**Vaccine Recommendations for Health Professionals: Science, Perceptions & Myths**

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**Categories of Immunity**

- **Natural Active**: recovery from symptomatic or asymptomatic disease.
- **Natural Passive**: cross-placental transfer of Ab; colostrum.
- **Artificial Active**: vaccination with Ag.
- **Artificial Passive**: temporary protection from injection of exogenous Ab.

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**Protection Against Infection**

- Antimicrobials -- therapeutic or prophylactic
- Recovery from Disease
- Immunization -- prophylactic

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**Impact of Vaccine in the 20th and 21st Centuries**

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Morbidity</th>
<th>2013 Reported Cases</th>
<th>% Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>29,005</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21,053</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>28,639</td>
<td>86%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>28</td>
<td>96%</td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>16,316</td>
<td>1</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>187</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>584</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>9</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>CRS</td>
<td>152</td>
<td>1</td>
<td>99%</td>
</tr>
<tr>
<td><em>Haemophilus influenza</em></td>
<td>20,000 (est.)</td>
<td>31$^\dagger$</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>
Comparison of Pre-Vaccine Era Estimated Annual Morbidity with 2013 Estimate

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pre-Vaccine Era Annual Estimate</th>
<th>2013 Estimate (unless otherwise specified)</th>
<th>% Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>117,333</td>
<td>2,890</td>
<td>98%</td>
</tr>
<tr>
<td>Hepatitis B (acute)</td>
<td>66,232</td>
<td>18,800</td>
<td>72%</td>
</tr>
<tr>
<td>Pneumococcus (invasive)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages &lt;5 years of age</td>
<td>63,067</td>
<td>33,500</td>
<td>47%</td>
</tr>
<tr>
<td>Rotavirus (hospitalizations &lt;3 years of age)</td>
<td>62,500</td>
<td>12,500**</td>
<td>80%</td>
</tr>
<tr>
<td>Varicella</td>
<td>4,085,120</td>
<td>167,490</td>
<td>96%</td>
</tr>
</tbody>
</table>

US Childhood Infections / Year Before Vaccines

- Polio: paralyzed 10,000 children.
- Rubella (German measles): birth defects & mental retardation in as many as 20,000 newborns.
- Measles: infected about 4 million children, killing 3,000.
- Diphtheria: one of most common causes of death in school-age children.
- Haemophilus influenzae type b (Hib): caused meningitis in 15,000 children.
- Pertussis (whooping cough): killed thousands of infants.

Burden of Vaccine-Preventable Diseases – U.S.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Annual Burden of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>200,000 hospitalizations; 36,000 deaths (&gt;90% in older adults)</td>
</tr>
<tr>
<td>Invasive pneumococcal disease</td>
<td>44,000 cases, 4500 deaths (higher rates of both in older adults and persons with comorbidities)</td>
</tr>
<tr>
<td>Hepatitis B (HBV)</td>
<td>51,000 infections (95% adults); 2000-3000 deaths; 1.25 million with chronic HBV infection</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>6.2 million new infections</td>
</tr>
<tr>
<td>Pertussis</td>
<td>10,454 cases reported in 2007 (3152 adults) Severe illness in infants; often transmitted by older child or adult</td>
</tr>
<tr>
<td>Zoster</td>
<td>1 million cases; risk for shingles and postherpetic neuralgia increases with age</td>
</tr>
</tbody>
</table>

Properties of an Ideal Vaccine

- Immunogenic: stimulates protective immune response
- Safe, no side effects, non-allergenic
- Provides lifelong immunity
- Requires only one administration
- Does not increase susceptibility to other diseases
- Can be administered to immune competent & immune compromised recipients
- Inexpensive

NO VACCINE IS 100% FULL-PROOF
Time to Develop a Vaccine
Duration between discovery of microbial etiology of selected Infectious Diseases & development of a Vaccine

