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Alan C. Jackson *Editor*

Viral Infections of the Human Nervous System

Springer

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Foreword

As a young Army Medical Corps officer, I was assigned to work in the Department of Virus Diseases of Walter Reed Army Institute of Research during the Asian influenza epidemic of 1957. At that time, we knew nothing of the genomic structure of influenza viruses and had no idea that we were working with a recombinant of a human and a duck virus. In the spring, the influenza epidemic waned. The focus of the diagnostic laboratory was shifted to the three clinical syndromes putatively caused by viral infections of the nervous system—aseptic meningitis, encephalitis, and paralytic poliomyelitis. In those days, rabies with its long incubation period, unique clinical features, and uniformly fatal course was regarded as a strange outlier.

Amazing how the landscape has changed over the past 50 years and how two very divergent paths evolved in clinical virology. The latency and reactivation of herpesviruses, the chronic infection with measles virus in the form of subacute sclerosing panencephalitis, the prominent fetal damage caused by rubella virus, the role of viruses in demyelinating diseases (postinfectious encephalomyelitis and progressive multifocal leukoencephalopathy), and the role of infectious prions in chronic degenerative diseases led to an expanding interest in viral infections of the human nervous system.

Conversely in the middle of the twentieth century, the interest in infectious diseases faded. The discovery of antibiotics and antiviral drugs, the eradication of smallpox, and the control of measles and poliomyelitis with vaccines all led to death knells for the specialty of infectious diseases. Infectious disease services were minimized. Prominent infectious disease physicians moved into "healthcare delivery" careers; several published obituaries for the specialty. Infectious diseases were disappearing as a specialty despite the foreboding of *new* diseases such as Legionnaire's disease, a paralytic form of enterovirus 71, and the evolution of an encephalitic strain of California virus in the Midwestern USA. Then in 1981, the surprising and frightening onslaught of acquired immune deficiency disease dramatically changed all of medicine and society.

Why are we now seeing new diseases every year? Greater surveillance and reporting is one explanation, but some new diseases are caused by mutations of

familiar viruses, some result from transportation of exotic viruses to new sites, and some result from animal viruses that have been introduced into human populations. All these factors are propelled by the burgeoning global human population and its mobility and speed of global movement. Today, a new exotic virus transmitted to a human in Asia or Africa can be in your local airport or indeed at your church social within one incubation period or even a single day.

This book addresses many of the factors that have made the study of viral infections of the nervous system so compelling and raises intriguing questions that must be addressed over the next decades.

Baltimore, MD Richard T. Johnson
March 2012

Preface

Viral infections of the nervous system are a challenging group of diseases for clinicians and for researchers. The pathogenetic mechanisms involved in this group of diseases are very diverse. Although some, like enteroviral meningitis, are common. However, many are rare and have limited and unpredictable distributions, both geographically and in time (e.g., Nipah virus infection). Specialized diagnostic investigations are often necessary for definitive diagnosis, although a presumptive diagnosis should often be suspected on the basis of the clinical features. Many of these infections are serious diseases with high morbidity or mortality or with fatal outcomes (e.g., Creutzfeldt–Jakob disease and rabies). A majority of the authors are neurologists and most have either a background or a distinguished career in basic neurovirology research, which gives them unique insights in writing about these diseases. Only further research will give us a better understanding of the basic mechanisms involved in all aspects of these infections, which will, hopefully, lead to future advances in their therapy.

My interest in the field of neurovirology became solidified when 30 years ago I first read Dr. Richard T. Johnson's book entitled *Viral Infections of the Nervous System* (Raven Press, 1982). Two years later, I became a postdoctoral fellow in Dr. Johnson's research laboratory at The Johns Hopkins University in Baltimore. I hope this volume will also stimulate the interest of young people in this intriguing field. I would like to thank Dr. Beatrice Menz at Springer Basel for giving me the opportunity of putting together a volume on these infections and to all of the expert contributors for their hardwork in preparing up-to-date chapters and sharing their expertise and insights on this diverse group of diseases. They have all done a superb job.

Winnipeg, MB, Canada — Alan C. Jackson
February 2012

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Part I
Encephalitis

Measles Virus Infection and Subacute Sclerosing Panencephalitis

Banu Anlar and Kalbiye Yalaz

Abstract Measles virus can cause two acute neurological disorders: acute infectious encephalitis and postinfectious autoimmune encephalitis, each with a risk of about 1 in 1,000 measles cases. Two other rare neurological problems manifest after a latent period: subacute measles encephalitis occurring in immunocompromised individuals, and subacute sclerosing panencephalitis (SSPE) in immunocompetent hosts. SSPE develops 1–10 years after measles infection; it is usually progressive and fatal. Mental and behavioral changes, myoclonia, and ataxia are typical initial manifestations. The diagnosis is based on the demonstration of intrathecal anti-measles virus immunoglobulin G synthesis. Pathological examination of brain biopsy or autopsy material demonstrates inflammation, neuronal loss, gliosis, demyelination, and typically, inclusion bodies containing measles virus antigens or RNA. Treatment with inosiplex and interferons may induce temporary stabilization or remission in about 30–35 % of the cases. Immunization against measles virus and maintenance of immunization rates above 90 % in the population are of extreme importance for the prevention of these debilitating or fatal disorders.

Keywords Demyelinating • Immunoglobulin • Magnetic resonance imaging • Measles • Subacute sclerosing panencephalitis

Abbreviations

ADEM	Acute disseminated encephalomyelitis
CSF	Cerebrospinal fluid
EEG	Electroencephalography

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