MAYO CLINIC LABORATORIES

Test Definition: MMRV

Measles, Mumps, Rubella, and Varicella (MMRV) Immune Status Profile, Serum

Overview

Useful For

Determining immune status of individuals to measles, mumps, rubella, and varicella-zoster viruses (VZV)

Documentation of previous infection with measles, mumps, rubella, or VZV in an individual without a previous record of immunization to these viruses

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
ROPG	Measles (Rubeola) Ab, IgG, S	Yes	Yes
MPPG	Mumps Ab, IgG, S	Yes	Yes
RBPG	Rubella Ab, IgG, S	Yes	Yes
VZPG	Varicella-Zoster Ab, IgG, S	Yes	Yes

Method Name

Multiplex Flow Immunoassay (MFI)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Instructions: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-Kidney Transplant Test Request
-Infectious Disease Serology Test Request (T916)

Specimen Minimum Volume

0.4 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

The measles virus is a member of the Paramyxoviridae family of viruses, which includes parainfluenza virus serotypes 1-4, mumps, respiratory syncytial virus (RSV), and metapneumovirus. The measles virus is among the most highly contagious infectious diseases among unvaccinated individuals and is transmitted through direct contact with aerosolized droplets or other respiratory secretions from infected individuals. Measles has an incubation period of approximately 8 to 12 days, which is followed by a prodromal phase of high fever, cough, coryza, conjunctivitis, and malaise. Koplik spots may also be apparent on the buccal mucosa and can last for 12 to 72 hours.(1) Following this phase, a maculopapular, erythematous rash develops beginning behind the ears and on the forehead, and spreads centrifugally to involve the trunk and extremities.

Immunocompromised individuals, pregnant women, and those with nutritional deficiencies are particularly at risk for serious complications following measles infection, which include pneumonia and central nervous system (CNS) involvement.(1)

Following implementation of the national measles vaccination program in 1963, the incidence of measles infection has fallen to fewer than 0.5 cases per 1,000,000 individuals, and the virus is no longer considered endemic in the United States. Measles outbreaks continue to occur in the United States due to exposure of nonimmune individuals or those with waning immunity to infected travelers. The measles outbreak in 2011 throughout Western Europe emphasizes the persistence of the virus in the worldwide population and the continued need for national vaccination programs.(2)

The diagnosis of measles infection is often based on clinical presentation alone. Screening for IgG-class antibodies to measles virus will aid in identifying nonimmune individuals.

Mumps:
The mumps virus is a member of the Paramyxoviridae family of viruses, which includes parainfluenza virus serotypes 1-4, measles, RSV, and metapneumovirus. Mumps is highly infectious among unvaccinated individuals and is typically transmitted through inhalation of infected respiratory droplets or secretions. Following an approximately 2-week incubation period, symptom onset is typically acute with a prodrome of low-grade fever, headache, and malaise.(3,4) Painful enlargement of the salivary glands, the hallmark of mumps, occurs in approximately 60% to 70% of infections and in 95% of patients with symptoms. Testicular pain (orchitis) occurs in approximately 15% to 30% of postpubertal men and abdominal pain (oophoritis) is found in 5% of postpubertal women.(3) Other complications include mumps-associated pancreatitis (<5% of cases) and CNS disease (meningitis <10% and encephalitis <1%).

Widespread routine immunization of infants with attenuated mumps virus has dramatically decreased the number of reported mumps cases in the United States. However, outbreaks continue to occur, indicating persistence of the virus in the general population.

Laboratory diagnosis of mumps is typically accomplished by detection of IgM- and IgG-class antibodies to the mumps virus. However, due to the widespread mumps vaccination program, in clinically suspected cases of acute mumps infection, serologic testing should be supplemented with virus isolation in culture or detection of viral nucleic acid by polymerase chain reaction in throat, saliva, or urine specimens.

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 and self-limited and is characterized by a maculopapular rash beginning on the face and spreading to the trunk and extremities, as well as 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, and 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 of Disease Control and Prevention 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) Immunity may, however, wane with age as approximately 80% to 90% of adults will show serologic evidence of immunity to rubella.

Varicella-Zoster Virus:
Varicella-Zoster virus (VZV), a herpes virus, causes 2 distinct exanthematous (rash-associated) diseases: chickenpox (varicella) and shingles (herpes zoster). Chickenpox is a highly contagious, though typically benign, disease, usually contracted during childhood. Chickenpox is characterized by a dermal vesiculopustular rash that develops in successive

crops approximately 10 to 21 days following exposure.(10) Although primary infection with VZV results in immunity and protection from subsequent infection, VZV remains latent within sensory dorsal root ganglia and upon reactivation, manifests as herpes zoster or shingles. During reactivation, the virus migrates along neural pathways to the skin, producing a unilateral rash, usually limited to a single dermatome. Shingles is an extremely painful condition typically occurring in older, nonimmune adults, those with waning immunity to VZV, and in patients with impaired cellular immunity.