<table>
<thead>
<tr>
<th>Disease</th>
<th>Year of Discovery</th>
<th>Year of Vaccine</th>
<th>Years Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid</td>
<td>1884</td>
<td>1989</td>
<td>155 years</td>
</tr>
<tr>
<td>Pertussis</td>
<td>1906</td>
<td>1955</td>
<td>49 years</td>
</tr>
<tr>
<td>Polio</td>
<td>1908</td>
<td>1955</td>
<td>47 years</td>
</tr>
<tr>
<td>Measles</td>
<td>1953</td>
<td>1955</td>
<td>42 years</td>
</tr>
<tr>
<td>HPV</td>
<td>1974</td>
<td>2007</td>
<td>33 years</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>1973</td>
<td>1980</td>
<td>23 years</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1955</td>
<td>1991</td>
<td>16 years</td>
</tr>
<tr>
<td>HIV</td>
<td>1983</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Evolution of Immunization Programs and Prominence of Vaccine Safety

Annual Impact of Influenza: U.S.
- Highly infectious viral respiratory illness caused by influenza viruses.
- Est. 10-20% US population get the flu each year.
- ~ 114,000 excess hospitalizations / year for flu-related complications since 1969.
- Up to 40 million require outpatient visits.
- ~ 24,000 annual deaths from complications (1976-2007)
- Highest rates of complications & hospitalizations among young children & persons > 65 yrs old.
- > 90% of deaths occur in person age 65 or older.
- 7th leading cause of US death. CDC
Influenza Virus Nomenclature

3 Influenza Virus Types:
A: epidemics & pandemics
B: epidemics only
C: rare in humans

- A/Moscow/21/99 (H3N2)

<table>
<thead>
<tr>
<th>Type of nuclear material</th>
<th>Hemagglutinin</th>
<th>Neuraminidase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus type</td>
<td>Geographic origin</td>
<td>Strain number</td>
</tr>
<tr>
<td>Virus subtype</td>
<td>Year of isolation</td>
<td>Virus subtype</td>
</tr>
</tbody>
</table>

Influenza Virus Transmission

- Person-to-person: respiratory droplets
- Direct contact with person-contaminated object before washing hands.
- Incubation period 2 days (range 1-4 days)
- Adults infectious 1 day before symptoms thru 5 days after onset of illness (children up to 10 days).
- Abrupt symptoms: fever, myalgia, sore throat, malaise, nonproductive cough, headache
- HCW at high risk
- Confused with “bad cold?”
- cross-rx Ab’s between strains

Influenza Vaccine (2014-2015)

- an A/California/7/2009 (H1N1)pdm09-like virus
- an A/Texas/50/2012 (H3N2)-like virus
- a B/Massachusetts/2/2012-like virus.

CDC (9/2014)

2015-2016 Flu Vaccine

All of the 2015-2016 influenza vaccine is made to protect against the following three viruses:
- an A/California/7/2009 (H1N1)pdm09-like virus
- an A/Switzerland/9715293/2013 (H3N2)-like virus
- a B/Phuket/3073/2013-like virus. (a B/Yamagata lineage)

CDC (8/2015)
Influenza Vaccine

- Preparations are strain specific—use of current year strain for vaccine (due to viral “antigenic drift”)
- High-dose vaccine for elderly
- Recent vaccine advance for people c egg allergy (Flublok)
- Goal: reduce influenza complications and mortality
- ~70-90% recipients develop protective Ab’s
- Contraindications:
  - Pregnancy (1st trimester)
  - Allergy to eggs (?) or thimerosal (only in multi-dose vials)

Note: Do not get flu from vaccine!!

Influenza Vaccines

- Inactivated Trivalent (IIV₃), Standard Dose
- Inactivated Trivalent (IIV₃), High Dose
- Inactivated Quadrivalent (IIV₄), Standard Dose
- Live Attenuated Quadrivalent (LAIV₄) Vaccine
- Recombinant Trivalent (RIV₃) Vaccine – new for 2013-2014
  - Flublok: approved for adults 18-49 yrs old
  - does not use influenza virus or eggs in manufacturing process
  - consists only of HA from influenza virus (prepared by placing gene for HA into a virus that infects insect cells)
  - altered cells grown in culture & produce HA antigens
  - meets FDA stds for safe & suitable vaccines

Dental Occupational Risks & Influenza Control

Surveys in mid-1980’s: high risk for dental hygienists failure to wear protective masks during tx.

