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Treatment outcome of imported cutaneous leishmaniasis among travelers and migrants infected with *Leishmania major* and *Leishmania tropica*: a retrospective study in European centers 2013 to 2019

Hedvig Glans[1,2,*], Leif Dotevall[3], Gert Van der Auwera[4], Aldert Bart[5,a], Johannes Blum[6,7], Pierre Buffet[8], Romain Guery[9], Jean-Pierre Gangneux[10], Saskia van Henten[4], Gundel Harms[11], Stefania Varani[12,13], Florence Robert-Gangneux[10], Robert Rongisch[14], Björn Andersson[15], Maria Bradley[2]

[1] *Department of Infectious Diseases, Karolinska University Hospital, Stockholm, Sweden*
[2] *Division of Dermatology and Venereology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden*
[3] *Department of Communicable Disease Control Region, Västra Götaland, Gothenburg, Sweden*
[4] *Institute of Tropical Medicine, Antwerp, Belgium*
[5] *Department of Medical Microbiology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands*
[6] *University of Basel, Petersplatz 1, Postfach 4001, Basel, Switzerland*
[7] *Swiss Tropical and Public Health Institute, Basel, Switzerland*
[8] *Université Paris Cité, Biologie Intégrée du Globule Rouge, UMR_S1134, INSERM, F-75015, Paris, France*
[9] *Department of Internal Medicine and Infectious Diseases, Hôpital du Confluent, Nantes, France*
[10] *Univ Rennes, CHU Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail)—UMR_S 1085, 2 rue du Pr Léon Bernard, 35000 Rennes, France*
[11] *Institute of Tropical Medicine and International Health, Charité–Universitätsmedizin Berlin, corporate member of Freie Universität, and Humboldt-Universität zu Berlin, Berlin, Germany*
[12] *Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Bologna, Italy*
[13] *Microbiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy*
[14] *Department of Dermatology and Venereology, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany*
[15] *Department of Cell & Molecular Biology, Karolinska Institutet, Stockholm, Sweden*

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ABSTRACT

Objectives: Cutaneous leishmaniasis (CL) in Asia, Northern, and Sub-Saharan Africa is mainly caused by *Leishmania major* and *Leishmania tropica*. We describe and evaluate the treatment outcome of CL among travelers and migrants in Europe.

Methods: We conducted a retrospective study of parasitological confirmed CL cases caused by *L. major* and *L. tropica* during 2013-2019 in Europe. Data were collected from medical records and databases within the LeishMan network.

Results: Of 206 included cases of CL, 75 were identified as *L. major* and 131 as *L. tropica*. Of patients with *L. tropica* infection, 80% were migrants, whereas 53% of patients with *L. major* infection had been visiting friends and relatives. Among patients with *L. tropica*, 48% were younger than 15 years. Pentavalent antimony cured 73% (*L. major*) and 78% (*L. tropica*) of patients. The cure rate for intralesional administration was 86% and 67% for systemic, on *L. tropica*. Liposomal amphotericin B had a cure rate of 44-63%.

Conclusion: *L. major* infections were mostly found in individuals visiting friends and relatives, whereas *L. tropica* were mainly identified in migrants. No patients with *L. major* relapsed. Pentavalent antimony, liposomal amphotericin B, and cryotherapy had cure rates in accordance with previous studies.

* Corresponding author: Hedvig Glans, Division of Infectious Diseases, Department of Medicine Solna, Karolinska Institutet, 17176 Stockholm, Sweden.
E-mail address: hedvig.glans@ki.se (H. Glans).

[a] Present address: Department of Medical Microbiology, Tergooi MC, Hilversum, The Netherlands

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Introduction

Leishmaniasis, caused by parasites from the genus *Leishmania*, is classified as a neglected tropical infectious disease by the World Health Organization (WHO), with 350 million people living in endemic areas (World Health Organization, 2010). The parasite is transmitted by a phlebotomine sand fly bite and can cause different clinical manifestations, where cutaneous leishmaniasis (CL) is the most common form. Several *Leishmania* species can cause CL. *Leishmania major* and *Leishmania tropica* circulate in several continents but are most common in the Middle East, Northern and Sub-Saharan parts of Africa, and western Asia (World Health Organization, 2016, 2017).

