

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



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 National Institutes of Health  
 December 5, 2011



## National Institutes of Health

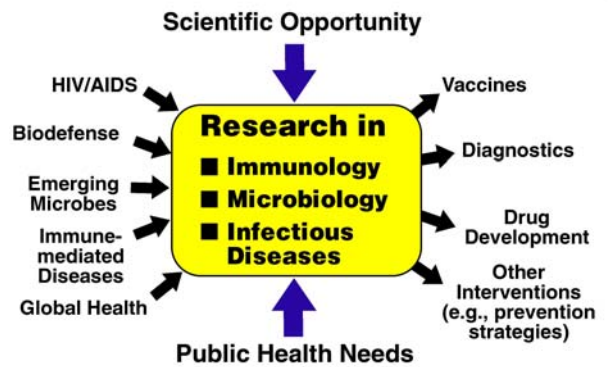


**NIH's Mission:**  
 Science in Pursuit of Knowledge to Improve Health

### 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 Institute of Allergy and Infectious Diseases (NIAID) National Institutes of Health (NIH)



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

NCI	\$5.1B
<b>NIAID</b>	<b>\$4.8B</b>
NHLBI	\$3.1B
NIGMS	\$2.0B
NIDDK	\$1.8B
NINDS	\$1.6B
NIMH	\$1.5B
NICHD	\$1.3B

NIAID includes \$297M for Global Fund

### 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

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Emerging and Re-Emerging Infectious Diseases

## Global Health and Infectious Diseases

Established Infectious Diseases

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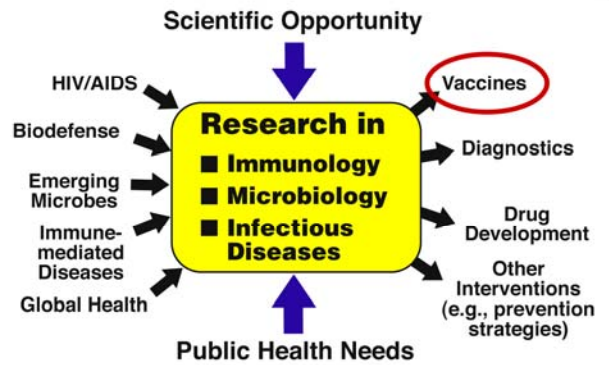
Emerging and Re-Emerging Infectious Diseases

### Selected Established Infectious Diseases of Global Public Health Importance

	Estimated Annual Deaths
Respiratory Infections	4.0 million
HIV/AIDS	1.8 million
Diarrheal Infections	1.8 million
Tuberculosis	1.7 million
Vaccine Preventable Childhood Diseases (measles, pertussis, tetanus, etc.)	1.1 million
Hepatitis (B and C)	950,000
Malaria	781,000
Neglected Tropical Diseases	547,000

Sources: WHO; Hotez et al., *Lancet* 373:1570, 2009

### National Institute of Allergy and Infectious Diseases (NIAID) National Institutes of Health (NIH)



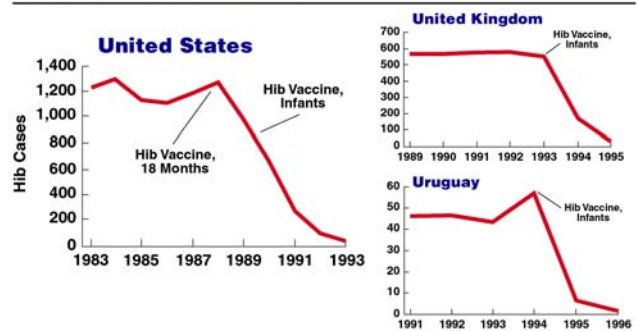
### 3 Recently Developed Vaccines and their Life-Saving Potential in Children <5 Years

	Worldwide Deaths/Yr. Children <5 yrs.
Pneumococcal conjugate	1,000,000
<i>Haemophilus influenzae</i> type b (Hib)	700,000
Rotavirus	600,000



