Neuroinfectious disease

A rapidly evolving challenge

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Infectious diseases of the nervous system constitute a unique challenge for the practicing clinician: they are relatively uncommon, and are often serious enough to cause disability or death, yet frequently are treatable. By their nature, the organisms that cause neuroinfectious disease can evolve rapidly. Likewise, knowledge about these conditions can emerge and radically change during the practice life of a clinician. This necessitates regular updating of neurologists about neuroinfectious disease to provide optimal care for patients. In this issue of *Neurology® Clinical Practice*, we present a series of articles aimed at helping practicing clinicians stay abreast of emerging information needed to manage these critical neurologic disorders.

Infections can have a bewildering breadth of presentations, challenging the clinician always to consider them when assessing the etiology of patient complaints. Rapid detection of the causative organism is a key to diagnosis and selection of the best therapy. While culturing the organisms remains common for bacterial pathogens, more rapid identification is often needed. Antigen detection is critical in rapid diagnosis of some fungal infections such as *Cryptococcus*, and immune response may assist in identification of other conditions like syphilis. Previous challenges of etiologic diagnosis of viral illness have been substantially addressed with increasing availability of PCR tests. Knowledge about how to interpret these highly sensitive and specific methods to detect the DNA or RNA of specific organisms has expanded rapidly and made speedy diagnosis of such disorders as herpes simplex encephalitis reliable without requiring brain biopsy. The intricacies of use of PCR are highlighted in almost every report in this series. Microbial DNA technology is emerging for bacterial and fungal infections, illustrated by a challenging case of neurosyphilis reported by **Takahashi et al.** In another article, **Chin** explains how nucleic acid amplification tests (Xpert MTB/RIF) contribute to identification of tuberculosis. PCR has assisted in identification of the causes of viral encephalitis leading to more rational management as outlined by **Venkatesan and Geocadin**. Varicella-zoster virus (VZV), which can be clinically inferred quite reliably when a typical dermatomal chickenpox rash is observed, can now be etiologically linked with

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neurologic syndromes through VZV DNA detection even without the typical cutaneous manifestations (**González-Otárula et al.**).

Emergence of HIV has illustrated the rapidly evolving nature of neuroID as a field, and resulted in the special focus of neuroHIV. This virus that was unknown when some of us trained now affects more than 30 million people worldwide, and has been associated with a challenging array of primary neurologic complications as well as vastly increased risks of previously uncommon opportunistic conditions. It is not a uniform and constant foe, but has evolved in genetically differing subtypes prevalent in various global sites. Rapid development of therapies has already dramatically improved the outlook for HIV-affected patients, but the brain is a sanctuary from which it sometimes emerges even when traditional systemic disease markers appear reassuring. Articles in this issue help clinicians become familiar with emerging areas of knowledge relevant to HIV, highlighting acute HIV infection (Andrade et al.) and the escape of the virus during long-term suppression by therapy (Hoogland and Portegies).

The chronic immune-suppressed population with HIV has allowed research previously almost impossible, thereby improving diagnosis and care for a variety of opportunistic brain diseases. Neurosyphilis, Epstein-Barr virus-associated primary CNS lymphoma, and cytomegalovirus encephalitis are among conditions now much more easily diagnosed based on experience gleaned from AIDS management. Cryptococcal meningitis therapy has evolved, helping a wide spectrum of patients at risk for this condition as well as HIV-infected patients. Progressive multifocal leukoencephalopathy (PML) similarly was rarely recognized until the HIV epidemic. In the past decade, PML has emerged as a serious challenge for development of immune-modulating therapies for various inflammatory and neoplastic conditions. Identifying those at risk and more effectively treating those with PML remains a work in progress critical both to neurology and to therapeutics for numerous systemic inflammatory conditions.

The shrinking world we live in—where health problems any place in the world, particularly infectious diseases, can easily appear in our own communities—has given urgency to understanding and addressing global health problems. Tuberculosis is the poster child of such a problem, long known but rare and low on the list of priorities in the United States. Fueled by the AIDS epidemic, conditions for spread of tuberculosis—including drug-resistant forms that are even more dangerous—have underscored the importance of supporting a worldwide approach to control of infectious diseases (Chin). From severe acute respiratory syndrome, to emerging influenza, to dengue, to poliomyelitis, to chikungunya, previously rare infectious diseases can suddenly emerge anywhere in the world.

It is important for all engaged in neurology to participate in lifelong learning about the emerging topics in infectious disease as it relates to the nervous system. Furthermore, our national research enterprise must support the work of a cadre of specialists dedicated to this discipline. We cannot afford to ignore these often dangerous, yet treatable, neurologic diseases. Leaving their care to physicians without special skills in neurologic diagnosis and management is likely to result in suboptimal outcomes. The American Academy of Neurology (AAN) has fewer than 300 from its membership of ~26,000 identifying neuroID as a special interest. Fortunately, through the AAN and 21st century communications, it is easier for practitioners throughout the world to access those with special expertise. However, it is critical that we maintain a vital group of specialists with in-depth knowledge of both the science of infectious disease and clinical expertise in its neurologic manifestations. Emerging tools with molecular mechanisms, as well as the power of new imaging techniques, provide exciting career opportunities for those who wish to study neuroID. NeuroID training is only available at a handful of larger academic departments, and does not have a formal certification process. The numbers of trainees have been too small to support the costs of formal testing that certified fellowship programs require. However, current leaders regularly mentor trainees interested in this discipline, generally providing a several-year clinical and research fellowship launching the academic career of the trainee. Often training combines special emphasis on

neuroimmunology and neuroID, a rational and synergistic career mix that enlarges practice opportunities to include common neurologic conditions such as multiple sclerosis. Alternative pathways discussed include combining neuroID with hospitalist training, neurologic intensive care training, or global health careers. These neuroID experts are necessary to support training clinicians worldwide about these diseases; to lead the research required to understand the pathophysiology contributing to the disorders; and to maintain and improve diagnostic and therapeutic tools that can save lives in years to come. We encourage neurologists to participate in the NeuroID Section of the AAN, where those interested in further training can obtain mentoring through the leaders of this Section.

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