Vaccine Safety
Reaction or Coincidence?

April 22 & 23, 2015
Karen Lewis, M.D.
22nd Annual Immunization Conference
Cowpox Vaccination Cartoon 1802
Possible Local Reactions at Vaccine Site

• Common
  – Redness, swelling, warmth, pain

• Local reactions more common when...
  – Pre-existing immunity
  – Strong immune response
  – Adjuvant
  – Subcutaneous versus intramuscular
Examples of Possible Systemic Reactions after Vaccination

• More common
  – Fever
  – Malaise, tiredness, headache
  – Rash

• Rare events
  – Febrile seizure
  – Anaphylaxis
  – Autoimmune
  – Neurologic: Guillain Barré Syndrome, ADEM, seizure
# Measles

Source: [cdc.gov](http://cdc.gov)

<table>
<thead>
<tr>
<th>US &amp; Measles</th>
<th>1950</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>319,124</td>
<td>43</td>
</tr>
<tr>
<td>Deaths</td>
<td>468</td>
<td>0</td>
</tr>
</tbody>
</table>
# Rubella

<table>
<thead>
<tr>
<th></th>
<th>1970</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>US &amp; Rubella</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rubella Cases</td>
<td>57,686</td>
<td>11</td>
</tr>
<tr>
<td>Deaths from Rubella</td>
<td>29</td>
<td>1</td>
</tr>
<tr>
<td>Congenital Rubella Syndrome</td>
<td>62</td>
<td>0</td>
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</table>

Source: cdc.gov
Mumps

<table>
<thead>
<tr>
<th>US &amp; Mumps</th>
<th>1968</th>
<th>2007</th>
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</thead>
<tbody>
<tr>
<td>Cases</td>
<td>152,209</td>
<td>800</td>
</tr>
<tr>
<td>Deaths</td>
<td>25</td>
<td>0</td>
</tr>
</tbody>
</table>

Source: cdc.gov
MMR Vaccine Reactions

• Live attenuated viruses
• Reactions usually within 5-14 days
• MMR recipient is not contagious
• Anaphylaxis (< 1/1,000,000)

• Mild problems
  – Fever (1/6)
  – Mild rash (1/20)
  – Swelling in glands of cheek or neck (1/75)

• Moderate problems
  – Febrile seizure (1/3,000)
  – Temporary joint pain, esp. women (up to 1/4)
  – Temporary low platelet count (1/30,000)
Quiz: Adverse Events after MMR Likely due to vaccine?

• Fever of 102°F. two days after MMR.
• Swollen lymph nodes along back of the neck one week after MMR
• Low platelets 1 week after MMR
• Small red spots on the trunk 10 days after MMR
• Unilateral swelling of parotid gland 2 months after MMR
**CHICKEN POX**

<table>
<thead>
<tr>
<th></th>
<th>US &amp; Varicella</th>
<th>1972</th>
<th>2007</th>
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</thead>
<tbody>
<tr>
<td>Cases</td>
<td>154,114</td>
<td></td>
<td>40,146</td>
</tr>
<tr>
<td>Deaths</td>
<td>122</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>
Shingles (Herpes Zoster)

Source: CDC PHIL 6886
Varicella Vaccine Reactions

• Vaccine site pain, soreness, redness, swelling
  – 1/5 children; 1/3 adolescents and adults
• Fever 5-12 days after vaccine (<10%)
  – Febrile seizure (very rare)
• Generalized maculopapular or vesicular rash within one month after vaccine (4%)
  – Could be contagious until vesicles scab or M/P rash stops appearing for 24 hours
• Pneumonia (very rare)
MMR-V Vaccine

• Combination of MMR vaccine and varicella vaccine
• Nine times as much varicella virus as with separate varicella vaccine
• Fever and febrile seizures more likely after MMR-V than after MMR + Varicella vaccines given at same time but separately
Adverse Events after Varicella Vaccine Likely due to vaccine?