Source: PATH

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



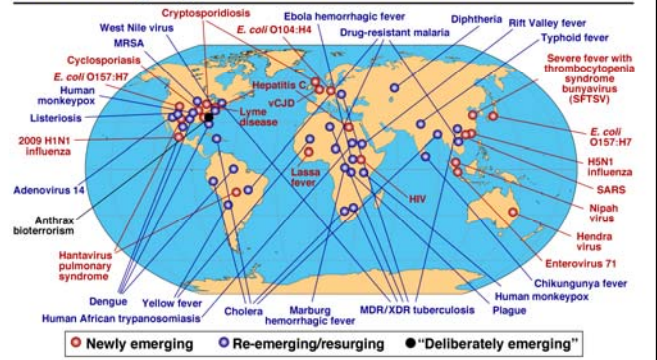
## Global Health and Infectious Diseases

Established Infectious Diseases

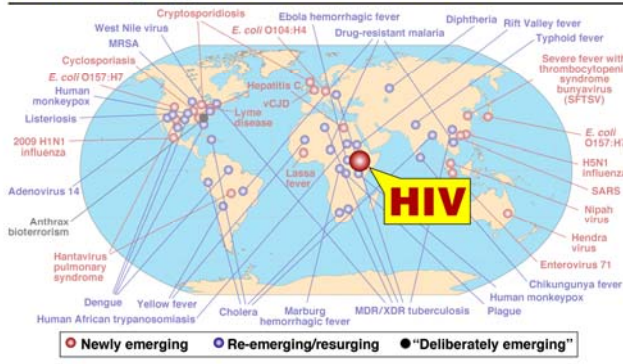
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Emerging and Re-Emerging Infectious Diseases

## Global Examples of Emerging and Re-Emerging Infectious Diseases



## Global Examples of Emerging and Re-Emerging Infectious Diseases



## 30 Years of AIDS

CENTERS FOR DISEASE CONTROL

**MMWR**  
MORBIDITY AND MORTALITY WEEKLY REPORT

June 5, 1981

**Pneumocystis Pneumonia - Los Angeles**

July 4, 1981

**Kaposi's Sarcoma and Pneumocystis Pneumonia Among Homosexual Men - New York City and California**

## 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

UNAIDS estimates, 11/2011



## HIV/AIDS in the United States - Latest Estimates

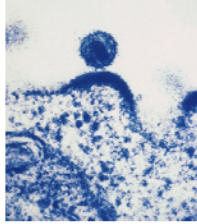
- 594,496 cumulative deaths
- ~1.2 million living with HIV, 20% unaware of their infection
- ~50,000 new infections/yr.
  - 61% male-to-male sexual contact, 27% heterosexual contact
  - incidence rates among blacks >7 times higher than whites

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



## Rounding on AIDS Ward, NIH Clinical Center, Early 1980s



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

## FDA-Approved Antiretroviral Drugs

### NRTI

- Zidovudine
- Didanosine
- Zalcitabine
- Stavudine
- Lamivudine
- Abacavir
- Tenofovir
- Emtricitabine

### NNRTI

- Nevirapine
- Delavirdine
- Efavirenz
- Etravirine
- Rilpivirine

### PI

- Saquinavir
- Ritonavir
- Indinavir
- Nelfinavir
- Amprenavir
- Lopinavir
- Atazanavir
- Fosamprenavir
- Tipranavir
- Darunavir

### Fusion Inhibitor

- Enfuvirtide (T-20)

### Entry Inhibitor

- Maraviroc

### Integrase Inhibitor

- Raltegravir

### Combinations

- 6 available, combining 2 or 3 drugs



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

A. van Sighem et al. on behalf of the ATHENA National Observational Cohort Study

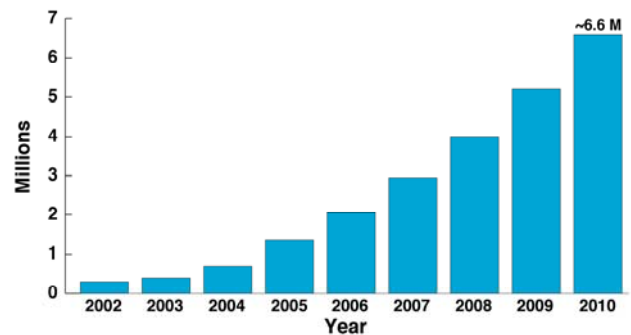
- **Life expectancy** for HIV-infected patients (without AIDS) aged 25 yrs at six months postinfection
  - Men: an additional 52.7 yrs** (versus 53.1 yrs in general population)
  - Women: an additional 57.8 yrs** (versus 58.1 yrs in general population)

