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Invited review

The current status of zoonotic leishmaniases and approaches to disease control

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Abstract

Leishmaniases are a complex of world-wide diseases with a range of clinical and epidemiological features caused by *Leishmania* spp. of protozoan parasites. Among 15 well-recognised *Leishmania* species known to infect humans, 13 have zoonotic nature, which include agents of visceral, cutaneous and mucocutaneous forms of the disease in both the Old and New Worlds. Currently, leishmaniases show a wider geographic distribution and increased global incidence of human disease than previously known. Environmental, demographic and human behavioural factors contribute to the changing landscape of leishmaniasis, which includes increasing risk factors for zoonotic cutaneous leishmaniases and new scenarios associated with the zoonotic visceral leishmaniases. The latter consist of the northward spread of *Leishmania infantum* transmission in Europe and America, the identification of unusual mammal hosts, and the decline of HIV-*Leishmania* co-infections in southern Europe following the introduction of the highly active antiretroviral therapy. Few advances have been made in the surveillance and control of the zoonotic leishmaniasis, however a number of tools have been developed for the control of the canine reservoir of *L. infantum*. These include: (i) several canine vaccine candidates, in particular an FML *Leishmania* enriched fraction showing good clinical protection, has been registered in Brazil for veterinary use; (ii) a number of insecticide-based preparations have been specifically registered for dog protection against sand fly bites. Laboratory and field studies have shown improved efficacy of these preparations for both individual and mass protection.

Keywords: Leishmaniasis; Zoonosis; Emerging diseases; Control

1. Introduction

Leishmaniases are protozoan diseases caused by members of the genus *Leishmania*, parasites infecting numerous mammal species, including humans, and transmitted by the bite of phlebotomine sand flies. Human leishmaniases have diverse clinical manifestations. Visceral leishmaniasis (VL), caused by *Leishmania donovani* in the Old World and *Leishmania infantum* in both the Old and New Worlds, is the most severe form, which if left untreated, invariably leads to death. A number of different species of *Leishmania* cause cutaneous (CL) or mucocutaneous (MCL) leishmaniasis which, if not fatal, are responsible for considerable morbidity of a vast number of people in endemic foci. According to available figures, 66 Old World and 22 New World countries are endemic for human leishmaniases, with an estimated yearly incidence of 1–1.5 million cases of CL forms and 500,000 cases of VL forms (Desjeux, 1996). The incidence of leishmaniases is not uniformly distributed in endemic areas: about 90% of CL cases occur in seven countries only (Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia and Syria), whereas some 90% of VL cases occur in rural and suburban areas of five countries (Bangladesh, India, Nepal, Sudan and Brazil). These figures, however, must be regarded as approximate and, most probably, underestimated, as official data are often obtained through passive case detection and do not include information from private practitioners and non-government organisations.

Currently, it appears that the global incidence of human leishmaniases is higher than before, although it is difficult to

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differentiate between a real and artificial increase, due to better awareness, case detection, improved reporting and accessibility to treatment. For example, in Brazil CL cases were 21,800 in 1998, while there were 40,000 in 2002; VL cases recorded in the same periods were 1840 and 6000, respectively; in Kabul, Afghanistan, CL cases were 14,200 in 1994, 65,000 in 2002 (Desjeux, 2001; 2004).

Undoubtedly, human and animal leishmaniases show a wider geographic distribution than previously known. Autochthonous *Leishmania* transmission has been recently recorded in traditionally non-endemic areas, for example in western Upper Nile, Sudan (Desjeux, 2001), a number of US states and Canadian provinces (Enserink, 2000), Australia's Northern Territory (Rose et al., 2004), and in some parts of Europe (Koehler et al., 2002; Capelli et al., 2004). It is widely accepted that the leishmaniases are dynamic diseases and the circumstances of transmission are continually changing in relation to environmental, demographic and human behavioural factors. Changes in the habitat of the natural host and vector, immunosuppressive conditions (e.g. HIV infection or organ transplantation-associated therapies) and the consequences of conflicts, all contribute to the changing leishmaniasis landscape.

