Human Immunodeficiency Virus (HIV) History, Epidemiology and Testing

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August 2018
June 5, 1981

Pneumocystis Pneumonia – Los Angeles

July 4, 1981

Kaposi’s Sarcoma and Pneumocystis Pneumonia Among Homosexual Men – New York City and California
What kind of Virus is HIV?

Lentivirus

- A genus of retroviruses with long latent interval
Primate Lentiviruses

1) Chimpanzees; gorillas

2) Monkeys; Mandrills

3) African green monkeys; baboons

4) Sooty mangabeys

5) Sykes’ monkeys

Slide courtesy of Dr. Monica Ghandi
How did Lentiviruses get to Humans?

Slide courtesy of Dr. Monica Ghandi
First theory – “The River”

- Polish scientist competing with Sabin for first oral polio vaccine (Sabin won)
- Scientist (Koprowski) administered his vaccine to 1 million people in Belgium-controlled Africa
- Likely not reason (wrong primate; wrong timing) but led to greater safety with primate cells

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1Plotkin SA. CHAT oral polio vaccine was not the source of human immunodeficiency virus type 1 group M for humans. *Clin. Infect. Dis* 2001
To know when – we need to go back in time and get human specimens!

• 1213 plasma specimens from Kinshasa, DRC, UW, 1959
• HIV-1 found in 1 patient ("Bantu male", ZR59)
• "Phylogenetic analysis"
  • ZR59 and SIV in chimpanzees
  • ZR59 and modern human strains
• Estimated HIV entered humans ~1930

Hahn BH. Science 2000.
Slide courtesy of Dr. Monica Ghandi
Found another human specimen!

- Lymph node in paraffin found, adult female, Kinshasa, 1960 “DRC60”
- DRC60 very different than ZR59
- Family tree constructed, rate of mutation calculated
- Ancestor of HIV-1 M probably entered humans 1884-1924

What was the cross over event?

• Likely “bushmeat” trade-hunting primates for food
• Hunters and other highly exposed populations: many SIV strains incorporated
• General human population – one cross over event and SPREAD due to social disruption, colonization, city growth

What happened from there?

- Carried from West to Eastern Africa in ’70’s
- Spread fast in E. Africa, epidemic form in early ’80’s
  - Labor migration (35% truck drivers positive Uganda ’88)
  - High ratio of men urban centers, sex trade, STDs
  - Low status of women, low rates circumcision
  - 85% Nairobi sex workers infected by ‘86)
- By mid and late ’80’s, on to sub-Saharan Africa
  - Tanzam road between Tanzania and Zambia

Slide courtesy of Dr. Monica Ghandi
Adults and children estimated to be living with HIV | 2016

- North America and western and central Europe: 2.1 million [2.0 million–2.3 million]
- Caribbean: 310,000 [280,000–350,000]
- Latin America: 1.8 million [1.4 million–2.1 million]
- Middle East and North Africa: 230,000 [160,000–360,000]
- Western and central Africa: 6.1 million [4.9 million–7.6 million]
- Eastern and southern Africa: 19.4 million [17.6 million–21.1 million]
- Eastern Europe and central Asia: 1.6 million [1.4 million–1.7 million]
- Asia and the Pacific: 5.1 million [3.9 million–7.2 million]

Total: 36.7 million [30.8 million–42.9 million]
Estimated HIV Incidence among Persons Aged ≥13 Years, 2010–2015—United States

HIV infections decreased 18% from 2008-2014
Nearly $15 billion saved in health care costs

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.
*Difference from the 2010 estimate was deemed statistically significant (P < .05).
Estimated HIV Incidence among Persons Aged ≥13 Years, by Sex, 2010–2015—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.

* Difference from the 2010 estimate was deemed statistically significant (P < .05).
Estimated HIV Incidence among Persons Aged ≥13 Years, by Age, 2010–2015—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.

* Difference from the 2010 estimate was deemed statistically significant (P < .05).
Estimated HIV Incidence among Persons Aged ≥13 Years, by Transmission Category, 2010–2015—United States

Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Data have been statistically adjusted to account for missing transmission category. Heterosexual contact is with a person known to have, or to be at high risk for, HIV infection.

* Difference from the 2010 estimate was deemed statistically significant (P < .05).
Time course of HIV-1 infection

- HIV-1 p24 antigen
- HIV proviral DNA
- HIV antibodies
- HIV-1 p24 antigen

'window' period

Time following infection

1st infection
weeks
years
**Pathophysiology**

CD4 T-Lymphocytes are target cell

- Depleted by HIV infection
- Circulating CD4 count is:
  - marker of progression
  - Indicator of susceptibility to opportunistic infections

Immunodysregulation occurs

- Increased immune activation
- Elevated cytokine levels
- Persistent inflammatory state may predispose to accelerated cardiovascular disease
Typical Course of HIV Infection

- Primary Infection
- Acute HIV syndrome
- Wide dissemination of virus
- Seeding of lymphoid organs
- Clinical Latency
- Opportunistic diseases
- Constitutional symptoms
- Death

