CONTROL OF VIRUS DISEASES

Editor
EDOUARD KURSTAK

Preface

A wise, extensive, long-term, and worldwide program of vaccination under the guidance of the World Health Organization (WHO), and with the concerted effort of public health services in participating countries, effected the eradication of smallpox, one of the most dangerous human virus diseases. Today, smallpox vaccination has been discontinued, and no more cases of smallpox are reported. Such an effort to eradicate a worldwide virus disease epidemic, needed not only scientific and medical expertise but also substantial financial help. It should be recognized that beside the expertise involvement of, among others, the WHO, and the Centers for Disease Control (CDC), the financial support of the U.S. Department of State's Agency for International Development (AID) was of great importance. The smallpox eradication effort undertaken in 1966 had succeeded in 20 countries in West Africa by 1971 and, by 1975, in India, both areas were all important reservoirs of this virus.

Undoubtedly, if such an eradication program is implemented for another dangerous human virus disease, such as measles, poliomyelitis, or for animal virus diseases (e.g., foot-and-mouth disease) for which vaccines are available, similar results could be obtained.

The control of virus diseases to an acceptable level, or if possible, their eradication, depends mainly on: (1) appropriate specific diagnostic technology; (2) availability of highly immunogene and safe vaccines; and (3) to vector containment and to the detailed knowledge of the epidemiology of viruses and their interaction with the environment.

In all of these areas, tremendous progress has been made since the smallpox eradication was certified by WHO in 1979. The virus diagnosis technology is enriched with very sensitive tools, such as monoclonal antibodies, nucleic acid hybridization, or enzyme immunoassays. Vaccine production expanded to genetic engineering, safe virus immunogenes are produced in bacteria, and synthetic vaccines are envisaged. The monoclonal antibodies technology enables detailed study of the antigen variation of viruses, and the quality control of produced vaccines is achieved more efficiently, resulting in vaccines with enhanced specificity. In addition, the scientific community realized the usefulness of the comparative unifying concept to study viruses or to control them.

Recent experience in veterinary virology in the production of immunogene polypeptides of foot-and-mouth disease virus in *Escherichia coli*, using genetic engineering technology, serves medical virology also in the case of poliovirus or hepatitis B virus vaccine production attempts. Methods of monoclonal antibodies used for the study of the variation of influenza virus may also be used in the diagnosis of animal or plant virus diseases.

The present treatise, *Control of Virus Diseases*, is built in this spirit of unity in virology and was prepared according to the program of the IVth International Conference on Comparative Virology. This conference organized by the International Comparative Virology Organization (ICVO) under the auspices of the WHO, was held in Banff, Alberta, Canada at the end of 1982. The plenary sessions of the conference were devoted to the evaluation of the recent achievements and progress in the prevention, control, and diagnosis of virus diseases. Professor Edouard Kurstak, the editor of this treatise, chaired the conference and Professor Raymond G. Marusyk, associate editor, acted as chairman of the local organizing committee. The eminent virologists participating in this conference, from all parts of the world, assured its remarkable success.

The present treatise emphasizes the control of virus diseases of man, animals, fish, mollusks and plants, and reflects our efforts to bring the concept of comparative virology into a broader practical application. The rapid progress of virology as a science and new concepts and technology to produce safe vaccines and to control several dangerous and economically important viruses, are presented in 30 chapters by well known and reputed virologists. Moreover, special attention is given to new developments in immunological and biochemical diagnosis and containment of highly infectious viruses, to antiviral chemotherapy and its clinical application, and to new strategies for vaccine development including those for hepatitis B and foot-and-mouth disease. The virus-induced immunopathology and defense mechanisms are also reviewed, as well as new concepts to control viral zoonoses and plant virus infections. Special attention is given to the variation of antigenic spectrum of viruses, in particular of influenza viruses, which complicate the prevention and control of diseases.

The ecology and epidemiology of arthropod-, nematode-, animal-, or seed-transmitted viruses is reviewed in connection with the control perspectives and new strategies. Finally, the WHO recent programs for the control of virus diseases are presented in a separate chapter.

The uniqueness of this treatise is attested by its comparative approach to resolve problems of prevention and control of virus diseases and by very recent information on the achievements, from areas of both basic research and practical applications related to the containment of viruses.

The contributors to this treatise are well known for their expertise in their chosen field. Each has prepared a thoughtful and well-documented treatment of the subject. Personal interpretations and conclusions of the authors, as well as the numerous illustrations and unpublished material, provide a large body of information which brings into sharp focus current findings and new directions and strategies in the control of virus diseases.

It is our hope that this treatise will provide a useful tool for all concerned with viral diseases, particularly in hospitals; veterinary clinics; centers of infectious diseases; medical, veterinary, and agricultural schools; plant protection institutes; departments of public health and agriculture, and authorities involved with the prevention, control, and quarantine measures of virus diseases. We also hope that virologists working in isolation, mainly in developing countries, will appreciate this treatise containing the newest information in control and diagnosis technology of virus diseases.

We wish to express our sincere gratitude to the contributors for the effort and care with which they have prepared their chapters and to the staff of Marcel Dekker, Inc. for their part in the production of this treatise.

Edouard Kurstak
Raymond G. Marusyk

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Introduction

Virus diseases remain a world-scale problem by contributing enormously to human disability and mortality, and causing severe economic losses by affecting livestock and crops in all countries. The estimated annual cost due to a few selected virus diseases, such as hepatitis, influenza A, measles, poliomyelitis and rubella, in the absence of immunization would be more than $1 trillion in the United States alone. Personal misery, serious sequellae, and economic losses can be staggering. Even with all the preventive measures taken in the United States, costs exceed billions of dollars annually. Worldwide, an estimated 200 million persons are chronically infected with hepatitis B and mortality due to measles is estimated at 1 million children per year, of which about 90% were undernourished. Acute gastroenteritis, mainly due to rotaviruses, is estimated to be the cause of death of 5 million persons annually, and the list goes on and on, even poliovirus continues to kill children in developing countries. On the other hand, smallpox virus has been eradicated, a feat which could be repeated with several other viruses which depend on human-human transmission.

