The History of HIV

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Conflicts of interest: None
Epidemiologic Notes and Reports

**Pneumocystis Pneumonia --- Los Angeles**

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 21-year-old man, who denied any prior illness associated with elevated CD4 counts 

* The patient's condition was stable for the 2 months since he was first seen. He died May 3, 1981, of *Pneumocystis* pneumonia, a 2-month history of fever, and a 1-month history of lymphadenopathy and acyclovir. He died May 3, 1981, of *Pneumocystis* pneumonia, a 2-month history of fever, and a 1-month history of lymphadenopathy and acyclovir.
The Science-Director of NIAID made this a new almost singular priority

“Goose pimples” 1981
PNEUMOCYSTIS PNEUMONIA
TOXOPLASMOSIS
WHO WINNING PHOTO AWARD: AIDS – THE HUMAN TRAGEDY
The stigma- Ryan White

Child with hemophilia – HIV discovered 12/17/84 – banned from school and given 6 months to live. Died 5 years later, 4 months before passage of the Ryan White Care Act
Government leadership
C. Everett Koop
“The Letter” 1987

Surgeon General under President Reagan
Champion of –
Sex education
Condoms
Handicapped children
Cigarette harm
“The Letter” was an AIDS wakeup call
The Response: AIDS COALITION to UNLEASH POWER: 1987 ACT-UP

Martin Delaney HIV Activist
1945-2008

Founded Project Inform “for medically supervised guerrilla trials” – Major force in NIAID, FDA and ethics (“First in the tent”)
MAGIC JOHNSON
Olympic hero & greatest guard in NBA history

The Announcement: 1991

“I have AIDS”
Trumped efforts of millions to
destigmatize HIV infection
The beginning of ART: Jerome Horwitz 1919-2012

Discovered AZT (1964) for cancer
Then ddl & d4T → failed & shelved
“Great drugs waiting for the right disease”

Broder, Mitsuya and Yarchoan (NCI) showed anti-HIV action in CD4 cells

BW got the drug (and the patent)

AZT trial → First HIV → FDA record for approval: one cohort, 282 patients, stopped at 6 months
The Trial: AZT vs. placebo (n=282). DSMB stopped study: 19 deaths (placebo) vs 1 (AZT) (Fischl MA. NEJM 1987;317:185)
Agency Hero: Jeff Murray, MD
Deputy Director
Division of Antimicrobial Drug Products for FDA

Major facilitator of HIV drugs (n=28) and, more recently HCV (#37 approved or in trials)
Reduction of Maternal-Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment


Perinatal tx rates: Placebo-23%; AZT-8% (p=0.0006)
Estimated Numbers of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2010 — United States and Dependent Areas

Note: Data have been adjusted for reporting delays and missing risk-factor information.
The development of protease inhibitors and beginning of HAART
THE STUDY THAT CHANGED AIDS

Gulick RM. Merck 035 NEJM 1997;337:734

HAART: IDV/AZT/3TC

Results for NDV at 52 weeks – 80% vs. zero
David Ho:
Post Vancouver IAS Meeting

“Hit hard and hit early”
(3 ART agents for all with HIV starting at diagnosis)

...

Time Magazine:
Man-of-the-year, 1996
## RECOMMENDATIONS FOR WHEN TO START ART
(DHHS Panel on ART 1996-2012)

<table>
<thead>
<tr>
<th>Year</th>
<th>Who by CD4 count</th>
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<tbody>
<tr>
<td>1996</td>
<td>CD4 &lt;500: Merck 035</td>
</tr>
<tr>
<td>2000</td>
<td>CD4 &lt;200: Toxicity/Resis</td>
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<tr>
<td>2006</td>
<td>CD4 &lt;350: Half between</td>
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<tr>
<td>2009</td>
<td>CD4 &lt;500: 14 ART drugs</td>
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<tr>
<td>2012</td>
<td>All pts; Any CD4 count</td>
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<tr>
<td>Year</td>
<td>NRTI</td>
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<td>--------</td>
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<tr>
<td>1987</td>
<td>AZT</td>
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<tr>
<td>1991-92</td>
<td>ddi, ddC</td>
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<tr>
<td>1995</td>
<td>d4T</td>
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<tr>
<td>1996</td>
<td>3TC</td>
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<td>2012</td>
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<tr>
<td>2013</td>
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The START Trial

Trial: Start ART at CD4 <350 vs >500

Sample size: 4400 in 230 clinics, 36 countries

Started: 1/1/14; first data review 2016

Web statement: Early start is based on “embarrassingly uninterpretable studies like NA-ACCORD”

Early review, May 2015: Early ART clearly superior (53% reduction in HIV complications)
### Average duration of life after AIDS diagnosis in a 25 year old man

<table>
<thead>
<tr>
<th>Year</th>
<th>Age of Death</th>
<th>Added years</th>
</tr>
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<tbody>
<tr>
<td>1995</td>
<td>28 years</td>
<td>3</td>
</tr>
<tr>
<td>1997-99</td>
<td>48 years</td>
<td>25</td>
</tr>
<tr>
<td>2000-05</td>
<td>64 years</td>
<td>39</td>
</tr>
<tr>
<td>2011-12</td>
<td>73 years*</td>
<td>48</td>
</tr>
</tbody>
</table>

* Moore Clinic
GLOBAL HIV - Subsaharan Africa: 12% global population 69% of HIV cases

Figure 1: Adult HIV Prevalence Rate (Ages 15–49), 20111,7

Current Global Snapshot
Zimbabwe: Lifetime Probability of AIDS - 60%!
White House meeting of President Bush & Joe O’Neill
President George W. Bush
PEPFAR: 2002

Bush: Do those HIV drugs work?