Infection prevention steps:
- Get vaccinated.
- Take approved anti-influenza prophylactic drugs (amantadine, rimantadine, & oseltamivir)
- Avoid close contact with people who are sick.
- Keep distance from others when you are sick.
- Wash hands often.
- Cover mouth & nose when coughing / sneezing.
## Est. Number & Proportion of Deaths in Persons < 65 Yrs in U.S. for Seasonal & Pandemic Influenza

<table>
<thead>
<tr>
<th>Pandemic/ Season</th>
<th>Total Estimated Deaths</th>
<th>% Deaths &lt; 65 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918 H1N1 Pandemic</td>
<td>546,000</td>
<td>99%</td>
</tr>
<tr>
<td>1957-58 H2N2 Pandemic</td>
<td>66,000</td>
<td>36%</td>
</tr>
<tr>
<td>1968-69 H3N2 Pandemic</td>
<td>36,400</td>
<td>48%</td>
</tr>
<tr>
<td>1976-2007 Seasonal</td>
<td>23,000</td>
<td>10%</td>
</tr>
<tr>
<td>2009-2010 H1N1 Pandemic</td>
<td>12,470</td>
<td>87%</td>
</tr>
</tbody>
</table>

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## Pneumococcal Disease

- Most common cause of US vaccine-preventable death.
- Most common cause of infant/young child bacterial meningitis.
- Increasing antibiotic resistance
- ~100,000 - 135,000 hospitalized cases/year.
- ~36% of adult community-acquired pneumonia & 50% of hospital-acquired pneumonia.
- Common bacterial complication of influenza and measles.
- Case-fatality rate 5%-7%, higher in elderly.  
  
  CDC (2010)

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## S. pneumoniae Pneumonia

Images A and B show typical symptoms of S. pneumoniae pneumonia, including lung consolidation and bacterial colonies.
**Pneumococcal Bacteremia**

- More than 50,000 cases per year in US
- 4-12% hospital-associated bacteremic infections
- 5-10% pts hospitalized with community-acquired pneumonia
- Rates higher among elderly & very young infants
- Case fatality rate ~20%; up to 60% among the elderly

![Encapsulated Streptococcus pneumoniae](image)

**Pneumococcal Vaccines**

- 1977 14-valent polysaccharide vaccine licensed
- 1983 23-valent polysaccharide vaccine licensed (PPV23)
- 2000 7-valent polysaccharide conjugate vaccine licensed (PCV7)
- 2012 13-valent polysaccharide conjugate vaccine licensed (PCV13)

✓✓ ✓✓ Purified capsular polysaccharide antigen from multiple pneumococcus types
✓✓ ✓✓ Account for 88% of bacteremic pneumococcal disease
✓✓ ✓✓ Cross-react with types causing additional 8% of disease

**Varicella Epidemiology**

- Reservoir: Human
- Transmission: Airborne droplet
- Direct contact with lesions
- Temporal pattern: Peak in winter and early spring (U.S.)
- Communicability: 1-2 days before to 4-5 days after onset of rash; may be longer in compromised pts
- Most transmissions via droplets (efficient with close contact)
- Serious morbidity & mortality in neonates & adults
- Lower transmission risks from herpes zoster cases to non-immune

[Source: CDC]
### Varicella-Zoster Virus (VZV)

- Human alpha-herpesvirus
- Causes varicella (chickenpox) and herpes zoster (shingles)
- Primary VZV infection leads to varicella
- VZV latency in dorsal root ganglia after primary infection
- VZV can reactivate at a later time, causing herpes zoster
- 3 licensed vaccines to prevent varicella (Varivax®, Proquad®) and herpes zoster (Zostavax®) in the US:
  - Varivax® (licensed 1995); Proquad® (licensed 2005)
  - Zostavax® (licensed 2006)

### Varicella Complications

- Bacterial infection of lesions
- CNS manifestations
- Pneumonia (rare in children)
- Hospitalization ~3 per 1,000 cases
- Death ~1 per 60,000 cases

Varicella super-infected with *S. aureus* pyoderma

### Varicella & Adults

- Adult chickenpox more severe
- ~1-2% adults with chickenpox require hospitalization
- 60-86% US HCW report previous chickenpox
- Can check for primary Varicella Hx by serology assay
- Hx of prior household exposure in absence of clinical illness NOT reliable immunity indicator
- Overall HCW susceptibility 1 – 7% CDC/UDM
### 3 Types of Varicella – Containing Vaccines:

