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Adapting to vector borne main diseases under climate change in Algeria

Présenté par **ACHOUR Serine**

Devant le jury :

Président(e):	**Kaidi R.**	**Professeur**	**ISV- Blida**
Examinatrice:	**Yahiaoui W.I**	**MCB**	**ISV- Blida**
Promotrice:	**Sahraoui N.**	**Professeur**	**ISV- Blida**

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Dedication

Dear family, Dear friends and team of work

I came here to thank you and to express my deep gratitude for your solidarity and support.

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RÉSUMÉ

Les données actuelles suggèrent que la variabilité climatique interannuelle et inter décennale a une influence directe sur l'épidémiologie des maladies à transmission vectorielle.
Et Le climat tropical de l'Algérie est favorable à la plupart des principales maladies à transmission vectorielle y compris : la leishmaniose et les fièvres hémorragiques à tiques.
La température, les précipitations, l'humidité et d'autres facteurs climatiques sont connus pour affecter la reproduction, le développement, le comportement et la dynamique des populations des arthropodes vecteurs de ces maladies. Le climat peut également affecter le développement d'agents pathogènes dans les vecteurs

L'objectif de cette étude est d'étudier le risque majeur de maladie à transmission vectorielle sous le changement climatique en Algérie (leishmaniose et maladie de Lyme).

La leishmaniose est une maladie causée par un parasite protozoaire intracellulaire (genre Leishmania) transmis par la morsure d'une phlébotomine femelle. Le spectre clinique de la leishmaniose s'étend d'un ulcère cutané de self-resolving à une maladie mucocutaneous mutilante et même à une maladie systémique viscérale.

La borréliose de Lyme, également connue sous le nom de maladie de Lyme est une maladie à organes multiples d'origine animale, causée par des spirochètes de Borrelia burgdorferi (Bb) transmis par une morsure de tiques, qui affectent généralement la peau, le système nerveux, le système musculo-squelettique et le cœur.

Mots clés : vectorielle, leishmaniose, phlébotomie, borréliose, tiques, Borrelia burgdorferi.

ABSTRACT

Current evidence suggests that inter-annual and inter-decadal climate variability have a direct influence on the epidemiology of vector-borne diseases.

The tropical Algeria climate is favorable to most major vector-borne diseases including: leishmaniosis and tick-borne hemorrhagic fevers.

Temperature, precipitation, humidity, and other climatic factors are known to affect the reproduction, development, behavior, and population dynamics of the arthropod vectors of these diseases. Climate also can affect the development of pathogens in vectors

The objective of this study was to study the major vector-borne disease risk under climate change in Algeria (leishmaniosis and Lyme disease).

Leishmaniasis is a disease caused by an intracellular protozoan parasite (genus *Leishmania*) transmitted by the bite of a female phlebotomine sand-fly. The clinical spectrum of leishmaniasis ranges from a self-resolving cutaneous ulcer to a mutilating mucocutaneous disease and even to a visceral systemic illness.

Lyme borreliosis, also known as Lyme disease is a multi-organ animal-borne disease, caused by spirochetes of *Borrelia burgdorferi* (Bb) transmitted by a bite of ticks, which typically affect the skin, nervous system, musculoskeletal system and heart.

Keywords: vector, leishmaniasis, phlebotomine sand-fly, Lyme borreliosis, ticks, Borrelia burgdorferi.

ملخص:

تشير البيانات الحالية إلى أن تقلب المناخ بين السنوات والعقود لها تأثير مباشر على وبائيات الأمراض المنقولة بالنواقل كما أن المناخ الاستوائي في الجزائر ملائم لمعظم الأمراض الرئيسية المنقولة بالنواقل بما في ذلك: داء الليشمانيا والحمى النزفية التي ينقلها القراد.

من المعروف أن درجة الحرارة والرطوبة والعوامل المناخية الأخرى تؤثر على تكاثر وتطور ناقلات مفصليات الأرجل لهذه الأمراض. يمكن أن يؤثر المناخ أيضًا على تطور مسببات الأمراض في النواقل.

الهدف من هذه الدراسة هو دراسة المخاطر الرئيسية للأمراض المنقولة بالنواقل في ظل تغير المناخ في الجزائر (داء الليشمانيا وداء لايم).

داء الليشمانيا هو مرض يسببه طفيلي البروتوزوان داخل الخلايا (جنس الليشمانيا) الذي ينتقل عن طريق لدغة ذبابة رملية أنثوية. يتراوح الطيف السريري لداء الليشمانيا من قرحة جلدية ذاتية الحل إلى مرض مخاطي مشوه وحتى إلى مرض نظامي حشوي.

داء لايم بوريليوسيس، المعروف أيضا باسم مرض لايم هو مرض متعدد الأعضاء ينتقل عن طريق الحيوان، بسبب سبيروشيهات بوريليا بورغدورفيري التي تنتقل عن طريق لدغة القراد، والتي تؤثر عادة على الجلد والجهاز العصبي والجهاز العضلي الهيكلي والقلب.

الكلمات الدالة: الأمراض الرئيسية المنقولة بالنواقل، الليشمانيا، داء لايم، القراد، لايم بوريليوسيس.

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Abbreviation List:

LD: Lyme disease

Bb: Borrelia burgdorferi

OmpA : Outer membrane protéine A

FlaB: Lyme disease spirochete - flab gene & protein - Borrelia burgdorferi

OspA : outre surface (lipo)protéine A

OspC : outer-surface protein C

Osp : outer-surface protein

ZVL: Zoonotic Visceral Leishmaniasis

ZCL: Zoonotic Cutaneous Leishmaniasis

ACL: anthropontic Cutaneous Leishmaniasis

VL: Visceral Leishmaniasis

CL: Cutaneous Leishmaniasis

CanL: Canine leishmaniosis

HIV/AIDS: human immunodeficiency virus

PKDL: Post-kala-azar dermal leishmaniasis

KDNA: Leishmania kinetoplast DNA

L. tropical: Leishmania tropical

L. major: Leishmania major

FIV (FeLV): Feline immunodeficiency virus and feline leukemia virus in cats from an area endemic for visceral leishmaniasis

Introduction

Diseases transmitted by insect vectors have a major impact on human and animal health, as well as on the economy of societies.

In addition, the Global climate change might expand the distribution of vector-borne pathogens in both time and space, thereby exposing host populations to longer transmission seasons.

This has focused on important multivoltine insects and hard-bodied (ixodid) ticks diseases that are transmitted by the vectors from infected to uninfected humans (Ogden and Lindsay, 2016).

The aim of this research is to describe how the climate change can make an impact on spatiotemporal occurrence and abundance of vectors and how the spread altering conditions can affect the development and dynamics of the disease vectors and the pathogens they carry.

In Algeria the main diseases concerned are leishmaniasis and Lyme disease due to the abundance of mosquitoes, ticks, and flies. Which they're the disease vectors.

So as a first main disease, Lyme disease is a multi-organ animal-borne disease, caused by spirochetes of *Borrelia burgdorferi* (Bb), which typically affect the skin, nervous system, musculoskeletal system and heart. A history of confirmed exposure to tick bites is the reason, and typical signs and symptoms of Lyme borreliosis was confirmed most frequently appear in spring, summer and early autumn which explain the input of the climate change in the disruption of this tick and the damage that it can cause (Biesiada *et al*., 2012).

Furthermore, for the Leishmaniosis disease, Leishmaniasis is caused by an intracellular parasite transmitted to humans and animals by the bite of a sand fly Clinical features depend on the species of *Leishmania* involved and the immune response of the host. Manifestations range from the localized cutaneous to the visceral form with potentially fatal outcomes (Torres-Guerrero et al., 2017).And the activity season revealed that weeding and harvesting time (July–December) had higher incidence of leishmaniasis than dry time (January–June)(Gebremichael Tedla *et al*., 2018).

Chapter I:

Vector borne disease and climate change

Vector-borne diseases and climate change

1. Climate change and vector-borne disease challenge:

Climate change is a complex phenomenon that is threatening all aspects of human society including increasing risks to human and animal life and health (Tubiello, 2018). Most climate-related health impacts are mediated by complex ecological, environmental and social processes, while the impacts vary in magnitude, scale and duration as a function of the local environmental conditions and the vulnerability of the human population; (Shuman, 2010) (Smith *et al*., 2010) (Goldstraw *et al*., 2016) . Climate change impacts human health directly through extreme heat, cold, drought or storms, or indirectly by changes in air quality, water availability, food provision and quality, and other stressors. The main health effects are related to extreme weather events (including extreme temperatures, droughts and floods), changes in the distribution of climate-sensitive diseases (such as vector-, water- and food-borne diseases), and changes in environmental and social conditions.

According to the WHO, between 2030 and 2050, climate change is expected to cause approximately 250,000 additional deaths per year, from malnutrition, malaria, diarrhea and heat stress alone. The direct damage costs to health is estimated to be between 2–4 billion dollars per year by 2030 (Orru *et al*., 2021).

In a particular case due to the inherent sensitivity of arthropod vectors to weather and climate which affect vector habitat range, distribution and abundance, vector-borne diseases have been identified as likely candidates that will be affected by climate change (Martens et al., 1995).

However, the link between climate change and vector-borne disease has been a topic of intense debate over the years owing to the numerous interacting drivers, especially non-climatic, that also affect vector-borne disease dynamics (Patz *et al*., 2005) (Rogers and Randolph, 2006) (Altizer *et al*., 2013) (Campbell-Lendrum et al., 2015). Climate has likely played an important role on human health to date, but this has been highly mediated by the numerous interacting other stressors and drivers of disease risk which to date have been poorly quantified (Smith *et al*., 2010).
Climate warming is likely to increase disease risk in areas currently limited by lower temperatures; however, the nature of public health measures in place in these locations are likely to significantly modify the impacts of these changes.

