Test Definition: TRCHG

ToRCH Profile IgG, Serum

Overview

Useful For

Determining immune status of individuals to the rubella virus following vaccination or prior exposure

Indicating past or recent infection with *Toxoplasma gondii*, cytomegalovirus, or herpes simplex virus (HSV)

Distinguishing between infection caused by HSV types 1 and 2, especially in patients with subclinical or unrecognized HSV infection

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
TOXGP	Toxoplasma Ab, IgG, S	Yes	Yes
RBPG	Rubella Ab, IgG, S	Yes	Yes
CMVG	Cytomegalovirus Ab, IgG, S	Yes	Yes
HS1G	HSV Type 1 Ab, IgG, S	No	Yes
HS2G	HSV Type 2 Ab, IgG, S	No	Yes

Method Name

Multiplex Flow Immunoassay (MFI)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

To evaluate recent or acute infection with *Toxoplasma gondii,* order TXM / *Toxoplasma gondii* Antibody, IgM, Serum.

For patients presenting with presumed acute infection with herpes simplex virus, order HSVPB / Herpes Simplex Virus, Molecular Detection, PCR, Blood.

Immunoglobulin G antibodies in patients younger than 6 months are typically the result of passive transfer from the mother. To assess possible infection in patients younger than 6 months, consider ordering IgM testing.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send Infectious Disease Serology Test Request (T916) with the specimen.

Specimen Minimum Volume

1.2 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Toxoplasma gondii:
Toxoplasma gondii is an obligate intracellular protozoan parasite 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.(1) 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, *T gondii* can remain latent for the life of the host; the risk for reactivation is highest among individuals who are immunosuppressed.

Seroprevalence studies performed in the United States indicate approximately 6.7% of individuals between the ages of 12 and 49 have antibodies to *T gondii*.(2)

Infection of immunocompetent adults is typically asymptomatic. In symptomatic cases, patients most frequently 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 that are otherwise immunosuppressed. These infections are thought to be caused by reactivation of latent infections and commonly involve the central nervous system.(3)

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.(4) 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.

Rubella:
Rubella (German or 3-day measles) is a member of the Togavirus family, and humans remain the only natural host for this virus. Transmission is typically through inhalation of infectious aerosolized respiratory droplets, and the incubation period following exposure can range from 12 to 23 days.(5) Infection is generally mild, self-limited, and characterized by a maculopapular rash beginning on the face spreading to the trunk and extremities, fever, malaise, and lymphadenopathy.(6)

Primary, in utero rubella infections can lead to severe sequelae for the fetus, particularly if infection occurs within the first 4 months of gestation. Congenital rubella syndrome is often associated with hearing loss and cardiovascular and ocular defects.(7)

The United States 2-dose measles, mumps, rubella (MMR) vaccination program, which calls for vaccination of all children, leads to seroconversion in 95% of children following the first dose.(5) A total of 4 cases of rubella were reported to the Centers for Disease Control and Prevention (CDC) in 2011 without any cases of congenital rubella syndrome.(8) Due to the success of the national vaccination program, rubella is no longer considered endemic in the United States.(9) However, immunity may wane with age as approximately 80% to 90% of adults will show serologic evidence of immunity to rubella.

Cytomegalovirus:
Cytomegalovirus (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.(10) 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.

Cytomegalovirus 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.(11,12) Infection in these patient populations can affect almost any organ and lead to multi-organ 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]).

Cytomegalovirus seroprevalence increases with age. In the United States, the prevalence of CMV-specific antibodies increases from approximately 36% to over 91% in children between the ages of 6 and 11 years and adults over 80 years old, respectively.(13)

Herpes Simplex Virus Types 1 and 2:
Herpes simplex virus types 1 and 2 are members of the Herpesviridae family and produce infections that 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 is routinely made based on clinical findings and supported by laboratory testing using a polymerase chain reaction assay 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.(14) For example, the risk for reactivation is highest for HSV type 2, and the method of antiviral therapy may be different 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.(15,16)

