Status of varicella surveillance and challenges in the 2-dose varicella vaccination era

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Outline

- Varicella and varicella vaccine background
- Varicella surveillance
- Implementation and impact of the varicella vaccination program
- Varicella surveillance in Arizona
- Challenges with varicella surveillance
- Summary
Varicella: Transmission, Incubation Period, Contagiousness

- Humans only reservoir of infection
  - Primary infection → varicella (chickenpox)
  - Reactivation → herpes zoster (shingles)
- Person-to-person transmission through
  - Direct contact
  - Inhalation of aerosols from vesicular fluid of skin lesions, or infected respiratory tract secretions
- Average incubation period
  - 14-16 days after exposure to rash (range: 10-21 days)
- Contagiousness
  - 1-2 days before rash onset until all lesions crusted or disappear if maculopapular rash (typically 4-7 days)
- Varicella in unvaccinated persons is highly contagious
  - 61-100% secondary household attack rate

Varicella: Clinical Features in Unvaccinated Persons

- Can start with prodrome of fever, malaise, headache, abdominal pain 1-2 days before rash
- Vesicular rash, occurring in crops, lesions in different stages of development, centralized distribution
- Rash usually starts on face and trunk, then spreads to extremities
- Rash involves 250-500 lesions that are pruritic
- Lesions typically crusted 4-7 days after rash onset

Varicella Complications

<table>
<thead>
<tr>
<th>Virally mediated</th>
<th>Bacterially mediated</th>
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<tbody>
<tr>
<td>Neurological</td>
<td>Skin and soft tissue</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Hemorrhagic, other</td>
<td>Pneumonia, other</td>
</tr>
</tbody>
</table>

- Certain groups at increased risk of complications:
  - Adults
  - Immunocompromised persons
  - Pregnant women
  - Newborns

- However, most severe complications and deaths occur in healthy persons
Varicella Disease Burden in the U.S. Before Varicella Vaccine Introduction

- Annually, before 1996, varicella caused:
  - Cases ~ 4 million
    - 15.0 – 16.0/1,000 population per year
    - Highest incidence children < 10 years
  - Hospitalizations ~ 11,000 to 13,500
    - ~ 4.0-6.0/100,000 population per year
  - Deaths ~ 100 – 150
    - ~ 0.4-0.6/million population per year
  - Congenital varicella syndrome ~ 44
    - Risk = 1-2% for pregnancies affected 0-20 weeks

- Greatest disease burden in children
  - >90% cases, 70% hospitalizations, 50% deaths

US Varicella Vaccination Program

- 1996 - Universal one-dose varicella vaccination program recommended by Advisory Committee on Immunization Practices (ACIP)

- 2007 - ACIP changed from a routine 1-dose to a 2-dose varicella vaccination program for children
  - First dose: 12-15 months
  - Second dose: 4-6 years

- Rationale for routine 2-dose program
  - Outbreaks in highly vaccinated school populations placed resource burden on state health departments
  - Incomplete protection after 1 dose
  - Improved disease control anticipated with 2-dose program
    - 2nd dose expected to provide protection to the 15-20% of children who do not respond to the 1st dose
    - Risk of varicella 3-fold lower in 2-dose vaccinees compared to 1-dose vaccinees
Varicella: Clinical Features in Vaccinated Persons (“Breakthrough Varicella”)

- ~15-20% of 1-dose vaccinated persons develop breakthrough varicella if exposed to VZV
- Varicella in vaccinated persons usually milder than varicella in unvaccinated persons
- 25-30% breakthrough cases not mild and have clinical features more similar to unvaccinated cases
- 1-dose vaccinees with <50 lesions 1/3 as contagious as unvaccinated persons
- Vaccinees with ≥50 lesions as contagious as unvaccinated persons

