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SP.718 Special Topics at Edgerton Center: D-Lab Health: Medical Technologies for the Developing World  
Spring 2009

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Massachusetts Institute of Technology

# D-LAB HEALTH

## SP.718/755

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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



**D**isability **A**adjusted **L**ife **Y**ears

*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/documents/BVGH\\_Global\\_Health\\_Primer\\_2007.pdf](http://www.bvgh.org/documents/BVGH_Global_Health_Primer_2007.pdf)

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  $\approx$  {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.
- 1/2 million deaths annually.
- Lymphatic filariasis patients lost 20% productive working days each year. 1/3<sup>rd</sup> 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	<i>Trypanosoma gambiense</i> , <i>T. rhodesiense</i>
Kala-azar (visceral leishmaniasis)	<i>Leishmania donovani</i>

### Helminth Infections

#### STH Infections

Ascariasis	<i>Ascaris lumbricoides</i>
Trichuriasis	<i>Trichuris trichiura</i>
Hookworm infection	<i>Necator americanus</i>

#### Schistosomiasis

Urinary schistosomiasis	<i>Schistosoma haematobium</i>
Hepatobiliary schistosomiasis	<i>Schistosoma mansoni</i>

#### Lymphatic filariasis

Onchocerciasis	<i>Wuchereria bancrofti</i>
	<i>Onchocerca volvulus</i>

#### Dracunculiasis

	<i>Dracunculus medinensis</i>
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### Bacterial Infections

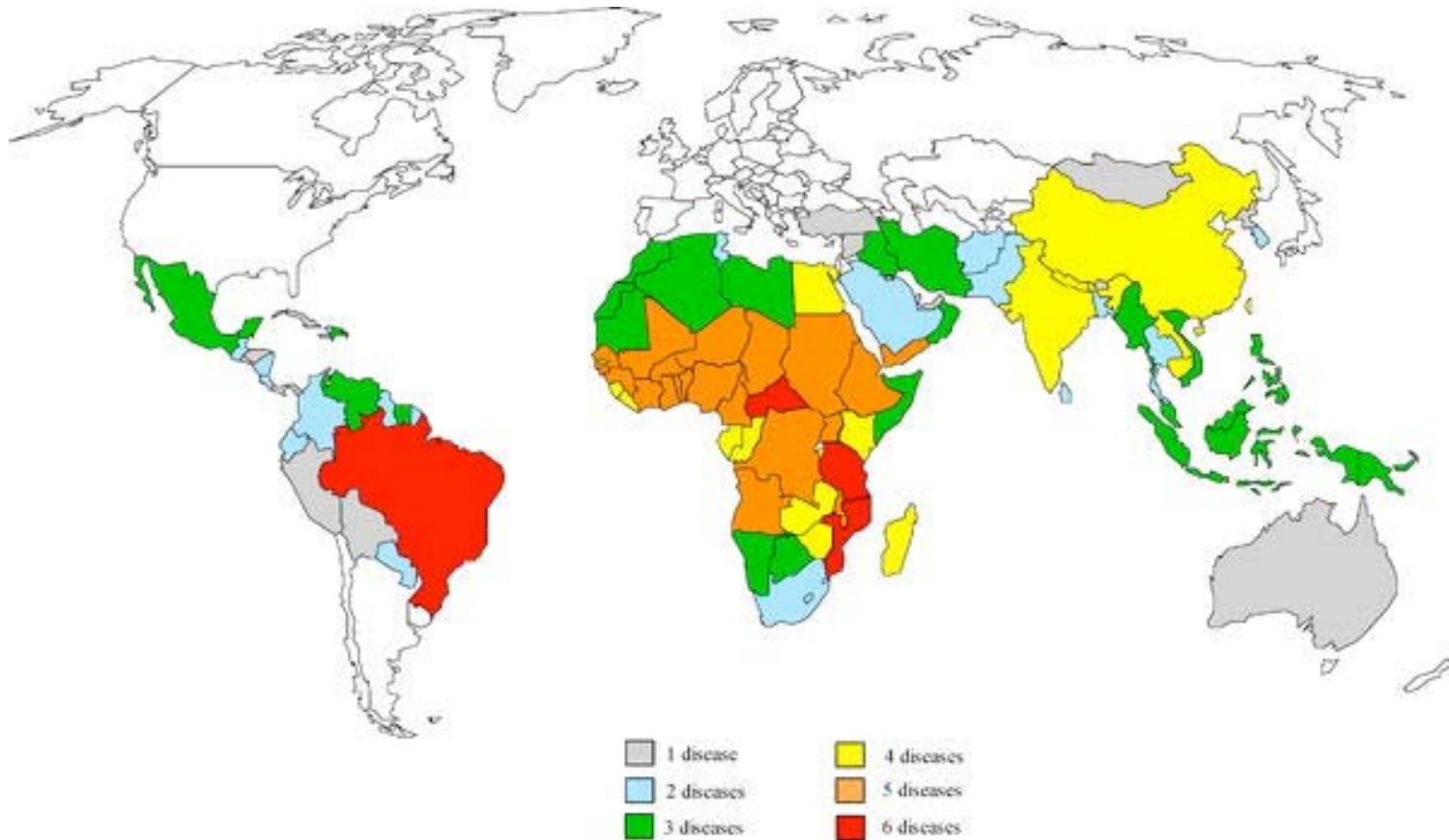
Trachoma	<i>Chlamydia trachomatis</i>
Leprosy	<i>Mycobacterium leprae</i>
Buruli ulcer	<i>Mycobacterium ulcerans</i>

