*Institute of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna; Kinderspitalgasse 15, 1090 Vienna, Austria*

# *Leishmania* infections and *Leishmania* species in central Europe

E. Kniha[a], H. Aspöck[b], H. Auer[c] and J. Walochnik[d,*]

ORCID: a) 0000-0002-6875-7056
b) 0000-0001-9407-3566
c) 0000-0001-7020-9705
d) 0000-0003-0356-2853

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## Summary

Species of the genus *Leishmania* (Trypanosomatidae) are parasitic protists that are transmitted to vertebrates by the bites of female sandflies (Phlebotominae) and are the causative agents of Visceral Leishmaniosis (VL) and various forms of Cutaneous Leishmaniosis (CL) in humans and animals. Worldwide, around 12 million humans are infected and more than 50,000 deaths are recorded every year, mainly due to VL. Numerous animal species are affected with various forms of leishmaniosis and canine leishmaniosis is a major global zoonosis. *Leishmania* infections diagnosed in central Europe are generally imported cases, the main drivers being travelling and migration. However, occasional autochthonous cases have also been recorded, suggesting that *Leishmania* may have arrived in central Europe. This review addresses the issue by evaluating cases of *Leishmania* infections reported from central European countries and by summarizing the knowledge of reservoirs and vectors for *Leishmania* spp. in central Europe.

## Zusammenfassung

### *Leishmania*-Infektionen und *Leishmania*-Spezies in Mitteleuropa

Bei den Arten der Gattung *Leishmania* (Trypanosomatidae) handelt es sich um parasitische Protisten, die durch den Stich von weiblichen Sandmücken (Phlebotominae) auf Vertebraten übertragen werden und bei diesen die Viszerale Leishmaniose (VL) und mehrere Formen von Hautleishmaniose (CL) hervorrufen können. Weltweit sind etwa 12 Millionen Menschen mit Leishmanien infiziert, und es kommt jedes Jahr zu geschätzten 50.000 Todesfällen, vor allem durch VL. Außerdem sind zahlreiche Tiere von verschiedenen Ausprägungen der Leishmaniose betroffen; die Kanine Leishmaniose gilt als bedeutende globale Zoonose. Bei den in Mitteleuropa diagnostizierten Leishmanien-Infektionen handelt es sich in der Regel um importierte Fälle, meist in Zusammenhang mit Reisetätigkeiten oder Migration. Jedoch werden auch immer wieder autochthone Fälle beschrieben, was die grundsätzliche Frage aufwirft, ob Leishmanien in Mitteleuropa vorkommen (können)? Dies soll in der vorliegenden Übersichtsarbeit erörtert werden, wobei Daten zu beschriebenen Leishmaniose-Fällen ebenso berücksichtigt werden wie der derzeitige Stand des Wissens zu in Mitteleuropa vorhandenen möglichen Reservoiren und Vektoren von Leishmanien.

**Abbreviations:** CL = Cutaneous Leishmaniosis; EDTA = Ethylenediaminetetraacetic acid; IgG = Immunoglobulin G; kDNA = Kinetoplast DNA; LAMP-based = Loop-mediated isothermal amplification-based; MB = Megabases; PCR = Polymerase chain reaction; VL = Visceral Leishmaniosis; WHO = World Health Organization

*E-Mail: julia.walochnik@meduniwien.ac.at

## Introduction

Species of the genus *Leishmania* (Trypanosomatidae: Leishmaniinae) are parasitic protists that can cause disease in a large number of animals and humans. The symptoms and progression of the disease depend on the species, the localization of the infection and the immune status of the host. Generally, the disease can be divided into two main entities, Visceral Leishmaniosis (VL) and various forms of Cutaneous Leishmaniosis (CL) (Fig. 1). While human VL, as canine VL, are fatal if untreated, many forms of CL are self-limited, although they nevertheless cause a permanent local destruction of the skin and are often associated with social stigmatization in humans. More than one billion humans live in areas endemic for leishmanioses. According to the WHO, up to 90,000 new cases of VL and between 600,000 to 1 million new cases of CL occur annually. HIV-infected individuals are particularly susceptible to VL and difficult to treat (WHO 2021, 2022). The annual number of canine VL cases is estimated to be as high as 50–100/ 1000 dogs in several Mediterranean regions, with well over 50 % of dogs infected in many endemic areas worldwide (Moreno & Alvar 2002; Le Rutte et al. 2021; Vaselek 2021).

*Leishmania* parasites are transmitted by the bites of female sandflies (Diptera: Psychodidae: Phlebotominae). Around 100 of the 1000 described sandfly species are confirmed vectors of *Leishmania* species (Cecílio et al. 2022). However, when discussing possible autochthonous cases in non-endemic regions it is important to note that in dogs, but potentially also in humans, other routes of transmission may play a part, such as blood contacts (in dogs: bites), or venereal and transplacental transmission (Walochnik & Aspöck 2005; Silva et al. 2009; Guedes et al. 2020). Transmission by blood transfusion has been long known for and also has to be excluded when confirming suspected autochthonous cases (Jimenez-Marco et al. 2016).

The leishmanioses, particularly the cutaneous forms, were already known to ancient civilizations in Egypt, the Middle East and central and South America. The first detailed description of CL is given in the Canon of Medicine ("al-Qanun fi'l-tibb") written around 1030 by Avicenna (Ibn Sina), a Persian physician born in what is today Uzbekistan, who stated that the disease often starts with an insect bite (Walochnik & Aspöck 2010). One of the first to see *Leishmania* parasites was David Cunningham (1843–1914), who described parasites in a skin biopsy of an Indian patient with an "Oriental sore" in 1885 but mistook them for mycetozoans. A year later, the Viennese physician Gustav Riehl identified "micrococcae" as causative agents of the "Aleppo boil" in a patient returning from India and in 1898, Piotr Fokich Borovsky, a Russian military physician serving in Tashkent (the present capital of Uzbekistan), described protistan parasites as the causative agents of the Oriental sore. The genus was named after Sir William Boog Leishman, who detected the parasites in 1900 in spleen samples from a soldier who had died after returning from India from what we today know as VL. He published his finding in 1903, almost synchronously with Charles Donovan, who was Professor at the Medical College in Madras, India and had also detected the parasites in spleen samples (Donovan 1903; Leishman 1903). In the same year, the American pathologist James Wright published a description of the causative agent of a sore in an Armenian girl as *Heleosoma tropicum* (Wright 1903). Ronald Ross established the genus *Leishmania* with the species *Leishmania donovani*, *H. tropicum* was included as *L. tropica* by Max Lühe (Ross 1903a,b; Lühe 1906) and later divided into *L. tropica* and *L. major*.

