Infectious Disease Epidemiology
BMTRY 713 (A. Selassie, DrPH)
February 27, 2017
Lecture 13
HIV/AIDS

Learning Objectives
1. Describe the epidemiology of HIV/AIDS
2. Explain the key viral characteristics of HIV
3. Describe the major clinical pictures of HIV/AIDS
4. Explain the prevention strategies

HIV & Acquired Immunodeficiency Syndrome (AIDS)
- First recognized in the US in 1980-81 among men who have sex with other men (MSM); intravenous drug users (IVDU); and hemophiliacs
- Rare fungal infection of the lung (PCP) and Kaposi sarcoma, heretofore found in immune compromised persons, in young healthy men alerted epidemiologists (Figure)
- Contact tracking indicated chain of transmission suggestive of unique pattern of infection and perhaps new etiologic agent

![Image of diagram showing HIV transmission]

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Epidemiological milestones

- **1981**
  - Increase in PCP and KS among young homosexual men
  - PCP among children of injection drug users
- **1983**
  - Recognized in hemophiliacs
  - HIV isolated
    - Detected in 99% of AIDS patients

The HIV Virus

- Virus was discovered in 1984, four years after the epidemic, by Robert Gallo (NIH) and Luc Montagnier (Pasteur Institute)
- Serological sample stored in Zaire in 1959 was later discovered to have evidence of HIV leading to speculation of the origin of the virus in chimpanzees
- Another HIV, HIV-2, was later discovered in green monkeys in West Africa

Acquired Immunodeficiency Syndrome (AIDS)

- **1980s** – epidemic; 1984 HIV discovery
- **1990’s** – pandemic
- Deaths through end of 1997 (in millions)
  - 5.1 males; 3.9 females; 2.7 children
- Same as malaria deaths in 1997
- Disproportionate burden in sub-Saharan Africa with adult prevalence ↑ 7%
- Estimated worldwide prevalence among adults is 1.1%
Impact of AIDS Epidemic

- Reduced life expectancy of its victims by 20 or more years
- Main cause of death in many sub-Saharan African countries
- Higher rates among adolescents, leading to death at the prime of life
- Catastrophic effect in many societies and economies

Global data & trend, 1982-2013

- 78 million people infected with the HIV
- 39 million people have died of HIV
- 35 million were living with HIV in 2013
- An estimated 0.8% of adults, age 15–49, have HIV
- Sub-Saharan Africa remains most severely affected,
  - Nearly 1 in every 20 adults are living with HIV
  - Accounting for nearly 71% of the people living with HIV worldwide

Estimated number of people who have HIV infection and AIDS

- 850,000
- 480,000
- 190,000
- 42,000
- 310,000
- 210,000
- 2 million
- 1.3 million

- 12,000
Current Facts and Figures

- More than 25 million people have died of AIDS since 1981.
- By December 2005 women accounted for 46% of all adults living with HIV worldwide, and for 57% in sub-Saharan Africa.
- Young people (15-24 years old) account for half of all new HIV infections worldwide - more than 6,000 become infected with HIV every day.
- Of the 6.5 million people in developing and transitional countries who need life-saving AIDS drugs, only 1 million are receiving Rx in 2005.
Africa has 12 million AIDS orphans.

Regional statistics for HIV & AIDS end of 2005

<table>
<thead>
<tr>
<th>Region</th>
<th>Adults &amp; Children</th>
<th>Adults</th>
<th>Adult</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>29.8</td>
<td>3.2</td>
<td>7.2</td>
<td>2.4</td>
</tr>
<tr>
<td>East Asia</td>
<td>8.0</td>
<td>0.14</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>South and South-East Asia</td>
<td>7.4</td>
<td>0.56</td>
<td>0.7</td>
<td>0.43</td>
</tr>
<tr>
<td>Oceanic</td>
<td>0.024</td>
<td>0.0082</td>
<td>0.0</td>
<td>0.0035</td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Asia</td>
<td>1.6</td>
<td>0.27</td>
<td>0.6</td>
<td>0.956</td>
</tr>
<tr>
<td>Western &amp; Central Europe</td>
<td>0.72</td>
<td>0.032</td>
<td>0.5</td>
<td>0.012</td>
</tr>
<tr>
<td>North Africa &amp; Middle East</td>
<td>5.0</td>
<td>0.647</td>
<td>0.2</td>
<td>0.553</td>
</tr>
<tr>
<td>North America</td>
<td>5.2</td>
<td>0.643</td>
<td>0.7</td>
<td>0.318</td>
</tr>
<tr>
<td>Caribbean</td>
<td>0.5</td>
<td>0.053</td>
<td>1.6</td>
<td>0.624</td>
</tr>
<tr>
<td>Latin America</td>
<td>1.0</td>
<td>0.2</td>
<td>0.6</td>
<td>0.999</td>
</tr>
<tr>
<td>Global Total</td>
<td>48.5</td>
<td>4.8</td>
<td>11.1</td>
<td>5.1</td>
</tr>
</tbody>
</table>