Varicella Surveillance
History of varicella surveillance

- 1999 – Varicella deaths become reportable
- 2002 – Council of State and Territorial Epidemiologists (CSTE) recommended states move to case-based reporting by 2005
- 2003 – Varicella added back to national notifiable diseases list for case reporting
- 2007 – 2nd dose varicella vaccination program implemented
- 2010 – Varicella reportable in 39 states and 38 states conducting case-based surveillance
Case-Based Surveillance

- Needed to monitor impact of the varicella vaccination program

- Critical variables:
  - Standard case-based surveillance data:
    - Demographics
    - Clinical information (e.g., rash description, fever, medications)
    - Epidemiologic (e.g., transmission setting, outbreak-related)
    - Outcomes of case (e.g., hospitalized, died)
  - Varicella-specific variables needed to monitor varicella surveillance program:
    - Age
    - Vaccination status and number of doses
    - Disease severity (i.e., number of lesions)
Sources of Varicella Surveillance Data

- **Varicella Active Surveillance Project (VASP)**
  - Established in 1995 in 3 sites (Antelope Valley, CA, West Philadelphia, PA, and Travis County, TX) to monitor impact of varicella vaccination program
  - Not nationally representative – only 2 sites participated from 2000-2012
  - Expensive to maintain
  - Project ended June 2012

- **National Notifiable Diseases Surveillance System (NNDSS)**
  - Relies on passive reporting from sites to state
  - Limited to states where varicella reportable
Implementation and Impact of the Varicella Vaccination Program
One-dose Varicella Vaccination Program (1996-2005)

- One-dose vaccine effectiveness 80-85% against all varicella; >95% against severe varicella
- National one-dose varicella vaccination coverage reached 90% in 2010
- One-dose varicella vaccination coverage in Arizona reached 88.2% in 2010
- Varicella active surveillance sites reported 90% decline in varicella incidence

MMWR Sept 2 2011 Vol 60/No 34; MMWR 2007 Varicella Recommendations; Guris JID 2008
Varicella Active Surveillance Project sites experience further declines in varicella incidence during two-dose vaccination era, 2006-2010

2006-2010:
78% decline Antelope Valley
67% decline West Philadelphia

Routine 2 dose program recommended
Reductions in age-specific incidence greatest in age groups targeted for 2\textsuperscript{nd} dose – Varicella Active Surveillance Project sites, 2006-2010

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Antelope Valley, CA (%)</th>
<th>West Philadelphia, PA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>-81.3</td>
<td>40.8</td>
</tr>
<tr>
<td>1-4</td>
<td>-54.0</td>
<td>-72.7</td>
</tr>
<tr>
<td>5-9</td>
<td>-88.3</td>
<td>-78.7</td>
</tr>
<tr>
<td>10-14</td>
<td>-75.3</td>
<td>-91.4</td>
</tr>
<tr>
<td>15-19</td>
<td>-29.3</td>
<td>-25.1</td>
</tr>
<tr>
<td>20+</td>
<td>-50.0</td>
<td>-17.3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>-76.3</strong></td>
<td><strong>-67.1</strong></td>
</tr>
</tbody>
</table>
Proportion of Case-patients with Breakthrough Varicella
Varicella Active Surveillance Project, 1995-2010

* 2010 data provisional
National varicella incidence rates from states meeting inclusion criteria* (n=12-31 states) that reported to NNDSS, 2000-2010

- * Inclusion criteria includes: reporting a minimum incidence of 1/100,000 for at least 3 consecutive years between 2000-2010.
### Characteristics of varicella cases reported to NNDSS, 2009-2010

