Massachusetts Institute of Technology

D-LAB HEALTH
SP 725

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Infectious Diseases in Global Health

- Scope and magnitude of the problem
- What can we do?
- Framework for designing solutions and interventions
- Examples and case studies.

The Burden of Disease

Disability Adjusted Life Years

The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.

Infectious Diseases in Global Health

Leading Causes of Mortality and Disease Burden from Infectious Diseases (2002)

	Deaths (millions)	DALYs* (millions)
Respiratory Infections	3.96	94.60
Diarrheal Diseases	1.80	61.97
HIV/AIDS	2.78	84.46
Tuberculosis	1.57	34.74
Malaria	1.27	46.49

Source: WHO Death & DALY Estimates Report for 2002

Source: BVGH Global Health Primer, 2007.
http://www.bvgh.org/LinkClick.aspx?fileticket=aqnG6VPYW_o%3D&tabid=91
Courtesy of BIO Ventures for Global Health. Used with permission.

Infectious Diseases in Global Health

Cause the greatest burden of disease. Each year **>10 million** children under 5 years die from preventable or treatable diseases.

- {Respiratory infections + diarrheal diseases} kill ≈ {AIDS + TB + Malaria}
- Each year 2-3 million children die from acute diarrheal illnesses (ADI) including rotavirus, enterotoxigenic *E. coli* (ETEC) and Shigella. Some 60% of the deaths from diarrhea occur in 10 developing countries.
- Nearly 40 million people (including 2.3 million children) are currently living with HIV/AIDS - 63% live in Africa.
- > 2.4 billion people (40% of global population) in over 100 countries are at risk for malaria. 300-400 million cases of acute malaria each year.
- Multidrug-resistant or MDR-TB is in every country worldwide - resistant to at least isoniazid and rifampicin, the two principal first-line drugs.

Infectious Diseases in Global Health

- Neglected Diseases
- 1 billion people affected.
- ½ million deaths annually.
- Lymphatic filariasis patients lost 20% productive working days each year. 1/3rd of S. Africa's workforce is HIV-positive.
- Repeated bouts of childhood diarrheal infections are associated with malnutrition and growth stunting and diminishing mental development in children.

Box 1. The Thirteen Neglected Tropical Diseases in Africa and Their Major Etiologic Agents

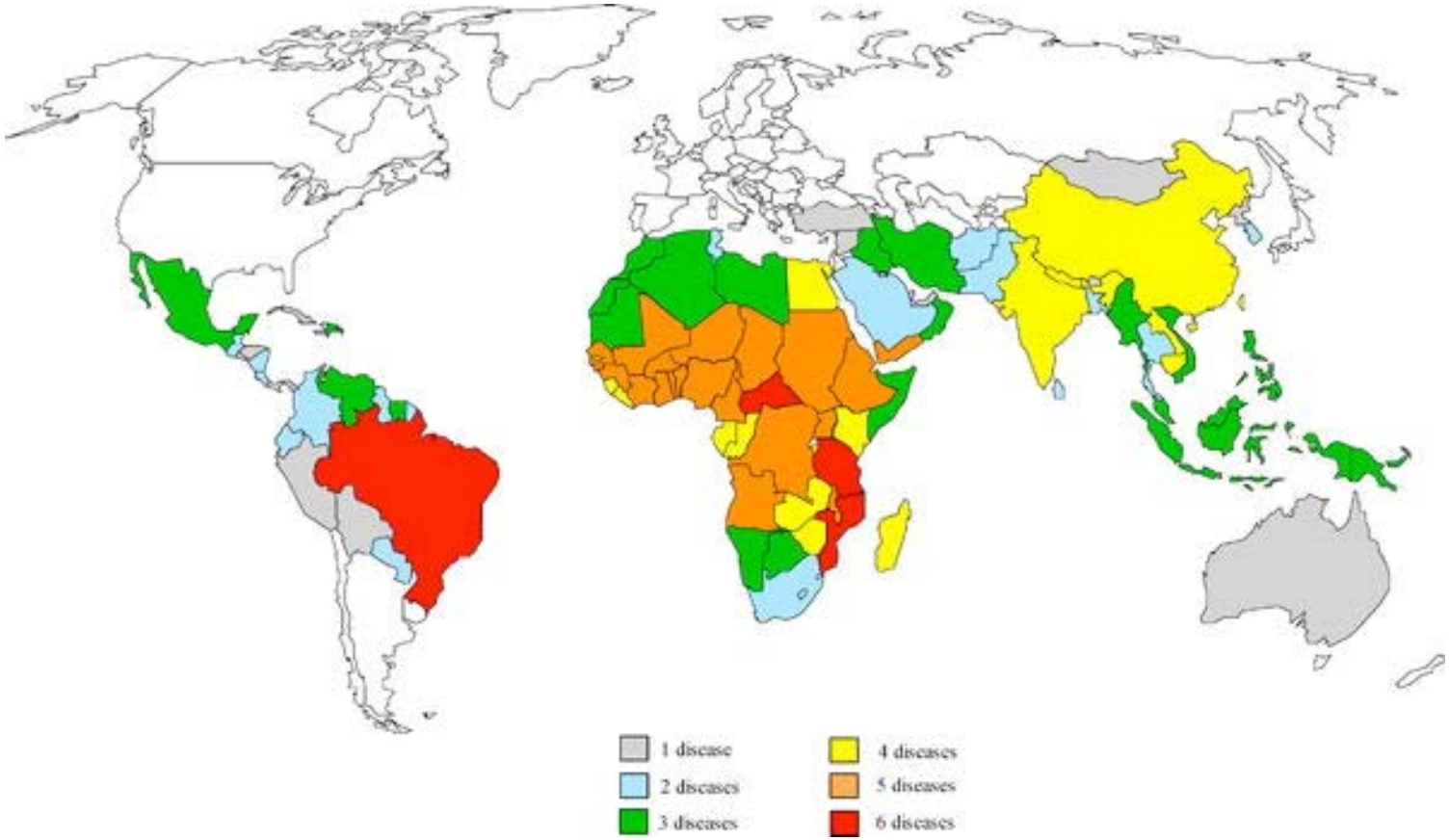
Protozoan Infections	
African trypanosomiasis	*Trypanosoma gambiense, T. rhodesiense*
Kala-azar (visceral leishmaniasis)	*Leishmania donovani*
Helminth Infections	
STH Infections	
Ascariasis	*Ascaris lumbricoides*
Trichuriasis	*Trichuris trichiura*
Hookworm infection	*Necator americanus*
Schistosomiasis	
Urinary schistosomiasis	*Schistosoma haematobium*
Hepatobiliary schistosomiasis	*Schistosoma mansoni*
Lymphatic filariasis	*Wuchereria bancrofti*
Onchocerciasis	*Onchocerca volvulus*
Dracunculiasis	*Dracunculus medinensis*
Bacterial Infections	
Trachoma	*Chlamydia trachomitis*
Leprosy	*Mycobacterium leprae*
Buruli ulcer	*Mycobacterium ulcerans*

