Getting to an AIDS-Free Generation: What Will it Take?

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
May 8, 2013
Global Summary of the HIV/AIDS Pandemic, November, 2012

- >60 million total HIV infections
- >30 million total AIDS deaths
- 34.0 million people living with HIV
- 1.7 million AIDS deaths in 2011
- 2.5 million new HIV infections in 2011
Ending the HIV/AIDS Pandemic

Implementation Research

Implementation of Interventions

Interventions: Treatment and Prevention

Basic and Clinical Research

The End of AIDS
FDA-Approved Antiretroviral Drugs

**NRTI**
- Zidovudine
- Didanosine
- Zalcitabine*
- Stavudine
- Lamivudine
- Abacavir
- Tenofovir
- Emtricitabine
- 4 multi-drug combinations

**NNRTI**
- Nevirapine
- Etravirine
- Delavirdine
- Rilpivirine
- Efavirenz

**PI**
- Saquinavir
- Ritonavir
- Indinavir
- Nelfinavir
- Amprenavir*
- Lopinavir + Ritonavir
- Atazanavir
- Fosamprenavir
- Tipranavir
- Darunavir

**Fusion Inhibitor**
- Enfuvirtide (T-20)

**Entry Inhibitor**
- Maraviroc

**Integrate Inhibitor**
- Raltegravir

**Multi-Class Combinations**
- Atripla
- Complera
- Stridbild

*no longer marketed

Source: FDA, 2013
Global Summary of the HIV/AIDS Pandemic, November, 2012

- >60 million total HIV infections
- >30 million total AIDS deaths
- 34.0 million people living with HIV
- 1.7 million AIDS deaths in 2011
  ↓ 24% since 2005
- 2.5 million new HIV infections in 2011
Combination HIV Prevention

- HIV Testing/Counseling
- ARVs for PMTCT, PEP, PrEP
- Treatment as Prevention
- Medical Male Circumcision
- Microbicides
- Treatment/Prevention of Drug/Alcohol Abuse
- Clean Syringes
- Education/Behavior Modification
- Blood Supply Screening
- Condoms
Global Summary of the HIV/AIDS Pandemic, November, 2012

- >60 million total HIV infections
- >30 million total AIDS deaths
- 34.0 million people living with HIV
- 1.7 million AIDS deaths in 2011
- 2.5 million new HIV infections in 2011
  ↓ 22% since 2001
Too Soon for a Victory Lap!

Much to do with regard to:
- Implementation
- Discovery
HIV/AIDS: A Look to the Future

Improving implementation of existing interventions

- Treatment
- Prevention

Discovery of new interventions

- Treatment
- Prevention
HIV/AIDS: A Look to the Future

Improving implementation of existing interventions

Discovery of new interventions

Treatment  Prevention

Treatment  Prevention
Improving Implementation of Existing Treatment Interventions: Challenges

- 46% of HIV-infected people eligible for ART, including 28% of eligible children, do not have access.

- Levels of access to testing, entry and retention in care, initiation and adherence to ART are inadequate in many settings.

- Conclusive data on optimal time to start ART remain elusive.
Improving Implementation of Existing Treatment Interventions: Challenges

- 46% of HIV-infected people eligible for ART, including 28% of eligible children, do not have access.

- Levels of access to testing, entry and retention in care, initiation and adherence to ART are inadequate in many settings.

- Conclusive data on optimal time to start ART remain elusive.
HPTN 065: "TLC-Plus" - Feasibility of an Enhanced Test, Link-to-Care, Plus Treat Approach in the United States

- Testing
- Linkage to care
- Viral suppression
- Prevention for positives
- Patient and provider survey

3-year study; interventions initiated October 2010
HIV/AIDS: A Look to the Future

- Improving implementation of existing interventions
  - Treatment
  - Prevention

- Discovery of new interventions
  - Treatment
  - Prevention
Improving Implementation of Existing Prevention Interventions: Challenges

- Validate the concept of treatment as prevention
- Optimize adherence to PrEP regimens
- Scale-up medical male circumcision
- Eliminate mother-to-child transmission
Improving Implementation of Existing Prevention Interventions: Challenges

- Validate the concept of treatment as prevention
- Optimize adherence to PrEP regimens
- Scale-up medical male circumcision
- Eliminate mother-to-child transmission
Prevention of HIV-1 Infection with Early Antiretroviral Therapy

HPTN 052 Study Team

- 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
The PopART Study (HPTN 071)

- **PopART**: Population effect of universal testing and immediate ART therapy to Reduce HIV Transmission

- Targeted for intervention: 1.2 M people in 21 clusters in South Africa and Zambia

- Full field launch: Q2 2013
HIV/AIDS: A Look to the Future

- Improving implementation of existing interventions
  - Treatment
  - Prevention

- Discovery of new interventions
  - Treatment
  - Prevention
Discovery of New Treatment Interventions: Selected Examples

- Longer acting ARVs to improve adherence
- Passive transfer of broadly reactive neutralizing antibodies (bNAbs)
- Gene-based delivery of bNAbs
- Therapeutic strategies towards a cure
Discovery of New Treatment Interventions: Selected Examples