Syria is a highly endemic country for *L. tropica*. After the onset of the Syrian Civil War, the number of reported cases of CL in Syria and neighboring countries has increased (Al-Salem et al., 2016; Du et al., 2016; Kanani et al., 2019), and because of migration, it also became more common in European countries (United Nations High Commission for Refugees, 2017). *L. tropica* can cause chronic manifestations, lack of healing, and recurrence as late as 12 months after resolution (Bamorovat et al., 2021; Khosravi et al., 2017).

L. major is more common in other regions, including Northern and Sub-Saharan Africa. Migrants from these countries enter Europe by crossing the Mediterranean Sea (Kassar et al., 2014).

For most areas endemic to *L. major* and *L. tropica*, pentavalent antimony is still used as the first line of treatment, either intralesional or intramuscular/intravenously. The outcome of treatment varies between 60% and 70% for Old World CL (Khatami et al., 2007). *L. tropica* is known for the recurrence of CL (Akilov et al., 2007). In Aleppo, Syria, more than 30% of the CL caused by *L. tropica* was reported as recurrence after or due to unresponsiveness to antimony treatment (Douba et al., 1997). The WHO has established recommendations for the region (World Health Organization, 2010, 2014); nevertheless, the best treatment option for CL caused by *L. tropica* in the Middle East has not yet been fully proved (González et al., 2008). A spontaneous cure rate of 50-90% after several months has been reported for *L. major* (Morizot et al., 2013; World Health Organization, 2014). The lesions are often managed with local care and thus do not always require treatment (Bailey and Lockwood, 2007; World Health Organization, 2010, 2014).

Data on treatment and outcome in patients with CL because of *L. major* and *L. tropica* in Europe are scarce. Studies on clusters of Syrian refugees with complicated CL because of prolonged delay of treatment (Glans et al., 2018; Lindner et al., 2020) and outbreaks of imported CL among military personnel, mainly because of *L. major*, have been reported from European countries and the US (Bart et al., 2013; van Thiel et al., 2010; Woodrow et al., 2006). Larger European studies have focused on the clinical manifestation, treatment, and outcome and have usually not separated the different *Leishmania* species in the analysis (Blum and Hatz, 2009; Blum et al., 2014, 2004; World Health Organization, 2014). Size, number, and location of the lesions, apart from the *Leishmania* spp. and immunosuppression, have to be considered when treating travelers with CL in Europe, and local treatments have been most commonly used (Guery et al., 2021; Morizot et al., 2013). Systemic treatment is recommended in case of >3 lesions or a lesion size >3 cm or a lesion in a delicate site, such as the face, hands, and joints (Blum et al., 2014). The importance of identifying the infecting species to provide a species-specific treatment of CL has been highlighted (Blum and Hatz, 2009; Blum et al., 2014).

This study aimed to describe the data obtained on experience from various European centers in the identification and treatment of patients with imported CL caused by *L. major* and *L. tropica* for 7 years, between 2013 and 2019. The primary aim was to focus on the epidemiological data and the treatment outcome, including spontaneous healing and relapses, underlining the differences between *L. tropica* and *L. major* in this context.

Methods

Ethical approval

All data were shared and analyzed anonymously in accordance with respective national guidelines. Specific ethical approval for using routinely collected data from patients with CL was obtained from ethical committees and institutional review boards from the respective centers.

Inclusion criteria

Inclusion criteria were cases of CL caused by *L. tropica* or *L. major*, identified between 2013 and 2019 and confirmed by polymerase chain reaction.

Cohort

Patient records were collected from a common database within the LeishMan network and treating hospitals. LeishMan is a multicenter, international consortium aiming to improve the diagnosis, management, and surveillance of leishmaniasis through harmonization of medical practice and collection of data in a common system. The consortium gathers 50 experts affiliated with 30 institutions in 11 European countries (Belgium, France, Germany, Italy, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom, and The Netherlands). Data were collected pseudonymously through an electronic case report form (demographic, clinical, laboratory, and biological data) and retrospectively collected by experts from each institute. Clinical and treatment data were collected according to the protocol (Supplementary Table 1). Some records had missing data, and the denominators mentioned in the text count only those where data were available.

Definitions

Immunocompromised patients were defined as patients with the following conditions or treatments: HIV infection, primary immunodeficiency, and immunosuppressive treatment; >5 mg/day prednisolone, or equivalent; >3 months, chemotherapy, methotrexate, monoclonal antibodies, or other molecular targeting immune cells or their products (e.g., anti–tumor necrosis factor agents).

