

CRC

HANDBOOK
of
PARVOVIRUSES
Volume II

Peter Tijssen

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CRC Handbook of Parvoviruses

Volume II

Editor

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CRC Press, Inc.
Boca Raton, Florida

Library of Congress Cataloging-in-Publication Data

CRC handbook of parvoviruses / editor, Peter Tijssen.

p. cm.

Includes bibliographies and index.

ISBN 0-8493-3217-6 (v. 1). -- ISBN 0-8493-3281-4 (v. 2)

1. Parvoviruses--Handbooks, manuals, etc. I. Tijssen, P.

[DNLM: 1. Parvoviridae. 2. Parvovirus Infections. QW 165 C911]

QR408.C73 1990

576'.6484--dc20

DNLM/DLC

for Library of Congress

89-15895

CIP

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Direct all inquiries to CRC Press, Inc., 2000 Corporate Blvd., N.W., Boca Raton, Florida 33431.

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International Standard Book Number 0-8493-3217-6 (Volume I)

International Standard Book Number 0-8493-3218-4 (Volume II)

Library of Congress Card Number 89-15895

Printed in the United States

PREFACE

In the last 30 years, the importance of parvoviruses has become increasingly recognized. At first they were viewed as viruses with peculiar properties, but later it was realized that they are the cause of potentially serious diseases in animals and man. Most of the research on parvoviruses has been directed toward the characterization of the virus particle and to the molecular biology of its propagation. Reviews and the two, increasingly outdated, books tend to expand on these particular topics only.

When asked by CRC Press to edit a book on parvoviruses, I responded positively, for this was an opportunity to review not only the molecular biology of this virus group in detail, but also other, in practice perhaps more urgent, topics such as the involvement of parvoviruses in disease, diagnosis and treatment, epidemiology, and their use as research tools. The work was divided into five different sections (on a scale increasing from virion, via cell to individual): i.e., virion characterization, molecular biology, epidemiology, involvement in disease, and particular applications. The resulting work is in the form of a handbook since all areas of parvovirology are comprehensively covered, which I hope will improve substantially the useful life of this review. Later, it became evident that, in order to conform to the CRC Press publishing format regarding handbooks, the work had to be divided into two volumes.

These volumes are aimed at two major groups: those involved in research on parvoviruses or who use these viruses as research tools, and those involved in diagnostic kit and vaccine development for parvoviruses and in the general practice of diagnosis of parvovirus-related diseases. Moreover, this will expose both groups to what happens on the other side of the fence. Some of the most recent developments, those that have occurred since completion of writing these volumes, are not covered, which I regret, but cannot help due to problems in editing a multiauthored work of 33 chapters.

I wish to thank wholeheartedly the Editorial Board for their excellent suggestions and the authors who agreed to contribute their precious time to write one or more chapters for this work. I believe their efforts have resulted in valuable reviews of their respective fields. Some of this material has not been published before in either reviews or in primary literature. I hope the readers will profit as much from these essays as I have. In addition, I wish to thank Dr. R. Ruppner, Director of this Center, for his support, Laure Bourgoin for (re)typing many of the chapters and her secretarial help, and the CRC editorial staff for their help. Finally, I thank my wife, Trics, for her help and express my gratitude to her and our children, Andrew and Janice, for putting up with being without their father during the many hours needed for editing these volumes.

Peter Tijssen

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Peter Tijssen, Ph.D., is professor of virology at the Institut Armand-Frappier (Université du Québec), Ville de Laval (twin-city of Montréal, Canada), where he heads a research laboratory in the Center for Research in Comparative Medicine.

Dr. Tijssen attended the University of Wageningen (the Netherlands) for his undergraduate and doctoral studies (1972), and the Université de Montréal for his Ph.D. studies. After joining the Department of Microbiology and Immunology at the Université de Montréal in 1976, he moved to his current position at the Institut Armand-Frappier in 1985.

His major research interests include the development of virus detection methods, the study of animal coronaviruses, and the study of the replication of parvoviruses of vertebrates and invertebrates. He is the author of two books on detection methods (Elsevier), one of which is in press whereas the other has been reprinted more than once a year since its publication in 1985 and has been translated. He has lectured on this topic as a result of bilateral agreements with governments in countries in Europe, Africa, Asia, and for the World Health Organization. He serves also as member of the Editorial Board of the *Journal of Immunoassay*.

His main interests in parvoviruses are directed to porcine parvovirus and densovirus virus and he serves as a member of the International Committee for Taxonomy of Viruses (Parvovirus Study Group). Dr. Tijssen has presented a large number of lectures at national or international meetings, is author of many reviews, and has published more than 70 research papers.

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Biological Properties of Parvoviruses

Chapter 1

TISSUE TROPISM OF PARVOVIRUSES

Michael J. Studdert

INTRODUCTION

Some of the factors that influence the tissue tropism, more specifically cell tropism, of autonomously replicating parvoviruses are set down in Table 1. Of the four factors listed, the most obvious are the presence of an appropriate receptor on the cell surface and a requirement of cycling cells in late S-phase. The cell tropism of a virus is a central feature of its pathogenesis. We may consider parvovirus-cell tropism in the context of pathogenesis at four, somewhat overlapping, levels: (1) molecular, (2) cellular, (3) animal, and (4) population. Some remarks will be made about tropism and pathogenesis at each of these levels, although most will be said about the cell and animal. The remarks are particularly influenced by our studies of the most dramatic, naturally occurring diseases caused by parvoviruses: the long-recognized, worldwide, frequently fatal disease feline panleukopenia and the remarkably similar, recently emerged (1978) canine parvovirus disease. Recent reviews of canine and feline canine parvovirus diseases have been published^{1,3} and may be consulted for more detailed aspects of the disease and extended bibliographies. More specific and detailed accounts of the feline and canine as well as other parvovirus diseases follow in this volume. The intention here is to use aspects of our understanding of the feline and canine diseases to provide a general account of parvovirus tropism and pathogenesis and to identify some of the deficiencies in coming to a more complete understanding of these matters.

MOLECULAR ASPECTS OF CELL TROPISM

A detailed description of the genes, the gene products, and the mode of replication of parvovirus DNA is in part a description of the molecular pathogenesis of the virus, and these aspects, which are now understood in increasing detail, are reviewed elsewhere in the volume. Corollaries to these events in the viral replication cycle are to define in molecular terms the mechanisms whereby the entering single-stranded virion DNA molecule usurps the cellular machinery and the consequences in terms of loss of cell function. It is also necessary to define the kinetics of the production of viral specific antigens at the cell surface that are targets for one of several immune cytolytic mechanisms which probably also influence pathogenesis.

These notions of viral pathogenesis are of course applicable to any virus; they are mentioned, perhaps somewhat unnecessarily, at the outset of this review simply to draw attention to the oft-quoted belief that because of the "simplicity" of parvoviruses — a "simplicity" exceeded only by viroids and perhaps the scrapie agent — it should be possible in the coming years to specify in quite complete and precise terms the molecular events in the viral replication cycle and the consequences of these events for the cell. We shall note, however, that many aspects of *in vivo* pathogenesis, which are the emphasis of this chapter, are not so accessible to study. Indeed, experimental *in vivo* models for studying the pathogenesis of the feline and canine parvoviruses have generally been only partially successful. There is a complex set of factors that are poorly defined, in addition to the role of the virus itself, and a susceptible animal, that determine and influence tropism and pathogenesis.

A critical feature of the molecular basis for parvovirus tropism and pathogenesis about