Reference Values

Toxoplasma ANTIBODY, IgG
Negative

Toxoplasma IgG
< or =9 IU/mL (Negative)
10-11 IU/mL (Equivocal)
> or =12 IU/mL (Positive)

RUBELLA ANTIBODY, IgG
Vaccinated: Positive (> or =1.0 AI)
Unvaccinated: Negative (< or =0.7 AI)

CYTOMEGALOVIRUS
Negative

HERPES SIMPLEX VIRUS (HSV), TYPE 1 AND TYPE 2 ANTIBODIES, IgG
Herpes Simplex Virus (HSV) Type 1, IgG
Negative

Herpes Simplex Virus (HSV) Type 2, IgG
Negative

Interpretation

Toxoplasma gondii:
A positive *Toxoplasma* IgG result is indicative of current or past infection with *T gondii*. A single positive *Toxoplasma* IgG result should not be used to diagnose recent infection.

Equivocal *Toxoplasma* IgG results may be due to very low levels of circulating IgG during the acute stage of infection. A second specimen should be submitted for testing if clinically indicated.

Individuals with negative *Toxoplasma* IgG results are presumed to not have had previous exposure to *T gondii*. However, negative results may be seen in cases of remote exposure with subsequent loss of detectable antibody. Seroconversion from negative to positive IgG is indicative of *T gondii* infection subsequent to the first negative specimen.

Rubella:
Positive: The presence of detectable IgG-class antibodies to rubella indicates prior exposure through infection or immunization. Individuals testing positive for IgG-class antibodies to rubella are considered immune.

Equivocal: Submit an additional specimen for testing in 10 to 14 days to demonstrate IgG seroconversion if recently vaccinated or if otherwise clinically indicated.

Negative: The absence of detectable IgG-class antibodies to rubella suggests no prior exposure to this virus or the lack of a specific immune response to immunization.

Cytomegalovirus:
Positive cytomegalovirus (CMV) IgG results indicate past or recent CMV infection. These individuals may transmit CMV to susceptible individuals through blood and tissue products.

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

Individuals with negative CMV IgG results are presumed to not have had prior exposure or infection with CMV and are therefore considered susceptible to primary infection.

Herpes Simplex Virus:
The presence of IgG-class antibodies to herpes simplex virus (HSV) types 1 or 2 indicates previous exposure and does not necessarily indicate that HSV is the causative agent of an acute illness.

Cautions

Toxoplasma gondii:
Sera collected very early during the acute stage of infection may have *Toxoplasma* IgG levels less than 9 IU/mL.

The *Toxoplasma* IgG assay should not be used alone to diagnose recent *T gondii* infection. Results should be considered in conjunction with clinical presentation, patient history, and other laboratory findings.

The performance characteristics of this assay have not been evaluated in immunocompromised individuals and have not been established for cord blood or for testing of neonates.

Rubella:
Specimens collected early during the acute phase of infection or shortly (1-2 weeks) following vaccination may be negative for IgG class antibodies.

Cytomegalovirus:
Sera collected very early during the acute stage of infection may have undetectable levels of cytomegalovirus (CMV) IgG.

The CMV IgG assay 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 diseases, submit a second specimen for testing in 10 to 14 days.

The performance characteristics of this assay have not been evaluated in immunosuppressed or organ transplant recipients and have not been established for cord blood or for testing of neonates.

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

Potential cross-reactivity for CMV with human chorionic gonadotropin, HIV IgG, multiple myeloma IgG, rheumatoid factor IgM, and *T gondii* IgG have not be ruled out.

Herpes Simplex Virus Types 1 and 2:
Detection of IgG-class antibodies to herpes simplex virus (HSV) should not be used routinely as the primary means of diagnosing HSV infection. For patients presenting with presumed acute infection with HSV, a clinical specimen (eg, oral, dermal, or genital lesion) should be sampled and submitted for detection of HSV types 1 and 2 by rapid polymerase chain reaction (PCR) (HSVPB / Herpes Simplex Virus, Molecular Detection, PCR, Blood).

