AIDS Course: Virology and Immunology

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Professor of Medicine
Well, I've got no job, my kids' ve got no health insurance, my brother's in Iraq, but thank God gay people I don't even know who care about each other won't be able t'get married!

Yeah, first things first....
HIV attachment and fusion

CD4 Binding → Coreceptor Binding → Virus-Cell Fusion

gp41

gp120

V3 loop

CD4

CCR5/CXCR4

Cell membrane

Chemokine Antagonists

Enfuvirtide
Symptomatic Primary HIV Infection

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Schacker</th>
<th>Kinloch-Loes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>93%</td>
<td>87%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>90%</td>
<td>26%</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>70%</td>
<td>48%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>70%</td>
<td>13%</td>
</tr>
<tr>
<td>Myalgias</td>
<td>60%</td>
<td>42%</td>
</tr>
<tr>
<td>Headache</td>
<td>55%</td>
<td>39%</td>
</tr>
</tbody>
</table>
Man’s Protection from Disease

- Skin or Mucous Membrane
- Humoral or Antibody Mediated Immunity (B lymphocytes)
- Cell Mediated Immunity (Other lymphocytes)
Antigen

A molecule which is recognized by antibody and by cells of the immune system
Macrophage Processes Antigen

Recognition  Processing  Presentation
Virus and Antibodies
Pathogenesis of HSV Infections

Synthesis of infectious virions.
Centrifugal migration of infectious virions to epidermis
Viral dynamics of HIV-1 *in vivo*

Perelson et al. Science. 1996

Productively infected CD4 lymphocytes

>99% of replication

2.6 days per generation

Uninfected, activated CD4 lymphocytes

Latently infected CD4 lymphocytes

<1% of replication

T₁/₂ ~6 hours

Long-lived cell populations (macrophages)

<1%

Uninfected CD4 lymphocytes

CD4 lymphocytes infected with defective virus

HIV-1
The course of HIV infection. Variable virologic setpoints after acute HIV-1 infection and their prognostic values. [Drawn from the data in (3)]
Prognosis for Anti-retroviral Naive CD4>500 cells/mm³

<table>
<thead>
<tr>
<th>HIV Load (copies/ml)*</th>
<th>in 3 years</th>
<th>in 6 years</th>
<th>in 9 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3,000</td>
<td>1</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>3,000-14,000</td>
<td>2</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>14,000-41,000</td>
<td>7</td>
<td>26</td>
<td>50</td>
</tr>
<tr>
<td>41,000-110,000</td>
<td>15</td>
<td>48</td>
<td>71</td>
</tr>
<tr>
<td>&gt;110,000</td>
<td>33</td>
<td>67</td>
<td>76</td>
</tr>
</tbody>
</table>

* PCR
Mellors et al. Annals of Internal Medicine June 1997
Development of AIDS: Like an Impending Train Wreck

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

Courtesy of Douglas D. Richman, MD.
The Clinical Spectrum of HIV Infection

"Iceberg"

CDC-Reportable AIDS
Opportunistic Diseases
and Related Conditions

Nonspecific signs and symptoms
of illness secondary to
immunodeficiency (including
"AIDS related complex")

Immune complex disease
(e.g. thrombocytopenia)

Asymptomatic infections
Opportunistic Infections Over the Course of HIV Infection

- CD4 Lymphocyte Count
- Years
- Pneumocystis Pneumonia
- Toxo encephalitis
- Crypto meningitis
- MAC Bacteremia
- CMV Retinitis
- TB
- Shingles/Hairy Leukoplakia
- Thrush/Herpes

University of North Carolina 1/18/2006
Elisa: Detects Antibodies to HIV

Positive at All Titrations
HIV 1 Western Blot

- Indeterminate
- Weak positive
- Strong positive

A positive result generally requires the presence of bands at p24, p31, gp41 and gp120 or gp160
Semen HIV in patients with suppressed viral load

Vernazza et al., AIDS, 2000 in press
Changes in $\log_{10}$ HIV RNA Levels in Vaginal Lavage

Courtesy of Jeff Lenox Emory University

Controls: Women on no rx or stable for 12 wks
Cases: Unrx or stable for > 12 weeks starting at least 1 new ART
Samples obtained 2-10 weeks after change in rx
Course of HIV Without Intervention

Free Virus

Protective Immune Responses

Cellular Contagion, Latency, Genomic Diversity, and Immune Destruction

Asymptomatic
WR-1
WR-2
ARC
WR-3/4
AIDS
WR-5/6
Course of HIV with Early Intervention

- **Free Virus**
- **Protective Immune Responses**
- **Asymptomatic**
  - WR-1
  - WR-2
- **ARC**
  - WR-3/4
- **AIDS**
  - WR-5/6
## Change in Viral Load and Risk of Death at 3 Years*

<table>
<thead>
<tr>
<th>Baseline RNA</th>
<th>Drop in RNA</th>
<th>Risk of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000,000</td>
<td>$1 \log_{10}$</td>
<td>100% to 35%</td>
</tr>
<tr>
<td></td>
<td>$2 \log_{10}$</td>
<td>100% to 13%</td>
</tr>
<tr>
<td>100,000</td>
<td>$1 \log_{10}$</td>
<td>17% to 4%</td>
</tr>
<tr>
<td></td>
<td>$2 \log_{10}$</td>
<td>17% to 1%</td>
</tr>
</tbody>
</table>

*ACTG 175
Trends in Rates of Death from Leading Causes of Death Among Persons 25-44 Years Old, USA, 1982-1997

From national vital statistics, Centers for Disease Control & Prevention

*Preliminary data