The challenge in attributing climate change to changes in vector-borne disease incidence lies in clearly linking the effect of climate change on elements which affect the basic reproduction number of a disease and disentangling this effect from the numerous confounders which can also affect these parameters doing so requires extensive data over time which in many cases is simply not yet available at a level of detail that would allow confident predictions.

2. Climate sensitive vector-borne diseases in Algeria:

Several studies have sought to make predictions on the effects of climate change on diseases and the exact change in distribution that leishmaniosis or Lyme disease and other vector-borne diseases in Algeria will exhibit as a result of climate change remains unclear, with some areas likely to experience decline as a result of temperatures exceeding the vector or pathogen`s tolerance levels while other areas will likely experience emergence as a result of temperatures favoring transmission (Rogers and Randolph, 2006).

Changes in seasonality and length of the transmission season are expected as has been suggested by models of the health impacts of emerging and re-emerging vector-borne disease will inevitably depend on localized factors and the interacting effects of climate and socioeconomic conditions (Morin *et al*., 2013).

In Algeria, the largest country in Africa, there are three types of climates:

(1) the Mild Mediterranean climate of the coast

(2) the transitional climate of the Northern hills and mountains in the north of the country, which is slightly more Continental and moderately rainy.

(3) the desert climate of the vast area Occupied by the Sahara, when reaching the Algerian south.

The northern climate Is conducive to the development of arthropods such as ticks, fleas, lice, Mosquitoes and sandflies and therefore to diseases that can be transmitted Causing a public health problem (Gage *et al*., 2008) .

A recent review of emerging vector-borne diseases of concern in Algeria identified Lyme. Disease and leishmaniosis because they are the major diseases that threaten public health.

Leishmaniosis is a re-emerging disease in Algeria and seems to spread because of a combination of factors: environmental changes as well as factors related to the immune status of the host and drug resistance (Adel *et al*., 2014) .

For the Lyme disease since Algeria is one of the Mediterranean regions known for its great bioclimatic variety. The research is showing that the seasonal abundance of ticks and the prevalence of tick-borne pathogens is essential to describe in order to better understand the risk of tick-borne diseases. Many studies are therefore being conducted on the detection of *Rickettsia* in different tick species, and studying the dynamics of transmission of this bacterium. Because of these main climatic characteristics, the composition of tick fauna in the mediterranean region is highly variable, and the distribution of the most important tick species can change significantly depending on the specific characteristics of the region concerned (Dib *et al*., 2019).

Chapter 2:

Lyme disease

Lyme disease (Borreliosis)

1. Main disease:

Lyme disease or Lyme borreliosis, is an infectious disease caused by the Borrelia bacterium which is extended by ticks. It is transmitted to humans and animals through the bite of infected blacklegged ticks. Typical symptoms include fever, headache, fatigue, and a characteristic skin red rash which is the most common sign of infection, known as erythema migrans (fig.1), that appears at the site of the tick bite about a week after it occurred. If Lyme disease is left untreated it can lead to damage in the kidneys, nervous system, and heart (Biesiada *et al*., 2012).

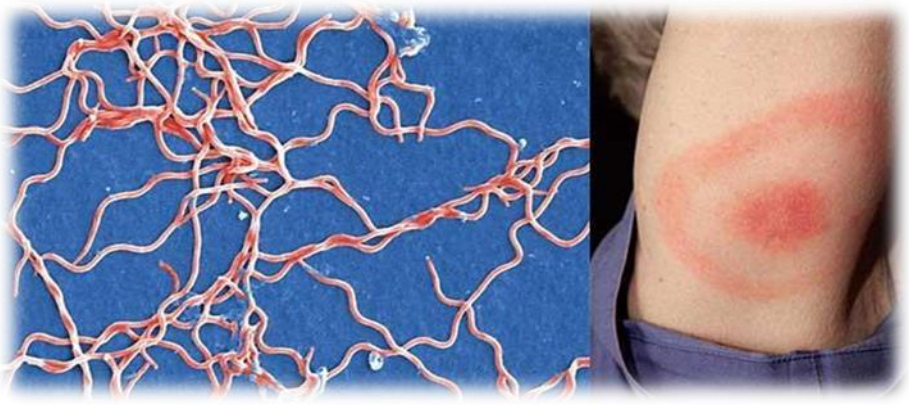

Figure 1: Pathogenesis of Lyme disease caused by Borrelia burgdorferi (James G,2007)

On the right we have a skin lesion showing an erythma migran after a bite of a tick and on the left Borrelia burgdorferi form under a Microscope

2.Etiology:

Lyme disease (Lyme borreliosis) is caused by a group of related spirochetes isolated from the main vector, that is, hard ticks (Ixodes spp.) and from patients with Lyme borreliosis belonging to the genus Borrelia. They are Gram-negative and have a typical spirochetal structure with a protoplasmic cylinder surrounded by an internal membrane and a peptidoglycan wall. The protoplasma contains a linear chromosome and many linear and circular plasmids. Flagella in variable numbers (7 to 11 in B.burgdorferi; 15 to 30 in B. recurrentis) originate at the ends of the protoplasmic cylinder and they are enveloped by the outer membrane. Thus, they are endoflagella that cause the spiral shape as well as the screw-like motility. The outer membrane contains immunogenic proteins used in diagnostic tests (Biesiada *et al*., 2012).

The Lyme borreliosis spirochetes form a complex (B.burgdorferi s.l.) that by now contains 37 named genospecies . Within this complex, B. burgdorferi sensu stricto, B. garinii, and B. afzelii are the most important human pathogens. All of them isolates belong to B. burgdorferi s.s., while in Europe, all three species have been isolated, although most of them belong to the latter two species. These epidemiological differences may account for regional differences in clinical symptomatology (Mertz, 2016).

3.Occurrence:

Lyme borreliosis has been found in the entire Northern Hemisphere. The incidence in Central Europe is estimated at 60 to 130 cases per 100 000 inhabitants per year that is, 40 000 to 90 000 new cases per year in Germany.

The tick responsible of the disease may nevertheless contribute to the spread of the disease as it can be found in many wild and domestic animals, including birds. The occurrence of Lyme borreliosis in humans is closely associated with tick infestation. Ticks prefer moist areas: lightly grown deciduous forests, meadows adjacent to rivers, parks, and gardens. At special risk are forest workers, tourists sleeping in tents, and walkers (Mertz, 2016).

In Algeria:

In our country, twenty-one cases of Lyme disease were reported in Algiers for the first time. (fig.3)(Benredjem et al., 2014) . However, these cases were diagnosed by detection of only serum antibodies against *B. burgdorferi* by ELISA without confirmation by Western blotting.

To investigate of Lyme disease and tick-borne rickettsioses transmitted by *I. ricinus* ticks in northeastern Algeria, started when they collected ticks by using the flag method in El Ghora (Bougous, El Tarf). Results showed that in Algeria (Borrelia burgdorferi sensu lato) is the responsible agent which include more than 11 species (Benredjem *et al*., 2014) .

In northern Africa, the main vector of Lyme disease is same in Europe (Ixodes ricinus ticks) , and this disease has been suspected to be present in this region of north Africa (*Algeria ,Morocco and Tunisia*) and it were reported first time in ALgeria, during 1996–1999 (Benredjem *et al*., 2014).

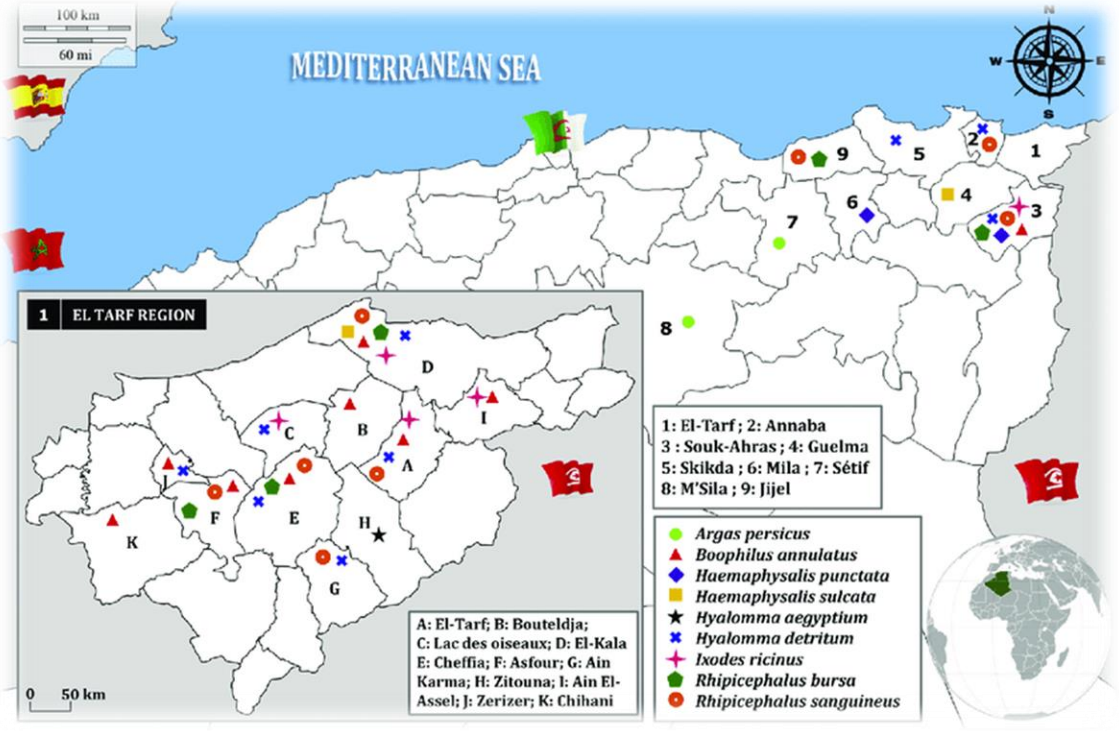

Figure 2: *Geographical distribution of tick species collected in nine regions of northeastern Algeria(Boucheikhchoukh et al., 2018)*

In the Investigation of Lyme disease and tick-borne rickettsial disease transmitted by I. ricinus ticks in northeastern Algeria, they use the flag method to collect ticks in El Ghora (Bougous, El Tarf).

