PHYSICIAN UPDATE

Epstein-Barr Virus (EBV) Viral Load Testing by Real-Time PCR Now Available

SUMMARY
Effective Wednesday, June 6, Epstein-Barr virus (EBV) viral load testing by real-time PCR will be available from PeaceHealth Laboratories at the central laboratory in Springfield, Oregon. This comes as a result of an extensive analytical verification and clinical validation process for this laboratory-developed test.

EBV is associated with malignant proliferative disorders of both epithelial and lymphoid origins, including:
- Hodgkin's and Burkitt's lymphoma
- B- and T-cell non-Hodgkin's lymphoma
- Nasopharyngeal and gastric carcinoma

EBV also causes substantial disease from lymphoproliferative disorders among immunocompromised individuals such as transplant recipients and patients with AIDS.2,3

MONITORING EBV INFECTIONS AND THERAPEUTIC TREATMENT
Quantitative methods to measure EBV are now widely used to diagnose, monitor and treat EBV-related diseases. This is particularly true in the case of PTLD.4

In addition, studies indicate that preemptive treatment of EBV and reducing immunosuppressive therapy can reduce the incidence of PTLD in immunocompromised patients.4,5 EBV-related PTLD is usually accompanied by increased EBV DNA in the peripheral blood. EBV viral load monitoring is used to guide initiation of preemptive or anti-EBV-related tumor therapy.

BENEFITS
- Assists in early diagnosis of infectious mononucleosis when serology testing is inconclusive1
- Assists in diagnosing and monitoring patients with post-transplant lymphoproliferative disease (PTLD), nasopharyngeal carcinoma, or AIDS-related brain lymphoma
- Improves turnaround time

BACKGROUND
By the time U.S. adults reach the ages of 35-40, 95% of them will test positive for EBV. It persists in the host after primary infection and may reactivate at any time. Since EBV may replicate without causing apparent harm, it is important to distinguish asymptomatic infection from EBV disease.

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SERIAL MONITORING
Increasing EBV DNA levels rather than a stable elevated EBV DNA load may be a more reliable marker of PTLD. Serial monitoring with the same specimen type is important to identify patients at risk of disease because a high EBV DNA load (DNAemia) alone cannot always predict impending PTLD.

WHOLE BLOOD VERSUS PLASMA
The choice of optimal clinical specimen may differ with regards to the type of EBV infection because the status of EBV DNA can differ in different disease states and furthermore require a different interpretation. Viral load testing of whole blood detects EBV DNA in both lymphocyte and cell-free compartments. Whereas, EBV DNAemia in plasma may reflect virus released from necrotic cells, as well as virus that is shed intermittently from the epithelium and from lytically infected B cells.

Generally, in transplant recipients, quantitative viral load testing of whole blood correlates extremely well with the viral load measured in peripheral blood mononuclear cells and may predict EBV disease at the earliest time. However, normal adults previously infected with EBV may have low levels of EBV DNA in their lymphocytes (i.e. whole blood testing) that might not be present in their plasma.

METHODOLOGY
The real-time PCR assay targets a conserved region of the Epstein-Barr nuclear antigen (EBNA) gene. The real-time quantitative EBV PCR assay has been shown to have both very high precision and reproducibility.

This assay has a dynamic range that permits the quantitation of EBV, with acceptable precision and linearity, between 1,000 and 1,250,000 copies/mL. The quantification limit for this DNA assay is 3.0 log copies/mL (1,000 copies/mL).

QUESTIONS?
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**ORDERING INFORMATION**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>58110</td>
<td>EBV Quantitative PCR, Plasma</td>
</tr>
<tr>
<td>58114</td>
<td>EBV Quantitative PCR, Whole Blood</td>
</tr>
<tr>
<td>58112</td>
<td>EBV Quantitative PCR, CSF</td>
</tr>
<tr>
<td>58116</td>
<td>EBV Qualitative Detection by PCR</td>
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**Methodology:** Real-Time PCR  
**Performed:** Monday, Wednesday, Saturday  
**Reported:** Same day as tested  
**CPT Code:** 87799 (for 58110, 58114, 58112)  
87798 (for 58116)

**SPECIMEN REQUIREMENTS**

**Collect:** One 4 mL lavender top tube, (EDTA) or CSF in a sterile, leak-proof container.

**Handling:**  
Whole Blood: Do not freeze. Ship refrigerated at 2-8°C.  
Plasma: Centrifuge and immediately separate plasma into a plastic vial. Refrigerate. Freeze at -20°C if specimen cannot be assayed within 3 days.  
CSF: Refrigerate or freeze CSF within 30 minutes. If transport is delayed, freeze at -20°C.

**Stability:**  
Whole Blood: Ambient 24 hours; Refrigerated 72 hours; Frozen unacceptable.  
Plasma: Ambient 24 hours; Refrigerated 72 hours; Frozen 14 days.  
CSF: Ambient 30 minutes; Refrigerated 72 hours; Frozen 14 days.

**Standard Volume:** 1 mL plasma, whole blood or CSF.

**Transport:**  
Whole Blood: Do not freeze. Ship refrigerated at 2-8°C.  
Plasma: Ship frozen at -20°C.  
CSF: Ship frozen at -20°C.

**Rejection Criteria:** Non-sterile or leaking container; amniotic fluid; ocular fluid; bone marrow; BAL or biopsy tissue; heparinized specimen; frozen whole blood; hemolyzed or clotted whole blood.

**Reference Range:** Not detected.
Epstein-Barr Virus (EBV) Viral Load Testing by Real-Time PCR Now Available (Continued)

REFERENCES


