Vaccines: Then and Now
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Immunization Action Coalition

Michigan Regional Immunization Conferences
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Note: slides are arranged in vertical rows rather than horizontal rows

Comparison of 20th Century Annual Morbidity and Current Morbidity: Vaccine-Preventable Diseases

**Table:**

<table>
<thead>
<tr>
<th>Disease</th>
<th>20th Century Annual Morbidity</th>
<th>2016 Reported Cases</th>
<th>Percent Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>29,055</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21,853</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Measles</td>
<td>530,217</td>
<td>69</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>Mumps</td>
<td>162,344</td>
<td>5,311</td>
<td>97%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>200,762</td>
<td>15,737</td>
<td>92%</td>
</tr>
<tr>
<td>Polio (paralytic)</td>
<td>16,216</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>5</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>Congenital Rubella Syndrome</td>
<td>152</td>
<td>1</td>
<td>99%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>580</td>
<td>33</td>
<td>94%</td>
</tr>
<tr>
<td>Haemophilus influenza type b</td>
<td>20,000</td>
<td>22*</td>
<td>&gt; 99%</td>
</tr>
</tbody>
</table>

*JAMA. 2007;298(18):2155-2163
†† CDC. MMWR January 6, 2017/65(52); ND-924 – ND-941. (MMWR 2016 week 52 provisional data)

* Haemophilus influenzae type b (Hib) < 5 years of age. An additional 11 cases of Hib are estimated to have occurred among the 222 reports of Hi (< 5 years of age) with unknown serotype.

Smallpox

- Acute illness caused by Variola virus
  - variola major – severe
  - variola minor – less severe
- Humans only known reservoir
- Transmitted by contact with infectious aerosols

Smallpox - day 8 of rash

Late hemorrhagic smallpox
Smallpox Complications

- Scarring
- Blindness
- Death
  - 30% overall for ordinary smallpox
  - 40%-50% for children <1 year
  - >90% for flat and hemorrhagic smallpox

Smallpox – Boston, 1752

<table>
<thead>
<tr>
<th>Cases</th>
<th>5,545</th>
<th>2,124</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>537 (9.7)</td>
<td>30 (1.4)</td>
</tr>
</tbody>
</table>

*28% of smallpox cases caused by variolation

The First Vaccination Strategy

Variolation

- “Artificial” infection of susceptible person with variola virus taken from a person with “mild” smallpox
- Practiced in China and probably India in the 9th century
- Cutaneous inoculation resulted in severe local lesions, usually with many satellite pustules
- Usually caused a generalized rash and severe constitutional symptoms
- Could be fatal, and could be transmitted to contacts
Protection from Smallpox

- Folklore in Europe that milkmaids rarely pockmarked
- Belief that protection from smallpox somehow resulted from contact with cows
- Edward Jenner observed that some with history of cowpox “resisted” variolation

Vaccination

- Jenner’s observations soon reproduced by others
- Practice quickly spread throughout Europe
- Benjamin Waterhouse performed first vaccinations in U.S. in Boston, 1800

“…it now becomes too manifest to admit of controversy, that the annihilation of the Small Pox, the most dreadful scourge of the human species, must be the final result of this practice.”

-Edward Jenner, 1801

Jenner’s Experiment

- Transferred “matter” from a cowpox lesion on the hand of a dairymaid to 8 year-old James Phipps on 14 May 1796
- Variolation of Phipps unsuccessful on 1 July 1796
- Phipps did not respond to variolation 5 years after original vaccination

Smallpox Eradication

- Last case of smallpox in the United States was in 1949
- Intensified Global Eradication program begun in 1967
- Initial strategy was mass vaccination
- Strategy evolved to “surveillance and containment”
- Routine smallpox vaccination discontinued in the United States in 1971
- Last case of variola major in India in October 1975
Last case of naturally occurring smallpox (variola minor)

Merca, Somalia
October 26, 1977

Quick Quiz
Smallpox was the first disease intentionally eradicated from Earth. What was the second?
A. Polio
B. Guinea Worm
C. Measles
D. Plague
E. Rinderpest

Eradication endorsed by the World Health Assembly
May 8, 1980

Rinderpest
- Disease that affects cattle, buffaloes, antelope, and other cloven-hoofed animals
- Closely related to measles virus and canine distemper
- Thought to have been the 5th plague of Egypt (Exodus 9:3-7)
- 95%-100% fatality rate in some outbreaks
Rinderpest epizootic, the Netherlands, 1745

Old Saint Dominic's Cemetery
Metz Township, Presque Isle County, Michigan

Diphtheria

- A toxin-mediated disease caused by Corynebacterium diphtheriae
- Most common clinical presentation is exudative pharyngitis with a tightly adherent membrane involving the pharynx and tonsils
- Complications attributable to toxin – severity generally related to extent of local disease
- Most complications are myocarditis and neuritis

Rinderpest Eradication

- World Organization for Animal Health (OIE) formed in 1924 in response to rinderpest
- Vaccine available in the 1960s
- Global Rinderpest Eradication Programme begun in 1994
- Last confirmed case in Kenya in 2011
- Eradication confirmed by OIE on May 25, 2011
- Eradication declared on June 28, 2011

Tonsillar diphtheria
History of Diphtheria

- 1884 – C. diphtheria isolated
- 1888 – toxin effects discovered
- 1890 – von Behring develops antitoxin*
- 1924 – toxoid developed
- 1936 – toxoid efficacy demonstrated
- 1943 – widespread use of toxoid

*awarded first Nobel Prize in Medicine 1901

Diphtheria - United States, 1940-1980

Diphtheria - United States, 1980-2015
Poliomyelitis

- Evidence of polio 1,400 BCE
- First described by Michael Underwood in 1789
- First outbreak described in U.S. in 1843
- Epidemics became increasingly severe during the next 100 years

