Varicella Vaccination Program in the United States

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Varicella disease

- Highly contagious, itchy vesicular rash (250-500 lesions)
  - Generally mild in childhood but severe cases occur
  - Complications include virally and bacterially mediated (e.g., skin and soft tissue infection, sepsis, pneumonia, neurologic, hemorrhagic)

- At increased risk of complications
  - Adults
  - Immunocompromised persons
  - Pregnant women
  - Newborns
Varicella public health burden

- Direct medical costs
  - Physician visits, hospitalizations, deaths

- Outbreak related costs
  - Schools, other closed settings especially involving adults (hospitals, ships, prisons etc.)

- Healthcare associated costs
  - Exposures and illness in healthcare settings

- Societal costs
  - Days of school and/or work missed for case and caretaker
  - Medications, other
Varicella disease epidemiology in the US – Pre-vaccine era

- **Annual Burden**
  - ~ 4 million cases (approximate to birth cohort)
  - ~ 11,000-13,500 hospitalizations (~ 4.0-6.0/100,000 population per year)
  - ~ 100-150 deaths (~ 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% of cases
  - 70% hospitalizations
  - 50% deaths
The US varicella vaccination program – Recommendations

- **1995:** 1st country to introduce varicella vaccine as part of routine childhood immunization program
  - 1-dose policy for children 12 – 18 months
  - 2-dose vaccination of susceptibles >13 years (4 – 8 weeks apart)

- **2006:** Routine 2-dose vaccination of children
  - 1st dose: 12 – 15 months
  - 2nd dose: 4 – 6 years
  - Catch-up vaccination (2nd dose if previously received 1 dose) and vaccination of all eligible persons without evidence of immunity
Cost effectiveness

- Analyses of 1-dose and 2-dose programs versus no vaccination suggested*
  - 1-dose program cost beneficial or breaks even from medical perspective
    - $4.40 saved for every $1 spent
  - 2 dose program is cost beneficial from societal perspective
    - Societal $2.70

*Not included: Varicella outbreak costs, herpes zoster – in vaccinees (expected decline) or in those with history of varicella (modeled increase)
US EXPERIENCE WITH ONE DOSE VARICELLA VACCINE
Varicella effectiveness and safety

- 1-dose vaccine effectiveness:
  - 85% varicella of any severity
  - >95% severe disease

- Vaccine safety*:
  - Excellent safety profile with >55 million vaccine doses distributed
  - Vaccine Adverse Event Reporting System – national passive system to report adverse events
    - Rate of severe adverse events**: 2.6/100,000 doses distributed
  - Rash, fever, and injection-site reactions accounted for 2/3 of all reports

*Chaves et al. JID 2008
** Rash, hepatitis, pneumonia, herpes zoster, meningitis, encephalitis; 2 vaccine strain VZV deaths, one immunocompromised and one with significant medical history suggestive of immunocompromise
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 (fewer lesions and shorter duration of rash) 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

One-dose varicella vaccination coverage, children 19-35 months
National Immunization Survey, 1997-2012

Coverage (%)

Year


26 43 58 68 76 81 85 88 88 89 90 91 90 90 91 90

*National Immunization Survey (NIS), coverage available at www.cdc.gov/vaccines/stats-surv/default.htm#nis
One-dose varicella vaccination program impact – Varicella Active Surveillance Project (VASP) sites, 1995-2005

Antelope Valley, CA

West Philadelphia, PA

Cases per 1000 population

Overall incidence

One dose vaccination coverage

Year


0 1 2 3 4 5 6 7 8

0 20 40 60 80 100

Year


0 20 40 60 80 100

0 1 2 3 4 5 6 7 8
Reduction in age-specific incidence rates – VASP sites, 1995-2005

<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>84</td>
<td>77</td>
</tr>
<tr>
<td>1-4</td>
<td>95 (circled)</td>
<td>89 (circled)</td>
</tr>
<tr>
<td>5-9</td>
<td>92</td>
<td>95 (circled)</td>
</tr>
<tr>
<td>10-14</td>
<td>64</td>
<td>98</td>
</tr>
<tr>
<td>15-19</td>
<td>86</td>
<td>78</td>
</tr>
<tr>
<td>20+</td>
<td>82</td>
<td>67</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td>93</td>
</tr>
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ACIP Recommendation (1 dose)

ACIP Recommendation (2 doses)

2000-2006
71% decline from 1988-1995


*Varicella as the underlying cause of death

Varicella vaccine program

2005-2007 88% decline from 1990-1994

Average 48 deaths/year

* NCHS, varicella as underlying cause of death
Reduction in varicella health care costs

- Total estimated direct medical expenditures for varicella hospitalizations and ambulatory visits
  - 1994-1995: $85 million
  - 2002: $22 million
  - 74% decline

