D-LAB HEALTH
SP 725
Jose Gomez-Marquez
Vaccine Preventable Diseases

Causes of 2.5 million child deaths out of 10.5 million child deaths globally, 2002

- Pneumococcal Diseases 28%
- Rotavirus 16%
- Measles 21%
- Hemophilus influenzae type B 15%
- Pertussis 11%
- Tetanus 8%
- Other 1%

Rationale for Immunization or Vaccination

- Prevention of life-threatening and prevalent disease
- Reduction of carriage
- Reduction of disease transmission
- Reduction of antibiotic resistance
- Retention of antibiotic effectiveness

Active immunization: induces immediate protective immunity and stable immunological memory

- Selective Immunization
- Universal Immunization
Universal Immunization Schedule

Image removed due to copyright restrictions.
“Recommended childhood immunization schedule in the United States, 2002.”
Effect of Polio Vaccination

Reported Polio Cases

1988

1998

Image by MIT OpenCourseWare.

D-LAB HEALTH
Vaccination

Properties of an Ideal Vaccine

- Effective protection against all forms of the disease
- Strong and durable immunological memory
- Easy administration
- Easy transport *i.e.*, refrigeration, clean needles and syringes *etc*
- Affordable
Vaccine Design and Development

Vaccines that elicit protective immunity and stable immunological memory

1. Whole organism vaccines
2. Purified macromolecules
3. Recombinant vector vaccines
4. DNA vaccines
5. Multivalent subunit vaccines
Vaccine Design and Development

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- **Attenuated bacteria and viruses**, e.g. BCG for tuberculosis, Sabin polio vaccine
  
  Advantages: transient growth favors cell-mediated response and therefore a single vaccination is sufficient

  Disadvantages: reversion and induction of disease-like symptoms

- **Inactivated/killed pathogens**, e.g. Salk polio vaccine.
Vaccine Design and Development

Vaccines that elicit protective immunity and stable immunological memory

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- **Bacterial polysaccharide capsules**, e.g. *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Hemophilus influenzae*. Conjugation with carrier ensures cell-mediated response
- **Toxoids**, e.g. Diphtheria and Tetanus toxin
- **Recombinant proteins**, e.g. Hepatitis B surface antigen
Vaccine Design and Development

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Genes encoding major antigens carried by benign or attenuated viruses or bacteria, e.g.

- Canarypox virus, BCG strain of *Mycobacterium*.
- **Vaccinia virus**, is able to carry several foreign genes. Easy administration.
- **Attenuated *Salmonella typhimurium*** is used to carry antigens from Cholera and Gonorrhea causing bacteria
Vaccine Design and Development

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Plasmid DNA encoding antigenic proteins injected directly into muscle. Uptake by dendritic cells elicits protective immune response.

**Advantages**
- Native antigen that triggers both humoral and cell mediated immunity and immunological memory
- Stable vaccine, easily delivered and multiplexing is possible

**Disadvantages**
- Cannot be used for non-protein antigens
Vaccine Design and Development

Vaccines that elicit protective immunity and stable immunological memory

1. Whole organism vaccines
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Synthetic carriers that contain immunodominant B and T cell epitopes

- Solid Matrix Antibody Antigen (SMAA)
- Immunostimulatory complexes (ISCOMs)
Focus Areas for Designing Solutions

- Development of new effective vaccines
- Formulation
- Delivery
The Cold Chain for Vaccines

Vaccines must be stored at 2-8 deg C

5% Waste

Vaccine Truck

Fridge

75-83% Waste

Waste = Thermally Damaged Vaccines

Image by MIT OpenCourseWare.
## Currently administered Vaccines

<table>
<thead>
<tr>
<th>Disease/Pathogen</th>
<th>Vaccine type</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>Inactivated virus</td>
<td>Injection</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Protein</td>
<td>Hep B surface antigen</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>Live, attenuated virus</td>
<td>5 Human-bovine reassortant viruses</td>
</tr>
<tr>
<td>Polio</td>
<td>Live, attenuated virus</td>
<td>Oral</td>
</tr>
<tr>
<td>Varicella</td>
<td>Live, attenuated virus</td>
<td>Injection</td>
</tr>
<tr>
<td>Influenza</td>
<td>Inactivated virus</td>
<td>Injection</td>
</tr>
<tr>
<td>MMR</td>
<td>Live, attenuated viruses</td>
<td>Measles, mumps, rubella</td>
</tr>
<tr>
<td>Diptheria</td>
<td>Protein</td>
<td>Diptheria toxoid</td>
</tr>
<tr>
<td>Tetanus</td>
<td>Protein</td>
<td>Tetanus toxoid</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Protein</td>
<td>Viral hemagglutinins</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>Polysaccharide-protein conjugate</td>
<td>Capsular polysaccharide</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>Polysaccharide</td>
<td>Capsular polysaccharide</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>Polysaccharide</td>
<td>Capsular polysaccharide</td>
</tr>
</tbody>
</table>
The Real Cost of Needles

1/3 of vaccine injections in the developing world are UNSAFE.

This leads to:
• 250,000 cases of HIV
• Millions of cases of hepatitis

Image removed due to copyright restrictions.
Photo of young boy at a trash dump in Nairobi, holding a scavenged hypodermic syringe.
See http://www.sfgate.com/cgi-bin/object/article?f=/c/a/1998/10/27/MN52NEE.DTL&o=1
Needle-free Vaccination Sites

Figure 1 | Schematic representation of various methods of needle-free immunization.

Cutaneous immunization

Mucosal immunization

Ocular immunization
(Drops)

Nasal immunization
(Sprays and drops containing adjuvants plus liquid formulations, liposomes or microspheres)

Pulmonary immunization
(Aerosols or powders)

Epidermal powder immunization
(DNA-coated gold particles or vaccine powders)

Liquid-jet injection
(Off-the-shelf vaccine formulations)

Topical application
(Adjuvant patches, colloidal carriers, ultrasound or microneedles)

Oral immunization
(Liquid formulations and pills containing adjuvants plus liposomes, microspheres or bacterial ghosts)

Vaginal or rectal immunization
(Creams containing adjuvants)

Courtesy of Samir Mitragotri. Used with permission.

DNA Vaccine Delivery by Propulsion into Skin via a “Gene Gun”

Allows rapid delivery of a vaccine to large populations without the requirement of huge supplies of sterile needle and syringes
Two images removed due to copyright restrictions.
“How to Make an Edible Vaccine” and
“How Edible Vaccines Provide Protection.”
Sanaria produces a vaccine for malaria.


Excerpt of Grand Challenges in Global Health grant recipient Hiroyuki Matsuoka's topic and grant summary have been removed due to copyright restrictions.
Standard Immunization Team

- **Drug Preparation**: 6 Physicians and Aides
- **Doctor Gives Shot**: 200 Patients in-clinic
- **Patient Registration and Disposal**: 70 Patients in the field

Sources: USAID, Becton Dickinson
Dry Powder Vaccines

Fig. 3. Electron micrograph of GFP-labeled *M. smegmatis* spray dried with leucine.

SI Fig 5. Newborn dry powder inhaler device with squeeze actuation.

Focus Areas for Designing Solutions

- Transcutaneous delivery of vaccines – Iomai/Intercell Inc Technology

EC.710 D-Lab: Medical Technologies for the Developing World
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