HIV/AIDS: The Status of the Epidemic Today

“The greatest single public health challenge that humanity has ever faced.”
Dr. Robert Lue, Harvard University

Kristine Thyng, HHMI-MCB Workshop
Summer 2004
Worldwide

- 3 million deaths in 2003
- Over 21 million deaths since the beginning of the epidemic
  - 17.5 million adults
  - 4.3 million children (under 15 years old)

Image from [www.avert.org/worldstats.htm](http://www.avert.org/worldstats.htm)

• Approximately 40 million people living with AIDS worldwide in 2003

• Approximately 14 million children orphaned by AIDS by the end of 2002

• Number of orphans expected to rise to 25 million by 2010

(www.avert.org)
Adult Prevalence of AIDS

People With HIV/AIDS, by Region

End 2002

Sub-Saharan Africa 71%

South and Southeast Asia 14%

North America 2%

Europe 1%

Latin America 4%

Caribbean 1%

North Africa and Middle East 1%

Eastern Europe/Central Asia 3%

East Asia and the Pacific 3%

Australia and New Zealand <1%


Image from www.prb.org
By the end of 2002: 384,906 people living with AIDS
- 46% White
- 34% Black
- 18% Hispanic

- 298,248 men
- 82,764 women

(www.avert.org/statsum.htm)
United States Cont’d

• Of the 298, 248 U.S. men living with AIDS,
  • 57% were men who had sex with men (MSM)
  • 23% were I.V. drug users
  • 10% were exposed through heterosexual contact
  • 8% were both MSM and IV

(www.avert.org/statsum/htm)
• Of the 82,764 U.S. women living with AIDS,
  • 61% were exposed through heterosexual contact
  • 36% were I.V. drug users

(www.avert.org/statsum/htm)
United States Cont’d

1999: Estimated that 800,000 to 900,000 Americans were infected with HIV

(www.avert.org/statsum/htm)
How A Healthy Immune System Works

• **Physical Barriers:** skin, mucus, etc.

• **Innate Immune System:** body’s immediate response to a pathogen. Not antigen specific. Immunity a person is born with.

• **Acquired Immune System:** Body takes a few days to build this immunity. Antigen specific. Immunity that is acquired through life.
Key Structures of the Immune System

Physical Barriers

**Skin**


**Mucosa**

Innate Immunity

If pathogens penetrate physical barriers, **phagocytic cells** in the area begin to engulf pathogen.

Image from http://health.yahoo.com/health/ency/adam/000821/i9478
Innate Immunity Cont’d

• Phagocytes also release chemical signals (cytokines) to “call” other phagocytes to the area, resulting in inflammation (redness, heat, swelling). The pus that we often observe is a combination of dead pathogen, white blood cells, and injured body cells.

Image from http://occawlonline.pearsoned.com/bookbind/pubbooks/campbell6e_awl/chapter43/deluxe.html
Acquired Immunity

- If pathogens are not completely eliminated by the innate immune system, the acquired immune system is activated.

- Key Players: Lymphocytes (T and B cells)

Image from http://occawlonline.pearsoned.com/bookbind/pubbooks/campbell6e_awl/chapter43/deluxe.html
Phagocytes active in the innate immune system display some of the proteins from the pathogen on their surfaces, “advertising” that the pathogen is present.

These cells then travel to the lymph nodes and spleen, where they help to activate T and B cells. The increase in T and B cell production when you are ill can often be detected by swollen lymph nodes (glands).

Macrophage (yellow) attacking bacteria (blue)

Acquired Immunity Cont’d

B cells – Defend against pathogens located outside of body’s cells. *

- Plasma cells – produce antibodies which attach to antigens and help to destroy them, or block the harmful effects of the antigen
- Memory cells – Can react quickly to produce antibodies upon additional exposures to the antigen

*Dr. Starnbach lecture 7/13/04

Image from http://www.accessexcellence.org/AB/GG/Antibody.html
Acquired Immunity Cont’d

- T cells – Defend against pathogens located inside of body’s cells.*
  - Helper T cells: secrete cytokines to call in other T, B, and phagocytic cells, activate B cells to produce antibodies
  - Killer T cells: recognize an infected cell and lyse it
  - Memory T cells: remain in body to react when pathogen is encountered again.

T cell (SEM)

Image from http://ca.encarta.msn.com/media_461519550/Lymphocyte.html

*Dr. Starnbach lecture 7/13/04
How it all works together

Humoral (antibody-mediated) immune response

- Antigen (1st exposure)
  - Engulfed by
    - Macrophage (APC)
    - Stimulates
      - Helper T cell
        - Stimulates
          - Cytotoxic T cell
            - Gives rise to
              - Memory T cells
            - Gives rise to
              - Active cytotoxic T cells

- Free antigens directly activate
  - B cell
    - Stimulates
      - Helper T cell
      - Memory helper T cell
        - Gives rise to
          - Memory B cells
          - Active cytotoxic T cells

- B cell
  - Secretes
    - Antibodies
      - Defend against extracellular pathogens by binding to antigens and making the pathogens easier targets for phagocytes and complement.

