

Expanding Molecular Diagnostics for Central Nervous System Infections

Mavel Gutierrez, MD, Patricia J. Emmanuel, MD*

Department of Pediatrics, University of South Florida, College of Medicine, 2 Tampa General Circle, 5th Floor, STC 5016, Tampa, FL 33606, USA

Keywords

- CNS infections • Meningitis • Encephalitis • Polymerase chain reaction
- Multiplex PCR • Next-generation sequencing

Key points

- Central nervous system (CNS) infections, although uncommon, require rapid, actionable diagnosis and treatment.
- Molecular diagnostics have greatly expanded the arsenal for detecting CNS infections; innovation continues to improve automation, turnaround time, and reliability.
- Multiplex syndromic polymerase chain reaction panels test for a variety of common CNS pathogens using a small aliquot of spinal fluid and are now commercially available at many hospital laboratories.
- Further clinical studies are needed to determine the panel's performance for the individual targets and in high-risk populations, such as neonates and immunocompromised and human immunodeficiency virus-infected patients. These panels do not replace traditional methods, including Gram stain and culture.
- Close collaboration with laboratory scientists is needed as these and other new technologies, such as next-generation sequencing and bioinformatics platforms, are implemented into clinical settings.

INTRODUCTION

Over the last 20 years, the evolution of molecular diagnostics has greatly expanded the clinician's ability to detect pathogens. Technology has advanced and focused on rapid turnaround times (TAT) and automation to make these

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*Corresponding author. *E-mail address:* pemmanue@health.usf.edu

technologies available to laboratories around the country [1]. One of the newer advances, the commercialization of multiplex polymerase chain reaction (PCR), allows hospital laboratories to offer syndromic panels of pathogens for diagnostic testing [2]. The newest set of panels is related to central nervous system (CNS) diseases. Although CNS infections are uncommon, there is often a critical need for rapid, actionable diagnosis and treatment.

CNS infections are challenging; symptoms are often nonspecific and overlap with many other infectious and noninfectious syndromes. The highest rates of meningitis and encephalitis occur in infants and young children, making it an important topic for all pediatric providers [3]. Despite a decreased incidence due to conjugated vaccines, there are more than 4000 cases of bacterial meningitis in the United States each year, and there are many more cases of viral meningitis and encephalitis [4]. Encephalitis alone causes \$2 billion in health care expenditures in the United States and significant morbidity and mortality [5].

The CNS is a sanctuary site with the blood-brain barrier offering some protection from pathogens but also inhibiting drug entry (Fig. 1) [6]. Infections can occur at almost every anatomic location of the CNS with certain pathogens having predilection for specific sites. Infection occurs primarily through hematogenous spread, through contiguous spread from a nearby infection, or

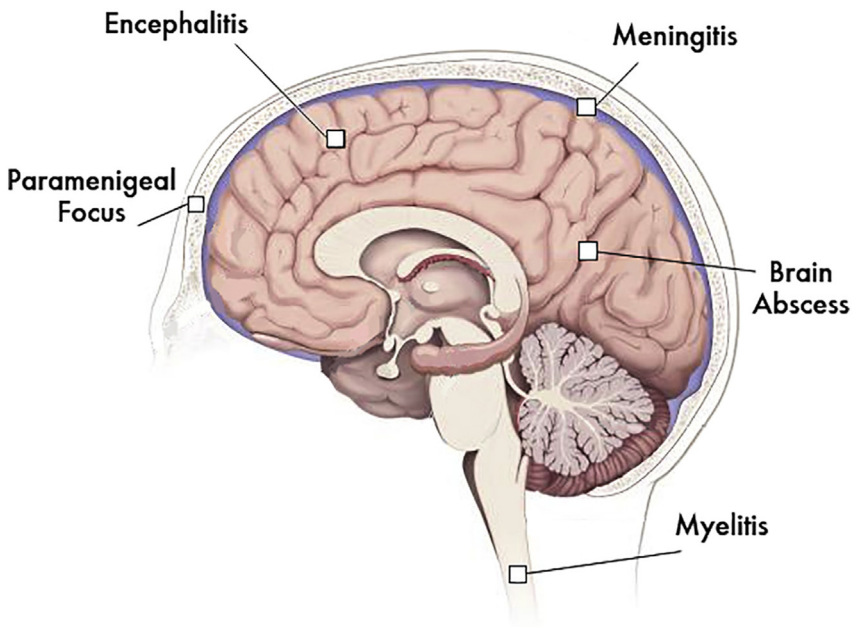


Fig. 1. Diagram of CNS anatomy. (Adapted from Swanson PA 2nd, McGavern DB. Viral diseases of the central nervous system. *Curr Opin Virol* 2015;11:45; with permission.)

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