

# The role of indigenous phlebotomine sandflies and mammals in the spreading of leishmaniasis agents in the Mediterranean region

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An updated view of the establishment and spread of the leishmaniasis in Europe is presented, mostly with respect to newly emerging and re-emerging foci and the incrimination of neglected as well as new reservoir hosts. At the same time, a concept of specific versus permissive vectors reassesses the potential role of various sandfly species in *Leishmania* transmission and considers the risk of introduction of exotic *Leishmania* species in Europe. The leishmaniasis are dynamic diseases and the circumstances of transmission are continually changing in relation to environmental, demographic and human behavioural factors. Changes in the habitat of the natural hosts and vectors, immunosuppressive conditions (like infection with human immunodeficiency virus (HIV) or organ transplantation-associated therapies in humans) and the consequences of war, all contribute to the transformation of the epidemiology of leishmaniasis. Such changes should be considered when studying the spread of the disease throughout Europe for targeted control measures to safeguard public health.

## Endemic burden of human leishmaniasis in Europe

The leishmaniasis are vector-borne diseases that have been endemic in southern Europe for centuries. They are transmitted by the bite of phlebotomine sandflies belonging to the genus *Phlebotomus* and most often exhibit one of two endemic clinical entities in humans, zoonotic visceral leishmaniasis (VL) and sporadic cutaneous leishmaniasis (CL). Four *Leishmania* species occur in the Mediterranean basin: *L. infantum*, the most frequent species, causing both VL and CL; *L. major*, occurring in North Africa and the Middle East, causing CL; *L. tropica*, found in Greece, Turkey, the Middle East and North Africa, causing CL; *L. donovani*, recently introduced in Cyprus, causing both VL and CL. These species are able to spread in new geographical areas where suitable sandfly vectors are present in sufficient

numbers and under favourable ecological conditions. The risk is greater when the anthroponotic species, *L. tropica* and *L. donovani*, are involved, because reservoir hosts other than human are not required to complete the transmission cycle. It is widely accepted that the leishmaniasis are dynamic diseases. As the conditions of transmission change (environmental, demographic, human behaviour and health), epidemiological studies and control measures to safeguard public health should be adapted for the application of successful monitoring measures.

The incidence of zoonotic VL caused by *L. infantum* in humans is relatively low (0.02–0.49/100,000 in the general population) with an average of about 700 clinical cases reported each year in southern Europe [1,2]. However, outbreaks or recrudescence may occur periodically in foci like the new focus in Spain where incidences increased up to 56 per 100,000 [3]. Incidence rates of sporadic CL, although generally accepted as high (in the range of one to a few 100), are not available because of poor notification.

Visceral leishmaniasis constitutes a problem in immunocompromised individuals. Starting from the early 1990s, the impact of co-infections with *Leishmania* and human immunodeficiency virus (HIV) was recognised as an alarming problem by international health authorities. Cases were reported from 35 countries worldwide, mostly in south-western Europe (France, Italy, Portugal and Spain), showing an association between the HIV pandemic and the zoonotic entity of VL caused by *L. infantum*. The cumulative number of co-infections recorded by a surveillance network from the World Health Organization (WHO) and UNAIDS was 692 by early 1995, 965 by 1998, and 1911 by early 2001. Spanish cases accounted for 57% of all co-infections worldwide, probably reflecting a relatively large area of *Leishmania*/HIV sympatry in Spain. The demonstration

of unusual modes of anthroponotic transmission (i.e. by syringe exchange) and the high rate of relapses following anti-leishmanial treatments, were alarming features indicating a trend toward an even higher incidence. By the end of the 1990s, however, several reports indicated that the *L. infantum*/HIV epidemic peak declined due to the introduction of the highly active antiretroviral therapy (HAART) which not only reduced the number of new cases of co-infection, but also the rate of VL relapses in individuals with restored immunological parameters (i.e. with a CD4+ count >200/μL). Currently, very few HIV-infected individuals with clinical VL are recorded annually in southern Europe, mainly in patients with acquired immunodeficiency syndrome (AIDS) who are unresponsive to HAART. Other countries, such as Germany, Greece, Switzerland and the United Kingdom currently report sporadic imported cases [4].