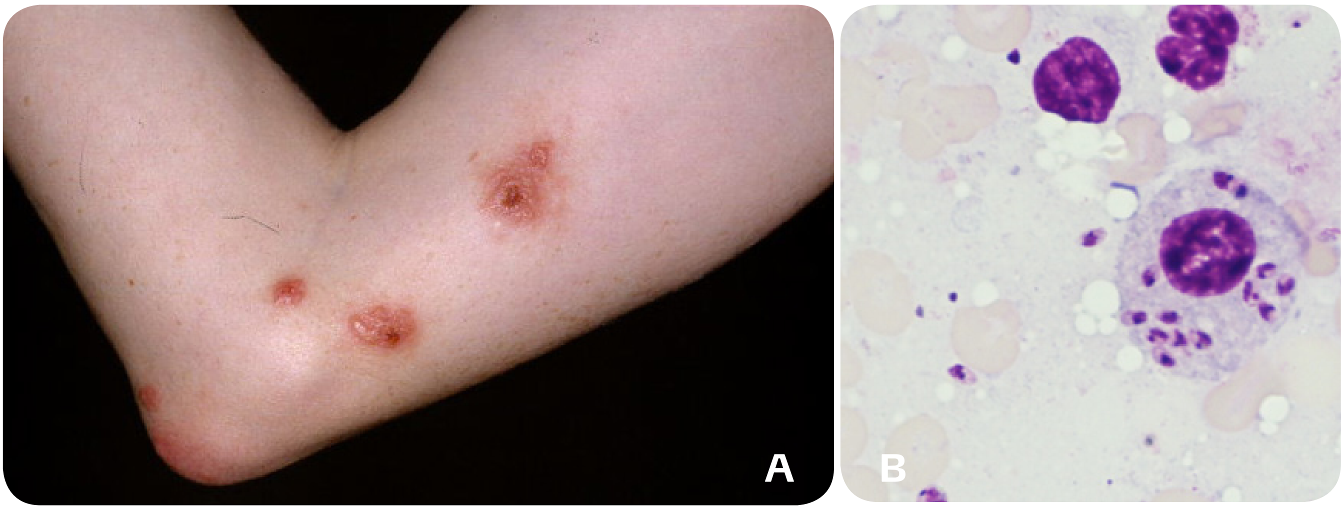

**Fig. 1:** Leishmaniosis. **A** Cutaneous Leishmaniosis, multiple lesions. Photograph: Dr Rosemarie Moser. **B** Amastigote *Leishmania* parasites in a human macrophage (bone marrow sample from a case of Visceral Leishmaniosis). Photograph: Authors / Leishmaniose. **A** Kutane Leishmaniose, mehrfache Läsionen. Foto: Dr. Rosemarie Moser. **B** Amastigote *Leishmania*-Parasiten in einem humanen Makrophagen (Knochenmarkspunktion eines Patienten mit viszeraler Leishmaniose). Foto von den Autor:innen

In 1908, Charles Nicolle isolated *Leishmania* parasites from a child, differentiating the disease from the Indian VL caused by *L. donovani* and proposing the name *L. infantum*, which in the same year he and Charles Compte also isolated from dogs (Nicolle 1908; Nicolle & Compte 1908). Charles Morley Wenyon (1911) identified sandflies of the genus *Phlebotomus* as the probable vector of *Leishmania* in the Old World and in 1922, Henrique de Beaurepaire Rohan Aragão confirmed in South America that *Leishmania* species are transmitted by sandflies, which were later recognized as belonging to the genus *Lutzomyia*. It is currently assumed that neotropical sandflies were already vectors for *Leishmania*-like parasites in the mid Oligocene to early Miocene (Steverding 2017).

The first *Leishmania* genome was published in 2005. The haploid genome of *Leishmania* has 32–35 megabases (MB), organized on 34–36 chromosomes and with a total gene number of around 9,000. The mitochondrial genome is organized in 20–50 maxicircles and $10^4$ minicircles within the single mitochondrion (Simpson et al. 1989; Aebischer & Mrva 2016). In the past years, particularly diagnostics but also treatment have improved significantly and there is a realistic chance that there will be a vaccine within the next decade (Malvolti et al. 2021). Currently, there is one live vaccine for humans licensed in Uzbekistan and four vaccines directed against leishmaniosis in dogs: Leishmune® (purified fraction isolated from *L. donovani* plus a saponin adjuvant; withdrawn in 2014), CaniLeish® (excretory-secretory proteins (ESP) of *L. infantum*; withdrawn from the European market), Leish-Tec® (recombinant protein A2 associated with saponin; licensed in Brazil) and LetiFend® (recombinant protein Q of *L. infantum* MON-1). A recombinant vaccine for use in humans is based on the Nucleoside hydrolase NH36 of *L. donovani*, the main antigen of the Leishmune® vaccine, and a vaccine against the sterol 24-c-methyltransferase from *L. infantum* has reached phase I clinical trials (Palatnik-de-Sousa & Nico 2020).

Within Europe, only the Mediterranean region has always been a region of endemicity, with *L. infantum* being the main pathogen and dogs, rodents and other small mammals the main reservoir hosts (Rocha et al. 2022). Presumably, the uncontrolled import of infected dogs from Mediterranean southern and eastern European countries has been a precondition for the occasional occurrence of autochthonous cases of leishmaniosis in central Europe (Leschnik 2020). However, in most central European countries, including Austria, leishmaniosis is not a notifiable disease, so case numbers can only be estimated and only few countries have implemented surveillance and control targeting both animal and human infections (Berriatua et al. 2021). With this review, we give an overview of the current relevance of *Leishmania* infections in central Europe from the One Health perspective and of the current state of knowledge on the possibility that *Leishmania* may become endemic in central Europe by reviewing the possible reservoirs and vectors.

## Cases of *Leishmania* infection in Europe/ central Europe

### Humans

Worldwide, most leishmaniosis cases occur in the tropics and subtropics, with a small number of countries bearing the major burden of the disease. According to the WHO, over 90 % of VL cases in 2020 occurred in Brazil, China, Ethiopia, Eritrea, India, Kenya, Somalia, South Sudan, Sudan and Yemen, with Brazil, East Africa and India reporting the highest numbers of new cases. The countries with the highest numbers of CL cases were Afghanistan, Algeria, Brazil, Colombia, Iraq, Libya, Pakistan, Peru, the Syrian Arab Republic and Tunisia, while over 90 % of all mucocutaneous cases occurred in Bolivia, Brazil, Ethiopia and Peru (WHO 2021).

Leishmaniosis has been endemic in the entire Mediterranean region since ancient times, including most southern European countries, where particularly *L. infantum* but also *L. tropica* are endemic. In France, for instance, 317 autochthonous and 1,154 imported cases of leishmaniosis were recorded between 1999 and 2012, with autochthonous cases mainly relating to VL (84.5 %) and all stemming from the south of France (Lachaud et al. 2013). However, *L. infantum* can also cause cutaneous and even mucocutaneous infections (Gaspari et al. 2020) and in several Mediterranean regions, including the Balkan peninsula, infections with *L. infantum* are considered to be re-emerging (Dvořák et al. 2020). In 2009, an outbreak of human leishmaniosis started in Madrid. It is currently declining and is considered the largest outbreak of human leishmaniosis recorded in Europe (Arce et al. 2013). In this outbreak, wild hares were identified as the main reservoir of the parasite. In 2021, a molecular follow-up study reported an average *L. infantum* infection rate of 8.97 % in *Ph. perniciosus* in the outbreak region, indicating ongoing transmission (González et al. 2021). In Italy, a continuous northward expansion has been recorded during the past 30 years (Gradoni et al. 2022). In Greece, 326 autochthonous cases of human leishmaniosis were registered between 2005 and 2010, including two cases of *L. tropica* from southern Greece (Ntais et al. 2013). Berriatua et al. (2021) surveyed 32 European countries, of which 18 declared autochthonous human cases of leishmaniosis, mainly VL, and 13 reported autochthonous human cases of both VL and CL. Human leishmaniosis was notifiable in 19 countries, 19 countries confirmed surveillance and 12 said that they had control programmes. Only four European countries reported control of leishmaniosis in animals: Greece, Italy, Montenegro and North Macedonia.

