Modern vaccines

- Modern vaccines are safe and effective
- However, they are neither perfectly safe nor perfectly effective
- Some persons who receive vaccines will have adverse events
- Some persons who receive vaccines will not be protected
Each public health problem is a slice of the cake

Vaccine safety

governmental, political
epidemiologic
public’s view

Perspectives on Vaccine Safety

- Epidemiologic Perspective on Risk
- Public Perspective on Risk
- Risk vs Benefits
- Government work in Vaccine Safety

Epidemiologic Risk

# new cases during a specified period
size of population at start of period

= "Attack rate"
= Probability of getting disease
= Risk of disease
Example of Risk Calculation

1. Deaths in diabetic men
   100 deaths
   189 men at start of follow-up period
   Risk = \( \frac{100}{189} = 0.529 = 52.9\% \)

2. Deaths in nondiabetic men
   811 deaths
   3151 men at start of follow-up period
   Risk = \( \frac{811}{3151} = 0.257 = 25.7\% \)

Risk Ratio / Relative Risk

\[
\text{Relative risk of death among diabetic men vs. nondiabetic men} \\
\text{RR} = \frac{100/189}{811/3151} = 0.529 \div 0.257 = 2.1
\]

Efficacy vs Effectiveness - 1

- Vaccine efficacy – performance of vaccine under ideal conditions
- Vaccine effectiveness – performance of vaccine in the field
Efficacy vs Effectiveness - 2

- Differences in recipients (e.g., nutrition)
- Vaccine storage & administration
- Interference from drugs/other things administered at same time (e.g., breast milk & OPV)
- Herd immunity

Herd Immunity - 1

Resistance of a group to spread of an infectious agent, based on the immunity of a high proportion of individuals of that group...

Herd Immunity - 2

![Diagram of herd immunity](image)
"...the proportion of the population required to be immune varies according to the agent, its transmission characteristics, the distribution of immunes and susceptibles, and other (e.g., environmental) factors."

Source: Last, Dictionary of Epidemiology

- Herd immunity threshold for polio
  ~80%

- Herd immunity threshold for measles
  ~95%

- In spite of immunization levels of 90%, an outbreak of 100 cases of measles occurs in a high school with 1,000 students

- Since 1/2 of cases occurred in students who had previously been vaccinated, the principal feels vaccine has not been effective
Vaccine efficacy - 2

1,000 students, 90% vaccinated =
900 vaccinated, 100 unvaccinated

100 cases, 1/2 in vaccinated =
50 vaccinated, 50 unvaccinated

Vaccine efficacy - 3

How much protection from disease does vaccine provide?

VE (%) = \frac{ARU - ARV}{ARU} \times 100

VE = vaccine efficacy
ARU = attack rate in unvaccinated
ARV = attack rate in vaccinated

Vaccine efficacy - 4

Attack rate in vaccinated (ARV) =
\frac{50}{900} \times 100 = 5.5%

Attack rate in unvaccinated (ARU) =
\frac{50}{100} \times 100 = 50.0%
**Vaccine efficacy - 5**

\[ \text{VE} (\%) = \frac{\text{ARU} - \text{ARV} \times 100}{\text{ARU}} \]

\[ = \frac{50.0 - 5.5 \times 100}{50.0} \times 100 = \frac{44.5 \times 100}{50.0} \]

\[ = 89\% \]

**Vaccine efficacy - 6**

\[ \text{VE} = \frac{\text{ARU} - \text{ARV} \times 100}{\text{ARU}} \]

\[ = \frac{\text{ARU} - \text{ARV} \times 100}{\text{ARU}} \times \frac{\text{ARU}}{\text{ARU}} \]

\[ = \left(1 - \frac{\text{ARV}}{\text{ARU}}\right) \times 100 \]

\[ = \left(1 - \text{RR}\right) \times 100 \]

**Immunity levels after 1 dose**

<table>
<thead>
<tr>
<th>Coverage</th>
<th>Efficacy</th>
<th>90%</th>
<th>95%</th>
<th>98%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% immune</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td></td>
<td>81.0</td>
<td>85.5</td>
<td>88.2</td>
</tr>
<tr>
<td>95%</td>
<td></td>
<td>85.5</td>
<td>90.2</td>
<td>93.1</td>
</tr>
<tr>
<td>98%</td>
<td></td>
<td>88.2</td>
<td>93.1</td>
<td>96.0</td>
</tr>
</tbody>
</table>
Governmental perspectives on Effectiveness and Safety