## 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)



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



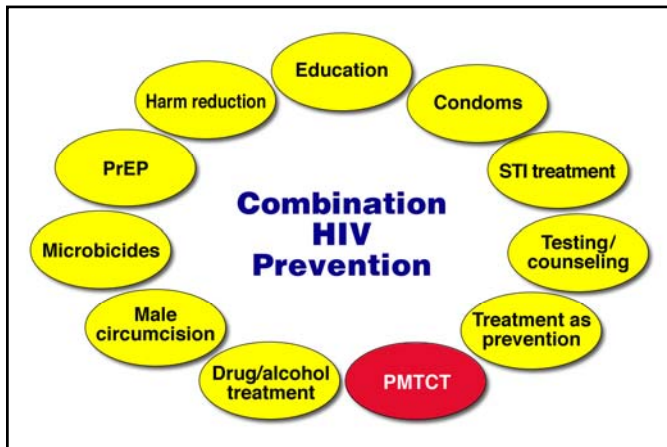
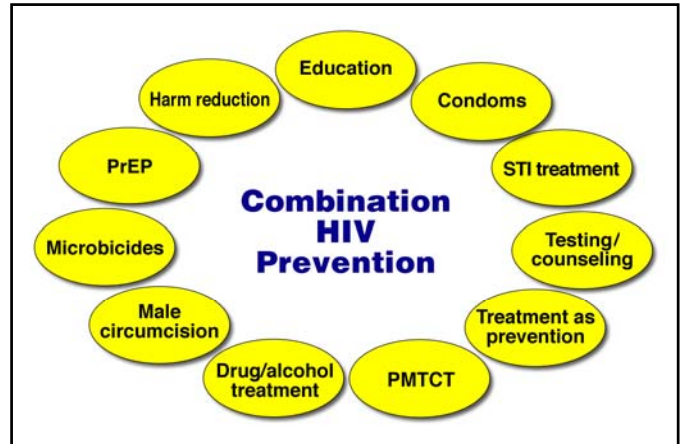
Source: UNAIDS, 2011

## Major Challenges Globally in the Treatment of HIV Disease

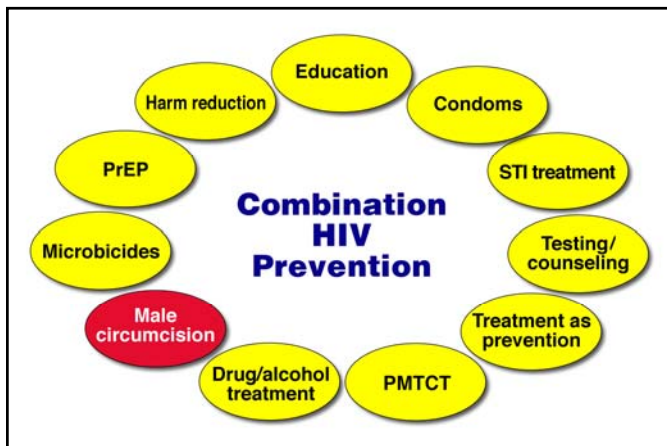
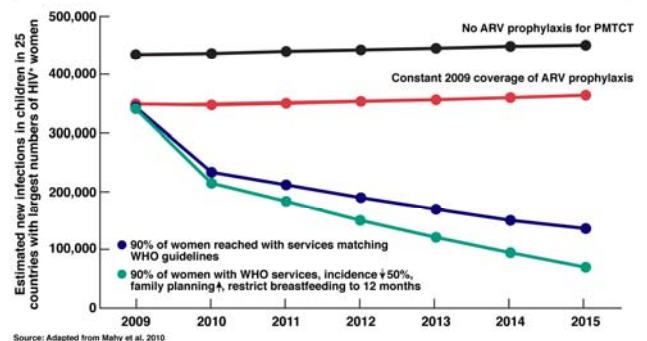
- 47% of people in need of ARV therapy in low- and middle-income countries are receiving it
- For every person put on ARV therapy in 2010, about 2 others were newly infected with HIV