The time of diagnosis was defined as the date of sampling because the exact infection date is often unknown.

The country of infection is the country where the patient most likely acquired the infection. For some patients, the country of infection was missing and was defined as “not applicable” (NA). For most migrants, we assumed that they were infected in their home country unless other specific information was available.

All cases were imported and categorized as migrants, tourists, military personnel, visiting friends or relatives, expatriates (workers, missionaries, volunteers, students), or others. Others were used when none of the previously mentioned reasons could be applied, and NA was used when data were missing.

CL cases were defined as cured when the lesion had healed, i.e., when a complete re-epithelization of the lesion or the disappearance of a papular lesion occurred within 6 months (Olliaro et al., 2013). Relapse was defined as the recurrence of a previously healed lesion without new exposure within 12 months after treatment started. Treatment failure is defined as the absence of clinical signs of re-epithelialization of the lesion during or within 2 months after treatment. In this study, data were collected 6 and 12 months after treatment.

Table 1
Comparative features of patients with cutaneous leishmaniasis caused by *L. major* or *L. tropica*.

		*Leishmania major*n = 75	*Leishmania tropica*n = 131
Male		44 (59)	69 (53)
Immunocompromised			
Yes		3 (4)	3 (2)
No		65 (87)	123 (94)
NA		7 (9)	5 (4)
Age	Median (IQR)	28 (11-46)	14 (9-32)
	0-4	8 (10)	17 (13)
	5-14	16 (21)	46 (35)
	15-24	6 (8)	25 (19)
	25-34	14 (19)	11 (8)
	35-44	9 (12)	13 (10)
	45-54	10 (13)	5 (4)
	55-64	9 (12)	9 (7)
	>65	3 (4)	5 (4)
Type of traveler			
	Tourist	17 (23)	3 (2,5)
	Visiting friends and relatives	40 (53)	18 (14)
	Migrants	6 (8)	105 (80)
	Military	1 (1.5)	0 (0)
	Expatriates[a]	3 (4)	0 (0)
	Others	1 (1.5)	2 (1)
	NA	7 (9)	3 (2.5)
Lesion localization			
	Face	5	42
	Head	5	17
	Upper limb	36	60
	Trunk	5	3
	Lower limb	31	29

Data are n (%) unless indicated otherwise.
IQR, interquartile range; NA, missing data.
[a] Workers, missionaries, volunteers, and students.

Results

A total of 206 patients with CL, caused by either *L. major* or *L. tropica*, during 2013-2019 were included in the study: 75 cases with *L. major* and 131 cases with *L. tropica*. To further evaluate the differences between *L. major* and *L. tropica*, we focused on epidemiological data, together with treatment regimens and outcomes.

Of 44 patients with *L. major*, 59%, and 69 patients with *L. tropica*, 53%, were men (Table 1). Most patients included in the study were immunocompetent, and only three patients in each group (*L. tropica* and *L. major*, respectively) were on immunosuppressive treatment: prednisolone, etanercept, and methotrexate or golimumab (Table 1).

The median age of the patients with *L. major* was 28 years (interquartile range [IQR] 11-46), whereas the median age of *L. tropica* was 14 years (IQR 9-32) (Table 1). A total of 32% (n = 24) of the patients with *L. major* infection and 48% (n = 63) of the patients with *L. tropica* infection were younger than 15 years.

Most patients with *L. major* (53%, n = 40) had been infected when visiting friends and relatives, whereas most patients infected with *L. tropica* (80%, n = 105) were migrants (Table 1).

The number of *L. major* cases was relatively consistent during the study period; between nine and 14 cases annually. For *L. tropica*, the number of cases varied during the study period and was higher in 2013-2016, with 20-30 cases annually and a decrease to 5-17 cases annually in 2017-2019 (Figure 1).

The country of origin with the highest number of *L. tropica* cases was Syria (n = 95, 72%), followed by Afghanistan (n = 11) and Pakistan (n = 9). In the case of *L. major*, the infection was most commonly acquired in Tunisia (n = 18), followed by Morocco (n = 16) and Israel (n = 8). Other countries in North and Sub-Saharan African and the Middle East regions were also represented, with only a few cases from each country (Supplementary Table 2).