(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](https://creativecommons.org/licenses/by/4.0/).

# Infectious Diseases in Global Health

- **Neglected Diseases:**
- 1 billion people affected and 1/2 million deaths annually.



From [http://www.who.int/neglected\\_diseases/en/](http://www.who.int/neglected_diseases/en/), accessed October 2009.  
 Courtesy of the World Health Organization. Used with permission.



# African Sleeping Sickness



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

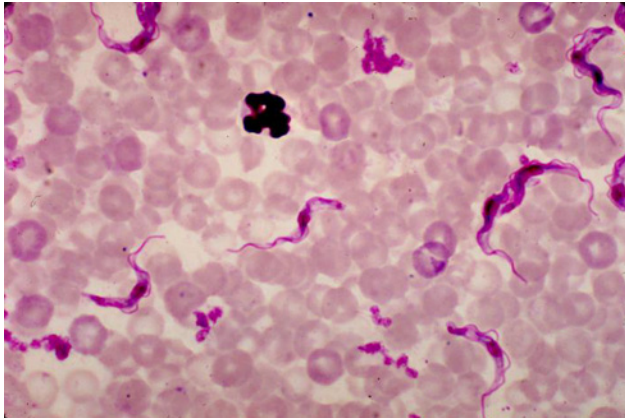
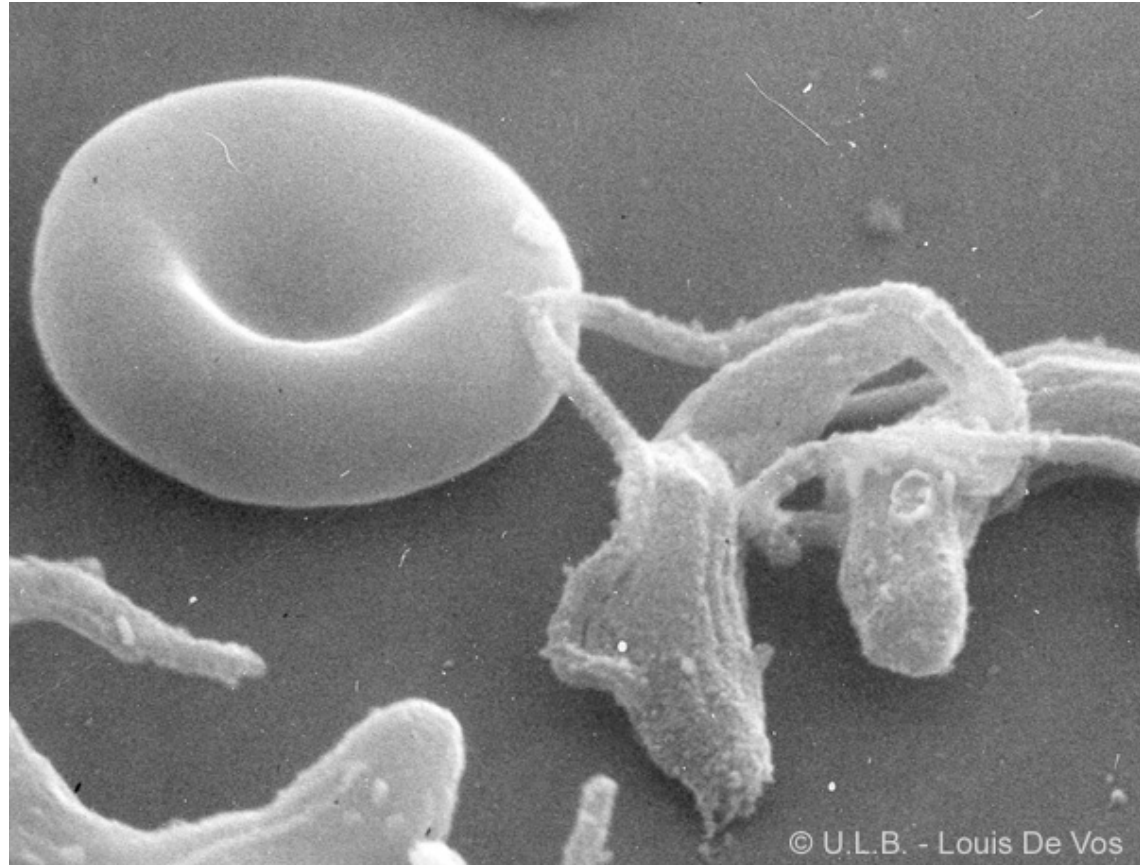