CDA+ T Lymphocyte Count (cells/mm²)

HIV RNA Copies per ml Plasma

CDC Testing Recommendations

• All persons age 13-64 should be tested at least once
• Those with HIV acquisition risk factors - annually
• Men who have sex with men (MSM) – annually
  • More frequent if at increased risk
### Types of HIV Diagnostic Tests

<table>
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<tr>
<th>HIV Antibodies</th>
<th>HIV-1 RNA</th>
<th>HIV p24 Antigen</th>
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<td><strong>Most Common Test for Established Infection</strong></td>
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- **HIV Antibodies**: Most Common Test for Established Infection
- **HIV-1 RNA**: Used for Acute HIV and Indeterminate WB
- **HIV p24 Antigen**: 4th Generation EIA
Enzyme Immunoassays (EIAs)

Quantitative assay to measure HIV antibodies

• Most detect antibodies to HIV-1 and HIV-2
• Antigens coated in microwells
• HIV Antigen / Antibody reaction is detected by color change
• Intensity of color reflects amount of antibody present serum
Enzyme ImmunoAssays (EIAs)

After several incubation and wash steps, a color reaction occurs if HIV antibody is present.

An automated reader gives a measurement of optical density (presence of color) for each well.

Lab workers

Health workers
Generation of EIA Tests

<table>
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<th>First</th>
<th>Second</th>
<th>Third</th>
<th>*Fourth</th>
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<td>Uses crude viral lysate</td>
<td>Uses recombinant HIV antigens or peptides</td>
<td>Detects IgM and IgG in “Sandwich” EIA</td>
<td>Detects HIV antibodies and p24 antigen</td>
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Timing of Diagnostic Tests after Initial HIV Infection

- HIV RNA Detectable
- HIV EIA* (3rd Generation, IgM-Sensitive EIA)
- HIV EIA* (2nd Generation EIA)
- Viral Lysate EIA

Weeks after HIV Infection

HIV-1 Western Blot Antigens

- **p** = protein
- **gp** = glycoprotein
- **Number** = molecular weight
HIV-1/2 Ag/Ab combination immunoassay
Automated, laboratory-based, p24/IgM/IgG sensitive

HIV-1/2 Ab differentiation immunoassay

(+)

Antibodies detected
Infected with HIV-1, HIV-2, or both

(-)

HIV-1 (-) or indeterminate
HIV-2 (-)
Biological false positive test or acute HIV-1 infection

HIV-1 nucleic acid test

(+)

HIV-1 nucleic acid test (+)
Acute HIV-1 infection

(-)

HIV-1 nucleic acid test (-)
Negative for HIV-1

Negative for HIV-1 p24 Ag, HIV-1 Ab, and HIV-2 Ab
Clinical Case 1

- 21 year old woman presents in labor – no prenatal care
- Cervix is completely dilated and she is emergently taken to L&D
- Normal term male infant delivered vaginally – good Apgars
- HIV test sent (4th generation and Western Blot) as woman wheeled into delivery and rapid HIV test negative
- Next day, 4th generation test is reported as positive but Western Blot is negative
- Patient signs out AMA
- Should baby be given antiretroviral agents???
HIV Rapid Tests

- Qualitative assay to detect HIV antibodies
- Most detect HIV 1 and HIV 2
- As reliable as EIAs
- Convenient with rapid answer
Reading Results: OraQuick

Non-Reactive

Reactive

Lab workers  Health workers  Counselors
Clinical Case 2

• 21 year old man presents for ED follow-up
• Three weeks ago he presented to ED with fever, cervical and inguinal adenopathy, pharyngitis, rash, and oral candidiasis
• Monospot was positive and patient was given a diagnosis of mononucleosis
• Now feeling well without complaints
• Patient reports that he has sex with men and sporadically uses condoms
• What are the considerations??
Primary HIV Infection

Rash

Trunk and face > limbs
Small pink macules

Mucosal Lesions

Oral ulcers, thrush

(Kahn, NEJM, 1998)
Primary HIV Infection: Signs & Symptoms

• 40-90% of patients will be symptomatic
• A mononucleosis-like illness of non-specific signs and symptoms
• Signs and symptoms typically begin 1-4 weeks post-exposure
• High index of suspicion is critical

Diagnosing Acute HIV: Clinical Manifestations

Signs and Symptoms of 160 Patients with Acute HIV

- Fever: 86%
- Lethargy: 74%
- Myalgias: 59%
- Rash: 57%
- Headache: 55%
- Pharyngitis: 52%
- Adenopathy: 44%

Primary HIV Infection: Other Signs & Symptoms

AIDS Drugs Have Saved 3 Million Years of Life in the United States

The Survival Benefits of AIDS Treatment in the United States

RP Walensky et al.
HAART Impact on Survival

Deaths per 100 Person-Years

HAART

Deaths

Palella FJ et al. NEJM 1998; 338: 853