AIDS at 25
Epidemiology and Clinical Management

HIV Transmission

- Blood
- Transfusion
- Injection drug use
- Sexual Intercourse
  - Heterosexual
  - Male to male
- Perinatal
- Intrapartum
- Breast feeding
**Proportion of AIDS Cases among Adults and Adolescents, by Exposure Category and Year of Diagnosis, 1985–2002—United States**

- Malicious intent contact
- Injection drug use (IDU)
- Heterosexual contact
- Male-to-male sexual contact and IDU

**Year of diagnosis**

Note: Adjusted for reporting delay.

**Proportion of AIDS Cases, by Race/Ethnicity and Year of Diagnosis, 1985–2002—United States**

- White, not Hispanic
- Black, not Hispanic
- Hispanic
- Asian/Pacific Islander
- American Indian/Alaska Native

**Year of diagnosis**

Note: Adjusted for reporting delay.

**percentage of those in need, 2002–2005**

<table>
<thead>
<tr>
<th>Year</th>
<th>Coverage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>75–100</td>
</tr>
<tr>
<td>2003</td>
<td>75–74.9</td>
</tr>
<tr>
<td>2004</td>
<td>35–49.0</td>
</tr>
<tr>
<td>2005</td>
<td>15–24.0</td>
</tr>
<tr>
<td>Less than 15</td>
<td></td>
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</table>
HIV Prevalence and Mortality in NYC

Plasma HIV-1 RNA Level After Acute HIV-1 Infection Predicts Disease Course


Probability of AIDS over 3 years

Development of AIDS: Like an Impending Train Wreck

Viral load = Speed of the train
CD4 count = Distance from site of crash

Frequency of HIV ‘Non-Progressors’
- San Francisco City Clinic Cohort
- 489 HIV+ Gay men with known seroconversion date.
- 13% developed AIDS by 5 years;
- 51% developed AIDS by 10 years.
- 89% had died, developed AIDS or had CD4<500 by 10 years.

[Rutherford et al. BMJ. 1990; 301:1183-8]
Explaining the variability of HIV disease

- **Viral Factors**
  - Nef deletion
  - Non-clade B subtypes?

- **Host Factors**
  - Chemokine co-receptors
  - Immune response
  - Gender?

- **Environmental Factors**
  - Infection, diet?, stress?

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HIV Co-receptors

CD4 necessary but not sufficient for infection. Beta chemokine receptors act as HIV co-receptors.

- CXCR4 (lymphocyte)
- CCR5 (macrophage)

Homozygous CCR5 deletion found in <1%.

MACS High risk cohort:
- No HIV+ among those homozygous for deletion.
- 3.6% of HIV Negative were homozygous.
- Among persistently HIV Neg: up to 33% were homozygous.

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Effect of Co-receptor Heterozygosity

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AIDS Restriction Genes

<table>
<thead>
<tr>
<th>Gene</th>
<th>Effect</th>
<th>Other</th>
<th>Mechanism of action</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>C5</td>
<td>Dominant</td>
<td>Race</td>
<td>Race related</td>
<td>95</td>
</tr>
<tr>
<td>CCR5</td>
<td>Dominant</td>
<td>Race</td>
<td>Race related</td>
<td>151</td>
</tr>
<tr>
<td>CXCR4</td>
<td>Dominant</td>
<td>Race</td>
<td>Race related</td>
<td>11</td>
</tr>
<tr>
<td>CCR2</td>
<td>Dominant</td>
<td>Race</td>
<td>Race related</td>
<td>11</td>
</tr>
<tr>
<td>CCR5</td>
<td>Non-dominant</td>
<td>Race</td>
<td>Race related</td>
<td>11</td>
</tr>
<tr>
<td>CCR2</td>
<td>Non-dominant</td>
<td>Race</td>
<td>Race related</td>
<td>11</td>
</tr>
<tr>
<td>Others</td>
<td>Dominant</td>
<td>Race</td>
<td>Race related</td>
<td>11</td>
</tr>
</tbody>
</table>

