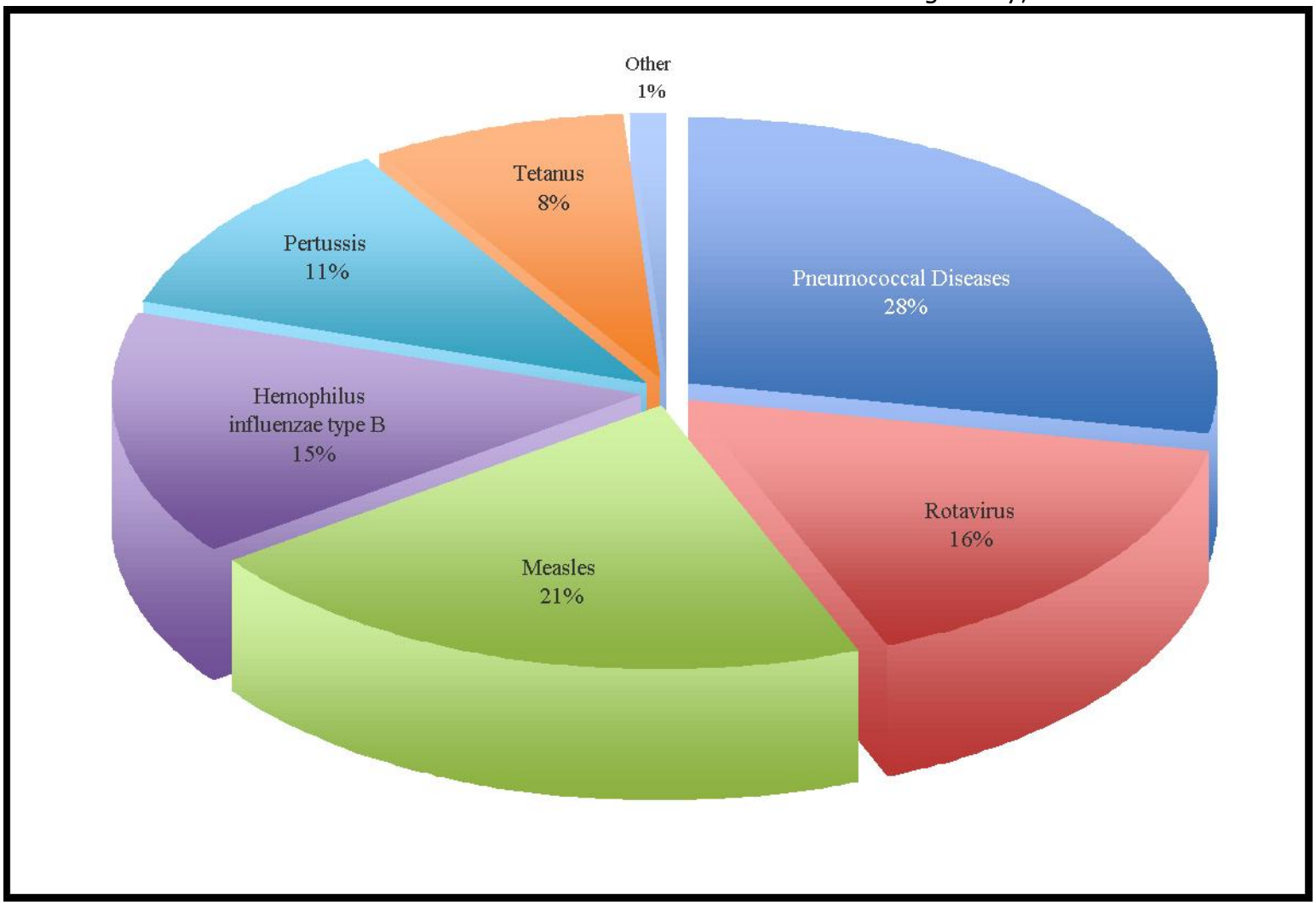
Massachusetts Institute of Technology

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



Source: WHO *Wkly Epidemiol Rec*. (2006) 81:189-196.

