

## Varicella-Zoster Virus - VZV

### Clinical Background

Varicella-zoster virus (VZV) is the cause of chickenpox in children and herpes zoster (shingles) in adults.

#### Epidemiology

- Incidence – estimated 1,000,000 new cases annually in the U.S.
- Age
  - Varicella – children (usually 1-9 years)
  - Herpes zoster – >60 years
- Sex – M:F, equal
- Climate variation
  - Temperate climates – 90% of people have infection before adolescence
  - Tropical climates – more adults are susceptible than in temperate climates

#### Organism

- DNA virus
- Member of the Herpesviridae family
- Establishes latency in sensory ganglia

#### Risk Factors

- For non-immune individuals, direct contact with large-particle droplets
- Risk factors for herpes zoster include immune deficiency, psychological stress and localized physical trauma

#### Clinical Presentation

- Varicella (chickenpox)
  - Fever and generalized vesicular exanthem
    - Rash begins as macules and rapidly progresses from papules to vesicles
    - Successive crops of lesions
- Complications
  - Secondary bacterial infections
  - Invasive infections – pneumonia, osteomyelitis
  - Central nervous system – strokes (vasculopathy), cerebellar ataxia, meningitis, transverse myelitis
- Herpes zoster (reactivation of VZV)
  - Characterizations:
    - Skin eruption (shingles)
      - Unilateral, painful maculopapular lesions followed by vesicular eruptions with dermatomal distribution (1-3 dermatomes is usual) that does not cross the midline
    - Facial nerve (7th cranial nerve) involvement (Ramsey-Hunt syndrome)
    - Pain from inflammation of sensory nerve ganglia
    - May mimic other serious medical conditions (eg, myocardial infarction, appendicitis, acute cholecystitis, renal colic, pulmonary embolism, glaucoma)
    - Less common manifestations include pneumonitis, acute retinal necrosis, myelitis, vasculopathy, hepatitis and meningoencephalitis
  - Complications
    - Postherpetic neuralgia (PHN)

- Secondary skin infection from *Streptococcus pyogenes* or *Staphylococcus aureus*
- Congenital infection – congenital VZV transmission (0.4-2% of children when mother had VZV during first 20 weeks of pregnancy) may cause severe disseminated neonatal infection with the following:
  - Pneumonia
  - Skin lesions
  - Hemorrhages
  - Death
  - Developmental problems, including hypoplastic limbs, cataracts, chorioretinitis, microphthalmos

#### Treatment

- Early treatment of zoster with antivirals accelerates resolution and may lessen post-herpetic pain

#### Prevention

- Childhood vaccination preventive for VZV in most cases
- Universal vaccination has decreased outbreaks and severity of secondary complications
- New vaccine recently approved for adults >60 years to prevent herpes zoster
  - Vaccine shown to reduce the incidence of PHN by 66.5%
- Passive immunization with varicella-zoster immune globulin (VZIG) can prevent severe disease in certain susceptible pediatric populations after an exposure

## Diagnosis

- Indications for testing
  - Rash of VZV primary or as shingles is usually a clinical diagnosis
  - Most common indication is to confirm severe or atypical disease
- Based on typical appearance of skin lesions
  - Chickenpox – skin lesions are in different stages of development (papule, vesicle, pustule, umbilication, and crusting) all at same time
  - Shingles – painful vesicles in a dermatomal distribution
- Laboratory testing
  - DFA or PCR – rapid identification of the virus
    - Performed on lesion swabs
    - Sensitivity and specificity exceed 90%
    - PCR is recommended in VZV-CNS syndromes where viral recovery of organisms from CSF is poor
  - Tzanck smear – rapid but not specific for VZV; performed on swabs from lesions
  - Viral culture
    - Takes >1 week
    - Only 60-70% sensitive
    - Difficult to grow organisms
  - Antibody testing
    - Significant change in titer from paired sera or a single high titer IgM is indicative of acute infection
    - IgG titer is useful in assessing immunity to VZV

