Progress in Medical Virology

Vol. 15

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Vol. 15

Edited by JOSEPH L. MELNICK, Houston, Tex.

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63 figures and 18 tables

S. Karger · Basel · München · Paris · London · New York · Sydney · 1973

Progress in Medical Virology

Vol. 1	VIII + 302 p.,	47 fig., 41 tab.,	1958
Vol. 2	VI + 234 p.,	36 fig., 23 tab.,	1959
Vol. 3	VIII + 496 p.,	59 fig., 40 tab.,	1961
Vol. 4	VIII + 303 p.,	27 fig., 34 tab., 3 cpl.,	1962
Vol. 5	X + 306 p.,	29 fig., 10 tab.,	1963
Vol. 6	X + 320 p.,	23 fig., 12 tab.,	1964
Vol. 7	XII + 376 p.,	58 fig., 22 tab.,	1965
Vol. 8	XII + 420 p.,	36 fig., 30 tab.,	1966
Vol. 9	XIV + 496 p.,	53 fig., 92 tab.,	1967
Vol. 10	XVIII + 502 p.,	55 fig., 25 tab., 1 cpl.,	1968
Vol. 11	XVIII + 470 p.,	120 fig., 45 tab.,	1969
Vol. 12	XVIII + 358 p.,	56 fig., 26 tab.,	1970
Vol. 13	XX + 503 p.,	86 fig., 42 tab.,	1971
Vol. 14	X + 339 p.,	43 fig., 30 tab.,	1972

S. Karger · Basel · München · Paris · London · New York · Sydney
Arnold-Böcklin-Strasse 25, CH-4000 Basel 11 (Switzerland)

Printed in Switzerland by F. Reinhardt AG, Basel
ISBN 3-8055-1388-7

Preface

The first six volumes of this series are now out of print. Rather than reprinting these previous volumes, current volumes of the series will include, in addition to new articles, reviews on selected topics from the early volumes, rewritten and updated – most of them by the authors who contributed the previous reviews nine to fifteen years ago.

Although total fetal and infant morbidity and mortality have declined in recent years, the incidence of congenital malformations has remained high. It has been estimated that each year, in the USA alone, 500,000 fetal deaths and 62,000 neonatal deaths are associated with congenital defects, and about 15 million individuals who survived have birth defects severe enough to affect their daily lives. In this volume, BLATTNER, WILLIAMSON, and HEYS up-date their review written more than a decade ago on the role of viruses in congenital malformations. The authors discuss important recent advances in the understanding and control of viral teratogenesis, particularly in understanding of rubella virus and of cytomegalovirus as teratogenes and of the previously unrecognized immunologic capabilities of the human fetus. Not only do they describe what has been learned to date, but they also point out important areas in which knowledge is incomplete and avenues of further investigation are promising, both in clinical investigations and in studies of experimental models in animals.

GEAR and MEASROCH review the status of knowledge concerning clinical illnesses, particularly of the newborn, which have been associated with coxsackievirus infections. This review is an up-dating of GEAR's review published in the first volume of this series, in 1958. In addition to surveying a number of outbreaks of severe illnesses due to coxsackieviruses of group A and of group B, the authors describe clinical, pathological and virological

studies, and outline recommended preventive measures. The authors suggest that the future pattern of epidemiology of the coxsackieviruses may follow that of poliomyelitis, i.e., where once immunizing infection with the coxsackieviruses occurred in early life, improved standards of living and hygiene may lead to postponement of initial infections into older age groups, in whom overt illnesses may occur more frequently. They also predict an increase in the proportion of women of childbearing age who lack immunity to coxsackie B viruses, and a corresponding increase in the proportion of babies born without the protection of maternal antibody.

Although virus myocarditis was reviewed only 8 years ago, developments in this field have been so rapid that LERNER and WILSON were asked to survey advances that have taken place since that 1965 publication. At the time of the earlier review, it was generally accepted that, while acute human infections of the myocardium and/or pericardium with coxsackievirus B might take place, including occasional lethal infections in newborns, there were no known sequelae in man or animals. Today, group B coxsackievirus infections have been associated with acute myopericarditis, valvulitis, chronic myocardiopathy, constrictive pericarditis, vena caval obstructions, endocardial fibroelastosis, and other congenital malformations of the heart. Group A coxsackieviruses and echoviruses also are now implicated in some of these disorders, and there are suggestions that some cases of rheumatic heart disease or glomerulonephritis may be due to enteroviruses. The authors critically review more than 100 selected new reports, both of human infections and of experimental animal models, discuss the pathogenesis of acute and chronic virus-associated disorders of the heart, and examine the evidence for the virus-disease associations.

When the 1858 review entitled 'The salivary gland viruses of man and animals' by MARGARET G. SMITH appeared in this series, the agent had been transmitted in tissue cultures only a few years previously. Since that time, a large amount of information has been acquired about the salivary-gland viruses – or cytomegaloviruses, as they are now known. Cytomegaloviruses of a variety of host species have been recognized; the cytomegaloviruses of man have been studied with regard to their epidemiology, pathogenesis, and clinical effects – as have a number of the animal cytomegaloviruses. Cytomegaloviruses have been of special concern in recent years, not only because of their primary involvement in the serious cytomegalic inclusion disease which they can produce in congenitally infected infants, but also because their ability to establish congenital infections and persistent infections, like that of the other herpesviruses, attracted special attention in

the search for viral etiologic agents of cancer and of other chronic diseases of unknown etiology. In this volume, PLUMMER reviews the progress that has been made in these investigations, the effects that they have on their hosts, and their taxonomic relationship to the other herpesviruses.