- **Varicella vaccine (Varivax)**
  - approved for persons 12 months and older
- **Measles-mumps-rubella-varicella vaccine (ProQuad)**
  - approved for children 12 months through 12 years
- **Herpes zoster vaccine (Zostavax)**
  - approved for persons 60 years and older

### Vaccine Recommendations for Adolescents & Adults:

- All persons 13 years of age and older without evidence of varicella immunity
- 2 doses separated by at least 4 weeks
- Do not repeat 1st dose because of extended interval between doses

### Incidence of varicella in states meeting criteria for adequate & consistent reporting & number of states reporting:

#### United States, 2000–2010

- 26/31 states reported varicella data were adequate & consistent
- Overall decline in these 26 states was 79% (2000 - 2010) [CDC (8/2012)]

### Herpes Zoster (Shingles)

- Reactivation of varicella zoster virus
- Can occur years or even decades after illness with chickenpox
- Generally associated with normal aging and with anything that causes reduced immune competence
- Lifetime risk (est.) ~32%
- Estimated 500,000-1 million cases of zoster diagnosed annually in the U.S
- 50% persons <85 yrs will develop zoster
VZV Vaccination for Older Adults: HCW Implications

- tested hypothesis: would VZV vaccination decrease incidence &/or severity of herpes zoster &/or post-herpetic neuralgia among older adults.
- 38,546 adults 60 yrs & older, placebo-controlled trial of investigational live, attenuated VZV vaccine.
- VZV vaccination:
  - reduced illness burden by 61.1%
  - reduced post-herpetic neuralgia by 66.5%
  - reduced herpes zoster incidence by 51.3%

Herpes Zoster Vaccine (Zostervax)

- 2006: Approved single dose among persons 60 years & older
- significantly reduces post-herpetic neuralgia risk
- may vaccinate regardless of prior history of herpes zoster (shingles)
- persons with a chronic medical condition may be vaccinated unless a contraindication or precaution exists for the condition
- 2011: FDA expanded age indication to include adults 50 - 59 years old
  - study showing vaccine reduced zoster risk by ~ 70% in certain adult groups, BUT efficacy decreased with recipient age:
    - 50 – 59 yrs: 68.9%
    - >70 yrs: 37.6%
- 2nd generation subunit vaccine being tested
  - 96.6 – 97.9% efficacy for all age groups tested

U.S. Adult Vaccination Coverage:
(Selected Vaccines by Age & High-risk Status)

- Pneumococcal, HR 19-64 yrs
- Pneumococcal, ≥65 yrs
- Herpes Zoster (Shingles), ≥60 yrs

Data Source: 2012 NHIS

*HP2020 Targets: 60% PPV1HR 19-64 years, 90% PPV≥65 years, 30% Shingles
Global Impact of Pertussis & Resurgence of a Vaccine-Preventable Disease

- "Whooping cough" caused by *Bordetella pertussis*
- 2014: 140,000 reported cases, c estimates # much higher
- 89,000 est. deaths
- high burden of disease in developing countries
- among leading causes of vaccine-preventable deaths.
- case-fatality rates in developing countries 4% in infants?
- high immunization coverage with effective vaccine is mainstay of prevention
- 85% global DTP3 vaccine coverage WHO 2015

Reported NNDSS pertussis cases: 1922-2014*

Changes in Pertussis Reporting by State from 2013 to 2014* 2015

18% increase over 2013
### Pertussis Epidemiology

- **Reservoir:** Human
  - Adolescents and adults
- **Transmission:** Respiratory droplets
- **Communicability:**
  - Maximum in catarrhal stage
  - Secondary attack rate up to 80%
- **Incubation period:**
  - Usually 7-10 days (range 4-21 days)
- **Insidious onset:**
  - Similar to minor upper respiratory infection with nonspecific cough
- **Fever:**
  - Usually minimal throughout course of illness
- **Coughing fits:**
  - Can last for up to 10 weeks or more
- **Institutional outbreaks:**
  - Common in schools as vaccine immunity fades