In central Europe, leishmanioses are typically travel-related diseases. It is assumed that several thousand human cases are imported into central Europe every year. However, as *Leishmania* infections are not notifiable in most European countries, there are no reliable data. In what is the probably largest study of the subject, Van der Auwera (2022) retrospectively analysed records of leishmaniosis cases diagnosed between 2014 and 2019 in 15 centres from eleven countries: Belgium, France, Germany, Italy, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom. They analysed a total of 1,142 cases, of which 76 %, 21 % and 3 % had cutaneous, visceral and mucosal disease, respectively. Sixty-eight percent were men and 32 % women, with a median age of 37 years (range: 0–90) at diagnosis. VL was mainly acquired in Europe (88 %; 167/190), while CL was primarily imported from outside Europe (77 %; 575/749). Sixty-two percent of CL cases from outside Europe were from the Old World and 38 % from the New World. A review of 223 cases of CL imported into the UK between 1998 and 2009 found 90 cases of Old World CL, mainly caused by representatives of the *L. donovani/infantum* complex (n=20) and mainly in tourists returning from the Mediterranean region, while 133 cases were diagnosed as New World CL, with *Leishmania* subgenus *Viannia* the principal causative agent and patients mostly backpackers, but also soldiers (Wall et al. 2012). A study (Glans et al. 2018) of all cases of microbiologically confirmed cases of leishmaniosis in Sweden between 1996 and 2016 revealed migration as the primary cause for the observed increase in cases between 2013 and 2016. Fifty-two percent of cases were linked to migration, with the most common countries of origin being Syria, Afghanistan and Iran. Medical reports were available from 156 of the 165 cases; 51 % of them were migrants, mainly young men, followed by tourists (25 %) and returning workers (8 %), volunteers and military personnel returning from Afghanistan. Migration and travel are the two factors with the highest impact on the number of leishmaniosis cases in central Europe and this is reflected in the gender distribution of the cases. More male migrants come to central Europe than females and male travellers have riskier travel habits, which are assumed to have a role (Boggild et al. 2019).

Between January 2010 and December 2020, 358 cases of leishmaniosis were recorded at the Institute of Specific Prophylaxis and Tropical Medicine of the Medical University of Vienna, with a median age of 41 years and 60.45 % of the patients being males (Fidelsberger 2021). Annual case numbers increased significantly from 2015, with a peak in 2018. Genotyping was performed in 21.5 % of cases and revealed the *L. donovani/infantum* complex in 37.7 % of the cases where the genotype was tested. Kniha et al. (2020a) evaluated the *Leishmania* seroprevalence in Austrian soldiers returning from the Kosovo. Fifty-five of them (21.1 %) had anti-*Leishmania* antibodies, with 13.8 % clearly positive and 7.3 % borderline. Kutyi (2020) evaluated the course of the disease and the personal perceptions of patients with leishmaniosis admitted to the Vienna University Hospital between 2011 and 2018 and found a low level of knowledge on the disease in the travelling population and a high degree of unsettledness during the course of disease and its management. Oeser (2011) performed a retrospective study of 21 patients who had received treatment for leishmaniosis at the Vienna University Hospital between 2004 and 2010 and found very heterogenous treatment approaches and outcomes.

## Animals

Only four European countries, Greece, Italy, Montenegro and North Macedonia, have control systems for leishmaniosis in animals (Berriatua et al. 2021). Although many animals, including a large number of mammalian species (e.g. red foxes, wolves, golden jackals, cats and many rodent species) and e.g. reptiles, can be infected with *Leishmania* spp., extensive and reliable data are available only for dogs. Dogs may develop canine leishmaniosis, which is lethal if left untreated, but most infected dogs remain asymptomatic. However, asymptomatic and treated dogs can still function as reservoirs for transmission of the parasites to sandflies (and occasionally also to vertebrates). Many Mediterranean countries have high infection rates in dogs. A study of 5,772 dogs in Greece found 22.09 % to be seropositive, with seropositivity generally higher in stray dogs and in some regions reaching >50 % (Ntais et al. 2013). More than 15 % of the entire canine population in southwestern European countries has been estimated to be infected with *L. infantum* (Moreno & Alvar 2002). Italy was reported to have the highest median seroprevalence (17.7 %) among these countries and has seen changing distribution patterns and a northward expansion of endemicity in the recent past (Mendoza-Roldan et al. 2020; Gradoni et al. 2022). Similar patterns have been reported for Spain and France, along with a general increase in canine leishmaniosis (Le Rutte et al. 2021).

## Diagnostics

*Leishmania* diagnostics has changed significantly in recent years, particularly in Europe. While microscopy is still the gold standard in many endemic regions, most central European labs – which have less experience with *Leishmania* microscopy – largely rely on molecular methods for diagnosis. This has the advantage that less invasive sampling techniques are required as sensitivity is usually very high. Moreover, molecular tests may allow the identification of species and strain, which is traditionally based on multilocus enzyme electrophoresis (zymodemes) that requires prior parasite isolation and culture. The diagnostic methods used for humans and animals are largely identical, although there are specific guidelines for the diagnosis and practical management of canine leishmaniosis (Solano-Gallego et al. 2011).

While numerous commercial (mainly serological, but also PCR-based) test systems are available for VL, laboratory diagnosis of CL can still be challenging. As in CL, the humoral immune response is low, except in disseminating forms, so the main focus is on direct detection, with molecular methods showing the highest sensitivity. In VL, parasites can be detected in bone marrow and (exceptionally) spleen aspirations; for PCR, EDTA blood is sufficient. Alternatively, commercial antigen tests are available or anti-*Leishmania* antibodies can be detected by serological methods. In humans, rapid tests, such as the K39 strip test based on the detection of IgG against the leishmanial antigen K39 or the so-called KAtex® test for *Leishmania* antigen in urine, are available for the rapid diagnosis of VL. To diagnose CL, punch biopsies from the margin of the lesion are the preferred sample but skin scrapings, slit skin smears, aspirates or even skin impressions on DNA-stabilizing filter paper usually give reliable and sensitive results with PCR-based techniques. The usual targets for the PCR are the kDNA (kinetoplast DNA, network of multiple copies of mitochondrial DNA exclusively found in the Kinetoplastida) or the 18S ribosomal DNA (rDNA). Multiplex real-time PCRs for the simultaneous discrimination of the various *Leishmania* complexes (Schulz et al. 2003) and Loop-mediated isothermal amplification (LAMP)-based point-of-care tests have been established (Adams et al. 2018), although the sensitivity in CL is well below 100 %.