<table>
<thead>
<tr>
<th>Varicella-specific variable (N states reporting data)</th>
<th>Total number of cases reported</th>
<th>Number of cases with characteristic, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated with varicella-containing vaccine (N=15)</td>
<td>12,313</td>
<td>7906 (64.2)</td>
</tr>
<tr>
<td>Number of lesions &lt;50 (N=12)</td>
<td>3942</td>
<td>2062 (52.3)</td>
</tr>
<tr>
<td>Fever present (N=12)</td>
<td>5934</td>
<td>1406 (23.7)</td>
</tr>
<tr>
<td>Itchy rash (N=11)</td>
<td>3193</td>
<td>1801 (56.4)</td>
</tr>
<tr>
<td>Hospitalized (N=14)</td>
<td>8884</td>
<td>132 (1.5)</td>
</tr>
<tr>
<td>Vaccinated (N=14)</td>
<td>5448</td>
<td>17 (0.3)</td>
</tr>
<tr>
<td>Laboratory testing for varicella performed (N=13)</td>
<td>8035</td>
<td>964 (12)</td>
</tr>
<tr>
<td>Outbreak-related (N=33)</td>
<td>31,793</td>
<td>4309 (13.6)</td>
</tr>
<tr>
<td>Case status (N=34)</td>
<td>35,676</td>
<td>14,896 (41.8)</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td>20,596 (57.7)</td>
</tr>
</tbody>
</table>
Impact on Varicella Outbreaks

- Connecticut (Kattan JID 2011)
  - 42 outbreaks 2005-2006, median size 14 cases
  - 2 outbreaks 2008-2009, median size 5 cases

- 6 state and local health departments funded to conduct varicella outbreak surveillance in schools
  - New York City: 120-330 schools (93,000-224,000 students)
    - reported 1 outbreak (n=7 cases) in a non-participating school during 2009-10 school year
  - Minnesota: 80 schools statewide (41,000 students)
    - reported 15 outbreaks from non-participating schools
    - Average outbreak size=9 cases
  - West Virginia: ~700 schools (281,000 students)
    - Reported 19 outbreaks (n=167 cases)
    - Case-control study being conducted to assess 2-dose VE

- VASP – Antelope Valley, CA
  - 46 outbreaks 2002-2005, median size 9 cases (range 5-45)
  - 21 outbreaks 2006-2009, median size 9 cases (range 5-17)
Varicella surveillance in Arizona
Varicella Reporting Form

Outbreak
- Indicate on School-based Case Form
- Also fill out the Outbreak Reporting Form

Received Varicella Vaccine?
- 1 dose
- 2 doses
- No
- Unknown

*Outbreak: 5+ cases (if ≤ 13 years old) or 3+ cases (if > 13 years old) within 21 days
Reported Varicella Cases by Age (≤14 years), Arizona, 2010
Reported Varicella Cases by Month (≤14 years), Arizona, 2010

Number of Reported Cases

Month

January  
February  
March  
April  
May  
June  
July  
August  
September  
October  
November  
December
Reported Varicella Cases by County (≤14 years), Arizona, 2010

Number of Reported Cases

County:
- Apache: 1
- Cochise: 2
- Coconino: 10
- Gila: 1
- La Paz: 8
- Maricopa: 367
- Mohave: 14
- Navajo: 4
- Pima: 98
- Pinal: 36
- Santa Cruz: 9
- Yavapai: 22
- Yuma: 23
593 varicella cases in 2010

- 340 (57%) were vaccinated
  - 232 (68%) received one dose
  - 108 (32%) received two doses

Grade of lesions for reported varicella cases, 2010

- Grade 1: 34%
- Grade 2: 17%
- Grade 3: 2%
- Unknown: 47%

Grade I: 50 spots or less easily counted within 30 seconds
Grade II: 50-500 spots (between Grades I and III)
Grade III: 500 or more spots or spots clumped so close together that little normal skin is visible
Challenges with varicella surveillance
Defining and identifying varicella cases in the 2-dose vaccination era

- Varicella case definition not sensitive or specific
  - Probable case: acute illness with generalized maculopapulovesicular rash
  - Confirmed case: acute illness with generalized maculopapulovesicular rash epi-linked to another probable or confirmed case or has lab confirmation
  - Two probable cases that are epi-linked considered confirmed even in absence of lab confirmation

