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Outline

• Background and Epidemiology
• Acute HIV Infection
• HIV-2
• Diagnostics
• Post-exposure prophylaxis (PEP)
June 5, 1981: 5 cases of PCP in homosexual men from UCLA (MMWR)
Background

• 1982:
  – Term “AIDS” coined
  – First cases in women reported
  – First transfusion and vertically transmitted cases

• 1983:
  – Isolation of a retrovirus from a patient with AIDS
Background

• Origin of HIV
  – Not completely understood
  – Studies suggest that HIV evolved from a lentivirus, simian immunodeficiency virus (SIV)

• HIV mainly targets CD4+ T lymphocytes
### Global summary of the AIDS epidemic | 2012

<table>
<thead>
<tr>
<th>Number of people living with HIV</th>
<th>Total</th>
<th>35.3 million [32.2 million – 38.8 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults</td>
<td>32.1 million [29.1 million – 35.3 million]</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>17.7 million [16.4 million – 19.3 million]</td>
</tr>
<tr>
<td></td>
<td>Children (&lt;15 years)</td>
<td>3.3 million [3.0 million – 3.7 million]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>People newly infected with HIV in 2012</th>
<th>Total</th>
<th>2.3 million [1.9 million – 2.7 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults</td>
<td>2.0 million [1.7 million – 2.4 million]</td>
</tr>
<tr>
<td></td>
<td>Children (&lt;15 years)</td>
<td>260 000 [230 000 – 320 000]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AIDS deaths in 2012</th>
<th>Total</th>
<th>1.6 million [1.4 million – 1.9 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults</td>
<td>1.4 million [1.2 million – 1.7 million]</td>
</tr>
<tr>
<td></td>
<td>Children (&lt;15 years)</td>
<td>210 000 [190 000 – 250 000]</td>
</tr>
</tbody>
</table>
## Regional HIV and AIDS statistics and features | 2012

<table>
<thead>
<tr>
<th>Region</th>
<th>Adults and children living with HIV</th>
<th>Adults and children newly infected with HIV</th>
<th>Adult prevalence (15–49) [%]</th>
<th>Adult &amp; child deaths due to AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>25.0 million [23.5 million – 26.6 million]</td>
<td>1.6 million [1.4 million – 1.8 million]</td>
<td>4.7% [4.4% – 5.0%]</td>
<td>1.2 million [1.1 million – 1.3 million]</td>
</tr>
<tr>
<td>Middle East and North Africa</td>
<td>260 000 [200 000 – 380 000]</td>
<td>32 000 [22 000 – 47 000]</td>
<td>0.1% [0.1% – 0.2%]</td>
<td>17 000 [12 000 – 26 000]</td>
</tr>
<tr>
<td>South and South-East Asia</td>
<td>3.9 million [2.9 million – 5.2 million]</td>
<td>270 000 [160 000 – 440 000]</td>
<td>0.3% [0.2% – 0.4%]</td>
<td>220 000 [150 000 – 310 000]</td>
</tr>
<tr>
<td>East Asia</td>
<td>880 000 [650 000 – 1.2 million]</td>
<td>81 000 [34 000 – 160 000]</td>
<td>&lt;0.1% [&lt;0.1% – 0.1%]</td>
<td>41 000 [25 000 – 64 000]</td>
</tr>
<tr>
<td>Latin America</td>
<td>1.5 million [1.2 million – 1.9 million]</td>
<td>86 000 [57 000 – 150 000]</td>
<td>0.4% [0.3% – 0.5%]</td>
<td>52 000 [35 000 – 75 000]</td>
</tr>
<tr>
<td>Caribbean</td>
<td>250 000 [220 000 – 280 000]</td>
<td>12 000 [9400 – 14 000]</td>
<td>1.0% [0.9% – 1.1%]</td>
<td>11 000 [9400 – 14 000]</td>
</tr>
<tr>
<td>Eastern Europe and Central Asia</td>
<td>1.3 million [1.0 million – 1.7 million]</td>
<td>130 000 [89 000 – 190 000]</td>
<td>0.7% [0.6% – 1.0%]</td>
<td>91 000 [66 000 – 120 000]</td>
</tr>
<tr>
<td>Western and Central Europe</td>
<td>860 000 [800 000 – 930 000]</td>
<td>29 000 [25 000 – 35 000]</td>
<td>0.2% [0.2% – 0.2%]</td>
<td>7600 [6900 – 8300]</td>
</tr>
<tr>
<td>North America</td>
<td>1.3 million [980 000 – 1.9 million]</td>
<td>48 000 [15 000 – 100 000]</td>
<td>0.5% [0.4% – 0.8%]</td>
<td>20 000 [16 000 – 27 000]</td>
</tr>
<tr>
<td>Oceania</td>
<td>51 000 [43 000 – 59 000]</td>
<td>2100 [1500 – 2700]</td>
<td>0.2% [0.2% – 0.3%]</td>
<td>1200 [&lt;1000 – 1800]</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>35.3 million [32.2 million – 38.8 million]</td>
<td>2.3 million [1.9 million – 2.7 million]</td>
<td>0.8% [0.7% - 0.9%]</td>
<td>1.6 million [1.4 million – 1.9 million]</td>
</tr>
</tbody>
</table>