- Generalized vesicular rash 1 day after vaccine
- Fever of 101°F seven days after vaccine
- Maculopapular, generalized rash 2 months after vaccine
- Vesicular, dermatomal, unilateral rash two years after vaccine
- Vesicular, generalized rash 8 days after vaccine
Rotavirus

• Yearly in US before 2006
  – 20-60 deaths
  – 55,000-70,000 hospitalizations
  – 205,000-272,000 emergency department visits

• WHO estimates globally ~527,000 deaths a year
Possible Reactions after Rotavirus Vaccination

• Live, attenuated vaccine

• Most have no problems

• Sometimes
  – Fussy
  – Mild, temporary diarrhea or vomiting

• Rare
  – Intussusception after 1\textsuperscript{st} or 2\textsuperscript{nd} dose
  – 1:20,000-1:100,000 U.S. infants
Pertussis (Whooping Cough)

<table>
<thead>
<tr>
<th></th>
<th>1950</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>120,718</td>
<td>10,454</td>
</tr>
<tr>
<td>Deaths</td>
<td>1,118</td>
<td>9</td>
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</table>
Pertussis (Whooping Cough)

<table>
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<tr>
<th>Pertussis</th>
<th>1950</th>
<th>2007</th>
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</thead>
<tbody>
<tr>
<td>Cases</td>
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<td>10,454</td>
</tr>
<tr>
<td>Deaths</td>
<td>1,118</td>
<td>9</td>
</tr>
</tbody>
</table>

cdc.gov

CDC PHIL 6379

Health and Wellness for all Arizonans
Diphtheria

<table>
<thead>
<tr>
<th></th>
<th>1950</th>
<th>2007</th>
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</thead>
<tbody>
<tr>
<td>Cases</td>
<td>5,796</td>
<td>0</td>
</tr>
<tr>
<td>Deaths</td>
<td>410</td>
<td>0</td>
</tr>
</tbody>
</table>
Tetanus

<table>
<thead>
<tr>
<th>US &amp; Tetanus</th>
<th>1950</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>486</td>
<td>28</td>
</tr>
<tr>
<td>Deaths</td>
<td>336</td>
<td>5</td>
</tr>
</tbody>
</table>
Antigenic and Biologically Active Components of *B. pertussis*

- pertussis toxin (PT)
- filamentous hemagglutinin (FHA)
- pertactin
- fimbriae
- agglutinogens
- adenylate cyclase
- tracheal cytotoxin
- dermatonecrotic toxin
- adenylate cyclase toxin
- Etc.

Stacey W. Martin, MSc.
CDC Webinar, May 30, 2012
# Components of Pertussis Vaccines

<table>
<thead>
<tr>
<th>Product</th>
<th>Type</th>
<th>PT µg</th>
<th>FHA µg</th>
<th>PERT µg</th>
<th>FIM µg</th>
<th>DIPH Lf</th>
<th>TET Lf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daptacel</td>
<td>DTaP</td>
<td>10</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Infanrix</td>
<td>DTaP</td>
<td>25</td>
<td>25</td>
<td>8</td>
<td>--</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Pentacel</td>
<td>DTaP+</td>
<td>20</td>
<td>20</td>
<td>3</td>
<td>5</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Pediarix</td>
<td>DTaP+</td>
<td>25</td>
<td>25</td>
<td>8</td>
<td>--</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>Adacel</td>
<td>Tdap</td>
<td>2.5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Boostrix</td>
<td>Tdap</td>
<td>8</td>
<td>8</td>
<td>2.5</td>
<td>--</td>
<td>2.5</td>
<td>5</td>
</tr>
</tbody>
</table>
Adverse Events after DTaP Vaccine

**MILD**
- Occurring 1-3 days after shot
- Fever (1/4)
- Redness, swelling, pain (1/4)
  - More severe after 4th or 5th
- Fussiness (1/3)
- Tiredness or poor appetite
  - 1/10
- Vomiting (1/50)

**MODERATE**
- Seizure (1/14,000)
- Non-stop crying for 3 hours or more (1/1000)
- Fever over 105°F. (1/16,000)

**SEVERE** (very rare)
- Anaphylaxis (< 1/1,000,000)
- Long-term seizures
- Permanent brain damage
### Adverse Events after Tdap Vaccine

**MILD**
- Local Pain
  - 3/4 teens; 2/3 adults
- Local redness/swelling (1/5)
- Fever to 100.4°F.
  - 1/25 teens; 1:100 adults
- Headache (3-4/10)
- Tiredness (1/3-4)
- Nausea, vomiting, diarrhea
  - 1/4 teens; 1/10 adults
- Chills, rash (uncommon)

**MODERATE**
- Local pain
  - 1/5 teens; 1/100 adults
- Local redness/swelling
  - 1/16 teens; 1/25 adults
- Fever over 102°F.
  - 1/100 teens; 1/250 adults
- Headache
  - 3/20 teens; 1/10 adults
- Nausea, vomiting, diarrhea
  - 1-3/100
- Entire arm swollen (3/100)
- Fainting
Adverse Events after DTaP or Tdap Likely due to vaccine?