The spread of leishmaniasis may be enhanced by globalisation, climatic change and other conditions which allow the parasite and its vectors to spread in space and time. Studies to foresee the effect of such changes have been undertaken by the EDENext EU FP7 ([www.edenext.eu](http://www.edenext.eu)) project in order to safeguard unaffected areas by preventing the introduction, establishment and spread of the *Leishmania* pathogen and its vectors. Data on the disease and its spatial distribution in Europe and the Mediterranean basin were composed and made accessible online to researchers and public health officials ([www.edenextdata.com](http://www.edenextdata.com)) so that knowledge-based decisions could be made for monitoring the disease.

Increasing evidence suggests that elevated rates of asymptomatic *L. infantum* carriers are an indicator of the intense *Leishmania* circulation in southern Europe. Infection prevalences, as high as 10–47% in particular age groups, were recorded in healthy individuals from endemic foci of France, Greece, Italy and Spain by traditional and molecular methods [5]. On the other hand, CL cases, autochthonous or imported, may not seek treatment, especially in cases with mild clinical forms or older people and illegal immigrants. When the disease is introduced in new areas, physicians who are not familiar with the problem often do not consider CL in their differential diagnosis, and hence appropriate treatment is not given, allowing parasite circulation.

### Literature search strategy

Scientific literature for the purposes of this review was searched in May 2012 by all participating co-authors, sourcing the PubMed and Scopus databases. An electronic search was conducted among articles from 1970 until recently, as well as a few relevant older references, cross-referencing the following combination of keywords: 'leishmaniasis' and '*Phlebotomus*' and 'emergence' and 'reservoirs'. Titles relevant to the scope of this review (an updated view of the establishment and spread of the leishmaniasis in Europe with respect to newly emerging and re-emerging foci and

the incrimination of neglected and new reservoir hosts) were obtained in full text and selected for inclusion. Unpublished data and titles from non-peer-reviewed literature were not considered.

### Sandfly vectors

The vectorial status of phlebotomine sandfly vectors of *Leishmania* in Europe and the Mediterranean area was recently reviewed [6,7] and new species have recently been incriminated [8,9]. Nine proven, or potential, vector species (*Phlebotomus ariasi*, *P. perniciosus*, *P. perfiliewi*, *P. neglectus*, *P. tobbi*, *P. kandelaki*, *P. balcanicus*, *P. papatasi* and *P. sergenti*) are indigenous in Europe. In addition, species of questionable taxonomic status (*P. similis*, *P. syriacus*) or of possible but unproven vectorial capacity (*P. mascittii*) should be further studied. Traditionally, the limited number of known vectors was explained by the inability of some sandfly species to support the development of infective stages in their gut or because of unidentified ecological contact with reservoir hosts [6]. However, experimental infections, under laboratory conditions, revealed that only two tested sandfly species, *P. papatasi* and *P. sergenti*, are 'specific vectors'; they allow only the maturation of a single *Leishmania* species they transmit in nature (*L. major* and *L. tropica*, respectively) and do not support development of other *Leishmania* species [10–13]. Nonetheless, most sandfly species tested to date support development of multiple *Leishmania* spp. allowing them to mature in their midguts, thus falling into a category of the permissive vectors [9]. These species are members of the *Larrousius* and *Adlerius* subgenera, namely *P. perniciosus*, *P. arabicus* and *P. halepensis*. Although in nature, *P. perniciosus* is the proven vector of *L. infantum* in the western Mediterranean, *P. arabicus* the proven vector of *L. tropica* in Israel and *P. halepensis* the suspected vector of *L. infantum* in the Caucasus region, all three species supported full development of *L. major* and *L. tropica* under experimental conditions [14–16].

The broad vectorial competence of permissive sandfly species may have important epidemiological consequences and should be taken into account while estimating the risk of new leishmaniasis foci. The most important example is the introduction of *L. infantum* (syn. *L. chagasi*) from the Iberian Peninsula to Latin America, where it adapted to the local permissive sandfly *Lutzomyia longipalpis* [9]. Similarly, we can speculate that *L. tropica* could be transmitted by permissive vectors in the Mediterranean area, although *P. sergenti* was for a long time considered to be its sole vector. The vectorial capacity of *P. similis*, a sister species of *P. sergenti*, which is widely distributed in the north-eastern Mediterranean, is yet to be tested. *P. arabicus*, a proven vector in a CL focus in northern Israel [14], demonstrated a clear potential of permissivity to transmit the parasite.