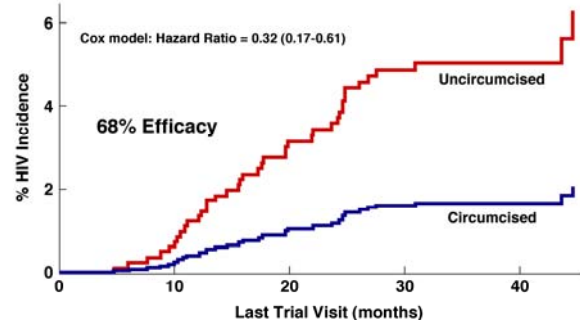
UNAIDS estimates, 11/2011



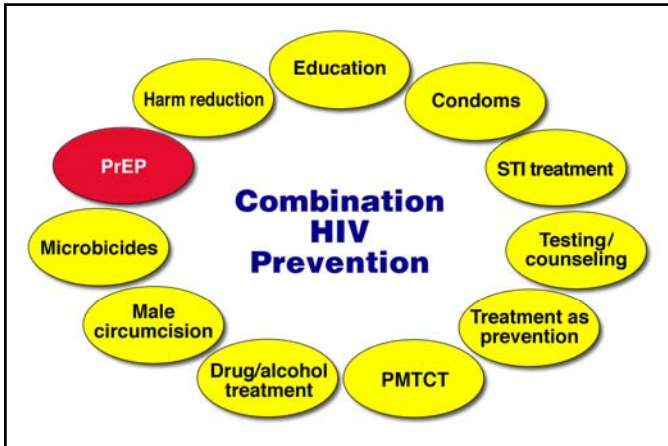
## The Virtual Elimination of Mother to Child Transmission of HIV is Possible



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



Kong et al., CROI 2011



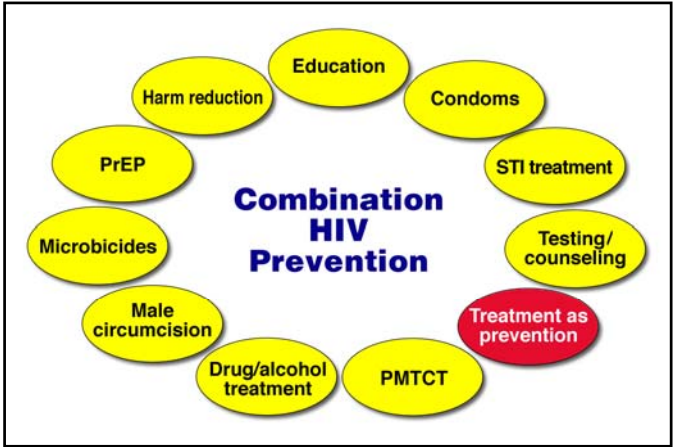
■ **44% reduction in incidence overall in patients receiving Truvada, 73% reduction with >90% adherence**

### 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

National Institute of Allergy and Infectious Diseases (NIAID)  
<http://www.niaid.nih.gov/>

FOR IMMEDIATE RELEASE  
Thursday, May 12, 2011

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

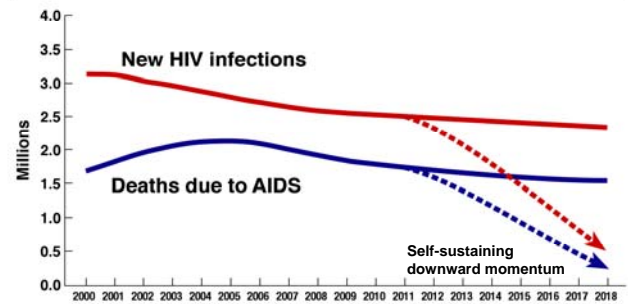
*Findings Result from NIH-funded International Study*

- 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

**Scientific Advances      Implementation**



**Global HIV Incidence and Mortality, 2000-2018: Two Hypothetical Scenarios**



**Toward an AIDS-Free Generation**



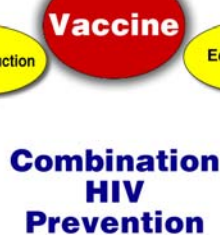
Secretary Hillary Rodham Clinton  
National Institutes of Health, November 8, 2011

