Varicella/Zoster Infections- What’s New?

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OVERVIEW (1)

- Herpes Zoster
  - Characteristics of the virus
  - Life Cycle
- Pathogenesis of Varicella Zoster Virus (VZV)
- Epidemiology of Chickenpox
- Pathogenesis of VZV in adults
  - Populations at risk
OVERVIEW (2)

✓ Waning immunity
✓ Asymptomatic endogenous reactivation

► Epidemiology zoster
✓ Prevaccine Era
✓ Post vaccine era

► Herpes Zoster Vaccine
HUMAN HERPESVIRUSES (HHV)

HHV family

Alpha-HHV
- HSV (HHV-1,2)
  - Primary infection: Varicella (chickenpox)

Beta-HHV
- VZV (HHV-3)
  - Reactivation: herpes zoster (shingles)
- (HHV-6A, 6B) (HHV-7)

Gamma-HHV
- EBV (HHV-4)
- CMV (HHV-5)
  - (HHV-8)

HSV = herpes simplex virus
VZV = varicella–zoster virus
EBV = Epstein-Bar virus
CMV = Cytomegalovirus


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HEMORRHAGIC VARICELLA
PRESENTATION OF HERPES ZOSTER (HZ)
VARICELLA-ZOSTER VIRUS (VZV)

- **Virions:** Spherical, but shape may vary\(^1\)
- **Genome:** Double-stranded DNA\(^1\)
- **Lipid envelope\(^1\)**
- **Tropism:** Infects many cell types
  - Skin cells, T-cells, neurons of the dorsal root ganglia\(^2\)
  - Cell receptor(s) needed for binding not fully identified\(^1, 2\)
- **Only 1 serotype\(^3\)**
- **Humans are the only known reservoir\(^3\)**


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VARICELLA HISTORY

- Herpes viruses alive and well in dinosaur time, 70 million years ago*
- 1767: differentiation varicella from smallpox
- 1892: occurrence of varicella after exposure to zoster
- 1943: consideration of herpes zoster as varicella reactivation

Grouse. Peds. 1999;103:5:1027-28
LIFE CYCLE

Primary infection with varicella-zoster virus (Varicella)

Latency

Reactivation

Zoster (Shingles)

- Immunocompetent patients
  - Myelitis
  - Large-vessel granulomatous arteritis

- Immunocompromised patients
  - Postherpetic neuralgia
  - Myelitis
  - Small-vessel encephalitis

Zoster sine herpete

VZV: IMMUNE RESPONSE

- Cell-mediated immunity (CMI) (more than humoral) plays a major role in recovery\(^1\)
  - Clears virally infected cells
  -Limits viral replication at dermal sites

- Humoral immunity\(^2\)
  - IgM, IgG and IgA are neutralizing antibodies

- Immunity persists following disease
  - Waning CMI with increasing age contributes to reactivation of VZV as herpes zoster (shingles)\(^3\)

PATHOGENESIS OF VARICELLA: CHICKEN POX

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Repeated episodes of viremia
- Multiple tissues, including sensory ganglia, infected during viremia
**PATHOGENESIS - INCUBATION**

**Day 0**
- Virus enters through conjunctivae and/or upper respiratory mucosa via airborne or direct contact
- Replicates in regional lymph nodes

**Days 4-6**
- Low-level primary viremia develops → viral replication in liver, spleen, and other organs

**Days 10-12**
- Secondary viremia occurs; virus reaches skin

**Day 14**
- Skin becomes infected and vesicular rash appears
HERPESVIRUSES

- Varicella-zoster virus (Human herpes virus 3)
- Transmitted by the respiratory route
- Causes pus-filled vesicles
- Virus may remain latent in dorsal root ganglia
LATENCY

- Virus in non infectious form with intermittent periods reactivation and shedding
- Only a few viral genes are expressed during latency and viral burden is low
- Latency occurs because host immune surveillance is able to prevent overt reactivation
- Herpes zoster is reappearance of one’s own chicken pox
EPIDEMIOLOGY OF VARICELLA (1)

- Occurs worldwide and equally affects both sexes and all races\(^1,\ 2\)
- Is highly contagious; infects at least 90% of the susceptible population\(^1\)
- Reservoir: Human
- Transmission: Airborne droplet; direct contact with lesions
- Temporal pattern: Peak in winter-early spring (U.S.)

EPIDEMIOLOGY OF VARICELLA (2)

- Communicability: 1-2 days before to 4-5 days after onset of rash; maybe longer in immunocompromised

- Pre vaccine in US-4 million cases
  - 11,000-13,500 hospitalization
  - 100-140 deaths

- Highest incidence in pre-school and elementary school aged children

- More significant cause of morbidity and mortality as other current vpd were controlled
CUMULATIVE INCIDENCE OF VZV

- Climate factor in age-susceptibility to varicella
- Epi studies in the 1980s—early 1990s showed approximately 90%-95% of the population in temperate climates (e.g. US and Japan) was VZV seropositive by 15 years of age\(^1,2\)
- In tropical climates, acquisition of varicella is delayed

CUMULATIVE INCIDENCE OF VZV

Seroprevalence (%) vs. Age (years)

- Pink: Japan, 1984
- Yellow: Philippines, 1995
- Green: Singapore, 1989
- Light Blue: St Lucia, 1985–1986


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VARICELLA VACCINE

- Composition: Live virus (Oka/Merck strain) introduced 1995
- Efficacy: 95% (Range, 65%-100%)
- Duration of Immunity: >7 years
- Schedule: 2 doses
- Coverage rates in most states in 2 >
Varicella Active Surveillance Project

