

Neuroinfectious Disease Inquiries within the Emerging Infections Network

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Infectious diseases have the potential to affect the nervous system of millions of people worldwide. For instance, approximately 3 million people contracted meningitis and 300 000 people died from the disease in 2016. With the discovery of new pathogens, a rise in the use of immunosuppressive therapy, improved diagnostics, and recent advances in infectious and autoimmune neurology, the field of neuroinfectious diseases is rapidly evolving.

A 1992 landmark report by the Institute of Medicine addressed the critical threat posed to society by emerging infectious diseases. This report highlighted infectious epidemics and pandemics and charged the infectious disease community to take steps to mitigate this threat. In response, the Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America (IDSA) launched the Emerging Infections Network (EIN) in 1997—a joint collaboration to identify and monitor new infectious diseases and syndromes. It now comprises more than 2570 infectious disease physicians and members of the public health community located in the United States and abroad. The EIN listserv has 2 member types: infectious diseases physicians and members of the public health community. Infectious diseases physician members are all members of the IDSA or the Pediatric Infectious Diseases Society who see patients on a regular basis [1]. These physician members practice in a variety of settings, including university hospitals, no university teaching hospitals, city/county public hospitals, community hospitals, and the Veterans' Affairs and Department of Defense hospital systems. Most members practice in the United States, with a small number of international members. Public health members include individuals working in a federal (eg, CDC, National Institutes of Health [NIH], US Food and Drug Administration [FDA], and other governmental entities), state, or local public health department and include veterinarians, microbiologists, epidemiologists, and pharmacists.

A major feature of this network is an exclusive, moderated listserv that allows physicians and members of the public health community, including CDC, FDA, NIH investigators and epidemiologists, to post inquiries related to challenging clinical issues, ranging from diagnostic dilemmas to management questions. Each post submitted to the listserv is reviewed by a moderator for appropriateness, edition, and removal of patient identifiers. Posts are then collated into a thread with an appropriate title and thread type (eg, clinical, epi, infection prevention, CDC update, FDA recall, etc) and sent out via the listserv platform on a once-daily basis (Monday through Friday only) with a disclaimer attached [2]. Once the inquiry is published, other EIN members provide suggestions to resolve the case. In recent years, the FDA's Center for Drug Evaluation and Research/Drug Shortage group joined the listserv to provide information to its members and surveil antimicrobial drugs. The average number of total separate listserv discussions has been stable over the last decade at approximately 200 inquiries per year, with a total number of responses for all topics ranging from 760 to 976 per year.

This article describes the prevalence and characteristics of inquiries related to neuroinfectious disease cases discussed by infectious disease physicians on the EIN listserv. Our goals were to identify the spectrum of inquiries, the pathogens most often discussed, the populations most

frequently affected, and finally to characterize recurring themes and unanswered questions to outline future opportunities on research and education in this complex field.

The EIN listserv is a forum for discussion of clinical aspects of emerging infectious diseases and new or unusual clinical events. However, data related to neuroinfectious diseases have not been described. Our findings suggest the important and challenging components of neuroinfectious diseases in infectious disease physicians' practice, as demonstrated by the large number of clinical inquiries dedicated to infections affecting the central and peripheral nervous system. It is notable that analysis of this data enables the identification of research and educational priorities that may aid physicians in the diagnosis and management of these complex conditions [3].

First, the inquiries demonstrate the challenge of diagnosis of neurologic infections in the setting of immunosuppression. Neurologic complications of immunosuppression are increasingly common—approximately one third of patients with solid organ transplants develop neurologic complications, and up to one half of patients with rheumatologic conditions have neurologic manifestations, many of which have been attributed to immunosuppression as opposed to the condition itself. Patients with malignancies are even more challenging diagnostically, because they may simultaneously be at risk for central nervous system (CNS) involvement of their malignancy, CNS infections due to immunosuppressive medications, and, more recently, neurologic immune-related adverse events due to novel immunotherapies. With a growing armamentarium of immunomodulatory medications, this challenge is likely to grow.

The EIN listserv also highlights the complexity of broader pathogen testing through neuroinfectious disease-directed diagnostic panels. There were 2 inquiries related to HHV6 before the approval of the Bio fire Film Array Meningitis Encephalitis PCR panel; both patients were tested for HHV6 due to their immunosuppressed status and a high clinical suspicion. However, 2 inquiries posted after the panel was approved involved immunocompetent cases in which the clinical suspicion for HHV6 was exceedingly low. After the panel revealed a positive result in these 2 cases, they both received treatment with antiviral agents. Numerous follow-ups suggested that these 2 results were likely clinically insignificant, perhaps related to chromosomal integration of the HHV6 genome. Although the availability of a multiplex PCR panel has shown benefit in improved pathogen

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identification, there is also concern with overutilization in patients with low clinical suspicion for CNS infections. With more advanced diagnostics such as next-generation sequencing becoming available, dedicated training may be required to properly interpret testing results within the appropriate clinical context [4].

Also of interest were inquiries involving patients with neurologic symptoms but without a clear infectious cause. A broad range of noninfectious neurologic etiologies were considered in the differential diagnosis. Noninfectious encephalitis is increasingly being recognized, with autoimmune cases now constituting 20%–30% of all encephalitis cases. This understanding was reflected in many inquiries suggesting anti-NMDA, post infectious and Para neoplastic encephalitis as possible differential diagnoses. Given the broad range of neurologic disorders entertained, infectious disease specialists may benefit from dedicated training to recognize these processes. There is currently no mention of neurology or neuroinfectious diseases in the Accreditation Council for Graduate Medical Education (ACGME) infectious disease fellowship curriculum requirements. Internal medicine residency curriculum requirements do include exposure to neurology as part of the training but do not specify type or length of exposure. Neurologists would also likely benefit from training in infectious diseases. The ACGME currently requires “sufficient exposure to faculty with special expertise in infectious diseases” as part of the neurology residency training but does not require any infectious disease-related training itself. As of July 2019, there were only 10 non-ACGME accredited fellowships dedicated to neuroinfectious diseases. Efforts are underway to standardize fellowship curricula for neurologists seeking training

in neuroinfectious diseases, although there may be additional benefit in development of joint training opportunities for neurologists and infectious disease physicians [5].

In summary, this retrospective study illustrates the significant and growing challenges related to the care of patients with neuroinfectious diseases in infectious disease physicians’ practice, identifies priorities for research and training in the field, and highlights the utility of forums such as the EIN in guiding areas of priority.

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Conflict of interest

None

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