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Early indicators of HIV Infection

- HIV causes profound defect mostly restricted to T cell-based immunity (restricted range of pathogens)
- OIs usually reflect reactivation of latent infections
- Reinfection may occur (e.g., tuberculosis)
- Chronic suppression needed after acute treatment
- Immune reconstitution with anti-retroviral therapy may reverseOI susceptibility (but may also trigger an inflammatory response to active OIs)

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Key features of OIs in AIDS

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Pneumocystis pneumonia in AIDS

- Commonest life threatening complication of AIDS in U.S.
- Subacute illness (fever, cough, dyspnea).
- Diffuse interstitial infiltrate on x-ray.
- Addition of corticosteroids to antimicrobials cuts mortality in severe disease 50%.
- Fully preventable with trimethoprim-sulfa.

Cryptococcal disease in AIDS

- Ubiquitous soil fungus.
- Initial asymptomatic pneumonia.
- Reactivation in advanced HIV disease (CD4<100).
- Meningitis commonest presentation but wide dissemination frequent.

CD4 count predicts risk of PCP

<table>
<thead>
<tr>
<th>CD4 count at baseline</th>
<th>N</th>
<th>PCP</th>
<th>6 mo</th>
<th>12 mo</th>
<th>26 mo</th>
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</thead>
<tbody>
<tr>
<td>0.1 – 100</td>
<td>12</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>101 – 200</td>
<td>20</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>201 – 300</td>
<td>20</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>301 – 500</td>
<td>20</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>501 – 700</td>
<td>20</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>&gt; 700</td>
<td>20</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>

CMV disease in AIDS

- Common viral infection (50% adult seroprevalence).
- Reactivation at CD4<50
- Retinitis commonest.
- Other sites: Colon, CNS.

CNS toxoplasmosis

- Protozoan parasite; cats shed oocysts; farm animals incidental hosts; humans infected from cysts, uncooked meat.
- Commonest cause of focal CNS disease in AIDS.
- Serum IgG antibody reliable marker of past infection.
- Reactivation in AIDS associated with CD4<100.

Disseminated Mycobacterium-avium complex (MAC) disease in AIDS

- Common in environment (water).
- Local lung disease known prior to AIDS.
- Widespread visceral dissemination in AIDS.
- Diagnosis by blood culture.
- Absence of inflammation in tissue sites.
**Prophylaxis of Opportunistic Infections**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Indication</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>CD4&lt;200</td>
<td>Trimethoprim-sulfasulfa</td>
</tr>
<tr>
<td>Toxo</td>
<td>CD4&lt;100 and IgG+</td>
<td>Trimethoprim-sulfadapsone +Pyrimethamine</td>
</tr>
<tr>
<td>MAC</td>
<td>CD4&lt;50</td>
<td>Clarithromycin/Pyrimethamine</td>
</tr>
<tr>
<td>TB +PPD (5mm)</td>
<td>INH (9 months)</td>
<td></td>
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</table>

**OI Guidelines November, 2001**

**Comparison of Indications to Discontinue Primary and Secondary Prophylaxis**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>PCP</td>
<td>1st CD4 &gt; 200 X 3 months</td>
</tr>
<tr>
<td></td>
<td>2nd CD4 &gt; 200 X 3 months</td>
</tr>
<tr>
<td>Toxo.</td>
<td>1st CD4 &gt; 200 X 3 months</td>
</tr>
<tr>
<td></td>
<td>2nd CD4 &gt; 200 X 6 months + initial Rx + asymptomatic</td>
</tr>
<tr>
<td>MAC</td>
<td>1st CD4 &gt; 100 X 3 months</td>
</tr>
<tr>
<td></td>
<td>2nd CD4 &gt; 100 X 6 months + 12 mo Rx + asymptomatic</td>
</tr>
</tbody>
</table>

**Immune Reconstitution with HIV Therapy**

- Focal MAC adenitis
- Inflammatory flare of CMV retinitis
- Worsening of previously stable hepatitis
- Development of cavitary TB