Getting to the Point: Childhood Immunizations

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Disclosure

• Neither I nor any member of my immediate family has a financial relationship or interest (currently or within the past 12 months) with any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients.

• The opinions presented are my own and do not necessarily reflect those of Fletcher Allen Health Care, University of Vermont College of Medicine, or the Vermont Children’s Hospital

• No unapproved use of pharmaceutical agents are discussed
Objectives

• Review the history of vaccines
• Describe how vaccines work
• Discuss vaccine controversies
• Discuss new developments in vaccines
Case of the Hour

• In January, a previously healthy 44 year old man goes to his physician for a health care supervision visit
• He is given an influenza vaccine (shot in the arm)
• Two days later, he complains of runny nose, chills, and fever
• The man tells his wife and two children to avoid getting the influenza vaccine because he got influenza from the shot
• Did the man get influenza from the vaccine?
Vaccine: definition

• A preparation of a weakened or killed pathogen, such as a bacterium or virus, or of a portion of the pathogen's structure that upon administration stimulates antibody production or cellular immunity against the pathogen
### Vaccine Preventable Diseases in the US

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Morbidity†</th>
<th>2007 Reported Cases‡‡</th>
<th>Percent 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>Measles</td>
<td>530,217</td>
<td>43</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>800</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,752</td>
<td>10,454</td>
<td>95%</td>
</tr>
<tr>
<td>Polio (Paralytic)</td>
<td>16,316</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>12</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Congenital Rubella Syndrome</td>
<td>152</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>28</td>
<td>95%</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>20,000</td>
<td>202*</td>
<td>99%</td>
</tr>
</tbody>
</table>
Question 1

• When were the first vaccines produced?
  – 2000 BC
  – 430 BC
  – 1000 AD
  – 1796 AD
  – 1937 AD
Infectious disease and the ancients

- Capricious gods
  - Punishment

- Small pox
  - 30% mortality
  - Disfigured survivors
Idea of immunity emerges

- Greeks realized that individuals who recovered from disease became resistant to same disease following subsequent contact

“it was with those who had recovered from the disease that the sick and the dying found most compassion. These knew what it was from experience, and had now no fear for themselves; for the same man was never attacked twice - never at least fatally.” *

*Thucydides describing the plague of Athens (430 BC)
Active prevention of disease: 1000 AD
Variolation in England

• Lady Mary Montagu
  – Stationed in Constantinople
  – 1718 had child variolated
  – Upon return to England, had other aristocrats do the same during 1721 epidemic
18th century England: cowpox

• Relatively uncommon disease of cattle
  – Milkmaids who handled cows frequently developed pox on their hands
  – Farmers noted milkmaids with a history of cowpox rarely got smallpox
Smallpox Vaccination in England

• In 1774, during an outbreak of smallpox, a farmer named Benjamin Jesty vaccinated his wife and two sons with cowpox taken from the udder of an infected cow and wrote of his experience*

His experiment succeeded; the two children remained immune even 15 years later, when they were deliberately inoculated with smallpox.11

*Jenner only noted Jesty’s work long after his own fame was secure
1796: Birth of the modern vaccine Era
May 14, 1796

• Jenner inoculated 8 y/o James Phipps from fluid taken from the cowpox infected hands of Sarah Nelmes

• Six weeks later James was inoculated with smallpox and survived without disease

• 23 (mostly children) ultimately “vaccinated”
Vaccination programs

Benjamin Waterhouse (1754-1846) Kine Pock Inoculation. Rules to Be Attended to During the vaccination: broadside, July 3, 1809
Complications of smallpox vaccine

- Material from humans not sterile
- Material from cattle not sterile
- Other diseases transmitted
# History of Vaccine Development

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Year introduced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>1796*</td>
</tr>
<tr>
<td>Rabies</td>
<td>1886</td>
</tr>
<tr>
<td>Typhoid</td>
<td>1886</td>
</tr>
<tr>
<td>Cholera</td>
<td>1896</td>
</tr>
<tr>
<td>Plague</td>
<td>1897</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1921</td>
</tr>
<tr>
<td>Whooping cough (pertussis)</td>
<td>1926</td>
</tr>
<tr>
<td>Influenza</td>
<td>1936</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>1937</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>1946</td>
</tr>
<tr>
<td>Killed polio</td>
<td>1955</td>
</tr>
<tr>
<td>Live polio</td>
<td>1961</td>
</tr>
<tr>
<td>MMR</td>
<td>1971</td>
</tr>
</tbody>
</table>
Biology of vaccines
Question 2

• In order to produce an effective immune response against the antigen , does the antigen have to be given with rest of the organism?
Types of vaccines
Types of vaccines