**President Obama Announces Ambitious New PEPFAR Goals - Dec. 1, 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

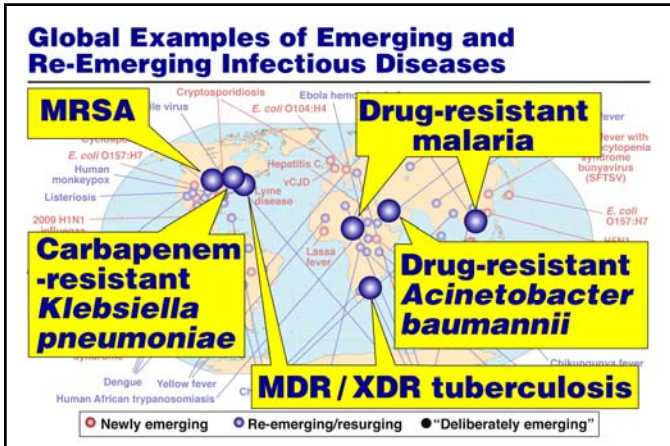


**First Signal of Efficacy in an HIV Vaccine Clinical Trial**



**Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand**

S Rerks-Ngarm, JH Kim et al. for the MOPH-TAVEG Investigators



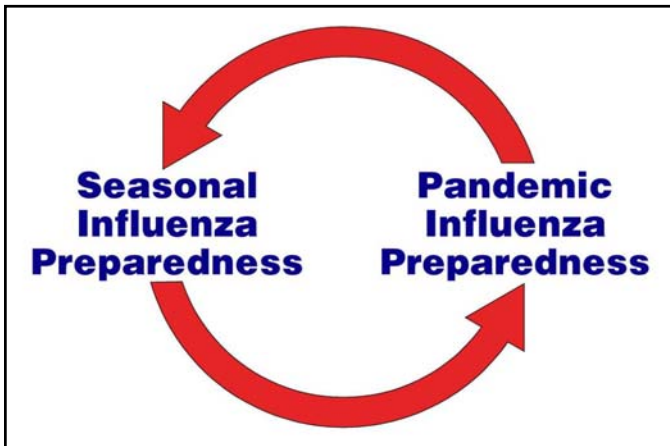
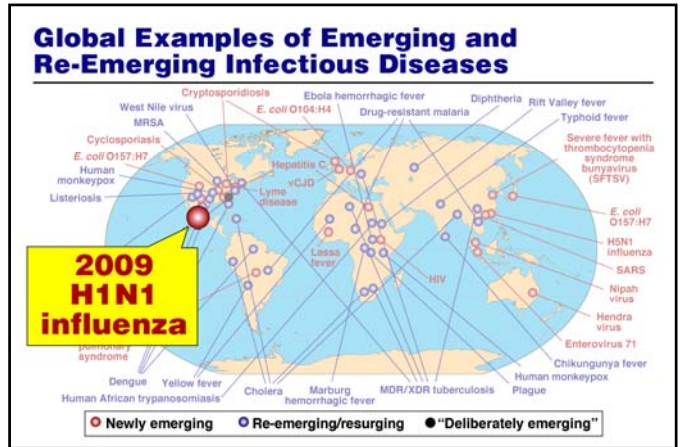
April 15, 2008  
Volume 197  
Number 8

## The Journal of Infectious Diseases

**The Research Agenda of the National Institute of Allergy and Infectious Diseases for Antimicrobial Resistance**

N. Kent Peters, Dennis M. Dixon, Steven M. Holland, and Anthony S. Fauci

- Basic Research
- Translational Research/Product Development
- Clinical Research



December 2010  
Volume 16 No 12

## nature medicine

**Induction of Unnatural Immunity: Prospects for a Broadly Protective Universal Influenza Vaccine**

GJ Nabel and AS Fauci

Recapitulating neoplasia in culture  
Multipotent progenitor cells from endothelial cells  
From Avandia to zebrafish: A look back at 2010



## **A Delicate Balance: The Perpetual Challenge**

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**The Extraordinary  
Capability of  
Microbial  
Pathogens to  
Persist, Emerge,  
and Re-Emerge**

**Public Health  
Measures,  
Biomedical  
Research, and  
Technological  
Advances**