### Treatment approaches

In Austria, treatment of *Leishmania* infections in humans generally follows the guidelines of the German Society for Tropical Medicine and International Health (DTG 2010, 2012). VL is treated systemically, with liposomal amphotericin B (AmBisome®) being the first-line therapy and miltefosine (Impavido®) the most important alternative. The antimony-based compounds sodium stibogluconate (Pentostam®) and meglumine antimoniate (Glucantime®) are now only rarely used in Europe due to their comparably severe side effects and possible resistances. The treatment of CL depends on the species involved and on the number, location and size of the lesion(s), as well as on the age and immune status of the patient and on cosmetic aspects. While mucosal and disseminating CL is generally treated systemically, again mainly with liposomal amphotericin B or miltefosine, localized CL is treated topically with paromomycin, fluconazole, ketoconazole or with thermotherapy. Small lesions on uncomplicated body sites may not need treatment. A new topical treatment for skin lesions based on sodium chlorite was recently introduced (Debus et al. 2022).

In animals, the decision for the necessity and justifiability of therapeutic interventions depends on the clinical condition and severity of the disease. Guidelines for dogs were published by the LeishVet Group (Solano-Gallego et al. 2011). Treatment in animals is generally based on Allopurinol (Lopurin®, Zyloprim®) and expanded when necessary (after staging) to meglumine antimoniate (Glucantime®) or miltefosine (Milteforan®). Immunostimulants such as domperidone (Leisguard®), which is also used for prevention, may be used in mild forms of the disease. In most cases, it is very difficult to achieve and to prove parasitological cure. In dogs, preventive measures, particularly repellents but also vaccines and immunostimulants, have a significant role in controlling the disease in endemic regions.

## Autochthonous cases in central Europe?

Leishmaniosis is endemic in all southern countries of Europe, with approximately 700 autochthonous human cases reported each year and many more asymptomatic infections. The main species involved is *L. infantum*, although *L. tropica* has also been documented in several regions and may become endemic in areas where *Ph. sergenti*, the main vector, is present or may become so (Barón et al. 2013; El Idrissi Saik et al. 2022) and *L. donovani* and *L. major* are on the rise. There is still no coordinated surveillance of the disease at the European level (Dujardin et al. 2008). The past years have seen several records of sandflies in central Europe (Fig. 2). Moreover, most regions have a reservoir of *Leishmania* in imported or travelling dogs, with dogs being the main reservoir host for *L. infantum* (Fig. 2). Is *Leishmania* transmission possible in central Europe?

Suspected autochthonous cases have been reported from several central European countries, in animals as well as in humans. In Germany, a case of VL in a 15-month-old German child was identified, congenital or blood transfusion-associated leishmaniosis ruled out (Bogdan et al. 2001). One year later, an autochthonous case of *Leishmania* infection in a horse was reported (Koehler et al. 2002) and there were multiple CL equine cases from different regions in Germany in the following years (Litzke et al. 2006; Müller et al. 2009; Kuhls et al. 2013; Sinning et al. 2014) (Fig. 2). Two autochthonous human cases have been described in Austria (Beyreder 1962; Kollaritsch et al. 1989) and there was an unexpectedly high seroprevalence of anti-*Leishmania* antibodies in asymptomatic Austrian individuals (Poeppl et al. 2013a). A suspected human case and autochthonous bovine and possibly autochthonous equine *Leishmania* infections have been reported in Switzerland (Mazzi 1976; Müller et al. 2009; Lobsiger et al. 2010) and autochthonous canine cases have been recorded in Hungary (Tánczos et al. 2012). Even northern Europe has seen cases with no travel

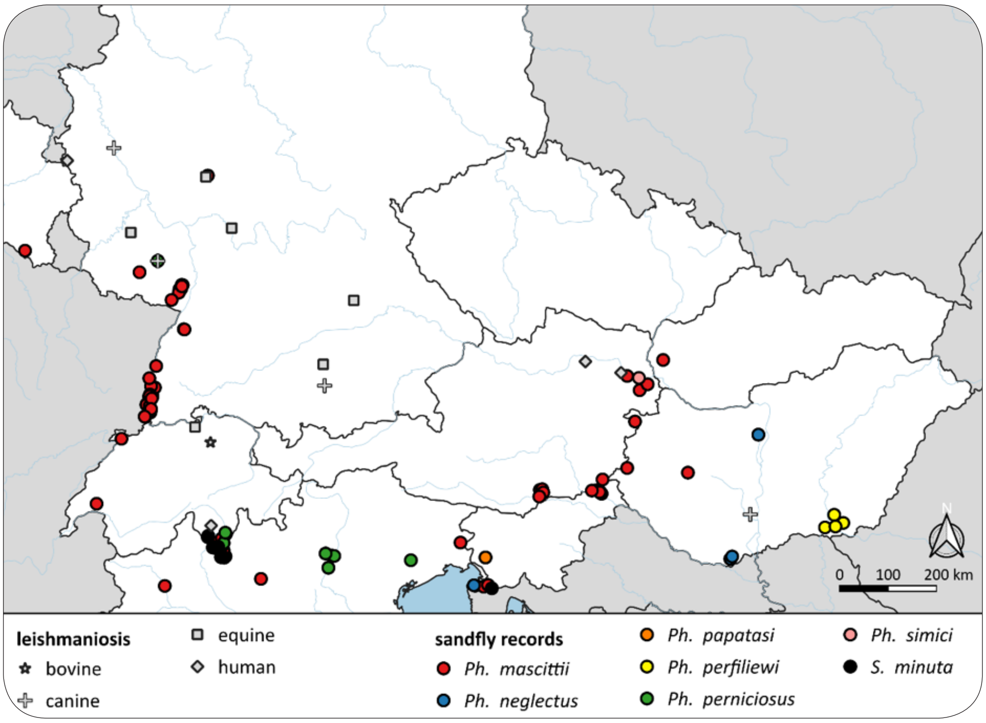

**Fig. 2:** Records of possible autochthonous leishmaniosis and sandflies (genera *Phlebotomus* and *Sergentomyia*) in central Europe / Mögliche autochthone Leishmaniose- und Sandmücken-Nachweise (Genera *Phlebotomus* und *Sergentomyia*) in Mitteleuropa

history (Slappendel 1988; Diaz-Espineira & Slappendel 1997). In a UK study, >95 % of dogs diagnosed with canine leishmaniosis had spent at least 6 months in an endemic country, mainly in Spain, although three affected dogs from UK re-homing centres had no history of travel (Shaw et al. 2009).

## Relevant *Leishmania* species

The genus *Leishmania* includes over 50 species, of which 30 are considered as pathogens for mammals. The genus is divided into four subgenera: *Leishmania*, *Sauroleishmania* and *Mundinia* occur in the Old and the New World, the subgenus *Viannia* is restricted to the New World (Table 1, Table 2). While the representatives of the Old World subgenera develop within the mid and foregut of the host sandflies, species of *Viannia* and *Endotrypanum* have an additional developmental stage in the hindgut. Over 20 species of the subgenera *Leishmania*, *Mundinia* and *Viannia* can cause disease in humans, the most important ones being the *L. donovani/infantum* complex, the *L. tropica* complex, the *L. major* complex, the *L. mexicana* complex, the *L. braziliensis* complex and the *L. guyanensis* complex. The majority of *Leishmania* species are zoonotic. Only two species, *L. donovani* and *L. tropica*, are anthroponotic but even these have repeatedly been isolated from animals. The representatives of the subgenus *Mundinia* have only recently been recognized as human pathogens (Sereno 2019). Some of the non-*Leishmania* Leishmaniinae have also been reported to cause disease in humans, e.g. *Endotrypanum columbiensis* (Kreutzer et al. 1991).