Image: US NIH.



© U.L.B. - Louis De Vos

Courtesy of Louis De Vos. Used with permission.

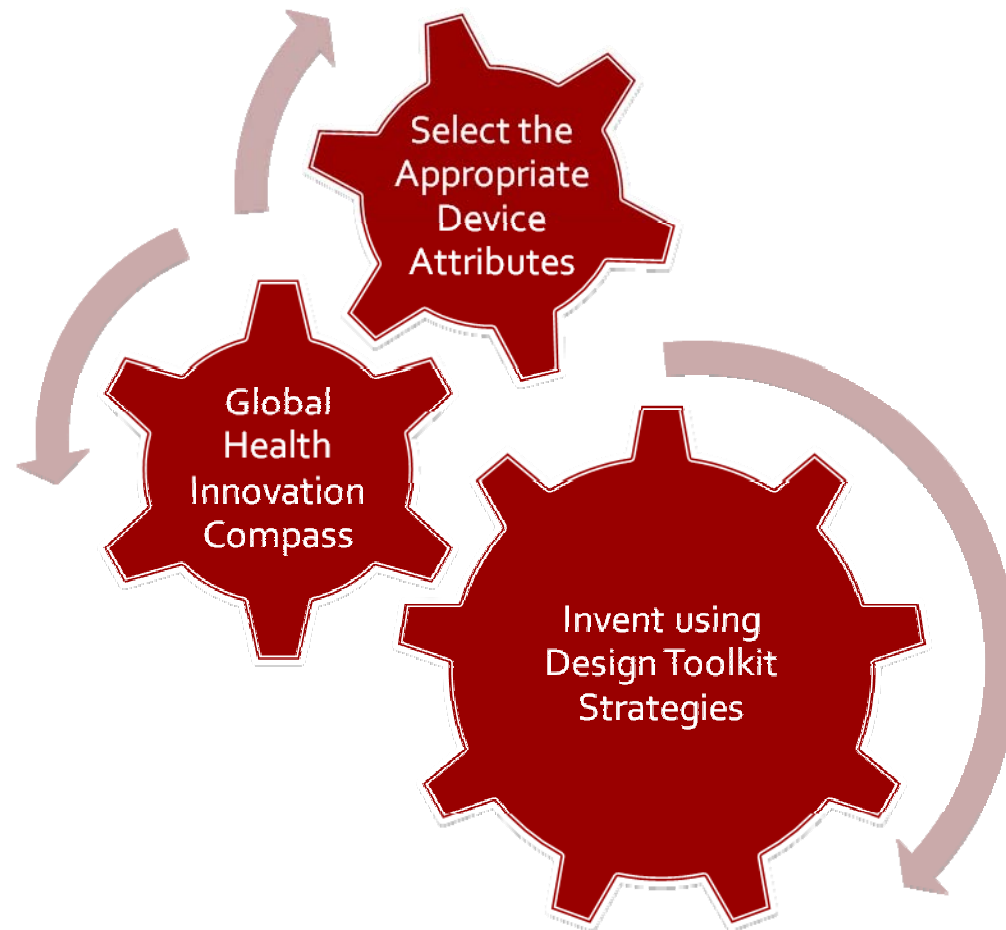
# Focus Areas for Designing Solutions



- 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

- SAFE
- Accurate
- Robust
- Longevity
- Cheap
- Reliable
- Reusable/Disposable

## Enhancing

- Mobile
- Connected
- Smart
- Plug n' Play

## Long-Term

- Local Mfg
- Local Innovation

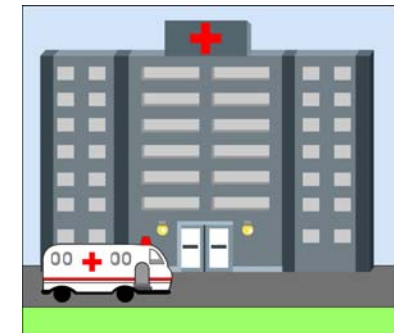
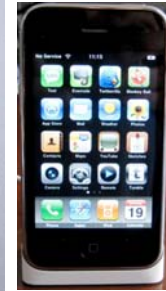
# Global Health Innovation Compass