(Modified from [3])

Source: "Rapid-Impact Interventions": How a Policy of Integrated Control for Africa's Neglected Tropical Diseases Could Benefit the Poor." Molyneux DH, Hotez PJ, Fenwick A PLoS Medicine Vol. 2, No. 11, e336 doi:10.1371/journal.pmed.0020336. Courtesy of the authors. License: CC Attribution.

Infectious Diseases in Global Health

- Neglected Diseases:
- 1 billion people affected and ½ million deaths annually.



From http://www.who.int/neglected_diseases/en/, accessed October 2009.
Courtesy of the World Health Organization. Used with permission.

African Sleeping Sickness

- Model of a extremely variant pathogen
- *Tse-tse* fly
- *Trypanosoma brucei*

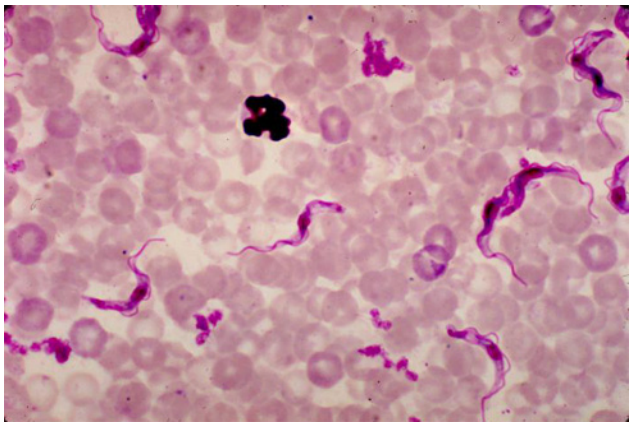
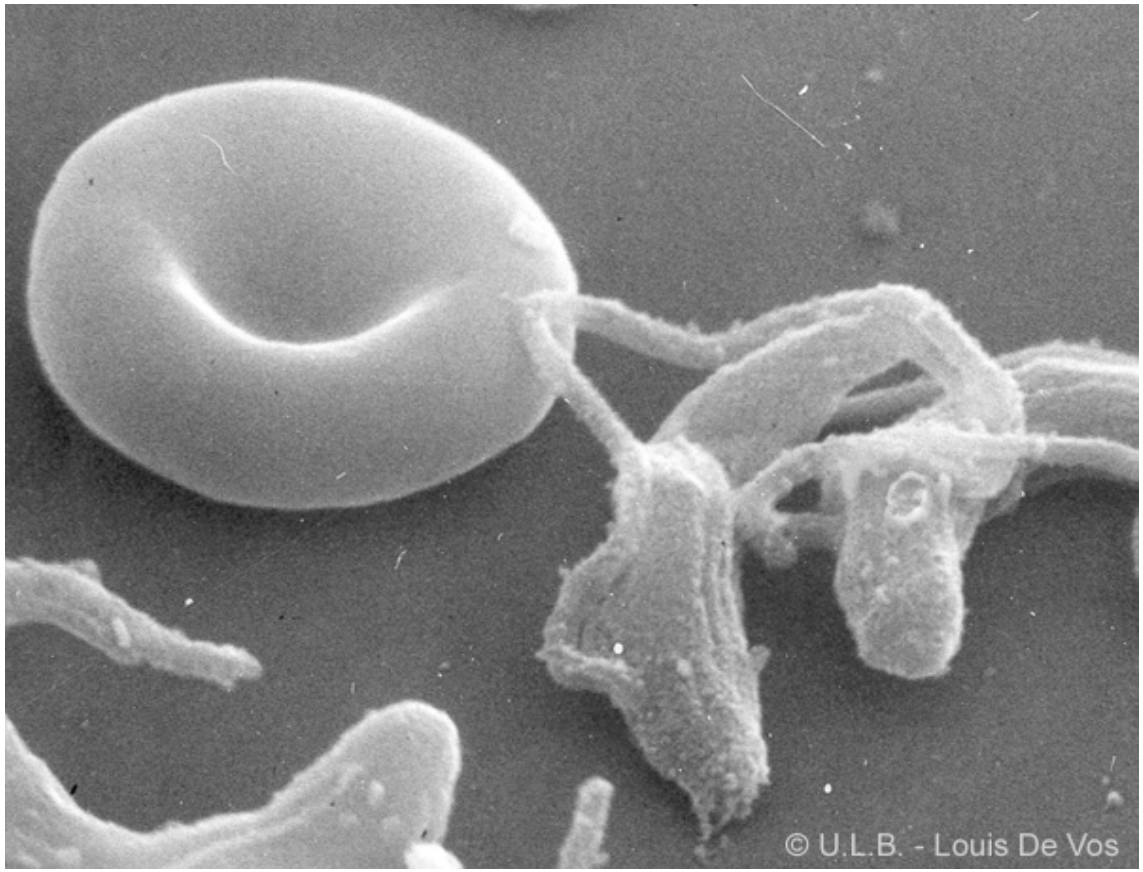