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 imunization: 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."
Table 18-3 in Goldsby, R. A. *Immunology*. 5th edition. New York, NY: Macmillian, 2003. p. 417.
See http://books.google.com/books?id=8281_jkbdhoC&pg=RA1-PA417

Effect of Polio Vaccination

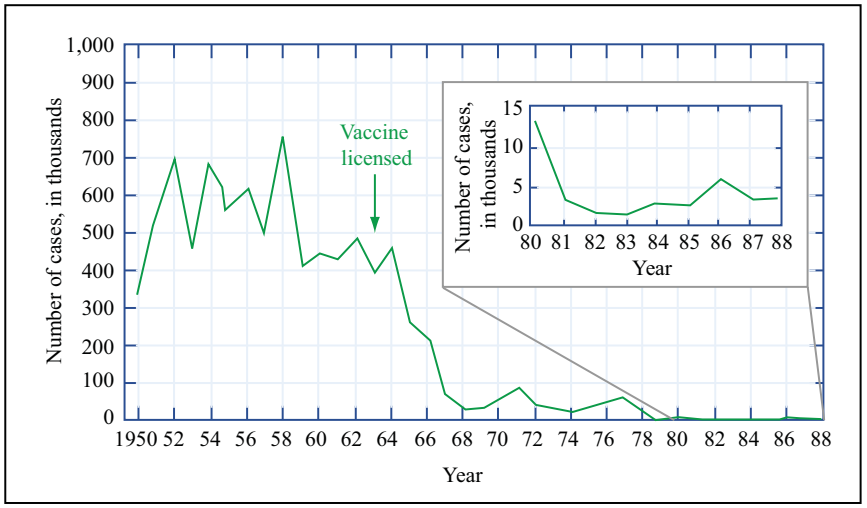


Image by MIT OpenCourseWare.

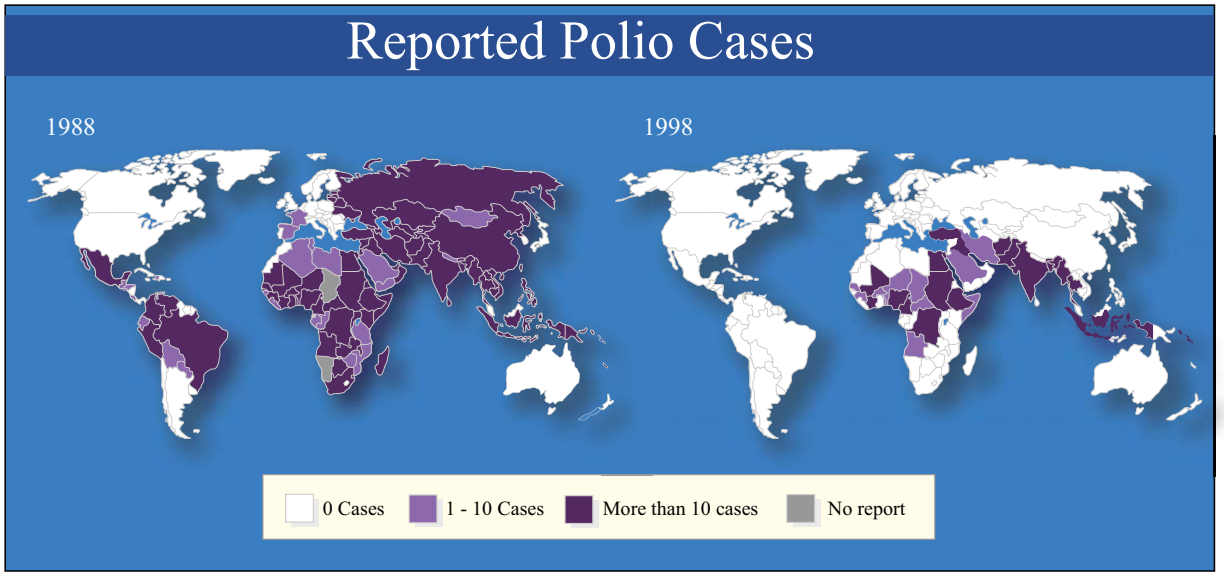


Image by MIT OpenCourseWare.