### Pertussis Stages

<table>
<thead>
<tr>
<th>Disease Progression:</th>
<th>Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1: Catarrhal Stage</td>
<td>0-2 weeks</td>
</tr>
<tr>
<td>May last 1 to 2 weeks</td>
<td></td>
</tr>
<tr>
<td>Symptoms: runny nose, low-grade fever, mild, occasional cough - highly contagious</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage 2: Paroxysmal Stage</th>
<th>Start from</th>
<th>Lasts from 2 weeks; may extend to 10 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms: fits of numerous, rapid coughs followed by &quot;whops&quot; sound; vomiting and exhaustion after coughing fits (called paroxysms)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage 3: Convalescent Stage</th>
<th>Lasts about 2-3 weeks; recoverable or other respiratory infections may occur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovery is gradual; Coughing lessens but fits of coughing may return</td>
<td></td>
</tr>
</tbody>
</table>

### Adults and Pertussis – HCW Tips?

- Neither acquisition of the disease nor vaccination provides complete or lifelong immunity
- 1 attack usually provides immunity for many years, but immunity wanes with time
- Attack rate over 50% reported when post-immunization interval is > 12 years
- Adult disease often milder than in infants/children
- Infection may be asymptomatic, or as classic pertussis
- Older persons often source of infection for children
Pertussis Vaccines

**Table: Pertussis-Containing Vaccines for Children and Adults**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Brand</th>
<th>Licensed Date</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP</td>
<td>INFANRIX/DAPTACEL</td>
<td>First licensed in 1991; used for all doses</td>
<td></td>
</tr>
<tr>
<td>DTaP+Hib</td>
<td>TRIVAX/HEPL ки</td>
<td>Used for the fourth dose only</td>
<td></td>
</tr>
<tr>
<td>DTaP+IPV+Hib</td>
<td>PEDIMAR</td>
<td>Used for the first three doses</td>
<td></td>
</tr>
<tr>
<td>DTaP+IPV+Hib</td>
<td>PENIONS</td>
<td>Approved in 2008; used for primary four-dose series</td>
<td></td>
</tr>
<tr>
<td>DTaP+IPV</td>
<td>KINRIX</td>
<td>Approved in 2008; used for booster dose at 4-6 years</td>
<td></td>
</tr>
</tbody>
</table>

**Tdap Recommendations for Adolescents**

- Preteens at age 11 or 12 years
- Teens aged 13 through 18 years who did not receive Tdap at age 11 or 12 years

**Tdap Recommendations for Adolescents and Adults**

- Tdap should be administered regardless of interval since the last tetanus or diphtheria toxoid-containing vaccine
- Tdap vaccine can be administered at the same time as other adolescent vaccines
Some People Should NOT Get Tdap Vaccine

- a life-threatening allergic rx after a previous dose of any diphtheria, tetanus or pertussis containing vaccine,
- severe allergy to any part of vaccine.
- coma or long repeated seizures within 7 days after a childhood dose of DTP or DTaP, or a previous dose of Tdap, should not get Tdap, unless a cause other than the vaccine was found.
- can still getTd.

Talk to your doctor if you:
- have seizures or another nervous system problem,
- had severe pain or swelling after any vaccine containing diphtheria, tetanus or pertussis,
- ever had Guillain Barré Syndrome (GBS), or aren't feeling well on the day the vaccine is scheduled.

CDC (2/24/2015)

Pertussis Vaccination Rates

Toddlers (19-35 months) Vaccinated 85%
Unvaccinated 15%

Teens (13 – 17 years) Vaccinated 78%

Adults (19 -64 years) Vaccinated 8%
Unvaccinated 92%

CDC (9/2012)

Human Papillomavirus (HPV)

- More than 100 types
- Established cause of cervical and other anogenital cancers (anal, penile cancer)
- Worldwide cervical cancer causes 233,000 deaths per year
- Genital warts
Human Papillomavirus (HPV)

- Most common sexually transmitted pathogen in males and females
  - 6.2 million new infections in US annually
  - 20 million people infected
  - Highest prevalence in sexually active adolescents and young adults
- First infection occurs soon after onset of sexual activity

Percentage of Adolescents Who Have Had Vaginal Sex, By Gender and Age

Human Papillomavirus (HPV)

- Small DNA virus
- More than 100 types identified based on the genetic sequence of the outer capsid protein L1
- 40 types infect the mucosal epithelium
- Most HPV infections asymptomatic --- no clinical disease
- Clinical manifestations of HPV infection include:
  - anogenital warts
  - recurrent respiratory papillomatosis
  - cervical cancer precursors (cervical intraepithelial neoplasia
  - cancer (cervical, anal, vaginal, vulvar, penile, some head & neck cancer)
Human Papillomavirus Types and Disease Association

