Overview

Useful For
Aiding in the diagnosis of acute or recent infection with *Toxoplasma gondii*, cytomegalovirus, or herpes simplex virus

Highlights
This panel may be used as a screening assay for detection of acute infection with *Toxoplasma gondii*, cytomegalovirus, or herpes simplex virus. Results should be interpreted alongside clinical presentation, exposure history, and other laboratory findings (eg, PCR).

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>TXM</td>
<td>Toxoplasma Ab, IgM, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CMVM</td>
<td>Cytomegalovirus Ab, IgM, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>HSMR</td>
<td>HSV Ab, IgM, S by IFA</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Method Name
TXM, CMVM: Multiplex Flow Immunoassay (MFI)

HSMR: Immunofluorescence Assay (IFA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Aliquot tube

Specimen Volume: 2 mL

Forms
If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Specimen Minimum Volume
1.5 mL
Test Definition: TCHM
Torch Profile IgM, S

Reject Due To

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
</tr>
<tr>
<td>Other</td>
<td>Heat-inactivated specimen</td>
</tr>
</tbody>
</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>14 days</td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Toxoplasma gondii:

Toxoplasma gondii is an obligate intracellular protozoan parasite that is capable of infecting a variety of intermediate hosts including humans. Infected definitive hosts (cats) shed oocysts in feces that rapidly mature in the soil and become infectious. Toxoplasmosis is acquired by humans through ingestion of food or water contaminated with cat feces or through eating undercooked meat containing viable oocysts. Vertical transmission of the parasite through the placenta can also occur, leading to congenital toxoplasmosis. Following primary infection Toxoplasma gondii can remain latent for the life of the host; the risk for reactivation is highest among immunosuppressed individuals.

Seroprevalence studies performed in the United States indicate that approximately 6.7% of individuals between the ages of 12 and 49 have antibodies to Toxoplasma gondii. Infection of immunocompetent adults is typically asymptomatic. In symptomatic cases, patients most commonly present with lymphadenopathy and other nonspecific constitutional symptoms, making definitive diagnosis difficult to determine.

Severe-to-fatal infections can occur among patients with AIDS or individuals who are otherwise immunosuppressed. These infections are thought to be caused by reactivation of latent infections and commonly involved the central nervous system.

Transplacental transmission of the parasites resulting in congenital toxoplasmosis can occur during the acute phase of acquired maternal infection. The risk of fetal infection is a function of the time at which acute maternal infection occurs during gestation. The incidence of congenital toxoplasmosis increases as pregnancy progresses; conversely, the severity of congenital toxoplasmosis is greatest when maternal infection is acquired early during pregnancy. A majority of infants infected in utero are asymptomatic at birth, particularly if maternal infection occurs during the third trimester, with sequelae appearing later in life. Congenital toxoplasmosis results in severe generalized or neurologic disease in about 20% to 30% of the infants infected in utero; approximately 10% exhibit ocular involvement only and the remainder are asymptomatic at birth. Subclinical infection may result in premature delivery and subsequent neurologic, intellectual, and audiologic defects.

Cytomegalovirus (CMV):

CMV is a member of the Herpesviridae family of viruses and usually causes asymptomatic infection after which it
remains latent in patients, primarily within bone marrow derived cells. Primary CMV infection in immunocompetent individuals may also manifest as a mononucleosis-type syndrome, similar to primary Epstein-Barr virus infection, with fever, malaise, and lymphadenopathy.

CMV is a significant cause of morbidity and mortality among bone marrow or solid organ transplant recipients, individuals with AIDS, and other immunosuppressed patients due to virus reactivation or from a newly acquired infection. Infection in these patient populations can affect almost any organ and lead to multiorgan failure. CMV is also responsible for congenital disease among newborns and is one of the ToRCH infections (toxoplasmosis, other infections including syphilis, rubella, CMV, and herpes simplex virus: HSV).

CMV seroprevalence increases with age. In the United States, the prevalence of CMV-specific antibodies increases from approximately 36% to over 91% in adolescents between the ages of 6 through 11 and adults over 80 years old, respectively.

Herpes Simplex Virus (HSV):

HSV types 1 and 2 are members of the Herpesviridae family of viruses and produce infections that may range from mild stomatitis to disseminated and fatal disease. Clinical conditions associated with HSV infection include gingivostomatitis, keratitis, encephalitis, vesicular skin eruptions, aseptic meningitis, neonatal herpes, genital tract infections, and disseminated primary infection.

Infections with HSV types 1 and 2 can differ significantly in their clinical manifestations and severity. HSV type 2 primarily causes urogenital infections and is found almost exclusively in adults. HSV type 1 is closely associated with orolabial infection, although genital infection with this virus can be common in certain populations.

The diagnosis of HSV infections are routinely made based on clinical findings and supported by laboratory testing using PCR or viral culture. However, in instances of subclinical or unrecognized HSV infection, serologic testing for IgG-class antibodies to type-specific HSV glycoprotein G (gG) may be useful. There are several circumstances in which it may be important to distinguish between infection caused by HSV types 1 and 2. For example, the risk for reactivation is highest for HSV type 2 and the method of antiviral therapy may differ depending on the specific type of HSV-causing disease. In addition, the results of HSV type-specific IgG testing is sometimes used during pregnancy to identify risks of congenital HSV disease and allow for focused counseling prior to delivery.