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

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

- 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

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

- 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

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

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

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

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
2. Purified macromolecules
3. Recombinant vector vaccines
4. DNA vaccines
5. Multivalent subunit vaccines

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

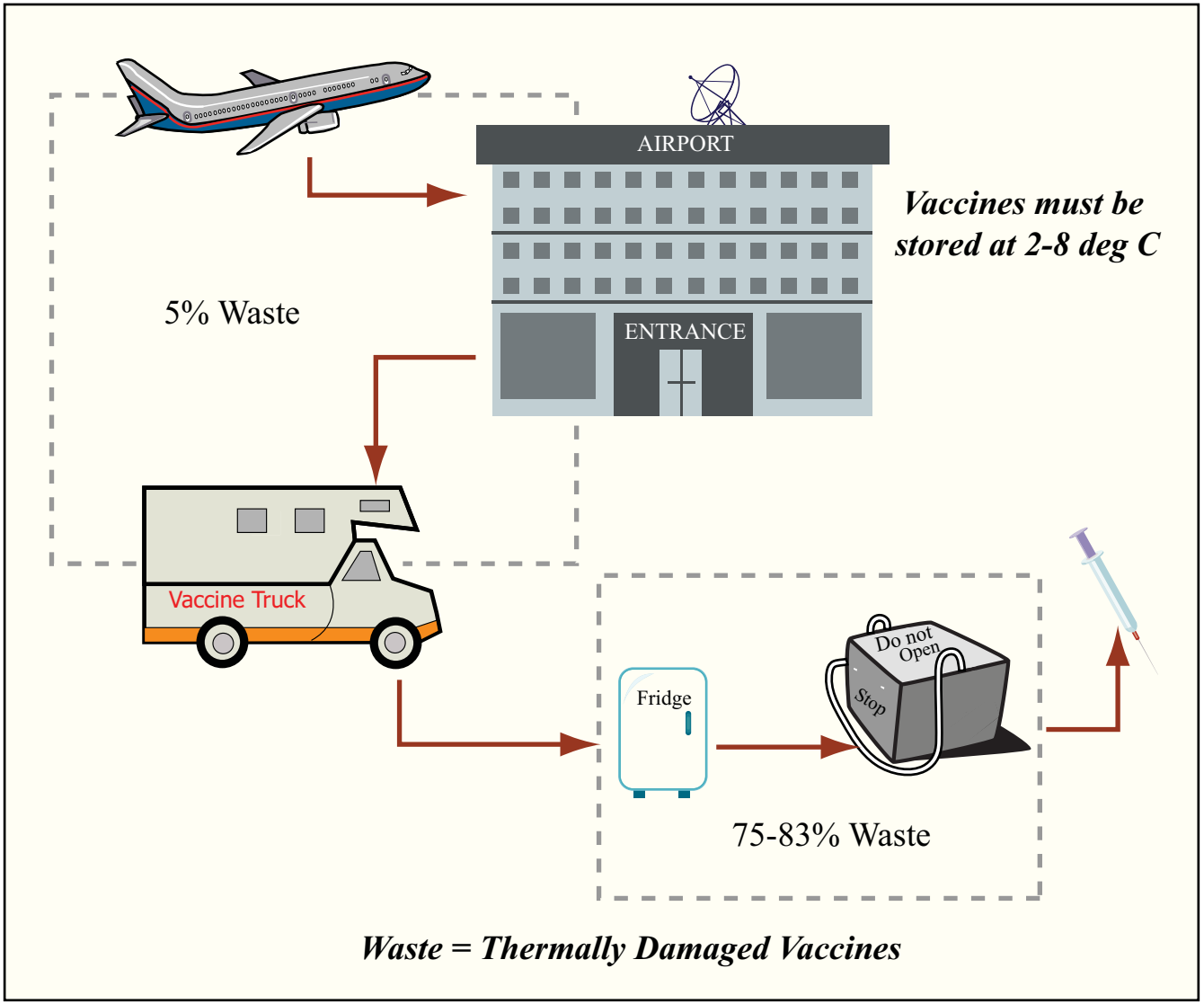
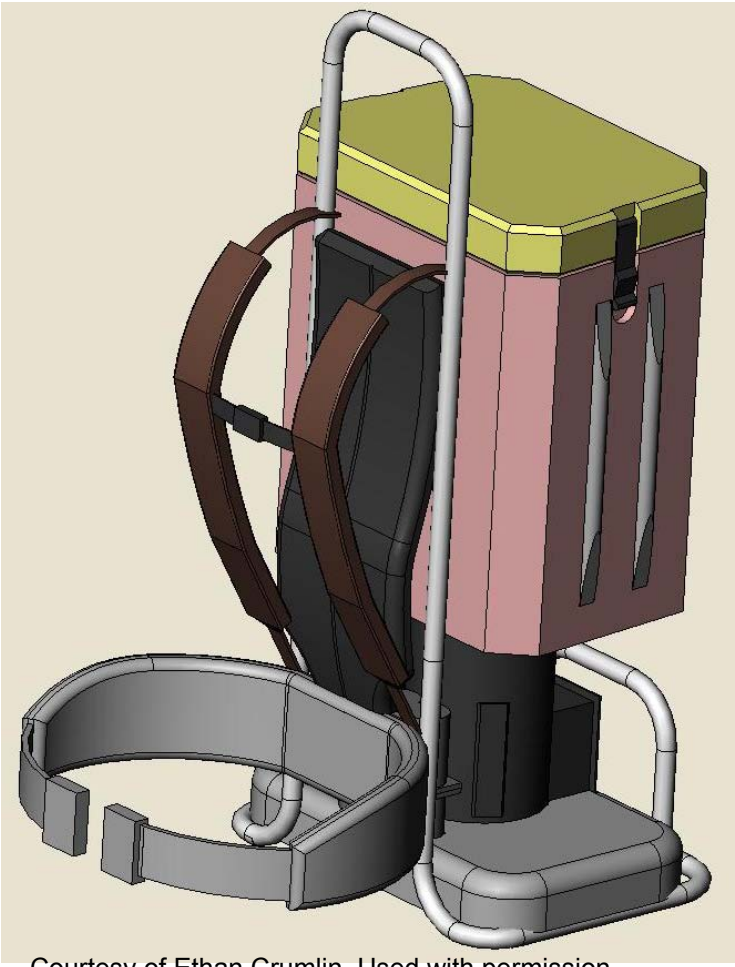