Human Papillomavirus (HPV) types can be categorized into:
- Mucosal/genital types (~40 types)
  - High-risk types: 16, 18, 31, 45 (and others)
  - Low-risk types: 6, 11 (and others)
- Nonmucosal/cutaneous types (~60 types)
  - Skin warts (hands and feet)

HPV types and their associations:
- **Woman**
  - Low grade cervical abnormalities
  - Cancer precursors
  - Anogenital cancers
- **Man**
  - Low grade cervical abnormalities
  - Genital warts
  - Laryngeal papillomas

HPV Epidemiology

- **Reservoir** Human
- **Transmission** Direct contact, usually sexual
- **Temporal pattern** None
- **Communicability** Presumed to be high

HPV-Associated Disease

<table>
<thead>
<tr>
<th>Type</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>16/18</td>
<td>70% of Cervical Cancer</td>
<td>70% of Anal Cancer</td>
</tr>
<tr>
<td></td>
<td>70% of Anal/genital Cancer</td>
<td>Transmission to women</td>
</tr>
<tr>
<td>6/11</td>
<td>90% of Genital Warts</td>
<td>90% of Genital Warts</td>
</tr>
<tr>
<td></td>
<td>90% of RRP lesions</td>
<td>90% of RRP lesions</td>
</tr>
<tr>
<td></td>
<td>Transmission to women</td>
<td>Transmission to women</td>
</tr>
</tbody>
</table>
HPV Vaccine (HPV4) Timeline

- Gardasil (HPV4) against HPV types 6, 11, 16, & 18 (FDA-licensed 6/2006)
- Bivalent vaccine (Cervarix) against HPV 6 & 18 (10/2009)
- HPV4 licensed for use in males 9-26 yrs to prevent genital warts (10/2009)
- FDA adds prevention of anal cancer (M & F) as indication for use (12/2010)
- ACIP 10/2011: (replaces 10/2009 recommendations)
  -- recommendation for HPV4 in males 11-12 yrs, & males 13-21 yrs who have not been vaccinated or completed 3-dose regimen

Available HPV vaccines

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Bivalent (Cervarix)</th>
<th>Quadrivalent (Gardasil)</th>
<th>9-valent (Gardasil 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GlaxoSmithKline</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
<td></td>
</tr>
<tr>
<td>Merck</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1 VLP types</td>
<td>16, 18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjuvant</td>
<td>AS04: 500 μg aluminum hydroxide, 50 μg 3-β-d-glucopyranosyl-2′,4′-nonsulfate lipid A</td>
<td>AS03A: 20 μg amorphous aluminum phosphate octahydrate, 500 μg amorphous aluminum phosphate dihydrate</td>
<td></td>
</tr>
<tr>
<td>Licensed</td>
<td>females 9-25 years</td>
<td>females 9-26 years</td>
<td>females 9-26 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>males 9-26 years</td>
<td>males 9-15 years</td>
</tr>
</tbody>
</table>

L1 – Major capsid protein; VLP – virus like particle

9-Valent HPV Vaccine (9vHPV)

- Licensed by FDA December 10, 2014
  - Females 9-26 yrs, males 9-15 yrs
  - Trials conducted with 3-dose schedule
- L1 VLP vaccine, similar to quadrivalent HPV vaccine
- Targets 5 additional high risk types (6,11,16,18,31,33,45,52,58)
- Males 16-26 yrs - not part BLA submitted in 2013
  - Data presented to ACIP October 2014
  - sBLA submitted to FDA
Human Papillomavirus Vaccine

- HPV L1 major capsid protein of the virus is antigen used for immunization
- L1 protein expressed in yeast cells using recombinant technology
- L1 proteins self-assemble into virus-like particles (VLP)
- VLPs are noninfectious and nononcogenic
- Routine 3-injection schedule: 0, 2, 6 months
HPV Vaccine Efficacy*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 16/18-related CIN2/3 or AIS</td>
<td>100</td>
</tr>
<tr>
<td>HPV 6/11/16/18 related CIN</td>
<td>95</td>
</tr>
<tr>
<td>HPV 6/11/16/18 related genital warts</td>
<td>99</td>
</tr>
</tbody>
</table>