- Longer acting ARVs to improve adherence
- Passive transfer of broadly reactive neutralizing antibodies (bNAbs)
- Gene-based delivery of bNAbs
- Therapeutic strategies towards a cure
Towards an HIV Cure

- Elite viral controllers
- Post-treatment viral controllers
- Viral eradication
Towards an HIV Cure

- Elite viral controllers
- Post-treatment viral controllers
- Viral eradication
Functional HIV Cure after Very Early ART of an Infected Infant

D Persaud, K Luzuriaga et al.
Re-Assessment of the Risk-Benefit Ratio of Treating High-Risk Newborns as if They Were Infected As Opposed To Post-Exposure Prophylaxis (PEP)
Post-Treatment HIV-1 Controllers with a Long-Term Virological Remission after the Interruption of Early Initiated Antiretroviral Therapy -- ANRS VISCONTI Study

A Sáez-Cirión, C Rouzioux et al.

- 14 patients treated with ART in primary HIV infection discontinued ART
- No viral rebound, very low levels of virus after 4 to 9.6 years, few HIV-infected central memory CD4+ T cells
- “Post-treatment controllers”
HIV/AIDS: A Look to the Future

- Improving implementation of existing interventions
  - Treatment
  - Prevention

- Discovery of new interventions
  - Treatment
  - Prevention
Towards an HIV Vaccine

- Preventive vaccine

- Therapeutic vaccine – possible application in pursuit of a “functional” cure
Neutralizing Antibody Epitopes on HIV-1 Trimer

Membrane proximal region

CD4 binding site

Glycan-V3

Glycan-V2

HIV virion

Viral membrane

Envelope protein

Sources: W. Schief, J. Mascola
Critical Challenge in the Development of an HIV Vaccine

Neutralizing Epitope → Immunogen
Co-Evolution of a Broadly Neutralizing HIV-1 Antibody and Founder Virus

HX Liao, R Lynch, T Zhou, JR Mascola, BF Haynes et al.

- Determination of precise viral and antibody evolutionary pathways over >2 years leading to induction of broadly neutralizing antibody CH103
- Next step: test sequential viral envelopes as experimental vaccines
Co-Evolution of Virus and Antibody in an HIV-Infected Individual

Transmitted/Founder Virus

Infection

2+ Years

Unmutated ancestor antibody

Broadly neutralizing antibody (20% of HIV-infected individuals)
HIV/AIDS: A Look to the Future

- Improving implementation of existing interventions
  - Treatment
  - Prevention

- Discovery of new interventions
  - Treatment
  - Prevention
Much to Do in a Time of Serious Fiscal Constraint
# National Institutes of Health

## Budget Comparison by Institute/Center

(Dollars in Thousands)

<table>
<thead>
<tr>
<th>IC</th>
<th>FY 2012 Actual</th>
<th>FY 2013 Enacted</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCI</td>
<td>$ 5,067,396</td>
<td>$ 4,779,406</td>
<td>-5.7%</td>
</tr>
<tr>
<td>NIAID</td>
<td>4,486,473</td>
<td>4,231,498</td>
<td>-5.7%</td>
</tr>
<tr>
<td>NHLBI</td>
<td>3,076,115</td>
<td>2,901,293</td>
<td>-5.7%</td>
</tr>
<tr>
<td>NHGRI</td>
<td>512,727</td>
<td>483,269</td>
<td>-5.7%</td>
</tr>
<tr>
<td>NCATS</td>
<td>574,823</td>
<td>542,155</td>
<td>-5.7%</td>
</tr>
<tr>
<td>NIGMS</td>
<td>2,427,742</td>
<td>2,291,294</td>
<td>-5.6%</td>
</tr>
<tr>
<td>Other ICs</td>
<td>$ 13,131,302</td>
<td>$ 12,368,808</td>
<td>-5.8%</td>
</tr>
<tr>
<td>Subtotal</td>
<td>$ 29,276,578</td>
<td>$ 27,597,723</td>
<td>-5.7%</td>
</tr>
<tr>
<td>OD</td>
<td>1,458,501</td>
<td>1,435,630</td>
<td>-1.6%</td>
</tr>
<tr>
<td>B&amp;F</td>
<td>125,308</td>
<td>118,109</td>
<td>-5.7%</td>
</tr>
<tr>
<td>Total</td>
<td>$ 30,860,387</td>
<td>$ 29,151,462</td>
<td>-5.5%</td>
</tr>
</tbody>
</table>
FY 2014 President’s Budget (PB)

- FY 2014 – $31.3 billion or $471 million over the final enacted 2013 CR prior to the sequestration (1.5% increase)

- However, the 2013 enacted budget adjusted for the sequestration is $29.3 billion, which makes the FY2014 PB ~7% increase, since the PB ignores the 2013 sequestration

- Likely “dead-in-the-water”
“Gentlemen (and Ladies), we have run out of money. It’s time to start thinking”.

- Ernest Rutherford
New Zealand Chemist & Physicist
Nobel Prize - 1908
Times are Tough

- Networks (and all of us) must prioritize research with a laser focus

- Studies must be kept current such that they are relevant when completed

- Partnerships are essential – PopArt as paradigm of collaboration
Questions?