While transcontinental import of new vectors to Europe by human activities appears improbable, due to the

fragile nature of sandflies in comparison to the rather robust invasive mosquito species, a shift of sandfly occurrence to northern areas of Europe, traditionally regarded as *Leishmania*-free, was recently well documented. In northern Italy, an increase in the density and geographical expansion of the *Leishmania* vectors *P. perniciosus* and *P. neglectus* was observed in 2003 and 2004 compared with the situation described in the 1960s and 1970s; this enabled the establishment and transmission of the parasite in the northern part of the country previously regarded as non-endemic [17]. In a similar manner, an increase in the incidence and distribution of canine leishmaniasis (CanL) was reported in 2007 from a new VL focus in southern France, a region outside the traditional endemic area of this disease. As no major changes in land use were observed, it was postulated that the increased CanL transmission could be attributed to vector dispersion (*P. perniciosus* and *P. ariasi*) due to an increase in the mean summer temperature during the two decades preceding the reported increase, a possible effect of global climate change [18]. A similar situation was described in Spain where the current distribution was compared to the predicted spreading of sandfly vectors based on expected climate changes [19]. In Germany, the detection of leishmaniasis cases in humans and animals (dogs, cats, horses) that had never travelled outside the country, has led to the hypothesis of a recent establishment of autochthonous transmission [20], suggesting a northward expansion of *L. infantum*, although entomological surveys have so far not provided solid evidence for the presence of competent vector species in Germany.

## Reservoirs

Dogs, which may suffer from severe disease (CanL), are the primary domestic reservoir hosts of zoonotic VL caused by *L. infantum*. Canine infections are widespread in southern Europe, representing both a public health threat and a veterinary problem. Infections in cats and horses have also been reported in areas where CanL is present, and cats may suffer from feline leishmaniasis syndrome, which is less severe compared to CanL [21]. In Europe, a number of other indigenous mammal species have been found infected by *L. infantum*, including *Mus spretus* (Algerian mouse), *Apodemus sylvaticus* (European wood mouse), *Rattus rattus* (black rat), *Rattus norvegicus* (brown rat), *Meles meles* (European badger), *Martes martes* (European pine marten), *Mustela nivalis* (weasel), *Geneta geneta* (common genet) and *Vulpes vulpes* (red fox) [6,21]. In addition to domestic dogs, the ability to transmit infection has been confirmed by xenodiagnosis in black rats and domestic cats [22], suggesting that they may represent a secondary reservoir host for *L. infantum*. The important question is: can any of these species serve as reservoir host, and can they participate in the establishment and spread of the parasite in new foci?

Zoonotic CL, caused by *L. major*, is not considered a threat for Europe, not even a very low risk, since its natural reservoir hosts, gerbils of the genera

*Rhombomys*, *Psammomys* and *Meriones*, are not found in European countries [6]. However, the recent finding that voles of the species *Microtus guentheri*, a common rodent in Balkan countries, were infected by *L. major* in Israel [5], has challenged this assumption. In contrast, CL caused by *L. tropica* is universally believed to be anthroponotic because it is prevalent in urban settings. However, dogs have been reported as possible reservoirs or accidental hosts of *L. tropica* in some countries [21]. In a broader geographical context of the Mediterranean region, several zoonotic foci have been described, with rock hyraxes (*Procapra capensis*) as reservoirs in Israel [7,14] and *Ctenodactylus gundi* rodents found infected and probably serving as reservoirs in the area of Maghreb [23]. These two examples from neighbouring areas to Europe illustrate that the traditional terms used for the diseases caused by *L. tropica* and *L. major*, 'anthroponotic CL' and 'zoonotic CL', respectively, may not be fully appropriate.