- Redness and pain in arm 2 days after shot
- Persistent cough starting the day after the vaccine
- Fever of 105°F. one week after DTaP
- Crying for 4 hours starting 4 hours after DTaP
- Fainting immediately after Tdap
- Sore throat with exudate one week after DTaP
SYMPTOMS OF INFLUENZA

• Rapid onset
• High fever, chills
• Extreme exhaustion
• Muscle aches
• Dry cough
• Runny nose
• Sore throat
Adverse Events after Influenza Vaccines

**INACTIVATED**

- Soreness, redness, swelling
  - Happen in 15-20%
  - Last 1-2 days
- Fever, chills, malaise, myalgia, fatigue (< 1%)
  - Occur 6-12 hours after shot
  - Last 1-2 days
- Anaphylaxis (< 1 in a million)
- Guillain-Barré Syndrome?

**LIVE, ATTENUATED (nasal)**

- Runny nose, cough, nasal congestion,
- Wheezing (children)

**LESS COMMON (after LAIV)**

- Headache, muscle aches
- Sore throat
- Tiredness
- Vomiting/diarrhea
Adverse Events after Influenza Vaccine Likely due to vaccine?

- Redness and soreness at vaccine site one day after influenza shot
- Fever of 102°F one week after influenza shot
- Pneumonia diagnosed one week after shot
- Vomiting and diarrhea starting 6 hours after an influenza shot
- Runny nose for two days after LAIV
- Sore throat one month after LAIV
Jaundice from Hepatitis A

<table>
<thead>
<tr>
<th></th>
<th>1980</th>
<th>2007</th>
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</thead>
<tbody>
<tr>
<td>US &amp; hepatitis A</td>
<td>30,407</td>
<td>2,979</td>
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<tr>
<td>Cases</td>
<td>129</td>
<td>34</td>
</tr>
<tr>
<td>Deaths</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Health and Wellness for all Arizonans
Adverse Events after Hepatitis A Vaccine

• Mild problems
  – Soreness at vaccine site (Children 1/6, adults 1/2)
  – Headache (Children 1/25, adults 1/6)
  – Loss of appetite (Children 1/12)
  – Tiredness (Adults 1/14)

• Anaphylaxis—very rare
  – Within minutes to hours
Hepatitis B
Causes
Liver Cancer and Cirrhosis

<table>
<thead>
<tr>
<th>US &amp; Hepatitis B</th>
<th>1979</th>
<th>2007</th>
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<tbody>
<tr>
<td>Cases</td>
<td>15,452</td>
<td>4,519</td>
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<td>Deaths</td>
<td>260</td>
<td>719</td>
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</table>
Adverse Events after Hepatitis B Vaccine

• Mild
  – Soreness at vaccine site (1/4)
  – Temperature to 99.9°F or higher (1/15)

• Test for hepatitis B surface antigen may test positive for up to 28 days

• Severe allergic reactions
  – About once in 1.1 million doses
Poliomyelitis

<table>
<thead>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>33,300</td>
<td>0</td>
</tr>
<tr>
<td>Deaths</td>
<td>1,904</td>
<td>0</td>
</tr>
</tbody>
</table>
Adverse Events after Polio Vaccines

Inactivated Polio Vaccine (IPV)
- Most people have no problem with IPV
- Soreness at vaccine site
- Anaphylaxis
  - Extremely small risk

Oral Polio Vaccine (OPV)
- Rarely can cause paralysis from polio infection
  - Risk of 1 case for every 2.4 million doses of OPV
- Close contact of OPV recipient can get infected with OPV and rarely could be paralyzed
- Anaphylaxis
  - Extremely small risk
Adverse Events after Vaccination Likely due to vaccine?

• Jaundice 1 week after hepatitis A vaccine
• Fever 1 day after hepatitis B vaccine
• Vomiting 1 week after IPV
• Runny nose 1 day after hepatitis A vaccine
• Anaphylaxis 6 hours after hepatitis B vaccine
• Paralysis one week after oral polio vaccine
• Diarrhea 1 week after hepatitis A vaccine
**Haemophilus influenzae type b (Hib)**

<table>
<thead>
<tr>
<th></th>
<th>US &amp; Hib</th>
<th>Early 1980s</th>
<th>2007</th>
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<tbody>
<tr>
<td>Cases</td>
<td>~20,000</td>
<td>202</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>~10,000</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>
Adverse Events after *Haemophilus influenzae* type b (Hib) Vaccines

- Most people do not have problems
- Mild problems
  - Redness, warmth, or swelling at injection site
  - Problems start soon after shot and last 2-3 days
- Severe shoulder pain at vaccine site—rare
- Fainting—occasional
- Anaphylaxis—very rare
Clinical presentations of *Streptococcus pneumoniae*