The ectoparasites were collected in March 2012, and the genera and species were determined by using taxonomic morphology keywords (Benredjem et al., 2014).

Positive results were confirmed by using a standard PCR specific for the ompA gene (*Outer membrane protein A*) of Rickettsia spp. and the 16S rRNA and flaB genes (*FlaB - Borrelia burgdorferi*) of Borrelia spp (fig.3),Ninety-four ticks were collected by using the dragging method; these ticks belonged to 2 species: 85.1% (80/174) were I. ricinus ricks and B. garinii is the most neurotropic of the genospecies of B. burgdorferi sensu lato; it causes meningo polyneuritis and, rarely, encephalomyelitis . Clinicians need to be aware of the prevalence of this bacterium in Algeria. The results help clarifies the epidemiology of B. garinii in Algeria. R. monacensis is an agent of tick borne diseases that was detected in Algeria in 2009 (Benredjem *et al*., 2014).

Figure 3: The blacklegged tick (ixodes spp), tick that carry Lyme Disease (Gary Alpert,2018)

The few cases that have been described were characterized by influenza-like symptoms, fever, an inoculation eschar, and a generalized rash, the early stage as a symptom was (erythema migrans) is seen most often during summer, with a peak in June/July. Weeks two months later, with a peak in October, neurological and cardiac symptoms will appear. The late stage with chronic skin and joint disease and neurological symptoms become manifest 2 to 3 years after infection. The most important reservoirs are wild rodents, particularly wood and yellow necked mice, bank voles, and hedgehogs whose complement does not affect bordelaise (by contrast, the complement of domestic animals and deer is able to lyse bordelaise). The main vectors of B. burgdorferi s.l. are various hard ticks that feed over several days.

The risk areas for Lyme disease and infection with *R. monacensis* include cool and humid areas in the Atlas Mountains. In this region, humans can come in contact with *I. ricinus* ticks, and these ticks might play a major role in transmission of *B. garinii* and *R.monacensis* (Benredjem et al., 2014).

4.Transmission:

B. burgdorferi s.l. residing in the midgut of a tick expresses outer surface protein A (OspA = *The outer surface protein A)* of the spirochete Borrelia burgdorferi. It was formerly used as an antigen in Lyme disease immunization. that mediates binding to the midgut epithelium of the tick. When the tick starts feeding on a host, most borreliae cease to express OspA at the higher temperature and begin to express OspC. These processes enable the borreliae to exit from the midgut, to spread via the hemolymph and to invade the salivary gland. They then manage to enter the bite wound via the infected saliva. During the first hours of tick attachment, the risk of infection is minimal but increases after 36 h. Prospective studies have estimated the risk of infection after any tick bite to be 4 to 8%. The risk after the bite of a tick infected with borreliae is, however, 23%. Whether other

blood-sucking insects such as deer flies (Stomoxys calcitrans) or horse flies (Tabanidae) may transmit borreliae has not been elucidated but it would probably be of sociological importance. Simultaneous infections with Babesia spp. or Ehrlichia spp. are possible and should be taken in consideration (Mertz, 2016).

Typical signs and symptoms of Lyme borreliosis was confirmed most frequently appear in spring, summer and early autumn which explain the input of the climate change in the disruption of this tick and the damage that it can cause (Biesiada *et al*., 2012).

5.Clinical Manifestations:

In analogy to infection with Treponema pallidum, the clinical course of Lyme borreliosis has been subdivided into three stages (Tab. 1).

- Stage 1 the early-localized infection;
- Stage 2, the dissemination;
- Stage 3 the persistent infection

Tableau 1 : Clinical stages of Lyme borreliosis (Mertz, 2016)

STAGE	INFECTION	CLINICAL MANIFESTATION
Stage 1	**Early localized**	● **Erythema chronicum migrans (fig.5)** ● **Lymphadenosis cutis (solitary lymphocytoma)**
Stage 2	**Disseminated**	● **Multiple erythema migrans (fig.4)** ● **Disseminated lymphocytoma** ● **Systemic infection with general malaise, myalgias, arthralgias** ● **Early Lyme borreliosis (aseptic meningitis, neuritis, meningoradiculitis Bannwarth)** ● **Carditis (tachyarrhyhmias, a-v block)**
Stage 3	**Chronic**	● **Acrodermatitis chronica atrophicans** ● **Arthritis** ● **Peripheral,neuropathies,progressive encephalomyelitis (very rare)**

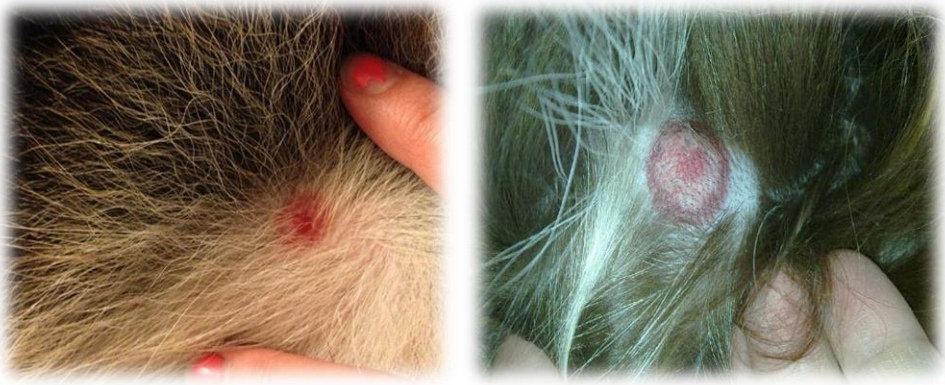

Figure 4: *Erythema migrans following tick bite in a dog (Paul Daniels,2017)*

Figure 5 : *Erythema migraine human with the Tick bite (Berríos-Torres et al., 2017)*

6.Animals infection:

The signs of Lyme disease vary for each animal. Many animals can have Lyme disease and show no signs rodents and wild animals seem to only have in apparent infections, dogs, possibly also horses and cattle may have overt borreliosis.

- **In dogs**: recurrent mono- or oligoarthritis, fever and malaise have been observed, and renal disease such as glomerulonephritis and kidney failure were seen in Bernese Mountain dogs and in retrievers. Neurological and cardiac manifestations are rare. After an incubation period of 2 to 4 months, one to five exacerbations will generally take place, each lasting from 2 to 5 days. Recovery occurs after 6 to 8 weeks, although the organisms may persist in various tissues.
- **In Horses*:*** may also show a multitude of symptoms, mostly recurrent arthritis, neuropathy, and ulcerative keratitis. They have been interpreted as signs of borreliosis as diagnostic tests were positive but could not be reproduced in controlled experiments.

- **In cattle*:*** arthritis, myocarditis, pneumonia, and stillbirth were seen and interpreted as signs of borreliosis (Littman *et al*., 2018).

7.Diagnosis:

7.1 Human:

Doctors diagnose it based on symptoms and a history of tick exposure.

Two-step blood tests are helpful if used correctly. but the accuracy of the test depends on when you got infected. In the first few weeks of infection, the test may be negative, as antibodies take a few weeks to develop. Tests aren't recommended for patients who don't have Lyme disease symptoms.

The test is an ELISA with purified or recombinant antigens. If it is positive, a confirmatory test, generally an immunoblot differentiating between IgM and IgG is required. In B. burgdorferi s.l. infections, many immunologically relevant proteins can be found which are located at the surface (Osp) and in the cell itself (Mertz, 2016).

7.2 Animals:

The diagnosis of Lyme disease is often based on the signs and history. For example, a veterinarian might suspect Lyme disease in a dog with recent lameness, a mild fever, and a history that includes possible exposure to ticks. Standard blood studies are not very helpful in diagnosis because the results tend to fall within normal ranges despite signs of infection. However, these tests may be important in order to rule out other causes of disease. Antibodies against the disease-causing bacteria can often be detected 4 to 6 weeks after the initial infection and help confirm the diagnosis (Aiello *et al*., 1998).

8 Differential Diagnosis:

The differential diagnosis of erythema migrants must consider erythema annular centrifuge (associated with rheumatic fever), erysipelas (which develops faster and spreads within days), erysipeloid (associated with a professional history, e.g., in butchers), and erythema exsudativum multiforme. Arthritis also occurs in primary chronic polyarthritis and as para- or postinfectious complication of infections with yersiniae, salmonellae, Campylobacter, and chlamydiae (Mertz, 2016).

9 Prophylaxis:

9.1 Human:

Individual prophylaxis, especially in an infested region has to focus on exposition, that is, wearing protective clothing, rubber boots, etc. Long trousers should be tucked into socks. Spraying of permethrin on clothing and of repellents on wrists will improve protection. Wearing light-colored clothing will facilitate the discovery of ticks. The risk of disease is low at 24 to 36 h after the bite. After walking through infested areas, the search for ticks should start right away, and at the latest, 24 h later. When trying to remove a tick, turn it with a tick tweezer at the mouth parts. Most tick forceps are not fine enough and they will crush the tick. Better are tick cards that are pushed underneath the tick (do not use oil or glue). If an area is known for a high degree of infestation and if the time of the bite is known. Elimination of ticks from their natural environment has so far not met with success. The use of fungal blastopores and of nematodes is in an experimental stage. (Bratton *et al*., 2008).

