

## Leishmania donovani leishmaniasis in Cyprus

Nicole Léger and Jérôme Depaquit emphasise “the importance of preventing an extension of this anthroponotic species in Europe”,<sup>1</sup> a point also stressed by Dujardin et al,<sup>2</sup> since leishmaniasis is not placed under public health surveillance in Europe.

We certainly agree with the authors that the indigenous transmission of *Leishmania donovani* to Cyprus needs to be proven, since the possibility of the invasion of Cyprus by anthropophilic *L donovani* vectors cannot a priori be excluded—particularly if we consider the geopolitical status of the island (figure, A). In this scenario, imported *L donovani*-infected sandflies would need either to transmit the parasite within their short lifespan or survive and spread. While the first hypothesis is contradicted by the 2–3 year observed infection period, the second is possible if the Cypriot ecosystem/microclimate is taken into account (figure, B). However, the five reported human cases,<sup>3</sup> including an additional cutaneous leishmaniasis case in Nicosia (unpublished), were found in three of the five prefectures of the government-controlled area. Each prefecture belongs to a distinct, relatively distant, biogeographical region (figure, B). Within the context of sandflies’ weak flight, there is little chance of even a small number of infected sandflies having traveled and spread to these different locations.

This raises the question of whether the Cyprus sandfly fauna, present since the Miocene period,<sup>4</sup> can transmit *L donovani*. This fauna is comprised of nine closely related species of the Phlebotominae subfamily (*Phlebotomus* and *Sergentomyia* genera), which are proven or probable

vectors of Mediterranean canine visceral leishmaniasis (CVL) caused by *L infantum*. *P neglectus*, a species with a wide distribution in eastern Mediterranean countries, was only recently identified in the northern non-government-controlled area of Cyprus.<sup>5</sup> Interestingly, the *Larrousius* species *P galilaeus* and *P tobbi*, are the most abundant in both the government-controlled and northern areas of Cyprus.<sup>4,7</sup> Notably, *P tobbi*, a broadly permissive vector, has been found in high dog seropositivity areas during several field surveys. As a result it is considered to be the vector of *L infantum* in Cyprus,<sup>8,9</sup> and this is also the case in the eastern Mediterranean region (figure, A). Léger and Depaquit question the role of *P tobbi* as a vector of *L donovani* in Cyprus based simply on their observation that, unlike in the north, no human leishmaniasis cases were reported in the southern part of the island.<sup>1</sup> However, in Turkey, it was recently shown through blood-meal identification that *P tobbi* feeds preferentially on cattle and people.<sup>10</sup> If we also consider the few reported cases due to *L infantum*,<sup>11</sup> and the identification of both species in a dog,<sup>3</sup> the trophic preferences of local populations of *P tobbi* remain to be established. In addition, the host immune response depends, not only on whether sandflies are infected, but also on their parasite load.<sup>12</sup> Pre-exposure to certain sandfly saliva components could affect immune response to *Leishmania* spp infection, and consequently disease outcome.<sup>13</sup> Therefore we consider that the conclusion reached, concerning the lack of anthropophily of *P tobbi* in Cyprus<sup>1</sup> may be illusive and

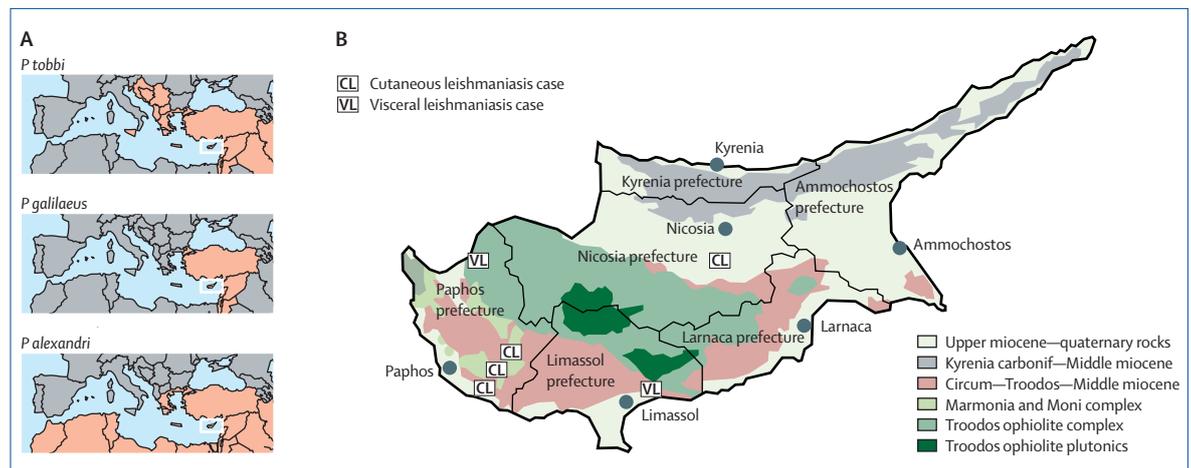


Figure: Regional distribution of three putative *Phlebotomus* spp vectors (A) and locations of the human *L donovani* cases in Cyprus (B)

that *P. tobbi* could be incriminated for the transmission of both *L. infantum* and *L. donovani*.