Both isolations of viruses of the respiratory tract and data about these agents and the diseases which they cause have proliferated greatly over the years since 1959, when WARD reviewed these viruses in Volume 2 of this series. His current review deals particularly with the myxovirus groups, the rhinoviruses, the adenoviruses, and the coronaviruses, surveying the characteristics of the agents, and their clinical and epidemiologic features.

The growth of the field of virology, and the increasing numbers of virus laboratories around the world, have been paralleled by the steady development of the virus programs of the World Health Organization and its network of virus reference centres and collaborating laboratories. COCKBURN, who reported to readers of this series in 1966 on the WHO program in medical virology, describes here the numerous and significant developments which have been achieved in the virologic activities of WHO since that time. The established role of WHO is to promote understanding of the epidemiology and ecology of virus diseases in a worldwide setting, in order to aid in control of these diseases. Particularly in recent years, WHO has stimulated laboratory and field studies and their application to public health problems. A part of the WHO program is implemented through the WHO Virus Reference Centres, which assist national laboratories in the identification of viruses, aid in furnishing reference and diagnostic reagents, assist in the training of national virologists, and participate in collaborative research studies conducted within the WHO network. Other important activities of the Virus Diseases Program include the regular collection and dissemination of epidemiological and virological information, aid in epidemic situations, and the organization of Scientific Groups for specific diseases.

For prevention of viral diseases, immunization programs have been shown to be efficient and relatively inexpensive public health measures, and have been increasingly used in recent years in both developing and developed countries. Well-planned and carefully-evaluated mass immunization campaigns offer particular promise for developing countries, not only for their economical use of funds but also for the logistic advantages of such mass programs in countries having scattered rural populations, limited transportation facilities, and few or widely separated permanent health institutions. With wider public acceptance of immunization, improved delivery techniques and reagents (such as jet-injector equipment and multiple-antigen combina-

tion vaccines), and more stable vaccine preparations, mass immunization campaigns are being conducted with increasing success. A dramatic example of what can be achieved is seen in the fact that serious predictions can now be made that smallpox may well be eradicated from the world by 1976 – a goal made realistic in recent years largely through the World Health Organization Smallpox Eradication Program in which mass immunization is an important tool. FOEGE & EDDINS discuss in this volume the considerable experience that has been gained recently in the conduct of such programs, and describe some of the important operational areas to be considered in planning mass immunization projects.

The serodiagnosis of viral infections has been made more reliable and efficient over the past decade through the development of micro-techniques, the standardization of test methods, wider availability of improved viral antigens and antisera, and automation of certain procedures. The review by SCHMIDT & LENNETTE in this volume constitutes an updating and extension of their chapter on the same topic published in 1961; it deals chiefly with new developments which have contributed to the diagnosis of human viral infections by serologic techniques.

Helper-dependent viruses, which are unable to replicate without the presence of another virus, have been of unusual interest ever since they were first recognized. This interest stems not only from the intrinsic significance of this phenomenon in terms of the nature of viruses, but also from the fact that defectiveness and helper-dependence were found to be characteristic of certain oncogenic viruses and have been explored as a possible key factor in oncogenesis. The opportunity to study a helper-dependent satellite virus model in a relatively simple system was provided by the recent isolation of a satellite, helper-dependent bacteriophage. BARRETT, CALENDAR, GIBBS, GOLDSTEIN, LINDQVIST & SIX, who have conducted much of the investigation of this phage, review the status of knowledge regarding its properties and life cycle, and discuss the potential implications for animal virology and viral oncology.

High resolution electron microscopy of thin-section preparations of virus-infected cells, correlated with accurate infectivity assays, contributes greatly to understanding not only of the structure of virus particles but also of their morphogenesis. HIGASHI, one of the pioneers in these studies, has updated and extended his previous review, which appeared in 1959. Selected illustrative material has been retained from the earlier version, and the author has added important new text sections and electron micrographs on virus development.

In the final chapter of the volume, the Editor reports on progress in classification and nomenclature of animal viruses. In the schematic diagrams showing separation of RNA- and DNA-containing viruses into major groups on the basis of physical and chemical properties, consideration has been given to certain new findings concerning some of the groups and to proposals for group names coming into general use but not yet officially approved. Also included is a tabulation of virus groups in terms of the polymerases which they induce and/or carry.

Readers of this series are encouraged to write regarding topics that they recommend for review, and also to offer suggestions for authors who might be invited to prepare such reviews. Topics requiring more lengthy coverage than would be available in this series may be proposed for inclusion as a single volume in the companion series, Monographs in Virology.

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Progr. med. Virol., vol. 15, pp. 1–41 (Karger, Basel 1973)

Role of Viruses in the Etiology of Congenital Malformations[1]

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I. Introduction

In recent years, while fetal and infant morbidity and mortality resulting from other causes have declined, the incidence of congenital malformations has remained high. Although the figures vary according to the types of studies made by different investigators it has been estimated that each year, in the United States alone, as many as 500,000 fetal deaths and 62,000 liveborn deaths may be associated with congenital defects, while approximately 15 million surviving persons have one or more birth defects which are

1 The early volumes of Progress in Medical Virology are now out of print. Rather than re-printing the entire volume, certain timely articles have been selected for up-dating. The previous review on this subject was written by Drs. BLATTNER and HEYS and appeared in volume 3.