Vaccination

“Artificially induced specific adaptive immunity”
## Is vaccination useful?

<table>
<thead>
<tr>
<th>Disease</th>
<th>Maximum Number of Annual Cases in Pre-vaccine Era (year)</th>
<th>Number of Cases in 2009</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>12,641 (1899)</td>
<td>0</td>
<td>-100.00</td>
</tr>
<tr>
<td>Measles</td>
<td>52,866 (1952)</td>
<td>2</td>
<td>-99.99</td>
</tr>
<tr>
<td>Mumps</td>
<td>18,709 (1957)</td>
<td>13</td>
<td>-99.93</td>
</tr>
<tr>
<td>Pertussis¹</td>
<td>13,333 (1937)</td>
<td>371</td>
<td>-97.22</td>
</tr>
<tr>
<td>Polio</td>
<td>3,950 (1955)</td>
<td>0</td>
<td>-100.00</td>
</tr>
<tr>
<td>Rubella</td>
<td>34,148 (1943)</td>
<td>1</td>
<td>-99.99</td>
</tr>
<tr>
<td>Tetanus</td>
<td>45 (1925)</td>
<td>0</td>
<td>-100.00</td>
</tr>
<tr>
<td>Hib ²(&lt; 5 yrs of age)</td>
<td>147 (1987)</td>
<td>1</td>
<td>-99.32</td>
</tr>
<tr>
<td>Chickenpox¹</td>
<td>23,768 (1953)</td>
<td>2,219</td>
<td>-90.66</td>
</tr>
</tbody>
</table>

¹ Preliminary Data
² First became reportable in 1985

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Examples</th>
<th>Form of protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live attenuated, or killed, bacteria</td>
<td>BCG, cholera</td>
<td>Antibody response</td>
</tr>
<tr>
<td>Live attenuated viruses</td>
<td>Polio, rabies</td>
<td>Antibody response; cell-mediated immune response</td>
</tr>
<tr>
<td>Subunit (antigen) vaccines</td>
<td>Tetanus toxoid, diphtheria toxoid</td>
<td>Antibody response</td>
</tr>
<tr>
<td>Conjugate vaccines</td>
<td><em>Haemophilus influenzae</em> infection</td>
<td>Helper T cell–dependent antibody response to polysaccharide antigens</td>
</tr>
<tr>
<td>Synthetic vaccines</td>
<td>Hepatitis virus (recombinant proteins)</td>
<td>Antibody response</td>
</tr>
<tr>
<td>Viral vectors</td>
<td>Clinical trials of HIV antigens in canary pox vector</td>
<td>Cell-mediated and humoral immune responses</td>
</tr>
<tr>
<td>DNA vaccines</td>
<td>Clinical trials ongoing for several infections</td>
<td>Cell-mediated and humoral immune responses</td>
</tr>
</tbody>
</table>
**Good vaccine characteristics**

<table>
<thead>
<tr>
<th>Features of effective vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safe</strong></td>
</tr>
<tr>
<td>Vaccine must not itself cause illness or death</td>
</tr>
<tr>
<td><strong>Protective</strong></td>
</tr>
<tr>
<td>Vaccine must protect against illness resulting from exposure to live pathogen</td>
</tr>
<tr>
<td><strong>Gives sustained protection</strong></td>
</tr>
<tr>
<td>Protection against illness must last for several years</td>
</tr>
<tr>
<td><strong>Induces neutralizing antibody</strong></td>
</tr>
<tr>
<td>Some pathogens (such as polio virus) infect cells that cannot be replaced (e.g., neurons). Neutralizing antibody is essential to prevent infection of such cells</td>
</tr>
<tr>
<td><strong>Induces protective T cells</strong></td>
</tr>
<tr>
<td>Some pathogens, particularly intracellular, are more effectively dealt with by cell-mediated responses</td>
</tr>
<tr>
<td><strong>Practical considerations</strong></td>
</tr>
<tr>
<td>Low cost per dose Biological stability Ease of administration Few side-effects</td>
</tr>
</tbody>
</table>

*Figure 16.23 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)*
Live attenuated vaccine

• Microbes are weak but alive
• Mimics natural immunization (infection): strong cellular and humoral immune response
• Limitations /downsides:
  – Possibility of mutation (back) to virulent forms
  – Not absolutely safe for everyone
  – Requires cooling during storage
Examples: morbilli, parotitis, varicella, ...
Inactivated (killed) vaccines

• Dead microbes: - whole or fractionated; killed by chemicals, temperature, irradiation
• Microbes can not mutate into virulent form
• Do not require cooling during storage

Limitations /downsides:
  – Weaker immune response in comparison to live vaccines (revaccinations (booster dose) are needed)

Examples: influenza, polio, pertussis, cholera, typhoid, diphteria, tetanus,...
Recombinant vaccines

• Antigens (epitopes) that are the most potent in stimulating immune response
• Usually contains several antigens
• Recombinant DNA technology is used for genetic cloning

Limitations /downsides:
- It is not easy to determine the most immunogenic antigens for the population

Examples: HBV, HCV, Ebola?, HIV?,...
Genetic engineering

1. Isolate pathogenic virus
2. Isolate virulence gene
   - receptor-binding protein
   - virulence
   - core proteins
3. Mutate virulence gene
4. Delete virulence gene

Resulting virus is viable, immunogenic but avirulent. It can be used as a vaccine.