Summary and Definitions

**Project Activities**
- Surveillance began 1995-present day and includes the Antelope Valley (SPA 1)
- Cases of varicella are reported bi-weekly by participating reporting sites
- VASP staff conduct telephone interviews with potential varicella cases
- Specimen collection performed by sites or project staff for lab testing

**Definitions**
- **Verified varicella case**
  - Acute onset of diffuse papulovesicular rash without other known cause diagnosed and/or reported by a licensed health care provider (LHCP), school nurse or parent
- **Breakthrough varicella case**
  - A verified varicella case where rash occurs >42 days after vaccination
ANNUAL VERIFIED VARICELLA CASES AND INCIDENCE RATES, ANTELOPE VALLEY, CA, 2000-2009

2010 Incidence rates not calculated, 2010 census data not yet available
VARICELLA CASES BY INCIDENCE RATES AND AGE GROUP, ANTELOPE VALLEY, CA, 2000-2009

Incidence rates = #Cases/1,000 Population
<table>
<thead>
<tr>
<th>Year</th>
<th>#Cases/Outbreaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>34</td>
</tr>
<tr>
<td>2001</td>
<td>30</td>
</tr>
<tr>
<td>2002</td>
<td>8</td>
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<td>2003</td>
<td>7</td>
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<td>25</td>
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<td>2006</td>
<td>11</td>
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<td>2007</td>
<td>8</td>
</tr>
<tr>
<td>2008</td>
<td>6</td>
</tr>
<tr>
<td>2009</td>
<td>2</td>
</tr>
<tr>
<td>2010</td>
<td>2</td>
</tr>
</tbody>
</table>

The number over the bar represents the number of reported outbreaks for that given year.
REDUCTION IN VARICELLA MORTALITY RATES IN 2001 COMPARED WITH AVERAGE RATES IN 1990-1995

<table>
<thead>
<tr>
<th>Age group</th>
<th>Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td>78</td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>88</td>
</tr>
<tr>
<td>1-4 years</td>
<td>100</td>
</tr>
<tr>
<td>5-9 years</td>
<td>94</td>
</tr>
<tr>
<td>10-19 years</td>
<td>83</td>
</tr>
<tr>
<td>20-49 years</td>
<td>92</td>
</tr>
<tr>
<td>≥50 years</td>
<td>28</td>
</tr>
</tbody>
</table>

RISK FACTORS FOR VACCINATION FAILURE

- Age (likelihood of exposure)
- Asthma/Reactive airway disease and/or steroids
- Younger at vaccination (not always consistent)
- Longer time since vaccination
- Varicella and MMR vaccine interval <28 days
- Other (eczema)

Aisha O. Jumaan, PhD, MPH
BREAKTHROUGH DISEASE (BT)

- Varicella BT is generally mild
- Lesions are maculopapular
- <50 lesions
- No fever, usually
- No complications, usually
- 1/3 less infectious
PERCENTAGE OF BREAKTHROUGH VARICELLA CASES, ANTELOPE VALLEY, CA, 2000-2010
Vaccination Coverage of 2nd Dose Varicella Vaccine in States with Mandatory 2-Dose Requirement for Kindergarten Entry, School Year 2009-2010, N=19
HERPES ZOSTER (SHINGLES): ETYMOLOGY

herpes = Derived from Greek “herpein” meaning “to creep”\(^1\)

zoster = A Greek word meaning “girdle”\(^2\)

shingles = Derived from Latin “cingere”\(^2\)

1. Dorland’s Illustrated Medical Dictionary. 28\(^{th}\) ed. 1994:759
ZOSTER: INCIDENCE

- Up to 800,000 cases of zoster occur annually in US\(^1\)
- Lifetime incidence is 10\%- 20\% in general population\(^2\)
- More than 67\% of zoster cases occur in people >50 years\(^3\)
- Estimated that up to 50\% of people surviving to 85 years will have an episode of zoster\(^2\)
- Frequency of recurrence of zoster: 1.7\% to 5.2\%\(^4\)


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POPULATIONS AT RISK FOR HZ

- As CMI decreases with age, the elderly, immunocompromised (HIV, cancer, transplants, immunosuppressive tx) more at risk
- Those who have had varicella disease before 1 year of age more at risk
- Some studies show females at greater risk (Fleming Epidemiol Infect. 2004 Jan; 132(1):1-5.)
- Some say stress imp; blacks less likely
- Most say more data needed
SHINGLES

- Reactivation of latent HHV-3 releases viruses that move along peripheral nerves to skin.
ZOSTER: LATENCY AND REACTIVATION

- In response to waning cell-mediated immunity (CMI) that often accompanies increasing age, VZV may reactivate and replicate within the ganglion.
- Virus is then transported down the sensory nerves, causing intense neuritis, and is released.
- Because VZV reactivation usually involves a single sensory nerve, the consequent vesicular rash occurs in the characteristic unilateral dermatomal distribution of zoster.¹

ZOSTER TRANSMISSION

- Reactivated VZV infections also play a role in maintaining VZV infections in pop
- Latently infected adults, pts with immuno-suppression impt reservoirs of infection as are more likely to reactivate
- With vesicles can transmit to seronegatives- cause chicken pox
- With seropositives, may boost VZV immunity
Annual incidence of zoster from 1947 to 1972 in a general practice population in the United Kingdom

ZOSTER: EPIDEMIOLOGY IN THE UNITED STATES

HERPES ZOSTER VACCINE
(ZOSTAVAX)

- Contains live attenuated varicella virus in an amount that is approximately 14 times greater than that in regular varicella vaccine
- Approved for persons 60 years of age and older
- Administered by the subcutaneous route
THANK YOU
Have a Nice Day