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## Leishmaniasis in Morocco: diseases and vectors

Kholoud Kahime<sup>1\*</sup>, Samia Boussaa<sup>1,2</sup>, Lahouari Bounoua<sup>3</sup>, Ouanaimi Fouad<sup>1</sup>, Mohammed Messouli<sup>4</sup>, Ali Boumezzough<sup>1\*</sup><sup>1</sup>Laboratory of Ecology and Environment, (URAC 32, CNRST; ERACNERS 06), Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco<sup>2</sup>Institut Supérieur des Professions Infirmières et des Techniques de Santé, Marrakesh, Morocco<sup>3</sup>Biospheric Sciences Laboratory, NASA's Goddard Space Flight Center, Maryland, USA<sup>4</sup>Laboratory of Hydrobiology, Ecotoxicology and Sanitation, Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakesh, Morocco

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## ABSTRACT

Leishmaniasis, a highly neglected disease, currently presents a significant health problem throughout Africa. This review presents a summarized analysis of its epidemiology in Moroccan context, a Mediterranean location in which leishmaniasis is prevalent and where both cutaneous and visceral leishmaniasis have been reported.

This study aims to determine the current leishmaniasis epidemiological situation in Morocco and the distribution of its different forms throughout the country. During the past 20 years, this disease has emerged as a major public health threat in Morocco. So, we gave a particular attention to vectorial status of Moroccan sandflies (Diptera: Psychodidae, Phlebotominae) in view of its major role in diseases spreading.

It seems clear that the risk of spread of the disease is rising in Morocco. Ecological characteristic of proven and potential vectors, according to climate and environmental changes, should be regarded as good marker to anticipate leishmaniasis distribution in Morocco.

## 1. Introduction

In Morocco, leishmaniasis are endemic diseases posing a major threat to public health. In 2011, Moroccan Ministry of Health reported 4319 cases of cutaneous leishmaniasis (CL) and 107 cases of visceral leishmaniasis (VL)[1].

CL is caused by three clinically important *Leishmania* species [*Leishmania major* (*L. major*), *Leishmania tropica* (*L. tropica*), and *Leishmania infantum* (*L. infantum*)], a flagellate protozoa of the family Trypanosomidae, while, VL is caused by *L. infantum*. Recently, the mucocutaneous form was also reported in Morocco, but remains rare[2].

*Leishmania* infection is transmitted to human host as a result of a bite by an infected female sandfly (Diptera: Psychodidae, Phlebotominae) of the genus *Phlebotomus*.

In Morocco, the *Phlebotomus papatasi* (*P. papatasi*) and *Phlebotomus sergenti* (*P. sergenti*) are the most common vectors for the spread of *L. major* and *L. tropica*, respectively[3]. *Phlebotomus ariasi* (*P. ariasi*), *Phlebotomus perniciosus* (*P. perniciosus*), and potentially *Phlebotomus longicuspis* (*P. longicuspis*) are reported to be the vectors of *L. infantum* in Mediterranean countries[3]. Previous studies in Morocco showed that the distribution of sandflies was due, in great part, to the bioclimate[4].

In Morocco, both zoonotic and anthroponotic forms were reported. The main reservoirs are dogs for zoonotic VL (ZVL), rodents for zoonotic CL (ZCL) and human for anthroponotic CL (ACL).

## 2. Epidemiology

Due to its geographical position, Morocco possesses different ecological and climatic conditions, which are important factors in the repartition and epidemiology of endemic neglected diseases such as leishmaniasis. According to Moroccan Ministry of Health, CL caused by *L. major* is the most dominant form (Figure 1), with