Serum specimens collected too early in the course of infection may not have detectable levels of HSV IgG. In cases of suspected early disease, a repeat serum specimen should be collected 14 to 21 days later and submitted for testing.

The presence of IgG-class antibodies to either HSV type 1 or 2 does not differentiate between remote infection and acute disease.

HSV serology cannot distinguish genital from nongenital infections.

The predictive value of positive or negative results depends on the prevalence of disease and the pretest likelihood of HSV type 1 and HSV type 2. False-positive results may occur. Repeat testing, or testing by a different method, may be indicated in some settings (eg, patients with low likelihood of HSV infection).

Supportive Data

Toxoplasma gondii:
To evaluate the accuracy of the BioPlex *Toxoplasma* IgG multiplex flow immunoassay, 600 prospective serum samples submitted for routine *Toxoplasma* IgG testing by the VIDAS enzyme-linked fluorescence immunoassay (ELFA;

bioMerieux) were also analyzed in a blinded fashion by the BioPlex assay within a 24-hour period. Samples with discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. Further resolution of discrepant results was performed by sending the samples to the Palo Alto Medical Foundation for testing. The results are summarized below.

Table 1. Comparison between BioPlex and VIDAS Toxoplasma IgG Assays

		Toxoplasma IgG (VIDAS ELFA)		
BioPlex Toxoplasma IgG		Positive	Negative	Equivocal
	Positive	63	2(a)	6
	Negative	0	528	0
	Equivocal	0	0	1

(a) Both serum samples were negative by the Sabin-Feldman dye test at the Palo Alto Medical Foundation Toxoplasma laboratory.
Sensitivity: 100% (63/63); 95% CI: 93.1% to 100%
Specificity: 99.6% (528/530); 95% CI: 98.5% to 99.9%
Overall percent agreement: 98.7% (592/600); 95% CI: 97.3% to 99.4%

Rubella:
To evaluate the accuracy of the BioPlex Rubella IgG multiplex flow immunoassay (MFI), 500 prospective serum samples were analyzed in a blinded fashion by the SeraQuest Rubella IgG IEA (Quest International) and the BioPlex Rubella IgG assay. Samples with discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. Further discrepancies were evaluated by the Rubella IgG VIDAS enzyme-linked fluorescent immunoassay (ELFA; bioMerieux, Inc.). The results are summarized below.

Table 2. Comparison between BioPlex and SeraQuest Rubella IgG Assays

		SeraQuest Rubella IgG EIA		
BioPlex Rubella IgG		Positive	Negative	Equivocal
	Positive	446	0	0
	Negative	7(a)	23	4
	Equivocal	17	0	3

(a) 6/7 samples tested as equivocal by the VIDAS Rubella IgG ELFA.
Sensitivity: 94% (446/470); 95% CI: 92.5% to 96.6%
Specificity: 100% (23/23); 95% CI: 83.1% to 100%
Overall Percent Agreement: 94.4% (472/500); 95% CI: 92.0% to 96.1%

Cytomegalovirus:
To evaluate the accuracy of the BioPlex cytomegalovirus (CMV) IgG multiplex flow immunoassay, 598 prospective serum samples submitted for routine CMV IgG testing by the VIDAS ELFA (bioMerieux) were also analyzed in a blinded fashion by the BioPlex assay within a 24-hour period. Samples with discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. Further resolution of discrepant results was performed by using the Diamedix CMV IgG enzyme immunoassay. The results are summarized below.