Individuals at risk for severe complications following primary VZV infection include pregnant women, in whom the virus may spread through the placenta to the fetus, causing congenital disease in the infant. Additionally, immunosuppressed patients are at risk for developing severe VZV-related complications, which include cutaneous disseminated disease and visceral organ involvement.

Serologic screening for IgG-class antibodies to VZV aids in identifying nonimmune individuals.

Reference Values

MEASLES, MUMPS and VARICELLA:
Vaccinated: Positive (> or =1.1 AI)
Unvaccinated: Negative (< or =0.8 AI)
Reference values apply to all ages

RUBELLA:
Vaccinated: Positive (> or =1.0 AI)
Unvaccinated: Negative (< or =0.7 AI)
Reference values apply to all ages

Interpretation

The reported antibody index (AI) value is for reference only. This is a qualitative test, and the numeric value of the AI is not indicative of the amount of antibody present. AI values above the manufacturer recommended cutoff for this assay indicate that specific antibodies were detected, suggesting prior exposure or vaccination.

Positive measles, mumps, varicella-zoster viruses: AI value > or =1.1
Positive rubella: AI Value > or =1.0
-The presence of detectable IgG-class antibodies to these viruses indicates prior exposure through infection or immunization. Individuals testing positive for IgG-class antibodies to measles, mumps, rubella, or varicella-zoster viruses (VZV) are considered immune.

Equivocal measles, mumps, VZV: AI value 0.9-1.0
Equivocal rubella: AI value 0.8-0.9
-Submit an additional sample for testing in 10 to 14 days to demonstrate IgG seroconversion if recently vaccinated or if otherwise clinically indicated.

Negative measles, mumps, VZV: AI value < or =0.8
Negative rubella: AI value < or =0.7
-The absence of detectable IgG-class antibodies to measles, mumps, rubella, or VZV suggests no prior exposure to these

viruses or the lack of a specific immune response to immunization.

Cautions

Immunoglobulin G-class antibodies to measles, mumps, rubella, or varicella-zoster virus may be present in serum specimens from individuals who have received blood products within the past several months but have not been immunized or experienced past infection with this virus.

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

Supportive Data

To evaluate the accuracy of the BioPlex MMRV assay, 500 prospective serum samples submitted to the laboratory for routine measles, mumps, rubella, and varicella (MMRV) testing by enzyme immunoassay (EIA) were also analyzed by the BioPlex assay within a 24-hour period. Routine testing for measles and varicella-zoster IgG was performed by Diamedix EIA, while routine analysis of mumps and rubella IgG was completed using the SeraQuest EIA assays. Samples that had discordant results after initial testing were repeated by both assays during the same freeze/thaw cycle. Further discrepancies were evaluated by a third method. Samples showing discordant results for measles and varicella IgG were tested using SeraQuest EIAs, while discrepant samples for mumps and rubella IgG were tested by enzyme-linked fluorescent immunoassay (ELFA) (VIDAS). Results are summarized in the tables below.

Table 1. Comparison between BioPlex and Diamedix Measles Assays

		Diamedix measles IgG EIA		
BioPlex measles IgG		Positive	Negative	Equivocal
	Positive	420	1(a)	0
	Negative	10(b)	27	17
	Equivocal	14	0	11

(a) This sample tested negative by the SeraQuest Measles IgG EIA

(b) All 10 samples tested positive by the SeraQuest Measles IgG EIA

Sensitivity: 94.6% (420/444); 95% CI: 92.1% to 96.4%

Specificity: 96.4% (27/28); 95% CI: 80.8% to 100.0%

Overall percent agreement: 91.6% (458/500); 95% CI: 88.8% to 93.8%

Table 2. Comparison between BioPlex and SeraQuest Mumps IgG Assays

		SeraQuest mumps IgG EIA		
BioPlex mumps IgG		Positive	Negative	Equivocal
	Positive	412	4(a)	8
	Negative	3(b)	48	3
	Equivocal	5	6	11