Zhou et al, JAMA, 2005
Change to a 2-dose vaccine policy  
- Rationale -

- Varicella epidemiology
  - Ongoing endemic transmission with outbreaks in highly vaccinated school populations (coverage >96%)
- Breakthrough cases are contagious
- Vaccine effectiveness one dose ~80-85%
  - Incomplete protection after 1st dose
- Improved vaccine efficacy* with 2 doses
  - 98% varicella of any severity
  - 100% severe disease

* Improved efficacy confirmed by field experiences which found a median of 95% 2-dose varicella vaccine effectiveness against varicella of any severity.
US EXPERIENCE WITH TWO DOSE VARICELLA VACCINE
Two-dose varicella vaccination program impact – VASP sites, 2005-2010

Routine 2 dose program recommended

2006-2010:
78% decline AV
79% decline WP

Cases per 1000 population

Year

Antelope Valley
West Philadelphia
## Reduction in age-specific incidence rates – VASP sites, 2006-2010

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<th>Age (years)</th>
<th>Antelope Valley, CA (%)</th>
<th>West Philadelphia, PA (%)</th>
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<tbody>
<tr>
<td>&lt;1</td>
<td>81.5</td>
<td>6.1</td>
</tr>
<tr>
<td>1-4</td>
<td>55.9</td>
<td>72.7</td>
</tr>
<tr>
<td>5-9</td>
<td><strong>88.3</strong></td>
<td><strong>92.9</strong></td>
</tr>
<tr>
<td>10-14</td>
<td><strong>78.5</strong></td>
<td><strong>95.7</strong></td>
</tr>
<tr>
<td>15-19</td>
<td>36.1</td>
<td>43.8</td>
</tr>
<tr>
<td>20+</td>
<td>55.6</td>
<td>58.6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>77.5</strong></td>
<td><strong>78.7</strong></td>
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</tbody>
</table>
# Varicella outbreak characteristics

**VASP - Antelope Valley, CA, 1995-2010**

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<thead>
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<tbody>
<tr>
<td>Number of outbreaks</td>
<td>236</td>
<td>42</td>
<td>46</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>Median cases (range)</td>
<td>15 (5-124)</td>
<td>11.5 (5-56)</td>
<td>9 (5-45)</td>
<td>9 (5-17)</td>
<td>8 (5-10)</td>
</tr>
<tr>
<td>% of outbreaks with 10 or more cases</td>
<td>72%</td>
<td>55%</td>
<td>41%</td>
<td>37%</td>
<td>25%</td>
</tr>
<tr>
<td>Duration outbreak (range)</td>
<td>45 (7-198)</td>
<td>39 (1-149)</td>
<td>30 (3-90)</td>
<td>29 (4-61)</td>
<td>43 (5-52)</td>
</tr>
<tr>
<td>Age case patients, median (range)</td>
<td>6 (0-59)</td>
<td>6 (0-40)</td>
<td>9 (0-49)</td>
<td>9 (0-19)</td>
<td>13 (6-41)</td>
</tr>
<tr>
<td>Percent cases vaccinated</td>
<td>2%</td>
<td>21%</td>
<td>49%</td>
<td>70%</td>
<td>68%</td>
</tr>
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Severe varicella disease in the 2-dose era

- Analysis of national varicella hospitalization data in progress
- Updated mortality analysis (unpublished data)
  - No varicella deaths were reported among persons <20 years in 2010-2011 versus an annual average of 2 deaths in the 1-dose era and 48 deaths during the pre-vaccine era
Varicella vaccine and herpes zoster (HZ)

- Effect in community will depend on effect in vaccinated and unvaccinated cohorts
- In vaccinated healthy and immunocompromised children
  - Varicella vaccine also prevents herpes zoster
    - VE 68% - 100%
  - Declines in HZ incidence in vaccinated cohorts described US, Canada
- In persons with history of varicella
  - Models predicted increases based on assumptions about role of and duration of external boosting from exposure to children with varicella
  - Real world data?
Is risk for HZ increasing in the US?

Yes, but ..... 

No evidence that this increase is related to the varicella vaccination program 

- Increased risk predates program 
- Increased risk in countries without varicella vaccination program 
- Increase seen in unvaccinated cohorts across all ages 
- An increase in some unrecognized risk factor for HZ is responsible?
Conclusions: impact of varicella vaccination program in US

- ≈20 years of experience with routine use of varicella vaccine in the US
- Varicella vaccine
  - Good safety profile with rare confirmed serious adverse events, most commonly in immunocompromised children
  - Markedly decreases the risk and severity of varicella and, over the short term, herpes zoster in vaccinated children
  - One dose is ≈ 85% effective in preventing all varicella and ≈ 100% effective in preventing severe varicella and 68-100% effective in preventing HZ; higher 2-dose effectiveness against all varicella
- Vaccine impact documented
  - Declines in varicella incidence, hospitalizations and mortality to very low levels
  - Herd immunity effect, no increase in incidence or severe outcomes in adults
  - Increases in herpes zoster cannot be attributed to varicella vaccination programs
THANK YOU

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov    Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.