"New" viruses inducing hemorrhagic fevers, such as Ebola, Lassa, Junin, Machupo, and Hantaan are recognized with increasingly advanced technology. These viruses cause a most complex zoonotic syndrome affecting man and have a variable geographic and ecologic specificity with endemic spots in Africa and South America. Recent data show that hemorrhagic fever with renal syndrome due to Hantaan virus may have worldwide epidemiological implications. As expected, the discovery of this virus, once again renewed the interest in this important group of viruses.

Economic losses due to animal and plant viruses are enormous and are a major factor for the high percentage of the world population which still suffers from chronic malnutrition. The cassave crop, essential in Kenya, was reduced by as much as 75% due to the infection of 90% of the plants by cassave mosaic virus. In Ghana, more than 100 million cacao trees were lost due to an infection by swollen shoot virus, and in several countries millions of citrus trees are lost annually due to the aphid-transmitted tristeza virus.

Some animal viruses (e.g., Rinderpest, Rift Valley fever) may in addition to their economic importance also be a threat to the health of the population. The viruses just mentioned recently caused thousands of human deaths, especially in the Middle East and North Africa.

Based on the premise of whether the host has an immune system and can be immunized (man, animals) or not (plants) two general approaches can be taken. Although plants cannot be vaccinated and diseased plants cannot as yet, be cured with chemotherapy, many cultivation factors can be undertaken to decrease the incidence of disease. These include: (1) starting with virus-free material and selection of more resistant varieties; (2) vector and diseased plant control (removal); and (3) taking epidemiologic parameters into account (plant spacing, crop rotation).

The last decade has been exciting in the development of very powerful and relatively simple techniques which should have a great impact on diagnosis and preventive immunization with noninfectious vaccines, namely, development of monoclonal antibodies, enzyme immunoassays, and genetic engineering. These techniques will have an enormous impact on virus control, but at the same time it should be emphasized that these advances may be delayed significantly if the technology transfer and the training of local virologists and auxiliary personnel in countries with the most urgent need is not increased. International organizations may aid greatly in furthering this purpose, for instance by stimulation of scientific exchange, such as with appropriate regional conferences in Asia, Africa, and Latin America, and the organization of frequent educational workshops in developing countries. The International Comparative Virology Organization (ICVO), which is an umbrella group of scientists, was created to promote the transfer and acquisition of knowledge on recent development and practical field expertise in the area of virology, especially for developing countries. It cannot be overrated that the emphasis for developing countries should be on the applied, practical side of virology and its interrelationship with the environments, and not on basic research. In fact, basic research is a form of world aid from countries which have the economic means to advance this field. However, most countries will and should have other priorities. In order to promote this transfer, I organize regularly with the aid of both local and international organizations (WHO, ICVO, UNEP), highly successful international conferences on topics of special interest for developing countries of those regions. It is hoped that these meetings help to break down the isolation of virologists in developing countries from those in the industrialized countries.

Production of vaccines is entering a new era with the development of genetic engineering. This technology enables the production of one or several antigens of the virus, which, without the presence of the viral genome, are noninfectious. Eventually, when costs are lower and natural variations of the virus in the environment have been adequately studied, this will provide the community with hitherto utopian synthetic vaccines. These vaccines would probably contain several immunogens to prevent the escape of an infectious variant. On the other hand, the possibility of mass production of vaccines in cell culture has been increased by the development of more efficient culture methods demonstrated by the replacement of bottles by beads. The tendency for developing tissue-culture prepared vaccines is to use killed instead of attenuated viruses, since live vaccines could revert. Nevertheless, live vaccines continue to serve in the control of several virus diseases.

Other control concepts involve: (1) understanding of the complex ecosystem in which the virus occurs, and (2) a complex interdependent system for disease diagnosis and information gathering. These elements of the programs seem to suffer in many parts of the world (see Chapter 21), their costs are escalating, while the costs and quality factors of vaccines improve.

The development of chemotherapeutic agents in the control of viral diseases is becoming more feasible due to the increasing understanding of the chemical nature of the virus and its replication. A detailed knowledge of the biochemistry and the way of multiplication of each group is necessary for a rational approach to treat the diseases they cause. The high hopes placed on interferon have not yet been fulfilled and its use for specific clinical applications need to be further investigated. Several antiviral agents have been found to be specific without or with only negligible side effects on the host. It is, therefore, expected that this field will expand considerably in the next few years.

The rapid progress in the development and concepts of the control of virus diseases has been the subject of the Fourth International Conference on Comparative Virology, conferences we have organized regularly in Canada since 1969. Eminent leading virologists from all parts of the world, and from all disciplines, contributed to the success of this conference by the high standing of the presentations and the fruitful and animated exchange of ideas and developments from usually isolated areas. This cannot fail to have an important influence on the virologists' community. Some of the topics discussed were virus diseases of man, animals, fish, mollusks, and plants from a comparative point of view, with an emphasis on new developments in diagnostic methods and the containment of viruses. This large, exciting body of information, so sharply brought into focus at this conference, has been compiled in a thoughtful and systematic way so that, as is our hope, it may serve virologists and other scientists in related areas everywhere, both in the field and the laboratory.

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HUMAN, FISH, ANIMAL, AND MOLLUSK VIRUS DISEASES

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