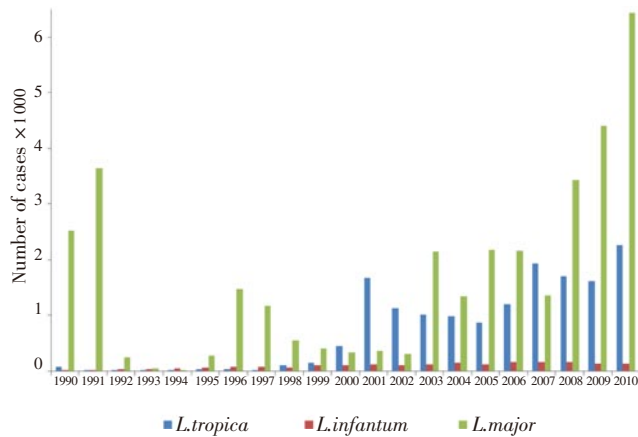
\*Corresponding author: Kholoud Kahime and Ali Boumezzough, Laboratoire Ecologie and Environnement L2E, Faculté des Sciences Semlalia, Université Cadi Ayyad, BP 2390, Marrakech 40000, Morocco.

Tel: +212 (0) 662 130 564

E-mail: kahimkholoud@gmail.com, aboumezzough@gmail.com

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more than 24000 cases reported during the last decade<sup>[1]</sup>. Epidemiological data show that *L. major* dominated in the 1990s, however starting in 2000, the apparition and growth of *L. tropica* and *L. infantum* is noticeable (Figure 1). Including *L. major* and *L. tropica*, the highest CL cases were noted between 2000 and 2010. While VL cases remains comparatively stable (Figure 1).



**Figure 1.** Evolution of cutaneous (*L. major*+*L. tropica*) and visceral (*L. infantum*) leishmaniasis cases between 1990–2010 in Morocco.

According to the same source, all ages are affected by the different forms of disease, with a high incidence for youth. Similar to the VL case<sup>[5]</sup>, young children are at high risk for both CL by *L. tropica*<sup>[6,7]</sup> and CL by *L. major*<sup>[8]</sup>. In the same way, leishmaniasis affects both genders almost equally with a slight increase in women<sup>[7,8]</sup>. The large numbers of women and children infected, indicates that *Leishmania* transmission may have occurred in the peridomestic habitat<sup>[6]</sup>.

There is evidence that changes in climate contribute to some extent to the incidence and expansion of the range of the CL<sup>[9,10]</sup>, but the absence of leishmaniasis epidemiological information collection system pre-1993 did not allow to accurately describe the epidemiological situation in Morocco<sup>[11]</sup> or to establish correlations between dynamics of the disease and global changes.

Since 1993, various studies of leishmaniasis foci together with the national incidence statistics confirmed the change in geographical distribution of leishmaniasis in Morocco, marked by the disappearance of the traditional North–South

dichotomy between visceral and cutaneous leishmaniasis, respectively (Figure 2). An overlap of foci, including *L. infantum* and *L. tropica* began then to emerge.

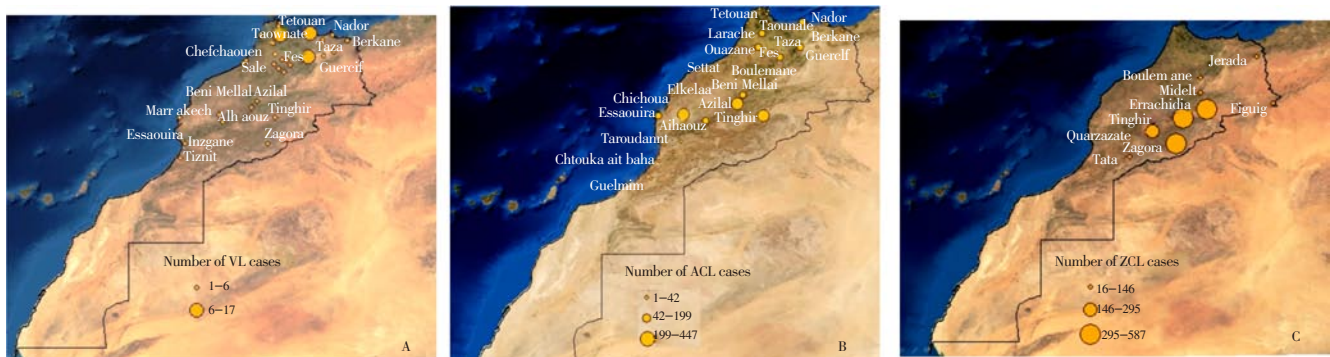
Currently, VL due to *L. infantum* is distributed mainly in Northern Morocco Rif and pre-Rif region (Figure 2A), geographically separated from other areas by mountains which constitute a natural barrier<sup>[12]</sup>. The ACL *L. tropica* has the widest geographic distribution with large foci in the Central and Western Morocco (Figure 2B), while, the ZCL *L. major* is dispersed in the south and south-east of the Atlas Mountain (Figure 2C) where the disease is located in the steppe fringes of the Sahara desert<sup>[10]</sup>.