Image: US NIH.

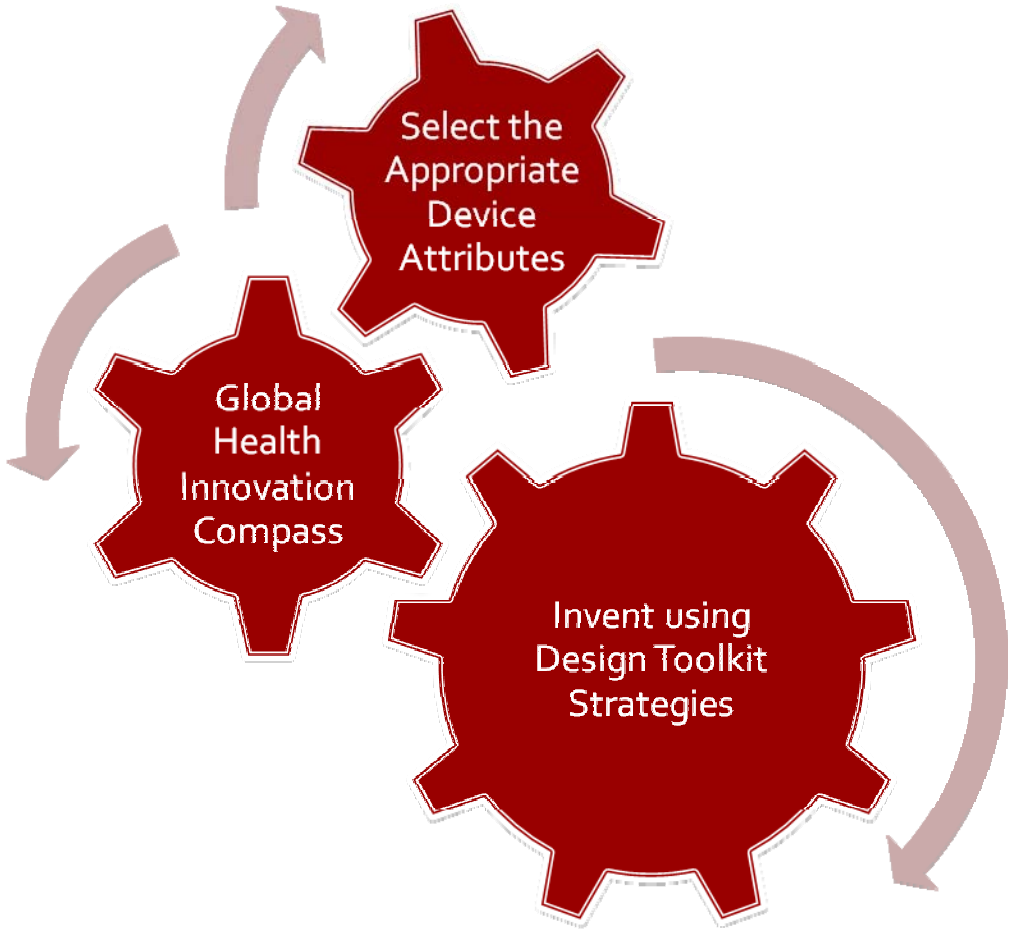


Courtesy of Louis De Vos. Used with permission.

