LEISHMANIA

World Class Parasites

VOLUME 4

Volumes in the World Class Parasites book series are written for researchers, students and scholars who enjoy reading about excellent research on problems of global significance. Each volume focuses on a parasite, or group of parasites, that has a major impact on human health, or agricultural productivity, and against which we have no satisfactory defense. The volumes are intended to supplement more formal texts that cover taxonomy, life cycles, morphology, vector distribution, symptoms and treatment. They integrate vector, pathogen and host biology and celebrate the diversity of approach that comprises modern parasitological research.

Series Editors

Samuel J. Black, *University of Massachusetts, Amherst, MA, U.S.A.*

J. Richard Seed, *University of North Carolina, Chapel Hill, NC, U.S.A.*

LEISHMANIA

edited by

Jay P. Farrell
University of Pennsylvania.

SPRINGER SCIENCE+BUSINESS MEDIA, LLC

Library of Congress Cataloging-in-Publication Data

Leishmania / edited by Jay P. Farrell

p. cm. — (World class parasites ; v. 4)

Includes bibliographical references and index.

ISBN 978-1-4613-5322-5

ISBN 978-1-4615-0955-4 (eBook)

DOI 10.1007/978-1-4615-0955-4

1. Leishmaniasis. 2. Leishmania. I. Farrell, J. (Jay) II. Series.

RC153 .L45 2002

616.9'364—dc21

2002025496

Copyright © 2002 by Springer Science+Business Media New York

Originally published by Kluwer Academic Publishers in 2002

Softcover reprint of the hardcover 1st edition 2002

All rights reserved. No part of this work may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise, without the written permission from the Publisher, with the exception of any material supplied specifically for the purpose of being entered and executed on a computer system, for exclusive use by the purchaser of the work

Permission for books published in Europe: permissions@wkap.nl

Permissions for books published in the United States of America: permissions@wkap.com

Printed on acid-free paper.

***The Publisher offers discounts on this book for course use and bulk purchases.
For further information, send email to <joanne.tracy@wkap.com>.***

TABLE OF CONTENTS

Preface	vii
CURRENT STATUS OF EPIDEMIOLOGY OF LEISHMANIASES Jean-Pierre Dedet	1
NEW WORLD LEISHMANIASIS: THE ECOLOGY OF LEISHMANIASIS AND THE DIVERSITY OF LEISHMANIAL SPECIES IN CENTRAL AND SOUTH AMERICA. Jeffrey J. Shaw	11
PHLEBOTOMINE SAND FLIES: BIOLOGY AND CONTROL Robert Killick-Kendrick	33
CANINE RESERVOIRS AND LEISHMANIASIS: EPIDEMIOLOGY AND DISEASE. Lenea Maria Campino	45
THE JOURNEY OF <i>LEISHMANIA</i> PARASITES WITHIN THE DIGESTIVE TRACT OF PHLEBOTOMINE SAND FLIES Shaden Kamhawi	59
MEMBRANE TRANSPORT AND METABOLISM IN <i>LEISHMANIA</i> PARASITES Scott M. Landfear	75
THE INTERACTION OF <i>LEISHMANIA</i> SPP. WITH PHAGOCYTIC RECEPTORS ON MACROPHAGES: THE ROLE OF SERUM OPSONINS David M. Mosser and Andrew Brittingham	89
<i>LEISHMANIA</i> INFECTION AND MACROPHAGE FUNCTION Greg Matlashewski	105

CLINICAL AND LABORATORY ASPECTS OF <i>LEISHMANIA</i> CHEMOTHERAPY IN THE ERA OF DRUG RESISTANCE	
Dan Zilberstein and Moshe Ephros	115
THE IMMUNOLOGY OF VISCERAL LEISHMANIASIS: CURRENT STATUS	
Paul M. Kaye	137
THE IMMUNOLOGY OF CUTANEOUS LEISHMANIASIS: EXPERIMENTAL INFECTIONS AND HUMAN DISEASE	
Jay P. Farrell	151
ANTI-LEISHMANIA VACCINE	
Antonio Campos-Neto	169
Index	191