Program Goal X Level of Pushing  
the Status Quo

*Inexpensive/  
Appropriate*

*Expensive/  
Appropriate*



*Inexpensive/  
Not Very Appropriate*

*Expensive/  
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Net Resources Expended (Time & Money – Resulting Impact)

# Diagnostics



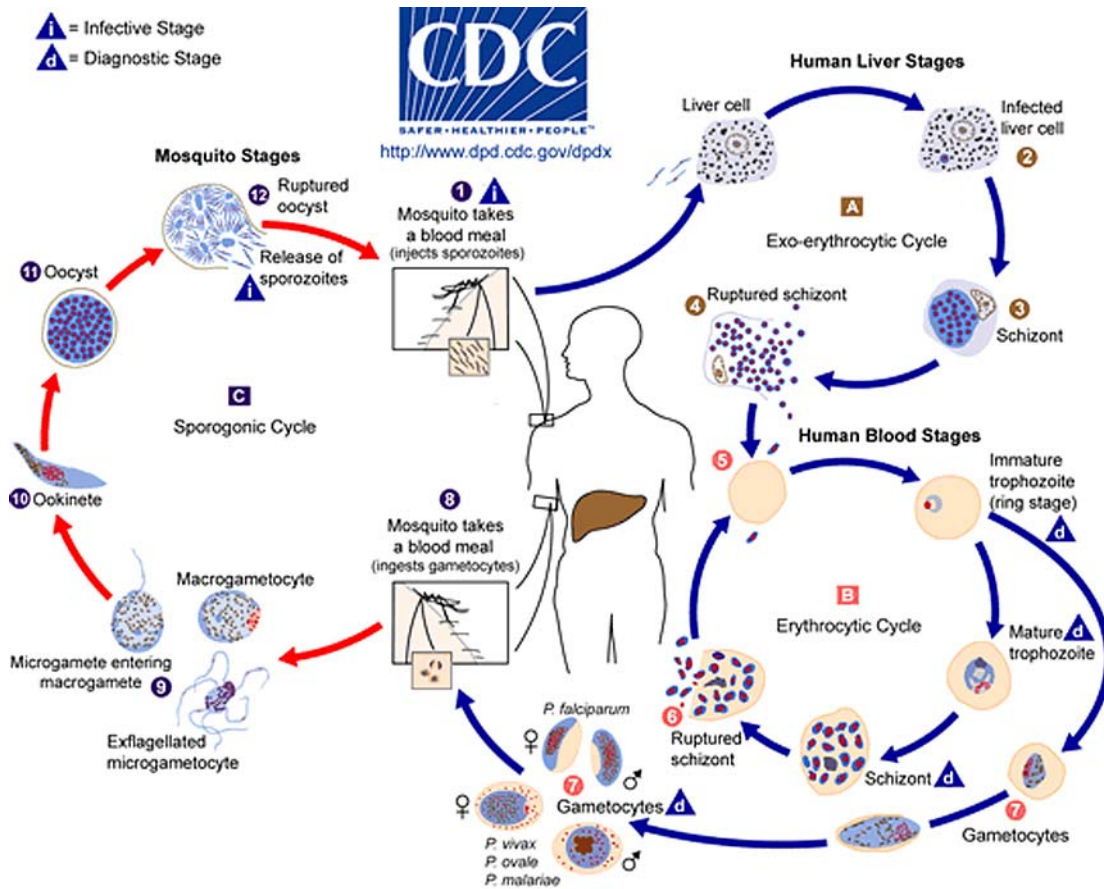
Photos removed due to copyright restrictions.  
Various medical diagnostic tools.



# Malaria

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

▲ = Infective Stage  
 ▲ = Diagnostic Stage



Merozoite penetrating a red blood cell



Merozoite multiplying in a red blood cell  
 Courtesy of the WEHI-TV. Used with permission.

