GERI 2015
21-22-23 April 2015 • Heraklion, Crete, Greece
Genes, Ecosystems and Risk of Infection

Epidemiology of Imported Cutaneous and Visceral Leishmaniasis in Italy: implications for a European endemic country

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Introduction

An increase of imported leishmaniasis cases in western European countries was reported in the last decades. The trend was associated to increasing travel and ecotourism in endemic destinations, military operations and immigration (Pavli et al, 2010, Int J Infect Dis). In endemic countries leishmaniasis is usually well diagnosed, however parasite identification is necessary to distinguish between autochthonous and imported cases. Indeed, without appropriate surveillance, new *Leishmania* species/genotypes may be introduced and transmitted locally by phlebotomine vectors with eco-epidemiological implications (Antoniou et al, 2013, Eurosurveillance; Gradoni, 2013, Eurosurveillance). The purposes of our study was to provide the magnitude and diversity of imported leishmaniasis in Italy over 27 years of surveillance. This was based, although not exclusively, on parasite identification. When this was impossible, other important information was considered in the analysis, that included clinical (e.g. incubation period, skin lesions appearance, etc) and epidemiological data (relative risk for visited/origin versus residence places).

Material and Methods

Clinical samples from patients were collected in the frame of routine diagnosis and/or post-treatment follow up, after obtaining patient's informed written consent delivered at the time of clinical examination. Patient records/information was anonymized and de-identified prior to analysis. Data were recorded according to the ISS ethic committee. Fifteen Italian regions with 34 regional diagnostic centers were involved in the study. Our methods of *Leishmania* species identification changed over time, having become more sensitive and rapid using reproducible and internationally validated PCR-RFLPs on clinical samples. Different identification methodologies were routinely employed: a) two molecular techniques, for both *Leishmania* diagnosis and typing (SSU rDNA n-PCR and ITS-1 n-PCR-RFLP) applied on samples (Cruz et al, 2002, Trans R Soc Trop Med Hyg; Minodier et al 1997, J Clin Microbiol; Shoenian et al, 2003, Diagn Microbiol Infect Dis); b) MLEE analysis on *Leishmania* isolates (Rioux et al, 1990, Ann Parasitol Hum Comp; Gramiccia, 2003, Ann Trop Med Parasitol).

Fig.1. Imported leishmaniasis in Italy, annual trend 1986-2012.
A) Distribution of VL and CL cases. B) Distribution of Old and New World cases.