Most lesions were found on exposed skin areas. Regarding CL caused by *L. tropica*, the most common location of lesions was the face and/or the head, whereas for CL caused by *L. major*, the upper and lower limbs were the most affected (Table 1). The patients often had more than one lesion in separate locations on the body. The presence of more than one lesion was reported in 18 patients with *L. tropica* and nine patients with *L. major* infection.

The most common drug used was pentavalent antimony (*L. major*, n = 15, and *L. tropica*, n = 36). Most patients received intralesional treatment (*L. major*, n = 12, and *L. tropica*, n = 21), whereas systemic treatment was used less often (*L. major*, n = 3, and *L. tropica*, n = 15). The second most common drug used was liposomal amphotericin B (*L. major*, n = 8, and *L. tropica*, n = 23), and the third most common treatment regimen used was cryotherapy as monotherapy (*L. major*, n = 2, and *L. tropica*, n = 21). The number of cryotherapy sessions varied between one to eight, with intervals of one to several times a week. Combination therapy, using cryotherapy and pentavalent antimony, or cryotherapy and liposomal amphotericin B, was used in both groups (Table 2).

Pentavalent antimony had a cure rate of 67% for *L. major* and 86% for *L. tropica* when administrated intralesional. Missing data were seen in 33% of the cases with *L. major*. A cure rate of 100% for *L. major* and 67% for *L. tropica* was observed following systemic administration (Table 2).

Liposomal amphotericin B had a cure rate of 63% (n = 5) for *L. major* and 44% (n = 10) for *L. tropica* (Table 2). The dose of liposomal amphotericin B was based on body weight, 3 mg/kg/day, and the duration was, in most cases, 5-6 days. The most common treatment schedule consisted of 5 consecutive days of 3 mg/kg, followed by a sixth dose on day 10.

Two of three immunosuppressed patients with *L. tropica* (n = 2) responded to liposomal amphotericin. One of three immunosuppressed patients with *L. major* (n = 1) was successfully treated with liposomal amphotericin B; in the other two patients with *L. major*, data were missing.

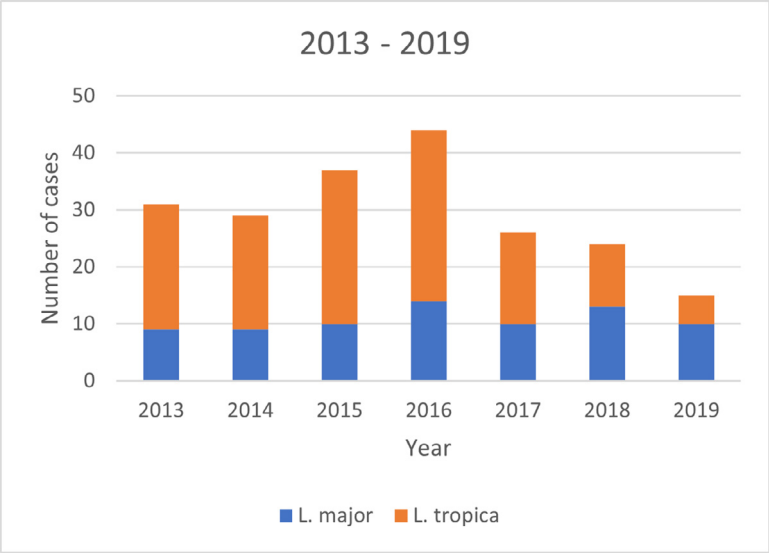

Figure 1. Number of *Leishmania major* and *Leishmania tropica* cases per year, 2013-2019.

Ten patients (*L. major*, n = 5, and *L. tropica*, n = 5), all immunocompetent, were treated with miltefosine and had a 100% cure rate (Table 2). Fluconazole was used for treatment in six patients with *L. major* and eight with *L. tropica*, and three of the patients with *L. tropica* relapsed (Table 2). Topical treatment with paromomycin 15% was also used for treatment on patients with *L. major* (n = 4) and *L. tropica* (n = 10). Two relapses (*L. tropica*) were seen after treatment, and three patients were lost to follow-up (Table 2).

The overall healing rate among treated cases was high. A total of 82% of the patients in the *L. major* group and 70% in the *L. tropica* group healed after treatment, without relapse, within 12 months. No patients infected with *L. major* had signs of recurrence of a healed lesion within 12 months after treatment, whereas 20% of patients with *L. tropica* relapsed after treatment. Among the patients with *L. major*, information on treatment and outcome was missing for 24 patients, and for *L. tropica*, data were missing for three patients.