REPORTED SEXUAL INTERCOURSE IN PAST 12 MONTHS IN NEVER MARRIED 15-19 YEAR OLDS

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AIDS in the developed countries

- Among the leading causes of death in the age group 25-44 in the US. Leading cause between from 1992 through 1995.
- In Europe, homosexual/bisexual transmission was leading cause for contracting HIV. Superseded by IDU since 1990.
- In developing countries transmission is mainly heterosexual

### Table: Surveillance of AIDS in the United States

<table>
<thead>
<tr>
<th>Stage</th>
<th>Laboratory evidence</th>
<th>Clinical evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Laboratory evidence: positive and CD4+ T lymphocyte count of less than 500 cells/mm³ or CD4+ T lymphocyte percentage of less than 14%</td>
<td>Note: lated (not an AIDS-defining condition)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Laboratory evidence: positive and CD4+ T lymphocyte count of less than 200 cells/mm³ or CD4+ T lymphocyte percentage of less than 14%</td>
<td>Note: lated (not an AIDS-defining condition)</td>
</tr>
<tr>
<td>Stage 2 (AIDS)</td>
<td>Laboratory evidence: positive and CD4+ T lymphocyte count of less than 200 cells/mm³ or CD4+ T lymphocyte percentage of less than 14%</td>
<td>Note: lated (not an AIDS-defining condition)</td>
</tr>
</tbody>
</table>

Note: All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.

a Hispanics/Latinos can be of any race.
b Includes Asian/Pacific Islander cases.
Characteristics of the agent

- HIV is a lentivirus of retrovirus subfamily
- Inserts itself into host’s DNA—provirus
- Remains latent in resting lymphocytes
- Transcription and translation occurs when cells are activated resulting in assembly of viral proteins to form virions
- Attacks and weakens immune system
- High replication rate ($10^9$ viral particles/day) and a high mutation rate (as high as $3\times10^6$ per day)
Types of HIV

- HIV-1 and HIV-2
  - Some genetic differences
  - Same mode of transmission
  - HIV-1
    - Worldwide transmission
    - Increased perinatal transmission 20-35%
    - Younger age group (20-34)
    - Classified into 10 genetic subtypes
  - HIV-2
    - Primarily West African and India
    - Perinatal transmission 0-4%, mean age 45-55

HIV Genotypes

- Three groups (strains) of HIV-1
  - M has 11 genetic subtypes
    - A, B, C, D, E, F, G, H, I, J, K
    - Viral recombination has been recognized, which occur by packaging RNA different subtypes into the same viral particles resulting in recombinant HIV in coinfected individuals.
      - Recombinant forms are either:
        - Circulating recombinant forms (CRF)—If same recombinants are found commonly circulating
        - Unique recombinant forms (URF)—If recombinants are found only in a few individuals
  - N
  - O Geographically limited to W. Africa

Host Susceptibility & Infectivity

Determined by

- Host factors—genetic polymorphism (see page 801 of Nelson textbook)
- Viral genotype—Subtypes C and E have higher replication rates compared to B; recombinant forms AC, AD, BE have higher infectivity and rapid progression
- Environmental—Parasitic infections, STDs, malaria, TB, nutritional deficiencies, and other environmental insults that result in chronic immune activation contribute to HIV infection rate and rapid progression of to fully blown AIDS
Is there immunity to HIV?

- May be there is ...
  - Genetic mutation in some people
    - Delta32 is a gene mutation that keeps CCR5 from latching to the surface of the CD4 T-cells preventing the HIV from infecting the cell, i.e., “door remains closed.”
    - 1% of Northern Europeans have it and it is believed to be mutation from surviving the massive epidemic of bubonic plague.
    - It is a recessive gene and for protection, both parents must pass the mutation to the offspring.

Timothy Ray Brown
“The Berlin Patient”

THE HIV-1 VIRION

Extracellular Protein gp120

Schematic Drawing of the HIV Life cycle
HIV natural history

- Three phases
  - Acute
    - High HIV levels, active immune response, symptoms of viral disease
  - Clinical latency
    - No clinical symptoms, viral replication
  - Chronic infection
    - Progressive symptomatic, clinical disease, non-AIDS defining conditions, AIDS
      - AIDS: PCP and TB most common
Manifestations of acute infection with HIV

- Constitutional symptoms of viremia characterized by:
  - Fever, malaise, joint pains, etc.
  - Maculopapular rash
  - Penile ulcers in males
Manifestations of HIV infection with progressive decline of immunity

- Aggravation of latent illnesses
- CD4 count is 300-400
  - Herpes zoster
  - Tuberculosis
  - Oral Candidiasis
  - Kaposi Sarcoma
HIV detection

- ELISA identifies presence of HIV
- Western blot confirmatory test
- The two tests are applied in series
- Staging of infection
  - Plasma viral load
    - HIV NAAT (nucleic acid amplification testing)
  - CD4 counts

Disease progression predictors

- The level of viral load at a set point
- Immunological insult manifested with comorbid infections
- Host genetic polymorphism
- Staging of infection
  - Plasma viral load (HIV NAAT)
  - CD4 counts

Series Testing

Two screening tests are said to be applied in series if both tests must be positive in order to establish a positive diagnosis.