Image by MIT OpenCourseWare.

oneworld medical devices

Vaccine Pack

making bridges to a healthy world



Courtesy of Ethan Crumlin. Used with permission.

Currently administered Vaccines

Disease/Pathogen	Vaccine type		Administration
Hepatitis A	Inactivated virus		Injection
Hepatitis B	Protein	Hep B surface antigen	Injection
Rotavirus	Live, attenuated virus	5 Human-bovine reassortant viruses	Injection
Polio	Live, attenuated virus		Oral
Varicella	Live, attenuated virus		Injection
Influenza	Inactivated virus		Injection
MMR	Live, attenuated viruses	Measles, mumps, rubella	Injection
Diptheria	Protein	Diptheria toxoid	Injection
Tetanus	Protein	Tetanus toxoid	Injection
Pertussis	Protein	Viral hemaglutinins	Injection
Pneumococcus	Polysaccharide-protein conjugat	Capsular polysaccharide	Injection
Meningococcus	Polysaccharide	Capsular polysaccharide	Injection
Hemolphilus influenzae	Polysaccharide	Capsular polysaccharide	Injection

The Real Cost of Needles

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

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

This leads to:

- **250,000** cases of HIV
- **Millions** of cases of hepatitis

Needle-free Vaccination Sites

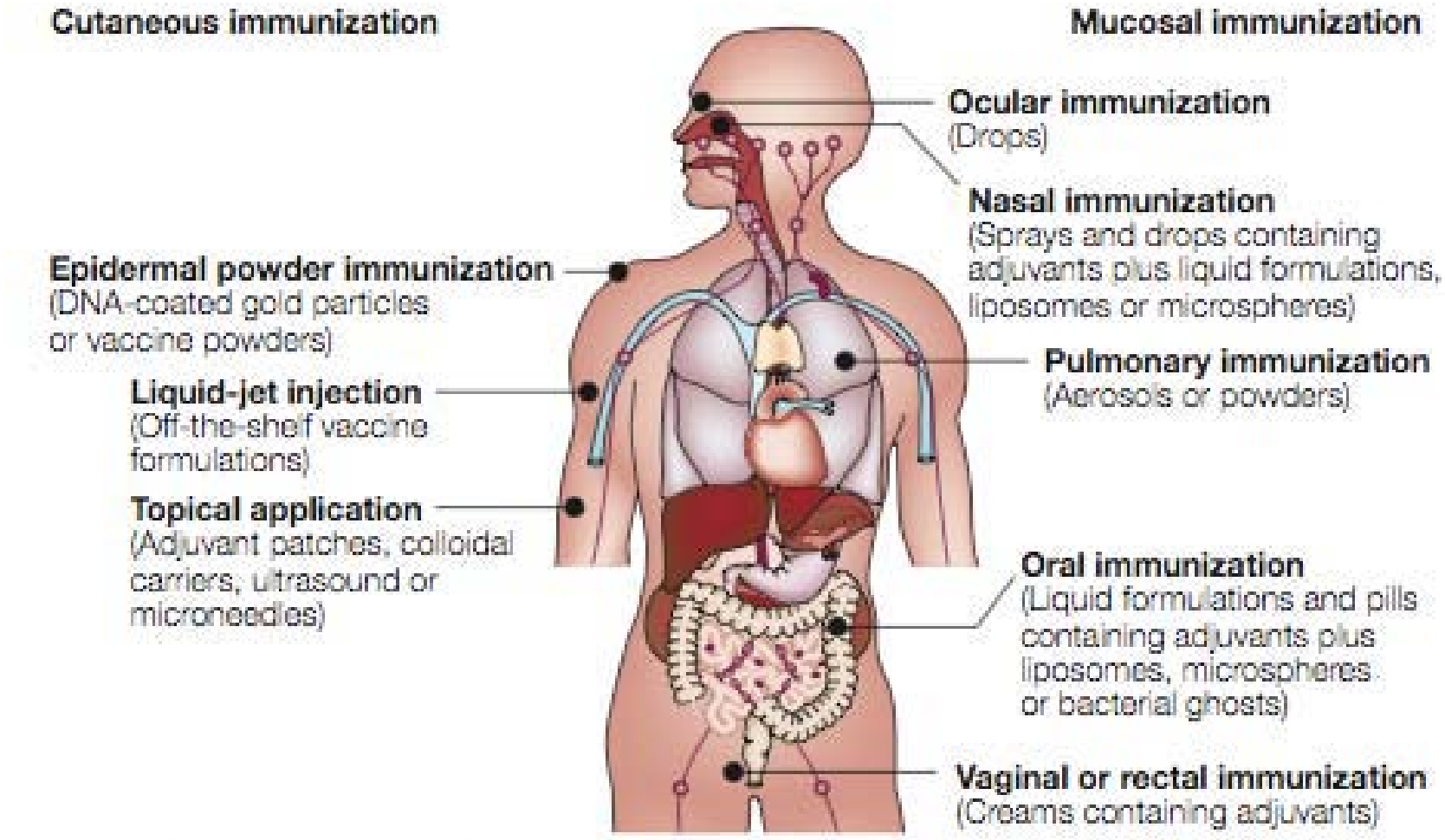
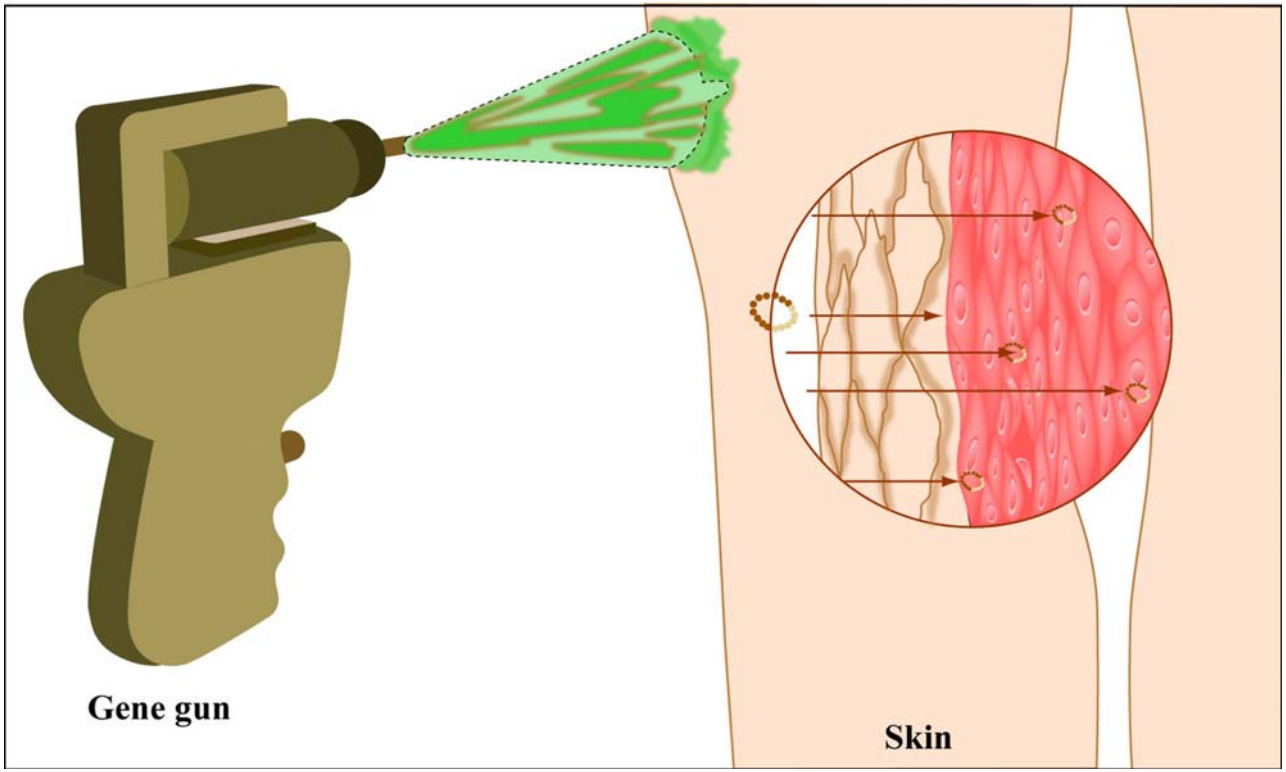