# Diagnosis of Malaria

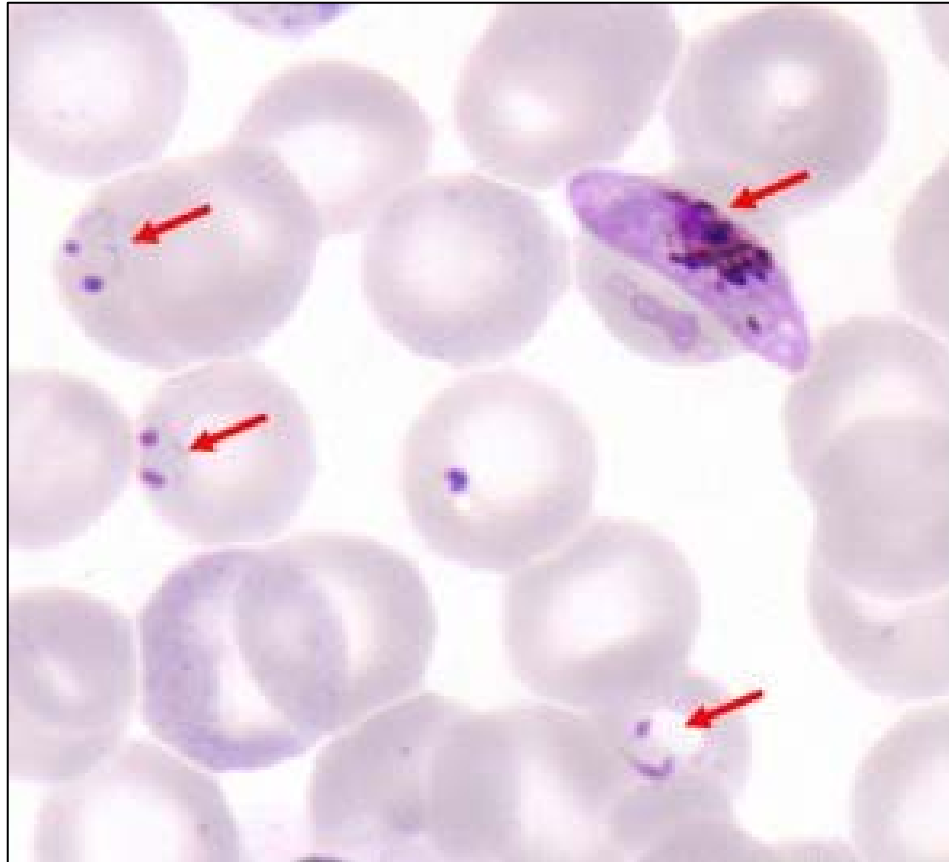


Image: US CDC



# 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



Image: US CDC



Courtesy of the Canadian Lung Association. Used with permission.