Focus Areas for Designing Solutions

- Diagnosis
- Therapy – Medicines, Compliance/Adherence.
- Prevention – Vaccines.
- Management – Monitoring/Surveillance
- SYSTEMS

The D-Lab Health Design Cycle
Elements for Device Design Success



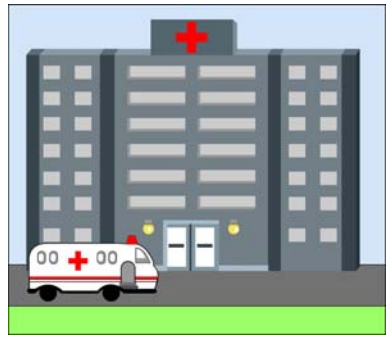
Attributes for Medical Devices

Essential	Enhancing	Long-Term
• SAFE • Accurate • Robust • Longevity • Cheap • Reliable • Reusable/Disposable	• Mobile • Connected • Smart • Plug n' Play	• Local Mfg • Local Innovation

Global Health Innovation Compass

Inexpensive / Appropriate

Expensive / Appropriate



Inexpensive / Not Very Appropriate

Expensive / Not Very Appropriate

Program Goal X Level of Pushing the Status Quo

Net Resources Expended (Time & Money – Resulting Impact)

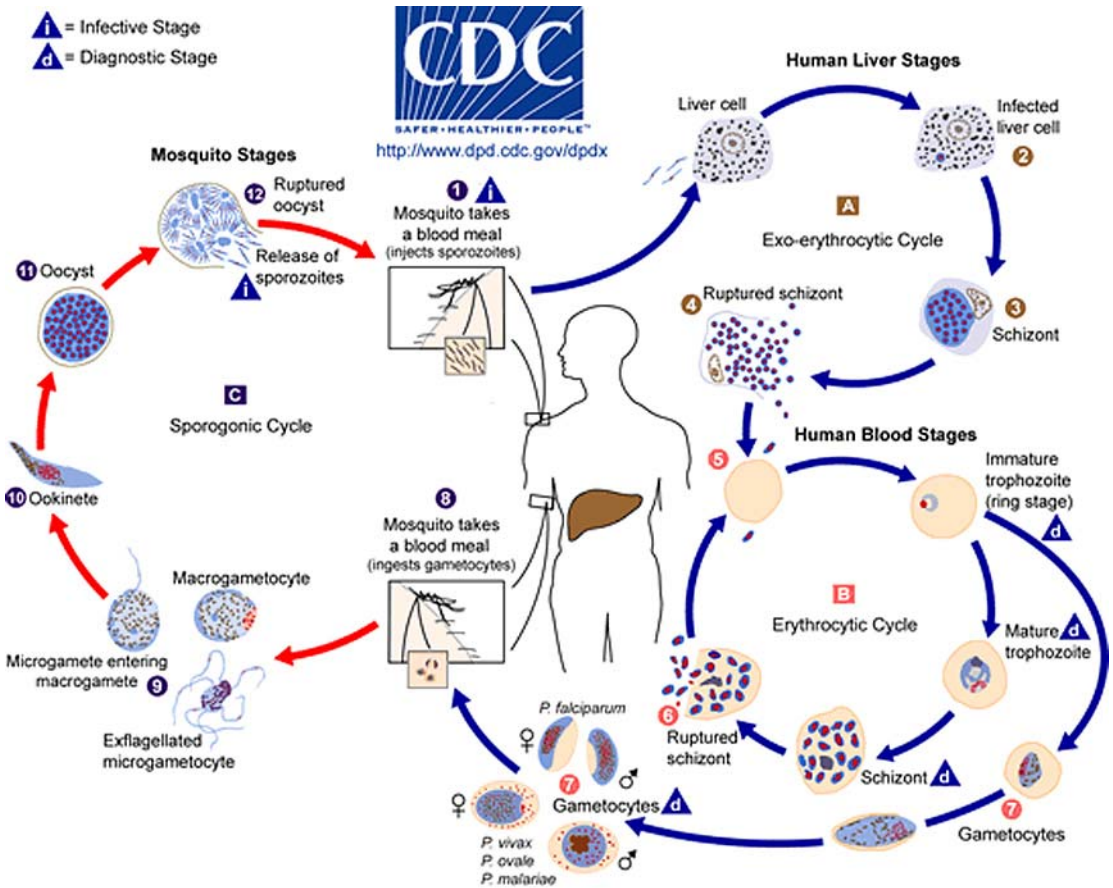
Diagnostics

Photos removed due to copyright restrictions.
Various medical diagnostic tools.

Malaria

- Model for a multi stage infectious disease
- *Anopheles* mosquito
- *Plasmodium vivax*,
- *Plasmodium falciparum*

Merozoite penetrating a red blood cell



Merozoite multiplying in a red blood cell

Courtesy of the WEHI-TV. Used with permission.

