The Role of NIH in Fighting Infectious Diseases: From Basic Science to Personal and Public Health

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NIH: A Two-Component System

- **INTRAMURAL** – Research and training conducted in NIH laboratories; ~10 percent of total
- **EXTRAMURAL** – NIH-supported research and training by non-federal investigators in universities, medical schools, hospitals, and research institutions throughout the USA and around the world; ~90 percent of total

National Institutes of Health – FY 2011 Budget Estimates for Eight Largest Institutes

<table>
<thead>
<tr>
<th>Institute</th>
<th>Budget Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCI</td>
<td>$5.1B</td>
</tr>
<tr>
<td>NIAID</td>
<td>$4.8B</td>
</tr>
<tr>
<td>NHLBi</td>
<td>$3.1B</td>
</tr>
<tr>
<td>NIGMS</td>
<td>$2.0B</td>
</tr>
<tr>
<td>NIDDK</td>
<td>$1.8B</td>
</tr>
<tr>
<td>NINDS</td>
<td>$1.6B</td>
</tr>
<tr>
<td>NIMH</td>
<td>$1.5B</td>
</tr>
<tr>
<td>NICHD</td>
<td>$1.3B</td>
</tr>
</tbody>
</table>

NIAID Research: A Dual Mandate

Maintain and “grow” a robust basic and applied research portfolio in microbiology, infectious diseases, immunology and immune-mediated diseases

Respond rapidly to new and emerging disease threats

New/Improved Interventions
Global Health and Infectious Diseases

Established Infectious Diseases

Emerging and Re-Emerging Infectious Diseases

Selected Established Infectious Diseases of Global Public Health Importance

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated Annual Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Infections</td>
<td>4.0 million</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1.8 million</td>
</tr>
<tr>
<td>Diarrheal Infections</td>
<td>1.8 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1.7 million</td>
</tr>
<tr>
<td>Vaccine Preventable Childhood Diseases (measles, pertussis, tctanous, etc.)</td>
<td>1.1 million</td>
</tr>
<tr>
<td>Hepatitis (B and C)</td>
<td>950,000</td>
</tr>
<tr>
<td>Malaria</td>
<td>781,000</td>
</tr>
<tr>
<td>Neglected Tropical Diseases</td>
<td>547,000</td>
</tr>
</tbody>
</table>

Sources: WHO, Kelis et al., Lancet 373: 1578, 2009

3 Recently Developed Vaccines and their Life-Saving Potential in Children <5 Years

Worldwide Deaths/Yr.
Children <5 yrs.

- Pneumococcal conjugate: 1,000,000
- Haemophilus influenzae type b (Hib): 700,000
- Rotavirus: 600,000

Decline in Invasive Haemophilus Influenzae Type b (Hib) Disease After the Availability of Conjugate Hib Vaccine

United States

<table>
<thead>
<tr>
<th>Year</th>
<th>Hib Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>1,400</td>
</tr>
<tr>
<td>1985</td>
<td>1,000</td>
</tr>
<tr>
<td>1987</td>
<td>800</td>
</tr>
<tr>
<td>1993</td>
<td>500</td>
</tr>
<tr>
<td>1999</td>
<td>200</td>
</tr>
</tbody>
</table>

United Kingdom

<table>
<thead>
<tr>
<th>Year</th>
<th>Hib Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>700</td>
</tr>
<tr>
<td>1995</td>
<td>300</td>
</tr>
</tbody>
</table>

Uruguay

<table>
<thead>
<tr>
<th>Year</th>
<th>Hib Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>60</td>
</tr>
<tr>
<td>1997</td>
<td>30</td>
</tr>
</tbody>
</table>

Source: PATH
Global Health and Infectious Diseases

Established Infectious Diseases +

Emerging and Re-Emerging Infectious Diseases

Global Examples of Emerging and Re-Emerging Infectious Diseases

30 Years of AIDS

The Scope of the Global HIV/AIDS Pandemic

- Cumulative HIV infections: 65 million
- People living with HIV/AIDS: 34 million
- New HIV infections in 2010: 2.7 million
- Deaths due to AIDS in 2010: 1.8 million
- Cumulative AIDS deaths: ~30 million

HIV/AIDS in the United States – Latest Estimates

- 594,496 cumulative deaths
- ~1.2 million living with HIV, 20% unaware of their infection
- ~50,000 new infections/yr.
  - 61% male-to-male sexual contact, 27% heterosexual contact
  - Incidence rates among blacks >7 times higher than whites

Source: CDC, 2011. Includes 50 States and District of Columbia.
**Advances in HIV Science**

- Etiology
- Diagnosis
- Molecular Virology and Epidemiology
- Natural History
- Pathogenesis
- Treatment
- Prevention
- Vaccine Development

**Examples of Programs Providing HIV/AIDS Prevention, Treatment and Care to Developing Nations**

- President's Emergency Plan for AIDS Relief (PEPFAR)
- Global Fund to Fight AIDS, Tuberculosis and Malaria
- Philanthropies and NGOs (e.g. Gates Fdn., Clinton Fdn., MSF)