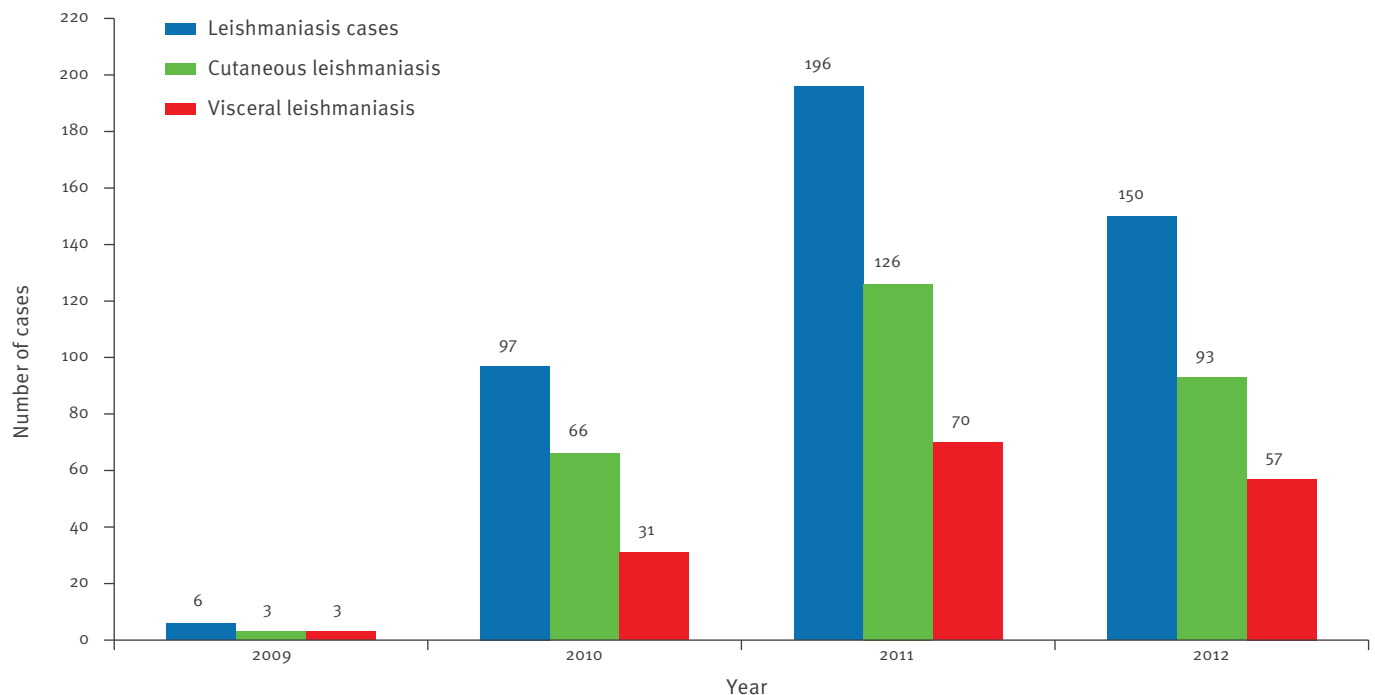
## Spread of endemic *L. infantum* and the risk of introduction of non-endemic *Leishmania* species

Being previously confined to coastal Mediterranean biotopes, autochthonous leishmaniasis caused by *L. infantum* does not appear to be limited to these habitats anymore, suggesting an expansion towards new biotopes at northern latitudes and higher altitudes. During the period from 2002 to 2009, the northward spread of CanL was monitored in northern Italy, in newly endemic regions, with mean seroprevalences increasing from 1.8 to 4.7%, and reported human VL and CL cases [17]. In a region of the French Pyrenees, outside the traditional area endemic for leishmaniasis, CanL seroprevalence rates increased 10-fold over a period of 13 years between 1994 and 2007 [18]. In south-eastern Spain, a progressive increase in CanL seroprevalence rates was reported at elevated altitudes in the Alpujarras region, climbing from 9.2% in 1984 to 20.1% in 2006 [24]. Furthermore, a new CanL focus was recently detected in a Pyrenean area of north-western Catalonia [25].