The “Supercontinent hypothesis” proposes that *Leishmania* parasites evolved in mammals in the Mesozoic on the supercontinent Gondwana, possibly from monoxenous insect flagellates and, after the breakup of Gondwana, separated into the subgenera *Viannia* in South America and *Leishmania*, *Mundinia* and *Sauroleishmania* in Africa (Harkins et al. 2016). The Old World *Leishmania* species, *L. aethiopica*, *L. donovani*, *L. infantum*, *L. major* and *L. tropica*, are assumed to have an African, possibly East African, origin and to have dispersed into Asia and Europe. One species of the subgenus *Leishmania*, possibly deriving from a common ancestor with *L. major*, later spread with its rodent hosts from Asia to the Americas, evolving to the *L. mexicana* complex, and *L. infantum* came to the Americas with the European conquerors (and their dogs). *L. infantum* has been introduced into the Americas on multiple occasions and as numerous different strains independently in the past centuries, adapting not only to new vector species but also to new reservoir hosts. Likewise, the current globalization is dispersing the species all over the world. In contrast to other *Leishmania* species, which have also been transported all around the globe, *L. infantum* seems to have an exceptional capacity for adaptation based on rapid karyotypic and genetic change (Boité et al. 2019; Patino et al. 2021; Schwabl et al. 2021). This is relevant to speculations that *L. infantum* may become endemic in central Europe. The association between sandfly and *Leishmania* species is also driven by the parasite density in the blood meal sources for the sandflies. In *L. infantum* infection it seems that the parasite density in the skin rather than in the blood affects the transmissibility of the parasite from the vertebrate host to the sandfly (Bourdeau et al. 2020).

Europe was probably first reached by *L. infantum* with dogs and by *L. tropica* with humans, most probably post-glacially. A recent study found evidence that the distribution of *L. infantum* during the last glacial period must have been rather small and concluded that the species may have survived in distinct western and eastern Mediterranean refugia, while the climate of large areas of

**Tab. 1:** Overview of the genera, subgenera and species in the subfamily Leishmaniinae, family Trypanosomatidae (based on Akhoundi et al. 2016 and Espinosa et al. 2016). Orange: Old World; Green: New World; Brown: Old and New World / Überblick über beschriebene Genera, Subgenera und Species der Subfamilie Leishmaniinae, Familie Trypanosomatidae (basierend auf den Arbeiten von Akhoundi et al. 2016 und Espinosa et al. 2016). Orange: Alte Welt; grün: Neue Welt; braun: Alte und Neue Welt

| Genus *Leishmania* Ross, 1908 | | | | | | | | | **Genus *Porcisia*** Shaw, Camargo & Teixeira, 2016 | **Genus *Endotrypanum*** Mesnil & Brimont, 1908 | **Genus *Zelonia*** Shaw, Camargo & Teixeira, 2016 | **Genus *Novymonas*** Kostygov & Yurchenko, 2016 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Subgenus *Leishmania*** Ross, 1908 | | | | **Subgenus *Sauroleishmania*** Ranque, 1973 | **Subgenus *Viannia*** Lainson & Shaw, 1987 | | | **Subgenus *Mundinia*** Shaw, Camargo & Teixeira, 2016 | ***P. hertigi*** Herrer, 1971<br>***P. deanei*** Lainson & Shaw, 1977 emend. Lainson & Shaw, 1987 | ***E. schaudinni*** Mesnil & Brimont, 1908<br>***E. monterogeii*** Shaw, 1969<br>***E. colombiensis*** Kreutzer et al., 1991<br>***E. equatorensis*** Grimaldi et al., 1992<br>***E. herreri*** Zeledón, Ponce & Murillo, 1979 | ***Z. costaricensis*** Yurchenko et al., 2006<br>***Z. australiensis*** Barrat et al., 2017 | ***N. esmeraldas*** Votypka, Kostygov, Maslov & Lukes, 2016 |
| ***L. donovani* complex** | ***L. tropica* complex** | ***L. major* complex** | ***L. mexicana* complex** | ***L. henrici*** Leger, 1918<br>***L. chameleonis*** Wenyon, 1921<br>***L. tarentolae*** Wenyon, 1921<br>***L. davidi*** Strong, 1924<br>***L. agamae*** David, 1929<br>***L. helioscopi*** Chodukin & Sofieff, 1940<br>***L. nicollei*** Chodukin & Sofieff, 1940<br>***L. adleri*** Heisch, 1954<br>***L. zmeevi*** Andruchko & Markov, 1955<br>***L. sofieffi*** Markov et al., 1964<br>***L. hoogstraali*** Mc Millan, 1965<br>***L. senegalensis*** Ranque, 1973<br>***L. gulikae*** Ovezmuchammedov Safjanova, 1987<br>***L. zuckermani*** Paperna et al., 2011 | ***L. braziliensis* complex** | ***L. guyanensis* complex** | ***L. lainsoni*** Silveira et al., 1987<br>***L. naiffi*** Lainson & Shaw, 1989<br>***L. lindenbergi*** Silveira et al., 2002<br>***L. utingensis*** Braga et al., 2003 | ***L. enriettii* complex** | | | | |
| ***L. donovani*** Laveran & Mesnil, 1903<br>***L. infantum*** Nicolle, 1908 syn. *L. chagasi* Cunha & Chagas, 1937<br>***L. archibaldi*** Castellani & Chalmers, 1919 | ***L. tropica*** Wright, 1903<br>***L. aethiopica*** Bray, Ashford & Bray, 1973 | ***L. major*** Yakimoff & Schokhor, 1914<br>***L. gerbilli*** Wang et al., 1964<br>***L. arabica*** Peters, Elbihari & Evans, 1986<br>***L. turanica*** Strelkova, Peters & Evans, 1990 | ***L. mexicana*** Biagi, 1953 syn. *L. pifanoi* Medina & Romero, 1959<br>***L. amazonensis*** Lainson & Shaw, 1972 syn *L. garnhami* Scorza et al., 1979<br>**L. aristidesi** Lainson & Shaw 1979<br>**L. venezuelensis** Bonfante-Garrido 1980<br>**L. forattinii** Yoshida et al., 1993 | | ***L. braziliensis*** Vianna, 1911<br>***L. peruviana*** Velez, 1913 | ***L. guyanensis*** Floch, 1954<br>***L. panamensis*** Lainson & Shaw, 1972<br>***L. shawi*** Lianson et al., 1989 | | ***L. enriettii*** Muniz & Medina, 1948<br>***L. martiniquensis*** Desbois et al. 2014 syn. *L. siamensis* Sukmee et al., 2008<br>***L. orientalis*** Bates & Jariyapan, 2018 | | | | |