Diagnosis of Malaria

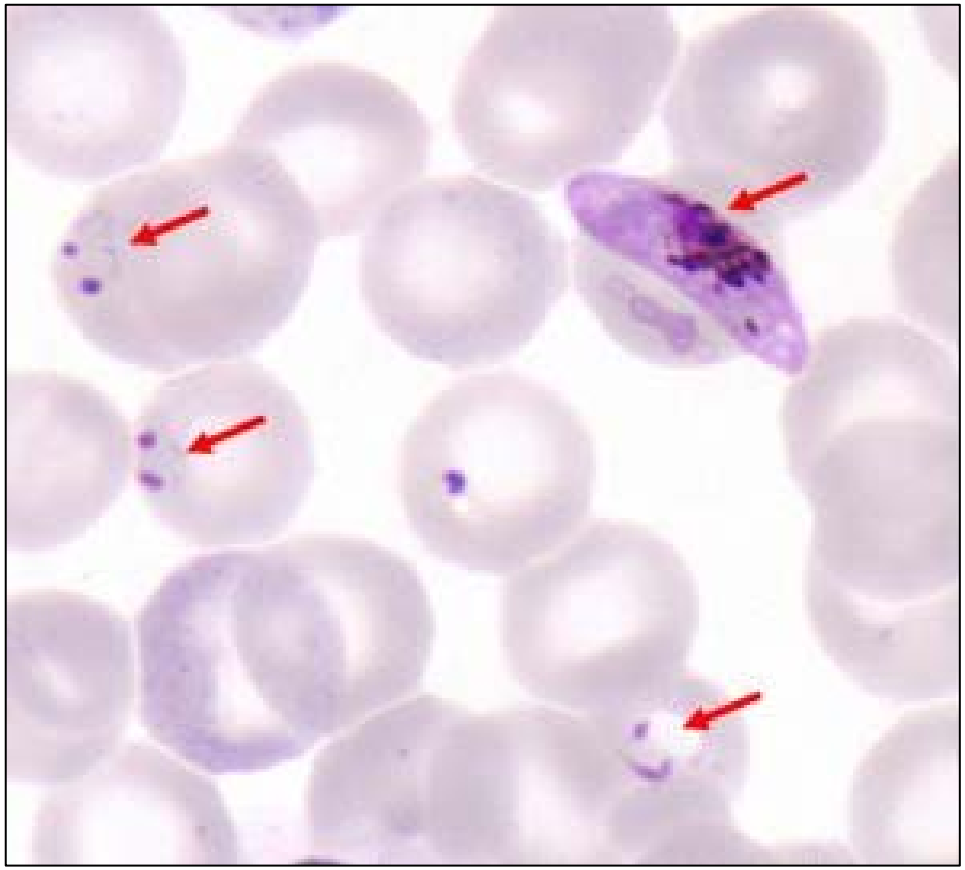


Image: US CDC

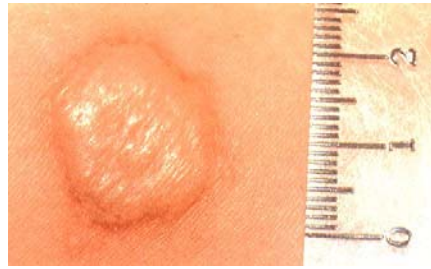
Diagnosis of Pneumonia

- Chest X-ray
- Viral vs. Bacterial:
  - Complete blood count
  - Sputum stain
  - Fluid from lungs
- Developing Countries:
  - Treat all pneumonias in children with antibiotics
  - Has reduced mortality
  - May encourage antibiotic resistance

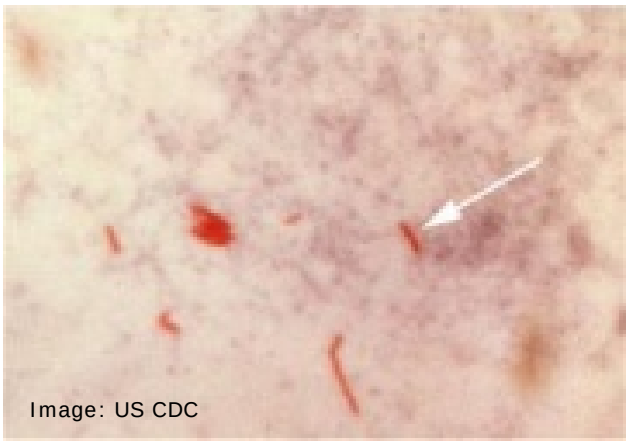
Image: US CDC

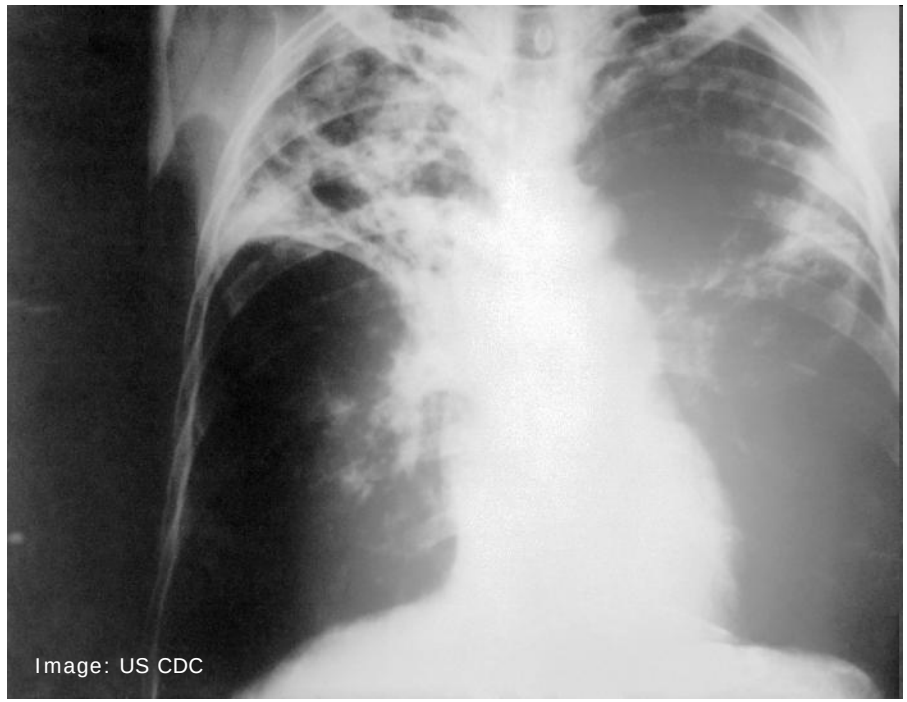
Diagnosis of Tuberculosis

- Skin test (PPD)
- Serum test
- Chest X-ray
  - Shows nodules in active TB
- Sputum
  - Acid-fast bacilli



Courtesy of the Canadian Lung Association. Used with permission.