Figure 16.25 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)
DNA vaccines
DNA vaccines

Clone gene for influenza hemagglutinin in a plasmid

Inject cloned gene into muscle tissue

Infect mice with influenza virus

Measure virus titer

Figure 14-28 Immunobiology, 6/e. (© Garland Science 2005)
Production of recombinant HBV vaccine

1. **Hepatitis B Virus**
   - **DNA / RNA**
   - **HB antigen producing gene**

2. **Recombinant DNA**
   - **Plasmid DNA cut with restriction enzymes**
   - **Bacterial DNA**

3. **Recombinant yeast cell**
   - **Plasmid DNA**
   - **HB antigen**
   - **Fermentation Tank**

4. **HB vaccine**
   - **Extraction & purification of HB vaccine**
   - **Recombinant yeast cell multiplying and producing HB antigen in fermentation tank**
Flu vaccine production

Recombinant DNA vaccine

Traditional method

(with technology based on chicken eggs 5 to 6 months in average is needed for mass production of influenza vaccine)
Adjuvans

Adjuvans are added to vaccines to stimulate immune response for specific antigen, while they do not induce specific immunity themselves.

Immune stimulation mechanism of adjuvans:
• Increase availability of antigen in the blood and tissue
• Increase adsorptions of antigen via APC
• Activate macrophages and lymphocytes
• Stimulate the production of cytokines
Types of adjuvans

- **Anorganic components**: aluminium salts, aluminium hydroxide, aluminium phosphate, calcium phosphate and hydroxide
- **Mineral oils**: paraffin oil (for „Depo” vaccines)
- **Bacterial products**: dead bacteria *Bordetella pertussis*, *Mycobacterium bovis*, toxoids
- **Nonbacterial organic compounds**: skvalen, thimerosal
- **Substances that facilitate delivery**: detergents (Quil A)
- **Plant saponins**: quillaja, Soy, Polygala senega,…
- **Cytokins**: IL-1, IL-2, IL-12
- **Combination**: Freund's complete adjuvans (exicated *M. tuberculosis* emulsified in mineral oil)
- **Other**: (adjuvant 65) – peanut oil
New vaccines development

• Develop better adjuvanses
  – ISCOMs (Immune Stimulatory Complexes) transfer peptides for MHC I presentation
  – Mucose adjuvans (modified pertussis toxin)

• The aim is to act on APC during simultaneous admission of cytokines

• Developing nasal or oral vaccines (molecular pharming)
Vaccine Adverse Reactions

**Adverse reaction** is extraneous effect caused by vaccine (side effect)

- **Adverse event:**
  - any medical event following vaccination
    (may be true adverse reaction or may be only coincidental)
- **Local adverse reactions:**
  - pain, swelling, redness at site of injection
    (occur within a few hours of injection; usually mild and self-limited)
- **Systemic adverse reactions:**
  - fever, malaise, headache
    (nonspecific; may be unrelated to vaccine)
- **Severe allergic: (anaphylaxis)**
  - due to vaccine or vaccine component
  - rare
  - risk minimized by screening
Contraindications and Precautions to Vaccination

Contraindication

• A condition that increases the likelihood of a serious adverse reaction to a vaccine for a patient with that condition

Precaution

• A condition in a recipient that might increase the chance or severity of an adverse reaction, or

• Might compromise the ability of the vaccine to produce immunity
## Contraindications and precautions for vaccination

<table>
<thead>
<tr>
<th>Condition</th>
<th>Live</th>
<th>Inactivated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy to component</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>---</td>
<td>C</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>C</td>
<td>V*</td>
</tr>
<tr>
<td>Immuno-suppression</td>
<td>C</td>
<td>V</td>
</tr>
<tr>
<td>Severe illness</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Recent blood product</td>
<td>P**</td>
<td>V</td>
</tr>
</tbody>
</table>

C=contraindication  
P=precaution  
V=vaccinate if indicated  
*except HPV  
**MMR and varicella containing (except zoster vaccine) only
Permanent contraindications to vaccination

• Severe allergic reaction to a vaccine component or following a prior dose
• Encephalopathy not due to another identifiable cause occurring within 7 days of pertussis vaccination
• Severe combined immunodeficiency (rotavirus vaccine)
• History of intussusception (rotavirus vaccine)
Literature:


http://www.cdc.gov/vaccines/pubs/pinkbook/index.html