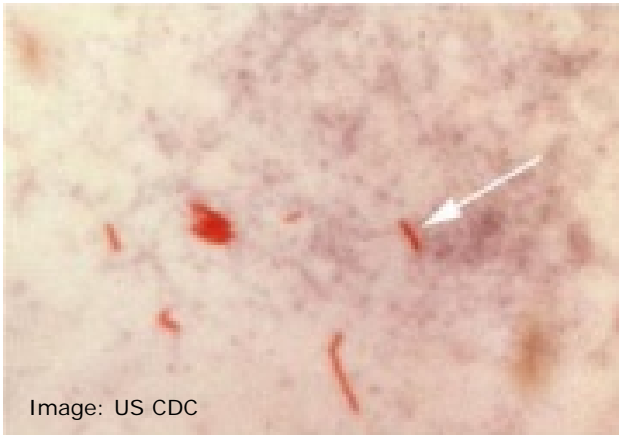


Image: US CDC

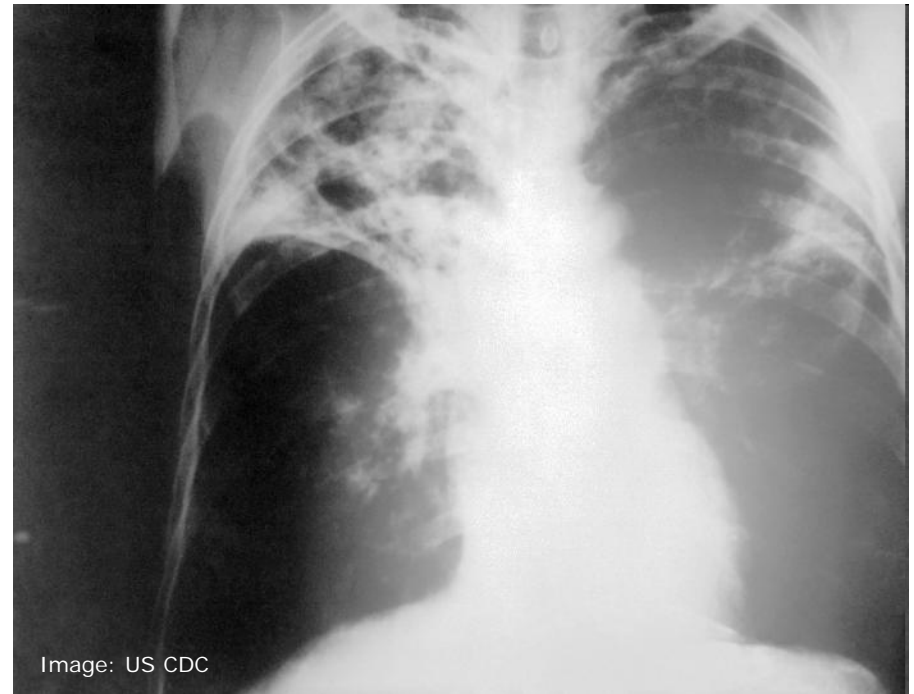


Image: US CDC

# 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

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>

# 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

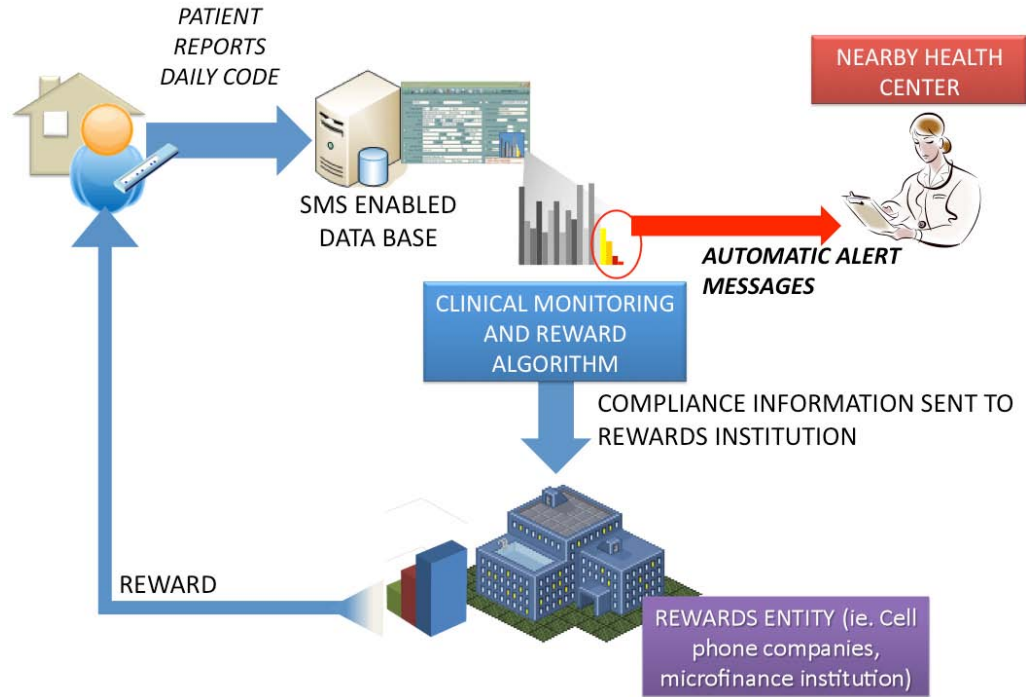
# SNAP

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