O’Neil: “Let me tell you about my morning in the Moore Clinic”

Bush: “Get Tony, we need to do something. Think big – really big”
President George W. Bush

Fauci: “Thinking big”

Collaborators – Dybul, Mugyeni, Goosby, Pape

Plan Proposed Would be considered

January 2003:

“Seldom have we been offered the opportunity to do so much for so many”
Bush: “$15 billion for AIDS in Africa”
Mugyeni: Jumped up → cheered → hugged the First Lady
Tony Fauci – Medal of Freedom

President Bush awarding Dr. Fauci the Presidential Medal of Freedom – June 18, 2008
Everett Koop Award
“The boys from Brooklyn”

2011
First C. Everett Koop Award – Dr. Fauci
(Forum, 2011)

2012
Second Award – from Dr. Fauci to Dr. Koop
(Forum, 2012)
1980: recruited to Hopkins to start an ID Division and continue *C difficile* work

1983: Frank Polk changed career-irreversible passion for starting an HIV program

1983: HIV program launched: Moore Clinic quickly filled & hidden in basement

1986: Hospital funded HIV in-pt Osler- 8

1988: Cardiology fellow- needlestick AIDS

1991: Hopkins surgeon dies with HIV; Test 1000: 1 positive; chair incident

2014: O8 closed & converted to Ebola Center
What was good about it

Filled a desperate need in tradition of Osler & J Hopkins

1984: Dr. Heyssel requested AIDS Program plan & budget
1985: Lambert
1989: AIDS Busters Softball team won the Hopkins league
    beating the Maintenance men in the playoffs 4-2
1993: 10th anniversary – Bo Diddly celebration
1983-2006: 24 faculty promoted-Prof based on work in 14 depts-Ob,Neuro,Basic,Card,Psych,Onc,Peds,Pharm,TB,HCV
The 1983 Career change

“There’s this new disease. Someone will find the virus— not me. BUT Epidemiology— That’s for me”

Started MACS and ALIVE cohorts: >1000 publications
Dr. Robert Heyssel:
President JHH-
Birth of Osler 8
“It doesn’t
matter (an
AIDS Ward).
It’s a moral
imperative”
1986
Osler 8 nurses:
1986-2013: Perennial best nursing unit-JHH. Unique service for knowledge of HIV and this patient population
Thomas Quinn, MD
Director of Johns Hopkins Center for Global Health.

Author of > 1000 publications

34 global HIV Centers, 450 faculty, 710 projects in 110 countries funded at $75M/yr
David Thomas, MD

CHIEF, Infectious Disease Division & international leader- HCV basic science
Mark Sulkowski, MD
National leader in HCV and HIV/HCV treatment

Director, Hopkins Center for Viral Hepatitis
Joel Gallant, MD
(Arguably) HIV’s best clinician; National and international HIV guidelines, President HIV Med Assoc
Richard Chaisson, MD

Co-PI JHU CFAR; International leader- TB & HIV
* Chair-NIH TB Clin TRIAL Group
* TB trials-INDIA, Brazil, Africa
* CHAIR-CREATE (TB-GATES)
RICHARD MOORE, MD
Internal Medicine

Master of design, management and analysis of cohorts.

PI of NA-ACCORD, NIH-sponsored, 8 yrs, 25 cohorts, >200 sites, 150,000 patients
Robert Siliciano, MD, PhD

H. Hughes
Investigator,
Leading
scientist
in HIV basic
research and
“the Cure”
Deborah Pursuad, MD
Pediatrician, HIV Basic Science
WENDY POST, MD
CARDIOLOGY
Leader in cardiac complications of HIV infection
Jean Anderson, MD
Ob/Gyn

Regional, national and international leader in Obstetric and gynecologic HIV care.
Rich Ambinder, MD
Oncology
Chair, NIH-HIV malignancy consortium;
Extraordinary in clinical care and research
Charles Flexner, MD
Pharmacology
*Pharmacology of HIV and role of immune activation in HIV
*Director Hopkins ACTG
*Consultant to Gates/Clinton
*Chair ACTG Translational Research
Simply extraordinary; Leader in HIV psychiatry and The meaning of life
WHAT HAS HIV TAUGHT US

• Science leadership: A. Fauci
• Pharma leadership: Merck – Indinavir
• Oslerian Medicine: HIV providers <1997
• Greatest humanitarian effort: PEPFAR (Bono)
• Government leadership: E. Koop
• Implementation science: 076
“AIDS Busters” Softball Championship vs Maintenance Department, 1989

Big Challenges Build Strong Bonds