It transpires, from both published and unpublished information that leishmaniasis cases due to *Leishmania* species that are not indigenous to Europe, are indeed frequent [6,21], occurring in migrants, visiting friends and relatives, or European citizens travelling to endemic countries outside Europe for tourism or work. Some 100 VL, 400 CL and 700 CanL imported cases have been diagnosed and published from traditionally non-endemic countries of Europe north of the regions with natural occurrence of leishmaniasis (Germany, the Netherlands and the United Kingdom). Information about non-indigenous *Leishmania* importation in endemic areas of southern Europe is scarce because it is difficult to discriminate between autochthonous and non-autochthonous cases that share similar clinical aspects. For example in Italy, during 2011 and 2012, about 20 cases (16 of them immunocompetent CL patients) from four New World and 10 non-European

**FIGURE 1**

Human leishmaniasis outbreak of Fuenlabrada, Spain, 2009–2012 (n=449)



Old World countries were diagnosed, indicative of the intense circulation of parasites at global level. Most imported cases are CL forms caused by *L. tropica* or *L. major*, but also by neotropical parasites of the *L. braziliensis*, *L. amazonensis* or *L. guyanensis* complexes. Although adaptation of the latter parasites to Old World phlebotomine vectors and reservoir hosts does not seem probable, phlebotomine species susceptible to full development of *L. tropica* (*P. sergenti*) or *L. major* (*P. papatasi*) have been recorded in several southern European countries. Notably, the geographical range of *P. sergenti* extends to Spain, Portugal and Italy (Sicily), where genetic competence of local sandfly populations for anthroponotic *L. tropica* transmission has been suggested [26]. Because of the zoonotic nature of *L. major*, the probability of its introduction appears to be low. Nevertheless, hybrid *Leishmania* from Portugal have been reported, which share genetic traits from *L. infantum* and *L. major*, suggesting that adaptation of novel parasites to southern European vectors may take place in the future [27].

## New foci in Spain, Crete and Cyprus

### Spain

Recently, a new *L. infantum* focus has been described in Spain. Since late 2010, an unusual increase of human leishmaniasis cases (VL and CL) has been observed in the south-western Madrid region, mainly in Fuenlabrada (204,838 inhabitants) and was considered as an outbreak (Figure 1). The incidence rate in this municipality rose from 2.44/100,000 inhabitants

in 2009 to 54.2/100,000 inhabitants in 2013. From July 2009 to December 2012, 449 leishmaniasis cases were diagnosed in Fuenlabrada and three affected neighbouring municipalities, Leganés, Getafe, and Humanes de Madrid, of which 158 (35.3%) were VL. This was the first reported outbreak of VL and CL of such magnitude in Spain.

From 2005 to 2011 a new periurban green park of around 450 hectares with an irrigation system was established very close to the residence of many of the VL and CL cases. This provided abundant food for hares in an area previously used for agriculture, now free of predators and hunters.

A survey revealed a large population of hares (*Lepus granatensis*) and a small population of rabbits living in this park, therefore the role of hares and rabbits as potential reservoirs of leishmaniasis in this focal area was studied during 2011 and 2012. Seroprevalence for *Leishmania*, studied during the same period in the same area in 2,070 dogs (by rK39 dipstick), was found to be 1.64% [28]. In addition, *Leishmania* was detected using a *Leishmania*-specific nested PCR (Ln-PCR) amplifying three targets (ITS1, ITS2, and *hsp70*) which proved to have 100% specificity for *Leishmania* [29]. Original R223 and R333 primers [30] used in this Ln-PCR assay detected *Leishmania* in four of 55 spleen samples from cats (7.3%) and in one of 66 spleen samples from rabbits (1.5%). However, the most interesting results were found in hares, as 43 of 148 animals studied (29%) were positive in Ln-PCR on spleen or