2. Zoonotic forms of leishmaniasis

There is no consensus about the named *Leishmania* species causing disease in humans (Ashford, 2000; Dedet and Pratlong, 2002). The New World species *Leishmania chagasi* is now widely accepted to be a synonym of *L. infantum*, however in recent work Latin American authors still consider these species to be distinct. Some authors describe *Leishmania archibaldi* and *Leishmania killicki* as species distinct from the closely related species *L. donovani* and *Leishmania tropica*, respectively. Finally, the taxonomic status of the New World species *Leishmania colombiensis* is still controversial (Kreutzer et al., 1991; Mendoza-Leon et al., 2002).

Among the 15 well-recognised *Leishmania* species known to cause disease in humans, 13 have a zoonotic nature (Table 1). Furthermore, for the only two species considered as having an exclusive or predominant anthroponotic transmission pattern, i.e. *L. donovani* (including *L. archibaldi*) and *L. tropica* (including *L. killicki*), the presence of animal reservoir hosts has been indicated in several endemic settings, such as eastern Sudan for *L. donovani* (Dereure et al., 2003), and Morocco (Dereure et al., 1991), northern Israel (Jacobson et al., 2003) and Iran (Mohebali et al., 2005) for *L. tropica*.

Finally, a number of *Leishmania* species have been recorded in animal hosts but not in humans: *Leishmania gerbilli*, *Leishmania turanica* and *Leishmania arabica*, from Old World rodents (Ashford, 2000); *Leishmania equatoriensis* from arboreal mammals in Ecuador (Grimaldi et al., 1992); *Leishmania* sp. from red kangaroo, *Macropus rufus* (Rose et al., 2004).

2.1. Zoonotic visceral leishmaniasis

Zoonotic visceral leishmaniasis is the most widespread entity of zoonotic leishmaniasis caused by a single parasite species, *L. infantum*. In the acute, life-threatening disease the agent multiplies in the macrophages of

Table 1
Leishmania agents of zoonotic leishmaniases

Leishmania species	Disease in humans	Geographical distribution	Main reservoir host
Leishmania (Leishmania) infantum (syn. Leishmania chagasi)	Visceral leishmaniasis; Localised cutaneous leishmaniasis	Mediterranean basin; Middle East and Central Asia to Pakistan; China; Central and South America	Dog
Leishmania (L) major	Localised cutaneous leishmaniasis	North Africa, Middle East and Central Asia; Subsaharian Africa and Sahel belt	Gerbillidae rodents various rodents
Leishmania (L) aethiopica	Localised cutaneous leishmaniasis; Diffuse cutaneous leishmaniasis	Ethiopia, Kenya	Rock hyraxes
Leishmania (L) mexicana	Localised cutaneous leishmaniasis	Central America	Various forest rodents
Leishmania (L) amazonensis (syns. Leishmania ganhami, Leishmania pifanoi)	Localised cutaneous leishmaniasis; Diffuse cutaneous leishmaniasis	South America, north of the Amazon	Various forest rodents
Leishmania (L) venezuelensis	Localised cutaneous leishmaniasis	Venezuela	unknown
Leishmania (Viannia) braziliensis	Localised cutaneous leishmaniasis; Mucocutaneous leishmaniasis	South America, Central America and Mexico	Numerous rain forest mammals (suspected)
Leishmania (V) guyanensis	Localised cutaneous leishmaniasis	Guyanas, Brazil	Sloths
Leishmania (V) lainsoni	Localised cutaneous leishmaniasis	Brazil, Bolivia, Peru	Rodents
Leishmania (V) naiffi	Localised cutaneous leishmaniasis	Brazil, French Guyana, Ecuador, Peru	Armadillos
Leishmania (V) panamensis	Localised cutaneous leishmaniasis; Mucocutaneous leishmaniasis	Central America, Colombia, Ecuador	Sloths
Leishmania (V) peruviana	Localised cutaenous leishmaniasis	Peruvian Andes	Dog
Leishmania (V) shawi	Localised cutaneous leishmaniasis	Brazil	Arboreal mammals (suspected)