PREFACE

Parasites of the genus *Leishmania* are dimorphic protozoans that exist as intracellular amastigotes within mammalian mononuclear phagocytes and as flagellated promastigotes within sand fly vectors. Although various species of *Leishmania* can infect a variety of hosts, the primary importance of these parasites is ability to produce disease in humans and dogs. Human leishmaniasis occurs in tropical, sub-tropical and temperate regions of the world with an estimated 1.5 to 2 million new cases each year. Continued research efforts have markedly increased our understanding of the ecology, epidemiology, and immunology of this disease and recent efforts have dramatically enhanced our knowledge of the cell and molecular biology of leishmanial parasites. However, we are still a long way from controlling this important disease.

This book comprises a series of chapters by authors who have devoted their research efforts to the study of *Leishmania* and leishmaniasis. Transmission and control are covered in the first four chapters with Jean-Pierre Dedet starting us off by reviewing the current worldwide epidemiology of leishmaniasis and pointing out the increasing problems associated with HIV-*Leishmania* co-infection. Next, Jeffrey Shaw discusses the incredible diversity of New World leishmanial species and the ecology of these parasites and their reservoir hosts. Robert Killick-Kendrick then takes up the biology of the sand fly and reviews methods to control transmission of infection to humans and important reservoir hosts such as the dog. Finally, Leana Campino discusses canine leishmaniasis, a topic central to understanding the transmission of human infection since dogs are important reservoir hosts for several species of *Leishmania*, especially those causing visceral disease.

The next several chapters focus on topics of a more experimental nature. The biology of promastigote development within sand flies and the biochemistry of parasite molecules that influence life in the sand fly intestine are covered by Shaden Kamhni. This has been an area of intense study since the discovery that leishmanial lipophosphoglycan mediates attachment of promastigotes to sand fly gut epithelial cells. Another area impacted by molecular technology is research on the metabolic biochemistry of leishmanial parasites and Scott Landfear uses one aspect of parasite metabolism, namely the nature and regulation of membrane transporters, to discuss our understanding of the cell biology of these parasites. The interaction of *Leishmania* with host macrophages is the topic of the next two chapters. David Mosser and Andrew Brittingham focus on the interaction of parasite molecules and host cell receptors that mediate entry into macrophages and discuss how opsonization by antibody may promote the production of cytokines that promote parasite survival.

Greg Matlaszewski takes a different tack and discusses how infection with different leishmanial species alters macrophage gene expression and signaling pathways. Dan Zilberstein and Moshe Ephros then cover an area critical to the control of leishmaniasis, namely chemotherapy. In addition to reviewing existing drug therapies, they discuss the current understanding of the modes of drug action and mechanisms of drug resistance.

The final three chapters are devoted to the immune response to leishmanial infections. Paul Kaye discusses the current state of knowledge of the immune response to human visceral leishmaniasis and relates it to insights gathered from studies of *L. donovani* in experimental models while I take a similar approach to cover the topic of immunity to human and murine cutaneous leishmaniasis. Finally, Antonio Campos-Neto reviews, in depth, the experimental basis of vaccine development and discusses recent efforts to move experimental vaccines from the laboratory to the field.

Leishmaniasis is a complex of infections caused by multiple leishmanial species that cause diverse forms of clinical disease. Each of these species has its own sand fly vectors and reservoir hosts and the ecological aspects that affect their transmission varies enormously. Thus, not all aspects of leishmaniasis are covered in this small volume. For example, little space is devoted to diagnosis and the clinical aspects of infection are only discussed in passing. However, these topics are detailed in multiple texts on clinical tropical medicine. Also missing is a discussion of a newly emerging area that will have enormous impact on our understanding of the biology of *Leishmania*, namely the *Leishmania* genome project. A number of laboratories are part of the *Leishmania* genome network and are actively sequencing leishmanial genes as well as pursuing the development and application of proteomics to complement these sequencing activities. As data continues to emerge from this effort, researchers will have exciting new tools to help tackle both clinical and experimental problems relevant to understanding and controlling this important infectious disease. We can only hope so since, as Professor Dedet concludes in his chapter about our current ability to control leishmaniasis, "there is much still to be done."

Jay P. Farrell, January 2002