*Among 16-26 year old females. CIN – cervical intraepithelial neoplasia; AIS – adenocarcinoma in situ

HPV vaccine safety monitoring - VAERS

- From 6/2006 through 3/2013 ~56 million HPV4 doses distributed in the United States
- No new safety concerns have been identified in post-licensure vaccine safety surveillance among male or female recipients of HPV4 vaccine
  - Among the 7.9% of reports coded as “serious”, most frequently cited are headache, nausea, vomiting, fatigue, dizziness, syncope, generalized weakness
- Syncope continues to be a frequently reported AEFI among adolescents
  - Adherence to a 15-minute observation period after vaccination is encouraged

Vaccine Protection Against Oral HPV Infection?

- Same types of HPV that infect genital areas can infect mouth & throat.
- HPV can cause oropharyngeal cancers
- Preliminary study (2013): - Costa Rica vaccine trial
  - 7,000 women (18-25 yrs old) rec’d either Cervarix or HAV vaccine (control)
  - 4 yrs later: only 16 women had oral HPV infection
    (1 in HPV vaccine group & 15 in comparison group)
  - 93% reduction in HPV infection in women ≥ HPV vaccine
  - Promising, but preliminary, evidence that HPV vaccines might prevent most oral HPV infections, AND have significant impact on prevalence of throat cancer
  - More investigations required – small sample size & more men get throat cancer than women.
General Vaccination Contraindications

**Absolute:**
1. acute systemic febrile illness
2. any severe, neurological reaction to previous vaccine dose.
3. anaphylactic reaction to eggs -- a contraindication to MMR.

**Special consideration needed:**
1. neonatal cerebral damage, convulsions, or idiopathic epilepsy
2. children with family HX of above
3. immune suppression
4. pregnancy

Severe Recurrent HSV Episode in Immune Compromised Patient
Importance of “Herd Immunity” on Public Health

- individuals who are immune to a communicable disease will not be carriers, & thus –
- cannot spread infection to susceptible persons
- occurrence of the pathogen will therefore be reduced in the population
- the larger the “herd” of protected people, the lower the risk for an epidemic to occur

Herd Immunity

The larger the immune “Herd,” the greater the protection for those in the population who are susceptible by not having immunity from disease recovery or vaccination.

Measles Timeline U.S.:
- 1920 - 469,924 U.S. cases (7,575 deaths)
- 1941 - 894,134 cases
- 1954 - measles virus isolated
- 1962 - 503,282 cases (432 deaths)
- 1963 - first live measles vaccine licensed
- 1968 - improved live measles vaccine licensed
- 1958 - first measles vaccine is tested
- 1970 - 47,351 cases (89 deaths)
- 1971 - MMR vaccine introduced
- 1978 - 26,871 cases (measles targeted for eliminated in U.S. by 1982)
- 1983 - 1,497 cases
- 2010 - 61 cases
- 2011 - 220 cases
- 2012 - 55 cases
- 2013 - 189 cases, including large NYC outbreak - 58 cases.
- 2014 - 644 cases

CDC/ JAM (2015)
Measles Epidemiology

- **Reservoir**: Human
  - Adolescents and adults
- **Transmission**: Airborne; respiratory droplets
- **Communicability**: 4 days before to 4 days after rash onset
- **Incubation period**: 10-12 days
  - **Prodrome**: 2-4 days before rash onset
    - Cough, coryza, conjunctivitis, Koplik spots (rash on mucous membranes)
  - **Rash**: 2-4 days after prodrome, 14 days after exposure
    - Persists 5-6 days (begins on face & upper neck)
    - Maculopapular, becomes confluent
    - Fades in order of appearance

Measles (Rubeola) Vaccine

- **Composition**: Live virus
- **Efficacy**: 95% at 12 months of age
  - 98% at 15 months of age
- **Duration of Immunity**: Lifelong
- **Schedule**: 2 Doses
  - Should be administered with mumps & rubella as MMR or with mumps, rubella and varicella as MMRV

Indications

- All children 12 months of age & older
- Susceptible adolescents & adults without documented evidence of immunity
- Single-antigen measles vaccine not available in U. S.

