**Leishmaniasis**

Leishmaniasis, the third most common vector-borne disease, is caused by protozoan flagellates and is transmitted by sandflies (family *Psychodidae*, genus *Phlebotomus* in the Old World and genus *Lutzomyia* in the New World) (Kato, Gomez et al. 2010; Rocha, Margonari et al. 2010). The number of sandfly species involved in the transmission of leishmaniasis is not known; at present the number of sandflies hosting *Leishmania* is larger than the number of sandflies involved in transmission (more than 17 species).

Human leishmaniasis is subdivided into three main clinical forms: visceral (VL) (Box 8a), cutaneous (CL) (Box 8b), and muco-cutaneous (ML) (Box 9). Two other forms are often considered distinct from the first three: asymptomatic (Banuls, Bastien et al. 2011) and post-kala-azar-dermal-leishmaniasis (post visceral leishmaniasis)(Box 9). The latter two forms have very long incubation periods and for this reason the infected people are considered reservoirs of *Leishmania* (Einalem 2011). The different types of disease are sometimes caused by the same *Leishmania* species group (Dedet, Pratlong et al. 1999) and the same phenotype of the disease may be caused by different *Leishmania* species (Zhang and Matlashewski 2010; Babiker, Ravagnan et al. 2011; Banuls, Bastien et al. 2011). For a general review on human leishmaniasis in Europe see (Ready 2010) and for canine (Box 10), feline and equines leishmaniasis see (Gramiccia 2011); leishmaniasis in travellers is reviewed by (Pavli and Maltezou 2010) that accounted for 507 cases worldwide between 1985 and 2009.

Sandflies are characterised by intra-specific (Azmi, Schonian et al. 2012; Miro, Checa et al. 2012; Nieves, Sanchez et al. 2012) and extra-specific variability. For example, (Orshan, Szekely et al. 2010) confirmed the exophilic behaviour of *P. sergenti* and endophilic behaviour of *P. papatasi*, but with *P. sergenti* more flexible according to the area. Moreover, sandflies are often parasite-specific and hence disease-specific. In Israel zoonotic CL is due to *L. major* transmitted by *P. papatasi* and *L. tropica* transmitted by *P. sergenti*. In the Middle East *P. alexandri* is a vector of visceral leishmaniasis, while *P. papatasi* is a vector of cutaneous leishmaniasis (Colaciccio-Mayhugh, Masuoka et al. 2010). Sometimes sandflies are also host-specific: e.g. in Iran *P. papatasi* is associated with four different hosts in four foci (Rassi, Oshaghi et al. 2011): central and northeast with *Rhombomys opimus* (Parvizi, Baghban et al. 2010), in the west and southwest with *Tatera indica*, in the southeast with *Meriones hurrianae*, and in the south with *Meriones lybicus* (Yavar, Abedin et al. 2011). Finally the parasite can be host-specific: in Israel, sand rats (*Psammomys obesus*) and jirds (*Meriones crassus*) are the reservoir of *L. major* whereas rock hyraxes (*Procavia capensis*) are the reservoir of *L. tropica* (Orshan, Szekely et al. 2010). For the main parasites of VL, *L. infantum* maintains a zoonotic cycle mostly involving canine hosts while *L. donovani* maintains an anthropogenic cycle or both zoonotic and anthropogenic cycles.

The abundance of sandflies is associated with host distribution, type of house, land cover, altitude and climate. Sandflies are found only at specific altitudes where the relative humidity is high enough (Morillas-Marquez, Martin-Sanchez et al. 2010). (Chamaille, Tran et al. 2010) found that canine leishmaniasis density associated probably with *P. perniciosus* is positively correlated with mean annual temperature and winter temperature; while canine leishmaniasis density associated probably with *P. ariasi* is positively correlated with summer...
rainfall and canine density, and negatively correlated with mean annual temperature. The two species are spatially clustered and positively correlated with human density (the variable with the highest significance). Other variables associated with endophilic sandfly abundance are land use and house characteristics (Baron, Morillas-Marquez et al. 2011; Adegboye and Kotze 2012). *P. alexandri* and *P. papatasi* are associated with land cover with a strong urban influence (Colacicco-Mayhugh, Masuoka et al. 2010) as is *Lu. longipalpis* (Ferro, Marin et al. 2011; Valderrama, Tavares et al. 2011; Valderrama, Tavares et al. 2011). There are similarities with South American sandflies, e.g. *Lu. longiflocosa, Lu. olmeca olmeca, Lu. shannoni* and *Lu. cruciate* are associated with forest environments and rainfall (Sanchez-Garcia, Berzunza-Cruz et al. 2010; Ferro, Marin et al. 2011). Other species (*Lu. cruzi* and *Lu. longipalpis*) with less pronounced seasonality show a weak correlation with temperature and precipitation.