A total of 41 cases had been treated previously, six of the *L. major* and 35 of the *L. tropica* cases. The most common previous treatments were intralesional and intramuscular pentavalent antimonial, liposomal amphotericin B, cryotherapy, paromomycin ointment/cream, and fluconazole. When now treated, 16 of the patients with *L. tropica* and three of the patients with *L. major* were cured. Relapses were only seen in *L. tropica* cases (n = 13). For four patients, this information was not available. There were more cases of relapse seen after treatment with liposomal amphotericin B and fewer cases seen after intralesional treatment with pentavalent antimonial (Supplementary Table 3).

Discussion

Our study retrospectively analyzed CL cases diagnosed with *L. major* or *L. tropica* infection in various European centers from 2013 to 2019 to evaluate the epidemiology and the treatment experiences.

We observed epidemiological differences between infection with *L. major* and *L. tropica* in the context of how the disease was acquired or "type of traveler." Most patients infected with *L. tropica* were migrants from Syria, and most patients infected with *L. major* had visited friends and relatives in North Africa. An increased risk of acquiring CL in these groups has previously been reported (Boggild et al., 2019; Guery et al., 2021).

During 2013-2016, there was increased migration from Syria to Europe as a result of the Syrian Civil War. The increased migration was clearly reflected in an increased number of *L. tropica* CL cases during these years. Migration patterns are affected by political decisions, and when new migration policies in different European countries changed in 2016, the number of CL cases from Syria dropped. No variation was observed in the number of patients infected with *L. major* during those years.

Among migrants infected with *L. tropica*, many had lesions on the face or the head. Sleeping outside during their migration may have affected their ability to protect themselves from sand fly bites during the evening and night (Munir et al., 2002). While being outside in the evening but sleeping inside during the night, the exposure of skin areas to the sand flies may be different. The different sand flies transmitting *L. major* and *L. tropica* and the different sand flies' feeding behavior when infected with *Leishmania* may also affect the localization of lesions in relation to the human/host supine position (Ajaoud et al., 2015; Rogers and Bates, 2007).

Pentavalent antimony has been the gold standard treatment for decades and is still a valuable drug, but it has been progressively replaced by treatments requiring shorter treatment courses and inducing less frequent alterations of laboratory parameters, such as local therapy (Morizot et al., 2013; Mosimann et al., 2016; Mosleh et al., 2008), miltefosine (Guery et al., 2021; Mosimann et al., 2016), and liposomal amphotericin B (Shirzadi, 2019; Solomon et al., 2011, 2013). The use of liposomal amphotericin B in CL is nevertheless not devoid of potentially severe adverse events (Guery et al., 2017). Today, several alternatives are available, and recommendation depends on the clinical manifestation, the infecting species, and the geographical region where the patient was infected (Blum et al., 2014; Hodiamont et al., 2014). In the case of larger lesions (>3 cm), multiple lesions (>3), or lesions in a delicate site (face, hands, joints), systemic treatment is recommended (Blum et al., 2014; Guery et al., 2021; Morizot et al., 2013; World Health Organization, 2010, 2014,).

In this study, we observed that both local and systemic treatment with pentavalent antimony had an overall cure rate for *L. tropica* of 78%. The cure rate of intralesional pentavalent antimony treatment was 86% (n = 18) and that of systemic treatment with pentavalent antimony was 67% (n = 10). Our results are in accordance with previous studies, both in endemic regions and among travelers in Europe (Blum and Hatz, 2009; Brito et al., 2017;

Table 2
Treatment and outcome of cutaneous leishmaniasis by infected *Leishmania* species; *L. major* and *L. tropica*.