9.2 Animals:

Animals should be treated regularly with a readily available, effective, tick-control product and should be routinely checked for ticks after they have been outside, especially if they have been in tall grass and brush during the spring, summer, or fall.

- Remove any ticks by using fine -pointed tweezers to grasp the head of the tick (right where it enters the skin). Pull the tick straight off, making sure not to grasp or squeeze its body.
- Dogs should be brushed regularly. watch carefully for any ticket that is removed and capture and dispose of them before they can either reattach to the dog or migrate to other pets or people household (Bratton *et al*., 2008).

Chapter 3:

leishmaniasis

Leishmaniosis disease

1. Main disease:

Leishmaniosis is a parasitic disease that is found in parts of the tropics, subtropics, and southern Europe. It is classified as a neglected tropical disease ,(NTD)Leishmaniosis is caused by infection with *Leishmania* parasites (fig.6), which are spread by the bite of phlebotomize sand flies (fig.7). There are several different forms of leishmaniosis in people. The most common forms are cutaneous leishmaniosis, which causes skin sores, and visceral leishmaniosis, which affects several internal organs (usually spleen, liver, and bone marrow)(Biesiada *et al*., 2012).

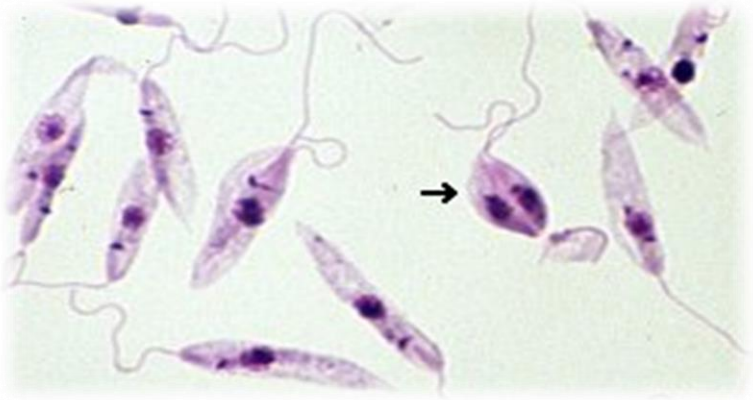

Figure 6 : Leishmania parasites(Janeaux, 2018)

Microscope image of Leishmania parasites form

Figure 7 : sandfly phlebotomize (Rogers et al., 2009)

2. Etiology:

Leishmaniosis is found in people in focal areas of approximately 90 countries in the tropics, subtropics, and southern Europe. The ecologic settings range from rain forests to deserts. Leishmaniosis usually is more common in rural areas than in urban areas, but it is found in the outskirts of some cities. Climate and other environmental changes have the potential to expand the geographic range of the sand fly vectors and the areas in the world where leishmaniosis is found (WHO .2020)

Leishmaniosis is found in people on every continent except Australia and Antarctica.

- In the Old World (the Eastern Hemisphere), leishmaniosis is found in some parts of Asia, the Middle East, Africa (particularly in the tropical region and North Africa, with some cases elsewhere), and southern Europe. It is not found in Australia or the Pacific islands.
- In the New World (the Western Hemisphere), it is found in some parts of Mexico, Central America, and South America. It is not found in Chile or Uruguay. Occasional cases of cutaneous leishmaniosis have been acquired in Texas and Oklahoma. (Mertz, 2016)

The number of new cases may vary or change over time and are difficult to estimate. For cutaneous leishmaniosis, estimates of the number of new cases per year have ranged from approximately 700,000 to 1.2 million or more. For visceral leishmaniosis, the estimated number of new cases per year may have decreased to <100,000, but previous estimates ranged up to 400,000 or more cases. The cases of leishmaniosis evaluated in the United States reflect travel and immigration patterns. For example, many of the cases of cutaneous leishmaniosis in U.S. civilian travelers have been acquired in common tourist destinations in Latin America, such as in Costa Rica(Steverding, 2017).

Overall, infection in people is caused by more than 20 species (types) of *Leishmanial* parasites, which are spread by about 30 species of phlebotomies sand flies; particular species of the parasite are spread by particular sand flies. The sand fly vectors generally are the most active during twilight, evening, and night-time hours (from dusk to dawn). In many geographic areas where leishmaniosis is found in people, infected people are not needed to maintain the transmission cycle of the parasite in nature; infected animals (such as rodents or dogs), along with sand flies, maintain the cycle (Muirhead-Thomson, 2013).

However, in some parts of the world, infected people are needed to maintain the cycle; this type of transmission (human—sand fly—human) is called anthropogenic. In areas with anthroponomics transmission, effective treatment of individual patients can help control the spread of the parasite (Inceboz, 2019).

3. Occurrence:

More than 90% of kala-azar (also known as visceral leishmaniasis) cases reported worldwide occur in Bangladesh, India, Nepal, Brazil, and Sudan. Other endemic areas are parts of Myanmar, China, Central Asia, Mediterranean littoral and regions of Sub-Saharan Africa, Central and South America. The number of new cases estimated worldwide is 400 000 per year and the number of related deaths is 50 000 per year. All age groups are susceptible, yet, the disease occurs mainly in children and adolescents up to an age of 20 years (~60% of cases). In the past, about 80% of the cases in the Mediterranean area concerned children below 5 years. Due to increasing numbers of clinical leishmanial disease in adult HIV infected people, the age-related distribution has changed. The disease is more common in rural areas, where living conditions of the human population and bionomics of phlebotomies fit closely together. However, rural exodus and increase of slums in bigger cities may result in the future in a higher prevalence in urban areas. Typical for visceral leishmaniosis caused by L. Donovan are epidemic outbreaks attributed to fluctuations in the human population and varying densities of the phlebotomies. A significant factor may also be general impairment of resistance to pathogenic agents due to malnutrition, particularly protein deficits, and helminth infections. The epidemiological type of the Mediterranean-Central Asian form of kala azar is found all over the Mediterranean basin, on the Atlantic coast of North Africa, Algeria, Portugal, the Caucasus, Iraq, and the Asian countries of the former Soviet Union as well as Central Asia and northern China(Mertz, 2016).

In Algeria:

Leishmaniosis has been classified primarily as a vector-borne disease that poses a major problem to public health in Algeria.

In the Mediterranean basin, leishmaniosis are neglected diseases that are emerging or re-emerging. Algeria belongs to the shortlist of the most affected countries for leishmaniosis, with more than 20,000 cases reported each year, and an incidence of 28.19 cases per 100,000 inhabitants. Zoonotic visceral leishmaniosis (ZVL) is caused by Leishman infimum, with dogs acting as the main reservoir and Phlebotomies longicuspis and P. pernicious acting as primary vectors. Historically present mainly in the humid and sub-humid regions of northern Algeria, it has extended from its historical foci of Kabyle (Tizi-Ouzou, Bejaïa) to Blida, Chlef, Medea, and Tipaza foci. The highest number of reported cases occurred in 1998 (310 reported cases) (fig.8) an overall increase recorded from 1994 to 2003 was followed by a decrease during the subsequent decade (Izri *et al*., 2021). In our country, cutaneous leishmaniosis (CL) caused by L. major, L. infimum, and L. tropical has a 30-fold higher incidence than the visceral form. Zoonotic are Phlebotomies papayas and Psammomys obesus, respectively. The disease is prevalent in 41 out of Algeria's 48 districts, spanning the North Saharan fringe, and the arid and semi-arid bioclimatic areas, including Biskra, Bordj Bou Arreridj, Batna, Djelfa, Saida, Sétif, M'sila, and Abadla. More recently, a spread of the disease has taken place towards M'sila, Ksar Chellala, Djelfa, and Bou-Saada foci, and the Northern part of the Tell Atlas, in the Soummam basin. Leishmania tropica causes anthroponotic cutaneous leishmaniasis (ACL), a chronic form with less than 100 cases per year that commonly occurs in sympatry with L. major. It is restricted to Constantine, Annaba, Ghardaia, and Tipaza. Phlebotomus sergenti is considered the proven vector of L. tropica, with humans as the primary reservoir. Nevertheless, some animals like Massoutiera mzabi (the Mzab gundi from the family Ctenodactylidae) are additional suspected reservoirs. Sporadic cutaneous leishmaniasis caused by L. infantum was first reported by Sergent in 1923. The parasitological, epidemiological, and clinical characteristics were individualized by Belazzoug et al. (1985). Izri and Belazzoug (1993) highlighted the vectorial role of P. perfiliewi in Ténès. It is responsible for sporadic cutaneous infections all over the coastal regions in northwestern Algeria (Oran, Tlemcen) and the Algerian Tell Atlas (Tizi-Ouzou, Bouira, Bord Menail, Tipaza, Blida, and Algiers). Herein, we diagnosed and identified Leishmania spp. from suspect CL patients originating from Algeria's geographical areas. This allowed us to update the geographical distribution of Leishmania sp. causing cutaneous infections in Algeria.(Izri *et al*., 2021).

