



PAML Introduces New Assay for CMV DNA: CMV DNA by Hybrid Capture®

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ON OCTOBER 30, 2000, PAML will begin offering the *Digene Hybrid Capture Assay* for the detection of CMV DNA in peripheral white blood cells. **This will replace the CMV antigenemia assay.**

Cytomegalovirus (CMV) is a member of the herpesvirus family. It is closely related to herpes simplex virus, varicella zoster virus and Epstein-Barr virus. Like all members of this family, CMV establishes latency in the host following primary infection. The virus may become reactivated and cause disease at a later time.

CMV infections are very common. In healthy individuals, primary CMV infection is mild or asymptomatic. However, in immunocompromised patients, CMV infection, whether primary or recurrent, can cause serious disease. In order to contribute to the clinical management of the immunocompromised patient, CMV testing must be rapid and detect the presence of active disease, not just latent infection.

Several laboratory procedures are available to detect CMV. The presence of IgG and IgM antibodies to CMV provides evidence of past and/or current infection but is not a reliable indicator of CMV disease. Viral culture, even centrifuged-enhanced (i.e., shell vial), has limited clinical value because it has a low sensitivity. As a result, the CMV antigenemia test has replaced culture in most transplant centers. Currently it is being succeeded by new molecular assays that detect CMV DNA or mRNA in white blood cells from anticoagulated peripheral blood. These new tests are rapid, specific, and sensitive and appear to be good predictors of CMV disease in the immunocompromised patient.

The Digene Hybrid Capture CMV test is a molecular assay that detects the presence of CMV DNA in white blood cells from blood collected in EDTA. It is more sensitive than CMV culture and has a sensitivity and specificity comparable to the CMV antigenemia assay for the detection of CMV viremia. Handling and shipping protocols are less stringent than those for the CMV antigenemia assay, permitting greater flexibility in specimen collection and processing.

Please note that culture for CMV is not included as part of the CMV DNA protocol. If CMV culture is needed, it must be ordered as a separate test, and a second specimen must be collected. An additional fee will be charged.

References

Mazzulli, T., et.al. 1999. Multicenter comparison of the Digene Hybrid Capture CMV DNA Assay (Version 2.0), the pp65 antigenemia assay, and cell culture for detection of cytomegalovirus viremia. *J Clin Microbiol* 37(4): 958-963.

Caissie, G., et.al. 2000. Comparison of Organon Teknika NucliSens CMV pp67 mRNA, Digene CMV Hybrid Capture System and Roche Amplicor Monitor Assay for the diagnosis and monitoring of CMV infections in bone marrow transplant recipients. PASCV 2000 Symposium, Paper T15.

Highlights

- ▶ **The Hybrid Capture System is a molecular assay for the detection of CMV DNA in peripheral white blood cells.**
- ▶ **This test replaces the CMV antigenemia assay.**
- ▶ **The test assists in the diagnosis and/or monitoring of CMV infection in immuno-compromised patients.**
- ▶ **The method is more sensitive than CMV culture and is comparable to the CMV antigenemia for the detection of CMV viremia.**
- ▶ **EDTA blood is stable for 48 hours.**
- ▶ **The test is FDA-approved for diagnostic use.**

**For more information, please
contact Virology at
1-800-541-7891**

Test Information

DESCRIPTION **CMV DNA IN WHITE BLOOD CELLS**

METHOD Digene Hybrid Capture

ORDER CODE CMVDNA

CPT CODE 87496

SPECIMEN 7 mL EDTA whole blood (lavender-top tubes). Store and transport at room temperature up to 24 hours after collection, or refrigerate up to 48 hours after collection. Total storage time is 48 hours from collection. This is a rapid and sensitive molecular test to detect CMV DNA in human peripheral leukocytes. This test is indicated for use as an aid in diagnosing CMV infection in solid organ transplant, bone marrow transplant, HIV-positive/AIDS, and other immunocompromised patients.

COMMENTS *Minimum amount:* 4 mL whole blood

Unacceptable conditions: Specimens older than 48 hours, collected in other than EDTA tubes, heparinized, frozen, or clotted specimens, or less than 4 mL whole blood.

Stability: 24 hrs at room temperature, 48 hours refrigerated.

SCHEDULE Monday, Wednesday, Friday

TURNAROUND 48 hours

RANGES CMV DNA by Hybrid Capture

Not detected.

DESCRIPTION **VIRAL CULTURE – BUFFY COAT**

METHOD Isolation in tissue culture

ORDER CODE BUFFY

CPT CODE 87015, 87252, 87206×2

SPECIMEN 15 mL freshly collected sodium heparinized (green-top tubes) or EDTA anticoagulated whole blood (lavender-top tubes). Maintain at room temperature. Maximum stability 24 hours. **TRANSPORT AT ROOM TEMPERATURE.**

COMMENTS *Minimum amount:* 3 mL

SCHEDULE Daily

TURNAROUND 72 hours for CMV shell vial, 10 days for preliminary culture, 14 days for final culture.

