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Epidemiology of the European Foci of Human Leishmaniasis

Introduction

The leishmaniasis are endemic in Southern Europe, where they are almost exclusively due to the species *Leishmania infantum*. This parasite is transmitted by Phlebotomine sandflies of the genus *Phlebotomus*, sub-genus *Larroussius*, and is responsible for a zoonosis of domestic and wild canids.

L. infantum is also responsible for visceral leishmaniasis in humans (VL), a form classically occurring in children, but for several decades has also shown incidence in immunosuppressed adults (HIV infection, organ transplantation). A high incidence of asymptomatic infections in the endemic areas was revealed as a result of the studies of *Leishmania*/HIV co-infection. Moreover, *L. infantum* can occasionally be responsible for cutaneous manifestations.

Geographical distribution

The endemic areas of leishmaniasis in Europe are restricted to the Mediterranean bioclimatic zones, of which thirty countries are concerned, including Portugal, Spain, France, Italy, Malta, Croatia, Bosnia and Herzegovina, Serbia, Montenegro, Albania, Greece, Turkey and Cyprus.

Epidemiology

Cases of leishmaniasis are registered differently according to each country and their clinical form. Human VL is a notifiable disease in Spain, Greece, Italy and Portugal, while CL is only notifiable in Greece and Italy. However, for all countries, it is presumed that the available figures for incidence are grossly underestimated, making the mean annual numbers of reported cases globally weak in all European countries. Between 300 and 400 new cases of human leishmaniasis are reported annually, in the whole of Southern Europe (fig. 1).

Parasite

Leishmania infantum is almost the only species present in Europe, and, with 33 different zymodemes, it shows a high level of enzymatic polymorphism. *L. infantum* MON-1 is the most common zymodeme (81.3%, 8 countries), particularly in dogs, the main reservoir, and in humans.

Vector

Four sandfly species are vectors for *L. infantum* in Europe. Out of them, *Phlebotomus perniciosus* has the largest geographical distribution, extending from west Portugal to Crete and Turkey. It is the main vector of the occidental part of Southern Europe. *P. ariasi* is more restricted in its distribution, where it is only found in Portugal, Spain, France and north-western Italy. In the oriental part of Southern Europe (Italy, the former Yugoslav Republic, Albania and Greece), there coexists *P. perfiliewi*, a north African sandfly species, and the oriental *P. neglectus*.

Reservoir

Leishmania infantum commonly infects domestic and wild canids, the dog, *Canis familiaris*, being its main reservoir. Canine leishmaniasis is enzootic in Southern Europe, with its incidence higher than that of human leishmaniasis (annual incidence of cases reaching several tens of thousands). A few apparently autochthonous cases of canine leishmaniasis, have been reported outside the common enzootic areas: Belgium, Germany, the Netherlands, Switzerland and the United Kingdom.⁸ In these cases the elucidation of transmission routes remain problematic.

Wild canids have been found harbouring *L. infantum*, particularly the fox, *Vulpes vulpes*, in southern France, Italy and Portugal. The position of the fox within the natural life cycle of the parasite remains unclear, as the number of cases reported is reduced. Leishmaniasis in the cat, *Felis catus*, first described in 1912 in Algeria, has, for a long time, been an exceptional phenomenon, but now appears more commonly in a few countries of Southern Europe (France and Spain), with its prevalence higher in Italy.⁶ The epidemiological status of the cat within the parasite life cycle remains to be elucidated: occasional host or true reservoir?

Clinical outcome

L. infantum is a viscerotropic parasite, mainly responsible for VL, but occasionally involving skin and, in rare cases, affecting the mucosae. Until the seventies, VL mainly occurred in young children, and was characterised by a triad of symptoms, including fever, anaemia and splenomegalia. However, from which time, cases were being reported in adults, the numbers of which increased yearly, notably from 1980, with the emergence of HIV infection. Since the first case of VL during AIDS, in 1985, *L. infantum* appears