**Reference Values**

**TOXOPLASMA ANTIBODY, IgM**

Negative

**CYTOMEGALOVIRUS, IgM**

Negative

**HERPES SIMPLEX VIRUS, IgM**

Negative

Reference values apply to all ages.

**Interpretation**

*Toxoplasma gondii:*

Diagnosis of acute central nervous system, intrauterine, or congenital toxoplasmosis is difficult by routine serological
methods. Active toxoplasmosis is suggested by the presence of IgM antibodies, but elevated anti-IgM titers are often absent in immunocompromised patients. In addition, elevated IgM can persist from an acute infection that may have occurred as long ago as 1 year.

A suspected diagnosis of acute toxoplasmosis should be confirmed by further testing at a toxoplasmosis reference laboratory or by detection of *Toxoplasma gondii* DNA by PCR analysis of cerebrospinal fluid or amniotic fluid specimens (PTOX / Toxoplasma gondii, Molecular Detection, PCR).

For confirmation of toxoplasmosis, the FDA issued a Public Health Advisory (7/25/1997) that recommends that sera found to be positive for *Toxoplasma gondii* IgM antibodies should be sent to a Toxoplasma reference laboratory.

Specimens interpreted as equivocal may contain very low levels of IgM. A second specimen should be drawn and tested.

**Cytomegalovirus (CMV):**

A negative CMV IgM result suggests that the patient is not experiencing an acute or active infection. However, a negative result does not rule out primary CMV infection.

It has been reported that CMV-specific IgM antibodies were not detectable in 10% to 30% of cord blood sera from infants demonstrating infection in the first week of life. In addition, up to 23% (3/13) of pregnant women with primary CMV infection did not demonstrate detectable CMV IgM responses within 8 weeks postinfection. In cases of primary infection, where the time of seroconversion is not well defined, as high as 28% (10/36) of pregnant women did not demonstrate CMV IgM antibody.

Positive CMV IgM results indicate a recent infection (primary, reactivation, or reinfection). IgM antibody responses in secondary (reactivation) CMV infections have been demonstrated in some CMV mononucleosis patients, in a few pregnant women, and in renal and cardiac transplant patients. Levels of antibody may be lower in transplant patients with secondary rather than primary infections.

Equivocal CMV IgM or IgG results may occur during acute infection or may be due to nonspecific binding reactions. Submit an additional sample for testing if clinically indicated.

**Herpes Simplex Virus (HSV):**

The presence of IgM-class antibodies indicates recent infection.

A negative result does not exclude the possibility of active disease. If lesions are present, a dermal swab and submission for HSV PCR is recommended.

**Cautions**

Results must be used in conjunction with clinical symptoms and patient history.

Positive test results may not be valid in persons who have received blood transfusions or other blood products in the past several months.

**Toxoplasma:**

Negative results do not preclude recent primary *Toxoplasma gondii* infection. A negative result could indicate either no previous exposure or also could be seen in cases of remote exposure with subsequent loss of detectable antibody. A second specimen drawn at a later point in time may be needed to rule out a recent infection.
Positive serologic results alone are not diagnostic of *Toxoplasma gondii* infection. For example, infections with Epstein-Barr virus (EBV) have been suspected to elicit antigen-specific IgM responses (eg, false-positive IgM *Toxoplasma* reactions) in individuals previously sensitized to a variety of non-EBV infectious agents.

Since persisting IgM levels may be detected long after the onset of acquired infection, the use of a single serological test result must be used with caution in those cases when it is critical to establish the time of infection. This applies to the diagnosis of acute *Toxoplasma gondii* infection acquired during pregnancy. Determination of the date of infection based solely on the results of detectable IgM antibody to *Toxoplasma gondii* is not recommended. That determination should include clinical history and previous serology, since low levels of IgM antibody may persist for a year or more. The use of a test to determine a rise in IgG antibody to *Toxoplasma gondii* (TOXGP / *Toxoplasma gondii* Antibody, IgG, Serum or TXMGP / *Toxoplasma gondii* Antibody, IgM and IgG [Separate Determinations], Serum) may provide additional information as to the date of infection. Therefore, the FDA has instructed commercial suppliers of *Toxoplasma* IgM kits to recommend *Toxoplasma* IgG testing also be performed.

Cytomegalovirus (CMV):

Sera drawn very early during the acute stage of infection may have undetectable levels of CMV IgM. Immunocompromised patients may have impaired immune responses, and nonreactive IgM results may be due to delayed seroconversion and do not rule-out current infection.

CMV IgM results should not be used alone to diagnose CMV infection. Results should be considered in conjunction with clinical presentation, patient history, and other laboratory findings. In cases of suspected disease, submit a second specimen for testing in 10 to 14 days.

The performance characteristics of these assays have not been evaluated in immunosuppressed or organ transplant recipients and have not been established for cord blood or for testing of neonates. These assays should not be used for screening blood or plasma donors.