The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.
Adults and children estimated to be living with HIV | 2012

- Western & Central Europe: 860,000 (800,000 – 930,000)
- Middle East & North Africa: 260,000 (200,000 – 380,000)
- Sub-Saharan Africa: 25.0 million (23.5 million – 26.6 million)
- Eastern Europe & Central Asia: 1.3 million (1.0 million – 1.7 million)
- East Asia: 880,000 (650,000 – 1.2 million)
- South & South-East Asia: 3.9 million (2.9 million – 5.2 million)
- North America: 1.3 million (980,000 – 1.9 million)
- Latin America: 1.5 million (1.2 million – 1.9 million)
- Caribbean: 250,000 (220,000 – 280,000)
- Oceania: 51,000 (43,000 – 59,000)

Total: 35.3 million (32.2 million – 38.8 million)
Estimated number of adults and children newly infected with HIV | 2012

- **Sub-Saharan Africa**: 1.6 million [1.4 million – 1.8 million]
- **North America**: 48,000 [15,000 – 100,000]
- **Caribbean**: 12,000 [9,400 – 14,000]
- **Latin America**: 86,000 [57,000 – 150,000]
- **Western & Central Europe**: 29,000 [25,000 – 35,000]
- **Middle East & North Africa**: 32,000 [22,000 – 47,000]
- **Eastern Europe & Central Asia**: 130,000 [89,000 – 190,000]
- **East Asia**: 81,000 [34,000 – 160,000]
- **South & South-East Asia**: 270,000 [160,000 – 440,000]
- **Oceania**: 2100 [1500 – 2700]
- **Total**: 2.3 million [1.9 million – 2.7 million]
Estimated adult and child deaths from AIDS | 2012

- Western & Central Europe: 7600 (6900 – 8300)
- Middle East & North Africa: 17,000 (12,000 – 26,000)
- Sub-Saharan Africa: 1.2 million (1.1 million – 1.3 million)
- Eastern Europe & Central Asia: 91,000 (66,000 – 120,000)
- East Asia: 41,000 (25,000 – 64,000)
- South & South-East Asia: 220,000 (150,000 – 310,000)
- Latin America: 52,000 (35,000 – 75,000)
- Caribbean: 11,000 (9,400 – 14,000)
- North America: 20,000 (16,000 – 27,000)
- Oceania: 1,200 (<1000 – 1800)
- Total: 1.6 million (1.4 million – 1.9 million)
HIV prevalence among adults (15-49) %  |  2012
Transmission

- Sexual contact (co-existing STI ↑ risk)
- Blood and body fluid exposures
- IV drug use
- Mother to child
  - In utero
  - Delivery
  - Breast feeding
## Transmission

**Estimated per-act risk for acquisition of HIV, by exposure route***

<table>
<thead>
<tr>
<th>Exposure route</th>
<th>Risk per 10,000 exposures to an infected source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood transfusion</td>
<td>9,000</td>
</tr>
<tr>
<td>Needle-sharing injection-drug use</td>
<td>67</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>50</td>
</tr>
<tr>
<td>Percutaneous needle stick</td>
<td>30</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>10</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>6.5</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>5</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>1</td>
</tr>
<tr>
<td>Insertive oral intercourse</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Performed on a male

Risk of perinatal HIV transmission 15-45% (without ART)
Natural History of HIV Infection

- **Primary Infection**: Wide dissemination of virus, Seeding of lymphoid organs
- **Acute HIV syndrome**: Constitutional Symptoms, Clinical Latency, Opportunistic Diseases, Death
- **CD4+ T Lymphocyte Count (cells/mm³)**
- **HIV RNA Copies per ml Plasma**
Acute HIV