Pre-Licensure Vaccine Safety Studies

- Laboratory
- Animals
- Humans

Pre-Licensure Human Studies

- Phase I, II, III trials
- Common reactions are identified
- Vaccines are tested in thousands of people before being licensed and on the market allowed
- Poorly detected reactions:
  - Rare
  - Delayed onset
  - Subpopulations
Post-Licensure Surveillance

- Identify rare reactions
- Monitor increases in known reactions
- Identify risk factors for reactions
- Identify vaccine lots with increased rates of reactions
- Identify signals

Vaccine Adverse Event Reporting System (VAERS)

- Jointly administered by CDC and FDA
- National reporting system
- Passive (depends on health care providers and others to report)
- Receives ~10,000 reports per year

- Detects
  - new or rare events
  - increases in rates of known events
  - patient risk factors
- Additional studies required to confirm VAERS signals
- Not all reports of adverse events are causally related to vaccine
Vaccine Safety Datalink

- Large-linked database
- Links vaccination and health records
- Population under “active surveillance”
  - 7 HMOs
  - 2.5% of the U.S. population
- Powerful tool for monitoring vaccine safety

Vaccine Safety Datalink

- 8 Managed Care Organizations
- 9 Million Individuals

Vaccine Safety Datalink

- Immunization histories on 5 million people
- Data on vaccine type, dates, concurrent vaccinations
- Medical outcomes (outpatient visits, emergency room visits, hospitalizations)
- Birth data, census data
- Studies on hypotheses generated by VAERS, medical literature, changes in immunization schedule, introduction of new vaccines
- 75 scientific articles since 1990
Vaccine Safety Datalink Studies

- Aseptic meningitis after MMR
- Safety of second dose of MMR
- Chronic arthropathy in women after rubella vaccination
- Safety of revaccination with pneumococcal polysaccharide
- Impact of sequential IPV/OPV schedule on vaccination coverage
- Varicella serology among school-age children with negative/uncertain history of chickenpox

The Public and Risk Communication

- When making decisions in their lives, people generally do not use quantitative measures, such as probabilities
- A risk from something people feel that they cannot control (West Nile Virus) is usually of more concern than a risk they think they can control (smoking, drinking)
- This is one reason why adverse reactions to vaccine may be of greater concern

The Public and Risk Communication

- People respond better to positive, rather than negative messages (If you do this you will be healthy. Vs. If you do this you will die.)
- People respond better to risk communication if it is personalized. (This is what I am doing. This is what I am doing for my children.)
- This is one reason why it is important to involve leaders or “champions” in vaccination programs
### Comparison of Risk vs Benefits of Vaccination United States

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pre-vaccine Era*</th>
<th>2002**</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>175,985</td>
<td>1</td>
<td>99.99</td>
</tr>
<tr>
<td>Measles</td>
<td>503,282</td>
<td>37</td>
<td>99.99</td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209</td>
<td>339</td>
<td>99.80</td>
</tr>
<tr>
<td>Pertussis</td>
<td>147,271</td>
<td>8,266</td>
<td>94.40</td>
</tr>
<tr>
<td>Polio paralysis(lyt.)</td>
<td>16,316</td>
<td>0</td>
<td>100.00</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745</td>
<td>14</td>
<td>99.97</td>
</tr>
<tr>
<td>Cong. Rubella Synd.</td>
<td>823</td>
<td>3</td>
<td>99.60</td>
</tr>
<tr>
<td>Tetanus</td>
<td>1,314</td>
<td>22</td>
<td>97.99</td>
</tr>
<tr>
<td>H flu b &amp; unk (&lt;5 yrs)</td>
<td>20,000+</td>
<td>167</td>
<td>98.60</td>
</tr>
<tr>
<td>Total</td>
<td>1,064,854</td>
<td>8,894</td>
<td>-99.16</td>
</tr>
<tr>
<td>Vaccine Adverse Events</td>
<td>0</td>
<td>7,773</td>
<td>+++</td>
</tr>
</tbody>
</table>

* Typically, average during 3 years before vaccine licensure
+ Estimated because no national reporting existed in the pre-vaccine era
** Provisional (01/06/2003)

### Problem with Risks vs Benefits

- Balance may change with time.
- Balance may change with place.
- Discussion: compare use of IPV vs OPV in the US vs India.

### References:

- [www.cdc.gov/vaccinesafety](http://www.cdc.gov/vaccinesafety) - see VAERS, VSD, Scientific Agenda