RANGES Culture, Buffy Coat
Status

CMV Diagnostic Antibody Assays

ASSAY	SPECIMEN	CLINICAL UTILITY AND DIAGNOSTIC SIGNIFICANCE
CMV IgG Antibody PAML CODES: CMV.IGG / CMVG	Serum	Indication: To determine past exposure status. Diagnose primary infection. Positive: Indicates CMV infection in the past. Paired sample seroconversion supports diagnosis of primary infection. Negative: Indicates absence of previous CMV infection. Caveat: A negative result does not rule out recent infection with CMV.
CMV IgM Antibody PAML CODES: CMV.IGM / CMVM	Serum	Indication: To determine CMV infection status. Diagnose primary infection. Positive: Indicates current primary CMV infection or possible reactivation of latent infection. Negative: Indicates absence of acute infection. Caveat: May remain positive for 8-9 months. Immunocompromised patients may fail to develop antibody. Of questionable value in the immunocompromised population.

CMV Diagnostic Immunofluorescence Assay

ASSAY	SPECIMEN	CLINICAL UTILITY AND DIAGNOSTIC SIGNIFICANCE
CMV Antigenemia	Whole blood in heparin processed within 4 hours of collection	Indication: To diagnose & monitor CMV disease in immunocompromised patients. Sensitivity is 50%-83%, and specificity is 71%-80% as a marker of future CMV disease. Positive: Indicates the presence of CMV viremia. May indicate impending CMV episode in the absence of current disease. Negative: CMV viremia not detected. Caveat: Must be interpreted in conjunction with patient signs and symptoms to determine association with disease.

CMV Diagnostic Culture Assays

ASSAY	SPECIMEN	CLINICAL UTILITY AND DIAGNOSTIC SIGNIFICANCE
Centrifuge-enhanced (shell vial) CMV Culture PAML CODES: CMV.CULT / CMVCUL	BAL Bronch Gastric biopsy	Indication: To detect the presence of CMV infection. Positive: Indicates the presence of CMV infection but not necessarily clinical disease. Must be interpreted in conjunction with patient signs and symptoms to determine association with disease. Negative: Does not rule out CMV disease due to the low sensitivity of this test. Caveat: Of questionable value in the immunocompromised population.
Centrifuge-enhanced (shell vial) CMV Blood Culture PAML CODE: BUFFY	Whole blood in heparin or EDTA	Indication: To diagnose and monitor CMV disease in immunocompromised patients. Sensitivity is 8%-63%, and specificity is 86%-88% as a marker of future CMV disease. Positive: Indicates the presence of CMV viremia but not necessarily clinical disease. May indicate impending CMV episode in the absence of current disease. Negative: Does not rule out CMV disease due to the low sensitivity of this test. Caveat: Must be interpreted in conjunction with patient signs and symptoms to determine association with disease. The method has a low sensitivity.

CMV Diagnostic Molecular Assays

ASSAY	SPECIMEN	CLINICAL UTILITY AND DIAGNOSTIC SIGNIFICANCE
CMV DNA by Hybrid Capture PAML CODE: CMVDNA	Whole blood in EDTA Refrigerate up to 48 hours.	Indication: To diagnose and monitor CMV disease in immunocompromised patients. Positive: Indicates the presence of CMV DNA. May indicate impending CMV episode in the absence of current disease. Negative: CMV DNA not detected. Caveat: Must be interpreted in conjunction with patient signs and symptoms to determine association with disease.
CMV DNA by PCR Amplification PAML CODE: CMVPCR	Serum/plasma Peripheral blood Mononuclear cells	Indication: To diagnose and monitor CMV disease in immunocompromised patients. Sensitivity is 50%-100% and specificity is 45%-63% for serum/plasma. Sensitivity is 20%-100% and specificity is 35%-91% for peripheral blood mononuclear cells. Sensitivity and specificity refer to the assay as a predictor of future CMV disease. Indication: To diagnose congenital infection. Positive: Indicates the presence of CMV DNA. May indicate impending CMV episode in the absence of current disease. Negative: CMV DNA not detected. Caveat: It is unresolved whether PCR can distinguish between active disease and asymptomatic infection or latency.
CMV mRNA by Nucleic Acid Sequence-Based Amplification (NASBA)	Whole blood in heparin or EDTA	Indication: To diagnose and monitor CMV disease in immunocompromised patients. Positive: Indicates the presence of CMV mRNA. May indicate impending CMV episode in the absence of current disease. Negative: CMV mRNA not detected. Caveat: Must be interpreted in conjunction with patient signs and symptoms to determine association with disease.

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