• Syndrome typically occurs **2-12 weeks after infection**
• Symptoms can be nonspecific, and last for several weeks (usually at least 7-10 days)
• Many are **asymptomatic**
• **High risk** for transmitting HIV to others
  – Very high viral load
  – Unaware of disease

• Diagnosis:
  – High index of suspicion + HIV RNA (viral load)
    • Viral load usually in the 100,000+ range
    • **Antibody testing generally not useful** as seroconversion may not have occurred yet (window period)
Acute HIV

Main symptoms of Acute HIV infection

- **Systemic:**
  - Fever
  - Weight loss

- **Central:**
  - Malaise
  - Headache
  - Neuropathy

- **Pharyngitis:**
  - Mouth:
    - Sores
    - Thrush

- **Esophagus:**
  - Sores

- **Muscles:**
  - Myalgia

- **Liver and spleen:**
  - Enlargement

- **Skin:**
  - Rash

- **Lymph nodes:**
  - Lymphadenopathy

- **Gastric:**
  - Nausea
  - Vomiting
# Acute HIV

## Table A-1. Signs and Symptoms of Acute HIV Infection

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>90</td>
</tr>
<tr>
<td>Morbilliform rash</td>
<td>40-80</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>50-70</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>40-70</td>
</tr>
<tr>
<td>Headache ± meningitis</td>
<td>24-70</td>
</tr>
<tr>
<td>Mucocutaneous ulcers</td>
<td>5-20</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>45</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>40</td>
</tr>
<tr>
<td>Transaminase elevations</td>
<td>20</td>
</tr>
</tbody>
</table>

## Table A-2. Comparison Between Acute HIV Infection and EBV Mononucleosis

<table>
<thead>
<tr>
<th>Acute HIV Infection</th>
<th>EBV Mononucleosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exudative pharyngitis rare</td>
<td>Exudative pharyngitis common</td>
</tr>
<tr>
<td>Painful mucocutaneous ulcers</td>
<td>No ulcers</td>
</tr>
<tr>
<td>Morbilliform rash common</td>
<td>Rash uncommon unless ampicillin administered</td>
</tr>
<tr>
<td>Vomiting and/or diarrhea</td>
<td>GI symptoms rare</td>
</tr>
<tr>
<td>Few atypical lymphocytes</td>
<td>Abundant atypical lymphocytes</td>
</tr>
<tr>
<td>Monospot negative</td>
<td>Monospot positive</td>
</tr>
</tbody>
</table>
HIV-2

- Serologic evidence in 1985 in Senegal
- Isolated in 1986 from a Cape Verdean patient
- Originally transmitted from West African Sooty mangabeys to humans
- Endemic in West Africa
- Less pathogenic than HIV-1
  - Longer asymptomatic stage of infection
  - Slower decline CD4 count
  - Lower levels of plasma viremia in chronically-infected patients
**HIV-2**

- **Diagnosis**
  - Most EIA (screening) test for HIV-1 and HIV-2
  - Confirmatory western blot testing may be indeterminate
    - gag (p55, p24, or p17) plus pol (p66, p51, or p32) bands
    - **NO** env (gp160, gp120, or gp41) bands
  - HIV-2 specific western blots and viral load assays are available (may not be widely available)
    - Contact WRAIR - MHRP (Dr. Sheila Peel’s lab)

- Treatment can differ from HIV-1 due to intrinsic resistance to some ART drugs (NNRTIs and enfuviritide)
Figure 1. Sequence of appearance of laboratory markers for HIV-1 infection
Diagnostics

• Antibody testing:
  – HIV-1/2 antigen/antibody combination immunoassay
    • 4th generation: HIV 1/2 Ab detection + p24 antigen
    • Confirmatory HIV 1/2 Ab differentiation immunoassay
    • Western blot no longer recommended as confirmatory test of choice but still done at some facilities
  – Rapid HIV testing (confirmatory testing required)
    • OraQuick (tests saliva sample) – 20 mins
    • Uni-Gold Recombingen – 10-12 mins

• HIV RNA viral load
Reporting results from the HIV diagnostic testing algorithm to persons ordering HIV tests and public health authorities

