Specialized Neuroscience Research Programs (SNRPs) and NINDS

SHANNON GARNETT, Ph.D., • BETHESDA, MD

The National Institute of Neurological Disorders and Stroke (NINDS)—in collaboration with the National Center for Research Resources and the Office for Research on Minority Health—supports a new, innovative funding mechanism called Specialized Neuroscience Research Programs (SNRPs). Dr. Al Gordon is the Director of the NINDS Office of Special Programs in Neuroscience. The purpose of the SNRPs is to augment and strengthen the research capabilities of faculty, students, and fellows at minority institutions by supporting the development of new or the enhancement of ongoing basic and clinical neuroscience research programs, and by developing the necessary infrastructures of these programs. This mechanism represents a long-term strategy to prepare future neuroscience research and health professionals who can assist the NINDS in reducing disease disparities of populations at increased risk for disorders of the nervous system. Additionally, the NINDS supports a SNRP in Health Disparities: HIV and the Nervous System to encourage research collaborations between established investigators, investigators at minority institutions, and health care providers to better deliver the benefits of research to all Americans as described by Dr. Joana Rosario, a program director in the NINDS Office of Special Programs. Institutions that develop successful research programs under this initiative will receive additional support to help them develop more intensive and larger research studies aimed at reducing the national burden of HIV and AIDS. Five institutions received SNRP awards in 1999 (University of Hawaii, University of Puerto Rico, Universidad Central del Caribe, University of Texas St. Antonio, and Howard University), and three additional awards are planned for this year.

Abundant viral antigen was observed in intraluminal necrotic debris in the upper and lower airways. In a small number of pigs, there was prominent central nervous system pathology with meningeal inflammatory infiltrates, and viral antigen was detected focally in inflammatory cells as well as within the nuclei of rare parenchymal cells. Nipah antigen was also detected in kidneys as focal staining in renal tubular epithelial cells. The presence of extensive infection in the upper and lower airways suggests that the respiratory secretions from infected pigs are likely to be a rich source of infectious virus. The finding of neutralizing antibodies to Nipah virus in two species of fruit bats (Pteropus vampyrus and Pteropus hypomelanus) and the results implicating fruit bats as a reservoir for Hendra virus led us to suspect a similar reservoir for Nipah virus. Recently, Nipah virus was reported to be isolated from bat urine of Pteropus sp. in Malaysia. If such findings can be confirmed, these large fruit bats might provide both a reservoir and the source of Nipah virus outbreak.
Diseases at 3rd International Symposium on NeuroVirology

NIAID and NINDS Panel Discusses Emerging Neurologic Diseases at 3rd International Symposium on NeuroVirology

Brian Wigdahl

Message from the President

BRIAN WIGDAHL, Ph.D. • HERSEY , PA

In conjunction with the 3rd International Symposium on NeuroVirology held September 14-16 in San Francisco, the National Institute of Allergy and Infectious Diseases and the National Institute of Neurological Disorders and Stroke sponsored a Blue-Ribbon Advisory Panel that convened to identify key scientific issues and research opportunities for future NIH support in the area of emerging neurovirologic diseases. During the course of this one-day meeting, participants met to assess the state of knowledge of neurovirology and relevant resources and technologies; identify questions that should be addressed in basic and clinical investigation, and to discuss proposed areas and mechanisms for research and resource allocation. The meeting was organized to allow maximum time for discussion and achievement of consensus. Selected presentations were used to provide an overview of critical aspects of the field and a framework for dialogue and synthesis. Topics included: Overview of Neurologic/Neuropsychiatric Disease Due to Viral Infections; Causation & Transmission (for other infectious agent) as a factor or cofactor in pathogenesis of disease?; Infrastructure Issues: Databases and Sample Repositories; Pathogen Discovery; Pathogenesis; and Clinical Intervention. The meeting was organized by Dr. Ian Lipkin, Department of Anatomy and Neurobiology, University of California, Irvine; Dr. Michael Buchmeier, Department of Neuropharmacology, The Scripps Research Institute; and Dr. Steven Jacobson, Viral Immunology Section, Neuroimmunology Branch, NINDS, NIH. Queries regarding this meeting may be directed to any one of these individuals.