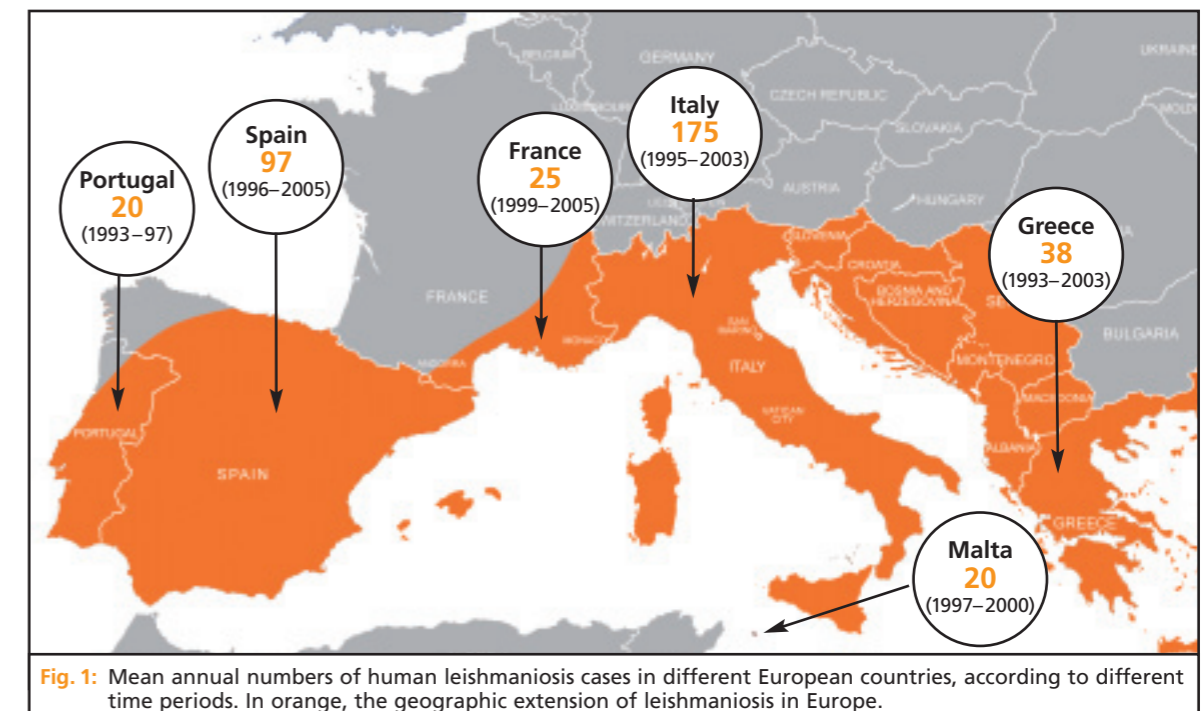


Fig. 1: Mean annual numbers of human leishmaniasis cases in different European countries, according to different time periods. In orange, the geographic extension of leishmaniasis in Europe.

as an opportunistic parasite occurring during HIV infection, particularly in Spain, Italy, France and Portugal, where 1,911 cases were detected between 1981 and 2001.³

The main risk factors for *Leishmania*/HIV co-infection in Europe are age (77.3% aged between 31 and 50 years), and intravenous drug use. In Spain, the sharing of syringes is suspected to be responsible for human-to-human transmission, which has led to the occurrence of a possible anthroponotic cycle of *L. infantum* free of a vector transmission stage.¹

While the prevalence of co-infection is decreasing, following the use of highly active antiretroviral therapy (HAART) in the treatment of AIDS, the multitude of therapeutic immunosuppressions favours occurrence of VL cases in endemic areas. A recent review reported 57 VL cases in organ-transplanted patients, of which 49 were from countries of Southern Europe.²

L. infantum can also be responsible for localised cutaneous leishmaniasis, particularly in some foci, such as that of the Pyrénées-Orientales in southern France.⁷ Moreover, it can also be responsible for isolated mucosal lesions, without any cutaneous extension or visceral involvement (fig. 2, 3).



Fig. 2: *L. infantum* cutaneous leishmaniasis from South of France. Diffusely infiltrative lesions. (Photograph of R. Perello)

Asymptomatic infection appears frequently in populations in endemic areas of Southern Europe, and was demonstrated in 1974 by Pampiglione *et al.*⁵ In the Alpes-Maritimes focus (southern France), 30% of the human population of an enzootic canine leishmaniasis area showed a positive skin test to the leishmanial antigen.⁴ In the same focus, some blood donors were also harbouring parasites.



Fig. 3: *L. infantum* cutaneous leishmaniasis from South of France. Ulcerative lesions. (Photograph of R. Perello)

Conclusion

L. infantum has a large geographic extension in Mediterranean Europe and is responsible for a large number of asymptomatic infections, which are susceptible to develop into symptomatic cases, in the event of immunosuppression. Symptomatic forms mainly include VL, less frequently, CL cases and rarely, mucosal lesions, which is illustrative of the complexity of the leishmaniasis pathology, related not only to the species tropism (visceral in principle), but also to host immunity.

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