		Leishmania major n = 75	*Leishmania tropica* n = 131
Healing rate			
Treated		44	117
	Cured	36 (82)	82 (70)
	Relapse	-	24 (21)
	NA	8 (18)	11 (9)
No treatment		7	11
	Cured	7 (100)	9 (82)
	NA	-	2 (18)
NA		24	3
Treatment			
Pentavalent antimony		15	36
Systemic - iv/im		3	15
	Cured	*3* (100)	*10* (67)
	Relapse	-	*5* (33)
Local - il		12	21
	Cured	8 (67)	18 (86)
	Relapse	-	1 (5)
	NA	4 (33)	2 (9)
Cryotherapy + Pentavalent antimony		4	8
Systemic - iv		0	1
	Cured	-	1 (100)
	Relapse	-	-
Local – il		4	7
	Cured	4 (100)	7 (100)
	Relapse	-	-
Cryotherapy		2	21
	Cured	2 (100)	18 (86)
	Relapse	-	3 (14)
Cryotherapy + liposomal amphotericin B		0	4
Systemic - iv	Cured	-	3 (75)
	Relapse	-	1 (25)
Liposomal amphotericin B		8	23
Systemic - iv	Cured	5 (63)	10 (44)
	Relapse	-	9 (39)
	NA	3 (37)	4 (17)
Miltefosine		5	5
Systemic - po	Cured	5 (100)	5 (100)
	Relapse	-	-
Fluconazole		6	8
Systemic - po	Cured	6 (100)	4 (50)
	Relapse	-	3 (38)
	NA	-	1 (12)
Paromomycin 15%		4	10
Topical	Cured	3 (75)	6 (60)
	Relapse	-	2 (20)
	NA	1 (25)	2 (20)
Itraconazole		0	1
	NA	-	1 (100)
Itraconazole + Pentavalent antimony		0	1
Systemic	NA	-	1 (100)
NA		22	3
No treatment		7	11
	Cured	7 (100)	9 (82)
	Relapse	-	-
	NA	-	2 (18)

Data are n (%) unless indicated otherwise.
Il, intralesional; im, intramuscular; iv, intravenous; NA, data missing; po, orally.

Guery et al., 2021; Khatami et al., 2007), and a result because of selection criteria when to use local and systemic treatment.

Liposomal amphotericin B was the second most used drug for lesions that had to be treated systemically, with a lower cure rate than pentavalent antimony and cryotherapy in our cohort. Only 44% of the patients with *L. tropica* infection were cured and 39% relapsed, whereas 63% of the patients with *L. major* infection were cured and 37% had missing data. Our cohort is small, and further studies on treatment with liposomal amphotericin B are needed to properly evaluate the efficacy of this drug on *L. tropica* CL cases. A suboptimal effect of liposomal amphotericin B on CL has previously been described in travelers in Europe when several *Leishmania* spp. were included (Guery et al., 2017). The efficacy seen in visceral and mucocutaneous leishmaniasis has not been confirmed in CL (Sundar et al., 2008; Rocio et al., 2014). The penetration of different formulas of liposomal amphotericin B, administrated systemically, to the skin (Fielding et al., 1991; Wijnant et al., 2018) and the variation of susceptibility between the different species have been discussed as possible reasons (Guery et al., 2017).

A drawback of treatment with liposomal amphotericin B is a prolonged healing period for skin lesions caused by *Leishmania*, demonstrating only a partial clinical response at 3-4 weeks after the start of treatment (Blum and Hatz, 2009; Blum et al., 2004). Safety aspects and reported adverse events must also be taken into consideration when treating a nonthreatening but disfiguring lesion (Guery et al., 2017; Morizot et al., 2013).

Cryotherapy as a single therapy showed a high cure rate, but the number of cases examined in this study is few. The treatment is efficient, but the limitations of this method are the size, number, and the localization of the lesion(s). For example, monotherapy with cryotherapy is highly effective for smaller lesions, whereas combination treatment with intralesional pentavalent antimony has been more effective for larger lesions (Asilian et al., 2004; Bumb et al., 2013). Previous data have shown an equal efficacy between cryotherapy and antimonial treatment but a synergic effect when combined (Mosleh et al., 2008; Layegh et al., 2009; López-Carvajal et al., 2016). Cryotherapy is less invasive and painful than pentavalent antimonial intralesional therapy, and in addition, it is less costly and results in fewer serious complications, together with greater tolerability than pentavalent antimonial (Layegh et al., 2009).