**FDA-Approved Antiretroviral Drugs**

<table>
<thead>
<tr>
<th>NRTI</th>
<th>PI</th>
<th>Entry Inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>Saquinavir</td>
<td>Maraviroc</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Ritonavir</td>
<td>Integrase Inhibitor</td>
</tr>
<tr>
<td>Zalcitabine</td>
<td>Indinavir</td>
<td>Raltegravir</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Nelfinavir</td>
<td>Combinations</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Amprenavir</td>
<td>6 available, combining 2 or 3 drugs</td>
</tr>
<tr>
<td>Abacavir</td>
<td>Lopinavir</td>
<td>Fusion Inhibitor</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Atazanavir</td>
<td>Enfuvirtide (T-20)</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>Fosamprenavir</td>
<td></td>
</tr>
<tr>
<td>NNRTI</td>
<td>Tipranavir</td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Darunavir</td>
<td></td>
</tr>
<tr>
<td>Delavirdine</td>
<td>Fusion Inhibitor</td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etavirenne</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rilpivirine</td>
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</tbody>
</table>

**Number of People Receiving Antiretrovirals in Low- and Middle-Income Countries**

**FDA-Approved Antiretroviral Drugs**

- Median survival of AIDS patients: ~6-8 months

**Life Expectancy of Recently Diagnosed Asymptomatic HIV-infected Patients Approaches that of Uninfected Individuals**

- **Life expectancy** for HIV-infected patients (without AIDS) aged 25 yrs at six months postinfection
  - **Men:** an additional 52.7 yrs (versus 53.1 yrs in general population)
  - **Women:** an additional 57.8 yrs (versus 58.1 yrs in general population)

**Graph:** Number of people receiving antiretrovirals in low- and middle-income countries.
Major Challenges Globally in the Treatment of HIV Disease

- 47% of people in need of ARV therapy in low- and middle-income countries are receiving it.
- For every person put on ARV therapy in 2010, about 2 others were newly infected with HIV.

![Image of people in a village](UNAIDS estimates, 1/2011)

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Combination HIV Prevention

- Harm reduction
- Education
- Condoms
- PrEP
- Microbicides
- Male circumcision
- Drug/alcohol treatment
- PMTCT
- STI treatment
- Testing/counseling
- Treatment as prevention

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The Virtual Elimination of Mother to Child Transmission of HIV is Possible

- No ARV prophylaxis for PMTCT
- Constant 2000 coverage of ARV prophylaxis

![Graph showing reduction in HIV transmission](Source: Adapted from Bailey et al., 2010)

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Durable Effect of Adult Male Circumcision on HIV Incidence in Rakai, Uganda

- Cox model: Hazard Ratio = 0.52 (0.17-0.81)

![Graph showing incidence rates](Source: Keng et al., CROI 2011)
**Pre-Exposure Prophylaxis Reduces HIV Infection Risk Among Heterosexuals**

- Two randomized studies in Africa found that daily antiretroviral therapy can reduce the risk for HIV infection among high-risk heterosexuals.

- Treating uninfected individuals with 1 or 2 antiretroviral drugs reduced the risk of HIV acquisition by 62-73%.

![Study site in Thika, Kenya](Source: U of Washington)

**The Rationale for ARV Treatment as Prevention**

- HIV RNA concentration ("viral load") is key driver of HIV transmission

- Low viral loads (either spontaneously or as a result of ARVs) are associated with reduced risk of transmission in:
  - Mother-to-child transmission
  - Discordant heterosexual couples
  - Cohort studies of "community viral load"

Source: Montaner, 2011

**Treating HIV-infected People with Antiretrovirals Significantly Reduces Transmission to Partners**

*Findings Result from NIH-funded International Study*

- HPTN 052
- 1,763 HIV-serodiscordant couples in 9 countries
- 96% reduction in HIV transmission when ART started in HIV-infected partner at CD4 count of 350-550 compared to <250

![NIH News](Source: National Institutes of Health)

**Combination HIV Prevention**

- PrEP
- Condoms
- Education
- STI treatment
- Testing/counseling
- Male circumcision
- Drug/alcohol treatment
- PMTCT
Toward an AIDS-Free Generation

Secretary Hillary Rodham Clinton
National Institutes of Health, November 8, 2011


Goals for next two years:
- 6 million people on ARVs by end-2013 (2 million more than current goal)
- 1.5 million pregnant women provided ARV prophylaxis
- 4.7 million medical male circumcisions in eastern and southern Africa
- 1 billion condoms distributed

First Signal of Efficacy in an HIV Vaccine Clinical Trial

Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand
S Rerks-Ngarm, JH Kim et al. for the MOPH-TAVEG Investigators
| The Extraordinary Capability of Microbial Pathogens to Persist, Emerge, and Re-Emerge | Public Health Measures, Biomedical Research, and Technological Advances |