The strong correlation between sandfly abundance and disease is reflected in the development of models that include vector abundance, temperature and proximity to other leishmaniasis cases (Fischer, Thomas et al. 2010; Valderrama-Ardila, Alexander et al. 2010; Ferro, Marin et al. 2011; Adegboye and Kotze 2012). Based on the environmental and climate characteristics, (Chamaille, Tran et al. 2010; Colacicco-Mayhugh, Masuoka et al. 2010; Baron, Morillas-Marquez et al. 2011) present maps of leishmaniasis risk for France, Iraq – Turkey – Afghanistan and Spain respectively. Apart from environmental and entomological data, social factors are an important component that need to be included in predictive models (settlements, human density and population structure and malnutrition rates, human age)(Faye, Bucheton et al. 2011; Ponte, Souza et al. 2011). A final component, disease transmission, is still not understood and mainly guessed in risk analysis models (Bern, Courtenay et al. 2010; Stauch, Sarkar et al. 2011). In Georgia, the high sero-prevalence in humans and dogs (Giorgobiani, Chitadze et al. 2011), low in the vector (1.8%) (Giorgobiani, Lawyer et al. 2012) and a very short season of the vector are indicative of a highly efficient transmission cycle or the presence of different, presently unknown vectors.

In endemic areas, sero-prevalence in vectors can be high (e.g. in Iran (Yaghoobi-Ershadi, Hakimiparizi et al. 2010)), but low values similar to the Georgian one are also possible (de Carvalho, Valenca et al. 2010; Missawa, Michalsky et al. 2010; Rocha, Falqueto et al. 2010; Sanchez-Garcia, Berzunza-Cruz et al. 2010).

How *Leishmania* species interact with the vectors (Rogers, Corware et al. 2010), how they cause human diseases (de La Llave, Lecoeur et al. 2011) and why the clinical symptoms are so variable remain unclear (Banuls, Bastien et al. 2011). Disease understanding is made more complicated by the fact that some of the parasite species are still indistinguishable: (e.g. *L. infantum* from *L. donovani* (Stevenson, Fedorko et al. 2010; Talmi-Frank, Nasereddin et al. 2010)) and by the intrinsic variability within the vector species. In addition, the high incidence of asymptomatic forms is the cause of the difficulties in the definition of the real distribution of the disease. For all these reasons, leishmaniasis risk management requires that entomologists, biologists, vector control and surveillance experts, and clinicians merge their forces for an efficient system of prevention (Desjeux 2010; Romero and Boelaert 2010; Harhay, Olliaro et al. 2011; Palatnik-de-Sousa and Day 2011) especially faced with the
increasing geographic range of the parasites (e.g. *L. infantum* found for the first time in Argentina and Palestine).

Box 8a. Human visceral leishmaniasis (“kala azar”, black fever).