**Tab. 2:** Known distribution of the Leishmaniinae (based on Alvar et al. 2012, Akhoundi et al. 2016, Espinosa et al. 2016 and Barratt et al. 2017) / Bekannte Verbreitung der Leishmaniinae (basierend auf Alvar et al. 2012, Akhoundi et al. 2016, Espinosa et al. 2016 und Barratt et al. 2017)

| Species | Known distribution |
|---|---|
| *Leishmania* | |
| *Leishmania* | |
| *L. donovani* complex | |
| *L. donovani* | Central Africa, South Asia, Middle East, India, China |
| *L. infantum* | Mediterranean countries of Europe, northern Africa, Arabian Peninsula, Central Asia, parts of China, South America (Brazil, Venezuela, Bolivia) and Mexico |
| *L. archibaldi* | East Africa (Ethiopia, Kenya, Sudan), Lebanon |
| *L. tropica* complex | |
| *L. tropica* | Central and North Africa, Middle East, Central Asia, India |
| *L. aethiopica* | Ethiopia, parts of Kenya |
| *L. major* complex | |
| *L. major* | Central and North Africa, Middle East, Central Asia |
| *L. gerbilli* | Mongolia, China, Russia, Middle East |
| *L. arabica* | Saudi Arabia |
| *L. turanica* | Mongolia, China, Russia, Middle East |
| *L. mexicana* complex | |
| *L. mexicana* | Belize, Costa Rica, Guatemala, Mexico, USA (Texas close to Mexican border), Columbia, Ecuador |
| *L. amazonensis* | North Argentina, Bolivia, Brazil, Columbia, Ecuador, French Guiana, Peru, Suriname, Venezuela |
| *L. aristidesi* | Panama |
| *L. venezuelensis* | Venezuela |
| *L. forrattinii* | Brazil |
| *Viannia* | |
| *L. braziliensis* complex | |
| *L. braziliensis* | Central America (including Mexico), South America (including northern Argentina) |
| *L. peruviana* | Peru |
| *L. guyanensis* complex | |
| *L. guyanensis* | Northern Argentina, Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guiana, Peru, Surinam, Venezuela |
| *L. panamensis* | Columbia, Panama |
| *L. shawi* | Brazil |
| *L. lainsoni* | Brazil, Peru, Bolivia, Surinam, French Guiana, Columbia, Ecuador |
| *L. naiffi* | Brazil |
| *L. lindenbergi* | Brazil |
| *L. utingensis* | Brazil |

**Tab. 2, continued:** Known distribution of the Leishmaniinae (based on Alvar et al. 2012, Akhoundi et al. 2016, Espinosa et al. 2016 and Barratt et al. 2017) / Bekannte Verbreitung der Leishmaniinae (basierend auf Alvar et al. 2012, Akhoundi et al. 2016, Espinosa et al. 2016 und Barratt et al. 2017)

| Species | Known distribution |
|---|---|
| *Sauroleishmania* | |
| *L. henrici* | Martinique island (?) |
| *L. chameleonis* | Egypt, Israel |
| *L. tarentolae* | North Africa, Malta, Sudan, Algeria, Italy, France |
| *L. davidi* | Central Africa |
| *L. agamae* | Eastern Mediterranean, Palestine, Lebanon, Israel, Turkmenistan |
| *L. helioscopi* | Turkmenistan |
| *L. nicollei* | Turkmenistan |
| *L. adleri* | Iran, Kenia |
| *L. zmeevi* | Turkmenistan |
| *L. sofieffi* | Russia |
| *L. hoogstraali* | Sudan, Senegal |
| *L. senegalensis* | Senegal |
| *L. gulikae* | Turkmenistan |
| *L. zuckermani* | Sudan, South Africa |
| *Mundinia* | |
| *L. enrietti* complex | |
| *L. enrietti* | Brazil |
| *L. martiniquensis* | Martinique, Thailand, Germany, Switzerland, USA (Florida) |
| *L. orientalis* | Thailand |
| *L. macropodum* | Australia |
| *Porcisia* | |
| *P. hertigi* | Panama, Costa Rica |
| *P. deanei* | South America, in particular Brazil |
| *Endotrypanum* | |
| *E. schaudinni* | Brazil, Panama |
| *E. monterogeii* | Costa Rica, Ecuador |
| *E. colombiensis* | Columbia, Venezuela |
| *E. equatorensis* | Ecuador |
| *E. herreri* | Costa Rica |
| *Zelonia* | |
| *Z. costaricensis* | Costa Rica |
| *Z. australiensis* | Australia |
| *Novymonas* | |
| *N. esmeraldas* | Ecuador |

west and central Europe during the middle Holocene period was suitable for the vectors of *L. infantum*, although the diversity was lower than in the Mediterranean region. The authors propose that archaic human populations of Europe were generally less impacted by sandfly-borne diseases than those of northern Africa or the Middle East, although they assume a possible sporadic occurrence of sandfly-borne infections in Neanderthal populations of the Apennine Peninsula in the late second part of the Middle Palaeolithic Period, probably not caused by *L. infantum* (Trájer & Sebestyén 2019). Interestingly, the genetic diversity of *L. infantum* is particularly high in Armenia (Kuhls et al. 2021). For southern France, genetic differentiation within *L. infantum* suggests two main populations: population A (primarily in the Provence and Alpes-Maritimes endemic areas with MON-1 and non-MON-1 strains) and population B consisting of only MON-1 strains mainly from the Alpes-Maritimes (Pomares et al. 2016). *L. tropica* is currently re-emerging in various regions around the Mediterranean, particularly in Syria and neighbouring countries, due to large migration events caused by the war but also in northern Africa, particularly in Morocco (El Idrissi Saik et al. 2022). Within Europe, *L. tropica* occurs sporadically in Greece (Ready 2010). To date, *L. donovani* has only been recorded in Cyprus (Antoniou et al. 2008).

In recent years, more and more endemic foci of leishmaniosis have been detected in the vicinity of central Europe. In the past decades, endemic foci of canine leishmaniosis have been recorded in northern Italy, mainly attributed to the northward expansion of vector populations and a growing reservoir in travelling/relocated dogs (Gradoni et al. 2022). Dogs certainly play a significant part in altering the distribution of *L. infantum* (Maia & Cardoso 2015). In the recent past, autochthonous cases of *L. major* and *L. donovani* infections have been also documented in the proximity of continental Europe, from the Manisa Province in Turkey (Özbilgin et al. 2022).

Although the genus *Leishmania* comprises many genetically distinct populations, it is debatable to speak of species in the biological sense. Generally, genetic exchange is possible during the insect phase of the transmission cycle in kinetoplastids and experimental hybridization has been shown in *Leishmania* (Ferreira & Sacks 2022), although meiosis seems not to be obligatory but rather an alternative developmental pathway in kinetoplastids (Gibson 2021).

## Vectors

At least 26 sandfly species have been recorded in Europe, including representatives of the genera *Phlebotomus* and *Sergentomyia* (Table 3).

An expansion of sandflies into previously non-endemic regions can be observed or at least assumed in many southern and eastern European countries (Maroli et al. 2002, 2006; Kasbari et al. 2012; Mihalca et al. 2019; Michelutti et al. 2021). There were recent reports of competent sandfly vectors, mainly *Phlebotomus perniciosus*, for the first time in 23 municipalities of northern Italy (Gradoni et al. 2022) and 14 sandfly species have been identified on the Balkan peninsula, including representatives of two genera (*Phlebotomus* and *Sergentomyia*) and six subgenera (*Phlebotomus*, *Paraphlebotomus*, *Larroussius*, *Adlerius*, *Transphlebotomus* and *Sergentomyia*) with *Ph. neglectus* being by far the most abundant and the most widely distributed species, followed by *Ph. perfiliewi* and *Ph. tobbi* (Dvořák et al. 2020).