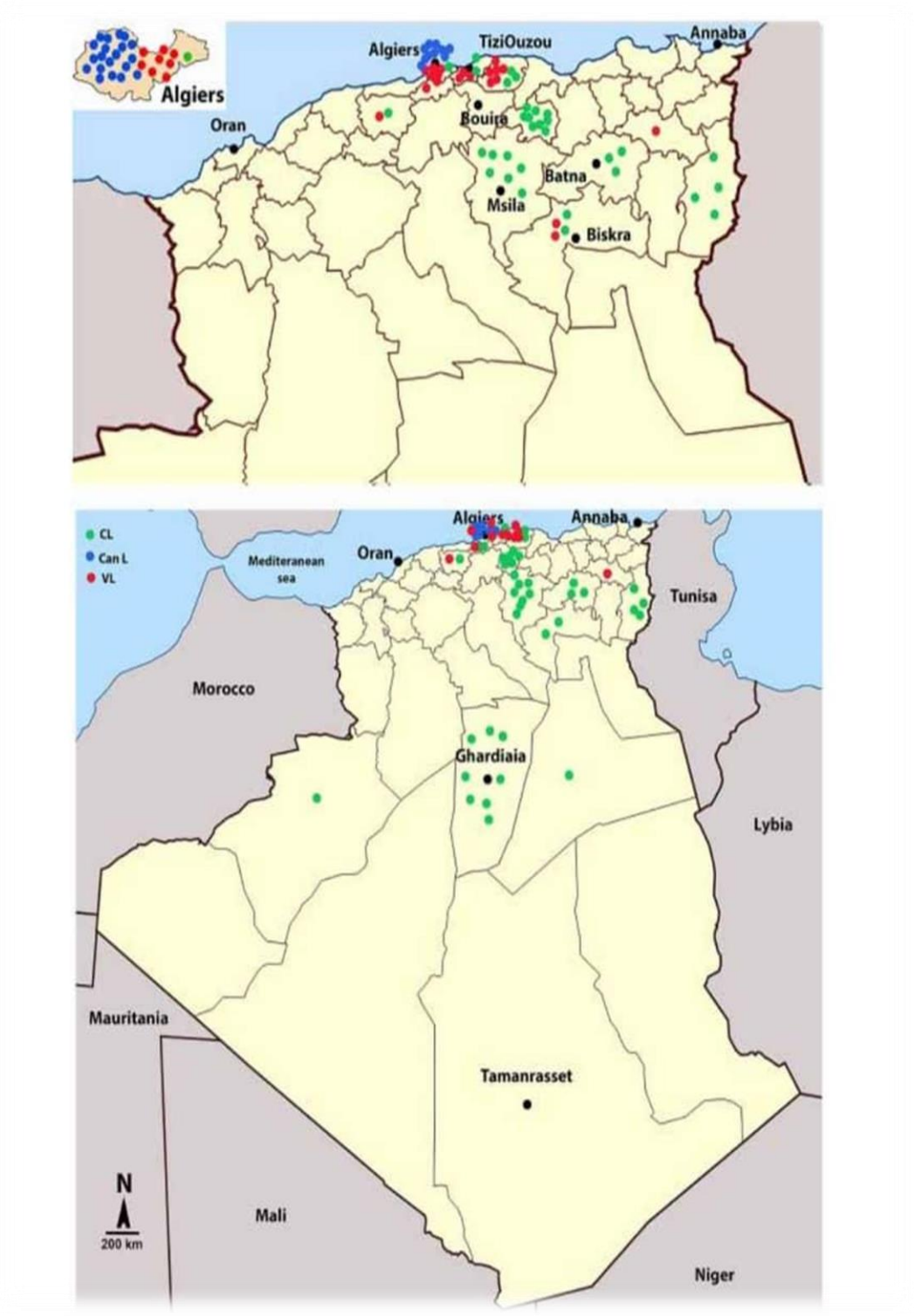

Figure 8 : Geographic disruption of Leishmania parasite isolated in Algeria (Aït-Oudhia et al., 2011).

Parasites were sampled from dogs (CanL) mentioned in the picture with the blue color and from human individuals with visceral (VL) mentioned with red color and cutaneous leishmaniosis (CL)mentioned zwith green color. The picture focus on northern territories of Algeria and of the Algiers region

4. Transmission:

Leishmanial parasites are transmitted through the bites of infected female phlebotomine sandflies, which feed on blood to produce eggs. The epidemiology of leishmaniasis depends on the characteristics of the parasite and sand-fly species, the local ecological characteristics of the transmission sites, current and past exposure of the human population to the parasite, and human behavior. Some 70 animal species, including humans, have been found as natural reservoir hosts of *Leishmanial* parasites(Postigo, 2010).

And the activity season revealed that weeding and harvesting time (July–December) had higher incidence of leishmaniasis than dry time (January–June)(Gebremichael Tedla *et al*., 2018)

4.1. Mode of transmission

Mainly, as a vector-borne disease through a bite of infective female phlebotomies (sandflies). L. major (leishmania major) is transmitted by Phlebotomies papayas from the animal reservoir to humans. L. tropical is transmitted by P. sergeant from person to person.

Very rarely, L. tropical (leishmania tropical) through transfusion.

4.2. Incubation period

- L. major: At least one week. Usually less than 4 months.
- L. tropical: At least one week. Usually 2–8 months.

4.3. Communicability period

- Not directly transmitted from reservoir to person, but infectious to sandflies as long as parasites remain in lesions in untreated cases, usually a few months to 2 years.
- Transmission is seasonal through adult sandflies. P. sergeant in Aleppo appears generally between May and October, with a usual peak in June and another in September.

4.4. Life cycle:

Life cycle of Leishman spp. and examples of molecules putatively involved in parasite infectivity and vascularization of infection. Phlebotomize sand flies release Leishmanial infective stages (i.e., met acyclic promastigotes) to the mammalian hosts during blood feeding. (fig.9)

(1): the parasites invade macrophages and granulocytes

(2 and 3): and develop to amastigotes inside the phagolysosome

(4): the amastigote stages replicate within the phagolysosome by simple division

(5): then, amastigote-containing macrophages are ingested by susceptible sand flies during the blood meal

(6): The parasites are released from the infected macrophages within the sand fly midgut

(7): where they transform into pericyclic promastigotes and divide. Then, the parasites migrate towards the stomodeal valve (anterior midgut) and transform into different promastigote subtypes that ultimately form met acyclic promastigotes

(8): These infective stages are then released into a new mammalian host during a subsequent blood meal and (9): include [10, 11, 12, and 13].

(10) =Amastigotes of viscerotropic Leishmania express A2 genes, implicated in visceral infection

(11)=Simultaneously,cox2 gens over pressed by infected macrophage promote parasite survival

(12)= Peritophins and chitins expressed by the sandfly midgut serve as a barrier to the migration of leishmania to the thoracic midgut, until their degradation by proteolytic enzyme

(13)= Salivary components(maxadilan,hyaluronidases)exacerbate parasite infectivity

Abbreviation: Cox2, prostaglandin-endoperoxide synthase 2(Cantacessi *et al*., 2015).

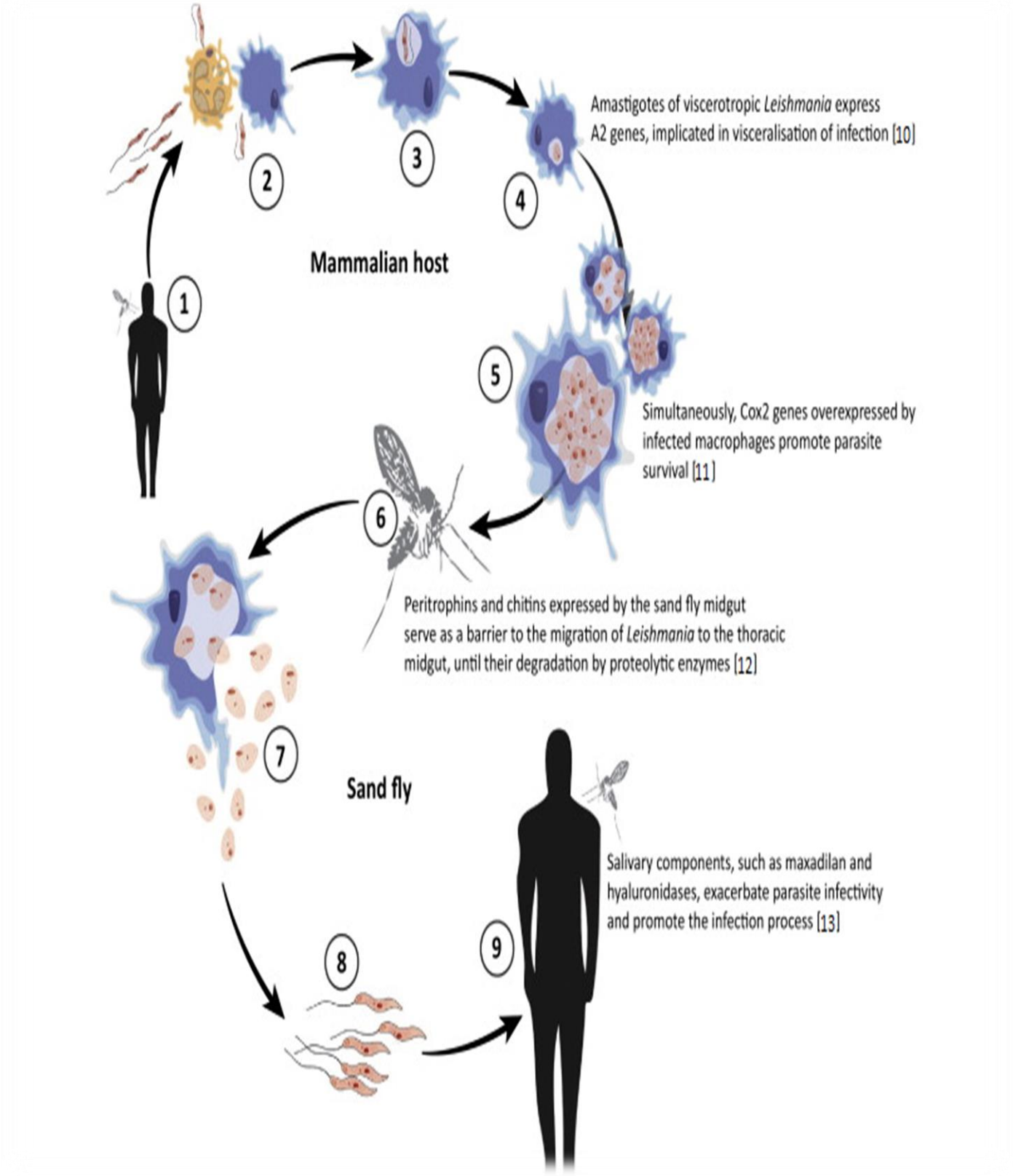

Figure 9: Life cycle of Leishmania Spp(Cantacessi et al., 2015)