Alive                 dead

Piece        product  linked
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type</th>
<th>Routine Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Whole live attenuated</td>
<td>x</td>
</tr>
<tr>
<td>Mumps</td>
<td>Whole live attenuated</td>
<td>x</td>
</tr>
<tr>
<td>Rubella</td>
<td>Whole live attenuated</td>
<td>x</td>
</tr>
<tr>
<td>Varicella</td>
<td>Whole live attenuated</td>
<td>x</td>
</tr>
<tr>
<td>BCG</td>
<td>Whole live attenuated (Jennerian)</td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Whole live attenuated (Jennerian)</td>
<td>x</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Subunit</td>
<td>x</td>
</tr>
<tr>
<td>Influenza</td>
<td>Subunit (or live attenuated)</td>
<td>x</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Subunit</td>
<td>x</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Toxoid</td>
<td>x</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Toxoid</td>
<td>x</td>
</tr>
<tr>
<td>Haemophilus</td>
<td>Conjugated polysaccharide subunit</td>
<td>x</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>Conjugated polysaccharide subunit</td>
<td>x</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>Conjugated polysaccharide subunit</td>
<td>x</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Whole inactivated</td>
<td>x</td>
</tr>
<tr>
<td>Polio</td>
<td>Whole Inactivated</td>
<td>x</td>
</tr>
<tr>
<td>Rabies</td>
<td>Whole Inactivated</td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>Subunit</td>
<td>x</td>
</tr>
</tbody>
</table>
Live vaccines

• Advantages:
  – Generally, best immune response occurs following natural infection
  – Stimulates complex immunologic reactions
  – Replicates at actual infection at the sites
  – Single dose usually sufficient

• Disadvantages
  – Complications in immunocompromised and pregnant
  – Potential to cause disease
  – Inactivated by circulating antibody

• Live virus vaccines
  – Measles, mumps, rubella, varicella zoster, rotavirus, some influenza
Inactivated or subunit vaccines

• Advantages
  – Well-defined antigen easy to produce
  – Cannot cause infectious disease
  – Can be given in the face of circulating antibody

• Disadvantages
  – Requires multiple doses

• Inactivated or subunit vaccines—many
  – Hepatitis B
  – Influenza
Efficacy of vaccines

CDC
MMWR. January 23, 2009; 58:1-3
Community Effects of Immunization: invasive vaccine associated pneumococcal disease in adults

Incidence / 100,000

PCV7 licensed

≥80 yo: -90%
65-79 yo: -88%
50-64 yo: -80%
18-49 yo: -88%

Year
Efficacy of vaccines
Vaccine efficacy
Vaccine controversies

James Gillray, 1802
Vaccine Refusal

• How many of you have personal experience with someone who has deferred at least one vaccine?
• How many of you have personal experience with someone who has refused at least one vaccine?
• How many of you have personal experience with someone who has refused all vaccines?
Complications of vaccines

• Local
  – Pain, erythema, tenderness at site

• Systemic
  – Fever, chills, malaise

• Catastrophic (and very rare)
  – Anaphylaxis (vascular collapse)

• Fear
  – Bad things happening to nice children
Recent controversies

• Measles
  – 1: 2,500-5,000 risk of death
  – 1:1,000 risk of encephalitis
  – 1:100 risk of hospitalization
  – Rarely seen

• Autism
  – Rising incidence
  – Most have heard about it
Parental attitudes toward vaccines (N=1552)

<table>
<thead>
<tr>
<th>Perspective</th>
<th>% Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Getting vaccines protects my children from disease</td>
<td>90</td>
</tr>
<tr>
<td>I generally do what my doctor recommends about vaccines</td>
<td>88</td>
</tr>
<tr>
<td>I am concerned about serious adverse effects of vaccines</td>
<td>54</td>
</tr>
<tr>
<td>New vaccines are recommended only if they are as safe as older ones</td>
<td>51</td>
</tr>
<tr>
<td>Parents should be able to refuse vaccines for any reason</td>
<td>31</td>
</tr>
<tr>
<td>Some vaccines cause autism in healthy children</td>
<td>25</td>
</tr>
<tr>
<td>I have refused at least one vaccine</td>
<td>11</td>
</tr>
</tbody>
</table>

Freed GL Pediatrics 2010;125;654-659
Reasons for increasing parental concern and vaccine refusal

• Vaccines are given to healthy children
• Perceived risk of disease has diminished
• Acceptable risk associated with the vaccine has diminished
• Safety is relative not absolute
Reasons for increasing refusal

• Information explosion
• Most internet sources are not necessarily favorable to vaccination
Reasons for increasing refusal

• Different definitions of causality
  – Medical
  – Legal
    – Cannot prove no association between a vaccine and an adverse event exists