<table>
<thead>
<tr>
<th>Test performed</th>
<th>Test results</th>
<th>Final interpretation for provider report</th>
<th>Test results to be reported to public health authorities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. HIV-1/2 Ag/Ab combination immunoassay</td>
<td>1. Nonreactive</td>
<td>Negative for HIV-1 antigen and HIV-1/HIV-2 antibodies. No laboratory evidence of HIV infection. If acute HIV infection is suspected, consider testing for HIV-1 RNA.</td>
<td>Reporting this test result is not required.</td>
</tr>
<tr>
<td>2. HIV-1/HIV-2 antibody differentiation immunoassay</td>
<td>1. Reactive</td>
<td>Positive for HIV-1 antibodies. Laboratory evidence consistent with established HIV-1 infection is present.</td>
<td>Report test results 1 and 2.</td>
</tr>
<tr>
<td></td>
<td>2. HIV-1 reactive and HIV-2 nonreactive</td>
<td>Positive for HIV-2 antibodies. Laboratory evidence of HIV-2 infection is present.</td>
<td>Report test results 1 and 2.</td>
</tr>
<tr>
<td>1. HIV-1/2 Ag/Ab combo immunoassay</td>
<td>1. Reactive</td>
<td>HIV antibodies were not confirmed and HIV-1 RNA was not detected. No laboratory evidence of HIV-1 infection. Follow-up testing for HIV-2 should be performed if clinically indicated.</td>
<td>Reporting this test result is not required.</td>
</tr>
<tr>
<td>2. HIV-1/HIV-2 antibody differentiation immunoassay</td>
<td>2. Nonreactive or indeterminate</td>
<td>Positive for HIV-1. Laboratory evidence consistent with acute HIV-1 infection is present.</td>
<td>Report test results 1, 2, and 3.</td>
</tr>
<tr>
<td>3. HIV-1 RNA assay</td>
<td>3. RNA not detected</td>
<td>Positive for HIV-1 antibodies. Laboratory evidence of HIV-1 infection confirmed by HIV-1 RNA.</td>
<td>Report test results 1, 2, and 3.</td>
</tr>
<tr>
<td>1. HIV-1/2 Ag/Ab combination immunoassay</td>
<td>1. Reactive</td>
<td>HIV-1 antibodies were not confirmed and HIV-1 RNA was not detected. No laboratory evidence of HIV-1 infection. Follow-up testing for HIV-2 should be performed if clinically indicated.</td>
<td>Reporting this test result is not required.</td>
</tr>
<tr>
<td>2. HIV-1/HIV-2 antibody differentiation immunoassay</td>
<td>2. Indeterminate</td>
<td>Positive for HIV-1 antibodies. Laboratory evidence of HIV-1 infection is present. HIV antibodies could not be differentiated as HIV-1 or HIV-2. Additional testing for HIV-1 RNA or HIV-2 RNA should be performed if clinically indicated.</td>
<td>Report test results 1 and 2.</td>
</tr>
<tr>
<td>3. HIV-1 RNA assay</td>
<td>3. RNA detected</td>
<td>HIV-1 antibodies were not confirmed and HIV-1 RNA testing was not performed. Testing of this specimen is incomplete. Follow-up testing for HIV antibodies and HIV-1 RNA is recommended as soon as possible.</td>
<td>Report test results 1 and 2.</td>
</tr>
</tbody>
</table>

Abbreviations: Ag/Ab, antigen/antibody; RNA, ribonucleic acid.
HIV PEP

• Resource:
a. Oraquick® is the only FDA approved test that rapidly detects antibodies to HIV-1/2 in saliva. The test is highly accurate with an estimated sensitivity of 99.9% (rare false negative results) and a specificity of 100% (very rare false positive results). Due to its ease of use and accuracy, Oraquick® is the recommended test for rapid HIV exposure testing.

b. DoD uses the Western blot (blood test) as the "gold standard" for the diagnosis of HIV infection. Service members or exposure sources with a positive Oraquick® will be "presumed" positive until confirmatory testing is completed.
Occupational Risk Exposures

- Percutaneous injury (needlestick, cut)
- Contact of mucous membrane or nonintact skin

**OR**

**WITH:**

- Blood
- Tissue
- Other body fluids that are potentially infectious (cerebrospinal, synovial, pleural, pericardial, peritoneal, or amniotic fluids; semen or vaginal secretions)
NOT Considered Infectious for HIV
Unless Visibly Bloody

• Feces
• Nasal Secretions
• Saliva
• Sputum
• Sweat
• Tears
• Urine
• Vomitus
Approximate Risk of Occupational Transmission of HIV