5. Clinical manifestation:

5.1. Visceral Leishmaniosis (VL)

Also known as kala-azar, which means black (*kala*) fever (*azar*) in Hindi—often is reserved for severe (advanced) cases of visceral leishmaniosis, the general term visceral leishmaniasis encompasses a broad spectrum of severity and manifestations. Although the incubation period generally ranges from weeks to months, asymptomatic infection can become clinically manifest years to decades after the exposure in people who become immunocompromised for other medical reasons (such as HIV/AIDS). Visceral leishmaniasis usually is caused by the species *L. Donovan* and *L. infant* (*L. Chagas* generally is considered synonymous with *L. infant*) and affects internal organs (particularly, spleen, liver, and bone marrow)(Postigo, 2010).

The stereotypical manifestations of clinically manifest visceral infection include:

- Fever
- Weight loss (cachexia; wasting)
- Hepatosplenomegaly, enlargement of the spleen and liver (usually, the spleen is more prominent than the liver)
- Pancytopenia—i.e., anemia, leukopenia, and thrombocytopenia
- A high total protein level and a low albumin level, with hypergammaglobulinemia

Lymphadenopathy may be noted, particularly in some geographic regions, such as Sudan and South Sudan. HIV-confected patients may have atypical manifestations, such as involvement of the gastrointestinal tract and other organ systems. (Fig.10)

Although the terms kala-azar and visceral leishmaniosis sometimes are used interchangeably. If untreated, severe cases of visceral leishmaniosis typically are fatal, either directly from the disease or indirectly from complications, such as secondary (mica) bacterial infection or hemorrhage(Mertz, 2016).

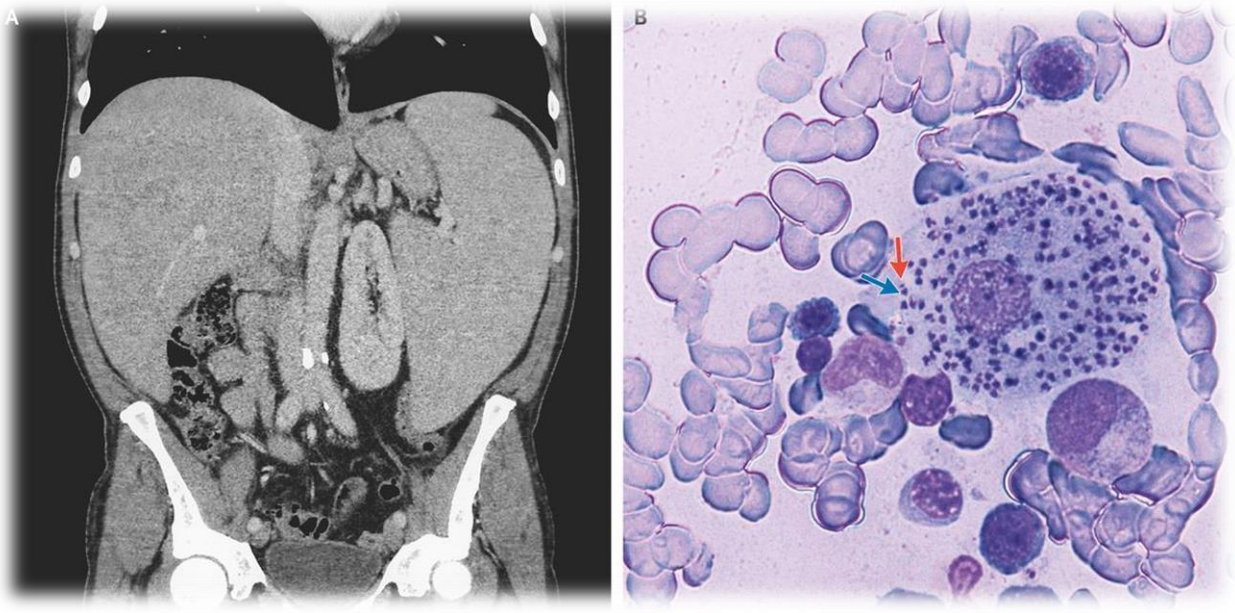

Figure 10 : clinic manifestation of Visceral Leishmaniosis on radiology and microscope image (Engle J, 2019)

The picture shows a radiology image for a patient infected with visceral leishmania parasite on the left and how his abdomen get dilation, we can see clearly Hepatosplenomegaly, enlargement of the spleen and liver and the picture on the right a show Microscope image how the cells get dilation.

Some patients develop post kala-azar dermal leishmaniosis (PKDL)(Post-kala-azar dermal leishmaniasis), a syndrome characterized by skin lesions (such as erythematous or hypo pigmented macules, papules, nodules, and patches), typically first noticed and most prominent on the face, that develop at variable intervals after (or during) therapy for visceral leishmaniosis. Persons with chronic PKDL can serve as important reservoir hosts of infection.

5.1.1. Life cycle:

The life cycle of *Leishmanial* is completed in two hosts, humans and sandflies. The adult female sand-fly is a bloodsucker, usually feeding at night on sleeping prey. When the fly bites an individual infected with *Leishmanial*, the pathogen is ingested along with the prey's blood. The protozoan is in the smaller of its two forms, called an amastigote, which is round, non-motile, and only 3–7 micrometers in diameter. Inside the stomach of the sand-fly, the amastigotes quickly transform into elongated and motile forms called the promastigotes. Promastigote is spindle-shaped, triple the size of the amastigote, and has a single flagellum that allows mobility. The promastigotes live extracellularly in the alimentary canal, reproducing asexually, then migrate to the proximal end of the gut where they become poised for a regurgitation transmission. As the fly bites, the promastigotes are released from the proboscis and introduced locally at the bite site.

Once inside the human host, promastigotes invade macrophages. Inside the cells they transform back into the smaller amastigote form (fig.11). The amastigotes replicate in the most hostile part of the macrophage cell, inside the phagolysosome, whose normal defensive response they are able to prevent. After repeated multiplication, they break down their host cell by sheer pressure of mass, but there is some recent speculation that they are able to leave the cell by triggering the exocytosis response of the macrophage.] The daughter cells protozoans then migrate to fresh cells or through the bloodstream to find new hosts. In this way the infection is progressive, spreading to the host's mononuclear phagocyte system, particularly the spleen and liver. The free amastigotes in peripheral tissues are then ingested by sand-fly to enter another cycle.(Cantacessi *et al*., 2015).

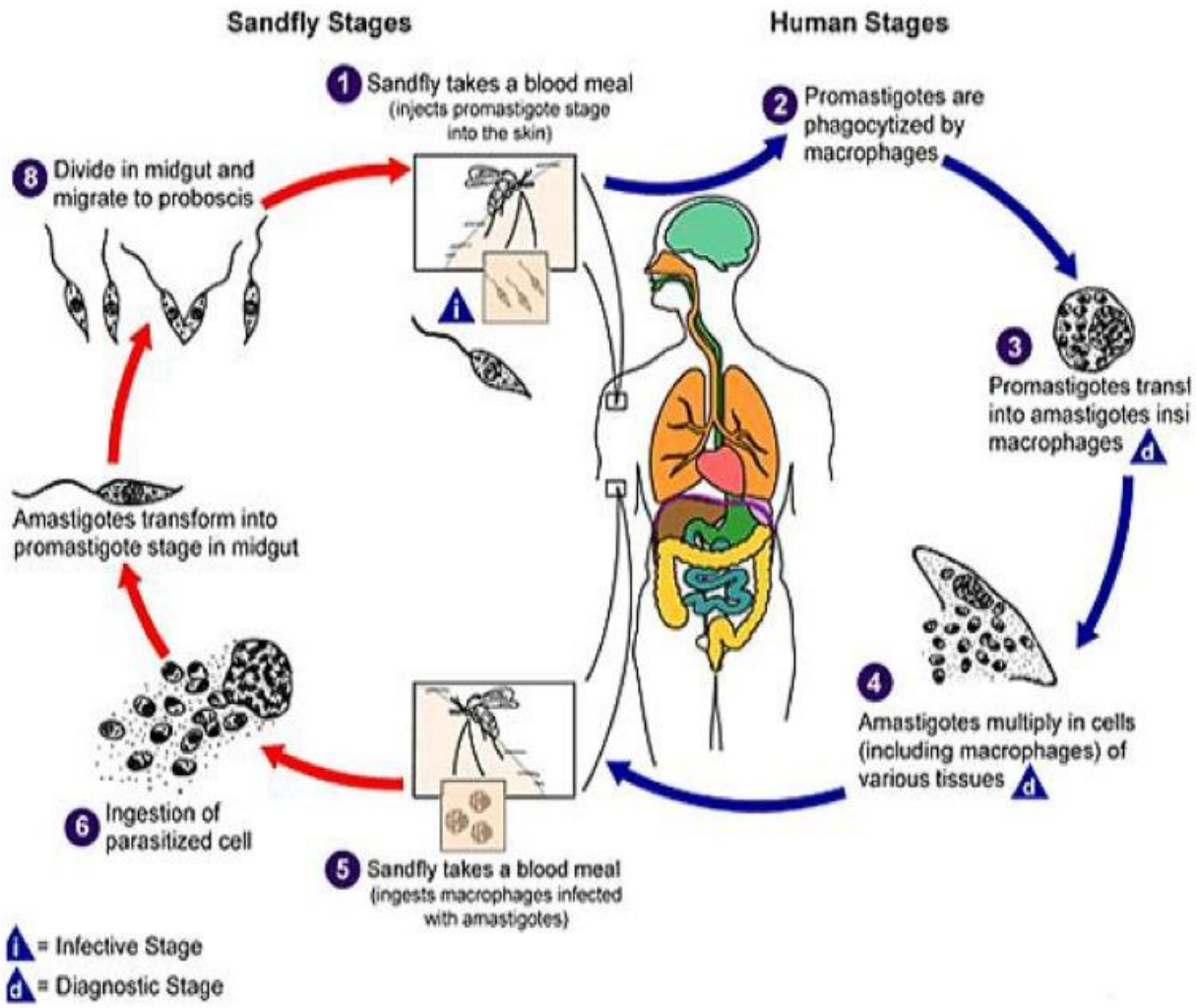

Figure 11 : life cycle of visceral leishmaniosis(Cantacessi et al., 2015)