skin samples collected between December 2011 and July 2012. Xenodiagnosis assay, carried out on seven hares (using a *P. perniciosus* colony) revealed four positive animals [3], proving for the first time that sandfly vectors acquire *L. infantum* by feeding on apparently healthy hares. Direct sequencing of the positive ITS1, ITS2, and *hsp70* PCR products was performed [31]. Molecular characterisation, based on the ITS1 and ITS2 regions and the *hsp70* gene of 30 isolates, 24 from humans and six from hares (six positive sandflies after xenodiagnosis of three hares), were consistent with *L. infantum* and 100% identical to the sequence of the *L. infantum* strain isolated in Spain in 1987 from a patient with CL. Between December 2011 and February 2013, about 1,200 hares were captured in the park, representing a high population density of around 265 hares/km<sup>2</sup>. A preliminary entomological study was conducted in September and October 2011, before starting the disease control measures, in order to analyse by PCR the blood feeding preferences of sandflies (based on the vertebrate *cytochrome b* gene), which showed a clear feeding preference for hares [32]. In the same study, the detection of *Leishmania* in the wild-caught *P. perniciosus* (studied by kDNA-PCR and cpb PCR) showed that 58.5% of flies were positive to *L. infantum*. This was the first evidence that hares can play a role as a reservoir of *L. infantum* in Europe, suggesting the existence of a sylvatic transmission cycle linked to the urban periphery. As noted above, the creation of the park resulted in an increase of hares as the reservoir host and sandfly populations, and thus led to the urbanisation of leishmaniasis. The new VL focus in Fuenlabrada is thus an example of leishmaniasis emergence due to environmental changes induced by man. The role of hares, and other possible sylvatic reservoirs, in the epidemiology of leishmaniasis deserves special attention in endemic sites.

## Crete

In the island of Crete, Greece, CL was so common sixty years ago that it had a local name, 'Chaniotico spyri', meaning 'the skin lesion found in the area of Chania'. Yet, after DDT spraying against malaria vectors during World War II, sandfly populations were drastically reduced [33,34] and Crete remained a latent focus for CL for over 25 years [35]. Recently however, CL due to *L. tropica* has re-emerged and spread to all parts of Crete, with an average of five CL cases per year observed in the last three years. The parasite was isolated from relapsed patients, over 60 years-old, who reported that they had 'Chaniotico spyri' during childhood, as most people in their village at that time [35]. Of the 19 CL cases known in Crete during the last three years, 15 were over 60 years-old. Possibly age-related changes in the immune system of these patients allowed the parasite to become activated and cause new lesions. Such cases are expected to appear in larger numbers as people infected at childhood get older. Currently, *L. infantum* and *L. tropica* are found circulating in the island of Crete, a closed ecosystem of 8,336 km<sup>2</sup> and with a population of 601,131 (Greek statistics department

2001). They are involved in zoonotic and anthroponotic cycles, with an increasing number of human cases and a reported mixed infection in a dog. The two prevailing *Phlebotomus* species in Crete are *P. neglectus* and *P. similis*, the first a proven vector of *L. infantum* and the second a suspected vector of *L. tropica*. However, 10 *Phlebotomus* species are found in the island [35], and vectorial capacities of most of them have not yet been investigated. These species, like *P. mascittii*, may be able to transmit the local parasites but also other parasite species and/or strains that could be introduced to the island, to humans and other hosts, a situation that may complicate the epidemiology of the disease and its implications for public health in the future.

## Cyprus

*L. donovani* is anthroponotic, causing VL, CL and post-kala-azar dermal leishmaniasis, depending on the geographical area. It is considered more aggressive than *L. infantum* and often does not respond to treatment with first-line drugs. For decades, *L. infantum* in Cyprus has been causing canine leishmaniasis without causing any human cases [36,37]. CanL was a serious veterinary problem until 1945 [38], but became latent after the mosquito eradication campaign [39] and the vast reduction in dog numbers (from 46,000 to 6,000) as a consequence of the successful anti-echinococcosis campaign between 1970 and 1975 [40,41]. Nevertheless, the reservoir host and vector populations for leishmaniasis gradually increased and CanL re-emerged on the island. In 1996, overall CanL seroprevalence was reported to be 1.7%; by 2006, it had increased six-fold, reaching 33.3% in some areas. Nevertheless, only one infantile VL case was reported during this period, in 1987 [42]. The situation is different in the northern part of the island not under effective control of the Government of the Republic of Cyprus, where an increasing number of human CL and VL, as well as CanL cases have been reported [43]. Although the population of the two parts of Cyprus has been free to cross the green line since 2003, leishmaniasis cases were not reported in the southern part until 2006, when three CL and two VL human cases were diagnosed.