#### Differential Diagnosis

- Cutaneous skin lesions (chickenpox) – HSV, smallpox, rickettsial pox, enterovirus, bullous impetigo, eczema with secondary superinfection
- Cutaneous skin lesions (Zoster) – HSV, contact dermatitis, poison ivy, poison oak, bullous impetigo

- Meningitis
- Viral encephalitis
- Fungal meningitis
- Vasculitis
- Congenital – syphilis, congenital histiocytosis, toxoplasmosis, cytomegalovirus, lesions

## Lab Tests

### Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

Test Name and Number	Recommended Use	Limitations	Follow Up
Varicella-Zoster Virus DFA with Reflex to Varicella-Zoster Virus Culture <b>0060282</b>  Method: Direct Fluorescent Antibody Stain	Confirm VZV, especially in active skin lesions  Culture considered gold standard	Not recommended for CSF samples	
Varicella-Zoster Virus DFA <b>0060290</b>  Method: Direct Fluorescent Antibody Stain	Confirm VZV	About 20% of samples submitted for VZV are positive for HSV; HSV testing is <b>NOT</b> included in this test	
Varicella-Zoster Virus & Herpes Simplex Virus DFA with Reflex to Varicella-Zoster Virus Culture & Herpes Simplex Virus Culture <b>0060283</b>  Method: Direct Fluorescent Antibody Stain	Confirm VZV or HSV especially in active skin lesions	Not recommended for CSF samples	
Varicella-Zoster Virus by PCR <b>0060042</b>  Method: Polymerase Chain Reaction	PCR is the most sensitive and rapid test  Given its expense, some laboratories may limit testing to <ul style="list-style-type: none"> <li>• CNS syndromes</li> <li>• Body fluids or tissues from unusual varicella or herpes zoster infections</li> <li>• Vesicle fluid specimens negative for VZV by culture and/or DFA negative for HSV by culture, where definitive etiologic determination clinically important</li> </ul>		

<p>Varicella-Zoster Virus Antibodies, IgG &amp; IgM <b>0050162</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	<p>Diagnose clinical infections with varicella or herpes zoster</p> <p>Identify hospitalized children with varicella</p> <p>Assess immune status of individuals exposed to varicella, especially pregnant women</p>		<p>Repeat testing in 10-14 days if results equivocal</p>
<p>Varicella-Zoster Virus Antibody, IgM by ELISA (CSF) <b>0054445</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	<p>Confirm VZV in acute infections</p>	<p>Antibody detection in CSF may reflect contamination by blood or antibody transfer across blood-brain barrier instead of VZV infection</p>	<p>Repeat in 10-14 days if results equivocal</p>

**Additional Tests Available**

Test Name and Number	Comments
<p>Varicella-Zoster Virus Antibody, IgM <b>0099314</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	
<p>Varicella-Zoster Virus Antibody, IgG <b>0050167</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	
<p>Varicella-Zoster Virus Antibody, IgG by ELISA (CSF) <b>0054444</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	
<p>Encephalitis Panel, CSF with Reflex to HSV Type 1 &amp; 2 Glycoprotein G-Specific Ab, IgG <b>2001741</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody</p>	
<p>Encephalitis Panel, Serum with Reflex to HSV Type 1 and Type 2 Glycoprotein G-Specific Ab, IgG <b>2001742</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody</p>	
<p>Meningoencephalitis Panel, CSF with Reflex to HSV Type 1 &amp; Type 2 Glycoprotein G-Specific Ab, IgG <b>2001765</b></p> <p>Method: Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody</p>	

Meningoencephalitis Panel, Serum with Reflex to HSV Type 1 & Type 2 Glycoprotein G-Specific Ab, IgG

2001764

Method:

Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody/Chemiluminescent Immunoassay

### General References

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- Cytomegalovirus - CMV
- Enterovirus
- Herpes Simplex Virus - HSV

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