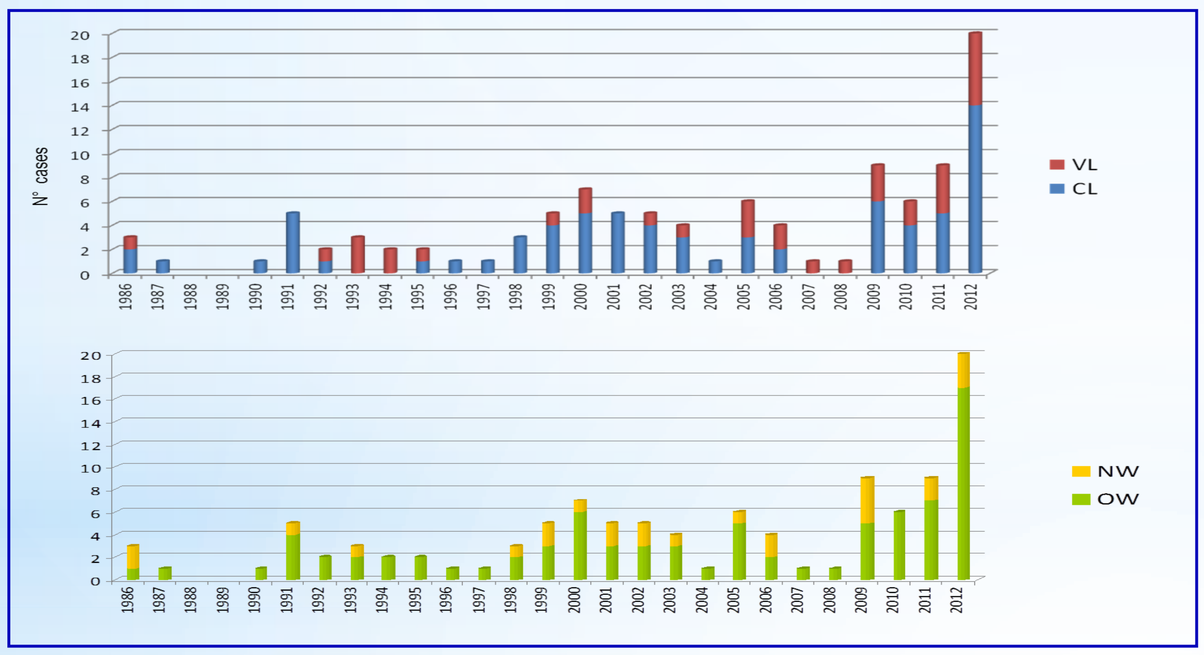
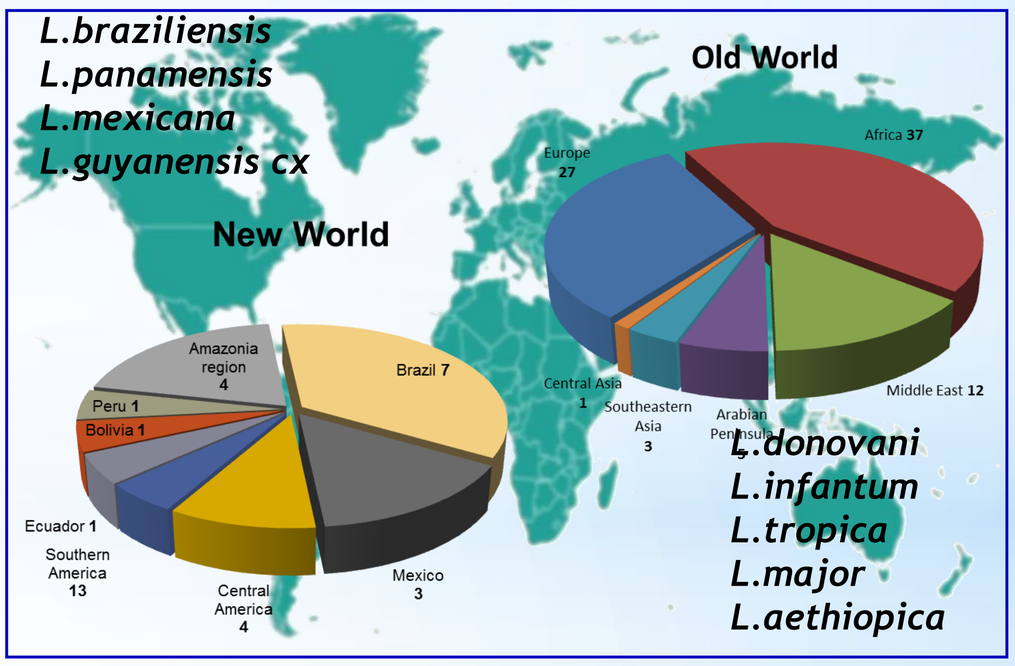