However, for the extreme south, there are no available epidemiological data. Rioux *et al.* have led an entomological survey carried out in the littoral zone of the Western Saharan region of Morocco, namely in Tan-Tan, Tarfaya, Layoun, Boujdour and Dakhla<sup>[13]</sup>. The authors noted the scarcity of vector species and absence of leishmaniasis cases. It's necessary to update these entomological data and assess the current status of human leishmaniasis in the entire extreme Southern Morocco.

### 3. ZCL

In the pre-Saharan area, ZCL has been identified since 1914<sup>[11]</sup>, in the palm grove of Oued Tata where a major CL epidemic manifested during the late 1970s. Currently, foci of ZCL are basically linked to palm groves, rural and periurban areas with degraded environmental and socio-economic conditions like poor housing and hygiene<sup>[8]</sup>. It is widespread from the Atlantic coast, south of the Anti-Atlas mountains to the north-east, crossing Saharan areas south of the Anti-Atlas and High Atlas mountains, and east of the Middle Atlas mountains<sup>[14]</sup>. Caused by *L. major*, this form is transmitted by the *P. papatasi*, with *Meriones shawi grandis* as the main reservoir host<sup>[10]</sup>. All strains isolated from the host, human and vector are identical and are identified biochemically as being due to *L. major* MON-25<sup>[15]</sup>. The same results were found on skin smears in 2007, in the provinces of Ouarzazate and Errachidia<sup>[16]</sup>.

*P. papatasi* was reported in Morocco as early as 1916<sup>[17]</sup>. This species is very common and has a significant ecological plasticity. It can be found in various biotopes, including



**Figure 2.** Geographical distribution of VL due to *L. infantum* (A), ACL cases due to *L. tropica* (B) and ZCL cases due to *L. major* (C) in Morocco (cases recorded in 2011).

houses, animal sheds and caves<sup>[17,18]</sup>, and is most frequent at 400–800 m above sea level<sup>[19]</sup>.

*P. papatasi* is well adapted to arid climate and its density increases with the aridity<sup>[10]</sup>. In Marrakech City, its seasonal fluctuation shows two peaks, the first in summer and the second in fall<sup>[20]</sup>. The establishment of *P. papatasi* in the city appears to have been favoured by urbanization<sup>[19]</sup>. The disease progresses as small localized epidemics and cases are diagnosed between late fall and late winter. Then, lull periods occur as the aboriginal population is protected by acquired immunity, as in the Errachidia region<sup>[10]</sup>. Genetically and phenotypically, *P. papatasi* populations are supposed to be highly homogeneous<sup>[21]</sup>, but this assumption still requires more investigations<sup>[22–25]</sup>. Besides this proven *L. major* vector, *P. papatasi* and *Phlebotomus bergeroti* are sympatric in Morocco, Algeria, Egypt, Sudan, and Ethiopia with possibility of cross-breeding<sup>[26]</sup>. *Phlebotomus bergeroti* may play a role in transmission of *L. major*, like in Iran<sup>[27]</sup> which suggests that future studies should include other factors related to this suspected vector and its vectorial competence/capacity in Morocco.