Cell-mediated immune response

- Antigen displayed by infected cells activate
  - Macrophage (APC)
    - Stimulates
      - Helper T cell
      - Memory helper T cell
        - Gives rise to
          - Memory T cells

- Memory B cells
  - Secretes
    - Antibodies
      - Defend against intracellular pathogens and cancer by binding to and lysing the infected cells or cancer cells.

Image from
http://occawlonline.pearsoned.com/bookbind/pubbooks/campbell6e_awl/chapter43/deluxe.html

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# Immune Response Summary

<table>
<thead>
<tr>
<th>Nonspecific defense mechanisms</th>
<th>Specific defense mechanisms (immune system)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line of defense</strong></td>
<td><strong>Second line of defense</strong></td>
</tr>
<tr>
<td>• Skin</td>
<td>• Phagocytic white blood cells</td>
</tr>
<tr>
<td>• Mucous membranes</td>
<td>• Antimicrobial proteins</td>
</tr>
<tr>
<td>• Secretions of skin and mucous membranes</td>
<td>• The inflammatory response</td>
</tr>
<tr>
<td></td>
<td>• Lymphocytes</td>
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<td></td>
<td>• Antibodies</td>
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Image from http://occawlonline.pearsoned.com/bookbind/pubbooks/campbell6e_awl/chapter43/deluxe.html
How does HIV interrupt the normal functioning of the immune system?

Image from http://ca.encarta.msn.com/media_461518877/TLymphocyte_Infected_With_HIV.html
What is HIV?

- HIV – human immunodeficiency virus
  - Works by infecting the cells of the immune system, using them to make more virus, and then killing them.
  - The immune system is able to battle this virus fairly successfully for up to 8-10 years, before the virus eventually wins.

Image from http://medlib.med.utah.edu/WebPath/TUTORIAL/AIDS/AIDS001.html
HIV Structure

- HIV is composed of three main layers:
  - Envelope
  - Viral Matrix
  - Core

Overview of how HIV works

• HIV attacks cells of the body, especially the helper T cells. (Approx. 100 billion new HIV particles generated/day during clinical latency)
• When the number of helper T cells is depleted, the body cannot fight infection
• Death results from infection or cancer that the body can’t fight off, not from AIDS itself.

(Dr. Lue’s lecture 7/16/04)
HIV infection

- Animation of HIV infection

(http://www.galaxygoo.org/hiv/hiv_lifecycle.html)
HIV proteins attach to receptors on cell membrane

HIV inserts genetic material (RNA)

Reverse transcriptase used to make viral DNA from RNA

Viral DNA inserted into one of the cell’s chromosomes

Cell manufactures viral proteins and RNA

New copies of virus bud off of host and infect new cells
Progression of HIV in the Body

Do some people have resistance to HIV?

- **Resistance to HIV**

- Mutations to HIV – will those without the ccr5 receptor still be resistant?
Why is HIV so hard to fight?

• Some antibodies that the body produces actually work to enhance HIV replication.

• Some antibodies that work to neutralize HIV replication can become enhancing antibodies when the virus mutates.

• Cells other than helper T-cells can be infected, therefore the virus can colonize many tissues of the body.

• HIV can kill cells that it doesn’t even infect.

(Dr. Lue’s lecture 7/16/04)
Growth of the AIDS Epidemic

People With HIV/AIDS, Cumulative Regional Totals

- Highly Industrialized*
- Sub-Saharan Africa
- South and East Asia
- Latin America/Caribbean
- Eastern Europe, other**

*North America, Europe (except Eastern Europe), Japan, Australia, and New Zealand.
**Eastern Europe, Central Asia, Middle East, and North Africa.

Image from http://www.prb.org/presentations/d_growth-aids-epidemic.ppt
Is there any reason to be optimistic?

• Drug Therapy
  – “Old” drugs - reverse transcriptase and protease inhibitors. BUT, many strains of the virus are becoming resistant.
  – Salvage drugs
    • T-20 in phase III trials (prevents fusion of HIV with T-cell)
    • T-1249 in phase II trials (prevents fusion of HIV with T-cell).
    • Both are promising, but already see some resistance.

(Dr. Lue, 7/22/04)
Availability of Drugs

• Widely available in U.S and other industrialized nations, but cost tens of thousands of dollars/year.

• Clearly not feasible in developing countries.

• Problems of patent infringement to produce generic versions.

(Dr. Lue, 7/22/04)
HIV/AIDS is a preventable disease, but controlling the epidemic will require behavioral changes worldwide.
References

• **TEXT SOURCES:**

“Averting AIDS and HIV”, [www.avert.org](http://www.avert.org)


• **IMAGE SOURCES:** All images were obtained from the web between the dates of 7/13/04 – 7/22/04

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