The Blight of Infectious Diseases

— Throughout history, millions succumbed to infectious diseases such as smallpox and polio
— By late 1700s, 400 000 people died per year in Europe from smallpox

Picture Source: Centers for Disease Control and Prevention
Common observation: dairymaids who have had cowpox (similar to smallpox but much milder) do not contract smallpox

Hypothesis: cowpox conferred immunity to smallpox
Jenner and the Invention of Vaccine

---

**Experiment (1796):**

- Cowpox
- Smallpox

Further confirmed with 22 other cases

Vaccine, from Latin *vacca* (cow)

---

No smallpox

6 weeks

Picture Source: Public Domain
Vaccines and the Triumph over Smallpox

By 1800, vaccines administered across Europe and North America

1975: Rahima Banu, one of the last people naturally infected by smallpox

1950: Pan Am Health Org - eradication program throughout Americas

By 1900: smallpox eliminated from much of industrialized world

1959: Beginning of global smallpox eradication program

12/9/1979: WHO declared smallpox eradicated

Picture Source: CDC
Other Successes, and Work in Progress

- Major diseases still to have reliable vaccine: tuberculosis, HIV, malaria
- Smallpox is the first, and only, human disease to be eradicated; polio eradication in progress
How do vaccines work?
Immunity

Innate

Adaptive

Natural

Artificial

Picture Sources: Public Domain, CDC
# Types of Vaccines

<table>
<thead>
<tr>
<th>Type</th>
<th>Component</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live, attenuated</td>
<td>Live microbe weakened by growth conditions in lab, or less dangerous relative</td>
<td>measles, rubella, mumps, yellow fever, typhoid, tuberculosis</td>
</tr>
<tr>
<td>Inactivated (Killed)</td>
<td>Microbe killed by chemicals, heat or radiation</td>
<td>flu, plague, polio, rabies, hep A, cholera</td>
</tr>
<tr>
<td>Subunit</td>
<td>1-20 parts of microbe that best stimulate immune response</td>
<td>hep B, HPV, flu</td>
</tr>
</tbody>
</table>
Other Components of a Vaccine

- Preservatives/stabilizers: antibiotics, formaldehyde, MSG, thimerosal
- Adjuvants: substances that enhance immune response by mimicking molecules common to pathogenic microbes
  - Aluminum salts (only type allowed in US)
  - Squalene (derived from shark liver or plant oils)
Vaccines in the US

Recommended Immunization Schedule:

- HepA; HepB
- DTaP (Diphtheria, Tetanus, Pertussis)
- MMR (Measles, Mumps, Rubella)
- Varicella (chickenpox); Polio; Rotavirus
- Hib (against Haemophilus influenzae type b); PCV (against Streptococcus pneumoniae)
- Meningococcus (at 11-12 years)
- Human papillomavirus (for females; at 11-12 years)
- Flu (yearly)
### Vaccines in the US

Immunization coverage in children of 19-35 months

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP</td>
<td>85%</td>
</tr>
<tr>
<td>Polio</td>
<td>94%</td>
</tr>
<tr>
<td>MMR</td>
<td>92%</td>
</tr>
<tr>
<td>Varicella</td>
<td>91%</td>
</tr>
<tr>
<td>HepB</td>
<td>94%</td>
</tr>
<tr>
<td>HepA</td>
<td>40%</td>
</tr>
<tr>
<td>Hib</td>
<td>91%</td>
</tr>
<tr>
<td>PCV</td>
<td>80%</td>
</tr>
</tbody>
</table>
How do we know a vaccine works and is safe?

- 3 types of evidence:
  - Clinical trials
  - Post-licensing safety monitoring
  - Population-level data
Clinical Trials

<table>
<thead>
<tr>
<th>Volunteer group size</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20-100</td>
<td>100-300</td>
<td>10000 or more</td>
</tr>
<tr>
<td>Duration</td>
<td>up to 2 yrs</td>
<td>2 or more yrs</td>
<td>up to 4 yrs</td>
</tr>
<tr>
<td>Looking for</td>
<td>safety, side effects, optimal dose / schedule</td>
<td>safety, immune response</td>
<td>safety, effectiveness</td>
</tr>
</tbody>
</table>

— When enough data is generated, a licensing application will be filed with FDA

National Center for Immunization and Respiratory Diseases
Post-Licensing Safety Monitoring

- National programs for reporting adverse events, e.g., Vaccine Adverse Event Reporting System (VAERS)
- Need to conduct formal scientific investigation to test link between vaccine and event
  - Coincidence or causal?

CDC, WHO
Vaccines Working at the Population Level
Herd Immunity

Vaccinated, immune
Unvaccinated, susceptible
Herd Immunity

- Vaccinated, immune
- Unvaccinated, susceptible
- Transmitting case
Herd Immunity

Vaccinated, immune
Unvaccinated, susceptible
Transmitting case
### Herd Immunity Threshold

Estimated % coverage needed to prevent disease from persisting in population

<table>
<thead>
<tr>
<th>Disease</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>85%</td>
</tr>
<tr>
<td>Pertussis</td>
<td>92-94%</td>
</tr>
<tr>
<td>Polio</td>
<td>80-86%</td>
</tr>
<tr>
<td>Measles</td>
<td>83-94%</td>
</tr>
<tr>
<td>Mumps</td>
<td>75-86%</td>
</tr>
<tr>
<td>Rubella</td>
<td>83-85%</td>
</tr>
</tbody>
</table>
Why Vaccines are Important
Why Vaccines are Important

<table>
<thead>
<tr>
<th>Disease</th>
<th>Annual Cases Pre-Vaccine</th>
<th>2008 Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>503 282</td>
<td>55</td>
</tr>
<tr>
<td>Mumps</td>
<td>152 209</td>
<td>454</td>
</tr>
<tr>
<td>Rubella</td>
<td>47 745</td>
<td>11</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>175 885</td>
<td>0</td>
</tr>
<tr>
<td>Pertussis</td>
<td>147 271</td>
<td>10 735</td>
</tr>
<tr>
<td>Tetanus</td>
<td>1314</td>
<td>19</td>
</tr>
<tr>
<td>Polio</td>
<td>16 316</td>
<td>0</td>
</tr>
<tr>
<td>Smallpox</td>
<td>48 164</td>
<td>0</td>
</tr>
</tbody>
</table>
Every dollar spent on childhood vaccine saves on direct healthcare cost and on indirect societal cost.

Why aren’t vaccines perfect?

— Individual variation from person-to-person, due to genetics, environment, other illnesses, etc
— Rare events
  — Serious side effects: 1 in 10000 - 1 in million
— Some people should not be vaccinated
  — Had previous allergic reaction
  — Compromised immune system, eg, HIV / cancer patients
What happens if we stop vaccinating?

MMR Coverage and Measles Cases Reported, 1985 - 2008
(England and Wales)

- 1988: Introduction of MMR
- 1998: Publication of MMR-autism study in *Lancet*

UK Health Protection Agency
What happens if we stop vaccinating?

Confirmed Measles Cases, 1996 - 2009
(England and Wales)

1998: Publication of MMR-autism study in *Lancet*
Summary

• Invention of vaccines had led to dramatic decrease in many infectious diseases

• Vaccines work by “teaching” immune system to respond quickly to real disease in future

• A vaccine is licensed only with enough evidence of its safety and efficacy

• Immunization coverage strongly correlated with changes in disease incidence