Sandflies were not considered endemic in central Europe, as populations were overlooked for a long time. During the last glacial period, which ended about 10,000 to 12,000 years ago, large parts of central and eastern Europe were covered by permafrost and tundra, resulting in a huge decrease of preglacial biodiversity. After the last glacial period, the onset of an interglacial period was marked by a fast rise of temperature with huge fluctuations. The Holocene Optima (two warm periods around 6,500 and 4,500 years ago) had mean temperatures comparable to recent climatic conditions, favouring the dispersal of sandflies from Mediterranean and Extramediterranean refugia to northern parts of Europe (Aspöck 2008, 2010; Aspöck et al. 2008; Aspöck & Walochnik 2009).

Within central Europe and surrounding countries, sandflies are known to occur in Belgium (Depaquit et al. 2005), Germany (Naucke & Pesson 2000; Naucke & Schmitt 2004; Oerther et al. 2020), Switzerland (Grimm et al. 1993), Austria (Poeppl et al. 2013b), Slovakia (Dvořák et al. 2016), Hungary (Farkas et al. 2011; Bede-Fazekas & Trájer 2015; Trájer 2017), Slovenia (Ivović et al. 2015; Praprotnik et al. 2019) and Serbia (Vaselek et al. 2017). By far the most widely occurring sandfly species in central Europe is *Ph. mascittii* (Figure 3), which also has the northernmost distribution (Melaun et al. 2014) (Figure 2).

*Ph. mascittii* is a suspected but unproven vector for *L. infantum*. The known anthropophilic behaviour and the detection of *L. infantum* DNA in a specimen from Montecristo, Italy, as well as in an unfed specimen from Lower Austria point towards a vector capacity of this species for *L. infantum* (Grimm et al. 1993; Zanet et al. 2014; Obwaller et al. 2016). While sandflies in Switzerland and Hungary were first found many decades ago, records in Austria, Germany and Slovenia are rather recent. *Ph. mascittii* was reported in the Swiss canton of Vaud in 1911 and 1956 (Langeron & Nitzulescu 1931; Gaschen 1956; Naucke & Pesson 2000), while *S. minuta*, known to mainly feed on reptiles, and *Ph. perniciosus* were found in southern Switzerland in the 1980s (Knechtli & Jenni 1989; Grimm et al. 1993). *Ph. perfiliewi* was reported from southwestern Hungary in 1932 (Szentkirályi & Lőrincz 1932) and *Ph. perfiliewi, Ph. papatasi, Ph. neglectus*, and *Ph. mascittii* were found during a more recent comprehensive study. *Ph. neglectus* and *Ph. mascit-*

**Tab. 3:** Sandfly species recorded in Europe (based on Morillas Marquez et al. 1983, Sáez et al. 2018, Dvořák et al. 2020 and Cruaud et al. 2021) / Nachgewiesene Sandmückenarten in Europa (basierend auf Morillas Marquez et al. 1983, Sáez et al. 2018, Dvořák et al. 2020 und Cruaud et al. 2021)

| **Sandfly species (genus, subgenus, author, year of description)** | **Known *Leishmania* spp. vector capacity** |
|---|---|
| genus *Phlebotomus* Rondani & Berté, 1840 | |
| subgenus *Adlerius* Nitzulsecu, 1931 | |
| *Phlebotomus balcanicus* Theodor, 1958 | *L. infantum* |
| *Ph. chinensis* Newstead, 1916 | |
| *Ph. simici Nitzulescu,* 1931 | suspected *L. infantum*[1] |
| subgenus *Anaphlebotomus* Theodor, 1948 | |
| *Ph. fortunatarum* Ubeda Ontiveros et al., 1982 | |
| subgenus *Laroussius* Nitzulescu, 1931 | |
| *Ph. ariasi* Tonnoir, 1918 | *L. infantum* |
| *Ph. galilaeus*[2] Theodor, 1958 | |
| *Ph. kandelakii* Shchurenkova, 1929 | *L. infantum* |
| *Ph. major* s.str. Annandale, 1910 | |
| *Ph. langeroni* Nitzulescu, 1930 | *L. infantum* |
| *Ph. neglectus* Tonnoir, 1921 | *L. infantum* |
| *Ph. pedifer* Lewis, Mutinga & Ashford, 1972 | |
| *Ph. perfiliewi* Parrot, 1930 | *L. infantum* |
| *Ph. perniciosus* Newstead, 1911 | *L. infantum* |
| *Ph. tobbi* Adler and Theodor, 1930 | |
| subgenus *Paraphlebotomus* Theodor, 1948 | |
| *Ph. alexandri* Sinton, 1928 | |
| *Ph. riouxi* Depaquit, Léger & Killick-Kendrick, 1998 | |
| *Ph. jacusieli* Theodor, 1947 | |
| *Ph. sergenti* Parrot, 1917 | *L. tropica* |
| *Ph. similis* Perfiliev, 1963 | *L. tropica* |
| subgenus *Phlebotomus* Rondani & Berté, 1840 | |
| *Ph. papatasi* Scopoli, 1786 | *L. infantum* |
| subgenus *Transphlebotomus* Artemiev, 1984 | |
| *Ph. economidesi*[2] Léger, Depaquit and Ferté, 2000 | |
| *Ph. mascittii* Grassi, 1908 | suspected *L. infantum*[2] |
| | |
| genus *Sergentomyia* França & Parrot, 1920 | |
| subgenus *Sergentomyia* França & Parrot, 1920 | |
| *Sergentomyia azizi* Adler, 1946 | |
| *S. dentata* Sinton, 1931 | |
| *S. fallax* Parrot, 1921 | |
| *S. minuta* Rondani, 1843 | |

[1]suspected by Chaskopoulou et al. 2016, [2]Only reported from Cyprus, [3]suspected by Zanet et al. 2014 and Obwaller et al. 2016

**Fig. 3:** *Phlebotomus mascittii.* **A** Female adult sandfly, **B** Pharynx, **C** Male genitalia / *Phlebotomus mascittii.* **A** Adultes Weibchen. **B** Pharynx. **C** Genitalpräparat eines Männchens

*tii* were also present close to Budapest (Farkas et al. 2011). In 1999 and 2001, *Ph. mascittii* and *Ph. perniciosus* were recorded for the first time in Germany (Naucke & Pesson 2000; Naucke & Schmitt 2004). The first record of a sandfly species in Austria, *Ph. mascittii*, was published in 2011, related to trappings in the year 2009 (Naucke et al. 2011). In the following years, there were additional findings in four federal states of Austria (Poeppl et al. 2013b; Obwaller et al. 2014) and the first record of *Ph. mascittii* in Slovakia close to the Austrian border (Dvořák et al. 2016). A second species, *Ph. simici*, was found in Lower Austria in 2019 (Kniha et al. 2021). Entomological surveys in Slovenia found *Ph. mascittii*, *Ph. perniciosus*, *Ph. papatasi*, *Ph. neglectus* and *S. minuta*, mostly in the Mediterranean parts of the country (Ivović et al. 2015; Praprotnik et al. 2019).

