
Preface

Leishmaniasis is an ancient disease, and indeed some lesions suggesting Old World cutaneous leishmaniasis were already described in tablets of the library of King Ashurbanipal from seventh century BC, while others were probably derived from earlier texts dating 1500 to 2500 BC.

Leishmaniasis is a worldwide, high-burden vector-borne disease with diverse clinical manifestations caused by protozoa belonging to the *Leishmania* genus. Different species of leishmaniasis have re-emerged in recent years with increasing global prevalence over a wide geographic range. A number of factors, including environmental, demographic and human behaviour, have contributed to the changing epidemiology of the disease and to its recent spread throughout the world.

The aim of this book is to update the readers interested in the different aspects of this ancient disease, included among the neglected tropical diseases by the World Health Organization (WHO) in 2010. Three years later, the 66th WHO General Assembly approved a resolution that represented an important milestone for the prevention, control, elimination and eradication of the disease.

In this book, various aspects are considered such as taxonomy of the different *Leishmania* species, vector biology, host immune response, immunopathological processes led by the parasite, diagnosis, clinical picture in both immunocompetent and immunocompromised patients, treatment of tegumentary and visceral forms and, finally, control perspectives.

Several eminent scientists in the field of parasitology have collaborated in the volume by providing an overview of topical issues on the different aspects of leishmaniasis.

In Chap. 1 Gradoni introduces the epidemiology of leishmaniasis, in order to help the reader to better understand the analyses of the more specialised chapters that will follow.

The chapter by Maurício is devoted to the rather complex taxonomy of the *Leishmania* genus, which includes at least 39 species that may differ highly not only in the ability to infect vertebrate hosts and vectors but also in the resulting clinical picture in humans. According to the author, as a result of recent molecular data and phylogenetic analyses, a simplification of *Leishmania* taxonomy could be possible by reducing the number of human-pathogenic species to six: *L. donovani*, *L. major*, *L. tropica* and *L. mexicana* within the sub-genus *L. (Leishmania)* and *L. braziliensis* and *L. guyanensis* within *L. (Viannia)*. A consensus on *Leishmania* taxonomy

should be reached among different scientists, especially clinicians and researchers, so as to avoid confusion and facilitate ease of interpretation.

In the chapter on vectors, Dvorak, Shaw and Volf describe finely the species of sandflies (Diptera: Psychodidae, Phlebotominae) and focus on their geographical distribution in both the Old and New World. Particular attention is given to the various mechanisms adopted by the parasite in order to survive in the vector's gut, and in the immunomodulatory molecules of sandfly saliva, which play a crucial role for successful transmission and infection in the vertebrate host. Both the classical phlebotomine vectors and the non-phlebotomines such as midges (recently suspected to transmit infection in some geographical regions like Australia, Martinica or Thailand) may fulfil a significant role.

In the chapter on the reservoirs of the parasite, Maia, Dantas-Torres and Campino consider different aspects of zoonotic and anthroponotic transmission, focusing in particular on the large number of host species that may be responsible for zoonotic transmission in the different geographical areas. Future research should be concentrated on food sources, breeding season, movement and migration activities and longevity of the potential reservoir host(s).

The immune response against *Leishmania* is a multifactorial process comprehensive of several components having different roles in the transmission chain since the bite of the sandfly in its very early phase of the infection. The molecules present in the vector's saliva trigger the initial inflammatory response up to the onset of the disease, where immunopathological phenomena such as autoimmune reactions occur.

Lauthier and Korenaga describe the most important mechanisms of the host immune response to the parasite, which differ between cutaneous, mucocutaneous and visceral forms of leishmaniasis. A first line of intervention is represented by neutrophils, which can kill the parasite by means of different mechanisms including NETosis (death of the cell by the release of nuclear extracellular traps). Particular focus is placed on the regulation of immune response, involving both CD4+ and CD8+Th1 cells. On the other hand, Th2 polarisation is responsible for the exacerbation of the disease.

In Chap. 6 Rojelio considers the clinical aspects of leishmaniasis, which encompass a spectrum of signs and symptoms, from nodular or ulcerative lesions occurring in cutaneous leishmaniasis (in some cases evolving to mucocutaneous leishmaniasis) to disseminated syndromes known as diffuse cutaneous leishmaniasis to visceral leishmaniasis. These different evolutions depend mostly on the infecting *Leishmania* species but also on the immunological status of the host.

A diagnosis of leishmaniasis is arduous, as it reflects the complexity of the disease. However, Gramiccia and Di Muccio have been able to elucidate the most important laboratory tools that make the parasitological diagnosis essential, in order to correctly identify the causes of such an extremely multifaceted clinical picture. In addition to the classic microscopical, immunoparasitological and more advanced molecular analyses, the *in vitro* study of cellular immunity is promising, not only in visceral but also in cutaneous leishmaniasis. However, further studies in different

geographical regions are needed to achieve more accurate results and to confirm these data.

Begoña Monge-Maillo and Rogelio López-Vélez discuss the most recent acquisitions concerning the treatment of visceral leishmaniasis, by differentiating the different choices, which depend on the geographical region of the infection and on the immunological status of the host. In consideration of the development of resistance to the traditional antimonials, amphotericin B deoxycholate or lipid formulations of amphotericin B are indicated as first-line treatment for their efficacy and lower toxicity in different world areas, in particular in the Mediterranean region. However, in low-income countries, the possibility of using parenteral paromomycin should be encouraged. The promising orally administered miltefosine drug, used mostly in India, Pakistan and Bangladesh, has shown very good cure rates, but clinical failures are still relevant and probably depend on the increased development of parasite resistance.

Blum, Neumayr and Lockwood have reviewed the criteria for selecting a reliable method of treatment for tegumentary leishmaniasis, mainly determined by the infecting *Leishmania* species. Treatment options include systemic treatment with antileishmanial drugs, local topical treatment with antileishmanial ointments/creams, local intralesional injection of antileishmanial drugs and local physical treatment (cryotherapy, thermotherapy). The choice of systemic or local treatment depends on the species, size, number and location of the lesions but also changes in reason of possible comorbidities. Treatment suggestions for cutaneous leishmaniasis are presented for each species. The treatment of mucosal leishmaniasis and leishmaniasis in pregnant women, in children and in patients with immunosuppression is discussed separately.

According to Boelaert, Burza and Romero, the control of leishmaniasis depends on a limited number of key control strategies, the most important of which are early diagnosis and case management, and limit of transmission of the disease, at least in its anthroponotic form. However, sandfly control measures (insecticide spraying, insecticide-treated materials, environmental management and personal protection) are also useful to reduce transmission, especially when the procedures are conducted near human dwellings or are well addressed to vector exposure. In case of zoonotic transmission of the disease, reservoir hosts need to be controlled. Unfortunately, no human vaccine is yet available and those commercialised against canine leishmaniasis have not shown good efficacy in reducing the transmission to humans.



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