E.g.: If the ELISA test is repeatedly positive (two ELISA tests applied in series) then a Western Blot test is given before making determination that HIV antibody is present.
Parallel Testing

Two screening tests, whether identical or different, are said to be applied in parallel if a positive result on either test is sufficient to establish a positive diagnosis.

E.g. Breast cancer screening frequently employs a combination of mammography and breast physical exam applied in parallel. If either test is positive, then biopsy is indicated.

<table>
<thead>
<tr>
<th>Screening test with Elisa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elisa Test</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{980}{1000} = 98.0\% \)

Specificity = \( \frac{89100}{99000} = 90.0\% \)

<table>
<thead>
<tr>
<th>Screening with Western Blot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Blot test</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{900}{1000} = 90.0\% \)

Specificity = \( \frac{98050}{99000} = 99.0\% \)
**Series Testing with Western Blot of those tested positive with Elisa (N=10,880)**

<table>
<thead>
<tr>
<th>Western Blot test</th>
<th>HIV Status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>HIV +</td>
<td>900</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td>HIV +</td>
<td>940</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>980</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{900}{980} = 91.8\% \)  
Specificity = \( \frac{9860}{9940} = 99.6\% \)

**Parallel Testing with Elisa (El) and Western Blot (WB)**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>HIV Status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>EL +</td>
<td>HIV +</td>
<td>190</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>9800</td>
</tr>
<tr>
<td>WB +</td>
<td>HIV +</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>4850</td>
</tr>
<tr>
<td>EL+ &amp; WB+</td>
<td>HIV +</td>
<td>760</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>100</td>
</tr>
<tr>
<td>EL- &amp; WB-</td>
<td>HIV +</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>84250</td>
</tr>
<tr>
<td>Total</td>
<td>HIV +</td>
<td>860</td>
</tr>
<tr>
<td></td>
<td>HIV -</td>
<td>84260</td>
</tr>
</tbody>
</table>

Sensitivity = \( \frac{990}{1000} = 99.0\% \)  
Specificity = \( \frac{84250}{99000} = 85.1\% \)

**Testing Summary**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elisa alone</td>
<td>98.0</td>
<td>90.0</td>
</tr>
<tr>
<td>WB alone</td>
<td>90.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Series +</td>
<td>91.8</td>
<td>99.6</td>
</tr>
<tr>
<td>Parallel +</td>
<td>99.0</td>
<td>85.1</td>
</tr>
</tbody>
</table>
Modes of transmission

- Sexual behavior (75-80% of HIVs)
  - Unprotected receptive anal intercourse is the most risky behavior (♂ to ♂ | ♂ to ♀)
  - Lowest risk among ♀ to ♀
  - Heterosexual moderate risk
  - Partner studies
    - Infected ♂ to uninfected ♀ ≈ 20.0%
    - Infected ♀ to uninfected ♂ ≈ 1.4-12.0%
  - Multiple sexual partners

Modes of transmission (2)

- Injection drug use (15-20%)
  - Higher in cocaine than heroin
    - Shorter half life and more frequent injections
  - Sharing needles
    - Social institution
    - Lack of access to clean needles

Modes of transmission (3)

- Perinatal transmission
  - Estimated 65-80% of transmission during delivery
    - Risk reduction with C/Sections OR=0.43
  - Zidovudine (AZT) administration reduces incidence by 67%
  - Breast feeding (12-15% of vertical)
Modes of transmission (4)

- **Blood transfusion**
  - Infrequent in developed countries
  - Historically very high among hemophiliacs (>90%)
  - Estimated acquisition from false negative is 26 per 1 million transfusion

Modes of transmission (5)

- **Transmission to health care workers**
  - HIV seroconversion from needle stick injury 0.4%
  - Greater risk with exposure to high quantities of blood
Impact of antiretroviral therapy on epidemicity

- Natural history of AIDS - death 2 years
- 17 years of treatment
  - 1987 AZT developed
  - 1990s triple combination
    - Viral suppression
      - 95% adherent: 81%
      - 70-80% adherent: 35%
      - <70% adherent: 6%
    - Mortality declined by nearly 6 fold with triple combination therapy

Prevention

- “Safe sex”
- Reduce needle sharing
- Identify and treat HIV+ mothers
- Screening of blood products
- Universal precautions
Effectiveness of Partner Notification

SEXUAL BEHAVIOR AND HIV/STD INCIDENCE IN YOUNG MALES IN NORTHERN THAILAND