Interestingly, no sandflies have been detected in Bavaria, Germany, although the area is climatically suitable for several species (Haeberlein et al. 2013), and no sandflies have been trapped in Upper Austria on the border with Bavaria (Kniha et al. 2020b). However, temperature conditions are becoming suitable for *Ph. perniciosus* across large areas of Germany, with the southwest (Upper Rhine Valley) and west (Cologne Bight) of the country assumed to represent risk areas (Fischer et al. 2010, 2011).

## Alternative vectors

Ticks and fleas have long been suspected to be vectors for *Leishmania* spp., a belief supported by the detection of *Leishmania* DNA in these arthropods. But, as strictly haematophagous organisms, ticks and fleas might take up various pathogens from their hosts without further survival or transmission of the pathogen. There is older evidence of the experimental transmission of *Leishmania* spp. to dogs by ticks and more recent routine PCR screenings of dog-biting ticks detected *Leishmania* DNA in ticks. However, the vectorial capacity of ticks and fleas has not been clarified and needs further evaluation (Dantas-Torres et al. 2010; Colombo et al. 2011; Dantas-Torres 2011).

Biting midges (Diptera: Ceratopogonidae) have recently been confirmed as vectors for *Leishmania*. In 2004, the first autochthonous case of leishmaniosis was reported from Australia, thereby identifying *Leishmania* (*Mundinia*) *macropodum*, a new species belonging to the *L. enrietti* complex (Rose et al. 2004). A subsequent study found no infected sandflies around the location where the host animals, red kangaroos (*Osphranter rufus* Desmarest, 1822), were located. However, biting midges of the genus *Forcipomyia* (*Lasiohelea*) Kieffer, 1921, were found to be infected by detection of promastigote forms and of DNA (Dougall et al. 2011). Experimental proof of the susceptibility of *Culicoides nubeculosus* (Meigen, 1830) to *L. infantum* followed shortly after (Seblova et al. 2012). DNA of *L. infantum* has been detected in *Culicoides imicola* Kieffer, 1913, and *Culicoides circumscriptus* Kieffer, 1918, in central Tunisia under natural conditions (Slama et al. 2014). In 2015, the New World species *Culicoides sonorensis* Wirth & Jones, 1957, was shown to be capable of developing late stage infections of *L. enrietti* under laboratory conditions (Seblova et al. 2015). Finally, three *Mundinia* species, *L. martiniquensis*, *L. orientalis* and *Leishmania* sp. from Ghana, were experimentally transmitted by *Culicoides sonorensis* to mice, proving the vectorial capacity of *C. sonorensis* for these *Leishmania* species (Becvar et al. 2021). As there are multiple autochthonous cases of equine and bovine leishmaniosis involving *Leishmania siamensis* (a synonym of *L. martiniquensis*) in Germany and Switzerland, biting midges should be taken into account as vectors, particularly in areas where no sandflies have been trapped (Müller et al. 2009; Lobsiger et al. 2010).

### Reservoirs

Dogs (*Canis lupus familiaris* Linnaeus, 1758) are the main reservoir for *L. infantum*. However, other canids such as wolves (*Canis lupus* Linnaeus, 1758), red foxes (*Vulpes vulpes* Linnaeus, 1758) and golden jackals (*Canis aureus* Linnaeus, 1758) meet the attributes of efficient reservoirs for *L. infantum*, although they are often asymptomatically infected (Dantas-Torres 2007; Reithinger et al. 2007; Ready 2010). In the recent past, there is growing evidence that a very broad spectrum of mammals can function as reservoir hosts (reviewed in Cardoso et al. 2021; Tomassone et al. 2018), particularly also rats in an urban setting (Galán-Puchades et al. 2022). Infected humans may likewise act as reservoirs, in particular immunocompromised individuals. Sandflies biting such individuals get infected with *Leishmania* (WHO 2022).

Although domestic dogs can be infected without apparent clinical signs for years or even their entire life, symptomatic infections can manifest as ulcers in the area of the ears and tail, or with hair loss, lymphadenopathy and splenomegaly (Solano-Gallego et al. 2009). Dogs may have cutaneous lesions with very high numbers of parasites and they live in close contact to humans, enhancing the maintenance of domestic *L. infantum* transmission cycles (Dantas-Torres & Brandão-Filho 2006; Dantas-Torres 2007). The infection in dogs can be passed on without a vector, from bitch to offspring and venereally (Walochnik & Aspöck 2005). Transplacental transmission in two generations of Boxers has been reported from the Czech Republic (Svobodova et al. 2017). Venereal *Leishmania* transmission in dogs in Germany and a series of autochthonous cases in Finland in the absence of a vector underline the relevance of transmission through bite wounds and semen (Naucke & Lorentz 2012; Karkamo et al. 2014).

A large German survey (with indirect and direct methods) showed a substantial risk that travelling dogs may import *L. infantum* to central Europe (Schäfer et al. 2019a). *L. infantum*-positive dogs were typically seen when returning from Spain, Italy and France. A reservoir of *L. infantum* in dogs has already been established in most central European countries (Mencke 2011). While military dogs that largely remained in Austria were negative for *L. infantum* (Sonnberger et al. 2021), a fairly high percentage of travelling dogs resident in central Europe may be *Leishmania*-positive (Leschnik et al. 2008; Schäfer et al. 2019b).

## Conclusion

Currently, *Leishmania* transmission by sandflies in central Europe can be assumed to be non-existent or very rare and limited to restricted regions. However, climate change and globalization will lead to growing populations and further dispersal of sandflies and possibly to the introduction of new species, including possible vector species. The future occurrence in or migration to central Europe of confirmed vector species, such as *Ph. perniciosus* and *Ph. neglectus*, up to the 10 °C isotherm can be expected. Rising travel activities will increase the number of imported leishmaniosis cases in humans and in animals and the continuous import of *Leishmania*-infected dogs provides a solid reservoir of *L. infantum*. Zoonoses with numerous animal reservoir hosts cannot be epidemiologically controlled by treatment. While the incidence of other vector-borne diseases, such as malaria, is declining due to large-scale control measures, the numbers of leishmaniosis cases are increasing worldwide because of shifts in natural transmission cycles to peridomestic areas through urbanization and deforestation and possibly also to climate change. The installation of reporting and surveillance systems can contribute to the early detection of changes in epidemiology and to countermeasures against the establishment of new transmission cycles.

**Fazit für die Praxis:**
Derzeit ist davon auszugehen, dass es in Mitteleuropa – wenn überhaupt – nur sehr selten und auch nur sehr fokal zu einer Übertragung von Leishmanien durch Sandmücken kommt, vermutlich abhängig von einer Koinzidenz mehrerer klimatischer und epidemiologischer Faktoren. Jedoch schaffen Klimawandel und Globalisierung günstige Voraussetzungen für die Ausbreitung der bereits vorhandenen Sandmücken-Populationen und die Einschleppung weiterer, möglicherweise besser als Vektoren für Leishmanien geeigneter Arten. Durch die zunehmende Reisetätigkeit der Bevölkerung, Tiertransporte und insbesondere Import von infizierten Hunden aus dem Mittelmeerraum ist jedenfalls bereits heute ein relevantes Erregerreservoir in Mitteleuropa gegeben und eine Übertragung von Leishmanien zumindest fokal grundsätzlich möglich, bei Hunden nicht zuletzt auch durch Bisswunden von Hund zu Hund.

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