Figure 1 | **Schematic representation of various methods of needle-free immunization.**

Courtesy of Samir Mitragotri. Used with permission.

Mitragotri. Immunization without needles. Nat Rev Immunol (2005) vol. 5 (12) pp. 905-16

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."
Source: Langridge, W. H. R. "Edible Vaccines." *Scientific American*.
September 2000.

Image of Sanaria website http://sanaria.com
removed due to copyright restrictions.
Sanaria produces a vaccine for malaria.

Article excerpt from Nature removed due to copyright restrictions.
See Butler, Declan. "Mosquito production mooted as fast track to malaria vaccine." Nature 425 (2003): 437.

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

92

Protective Immunity produced by the Injection of X-irradiated Sporozoites of *Plasmodium berghei*

STUDIES with avian malaria have shown that killed sporozoites as well as sporozoites inactivated with ultraviolet light can produce a partial immunity after injection into birds[1,2]. On the other hand, attempts to use the erythrocytic stages of the parasite as the source of antigen have met with only limited success with avian[3], rodent[4] and monkey malaria[3,4]. Previous attempts to use killed sporozoites of the rodent malarial parasite, *Plasmodium berghei*, to immunize rodents have been unsuccessful. We therefore sought to determine whether protective immunity to this parasite could be achieved by partial inactivation of the injected sporozoites as opposed to injection of dead parasites. X-irradiation was chosen as the inactivating agent, because of the partial immunity

er branches.

Reprinted by permission from Macmillan Publishers Ltd: Nature.
Source: Nussenzweig, R. S., et al. "Protective Immunity Produced by the Injection of X-irradiated Sporozoites of Plasmodium berghei." *Nature* 216 (1967). © 1967.

