

## Overview

### Useful For

Laboratory diagnosis of acute and recent infection with varicella-zoster virus (VZV)

Determination of immune status of individuals to the VZV

Documentation of previous infection with VZV in an individual without a previous record of immunization to VZV

### Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
VZM	Varicella-Zoster Ab, IgM, S	Yes	Yes
VZPG	Varicella-Zoster Ab, IgG, S	Yes	Yes

### Method Name

VZM: Immunofluorescence Assay (IFA)

VZPG: 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 Container/Tube:** 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 [Infectious Disease Serology Test Request](#) (T916) with the specimen.

### Specimen Minimum Volume

0.6 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**

Varicella-zoster virus (VZV), a herpesvirus, 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.<sup>(1)</sup> 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 or those with waning immunity to VZV and in patients with impaired cellular immunity.<sup>(2)</sup>

Individuals at risk for severe complications following primary VZV infection include women who are pregnant, 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.<sup>(2,3)</sup>

Serologic screening for IgG-class antibodies to VZV will aid in identifying nonimmune individuals. The presence of IgM-class antibodies to VZV is suggestive of acute or recent infection however results should be correlated with clinical presentation.

**Reference Values**

IgM

Negative

Reference values apply to all ages.

**IgG**

Vaccinated: positive ( $>$  or  $=1.1$  antibody index [AI])

Unvaccinated: negative ( $<$  or  $=0.8$  AI)

Reference values apply to all ages.

**Interpretation**

A positive IgG result coupled with a positive IgM result suggests recent infection with varicella-zoster virus (VZV). This result should not be used alone to diagnose VZV infection and should be interpreted in the context of clinical presentation.

A positive IgG result coupled with a negative IgM result indicates previous vaccination to or infection with VZV. These individuals are considered to have protective immunity to reinfection.

A negative IgG result coupled with a negative IgM result indicates the absence of prior exposure to VZV and nonimmunity. However, a negative result does not rule-out VZV infection. The specimen may have been drawn before the appearance of detectable antibodies. Negative results in suspected early VZV infections should be followed by testing a new serum specimen in 2 to 3 weeks.

Equivocal results should be followed up with testing of a new serum specimen within 10 to 14 days.

**Cautions**

Results from cord blood, neonates, or immunocompromised individuals should be interpreted with caution.

Testing for IgM-class antibodies to varicella-zoster virus (VZV) should be limited to patients with a clinically compatible disease.

The performance characteristics with individuals vaccinated with the VZV (OKA strain) have not been established.

Up to one-third of individuals with primary herpes simplex virus (HSV) infections who have experienced prior VZV infection show a heterotypic antibody response to VZV antigen making a differential diagnosis between VZV and HSV difficult in the absence of clear-cut clinical findings.

Immunoglobulin G-class antibodies to VZV 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.

Serum specimens collected early during acute phase of infection or soon after vaccination may be negative for IgM- or IgG-class antibodies to this virus, respectively.

**Supportive Data****IgG:**

To evaluate the accuracy of the BioPlex Varicella-Zoster Virus (VZV) IgG multiplex flow immunoassay, 500 prospective serum samples were analyzed in a blinded fashion by the Diamedix VZV IgG enzyme immunoassay (EIA) (Diamedix) and the BioPlex VZV 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 SeraQuest VZV IgG EIA (Quest International). The results are summarized in the table below:

Table. Comparison between Bioplex and Diamedix Varicella-Zoster Virus (VZV) Assays

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

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

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

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

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

### Clinical Reference

1. Yankowitz J, Grose C: Congenital infections. In: Storch GA, ed. Essentials of diagnostic virology. Churchill Livingstone; 2000:187-201
2. Gnann JW, Whitley RJ. Herpes Zoster. N Engl J Med. 2002;347(5):340-346
3. Cvjetkovic D, Jovanovic J, Hrnjakovic-Cvjetkovic I, Brkic S, Bogdanovic M. Reaktivacija herpes zoster infekcije varicela-zoster virusom [Reactivation of herpes zoster infection by varicella-zoster virus]. Med Pregl. 1999;52(3-5):125-128
4. Whitley RJ: Chickenpox and Herpes Zoster (Varicella-Zoster virus). In Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Elsevier; 2020: 1849-1856

### Performance

#### Method Description

Immunoglobulin M:

The presence or absence of IgM-class antibody to varicella-zoster virus (VZV) is determined by an indirect immunofluorescence assay. Serum is incubated with VZV antigen that is adhered to a glass microscope slide. Antibodies, if present, will bind to the antigen forming stable antigen-antibody complexes. If no antibodies are present, the complexes will not be formed, and the serum components will be washed away. Fluorescein-labeled antihuman-IgM antibody is added to the reaction side and binds to IgM antibodies if present. This results in a positive reaction of bright apple-green fluorescence when viewed with a fluorescence microscope. (Package insert: Bion Varicella Zoster Antigen Substrate Slide. Bion Enterprises; 11/2024)

Immunoglobulin G:

The BioPlex 2200 VZV IgG assay uses multiplex flow immunoassay technology. Briefly, serum samples are mixed and incubated at 37 degrees C with sample diluent and dyed beads coated with VZV antigen. After a wash cycle, antihuman IgG antibody conjugated to phycoerythrin (PE) is added to the mixture and incubated at 37 degrees C. Excess conjugate is removed in another wash cycle, and the beads are resuspended in wash buffer. The bead mixture then passes through a detector that identifies the bead based on dye fluorescence and determines the amount of antibody captured by the antigen based on 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 nonspecific 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 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**

86787 x2

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
VZGM	Varicella-Zoster Ab, IgM and IgG, S	81234-7

  

Result ID	Test Result Name	Result LOINC® Value
80964	Varicella-Zoster Ab, IgM, S	43588-3
VZG	Varicella-Zoster Ab, IgG, S	15410-4
DEXG4	Varicella IgG Antibody Index	5403-1