• Power of the anecdote over science

Insert video
Parental concerns about vaccines

• Vaccines
  – *Cause harm (neurodevelopmental)* 69%
  – Overwhelm the immune system 49%

• Child not at risk for disease 37%

• Disease not serious 21%

Bardenheier B. *Arch Pediatr Adolesc Med* 2004;158:569-575
Gust DA. *Pediatrics* 2008;122: 718-725
Vaccines and harm

• Vaccine ingredients
  – Measles virus
  – Mercury (thimerosal)
  – Aluminum
  – Other ingredients
MMR and autism rates in Canada

![Graph showing MMR coverage and autism rates over years.](image)

Fombonne E. *Pediatrics* 2006;118:e139-e150
MMR and Autism in Japan

![Graph showing MMR vaccination rate and cumulative incidence of autism over years](image)

- Year of birth: 1988 to 1996
- MMR vaccination rate (%)
- Cumulative incidence (/10,000)

Legend:
- without regression
- probable regression
- definite regression

Measles (MMR) and Autism

• Institute of Medicine
  – Rejects an association

• National Vaccine Compensation Board
  – Rejects an association
Autism and Thimerosal

• Thimerosal
  – A preservative in vaccines
  – 50% mercury
  – Metabolized to ethyl mercury

• Organic mercury toxicity
  – Central nervous system
  – Fetal>neonatal>adult
Autism and thimerosal: USA
Thimerosal and autism: Europe

Removal of thimerosal

Incidence per 10,000


Thimerosal and neurodevelopmental outcomes

- >1000 children
  - Various amounts of thimerosal
- No relationship between ethyl mercury exposure and neuropsychological outcomes at 7-10 years

Thompson WW. NEJM 2007;357:1281
Aluminum

• Most common metal on earth-everywhere
• Used to boost immune response of some vaccines (for 70 years)
• At six months of life:
  – 4 mg aluminum from vaccines
  – 10 mg in breast milk
  – 40 mg from cow’s milk formula
  – 120 mg from soy milk formula
Other Vaccine Ingredients

• “Anti-freeze”
  – Polyethylene glycol in many products
  – Ethylene glycol

• Formaldehyde
  – Trace amounts
  – Less than usually detected in infants
Question

• If measles is no longer considered endemic in the US, why should anyone get the measles vaccine?
Measles in the US: Jan-July 2008

- 131 cases
  - 76% < 20 years old
  - 91% unvaccinated
  - 89% imported or associated with importation

Eligible for vaccination but not given (N=95)

- Religious or philosophical
- Delayed vaccination
- Unknown
- Age 12-15 months

MMWR 2008;57(33):893
New developments

• Build on successes
• Adult vaccines
Future developments

The state’s duty to protect the public health vs.
An individuals right of free choice
Personal belief exemptions include religious, philosophical and any other unspecified non-medical exemption

All states allow for medical exemptions
48 states allow for religious exemption
Approximately 20 allow for philosophical exemptions
Immunization Exemptions and Risk of Disease

• Pertussis
  – States with philosophical exemptions:
    • 2.06 (1.8-2.4) rate over religious only*
  – Individuals who refused immunizations:
    • 22.8 (6.7-77.5) risk of disease^”

• Varicella
  – Refusal associated with 8.6 (2.2-33.3) risk of disease**

*Omer SB. JAMA 2006;296:1757
Background rate of exemptions

Omer SB. JAMA 2006;296:1757
Washington State Immunization Exemption Rates by School District; 2008-09

Data Source: WA State DOH Immunization Program CHILD Profile
June, 2009 Created with ArcGIS 9.2

www.doh.wa.gov/cfh/Immunize/
Measles and Refusal to Vaccinate

• San Diego 2008
  – Unvaccinated 7 year old acquired measles in Switzerland
  – 839 exposed people
    • 73 were unvaccinated children
      – 25 whose parents chose not to get them vaccinated
      – 48 children under 12 months too young to be vaccinated
    • 11 additional cases
      – $10, 376/case
      – $775 per quarantined child

Sugerman, DE. Pediatrics. 2010 Apr;125:747-55,
Vermont 2012

• Upheld philosophical exemption
• Recognized that vaccination could benefit others
  – Immunocompromised

• Consequences
  – Task force convened to discuss how to help prevent vaccine preventable diseases in people with compromised immune systems
    • Segregation
  – OK to Ask Program
Case of the Hour

• In January, a previously healthy 44 year old man goes to his physician for a health care supervision visit.
• He is given an influenza vaccine (shot in the arm)
• Two days later, he complains of runny nose, chills, and fever
• The man tells his wife and two children to avoid getting the influenza vaccine because he got influenza from the shot
• Did the man get influenza from the vaccine?
Community Medical School