FEATURED BRIEF

Nipah Virus: A Newly Emergent Deadly Paramyxovirus with an Extended Host Range that Includes Humans

WILLIAM J. BELLINI, Ph.D. • SHERIF ZAKI, Ph.D. • THOMAS G. KSIASEK, Ph.D. • ATLANTA, GA Division of Viral & Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control & Prevention

A n outbreak of severe febrile encephalitis associated with human deaths was reported in Peninsular Malaysia beginning in late September of 1998. The outbreak was first recognized nearIpoh, a city in the northern state of Pekur. Associated with respiratory illness in pigs, and was initially attributed to Japanese encephalitis. By February 1999, a severe increase in pigs and humans was recognized in other regions of Malaysia and was associated with the movement of a large number of pigs from Ipoh southward into the new outbreak areas. In March 1999, a cluster of 11 cases of respiratory and encephalitis illnesses was noted in Singapore in abattoir workers who handled pigs from the outbreak regions in Malaysia. The outbreak in Singapore ended when the importation of pigs from Malaysia was prohibited. The outbreak in Malaysia ceased when over one million pigs were culled from the outbreak and immediately surrounding areas. A total of 265 cases of encephalitis, including 105 deaths, were associated with the outbreak in Malaysia.

The virus, named Nipah virus after the village in which the first case death occurred, was determined to be a paramyxovirus related to Hendra virus, another recently emerged paramyxovirus. The virus is comprised of a single-stranded RNA genome (18,000 nucleotides) of negative polarity. The nucleocapsid structures are approximately 1.8 μm in length and 21 μm in diameter and the virus appears to assemble and bud from the plasma membrane. The assembled virions measure 500-700 nm in diameter, are enveloped, and appear to contain surface projections consistent with that of the family Paramyxoviridae and there are two genes encoding the fusion and attachment proteins. Nipah is both genetically and antigenically related to Hendra virus. Phylogenetic analysis suggests that these viruses form a new genus within the Paramyxovirinae subfamily.

Nipah virus was determined to be the etiologic agent of the outbreaks in Malaysia and Singapore. Isolation or serologic testing confirmed Nipah virus infection in all cases from Singapore and over 75% of the cases from Malaysia. The most notable illness in pigs implicated in transmitting the virus to humans was respiratory and included a loud and distinctive cough. Although serologic studies found evidence of Nipah virus infection in most of the pigs on farms with infected humans, only a minority of these pigs were noted to be ill with only a minimal (~5%) increase in pig deaths. Serologic studies also indicated that Nipah virus infection occurred in dogs, cats, two pongo pigs, and in bats.

Two key features of this outbreak were the fatal encephalitis and the nearly universal history of infected humans and other animals, including cats and dogs, in direct contact with pigs. Pathologic studies of infected human and pig tissues provided plausible explanations for these two features of the outbreak. Autopsy studies of humans suggested that the primary pathology was a multi-organ vasculitis associated with infection of endothelial cells. Infection was most prominent in the nervous system, where a diffuse vasculitis was noted in the cerebral cortex and brain stem with extension to parenchymal tissue. Eosinophilic, mainly intracytoplasmic, viral inclusions were observed in the affected neurons and other parenchymal cells. Intense immunostaining of endothelial cells and dead and dying parenchymal cells was noted in the central nervous system. These studies demonstrated that Nipah virus infection in humans can cause widespread central nervous system pathology consistent with a severe encephalitis.

Pathologic examination of pigs revealed extensive involvement of the respiratory tract. In the lungs, a giant-cell pneumonia with characteristic multi-nucleated syncytial cells was noted. By immunohistochemistry, Nipah virus antigens were demonstrated in syncytial cells in the lungs and epithelial cells lining the upper airways. 

NIAID and NINDS Panel Discusses Emerging Neurologic Diseases at 3rd International Symposium on NeuroVirology

STEVEN J. JACOBSON, Ph.D. • BETHESDA, MD

The “Featured Brief” section of the newsletter highlights an area of international importance that the editors feel deserves special attention. An update of current activity and information on a “featured” topic should help keep members aware of fast-paced studies and new results. The Editors are always interested in your ideas for future articles and brief comments on its topics.