5.1.2. Diagnoses:

In visceral leishmaniosis, diagnosis is made by combining clinical signs with parasitological, or serological tests (such as rapid diagnostic tests). One of them (the rK39 immunochromatographic test) gave correct, positive results in 92% of the people with visceral leishmaniosis .

The gold standard for diagnosis is visualization of the amastigotes in splenic aspirate or bone marrow aspirate. This is a technically challenging procedure that is frequently unavailable in areas of the world where visceral leishmaniosis is endemic (Akhoundi *et al*., 2017).

5.2. leishmaniosis cutaneous (LC)

In general, cutaneous leishmaniosis causes skin lesions, which can persist for months, sometimes years. The skin lesions usually develop within several weeks or months after the exposure but occasionally first appear years later (for example, in the context of trauma or immunosuppression). The lesions typically evolve from papules to nodular plaques to ulcerative lesions, with a raised border and central depression, which can be covered by scab or crust; some lesions persist as nodules(fig.12). The lesions usually are painless but can be painful, especially if ulcerative lesions become infected with bacteria or if the lesions are near a joint. The healing process typically results in atrophic scarring (Postigo, 2010).

Even patients with localized cutaneous leishmaniosis quite commonly develop more than one primary lesion (on the same or different parts of the body), satellite lesions, regional lymphadenopathy (occasionally bubonic), and/or nodular lymphangitis (sporotrichoid-like subcutaneous nodules). Sometimes lymphadenopathy is noticed, before skin lesions develop.

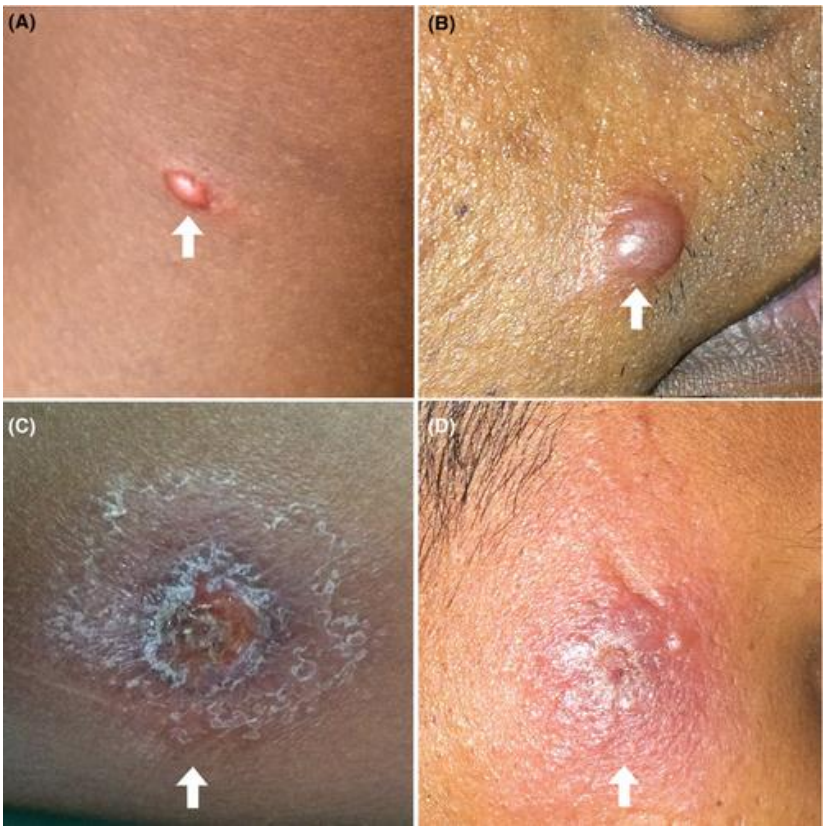

Figure 12: Types of skin lesions observed in cutaneous leishmaniasis(Karunaweera et al., 2020)
A) papule ; B) nodule ; C) ulcer; D) plaque

Leishmaniosis is transmitted by the bite of female phlebotomize sandflies. The sandflies inject the infective stage, promastigotes, during blood meals.

1. Promastigotes that reach the puncture wound are phagocytized by macrophages
2. and transform into amastigotes
3. Amastigotes multiply in infected cells and affect different tissues, depending in part on the *Leishmanial* species
4. This originates the clinical manifestations of leishmaniosis. Sandflies become infected during blood meals on an infected host when they ingest macrophages infected with amastigotes

(5,6)In the sand-fly's midgut, the parasites differentiate into promastigotes which multiply and migrate to the proboscis (Bates, 2007).

5.2.1. Diagnosis:

- The diagnosis of cutaneous leishmaniosis is mainly done on a clinical and epidemiological basis.
- The role of the laboratory is the confirmation of the causative agent by stained smear or culture from the skin lesion, especially in patients presenting atypical lesions or needing systemic treatment (Mertz, 2016).

6. Animal infection:

Even though the dog is the main reservoir of Leishmaniasis, there are other animals such as hares and rabbits, goats, rodents, cats, and even birds that can be effective reservoirs, and may therefore be involved in the transmission of *Leishmanial*. It is very important to control the pathogen in these animal populations in order to prevent their role as active reservoirs. These animal species do not directly spread the parasite, but the Infection is always conducted through the vector. Therefore, it is important to prevent sandflies bites by avoiding transit outside during dusk or at dawn, or by wearing appropriate protective clothing and using repellents(Álvarez et al., 2012).

6.1. LEISHMANIASIS IN DOGS:

Canine leishmaniosis (CanL) due to *Leishman infimum* is a major global zoonosis potentially fatal to humans and dogs, which comprise the main reservoir of infection to humans. It is endemic in more than 70 countries in the world. It is present in regions of southern Europe, Africa, Asia, South and Central America and has been reported also in the United States of America (USA). It is also an important concern in non-endemic countries where imported sick or infected dogs constitute a veterinary and public health problem (Nieto, 2004).

Canine leishmaniosis is a multisystem disease with a highly variable spectrum of immune responses and clinical manifestations. In endemic areas, the prevalence of dogs carrying infection is much higher than those demonstrating clinical disease. Clinical disease is associated with a marked antibody response that does not confer protection. In fact, immune-mediated mechanisms are responsible for much of the pathology in canine leishmaniosis (Nieto, 2004).

The typical history reported by owners of dogs with clinical disease due to *L infantum* includes the appearance of skin lesions, ocular abnormalities, or epistaxis. These are frequently accompanied by weight loss, exercise intolerance, and lethargy. The main physical examination findings are dermal abnormalities in 80%–90% of the dogs, lymph adenomegaly in 62%–90%, ocular disease in 16%–81%, splenomegaly in 10%–53%, and abnormal nail growth (onychogryphosis) in 20%–31%. Other clinical findings may include polyuria and polydipsia due

to kidney disease, vomiting, colitis, melena, and lameness due to joint, muscle, or bone lesions (Nieto, 2004)

The sole presenting signs of disease could be epistaxis, ocular abnormalities, or manifestations of kidney disease without dermal abnormalities. The dermal lesions associated with canine leishmaniosis include exfoliative dermatitis, which can be generalized or localized over the face, ears, and limbs. Ulcerative, nodular, or mucocutaneous dermatitis are also seen. Cutaneous ulcers over the ears or other locations may be associated with considerable bleeding. A mild form of papular dermatitis has been reported in dogs with no other signs of disease. Ocular or periocular lesions include keratoconj-unctivitis and uveitis (fig.13) (Nieto, 2004) .