94% Reduction in reported measles cases

Measles global annual reported cases and MCV1 coverage*, 1980-2012

* MCV1 coverage is coverage with first dose of measles-containing vaccine as estimated by WHO and UNICEF

\[ \text{Number of cases} \times \text{MCV1 Coverage} \]
Majority of people who have contracted measles were unvaccinated. Measles is still common in many parts of the world including some countries in Europe, Asia, the Pacific, and Africa. Travelers with measles continue to bring disease into U.S.

**June 29, 2015: California governor signed strict vaccination law exemptions only for children with serious health issues**

2014-15 Measles Outbreak: Latest Example of worsening public health problem

- Different State Rules
  - On Vaccinations: California (<51% preschool children measles vaccine)** vs. Mississippi (99.7%)
  - Majority of people who have contracted measles were unvaccinated.
  - Measles is still common in many parts of the world including some countries in Europe, Asia, the Pacific, and Africa.
  - Travelers with measles continue to bring disease into U.S.

**Issues - Concerns - Misconceptions**

- Is there a relationship between vaccines & autism spectrum disorders?
- Are we weakening children’s immune systems by giving too many vaccines?
- Are children getting more vaccines than necessary in today’s world?
- Is the mercury in the vaccine preservative thimerosal causing autism & other disorders?  
  JAM
Misperceptions About Vaccines

Myth 1: “I am healthy. I don’t need the flu vaccine.”
Myth 2: “Last time I got the influenza vaccine I came down with the flu.”
Myth 3: “I had a tetanus shot as a child. I don’t need another one.”
Myth 4: “I already had shingles. I don’t need a vaccine.”
Myth 5: “The shingles vaccine is not safe.”

By immunizing all babies in a given yr –
✓ prevent 14 million infections
✓ save 33,000 lives
✓ save $10 billion by the time children reach adolescence CDC

Opting Out:
2 – 3% of US school-age children whose parents have rec’d religious or philosophical exemption from state vaccination requirements, with the #’s increasing

Exemptions Permitted to School and Childcare Immunization Requirements
January 2015

CDC

*Adverse: Personal/medical exemptions permitted for school only
**Adverse: Personal/medical exemptions permitted for childcare only
### Rep. Childhood Vaccine Investigations

- Wakefield report in *The Lancet* determined to be a sham.
- Thimerosal preservative - ethyl vs. methyl mercury issues
- Children showed symptoms & were diagnosed with autism regardless of whether they were vaccinated before or after 18 months of age
- No epidemiological evidence for causal association between autism & MMR vaccine
- Population-based studies of MMR vaccination & autism (multiple published investigations)
- Early thimerosal exposure & neuropsychological outcomes at 7-10 years  
  *JAMA* (2016)

### Science Disproving a Risk for Autism from Vaccines (Representative Studies)

  
  “… analyses do not support a causal association between MMR vaccine and autism.”

  
  “study provides strong evidence against the hypothesis that MMR vaccination causes autism.”

  
  “results do not support a causal relationship between childhood vaccination with thimerosal-containing vaccines and development of autistic-spectrum disorders.”

  
  “does not support a causal association between early exposure to mercury …and deficits in neuropsychological functioning at...7 to 10 years.”

### Dangers & Risks of Not Vaccinating Children

- Disease can be more harmful than risks of vaccine side effects
- Parents too young to remember certain vaccine-preventable diseases (i.e. polio, smallpox, rubella)
- Parents question why their children need vaccines
- Increased concern regarding real & perceived side effects as disease incidence declines in US
- Public’s desire for absolute guarantees regarding vaccine efficacy & safety  
  *JAMA*
## WHAT WOULD HAPPEN IF WE STOPPED VACCINATIONS

- **Polio**: could reverse the virtual elimination of polio
- **Measles**: 99% reduction in disease with vaccine
- **Hib meningitis**: 98% incidence decline since vaccination
- **Pertussis**: in 8 countries who reduced immunizations, see a 10-100X increase in disease
- **Rubella**: congenital rubella syndrome
- **Chickenpox**: 4 annual million cases before vaccine
- **Hepatitis B**: major decline in cases since vaccines
- **Mumps**: 212,000 cases (1964); 266 cases (2001) \(\text{CDC/UDM (2005)}\)

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## THANK YOU