# X out TB



# The Cold Chain for Vaccines

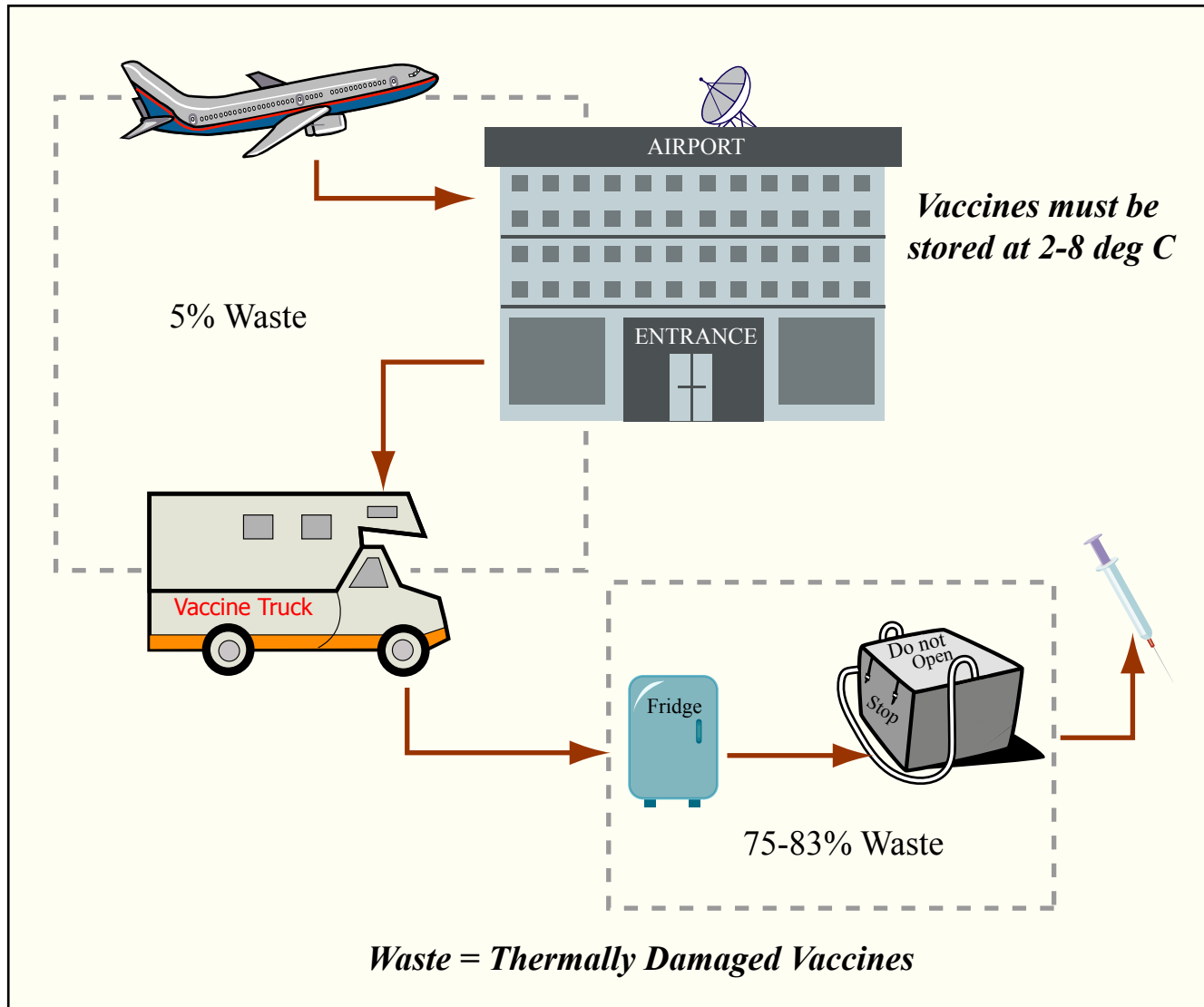


Figure by MIT OpenCourseWare.



# 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.

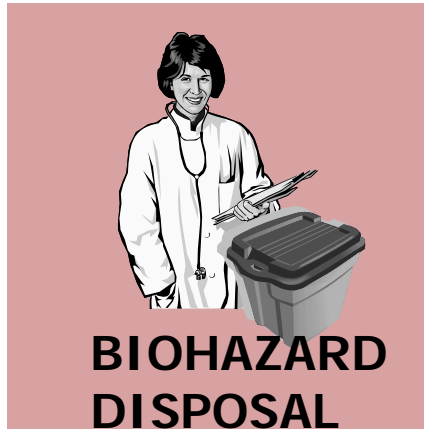
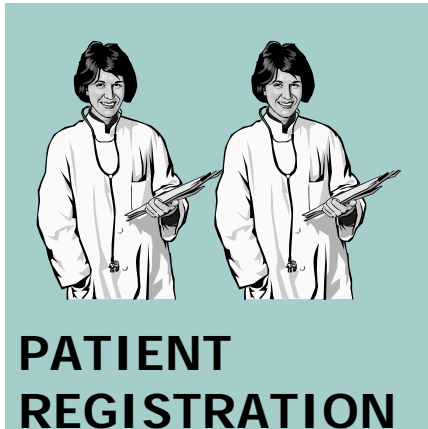
See <http://www.sfgate.com/cgi-bin/object/article?f=/c/a/1998/10/27/MN52NEE.DTL&o=1>

