Microchip Technology for Global Health Diagnostics

Xuanhong Cheng
Materials Science and Engineering
Bioengineering
Microchip Technology for Medicine
Overview of Presentation

1. Global Health Challenges
2. HIV/AIDS Statistics and Biology
3. HIV/AIDS Diagnostics
4. Microchip Technology for HIV/AIDS Diagnostics
Global Health

The area of study, research and practice that places a priority on improving health and achieving equity in health for all people

# Leading causes of death, high-income countries

<table>
<thead>
<tr>
<th>Cause</th>
<th>Deaths in millions</th>
<th>% of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>1.42</td>
<td>15.6%</td>
</tr>
<tr>
<td>Stroke and other cerebrovascular disease</td>
<td>0.79</td>
<td>8.7%</td>
</tr>
<tr>
<td>Trachea, bronchus, lung cancers</td>
<td>0.54</td>
<td>5.9%</td>
</tr>
<tr>
<td>Alzheimer and other dementias</td>
<td>0.37</td>
<td>4.1%</td>
</tr>
<tr>
<td>Lower respiratory infections</td>
<td>0.35</td>
<td>3.8%</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>0.32</td>
<td>3.5%</td>
</tr>
<tr>
<td>Colon and rectum cancers</td>
<td>0.30</td>
<td>3.3%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.24</td>
<td>2.6%</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>0.21</td>
<td>2.3%</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>0.17</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

## Leading causes of death, low-income countries

<table>
<thead>
<tr>
<th>Cause</th>
<th>Death (millions)</th>
<th>% of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory infections</td>
<td>1.05</td>
<td>11.3%</td>
</tr>
<tr>
<td>Diarrhoeal diseases</td>
<td>0.76</td>
<td>8.2%</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>0.72</td>
<td>7.8%</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>0.57</td>
<td>6.1%</td>
</tr>
<tr>
<td>Malaria</td>
<td>0.48</td>
<td>5.2%</td>
</tr>
<tr>
<td>Stroke and other cerebrovascular disease</td>
<td>0.45</td>
<td>4.9%</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0.40</td>
<td>4.3%</td>
</tr>
<tr>
<td>Prematurity and low birth weight</td>
<td>0.30</td>
<td>3.2%</td>
</tr>
<tr>
<td>Birth asphyxia and birth trauma</td>
<td>0.27</td>
<td>2.9%</td>
</tr>
<tr>
<td>Neonatal infections</td>
<td>0.24</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

33 million adults living with HIV/AIDS, 2008

Source: WHO/UNAIDS, 2008
Growth of the AIDS Epidemic

People With HIV/AIDS, Cumulative Regional Totals

*Western and Central Europe & North America.

Changes in Life Expectancy, 1950 - 2000

Projected changes in life expectancy in selected African countries with high HIV prevalence, 1995–2000


WHO and UNAIDS
AIDS’ Effect on African Agriculture

Percent of Agricultural Labor Force Lost to HIV/AIDS, 1985-2020 (Projected)

- Namibia: 26%
- Botswana: 23%
- Zimbabwe: 23%
- Mozambique: 20%
- South Africa: 20%
- Kenya: 17%
- Malawi: 14%
- Uganda: 14%
- Tanzania: 13%

Cell

Bacteria (TB, Typhoid)

Virus (HIV, hepatitis, SARS, influenza)

HIV emerging from a cell

HIV emerging from a cell
Global diversity of different HIV-1 strains

Source: Los Alamos Database http://hiv-web.lanl.gov/
HIV Pathophysiology - Life Cycle
HIV Pathophysiology - Life Cycle

CD4 Binding

Co-receptor (CCR5 or CXCR4)
HIV Pathophysiology - Life Cycle

Fusion
HIV Pathophysiology - Life Cycle

Virion entry
HIV Pathophysiology - Life Cycle
HIV Pathophysiology - Life Cycle

Reverse transcription

HIV DNA
HIV Pathophysiology - Life Cycle

Translocation to nucleus
HIV Pathophysiology - Life Cycle

Integration
HIV Pathophysiology - Life Cycle

Transcription / Translation of HIV mRNA / polyprotein
HIV Pathophysiology - Life Cycle

Protease processing and viral assembly
HIV infection

HIV attacks CD4 cells, the generals of the immune system’s army
HIV inserts itself into our genes
HIV creates many different strains
HIV infection

- Viral load
- CD4

Time (Weeks to Years)
Relationship Between CD4 count and Viral Load

Figure 1. T-cell count = distance to crash, HIV RNA = speed of train

HIV RNA (viral load) = speed of train

Slow: <5,000, Fast: 50,000+

Source: John Coffin, PhD, Tufts University.
WHO Stage 1: Asymptomatic HIV infection
CD4 >500

WHO Stage 2 and 3: Symptomatic HIV infection
CD4 200 - 500
Mild infections
Weight loss, fatigue
TB, Thrush

WHO Stage 4: AIDS
CD4 < 200
TB, infections
Death ~18 months

CD4 Count

Time (years)
Goals of HIV Treatment

- Improve quality of life
- Prevent opportunistic infections
- Prevent progression to AIDS
- Prevent death
- Reduce the likelihood of transmission to others (“Secondary prevention”)
HIV Treatment - Antiretrovirals

Fusion/Entry Inhibitors (1)

Maturation Inhibitors (~2008)

Protease Inhibitors (8)

Reverse Transcriptase Inhibitors (11)

Integration Inhibitors (~2008)
HIV Treatment - Timing of HIV Treatment

- Therapy is delayed until patients develop WHO Stage 3 or Stage 4 disease
  - Delaying therapy until Stage 3 or 4, if done carefully, does not decrease the likelihood of successful treatment
  - Treatment is lifelong and expensive, do not want to start unnecessarily early
  - Delayed therapy minimizes opportunity for side effects
  - Delayed therapy minimizes opportunity for drug resistance
CD4 and Mortality - Zimbabwe

- **CD4 > 200**
- **CD4 50-200**
- **CD4 < 50**

Survival Probability

Time from enrolment to death (years)
Impact of Treatment

Before
Impact of Treatment

After 9 months
Impact of Treatment

Begin ART

CD4

Viral load (HIV RNA level)

Weeks

Years

time→
Impact of Treatment - Society

Effective ARVs available

Unintentional injury
Cancer
Heart disease
Suicide
HIV infection
Homicide
Chronic liver disease
Stroke
Diabetes

Source: Centers for Disease Control, 2001
Number of Individuals Receiving ART

Number of people receiving antiretroviral therapy (end of year, lower- and middle-income countries)

- 5% in 2003
- 8% in 2004
- 19% in 2005
- 22% in 2006
- 33% in 2007
- 42% in 2008

Source: AVERT.org
Clinical Indicators

- 'Viral load' (copies/mL plasma)
- HIV RNA level (copies/mL plasma)
- CD4 cell count (cells/μL blood)

Graph showing the changes in viral load and CD4 cell count over weeks and years.
State of the Art Technologies

CD4-count
start treatment < 200 cells/ul

Viral load count
measure resistance to treatment
Lab Diagnostics in Resource Poor Settings
What is Needed

• Low cost
• Easy to use
• Rapid and Robust
• Portable
• Sensitive and specific
Microchip Technology for Medicine
CD4 counting microchip
Mechanism of the CD4 Counter
Nanoporous Membrane Fabrication

Cheng Lab: the Lab of Micro- and Nanotechnology for Medicine
Optically Forced Cytometry for Nanobead Counting

Cheng Lab: the Lab of Micro- and Nanotechnology for Medicine