<table>
<thead>
<tr>
<th>Topic</th>
<th>Findings</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasite systematic</td>
<td>Family <em>Mastigophora</em>, genus <em>Leishmania</em></td>
<td></td>
</tr>
<tr>
<td>Parasite species</td>
<td><em>L. donovani</em> (human specific) and <em>L. infantum</em> (<em>L. infantum/chagasi</em>) and occasionally <em>L. tropica</em>, <em>L. braziliensis</em>, <em>L. mexicana</em> and <em>L. amazonensis</em>. In Brazil <em>L. infantum chagasi</em> is the causative agent of human VL. <em>(Harhay, Olliaro et al. 2011)</em></td>
<td></td>
</tr>
<tr>
<td>Host species</td>
<td>Mainly dogs but also foxes, rats, equines, cats, and some wild animals.</td>
<td><em>(Baron, Morillas-Marquez et al. 2011)</em></td>
</tr>
<tr>
<td><strong>Recently:</strong></td>
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<tr>
<td></td>
<td>Vertical transmission of <em>L. infantum</em> has been demonstrated in beagles (in the laboratory), mice (in the laboratory) and dogs. In Greece for the first time one (out 16) <em>Rattus norvegicus</em> was found infected by <em>L. infantum</em>. <em>L. infantum</em> infected hares were recorded in Spain. In Brazil, <em>L. infantum chagasi</em> infection was found 18.9% in humans, 47.8% in dogs, and 1.56% in <em>Lu. Longipalpis</em>. <em>(Baron, Morillas-Marquez et al. 2011)</em></td>
<td><em>(Papadogiannakis, Spanakos et al. 2010)</em> <em>(Molina, Jimenez et al. 2012)</em> <em>(Felipe, Aquino et al. 2011)</em></td>
</tr>
<tr>
<td>Transmission pathway</td>
<td>Haematophagous female sandflies bite, usually at night.</td>
<td></td>
</tr>
<tr>
<td>Vector species</td>
<td>Sandflies in the genera <em>Phlebotomus</em> and <em>Lutzomyia</em>. In East Africa the vectors involved are: <em>P. orientalis</em>, <em>P. celiae</em>, and <em>P. martini</em>. <em>(Elnaiem 2011; Rosa, Pereira et al. 2012)</em></td>
<td><em>(Elnaiem, Hassan et al. 2011)</em> <em>(Tabbabi, Bousslimi et al. 2011)</em></td>
</tr>
<tr>
<td><strong>Recently:</strong></td>
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<td></td>
<td>Low man-biting rate <em>P. rodhaini</em> was found for the first time infected by <em>L. donovani</em> in eastern Sudan. <em>P. sergenti</em> a vector known to transmit <em>L. tropica</em> in Morocco, Middle East and Asia, was found infected by the same parasite (for the first time) in Tunisia in 2010.*(Elnaiem, Hassan et al. 2011) <em>(Tabbabi, Bousslimi et al. 2011)</em></td>
<td></td>
</tr>
<tr>
<td>Parasite transmission parameters</td>
<td>Incubation period variable from several months to years.</td>
<td></td>
</tr>
<tr>
<td>Disease distribution</td>
<td>Endemic in tropical and subtropical regions, and the Mediterranean basin.</td>
<td></td>
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</tbody>
</table>

From: New advances and persistent old questions in the emergence of some vector-borne disease in Europe. A critical and systematic review on the 2010/2012 literature.
Annually about 500,000 cases of visceral leishmaniasis occur, according to a WHO report in 2000. 90% of the cases occur in India, Bangladesh, Nepal, Sudan and Brazil. In South America, VL is reported in 12 countries, but most of the cases are reported in Brazil. In Europe, it is endemic and re-emerging in urban and rural areas of the Balkans (Albania, Bosnia and Herzegovina, Croatia, Greece, Montenegro, Serbia, Romania and Slovenia).

**Recently:**
- In 2002 and 2003 in Germany where recorded 27 cases (another 43 where CL).
- In southeast Madrid, the number of new cases increased from 3/100000 in 2009 to 55.7/100000 in 2011. From 2000 to 2009 173 cases of VL occurred in Portugal.
- In India, 90% of the VL cases are reported in Bihar state (parasite *L. donovani* and vector *P. argentipes*).

**Disease seasonality**
- In peri-Mediterranean countries the vector activity peaks in summertime.

**Recently:**
- In Georgia the sandfly season is from June to September. Adults diapause over winter.

**Disease clinical features**
- Systemic infection of the phagocytic and reticulo-endothelial system. The patient suffers fever, distress, hepatosplenomegaly, lymphadenopathies, pancytopenia, and anaemia but other clinical signs can develop. It is fatal if untreated, and it causes more than 50,000 deaths each year worldwide.

**Recently:**
- Mortality rate is 8% in Brazil.
- The DNA from 6,000 blood samples from India and Brazil was analysed; people with VL had similar DNA variations, but the mechanism why specific genes are common with the visceral form of Leishmaniasis is not understood.

**Disease diagnosis**
- Diagnosis is based on antibody-detection using rK39 immunochromatographic tests or by the direct agglutination test.

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From: New advances and persistent old questions in the emergence of some vector-borne disease in Europe. A critical and systematic review on the 2010/2012 literature.
Disease treatment: Treatment is with both old and new anti-leishmaniasis drugs that in poor endemic countries raised several problems of resistance, side effects and mortality (Maltezou 2010; Stauch, Sarkar et al. 2011).