For the typing of the isolates from Cyprus, a *K26*-PCR assay, which is specific for the *L. donovani* complex and discriminates between *L. donovani* and *L. infantum* [44], was used, together with multilocus enzyme electrophoresis (MLEE), the current reference method for characterising and classifying *Leishmania* strains [45], as well as microsatellite analysis [46]. All methods incriminated *L. donovani* MON-37 as the responsible strain. These isolates were found to be genetically very closely related to the Turkish *L. donovani* MON-37 and differed from the *L. donovani* MON-37 found in all other countries. This indicates that the parasite may have been introduced to Cyprus recently, probably from mainland Turkey, where human leishmaniasis is widespread, by Turkish immigrants and/or the army following the war in 1974. The fact that this strain was isolated from both human hosts and *P. tobbi* in Turkey

## FIGURE 2

Cutaneous leishmaniasis due to *Leishmania donovani*, Cyprus, 2011



Photograph by Maria Antoniou. The patient agreed for the photograph to be published.

[46], strengthens the hypothesis that this vector may be responsible for the transmission of both *Leishmania* species in southern Cyprus, where no *P. neglectus* has been recorded so far [37]. However, further studies should investigate the capacity of other species to transmit *L. donovani* in Cyprus, such as *P. galilaeus*. Four new human CL cases (Figure 2) and one VL case, caused by *L. donovani*, have been diagnosed in Cyprus since. *L. donovani* was also found, as a mixed infection with *L. infantum*, in a dog (one of 20 dogs examined by *K26*-PCR) living in the same district as three CL patients [37].

All evidence indicates that two different transmission cycles are taking place on the island, one of *L. infantum* in dogs and one of *L. donovani* in humans. However, the mixed infection in the dog suggests that the cycles meet, demonstrating that some of the sandfly species found on the island bite both dogs and humans, contrary to what was believed [47]. The question remains: why do humans in the southern part of Cyprus not get infected by *L. infantum*? A seroepidemiological study conducted in 600 people in two areas on Cyprus defined as high-risk in a seroepidemiological study conducted in dogs and one area defined as low-risk, did not reveal antibodies against the parasite [37]. However, a larger sample should be studied, to investigate the situation in depth before conclusions can be reached. It is also interesting to note that cases of VL have been reported in tourists visiting Cyprus [48,49] and that no *Leishmania* and HIV co-infections are known on the island. It is probable that genetic differentiation, in the parasite, the vector or the native population, has taken place, and these possibilities should be investigated to explain the Cyprus paradox [37].

## Conclusion

It is apparent that the epidemiology of the leishmaniasis in the Mediterranean basin is changing. Historical foci, silent for several decades, re-emerge and the threat of new strain/species introduction is evident. The new focus in Spain, with hares as reservoirs, clearly shows that hosts, neglected in previous epidemiological considerations, may play a major role in transmission cycles under changing conditions. At the same time, the concept of specific and permissive vectors draws attention to the possibility that a larger number of sandfly species could be incriminated in parasite transmission. Many reports indicate introduction and spread of exotic *Leishmania* species and zymodeme variants to areas of Europe that are already endemic. In areas where sandfly vectors are well established and circulating the local parasites, such introductions of for example a new *L. tropica* zymodeme in Crete and *L. donovani* in Cyprus [36], if able to support and transmit the new invaders, will enhance the possibility of genetic exchange between different species/strains of the parasite. As a result, new hybrids may be generated with different epidemiology, pathogenicity or drug resistance, a situation already shown in Portugal [27].

There is an urgent need to identify both *Leishmania* species and their vectors in detail. To safeguard public health, targeted control measures must be undertaken by local and European authorities. At the same time it is of vital importance for doctors in human and veterinary medicine to be well informed on the disease symptoms, therapy, and resistance of *Leishmania* to drugs. Scientific consortiums such as EDENext could prove appropriate platforms to accumulate, coordinate and integrate up-to-date knowledge and assist decision makers in assessing public health problems related to leishmaniasis, appropriately.

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