Vaccines: Then and Now

William Atkinson, MD, MPH
Immunization Action Coalition
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Note: The presentation may include slides not included in this handout and the order may be changed.
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

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

Smallpox – Boston, 1752

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

*28% of smallpox cases caused by variolation

Variolation was dangerous but not as dangerous as naturally acquired smallpox

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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

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

Jenner vaccinates James Phipps, 14 May 1796

Vaccination

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

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”

“...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

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Last case of naturally occurring smallpox
Somalia
October 26, 1977

Announcement of global smallpox eradication, World Health magazine, May 1980

Cover of book detailing the eradication of smallpox written by former CDC director Dr. William Foege

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

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

News article announcing the global eradication of rinderpest

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Woodcut showing rinderpest epizootic in the Netherlands, 1745

Photograph documenting rinderpest epizootic in the South Africa, 1900

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**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

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**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

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Diphtheria was the #10 cause of death among all ages in 1921.

Diphtheria was among the top 3 causes of death among children in England and Wales in 1937-1938.

Widespread use of diphtheria toxoid begins.

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Egyptian stone carving showing a man with probable polio, approximately 1100 BCE.

**Poliomyelitis**

- First described by Michael Underwood in 1789
- First outbreak described in U.S. in 1843

**Polio Outbreaks - 1916**

21,000 paralytic cases reported in the U.S. in 1952

**Jonas Salk**

Jonas Salk administering his experimental polio vaccination to his son, 1953

**Francis Field Trial**

The Francis Field Trial of Salk’s inactivated polio vaccine involved more than 1.8 million children, the largest clinical trial of a vaccine in history

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Francis Field Trial

Announcing the successful results of the Francis Field Trial, Ann Arbor, Michigan, April 12, 1955

People lined up to receive IPV, San Antonio, 1957

Poliomyelitis – United States, 1950-2002

Poliomyelitis - United States, 1964-2002

Poliomyelitis – United States, 1980-2002

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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 1988

Estimated 350,000 cases worldwide

Wild Poliovirus 2016

37 cases worldwide

More Vaccine-Preventable Diseases You Will Never See Again

Neonatal tetanus

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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>
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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

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**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 (~640,000 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

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