

THE PATHCARE NEWS

BioFire Meningitis/Encephalitis PCR test:

PathCare offers a Meningitis/Encephalitis Multiplexed PCR test with an expanded organism profile and reduced turn-around time, detecting 14 potential central nervous system (CNS) pathogens:

Table 1. Bacteria, Viruses, and Yeast Detected by the Meningitis/Encephalitis (ME) Panel

BACTERIA	
<i>Escherichia coli</i> K1	<i>Neisseria meningitidis</i>
<i>Haemophilus influenzae</i> (typeable and non-typeable strains)	<i>Streptococcus agalactiae</i> (group B)
<i>Listeria monocytogenes</i>	<i>Streptococcus pneumoniae</i>
VIRUSES	
Cytomegalovirus (CMV)	Enterovirus (EV)
Human herpesvirus 6 (HHV-6)	Herpes simplex virus 1 (HSV-1)
Human parechovirus (HPeV)	Herpes simplex virus 2 (HSV-2)
Varicella zoster virus (VZV)	
YEAST	
<i>Cryptococcus neoformans/gattii</i>	

The ME Panel is able to detect and identify multiple bacterial, viral, and yeast nucleic acids directly from cerebrospinal fluid (CSF) specimens obtained from patients with symptoms and signs of meningitis and/or encephalitis. The expanded profile include the ability to detect *E. coli* K1 strains, an important cause of neonatal meningitis which account for about 80% of *E. coli* isolated from CSF. The panel also can detect Human parechoviruses (HPeV). These viruses were originally classified as Enterovirus, but comprise another genus of the *Picornaviridae* family. Similarly to the Enteroviruses, respiratory and gastrointestinal illness are common. HPeV-3 is associated with severe disease, including encephalitis, meningitis, and hepatitis in infants < 3 months of age.¹ The Enterovirus PCR will fail to detect HPeVs due to genetic differences between these viruses. VZV has been found to be the third most frequent viral agent causing CNS disease in adults.² Encephalitis and meningitis may complicate both varicella (chickenpox) and zoster (shingles) infections. The vesicular rash is a characteristic finding for viral reactivation, but may be absent in more than a third of cases. HHV-6B, one of the causes of roseola in infants (HHV-7 being the other) and HHV-6A establish latency in host cells, including the CNS tissues.³ CNS disease may occur particularly in immunosuppressed individuals. In addition to the common bacterial and viral CNS pathogens, *Cryptococcus neoformans/gattii* can also be detected with this multiplexed PCR test.

Specimen collection:

The Meningitis/Encephalitis PCR test requires 0.5 ml unspun CSF. Due to the sensitive nature of this test, it is important to prevent contamination of the specimen during collection using aseptic technique. Some organisms detected with the ME Panel such as *Streptococcus pneumoniae* and *H. influenzae* can be shed from the respiratory tract of healthy individuals. HSV-1 may be shed from persons with or without active cold sores. Some studies indicate that 70% of individuals shed HSV-1 asymptomatically at least once a month and even up to 6 times a month.^{4,5} During sample collection, healthcare workers are advised to wear a surgical mask (or equivalent) and avoid touching the mask while collecting specimens.

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It is recommended to collect CSF specimen for the PCR test in a separate sterile tube to minimize handling of the specimen during processing. Ideally 2 CSF specimens must be submitted if both a molecular screen and culture are requested. CSF specimens for PCR should be transported in dedicated orange CSF specimen bags available from PathCare's warehouse (item number 702453).

The PCR test is not intended for use with CSF collected from indwelling CSF shunts.

Specimens should be transported at 2-8°C if > 8hrs transport time to the analysing laboratory.

Test result and Interpretation:

- The turn-around time for this test is < 8 hours from reaching the analysing laboratory.
- Please note that the ME Panel does not distinguish between latent and active CMV and HHV-6 infections. Detection of these viruses may indicate primary infection, secondary reactivation, or the presence of latent virus. These viruses may be reactivated during infection due to other pathogens, including agents not detected with the ME Panel such as *Mycobacterium tuberculosis*. The results should be interpreted together with other clinical and laboratory information.
- Viral shedding of VZV into the CSF may occur in cases of zoster due to reactivation. The detection of VZV in the CSF may not be the cause for CNS disease in these cases.
- False negative results may occur when the concentration of organism(s) in the specimen is below the limit of detection for the test.
- Results for this assay are generated by simultaneously performing several PCRs in a contained, automated procedure. Separation of the various targets (viral, bacterial and fungal) is not supported and as such, cannot be requested independently. However qualitative PCR tests for Enterovirus, HSV-1/2, VZV and CMV are offered separately.

Recommendation:

This encephalitis/meningitis PCR test is recommended for all patients with encephalitis and for those with viral meningitis of unknown origin in order to better target antiviral treatment, as well as for the identification of bacterial CNS pathogens in patients who received antibiotic therapy prior to CSF collection that may lead to negative cultures. The rapid diagnosis of a viral etiology may allow early discontinuation of antimicrobial therapy.

References:

1. Harvala, H et al. Parechoviruses in children: understanding a new infection. Curr Opin Infect Dis. 2010; 23: 224-30.
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3. Reynaud JM and Horvat B. Human Herpesvirus 6 and Neuroinflammation. ISRN Virology. 2013; doi.org/10.5402/2013/834890
4. Sacks SL et al. HSV shedding. Antiviral Res. 2004; 63: Suppl 1:S19-26.
5. Miller CS et al. Asymptomatic shedding of herpes simplex virus (HSV) in the oral cavity. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. Vol. 105, Issue 1, 2008, 43-50.

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