Jonas Salk

Dr. Salk developed the first inactivated polio vaccine in 1952

Polio Outbreaks - 1916

In 1949 Enders, Robbins and Weller discovered a method to grow poliovirus in tissue culture which allowed large amounts of virus to be produced. They received the Nobel Prize in Medicine for this discovery in 1954.
Francis Field Trial of Inactivated Polio Vaccine

- 440,000 vaccinated
- 210,000 placebo
- 1,200,000 unvaccinated controls

Findings
- 60%-79% effective against PV1
- 90% effective against PV2 and PV3
- 94% effective against bulbar polio

Francis Field Trial Results Announced
Ann Arbor, Michigan
April 12, 1955

People waiting in long lines for polio vaccine
San Antonio, 1957

Poliomyelitis – United States, 1950-2002

Cases

Inactivated vaccine
Live oral vaccine
Last indigenous case


Poliomyelitis - United States, 1964-2002

Cases

After 1979 almost all cases of polio in the United States were caused by oral polio virus. A few cases were imported.

Total Vaccine Assoc
Evolution of Polio Vaccination Recommendations

- 1955-1963 IPV only
- 1963-1996 OPV only
- 1996-2000 IPV-OPV
- 2001 IPV only
  OPV no longer available in the U.S.

Global Polio Eradication Initiative

- Begun in 1988
- Last case in Western Hemisphere in 1991
- Western Hemisphere certified polio free in 1994
- Type 2 virus eradicated in 1999
- No isolates of type 3 virus since November 2012

Wild Poliovirus 2016

37 cases worldwide

More Vaccine-Preventable Diseases You Will Never See Again

Neonatal tetanus
**Tetanus—United States, 1947-2010**

Combined DTP vaccine became available in 1948

- 29 cases reported in 2015
- None neonatal

Source: National Notifiable Disease Surveillance System, CDC

**Haemophilus influenzae type b**

**Congenital Rubella Syndrome**

**Invasive Hib Disease in Children <5 Years of Age—US, 1980-2012**

- 2015 – 29 cases reported


**Rubella - United States, 1966-2010**

- First rubella vaccine licensed in 1969
- 6 cases reported in 2015
- 1 CRS
- Last indigenous case 2004

Source: National Notifiable Disease Surveillance System, CDC

**Pneumococcal meningitis**
Number of Vaccines in the Routine Childhood and Adolescent Immunization Schedule

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td>Measles, Diphtheria, Tetanus, Pertussis, Polio, Smallpox</td>
</tr>
<tr>
<td>1985</td>
<td>Measles, Rubella, Mumps, Diphtheria, Tetanus, Pertussis, Polio</td>
</tr>
<tr>
<td>1995</td>
<td>Measles, Rubella, Mumps, Diphtheria, Tetanus, Pertussis, Polio, Hib (infant)</td>
</tr>
<tr>
<td>2017</td>
<td>Measles, Rubella, Mumps, Diphtheria, Tetanus, Pertussis, Polio, Hib (infant), HepB, Varicella</td>
</tr>
</tbody>
</table>

Vaccine Safety Concern
Can so many vaccines given at once overwhelm a baby’s immune system?

Antigen Exposure From Vaccines

<table>
<thead>
<tr>
<th>Year</th>
<th>Vaccines</th>
<th>Number of Antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900</td>
<td>Spox</td>
<td>200</td>
</tr>
<tr>
<td>1960</td>
<td>Spox, DTwP, OPV</td>
<td>3400</td>
</tr>
<tr>
<td>1980</td>
<td>DTwP, OPV, MMR</td>
<td>3000</td>
</tr>
<tr>
<td>2017</td>
<td>DTaP, IPV, MMR, Hib, Var, PCV, Hep A, HepB, Rota, Flu</td>
<td>130</td>
</tr>
</tbody>
</table>

More vaccines but fewer antigens
Offit PA, in Plotkin SA, et al (eds), Vaccines 2017
Vaccine Safety Concern
How do we know vaccines are safe?

Vaccine Adverse Event Reporting System (VAERS)
• National reporting system begun in 1990
• Jointly administered by CDC and FDA
• Passive (depends on healthcare providers and others to report)
• Receives about 35,000 reports per year

Vaccine Adverse Event Reporting System (VAERS)
• Detects
  – new or rare events
  – increases in rates of known side effects
  – patient risk factors
• Additional studies required to confirm VAERS signals
• Not all reports of adverse events are causally related to vaccine

Vaccine Safety Datalink (VSD)
• Involves partnerships with 8 large managed care organizations
• Links vaccination and health records
• Allows for planned immunization safety studies
• Allows for investigations of hypotheses that arise from review of medical literature, reports to VAERS, changes in immunization schedules, or the introduction of new vaccines

Estimated Return on Investment of Childhood Vaccines
• For each birth cohort vaccinated against 13 diseases in accordance with the schedule for DTaP, Hib, IPV, MMR, hep B, Varicella, Hepatitis A, Pneumo-7, and Rotavirus vaccines:
  – 42,000 lives are saved (~1.344 MI lives)
  – 20,000,000 cases of disease are prevented (~$40,000 MI lives)
  – $13.6 billion dollars in direct costs are saved
  – $68.9 billion dollars in direct plus indirect (societal) costs are saved
• For each dollar invested in these vaccinations, $10.20 is saved

Zhou et al, Arch of Ped and Adolesc Med 2005
Summary

- Vaccines have greatly reduced or eliminated the risk of vaccine-preventable diseases
- With the decline in risk from disease there has been an increasing focus on vaccine safety
- Technology has made vaccines safer
- The U.S. has a robust vaccine safety monitoring system to rapidly identify and investigate vaccine safety issues