Direct Fluorescence Assay

- Collect nasal secretions
- Spin down cells
- Place cells on slide
- Immerse in alcohol
- Apply solution containing antibodies which bind to viruses
- Antibodies are coupled to fluorescent dye
- Examine with fluorescence microscope

Microfluidics Applications

- **Diagnostics/Management**
  - **Point of Care (POC)**
  - **Disease Surveillance**

Various images of microfluidic devices removed due to copyright restrictions.

Sample Pre-processing for Diagnostics

Step 1
Use lancet to take blood from finger, and put into straw

Step 2
Open SNAP Device, and load with:
- Straw (containing blood sample)
- Blister Pack
- Waste and Sample Containers

Step 3
Close device, lock, and attach bicycle pump

Step 4
Pressurize device to 60 psi to push blood and buffer through straw

Step 5
Pull and rotate. Pressurize to push ethanol through straw.

Step 6
Pull and rotate. Pressurize to push water through straw.

Step 7
Open device to remove DNA solution and dispose of waste

How the System for Nucleic Acid Purification (SNAP) Works

SNAP

Simple Nucleic Acid Processing

Directly Observed Therapy (DOT)

- A health care worker watches and helps as the patient swallows anti-TB medicines in his/her presence.
- DOT shifts responsibility for cure from patient to health care system
- Requires political commitment, accurate diagnosis, quality drugs, observation, follow up
- DOT works well in many developing countries

Compliance by "electronic" pills

A Wireless Pharmaceutical Compliance Monitoring System Based on Magneto-Inductive Sensors

Xueliang Huo, *Student Member, IEEE*, and Maysam Ghovanloo, *Member, IEEE*

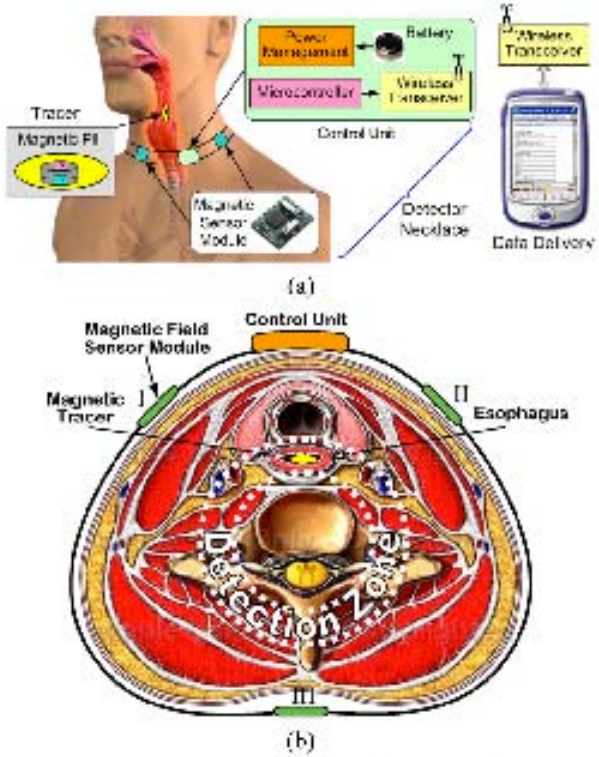


Fig. 1. (a) Schematic diagram of the wireless magnetic PCM system (MagneTrace) consisting of a magnetic tracer incorporated with the medication, a detector necklace, and a data delivery device. (b) Rendered cross section of the neck demonstrating the position of the sensor modules around the esophagus, as well as the detection zone, where the proposed PCM system looks for the passage of the tracer.