Disease prophylaxis: Vaccines are in a development phase. (Kaye and Aebischer 2011)

Disease prevention: Prevention from sandfly bite. Eradication and control of the vector is more efficient indoors than outdoors. (Desjeux 2010; Elnaiem 2011)

Coinfection: Although the seroprevalence of *L. infantum* can be associated with other viruses (e.g. Tuscana virus) to date no concomitant disease has been recorded. (Bichaud, Souris et al. 2011)

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Box 8b. Human cutaneous leishmaniasis (called “Uta” in Peru).

<table>
<thead>
<tr>
<th>Topic</th>
<th>Findings</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasite systematic</td>
<td>Family <em>Mastigophora</em>, genus <em>Leishmania</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Recently:</strong> <em>L. infantum</em> was isolated for the first time in Palestine in human in 2011. In Iran, <em>L major</em> is increasing its spatial extent.</td>
<td></td>
</tr>
<tr>
<td>Host species</td>
<td>Dogs, foxes and other mammals. <em>Arvicanthis niloticus</em> in west Africa.</td>
<td>(Sant'anna, Nascimento et al. 2010)</td>
</tr>
<tr>
<td></td>
<td><strong>Recently:</strong> Chickens are used by <em>L. longipalpis</em> for feeding and chicken blood can support the development of <em>L. Mexicana</em>.</td>
<td></td>
</tr>
<tr>
<td>Transmission pathway</td>
<td>Haematophagous female sandflies bite, usually at night.</td>
<td></td>
</tr>
<tr>
<td>Vector species</td>
<td>Sandflies of genus <em>Phlebotomus</em> and <em>Lutzomyia</em>.</td>
<td>(Rosa, Pereira et al. 2012)</td>
</tr>
<tr>
<td></td>
<td><strong>Recently:</strong> Confirmed <em>P. perniciosus</em> vector of <em>L. tropica</em> and <em>P. papatasi</em> of <em>L. major</em> in Israel. Confirmed that <em>P. papatasi</em> is the vector of <em>L. major</em> in Iran. Laboratory experiment showed that <em>P. duboscqi</em> originating from Kenya, was susceptible to infection by a strain of <em>L. tropica</em> from Turkey.</td>
<td>(Orshan, Szekely et al. 2010) (Yaghoobi-Ershadi, Hakimiparizi et al. 2010; Yaghoobi-Ershadi 2012) (Hanafi, El-Din et al. 2013). (Gonzalez, Rebollar-Tellez et al. 2011)</td>
</tr>
</tbody>
</table>
**Parasite transmission parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Incubation period</td>
<td>8 to 12 weeks.</td>
</tr>
<tr>
<td>Prevalence in endemic areas</td>
<td>CL prevalence typically increases with age up to 15 years, after which prevalence levels off, presumably because of the acquisition of immunity.</td>
</tr>
<tr>
<td>Bites per night per person</td>
<td>Lu. olmeca olmeca bites per night per person were 2.8 and the maximum risk was between 18.00 to 19.00.</td>
</tr>
</tbody>
</table>

**Disease distribution**

<table>
<thead>
<tr>
<th>Region</th>
<th>Description</th>
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<tbody>
<tr>
<td>Tropical and subtropical regions</td>
<td>It is distributed in arid margins of Asia, Africa, South Europe and the Mediterranean basin, South and Central America with 12 million people infected and 350 million of people at risk. Annually 400,000 to 1.5 million new cases of cutaneous leishmaniasis occur according to a WHO in 2000.</td>
</tr>
<tr>
<td>Germany</td>
<td>In 2002 and 2003 in Germany were recorded 43 cases.</td>
</tr>
<tr>
<td>Colombia</td>
<td>In 2002 and 2003 in Germany were recorded 43 cases.</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>From 2003 to 2009 (Kabul is the world’s largest focus of CL).</td>
</tr>
<tr>
<td>Iran</td>
<td>In 2009 30,000 cases were registered.</td>
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</tbody>
</table>

**Disease seasonality**

<table>
<thead>
<tr>
<th>Region</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Peri-Mediterranean countries</td>
<td>The vector activity peaks in summertime.</td>
</tr>
<tr>
<td>Libya</td>
<td>L. major infection peaks between November and January</td>
</tr>
</tbody>
</table>

From: New advances and persistent old questions in the emergence of some vector-borne disease in Europe. A critical and systematic review on the 2010/2012 literature.
L. Sedda & D. Rogers (2012) - Leishmaniasis

**Disease clinical features**
Torpid self-healing round ulcer, with permanent skin lesions (scar). A wider range of clinical manifestation also occurs

**Recently:**
In Tunisia *L. tropica* and *L. major* share equally the number of infected people. It has been shown that *L. tropica* causes single lesion while *L. major* causes multiple lesions.