- Rash presentation modified by vaccination
  - Increasingly challenging in 2 dose vaccine era to diagnose cases in vaccinated persons because often lack “classical” vesicles
  - Can be confused with other rashes or bug bites
Importance of laboratory testing for confirmation of varicella cases

- Laboratory testing not routinely done
  - Providers don’t rely on it for patient management and don’t recognize it is important for control to properly advise regarding exclusion from school, etc
  - If providers test, often not aware of best specimen to collect or test to order
    - Lesions/scabs better than serologic testing
    - IgM testing using commercial assays not sensitive
    - PCR of lesions most sensitive/specific for diagnosis

- Timing of specimen collection affects results and limits ability to confirm cases/outbreaks
Summary

- Impact
  - Varicella incidence has declined in all age groups coincident with implementation of routine 2-dose varicella vaccination program for children
    - Greatest declines among children aged 5-14 years
  - Outbreaks have become less common

- National varicella surveillance improving with more states reporting cases and varicella-specific variables to CDC
  - Data are now robust enough for monitoring impact of the varicella vaccination program
Varicella Surveillance Needs You...

- To identify cases
  - Identification and exclusion of mild cases can help prevent transmission

- To collect specimens for laboratory testing
  - Useful for diagnosis of mild cases that may be confused with other rash illnesses
  - Important for confirmation and implementation of appropriate control measures during outbreak investigations

- To report cases to your local/state health department
  - Data from Arizona will be used in analysis of national data for monitoring impact of the 2-dose varicella vaccination program
Acknowledgements

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Claire Newbern      Caroline Johnson

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Resources

- How to collect specimens for VZV testing: http://www.cdc.gov/shingles/lab-testing/collecting-specimens.html
- Instructions for sending specimens for VZV testing at CDC: http://www.cdc.gov/shingles/lab-testing/collecting-specimens.html
Contact Information

- For questions regarding varicella reporting, outbreak investigations, and laboratory testing in Arizona, please contact:
  - Office of Infectious Disease Services
    - Clarisse Tsang: 602-364-3817 (phone)
      602-509-7970 (cell)
      tsangc@azdhs.gov (email)
For questions about national varicella surveillance and testing at the CDC National VZV Laboratory, please contact:

CDC, Division of Viral Diseases, Herpes Virus Team

Adriana Lopez: alopez@cdc.gov (email) or 404-639-8369 (phone)

Thank you!
Severe Varicella Complications

Group A Strep

Severe disseminated varicella in child with ALL

Staph aureus
Varicella Vaccines

- Monovalent vaccine (VARIVAX)
  - Licensed 1995
  - Live, attenuated vaccine with VZV strain (Oka)
  - Vaccine-strain virus has potential to cause symptoms similar to those seen with wild-type infection (e.g., reactivation to cause herpes zoster, meningitis)

- Quadrivalent vaccine (MMRV; PROQUAD)
  - Licensed 2005 for children 1-12 years of age
  - Includes Measles, Mumps, Rubella, Varicella
### Published Estimates of 2-Dose Varicella Vaccine Effectiveness

<table>
<thead>
<tr>
<th>Study</th>
<th>1-dose VE</th>
<th>2-dose VE</th>
<th>Incremental Vaccine Effectiveness of 2&lt;sup&gt;nd&lt;/sup&gt; dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Efficacy</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Kuter, PIDJ 2004</td>
<td>94%</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td><strong>Vaccine Effectiveness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gould, PIDJ 2009</td>
<td>84%</td>
<td>88%</td>
<td>Incremental vaccine effectiveness of 2&lt;sup&gt;nd&lt;/sup&gt; dose =28%</td>
</tr>
<tr>
<td>Nguyen, PIDJ 2010</td>
<td>79%</td>
<td>95%</td>
<td>Incremental vaccine effectiveness of 2&lt;sup&gt;nd&lt;/sup&gt; dose =76%</td>
</tr>
<tr>
<td>Shapiro, JID 2011</td>
<td>86%</td>
<td>98%</td>
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