Immune complexes or other immunoglobulin aggregates present in patient specimens may cause increased nonspecific binding and produce false-positive results.

Potential cross-reactivity for CMV IgM may occur with specimens positive for EBV viral capsid antigen IgM and parvovirus B19 IgM.

Herpes Simplex Virus (HSV):

Individuals infected with HSV may not exhibit detectable levels of IgM antibody in the early stages of infection. This assay does not discriminate between antibodies to HSV-1 and HSV-2.

**Clinical Reference**


5. Soderberg-Naucler C, Fish KN, Nelson JA: Reactivation of latent human cytomegalovirus by allogeneic stimulation
of blood cells from healthy donors. Cell 1997;91:119-126


Performance

Method Description

Toxoplasma:

The BioPlex 2200 Toxoplasma gondii IgM assay uses multiplex flow immunoassay technology. Briefly, Toxoplasma antigen coated fluorescent beads are mixed with an aliquot of patient sample and sample diluent and incubated at 37 degrees C. During this time IgM anti-Toxoplasma antibodies in the specimen will bind to the Toxoplasma antigen on the beads. After a wash cycle, a fluorescently labeled antihuman-IgM antibody conjugate is added to the mixture and incubated at 37 degrees C. Following a wash step to remove unbound conjugate, the bead mixture is passed through a detector that identifies the bead based on dye fluorescence and determines the amount of antibody captured by the antigen based on fluorescence of the antihuman-IgM conjugate. Raw data is calculated in relative fluorescence intensity and is converted to an antibody index for interpretation.

- Antibody index (AI) values of 0.8 and below are considered negative.

- AI values of 0.9 and 1.0 are equivocal. AI values of 1.1 and above are considered positive.

Three additional dyed beads, an internal standard bead, a serum verification bead, and a reagent black bead are present in each reaction mixture to verify detector response, the addition of serum to the reaction vessel and the absence of significant nonspecific binding in serum, respectively. (Package insert: BioPlex 2200 System, ToRC IgM, Bio-Rad Laboratories, Clinical Diagnostics Group, Hercules, CA 8/2017)

Cytomegalovirus (CMV):
The BioPlex 2200 CMV IgM assay uses multiplex flow immunoassay technology. Briefly, CMV antigen-coated fluorescent beads are mixed with an aliquot of patient sample and sample diluent and incubated at 37 degrees C. During this time, IgM anti-CMV antibodies in the specimen will bind to the CMV antigen on the beads. After a wash cycle, a fluorescently labeled antihuman-IgM antibody conjugate is added to the mixture and incubated at 37 degrees C. Following a wash step to remove unbound conjugate, the bead mixture is passed through a detector that identifies the bead based on dye fluorescence and determines the amount of antibody captured by the antigen based on fluorescence of the antihuman-IgG conjugate. Raw data is calculated in relative fluorescence intensity and is converted to an antibody index (AI) for interpretation.

- Antibody index (AI) values of 0.8 and below are considered negative.
- AI values of 0.9 and 1.0 are equivocal. AI values of 1.1 and above are considered positive.

Three additional dyed beads, an internal standard bead, a serum verification bead, and a reagent black bead are present in each reaction mixture to verify detector response, the addition of serum to the reaction vessel, and the absence of significant nonspecific binding in serum, respectively. (Package insert: BioPlex 2200 System, ToRC IgM, Bio-Rad Laboratories, Clinical Diagnostics Group, Hercules, CA 8/2017)

Herpes Simplex Virus (HSV):

The indirect immunofluorescence test is used for the detection of IgM-class antibodies to HSV. After removal of IgG by specific immunoglobulin antibody, the serum is reacted with HSV-infected substrate cells on a slide. Specific fluorescence indicating the presence of IgM antibodies to HSV in the specimen can be detected by an immunofluorescence microscope. (Jerome KR, Morrow RA: Herpes simplex viruses and herpes B virus. In Manual of Clinical Microbiology. 11th edition. Edited by JH Jorgensen, MA Pfaller, KC Carroll, et al. Washington, DC, ASM Press, 2015, pp 1687-1703)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Saturday; 9 a.m.

**Analytic Time**

Same day/1 day

**Maximum Laboratory Time**

3 days

**Specimen Retention Time**

14 days

**Performing Laboratory Location**

Rochester

**Fees and Codes**

**Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).
Test Definition: TCHM
Torch Profile IgM, S

Test Classification
This test has been cleared or approved by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
86645-CMV IgM
86694-HSV IgM
86778-Toxoplasma IgM

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCHM</td>
<td>Torch Profile IgM, S</td>
<td>In Process</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>26589</td>
<td>HSV Ab, IgM, S by IFA</td>
<td>44507-2</td>
</tr>
<tr>
<td>CMVM</td>
<td>Cytomegalovirus Ab, IgM, S</td>
<td>24119-0</td>
</tr>
<tr>
<td>TXM</td>
<td>Toxoplasma Ab, IgM, S</td>
<td>40678-5</td>
</tr>
</tbody>
</table>