Brian Wigdahl

Dr. Lynn Pulliam (Chair of the Organizing Committee for the 3rd International Symposium on NeuroVirology) provided an overview of the Scientific Program and Objectives for the 2000 Symposium in her introductory remarks to more than 250 Symposium participants from around the world. We have been extremely pleased with the level of interest and excitement about the Symposium. This event has clearly become a major focal point for dissemination of research ideas in the area of neurovirology. We are very pleased to acknowledge the generous and essential support of the National Institute for Neurological Disorders and Stroke as well as the National Institute of Mental Health. The quality of our Symposium has been greatly enhanced by their involvement. We would also like to acknowledge additional Symposium support from The Pennsylvania State University and Temple University as well as support from the Journal of NeuroVirology, Pharmacia & Upjohn, Inc., Advanced Bioscience Resources, Inc., Medivacs, Inc., and Centaur Pharmaceuticals, Inc. The Board of Directors and Editorial Board of the International Society for NeuroVirology and the Journal of NeuroVirology is very proud of the high quality of the Symposium Speakers and the breadth and quality of the participants. The success of the Annual Symposium and the growing NSF Membership from around the world will continue to enhance our efforts to understand the pathogenesis of neurotropic viral diseases and to develop strategies to prevent and treat these often fatal processes.
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The purpose of the First Pan-American Symposium on Neurovirology is to bring together medical scientists from the United States, Canada, and Latin America to share knowledge with respect to the relatively new field of neurovirology. This is the first meeting of the Pan-American Society of Neurovirology, which was established to understand the impact of viral infections on the nervous system in the Americas. The meeting will take place from November 13 to 15, 2000, at the Princes Hotel, Acapulco, Mexico. This symposium is a scientific component of the Neuroscience 2000 Congress organized in collaboration with the Mexican Society of Neurology (November 10-18, 2000). The meeting will cover a broad range of topics in the field of neurovirology and will include workshops on the cutting-edge tools of molecular biology. The meeting will feature outstanding speakers in the fields of virology, neuroscience, and psychiatry.

The International Society for NeuroVirology has announced Volker ter Muenlen as the recipient of the 2000 ISNV Pioneer in Neuro-Virology Award. The award was presented to Dr. ter Muenlen at the Third International Symposium on Neuro-Virology held in September 2000. Dr. ter Muenlen’s contributions to the field of neurovirology span a period of more than thirty years in which his research has been directed toward the study of viruses in the CNS. His studies have focused on viruses in animal models or human diseases such as measles virus, coronavirus and more recently, simian immunodeficiency virus. Specifically, his research has targeted acute measles encephalitis, meningoencephalitis and subacute sclerosing panencephalitis. His seminal findings have greatly contributed to our current understanding of virus persistence and pathogenesis in the CNS. In addition, his work has been instrumental in determining the etiology of other neurological syndromes associated with viral infections. His studies on measles virus infection in the CNS have contributed to our understanding of the mechanisms of persistent viral infection and, in particular, the manner in which viruses are able to escape the immune response. To pursue the mechanisms of viral neuropathogenesis, Dr. ter Muenlen developed an animal model to examine human samples. Prior to the development of advanced molecular biology and immunological techniques, Dr. ter Muenlen studied viral homology, gene expression, and mutations. Through his studies he was able to demonstrate how measles and coronavirus infections are able to induce MHC class I and II expression and initiate an autoimmune response. One of the important implications of these findings was the notion that viral infections are able to trigger autoimmune responses. More recently, Dr. ter Muenlen has expanded his studies to include work on retroviruses, particularly HIV-1 and SIV. Dr. ter Muenlen received his M.D. from the University of Göttingen in 1960. Following an internship at the University of Göttingen, he completed a fellowship in virology at Children’s Hospital of Philadelphia under the direction of Dr. Werner Henle. He then returned to Germany to complete a residency in Pediatrics at the Universitäts-Kinderklinik in Göttingen. Dr. ter Muenlen returned to the United States as a visiting scientist at the Wistar Institute in Philadelphia where he worked on measles neuropathogenesis. In 1966, Dr. ter Muenlen accepted the position of Assistant Professor in the Departments of Pediatrics & Microbiology at the University of Göttingen. He quickly rose through academic ranks attaining the title see Pioneer Award