Leishmaniasis
Summary

Introduction

1. This note provides a brief summary of an analysis undertaken by a DISCONTOOLS group of experts on Leishmaniasis. They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details can be downloaded from the web site at http://www.discontools.eu/ by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting "create a report" which can then be downloaded as either a PDF or Excel spread sheet

Disease profile

2. Leishmaniasis represents a complex spectrum of diseases caused by intracellular protozoan parasites and transmitted by blood-sucking female phlebotomine sand flies. About 20 named *Leishmania* species and subspecies are pathogenic for humans, and 98 sand fly species are proven or suspected vectors (Maroli et al. 2013). The epidemiology and clinical manifestations of the diseases are diverse. The leishmaniases are usually grouped into 2 main entities: zoonotic leishmaniases, where domestic or wild animal reservoirs are involved in the transmission cycle and humans play a role of an accidental host, and anthroponotic leishmaniases, where man is the sole reservoir and source of vector infection. Most of leishmaniasis entities are zoonotic by nature and reservoir hosts are usually wild mammals.
3. Dogs are the primary reservoir for zoonotic VL due to *L. infantum*. This causes a severe disease in humans as well as a severe chronic disease in dogs. Zoonotic VL is currently reported in countries of the Mediterranean basin, the Middle East, Africa, Central Asia, Brazil and other countries of Latin America. A wide range of wild mammals (mainly rodents) are reservoirs of the other zoonotic entities of leishmaniasis in a range of different environments.
4. Clinically, leishmaniases are broadly divided into the two forms, visceral leishmaniasis (VL) and the cutaneous/mucocutaneous forms (CL). Human infection with *L infantum* or *L. donovani* can lead to severe systemic disease (VL) which is usually lethal in the absence of therapy. CL is a chronic skin disease in humans and non-human hosts which tends to resolve spontaneously over time. Humans are also susceptible to several other *Leishmania* species leading to a spectrum of clinical diseases.

Risk

5. About 2 million new cases of human visceral leishmaniasis are considered to occur every year in the endemic zones of Latin America, Africa, the Indian subcontinent, the Middle East, Central Asia, China, and the Mediterranean region. Public health and veterinary surveillance data remain fragmentary and these statistics are expected to be underestimates due to significant under-reporting.
6. In humans, risk factors include famine, malnutrition, mass migration, civil disturbance, poor economic conditions, and crowding. Proximity to infected dogs is a risk factor for both human and canine zoonotic VL infection. Cooler temperatures and a reduced vector activity season have limited the spread of infection northwards in the EU but global warming is likely to affect the distribution of zoonotic VL.
7. Vector control is difficult and insecticide spraying and the use of insecticide-impregnated bednets are not considered practical options to control zoonotic VL. In dogs, transient protection is possible using topical insecticides or insecticide-impregnated collars and community-wide application to dogs has been shown to impact on human and canine zoonotic VL incidence. Active case detection and drug treatment of infected individuals are recommended measures in both zoonotic and anthroponotic forms of leishmaniasis.

Diagnostics

8. Demonstration of parasites in smears, imprints or culture of infected tissues still represents the golden standard for leishmaniasis diagnosis worldwide, but is of low sensitivity. Commercial diagnostic kits are available for serological diagnosis with good performance to assess clinical disease. However, sensitivity is not always sufficient to detect some asymptomatic stages that may have an important role in transmission. Although new tests are being developed, there continues to be a need for better, easy to use, diagnostic tools that are sensitive and specific. Methods that can differentiate between exposed, infected and infectious hosts are needed. Molecular diagnostics (PCR) are available but are of limited sensitivity when performed on blood samples.

Vaccines

9. Currently, no vaccine for human leishmaniasis is available anywhere in the world. Lack of an effective, safe and affordable vaccine is the main obstacle for controlling the disease in dogs but also in humans. Several canine vaccine candidates are described in the literature but only two canine vaccines are available in EU: purified excreted-secreted proteins of L. infantum and recombinant Protein Q from L. infantum.. A canine vaccine licensed only for use in Brazil has shown efficacy but is not widely adopted. Several factors hinder the development of new vaccines, including the lack of fully reliable experimental models to test vaccine candidate efficacy and safety at an acceptable cost.

Pharmaceuticals

10. Several therapeutic agents exist for both humans and dogs including pentavalent antimonials, liposomal amphotericin B deoxycholate and paromomycin, Miltefosine is available for human (India) and dog treatment too (in Europe is mostly used in dogs. In general, human cases of VL or CL are successfully treated with cure rates exceeding 95%. Treatment of VL with antimonial drugs and liposomal amphotericin B in humans is, however, expensive and has to be administered parenterally by trained personnel. There is the potential for improvements in effectiveness at reduced costs with the use of combined drug treatments.
11. None of the currently available drugs leads to a definitive cure in dogs and relapses can occur after treatment. There is a need for new canine and human pharmaceutical options, and clinical trials of combined therapies.

Knowledge

12. Many aspects of the epidemiology and pathogenesis of the various *Leishmania* and vector species require further research. The environmental and climatic features that significantly affect the geographical spread of sandflies and canine transmission are still poorly understood. The mechanisms underlying recent northward spread of the canine infection in the EU are not fully elucidated.
13. Although the link between the canine reservoir and human VL due to *L. infantum* is well established the role of dogs in other *Leishmania* parasite cycles is unclear. There is also a need to elucidate the role of some domestic ruminants, expecially cats, as potential secondary reservoirs there are more studies, in fact, describing the presence of antibodies or L. infantum DNA in cats; the role of this animal species in the epidemiology of zoonotic VL needs to be elucidated. An understanding of the importance of infection and clinical disease in goats (mostly related with *L. donovani* in Nepal, not in Europe) and horses remains minimal at this stage. Although symptomatic patent infections play an important role in infection transmission, the significance of prepatent or asymptomatic patent infections is less well understood.

Conclusions

14. *Leishmania* are globally widespread but the number of species and the diverse epidemiology of infection leads to a complex spectrum of diseases.
15. The lack of an effective, safe and affordable vaccine is the main obstacle for controlling the disease in dogs but also in humans. It is anticipated that large scale canine vaccination could be instrumental in control the disease in dogs and hence eliminating the primary reservoir of zoonotic VL. Current approaches to the detection and control of disease are expensive and difficult to implement particularly in developing countries.