(a) All 4 samples tested positive by VIDAS Mumps IgG ELFA

(b) One of 3 samples tested negative by the VIDAS Mumps IgG ELFA

Sensitivity: 98.1% (412/420); 95% CI: 96.2% to 99.1%

Specificity: 82.8% (48/58); 95% CI: 70.9% to 90.6%

Overall percent agreement: 94.2% (471/500); 95% CI: 91.8% to 96.0%

Table 3. 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%

Table 4. Comparison between BioPlex and Diamedix Varicella Zoster (VZV) IgG Assays

		Diamedix VZV IgG EIA		
BioPlex VZV IgG		Positive	Negative	Equivocal
	Positive	436	0	0
	Negative	18(a)	22	4
	Equivocal	19	0	1

(a) All 18 samples tested positive by the SeraQuest VZV IgG EIA

Sensitivity: 92.2% (436/473); 95% CI: 89.4% to 94.3%

Specificity: 100.0 (22/22); 95% CI: 82.5% to 100.0%

Overall percent agreement: 91.8% (459/500); 95% CI: 89.0% to 93.9%

Clinical Reference

1. Perry RT, Halsey NA. The clinical significance of measles-a review. J Infect Diseases. 2004;189(Supp 1):S4-S16. doi:10.1086/377712

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3. Hviid A, Rubin S, Muhlemann K. Mumps. Lancet. 2008;371(9616):932-944

4. Hodinka RL, Moshal KL. Childhood infections. In: Storch GA, ed. Essentials of Diagnostic Virology. Churchill Livingstone; 2000; 168-178

5. American Academy of Pediatrics. Rubella. In: Pickering LK, ed. Red Book. Report of the Committee on Infectious Diseases. 2012

6. Best JM. Rubella. Semin Fetal Neonatal Med. 2007;12(3):182. doi:10.1016/j.siny.2007.01.017

7. Duszak RS. Congenital rubella syndrome-major review. Optometry. 2009;80(1):36. doi:10.1016/j.optm.2008.03.006

8. Notifiable diseases and mortality tables. MMWR Morb Mortal Wkly Rep. 2012;61(34):466-479

9. National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases: Rubella (German measles, three-day measles). CDC; Updated December 31, 2020. Accessed December 16, 2024. Available at www.cdc.gov/rubella/

10. Yankowitz J, Grose C. Congenital infections. In: Storch GA, ed. Essentials of Diagnostic Virology. Churchill Livingstone; 2000; 187-201

11. Theel ES, Sorenson M, Rahman C, Granger D, Vaughn A, Breeher L. Performance characteristics of a multiplex flow immunoassay for detection of IgG-Class antibodies to measles, mumps, rubella, and Varicella-Zoster viruses in presumptively immune health care workers. J Clin Microbiol. 2020;58(4):e00136-20. doi:10.1128/JCM.00136-20

Performance

Method Description

The BioPlex 2200 MMRV IgG kit uses multiplex flow immunoassay technology, which allows for the detection and identification of many different antibodies in a single tube. Four different populations of dyed beads are coated with antigens to identify the presence of IgG-class antibodies associated with measles, mumps, rubella, and varicella-zoster. The patient sample, sample diluent, and bead set reagent are mixed together in a reaction vessel and then incubated at 37 degrees C. After a wash cycle, anti-human IgG antibody conjugated to phycoerythrin (PE) is added to the dyed beads, and this mixture is incubated at 37 degrees C. Excess conjugate is removed during a wash cycle, and the beads are resuspended in wash buffer. The bead mixture next passes through the detector, and the identity of the beads is determined by the fluorescence of the dyes. The amount of antibody captured by the antigen on the bead is determined by the fluorescence of the attached PE. Raw data is calculated in relative fluorescence intensity.

Three additional dyed beads, an internal standard bead, a serum verification bead, and a reagent blank bead are present in each reaction mixture to verify detector response, the addition of serum to the reaction vessel, and the absence of significant non-specific binding in serum.(Package insert: BioPlex 2200 System MMRV IgG. Bio-Rad Laboratories; 02/2019)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

Same day/1 day

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

86735
86762
86765
86787

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MMRV	MMRV Immune Status Profile, S	104688-7

Result ID	Test Result Name	Result LOINC® Value
VZG	Varicella-Zoster Ab, IgG, S	15410-4
DEXG4	Varicella IgG Antibody Index	5403-1
RBG	Rubella Ab, IgG, S	40667-8
DEXG2	Rubella IgG Antibody Index	5334-8
DEXG5	Mumps IgG Antibody Index	25418-5
MUMG	Mumps Ab, IgG, S	6476-6
ROG	Measles (Rubeola) Ab, IgG, S	35275-7
DEXG3	Measles IgG Antibody Index	5244-9