**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



**6** *PHYSICIANS  
AND AIDES*

**200** *PATIENTS  
IN-CLINIC*

**70** *PATIENTS  
IN THE FIELD*

# Aerovax Man



**1**

**LOW SKILLED  
VOLUNTEER**

**650**

**PATIENTS  
IN THE FIELD**

**62%**

**SAVINGS**

# 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

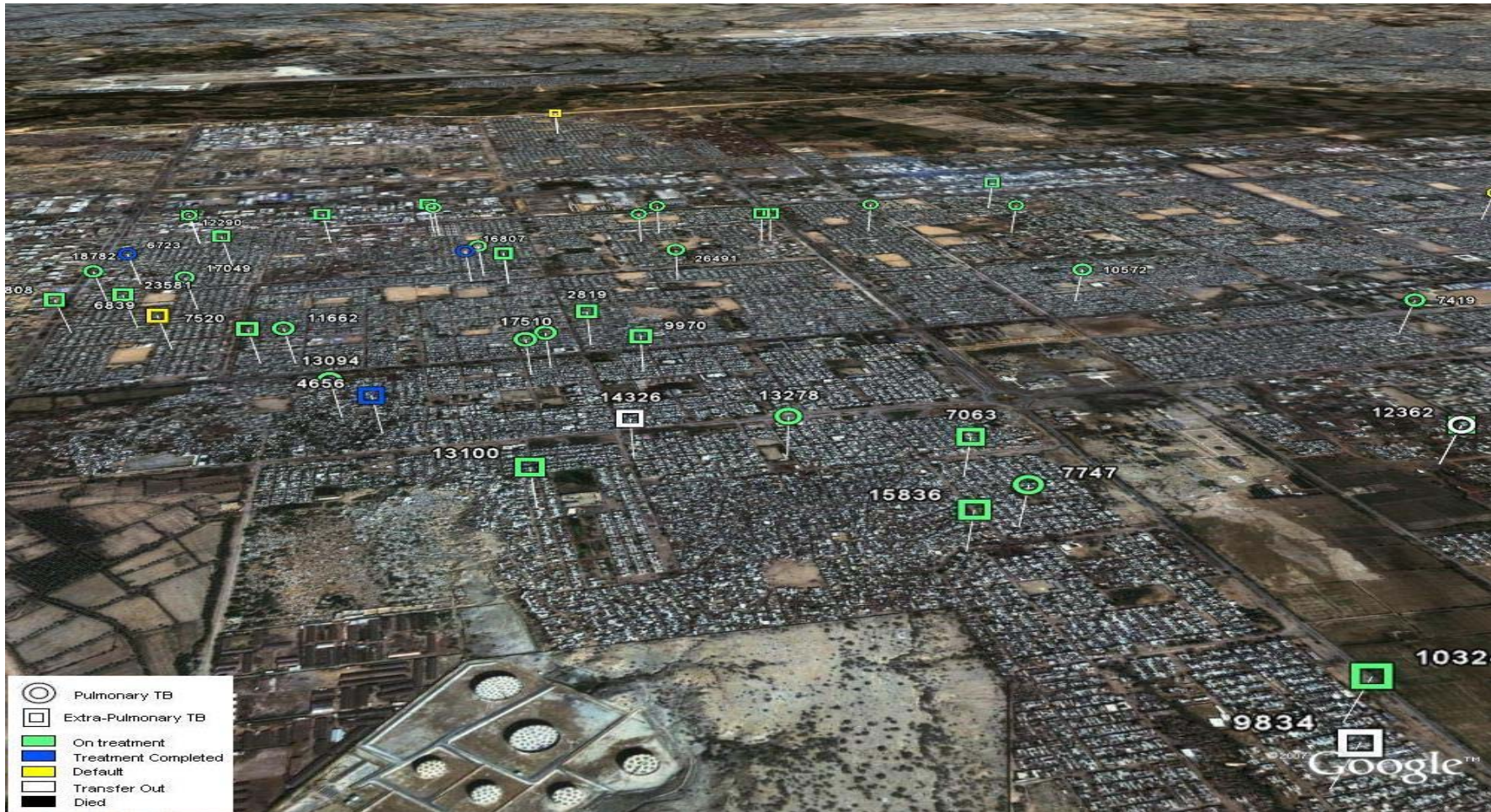
- Disease surveillance





# 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>

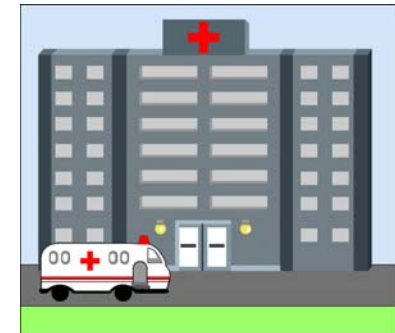
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Net Resources Expended (Time & Money – Resulting Impact)

# 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\*