Fluconazole showed a high cure rate on six patients with *L. major* in our cohort, with all cases healed. Previous studies have shown inconclusive results for treatment with fluconazole on CL caused by *L. major*. Studies of fluconazole treatment of patients infected with *L. major* in highly endemic areas reported positive results both with 200 mg daily and 400 mg daily treatment for 6 weeks (Alrajhi et al., 2002; Emad et al., 2011). However, modest efficacy of fluconazole was observed in returning travelers with *L. major* CL, regardless of dosage (Morizot et al., 2013). Furthermore, *L. major* has a high self-healing rate, which may affect the results (Akilov et al., 2007; Morizot et al., 2013), and only six patients with *L. major* infection were treated with fluconazole in our cohort. For all these reasons, our results on the efficacy of fluconazole on *L. major* CL must be interpreted with caution.

Evaluation of miltefosine on CL caused by *L. major* and *L. tropica* has only been performed in small cohorts (Guery et al., 2021; Mohebali et al., 2007; Mosimann et al., 2016; van Thiel et al., 2010). The outcome has so far been found to be superior to treatment with antimony, with a high cure rate for complicated CL (Mosimann et al., 2016). Evaluation of miltefosine as a treatment for CL caused by *L. tropica* in Pakistan showed a cure rate of 83% as first-line treatment and 70% as second-line treatment (Kämink et al., 2021). These results, and our results with a 100% cure rate on immunocompetent patients, indicate that miltefosine is an effective treatment for CL caused by *L. tropica* when local treatment cannot be used. However, larger prospective studies are necessary to evaluate properly this treatment option.

We observed that topical 15% paromomycin ointment showed a high cure rate in both groups. Several formulations exist with different degrees of local irritations and tolerance for the patient (Ben Salah et al., 2013; el-Safi et al., 1990). Local inflammation owing to the formulations has been discussed as part of the treatment (Garnier and Croft, 2002). The highest efficacy has been observed in CL caused by *L. major* (Ben Salah et al., 2013, 2014).

We evaluated the risk of relapse for the patients at 12 months after treatment. *L. tropica* is known to have a high rate of recurrence (Bamorovat et al., 2021; Khosravi et al., 2017), whereas *L. major* has a high rate of self-healing (Akilov et al., 2007; Minodier and Parola, 2007). The high rate of spontaneously healed lesions may affect the results in this study and explain the missing data among the *L. major* cases.

All patients showing healing of the lesions after 6 months of treatment were free of lesions at 12 months from therapy onset. Patients were only monitored for 12 months, and if they relapsed after 12 months, an event that is reported for *L. tropica* (Bamorovat et al., 2021; Khosravi et al., 2017), that information was not included in the study. Previous studies indicated that relapses of *L. tropica* CL might occur later than 12 months after starting the first treatment, even after healing (Bamorovat et al., 2021; Khosravi et al., 2017). This should be taken into consideration when our results are evaluated.

To our knowledge, this is the first European study that analyses the differences in the epidemiology and treatment outcome for patients with *L. major* or *L. tropica* CL in nonendemic European countries. Previous European studies have included all *Leishmania* spp. (Guery et al., 2021; Morizot et al., 2013). The evidence drawn by this cohort of 206 CL cases is valuable, as it cannot be gained from case reports or a clinician who only rarely treats CL cases. Our study also provides an overview of the patients with CL caused by *L. major* or *L. tropica* who seek health care in Europe.

This study includes only a fraction of the patients diagnosed and treated for CL caused by *L. major* and *L. tropica* in Europe during 2013-2019, which is its main limitation. The number of cases with missing data, both on treatment and follow-up, is also an important limitation. In addition, CL often heals spontaneously, and patients never contact the health care system for treatment.

In conclusion, most patients infected with *L. major* were infected while visiting friends and family in the North of Africa, whereas the patients infected with *L. tropica* were mainly migrants from Syria. Interestingly, this picture may reflect the political situation in Europe and neighboring regions during the study (2013-2019), and different living conditions and sand flies' behavior may affect the possibility of protecting people against being infected. In our study group, most patients were treated with pentavalent antimony; intralesional injection or systemic route of administration were used depending on the size, number, and location of the lesions, with a cure rate in line with previous studies. Therefore, antimony can still be used as the first-line treatment of CL caused by *L. major* and *L. tropica* when the infection is acquired in Africa or the Middle East. Treatment with cryotherapy and liposomal amphotericin B had also cure rates similar to previous studies. Finally, we observed that all patients with *L. major* were cured within 1 year after diagnosis and showed no signs of relapse, regardless of treatment.

Declarations of competing interests

The authors have no competing interests to declare.

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Supplementary materials

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