#### 4. ACL

ACL is caused by *L. tropica* and transmitted by the sandfly *P. sergenti* with humans as the only reservoir<sup>[3]</sup>. Domestic dogs were found infected with *L. tropica* in some rural areas, however these are not regarded as animal reservoirs and the transmission cycle is still considered to be anthroponotic<sup>[15]</sup>.

In Morocco, *L. tropica* was isolated, for the first time in 1987, from cutaneous lesion in a young child<sup>[28]</sup>. Since then, many eco-epidemiological studies were carried out in central and southern areas of the country with the aim to detect CL foci caused by *L. tropica*. Several foci have been reported in the rural areas of Azilal, Essaouira, Chichaoua and Al Haouz<sup>[6,28]</sup> and the urban and peri-urban regions of Taza and Zouagha Moulay Yaacoub<sup>[29]</sup>.

In Morocco, *L. tropica* is characterized by high enzymatic polymorphism. Seven zymodemes (*L. tropica* MON-102, MON-107, MON-109, MON-112, MON-113, MON-122, and MON-123) were detected in human, dogs and the sandfly *P. sergenti*<sup>[30]</sup>. In addition, a new zymodeme (*L. tropica* MON-279), responsible for canine VL, was detected in Al Hoceima in the north of country<sup>[29]</sup>. Actually, the ACL is widespread in the semi-arid regions of Central and South-western Morocco where it is transmitted anthroponotically by *P. sergenti*. This vector has an extensive geographical distribution<sup>[31,32]</sup>. Its role as vector was identified in Tanant-Azilal region, however it was also reported in all bioclimatic zones with 'preferences' for semi-arid regions<sup>[19]</sup>. *P. sergenti* is endophilic in Morocco, where it is abundant in rural as well as urban population habitats<sup>[18]</sup>. *P. sergenti* was collected up to 1400 m with the highest densities recorded between 800–999 m above sea level<sup>[33]</sup>.

As the *L. tropica*, *P. sergenti* shows considerable genetic variation in Morocco. Three mitochondrial-DNA haplotypes were identified among *P. sergenti* populations of Azilal,

Essaouira and Taza<sup>[34]</sup>. When its populations from Northern and Southern Morocco were investigated by isoenzymatic tools, *P. sergenti* did not present genetic characteristics of a single species<sup>[35]</sup>.

As closely related vectors, other endemic sandfly species are also present. Depending on the region, *P. sergenti* is sympatric with *Phlebotomus alexandri*, *Phlebotomus chabaudi*, *Phlebotomus kezeruni* and/or *Phlebotomus riouxi*, however the vectorial status of all these species is still not well unknown in Morocco.

#### 5. VL and CL due to *L. infantum*

The first human CL case caused by *L. infantum* in Morocco was detected in the central Rif region of Taounate in 1996, within an active focus of VL<sup>[11]</sup>. In contrast, VL was detected many years before. The first case of infantile kala-azar has been described in 1921 in the region of Tanger with a single adult case reported for one nurse in Meknes in 1922<sup>[15]</sup>.

*L. infantum* CL is a rare condition with a few sporadic cases in the north of the country. The enzymatic identification of the parasite showed that it is the *L. infantum* MON-24<sup>[36]</sup>. Molecular investigations, conducted in 2007 in the province of Sidi Kacem showed the existence of skin lesions caused by *L. infantum*, with domestic dogs as reservoir host and *P. ariasi* as vector<sup>[16]</sup>. Recently, in Sefrou Province, the coexistence of *L. tropica* and *L. infantum* by species-specific ITS1-PCR-RFLP assay was noted<sup>[37]</sup>. Anthroponotic foci of *L. tropica* CL are found around Fes and Taza in the eastern central parts of Morocco, not far from VL foci<sup>[29]</sup>. Furthermore, several cases of canine leishmaniasis caused by *L. tropica* have been reported in regions where canine leishmaniasis is caused by *L. infantum*<sup>[16]</sup>.

