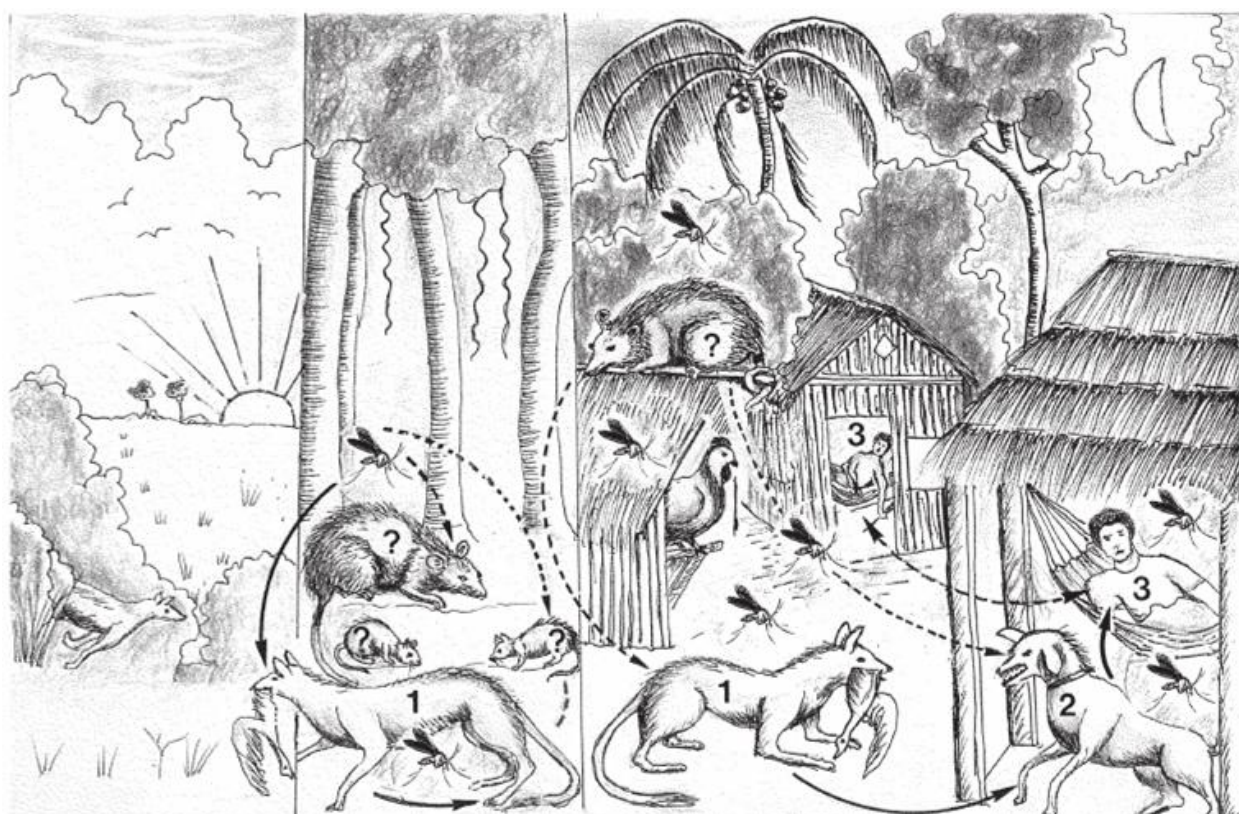


Figure 7. Scheme showing the life cycle of sandflies, reservoir hosts and humans, based on [46].

The human knowledge about leishmaniasis is not complete; many factors are still unknown or only partially known. Nevertheless, the current knowledge on this disease is adequate to develop accurate eradication strategies for the government and the public to work together developing specific protections with control of Phlebotomine by using insecticides, by removing organic material in the peridomicile areas [47, 48] and exterminating the contaminated reservoir hosts.

5. Conclusions

The aim of this chapter was simply to put together the collected information about the geographical and the environmental variables of leishmaniasis transmission. Leishmaniasis transmission is dependent on the association of contaminated sandflies with the reservoir hosts of *Leishmania* and the humans. In geographical terms association is favored in inter tropical regions, where the environmental factors such as the warm and the wet climate and certain types of the forest vegetation are predominant. In regional terms, the vicinity of the forest remnants or the woodland in the respective local periphery increases the density of sandflies thereby creating favorable conditions for the propagation of *Leishmania* life-cycle and its exposure to the people inhabiting that area.

Accurate and adequate public health policies and the proper dissemination of relevant information to the populations living in the endemic areas along with the severe control and the surveillance would be helpful in eliminating the contamination of humans and reservoir hosts by sandflies.

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