- Pneumonia
- Meningitis
- Bacteremia
- Otitis media
- Mastoiditis
- Sinusitis
- Periorbital Cellulitis
- Orbital Cellulitis
- Septic Arthritis
## Adverse Events after Pneumococcal Vaccines

<table>
<thead>
<tr>
<th>PCV13</th>
<th>PPSV23</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Drowsy, loss of appetite, redness or pain at site (1/2)</td>
<td>• Mild side effects (1/2)</td>
</tr>
<tr>
<td>• Swelling at vaccine site (1/3)</td>
<td>- Redness or pain at injection site</td>
</tr>
<tr>
<td>• Mild fever (1/3) or fever over 102.2°F (1/20)</td>
<td>• Fever (&lt;1%)</td>
</tr>
<tr>
<td>• Fussy or irritable (8/10)</td>
<td>• Muscle aches (&lt;1%)</td>
</tr>
<tr>
<td>• Anaphylaxis</td>
<td>• Severe local reaction (&lt;1%)</td>
</tr>
<tr>
<td>- Very rare</td>
<td>• Anaphylaxis</td>
</tr>
<tr>
<td></td>
<td>- Very rare</td>
</tr>
</tbody>
</table>
Neisseria meningitidis
Adverse Events after Meningococcal Vaccines

• Redness or pain at injection site (1/2)
  – More common after conjugate vaccine (MCV4) than polysaccharide vaccine (MPSV4)

• Fever
  – Occasional

• Fainting
  – Occasional

• Anaphylaxis—very rare
Adverse Events after Vaccination
Likely due to vaccine?

• Seizure and fever 1 month after meningococcal vaccine
• Runny nose, sore throat, cough starting 1 day after Hib vaccine
• Sore vaccine site for 1-3 days after pneumococcal vaccine
• Diarrhea starting 5 days after meningococcal vaccine
Cancers and Genital Warts Attributed to HPV Infections, U.S.

CDC; 2013. Available at http://www.cdc.gov/cancer/hpv/statistics/cases.htm
Adverse Events after Human Papillomavirus (HPV) Vaccines

- Injection site
  - Redness or swelling (4/10)
  - Pain (8/10)
- Fever
  - To 100.4°F. (1/10)
  - To 102°F. (1/65)

- Headache (1/3)
- Fainting
  - Occasional
- Anaphylaxis
  - Very rare
Vaccine Adverse Event Reporting System (VAERS)

- Created as part of National Childhood Injury Act of 1986
- Established in 1990
- Co-managed by CDC and FDA

➤ Report any clinically significant or unexpected event occurring after vaccination
# Summary of Vaccine Injury Table

## National Childhood Vaccine Injury Act

<table>
<thead>
<tr>
<th>Containing</th>
<th>Adverse Event Condition</th>
<th>Time interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any vaccine</td>
<td>Anaphylaxis / sequela / death</td>
<td>0-4 hrs / NA / NA</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Brachial neuritis</td>
<td>2-28 days</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Encephalopathy / encephalitis</td>
<td>0-72 hrs</td>
</tr>
<tr>
<td>MMR</td>
<td>Encephalopathy / encephalitis</td>
<td>5-15 days</td>
</tr>
<tr>
<td>Measles</td>
<td>Thrombocytopenic purpura</td>
<td>7-30 days</td>
</tr>
<tr>
<td></td>
<td>Vaccine infection in immune compromised</td>
<td>0-6 months</td>
</tr>
<tr>
<td>Rubella</td>
<td>Chronic arthritis</td>
<td>7-42 days</td>
</tr>
<tr>
<td>OPV</td>
<td>Paralytic polio--immune competent</td>
<td>0-30 days</td>
</tr>
<tr>
<td></td>
<td>Paralytic polio—immune compromised</td>
<td>0-6 months</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Intussusception</td>
<td>0-30 days</td>
</tr>
</tbody>
</table>
Vaccine Safety

“I don’t think that word means what you think it means.”

-- Íñigo in The Princess Bride
Safety Monitoring after FDA Licensing

- Licensing of manufacturing plant
- Each lot tested at the FDA
  - Safety, potency, purity
- Safety Monitoring
  - Vaccine Adverse Events Reporting System (VAERS)
  - Vaccine Safety Datalink (VSD)
  - Clinical Immunization Safety Assessment Centers (CISA)
Temporal Occurrence Does Not Prove Cause and Effect