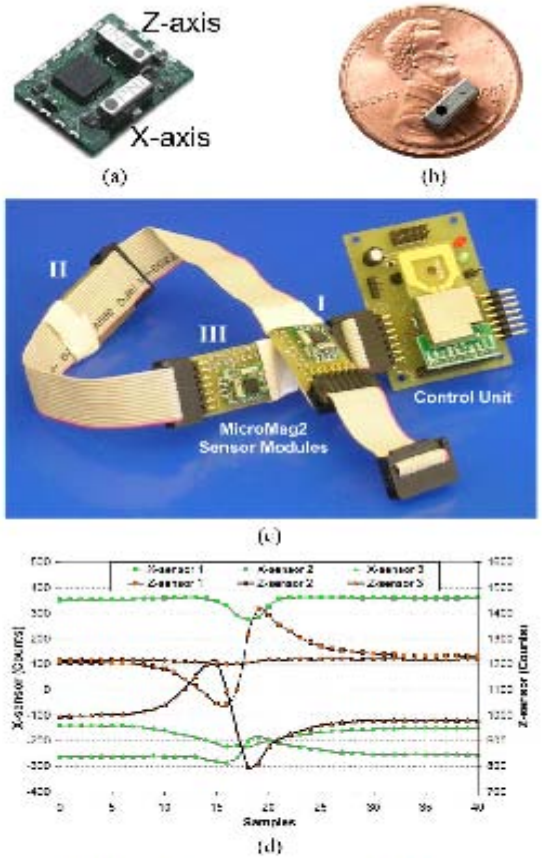


Fig. 3. (a) PNI MicroMag2 two-axis sensor module. (b) A PNI magneto-inductive sensor on a U.S. penny. (c) Prototype MagneTrace detector necklace consisting of three MicroMag2 sensor modules and a control unit. (d) Sample waveforms recorded at 11 samples/s from three X axis and three Z axis sensors while passing a magnetic tracer through the artificial neck, resembling ingestion (DIE). Sensor counts are proportional to the measured magnetic field strength [19].

The Cold Chain for Vaccines

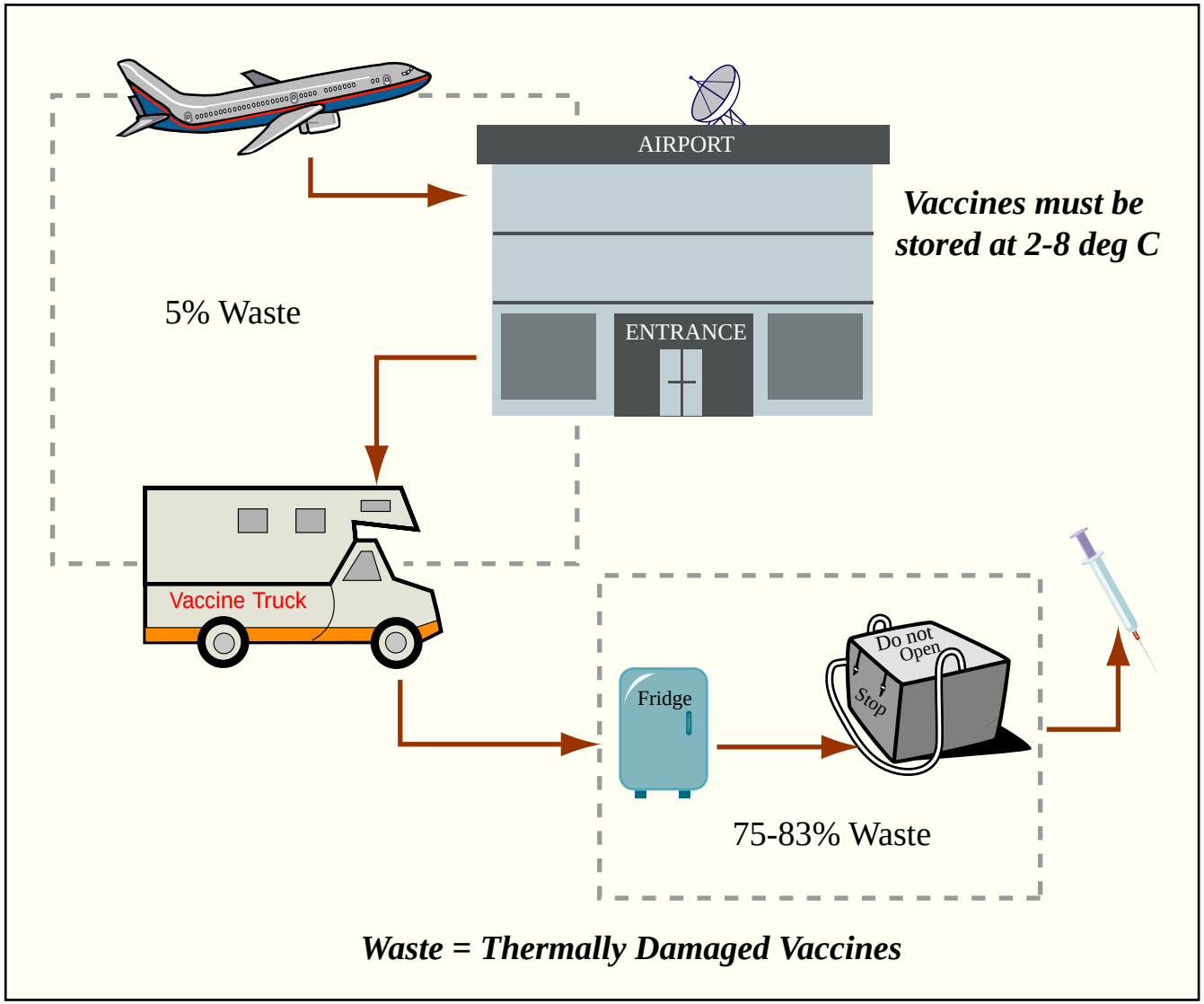


Image by MIT OpenCourseWare.

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

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

Aerovax Man

1 *LOW SKILLED VOLUNTEER*

650 *PATIENTS IN THE FIELD*

62% *SAVINGS*

Sources: Aerovax, MIT Analysis

Oral Rehydration Therapy

- 1975 WHO and UNICEF:
  - 90 mM sodium
  - 20 mM potassium
  - 80 mM chloride
  - 30 mM bicarbonate
  - 111 mM glucose
- Packet of ORT: 10 cents
- ORT in the U.S.

Photo of Pedialyte® products removed due to copyright restrictions.