(Goto and Lindoso 2010; Recalcati, Vezzoli et al. 2010; Romero, Tellez et al. 2010; Veraldi, Bottini et al. 2010)

(Bousslimi, Aoun et al. 2010)

**Disease diagnosis**
Visual and molecular (ELISA).

**Recently:**
Use of FTA card to collect samples directly from the patient’s lesions for a correct diagnosis (less invasive than usual methods).

(Souza, Andrade et al. 2010)

(Kato, Caceres et al. 2010)

**Disease treatment**
Treatment is by old and new anti-leishmaniasis drugs that in poor endemic countries raise several problems of resistance, side effects and mortality

(Maltezou 2010; Stauch, Sarkar et al. 2011)

**Disease prophylaxis**
New advances are in the development of transmission blocking vaccines.

(Coutinho-Abreu and Ramalho-Ortigao 2010; Coutinho-Abreu, Sharma et al. 2010)

**Disease prevention**
Prevention of sandflies bite. Eradication and control of the vector easier indoor that outdoor.

(Desjeux 2010; Elnaiem 2011)

**Coinfection**
*Leishmania and Wolbachia in Lu. Trapido*

(Azpurua, De La Cruz et al. 2010)

Box 9. Other forms of leishmaniasis (mucocutaneous leishmaniasis and post-kala-azar-dermal leishmaniasis).

Mucocutaneous leishmaniasis has lower incidence than CL and VL and is caused by *L. braziliensis* and occasionally by *L. panamensis*, *L. amazonensis*, *L. guyanensis*, *L. donovani*, *L. infantum* and *L. major* (Banuls, Bastien et al. 2011; Faucher, Pomares et al. 2011; Guerra, Prestes et al. 2011). The disease provokes severe destruction of the oro-nasal and pharyngeal cavities with consequent disfiguration (Ives, Ronet et al. 2011).

Post-kala-azar dermal leishmaniasis is distributed where *L. donovani* is endemic (Uranw, Ostyn et al. 2011). It is usually a consequence of VL and it develops six to several years (eight) after the visceral form. It is characterized by a wide spectrum of skin lesions ranging from hypo-pigmented macules, papules to nodules or combinations over the trunk and face (Ganguly, Das et al. 2010). The proportion of people developing post-kala-azar after VL ranges from 5% in India to 60% in Sudan (Rahman, Islam et al. 2010; Uranw, Ostyn et al. 2011). In the research of (Uranw, Ostyn et al. 2011) it was found that an adequate treatment can decrease the risk in developing post-kala-azar-dermal-leishmaniasis.

Box 10. Canine leishmaniasis.

Canine leishmaniasis is caused by *L. infantum* in dogs (and other mammals (Chitimia, Munoz-Garcia et al. 2011; Gramiccia 2011)) that are considered reservoir for human VL. The vectors are the sandflies of genus...
Seroprevalence of *L. infantum* in dogs can reach 52%, but commonly is between 1 and 30% (Kovalenko, Razakov et al. 2011; Santaella, Ocampo et al. 2011; Senghor, Fay et al. 2011; Shang, Peng et al. 2011; Wang, Ha et al. 2011; Hamarsheh, Nasereddin et al. 2012; Sun, Guan et al. 2012). The seroprevalence is higher in older dogs (Galvez, Miro et al. 2010; Hamarsheh, Nasereddin et al. 2012) or on very young (Miro, Checa et al. 2012). Other factors associated with *L. infantum* seroprevalence are weight, breed size, place of abode, sleeping outdoors and the use given to the dogs. Human and canine leishmaniasis cases in Hungary are usually imported (Farkas, Tanczos et al. 2011; Tanczos, Balogh et al. 2012), but recently a probable autochthonous *L. infantum* infection of dogs has been reported (Tanczos, Balogh et al. 2012).

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From: New advances and persistent old questions in the emergence of some vector-borne disease in Europe. A critical and systematic review on the 2010/2012 literature.


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