Standard Immunization Team

DRUG PREPARATION

DOCTOR GIVES SHOT

PATIENT REGISTRATION

BIOHAZARD DISPOSAL

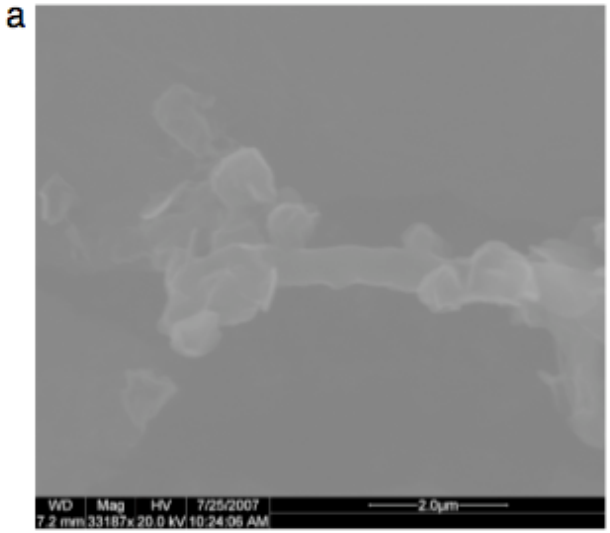
6 ***PHYSICIANS AND AIDES***

200 ***PATIENTS IN-CLINIC***

70 ***PATIENTS IN THE FIELD***

Sources: USAID, Becton Dickinson

Dry Powder Vaccines



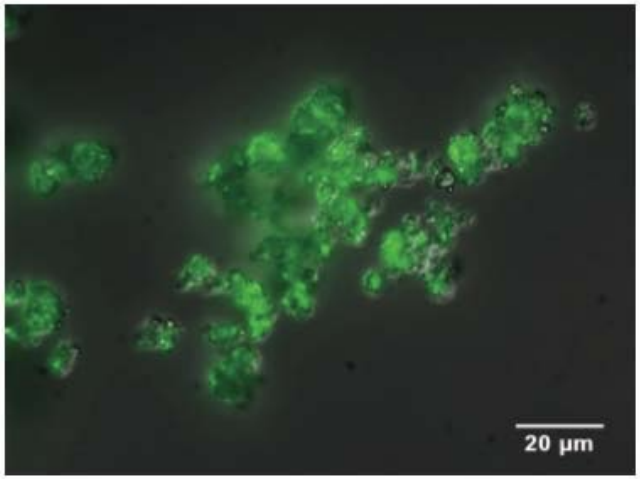
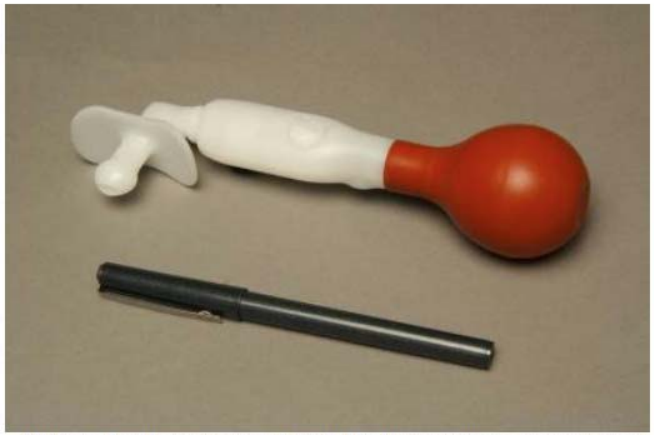


Fig. 3. Electron micrograph of GFP-labeled *M. smegmatis* spray dried with leucine.



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

Sources: Left: Wong, Y-L, et al. "Drying a tuberculosis vaccine without freezing." *Proc Natl Acad Sci USA* (2007) 104, no. 8: 2591-2595. Right: Garcia-Contreras, L, et al. "Immunization by a bacterial aerosol." *Proc Natl Acad Sci USA* (2008) 105 (12): 4656-4660. Courtesy of National Academy of Sciences, U. S. A. Used with permission. Copyright © 2007, 2008 National Academy of Sciences, U.S.A.

Focus Areas for Designing Solutions

- Transcutaneous delivery of vaccines – Iomai/Intercell Inc Technology

- See videos at http://www.intercell.com/main/forvaccperts/technologies/vaccine-patch/

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

Spring 2010