The VL form is widespread throughout the country. It is more frequent in the northern part with sporadic cases observed in other regions, particularly in the south<sup>[15]</sup>. Actually, the VL situation remained quasi-static since 1999 with hundreds of cases reported each year. Almost all of these cases originated in traditional northern foci, where this disease is sporadic<sup>[38]</sup>. *L. infantum* is transmitted by sandflies belonging to the subgenus Larrousius with dogs being the main host reservoir. Within this subgenus, little is known about the distribution and/or the vectorial role of its species (*Phlebotomus mariae*, *Phlebotomus chadlii*, *Phlebotomus perfiliewi*, *Phlebotomus langeroni*, *P. perniciosus*, *P. longicuspis* or *P. ariasi*) in Morocco.

Nevertheless, *P. ariasi* and *P. perniciosus* are the proven vectors in Mediterranean countries<sup>[33,36]</sup>, while *P. longicuspis* is a suspected one<sup>[39]</sup>.

The vectorial role of *P. ariasi* has been described in Northern Morocco in Taounate Province, where, one female *P. ariasi* was found infected by *L. infantum*<sup>[11]</sup>. *P. ariasi* distribution is limited to mountain. Guernaoui *et al.* collected *P. ariasi* in altitude ranging between 1000 and 1400 m<sup>[33]</sup>. However, in Morocco, VL is not limited to mountain and is mainly located in the northern regions and at different altitudes (Nador, 62 m; Al Hoceima, 14 m; Tetouan, 1 m; Taza,

1 100 m; Taounate, 567 m; Sidi Kacem, 55 m; Fez, 300 m and Meknes, 560 m) with sporadic cases in the south[36,38].

In north of Morocco, typical morphs of *P. perniciosus* are the most abundant forms of *L. infantum*[39]. Although in the southern regions, *P. perniciosus*, mainly as an atypical form, and *P. longicuspis* are sympatric, particularly in the mountainous regions[11]. However, in pre-Saharan regions, *P. longicuspis* is the only *Larroussius* species sufficiently abundant to be credibly suspected of transmitting VL[39]. Furthermore, the taxonomic status of the *P. perniciosus* complex (*P. perniciosus*, *P. longicuspis* and a potential cryptic species) should be confirmed as well as its vectorial capacity and competence of its species.

## 6. Conclusion

CL and VL are still significant public health issues in Morocco. The increase in transmission of *Leishmania* appears to be linked to changes in environment and disruption of its natural balance by ways of urbanization, rural exodus, unhealthy habitats and precarity, all of which promote settlement of the insect vector and/or reservoir that could exacerbate the epidemiological situation[8].

Significant attention and priority must be given to the studies of eco-epidemiology and spatio-temporal distribution of vectors, reservoirs as well as the diseases they transmit and their relationships to changes in climate. Only an integrated approach can give us a better understanding of these relationships and allow us to predict the associated risk level. Use of geographical information systems and remote sensing can help in investigations of large-scale distributions and geographical risk assessment of the disease, but so far such investigations on leishmaniasis have been absent or rare partly because of the complexity of the disease transmission cycle.

An health-ecosystemic approach seems prominent to allow for propose realistic and effective strategies for prevention, control and monitoring. Thus it is necessary to create a regional network in order to share information, and direct a collaborative programme of combined health education, risk assessment and mass screening of both infections in order to help early diagnosis and treatment. In order to be proactive, It is needed to:

- Improvement of the awareness and preparedness of the population to health problems such as leishmaniasis;
- Reappraisal of current plans to improve the robustness of design standards in those infrastructures which are usually rudimentary;
- Creating a strong partnership between the health sector and other sectors, an essential step in effective epidemic combat and control and orienting and charting the transverse measures.

## Conflict of interest statement

We declare that we have no conflict of interest.

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