Table 3. Comparison between BioPlex and VIDAS CMV IgG Assays

		CMV IgG (VIDAS ELFA)		
BioPlex CMV		Positive	Negative	Equivocal

IgG	Positive	336	2(a)	0
	Negative	3(b)	254	3
	Equivocal	0	0	0

(a) Both serum samples were negative by the Diamedix CMV IgG EIA

(b) All 3 serum samples were negative by the Diamedix CMV IgG EIA

Sensitivity: 99.1% (336/339); 95% CI: 97.3% to 99.8%

Specificity: 99.2% (254/256); 95% CI: 97.0% to 100%

Overall Percent Agreement: 98.7% (590/598); 95% CI: 97.3% to 99.4%

Herpes Simplex Virus Type 1:

To evaluate the accuracy of the BioPlex herpes simplex virus (HSV) assay, 505 prospective serum samples were tested by EIA (HerpeSelect, Focus Diagnostics) and the BioPlex HSV-1/2 IgG assay. Samples that had discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. Further discrepancies were evaluated by glycoprotein G (gG) type-specific Western blot (WB) at the University of Washington Virology laboratory. The results are summarized in Tables 4 and 5 below:

Table 4. Comparison between BioPlex and HerpeSelect HSV-1 Assays

		HSV-1 by HerpeSelect EIA		
BioPlex HSV-1 IgG		Positive	Negative	Equivocal
	Positive	254	5(a)	0
	Negative	2(b)	240	1
	Equivocal	0	3	0

(a) All 5 specimens were positive by WB

(b) Both samples were positive by WB

Sensitivity: 99.2% (254/256); 95% CI: 97.0% to 99.9%

Specificity: 96.8% (240/248); 95% CI: 93.7% to 98.5%

Overall Percent Agreement: 97.8% (494/505); 95% CI: 96.1% to 98.8%

Table 5. Comparison between BioPlex and HerpeSelect HSV-2 Assays

		HSV-2 by HerpeSelect EIA		
BioPlexHSV-2 IgG		Positive	Negative	Equivocal
	Positive	115	9(a)	2
	Negative	1(b)	376	0
	Equivocal	1	1	0

(a) Two of 9 samples were positive by WB; 2 of 9 samples were equivocal by WB.

(b) This sample was negative by WB

Sensitivity: 98.3% (115/117); 95% CI: 93.6% to 99.9%

Specificity: 97.4% (376/386); 95% CI: 95.2% to 98.7%

Overall Percent Agreement: 97.2% (376/386); 95% CI: 95.4% to 98.4%

Clinical Reference

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Performance

Method Description

Detection of IgG-class antibodies to *Toxoplasma gondii,* rubella, cytomegalovirus, and herpes simplex virus types 1 and 2 is performed on the BioPlex 2200 system, which uses multiplex flow immunoassay technology. Five different populations of fluorescently-dyed beads are each coated with antigens unique to each infectious organism. Patient sample is combined with sample diluent and the 5-bead set and then incubated at 37 degrees C. During this time, IgG antibodies will bind to the antigen-coated beads. After a wash cycle, a fluorescently-labeled antihuman IgG 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 are calculated in relative fluorescence intensity and is converted to an antibody index for interpretation.

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 inserts: BioPlex 2200 System, ToRC IgG. Bio-Rad Laboratories; 03/2012; BioPlex 2200 System, MMRV IgG. Bio-Rad Laboratories; 02/2019; BioPlex 2200 System, HSV1 and 2 IgG. Bio-Rad Laboratories; 04/2019)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
Same day/1 to 3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & 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 account representative. For assistance, contact Customer Service.

Test Classification
This test has been cleared, approved, or is exempt by the US 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
86644-CMV
86695-Herpes simplex, type 1
86696-Herpes simplex, type 2
86762-Rubella
86777-*Toxoplasma*

LOINC® Information

Test Definition: TRCHG

ToRCH Profile IgG, Serum

Test ID	Test Order Name	Order LOINC® Value
TRCHG	Torch Profile IgG, S	102088-2

Result ID	Test Result Name	Result LOINC® Value
HS1G	HSV Type 1 Ab, IgG, S	51916-5
HS2G	HSV Type 2 Ab, IgG, S	43180-9
RBG	Rubella Ab, IgG, S	40667-8
DEXG2	Rubella IgG Antibody Index	5334-8
CMVG	Cytomegalovirus Ab, IgG, S	13949-3
TOXG	Toxoplasma Ab, IgG, S	40677-7
DEXG6	Toxoplasma IgG Value	8039-0