Other candidate vectors of *L. donovani* MON-37 could be *P. galilaeus*<sup>1</sup> and also *P. economides* and *P. alexandri*, which are more abundant in Paphos and Limassol prefectures<sup>4</sup> where the human cases were detected. Notably, *P. alexandri* is considered the proven vector of *L. donovani* and *L. infantum* in China<sup>14</sup> and Iran,<sup>15</sup> respectively, and is also found in regions where *L. donovani* MON-37 is present.<sup>3</sup>

Therefore, the most probable scenario is that of importation and settlement of *L. donovani* MON-37 in Cyprus through infected individuals from *L. donovani* MON-37 endemic countries, including both legal and illegal laborers which most probably played or still play the part of parasite reservoir. Population genetic analysis of the *L. donovani* MON-37 strains from Cyprus, including those from other endemic countries, will give answers to the questions addressed above. Investigation of human exposure to the different sandfly species present in Cyprus and of sandfly blood meal preferences, as well as experimental transmission by their bite, will help assess their ability to act as *L. donovani* vectors. These actions aim to identify the responsible vector(s) among the putative candidates and assess the risk/danger of anthroponotic *Leishmania* species spread in Europe.

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- 1 Leger N, Depaquit J. *Leishmania donovani* leishmaniasis in Cyprus. *Lancet Infect Dis* 2008; **8**: 402.
- 2 Dujardin JC, Campino L, Canavate C, et al. Spread of vector-borne diseases and neglect of Leishmaniasis, Europe. *Emerg Infect Dis* 2008; **14**: 1013–18.
- 3 Antoniou M, Haralambous C, Mazeris A, Pralong F, Dedet JP, Soteriadou K. *Leishmania donovani* leishmaniasis in Cyprus. *Lancet Infect Dis* 2008; **8**: 6–7.
- 4 Depaquit J, Leger N, Ferte H, et al. Phlebotomines of the Isle of Cyprus. III. Species inventory. *Parasite* 2001; **8**: 11–20 (in French).
- 5 Rastgeldi S, Ozbel Y, Ozensoy TS, Ertabaklar H, Göçmen B. Phlebotominae sand flies (Diptera: Psychodidae) of the northern part of Cyprus island. *Arch Inst Pasteur Tunis* 2005; **82**: 121.
- 6 Adler S. The sandflies of Cyprus (Diptera). *Bulletin of Entomological Research* 1946; **36**: 497–511.
- 7 Aransay AM, Scoulica E, Chaniotis B, Tselentis Y. Typing of sandflies from Greece and Cyprus by DNA polymorphism of 18S rRNA gene. *Insect Mol Biol* 1999; **8**: 179–84.
- 8 Deplazes P, Grimm F, Papaprodromou M, et al. Canine leishmaniasis in Cyprus due to *Leishmania infantum* MON 1. *Acta Trop* 1998; **71**: 169–78.
- 9 Leger N, Depaquit J, Ferte H, et al. Phlebotomine sandflies (Diptera-Psychodidae) of the isle of Cyprus. II—Isolation and typing of *Leishmania (Leishmania infantum* Nicolle, 1908 (zymodeme MON 1) from *Phlebotomus (Larrousius) tobbi* Adler and Theodor, 1930. *Parasite* 2000; **7**: 143–6 (in French).
- 10 Svobodova M, Alten B, Zidkova L, et al. Cutaneous leishmaniasis caused by *Leishmania infantum* transmitted by *Phlebotomus tobbi*. *Int J Parasitol* 2008; published online Aug 14. DOI:10.1016/j.ijpara.2008.06.016.
- 11 Minter DM, Eitrem UR. Sandflies and disease in Cyprus; 1944–1985. In: Hart DT, ed. *Leishmaniasis, The current status and new strategies for control*, vol 3. Plenum Press, New York, 1989: 207–216.
- 12 Croft AM, Taylor NA, Rodenhurst KE. Sandflies and leishmaniasis. *Lancet* 2006; **367**: 112.
- 13 Gomes R, Teixeira C, Teixeira MJ, et al. Immunity to a salivary protein of a sand fly vector protects against the fatal outcome of visceral leishmaniasis in a hamster model. *Proc Natl Acad Sci USA* 2008; **105**: 7845–50.
- 14 Guan LR, Xu YX, Li BS, Dong JA. The role of *Phlebotomus alexandri* in the transmission of kala-azar. *Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi* 1985; **3**: 85–8 (in Chinese).
- 15 Javadian E, Nadim A. Studies on cutaneous leishmaniasis in Khuzestan, Iran. Part II. The status of sandflies. *Bull Soc Pathol Exot Filiales* 1975; **68**: 467–71.

## Vaccine immunogenicity in injecting drug users

Stefan Baral and colleagues published an interesting review on vaccination and injecting drug users in October 2007.<sup>1</sup> The authors argued that detectable hepatitis B virus (HBV) surface antigen specific antibodies (antiHBs) may not be the best measure of immunity to hepatitis B following vaccination.<sup>1</sup> The authors went on to quote the results of an Italian prospective cohort study by Lugoboni et al.<sup>2</sup> Baral et al claimed that the study showed that none of the 258 patients who received three or more doses of vaccine went on to contract

hepatitis B, despite a seroprevalence of protective antiHBs of only 71.9%.<sup>1</sup> This is not correct, since the study actually reported that two vaccinated patients developed hepatitis B (as measured by the detection of antibody to HBV core antigen (antiHBc)). One patient had received two doses of vaccine, while the other had received three doses. This was out of the 258 patients who were followed up. The article did not state that this group received three or more vaccinations. In fact, the article suggests (but does not explicitly state) that this