Fig.2. Number of leishmaniasis cases imported from Old and New Worlds



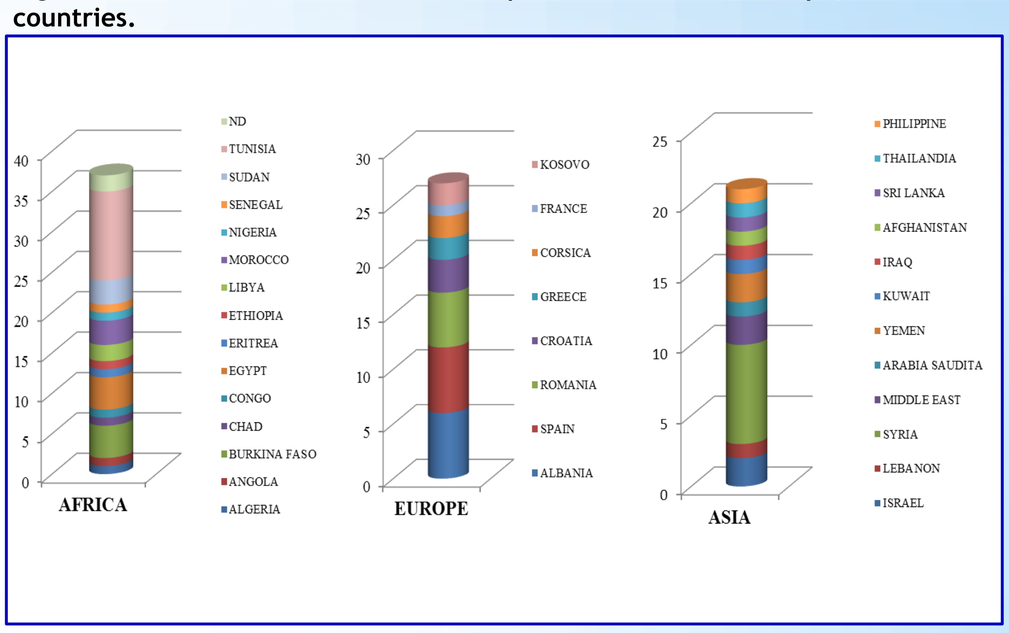
Result

Altogether 105 imported cases were diagnosed; 36 were visceral (VL) (16 HIV+) and 69 cutaneous (CL) cases; 85 (52 CL) were from the Old and 20 (17 CL) from the New World; there was a range of 0-20 cases/year (Fig.1, 2 and 3). Our findings indicated a relatively low incidence of leishmaniasis importation into Italy during the 1986–2012 period (n=105, for an average of 4 cases/year). These cases represented approximately 3.5% of all leishmaniasis cases notified in Italy (n=3028). The positive trend probably depends on better diagnosis, but we suspect that many CL cases remained unrecognized.

Agent identification was achieved in 84/105 patients. Eight *Leishmania* species were detected: *L.infantum* in 33 patients affected by VL or CL, *L.major* in 22 (CL), *L.tropica* in 10 (CL), *L.braziliensis* in 8 (CL), *L.panamensis* in 5 (CL), *L.mexicana* in 2 (CL), *L.aethiopica* (CL) and *L.donovani* (VL) in one patient each. Furthermore, parasites belonging to *L.donovani* complex (VL) and *L.guyanensis* complex (CL) were identified in one patient each.

Characteristics of the patients are changing: there are more immigrants classified as VFR and Italian tourists (Fig.4). VL importation until 1995 was associated to the increase in Mediterranean *Leishmania*-HIV co-infections. Following the introduction of HAART treatment, such cases became occasional in Italians but relatively frequent among immigrants. In contrast, a steady increase of CL cases was observed from different areas of the Old and New Worlds, which in recent years included mainly immigrants 'visiting friends and relatives' and Italian tourists. The immigrants and VFR represent a low percentage of evident "imported" cases (31/84, 36.9%), whereas they are the majority of those "probably imported" and mostly infected by *L.infantum* (17/21, 80.9%).

Fig.3. Number of leishmaniasis cases imported from Africa, Europe, and Asia countries.



Conclusions

In conclusion, despite our data are likely to be underestimated, they evidenced the introduction of a broad spectrum of parasites representative of eight human *Leishmaia* species. Given the low incidence of leishmaniasis importation, also the risk of introduction of exotic species/genotypes appears limited. However such risk should be diversified; zoonotic species such as *L. major* or neotropical *Leishmania* could unlikely be introduced in Italy because lacking of natural reservoir hosts; on the contrary, a risk associated with the importation of anthroponotic species (*L. tropica* and *L. donovani*) may require attention in the event of increased frequency. This emphasizes the importance of monitoring imported leishmaniasis prospectively so that changes in patterns and emerging risk factors can be identified.

Fig.4. Typology of travelers detected during the study period (1986-2012).

Type of traveler	1986-1988	1989-1991	1992-1994	1995-1997	1998-2000	2001-2003	2004-2006	2007-2009	2010-2012	Total (%)
Tourist	3	4	5	4	11	7	6	-	10	**50 (47.6)**
Immigrant	-	2	1	-	2	3	3	5	4	**20 (19.0)**
VFR	-	-	-	-	1	2	1	2	22	**28 (26.7)**
Soldier	-	-	-	-	-	1	1	-	-	**2 (1.9)**
Missionary	-	-	1	-	-	1	-	-	2	**4 (3.8)**
Adopted child	-	-	-	-	1	-	-	-	-	**1 (1.0)**
Total	3	6	7	4	15	14	11	7	38	**105**

This study was carried out in the frame of FP7-UE EDENext collaborative project of the 7th FP (2011-2014) founded by the European Commission under DG Health; Contract Number: 261504.