• Following percutaneous exposure: 0.3%
• Following mucous membrane exposure: 0.09%
• Risk following nonintact skin exposure: <0.09%
• Risk following exposure to fluids or tissues other than HIV-infected blood estimated to be “considerably lower” than for blood exposure
Factors Associated with ↑ Risk

- Visible contamination of device (such as needle) with patient’s blood
- Needle having been placed directly into vein or artery
- Hollow-bore (vs solid) needle
- Deep injury
- Source patient with terminal illness
- High viral load*

* Risk of transmission via occupational exposure to a source patient with undetectable viral load is thought to be very low but not impossible; PEP should be offered.  

www.aidsetc.org
PEP labs

• Exposed patient
  – HBV surface antibody (HBsAb)
  – HBV surface antigen (HBsAg)
  – HCV antibody
  – HIV antibody (EIA/ELISA)
  – Consider AST/ALT, RPR if available

• Source patient
  – Rapid HIV
  – HBsAg
  – HCV antibody
  – HIV antibody
  – Consider RPR if available
PEP

• Preferred PEP regimen:
  – Raltegravir 400 mg BID + TDF/FTC (Truvada) 1 pill daily

• PEP should be taken for 28 days

• Consult with ID, especially for:
  – Pregnant or lactating
  – Delayed exposure report (ie >72 hours)
  – Unknown source
  – Known or suspected ART resistance in source patient
  – Toxicity of the initial PEP regimen
  – Co-morbid conditions in the exposed person
  – Possible HIV-2 exposure
• Follow-up testing
  – HIV testing at baseline, 6 weeks, 12 weeks, and 6 months after exposure
  • If 4th-generation p24 Ag/HIV Ab test is used: HIV testing at baseline, 6 weeks, 12 weeks, and 4 months after exposure
PEP

• Hepatitis B Exposure
  – If the exposed is **unvaccinated** then give HBIG as soon as possible (<24 hours) and initiate hepatitis B vaccine series
    • HBIG effectiveness > 7 days after exposure likely ineffective
  
  – If the exposed is **vaccinated** (completed 3 dose series) no testing or treatment is needed
PEP

• Hepatitis C Exposure
  – There is no treatment to give (presently…)
  – Baseline testing for anti-HCV, HCV RNA (viral load), and transaminases (ALT, AST)
  – Repeat HCV RNA between 4 – 6 weeks after exposure
  – Repeat anti-HCV, HCV RNA, and transaminases 3 – 6 months after exposure

• Refer anyone who is found to have acquired HCV acutely to hepatology or infectious diseases as soon as possible
  – Early treatment during the acute phase leads to higher cure rates
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4. ADDITIONAL GUIDANCE.

a. If using a rapid HIV test kit, it should be FDA approved for detection of both HIV 1 and 2. Recommend against using a negative rapid test as justification for not initiating or stopping HIV PEP in light of the rapid test’s three (3) month window period and the relatively high prevalence of HIV on the continent.

b. PEP regimens should not include non-nucleoside reverse transcriptase inhibitors (e.g. efavirenz, etravirine, rilpivirine, nevirapine) since HIV 2 is resistant to this class of antiretrovirals.

c. Contact the AFRICOM infectious disease physician listed below if there are any questions regarding individual patient risk assessment, interpretation of test results and guidance on initiation and discontinuation of HIV PEP. If the AFRICOM infectious disease physician is unavailable, assistance may be requested via the Army Knowledge Online infectious disease teleconsultation service at id.consult@us.army.mil.
Further resources

• Managing exposure to hepatitis B and C
  – Hep B (MMWR 20 Dec 2013; Vol 62, No. 10)
  – Hep C (MMWR 2001;50(RR-11); online at
    http://www.cdc.gov/mmwr/PDF/rr/rr5011.pdf

• Non-occupational HIV exposure
  – July 2013 NYHD guidelines (www.hivguidelines.org)

• AKO ID consult: id.consult@us.army.mil
• National HIV/AIDS Clinicians’ Postexposure Prophylaxis Hotline (PEPline)
  – 24-hour telephone consultation service: 888-448-4911
ART costs (DoD) 30 day supply

- Atripla: $1055.55
- Complera: $1122.93
- Stribild: $1753.44
- FTC/TDF/ATV/rit: $1336.34
- FTC/TDF/DRV/rit: $1317.10
- FTC/TDF/Raltegravir: $1335.76
- FTC/TDF/Dolutegravir: $1583.56
QUESTIONS??

AIDS Orphans in Kenya