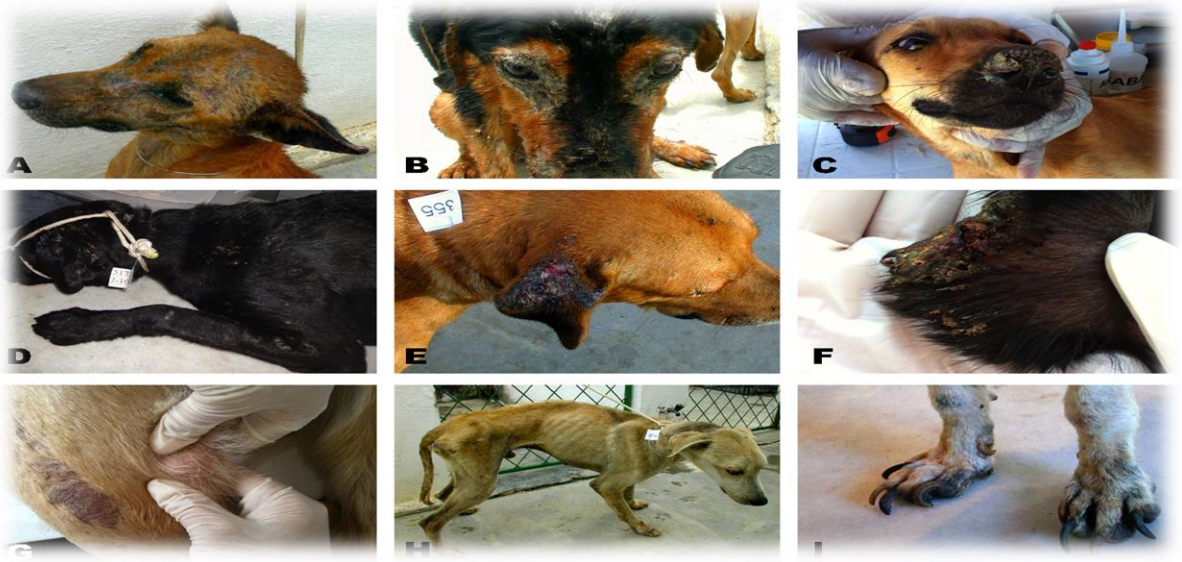

Figure 13: Leishmaniasis symptoms in dogs(Veras et al., 2014)

A =skin head lesions and aging aspect / B= ocular disease /C = nose bleed / D= body lesions / E and F= ears lesion / G= big ganglia /H= weight loss / I =lengthening of the claws

6.1.1. Diagnosis of leishmaniosis in dog:

Diagnostic tests for canine leishmaniosis include a biochemical profile, urinalysis, and one or more specific tests to confirm infection. Quantitative serology is best for diagnosis and particularly sensitive when compatible clinical signs are present. High antibody titers are found in 80%–100% of dogs with clinical disease and could be conclusive of a diagnosis. Various quantitative serologic methods to detect anti-*Leishmania* antibodies have been developed, including indirect immunofluorescence assays, ELISA, and direct agglutination assays. Purified recombinant antigens such as rK39 are also used to detect leishmaniosis in dogs and people in several rapid lateral flow formats as screening assays. Serologic cross-reactivity with trypanosomes may be found in regions where *Trypanosoma* infection is prevalent, particularly with *T cruzi* in the Americas (Paltrinieri *et al*., 2010).

Detection of parasite-specific DNA by PCR allows sensitive and specific diagnosis of infection. Several different assays with various target sequences using genomic or kinetoplast DNA (kDNA) have been developed for canine leishmaniosis. PCR can be performed on DNA extracted from tissues, blood, or even from histopathologic specimens. Assays based on kDNA are the most sensitive for direct detection in infected tissues, but these sequences have been shown to have wobble or variability over time. Bone marrow, lymph node, or spleen samples are superior to blood with most of the current PCR techniques (Paltrinieri *et al*., 2010).

Leishmania amastigotes can be demonstrated by cytology from lymph nodes, spleen, skin impressions, bone marrow, or joint fluids stained with Giemsa stain or a quick commercial stain. As mentioned earlier, *T cruzi*, a similar parasite, also has an amastigote form with a kinetoplastid, so in the Americas visualization of amastigotes does not necessarily diagnose *Leishmania* infection. Detection of amastigotes by cytology is sometimes unrewarding because of a low number of detectable parasites, even in dogs with full-blown clinical disease. *Leishmania* parasites may also be viewed in histopathologic formalin-fixed, paraffin-embedded biopsy sections of the skin or other infected organs. Identification of parasites within tissue macrophages may be difficult; immunolabeling with immunohistochemical staining can verify the presence of *Leishmania* in the tissue.

Detection of infection in dogs with no clinical disease for purposes such as importation to nonendemic countries or use as blood donors may require quantitative PCR, which is the most sensitive diagnostic technique. Cross-sectional studies of dog populations in highly endemic areas have shown that infection rates can reach 65%–80%. Typically, only approximately 10%–13% manifest clinical signs of disease, 26% are seropositive and include sick and subclinically infected dogs, and an additional 40%–60% are carriers positive only by tissue PCR (Nieto, 2004).

6.2. LEISHMANIASIS IN CATS

Infection by Leishmania in cats is not uncommon and has been described in virtually all areas where canine Leishmaniosis is endemic, although they are considered as a secondary reservoir. However, it seems that only a very small proportion of these animals develop the disease, probably due to the cat's immune system being able to control the infection of this parasite by either eliminating it or by keeping it in a chronic/subclinical state. More than 70% of the published cases were diagnosed in animals with compromised immunity (viral infections, immunosuppressive treatments, neoplasias, etc.). Retroviral infections such as Feline Leukemia and Feline Immunodeficiency creates an immunosuppression of the animal, making such kind of infected cats more vulnerable to other diseases such as Leishmaniosis. Whenever there is a FIV or FeLV infection, if the cat becomes infected with Leishmania the immune response of the cat to the parasite is severely reduced, leading to false negatives when serological techniques are used (Álvarez *et al*., 2012).

6.2.1. Symptoms of leishmaniosis in cats

Regarding the clinical presentation, the cutaneous symptoms predominate in 65% of the cases (dermatologic abnormalities include nodules, ulcerations and less often exfoliative dermatitis), similar to those observed in canine leishmaniosis. Other common symptoms in feline leishmaniosis include mucocutaneous lesions and lymph node enlargement, mainly in the head and neck, or the hands and feet. The systemic symptoms are nonspecific and among them we can find lympha-denomegaly, splenomegaly, anorexia, weight loss (Álvarez *et al*., 2012).

Figure 14 : Leishmaniasis symptoms in cats(Rodrigues et al., 2013)

The pictures show the different symptom of cats leishmaniasis (ocular diseases, skin lesion, lymph node enlargement in the head and neck, or the hands and feet.

6.2.2. Diagnosis of leishmaniosis in cats

Most diagnostic techniques for Leishmania infection which are available for dogs can be used in cats. Diagnosis is made in most cases by immunological, cytological, histological, culture or molecular methods.

- Cytological examination of samples from enlarged cutaneous lesions, mucous membranes and lymph nodes.
- Blood and bone marrow smears.
- Cutaneous biopsy for conventional staining and immunohistochemistry.
- Quantification of anti-Leishmania antibodies with serological techniques adapted to the cat. In the case of high suspicion and low antibody titers or even in the case of negative results, it is advisable to perform molecular techniques to rule out the disease(Álvarez *et al*., 2012)

In addition, it is highly probable that the cat might have an underlying or concurrent disease, so basic laboratory tests, including blood count, biochemistry, urinalysis and serum protein gram should be performed.

7. Differential Diagnosis:

It can be differentiated from other diseases that cause fever, weight loss, hepatosplenomegaly, and pancytopenia Bacterial infections, for example, typhus, typhoid fever, paratyphoid fever, brucellosis, tuberculosis, recurrent fever; viral diseases as mononucleosis, hepatitis, and rubella; parasitoses as sleeping sickness, malaria, schistosomiasis, amebiasis, and Chagas' disease; organic or systemic diseases as tropical splenomegaly and anemia, liver cirrhosis, Morbus Boeck, and rheumatic fevers must be considered (Mertz, 2016).

8. Prophylaxis:

Prevention and control of leishmaniasis requires a combination of intervention strategies because transmission occurs in a complex biological system involving the human or animal reservoir host, parasite and sandfly vector. Key strategies for prevention are listed below:

- Early diagnosis and effective prompt treatment reduces the prevalence of the disease and prevents disabilities and death. It helps to reduce transmission and to monitor the spread and burden of disease. Currently there are highly effective and safe anti-leishmanial medicines particularly for visceral leishmaniasis, although they can be difficult to use. Access to medicines has significantly improved thanks to a WHO-negotiated price scheme and a medicine donation programmed through WHO.
- Vector control helps to reduce or interrupt transmission of disease by decreasing the number of sandflies. Control methods include insecticide spray, use of insecticide–treated nets, environmental management and personal protection.
- Effective disease surveillance is important to promptly monitor and act during epidemics and situations with high case fatality rates under treatment.
- Control of animal reservoir hosts is complex and should be tailored to the local situation.

- Social mobilization and strengthening partnerships – mobilization and education of the community with effective behavioral change interventions must always be locally adapted. Partnership and collaboration with various stakeholders and other vector-borne disease control programmes is critical (Mertz, 2016).

Conclusion:

In this study, we have demonstrated how Vector life-history of Lyme disease and Leishmaniasis traits and parasite development respond in strongly nonlinear ways to changes in temperature. These thermal sensitivities create the potential for climate change to have a marked impact on disease transmission, for this reason there is a need to design effective and tailored strategies to adapt to vector-borne disease risk.

As such, approaches that can embrace this complexity are needed to inform adaptation research with evidence to make sure that everyone get the idea how danger this little insects can be and take their measure to reduce the risk of it.

So that's why we recommend to avoid the area risk specially in the season when they can be abundant or take your measures by checking the temperature, humidity and the time of day affect the likelihood of being bitten, so you can know when you need extra protective clothing and insect repellent, wear light-colored, long-sleeved shirts and long trousers, tucked into socks or boots, and use insect repellent on exposed skin and clothing to protect yourself from being bitten by mosquitoes, sandflies or ticks.

apply a skin disinfectant. examine your clothing, luggage and other belongings thoroughly before entering the place where you are staying.

If you are bitten and receive care abroad, remember to complete your course of treatment at home.

If you become ill upon your return from another place, inform the doctor where you have been, as you may have brought a disease back with you.so you ca get the necessary treatment.

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