Preventing Malaria

- Pregnant women and infants should sleep under insecticide treated nets
  - 25% reduction in low birth weight babies
  - 20% reduction in infant deaths
  - Cost: $1.70 (Retreatment: 3-6 cents)

Image: US Department of State / Timothy Ziemer

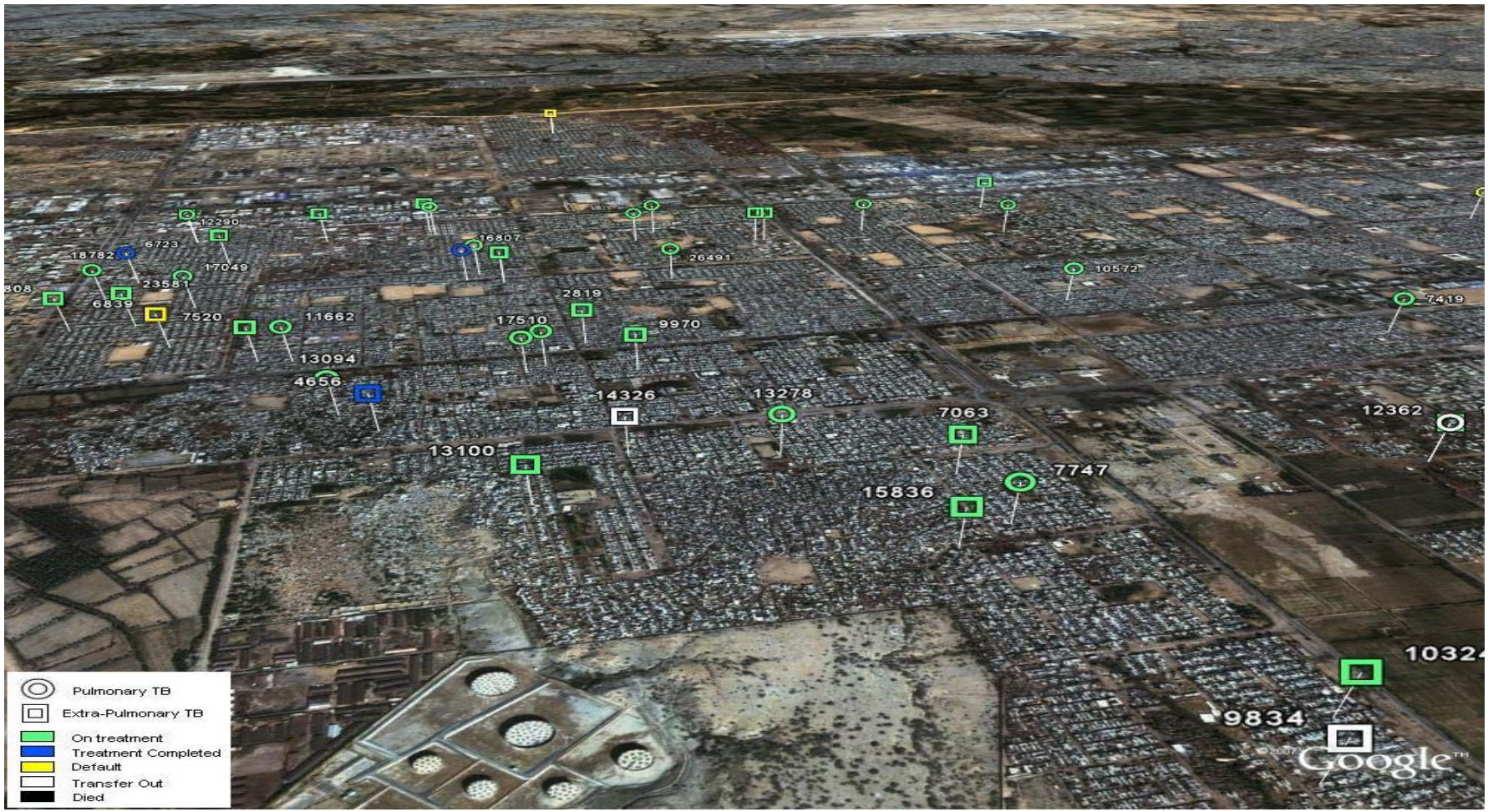
Preventing Neonatal Infections

Infection Management

- Disease surveillance

Infection Management

- Disease surveillance



Infection/Disease Surveillance

- Google FluTrends

Image removed due to copyright restrictions.

See graphic in Helft, Miguel. “Google Uses Searches to Track Flu’s Spread.” *The New York Times*, November 11, 2008. Accessed October 14, 2009. http://www.nytimes.com/2008/11/12/technology/internet/12flu.html?scp=1&sq=google%20flu&st=cse

How do we get there? Design Strategies

- Hybridization
- Vintage Technologies + Smart Design/Tech = New Solutions
- Taking the improvisation and engineering solutions
- Bottom up observation
- Be trendsetting, not trendy
- Context shifting
- Distributed Systems
- Crowd sourcing

The Stage & the Actors

Policy & Aid

- WHO
- UNICEF
- Multilateral aid agencies
- MSF
- Red Cross

- Solution Side
- PATH
- FIND
- Rice, Duke,
- MIT
- CIMIT
- MedMondiale
- IAVI*
- OneWorld Health*

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

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