Mechanisms and Manifestations of Disease Lecture 2

Part 5

Alterations in Immunity

Secondary (Acquired) Immune Deficiencies

- Acquired Immunodeficiency Syndrome (AIDS)-HTLVIII
- First recognized in 1981
- 1984-Recognized as cause of AIDS

HIV Big Picture (CDC,12/99)

- 650,000 to 900,000 cases in U.S.
- 40,000 new cases/year
  - 70% male
    - 50% Black
    - 30% White
    - 20% Hispanic
- 30% new female cases/yr
  - 30% Black
  - 18% White

Total Deaths-42% decline from 1996-1997

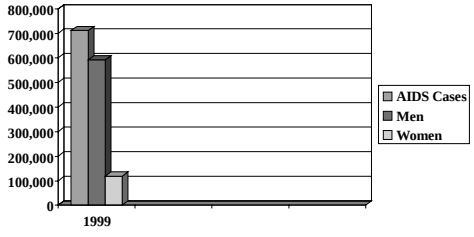
Delaware and AIDS

- I 95 connection-NY to Florida drug connection
- Relatively high rate considering size of state-6th in nation
- New Castle County highest followed by Sussex County

Gender Differences in Etiology

- Etiology of AIDS in Males
  - 60% MSM
  - 25% IVDA
  - 15% heterosexual sex
- Etiology of AIDS in Females
  - 75% heterosexual sex
  - 25% IVDA

The Toll of AIDS



HIV Transmission (CDC,2000)

- Spread primarily by:
  - Sexual contact
  - Sharing needles
  - Blood transfusions
- Babies-during birth or nursing

Other Transmission

- No additional routes of transmission documented:
  - air
  - water
  - insects

Why is HIV Different and More Lethal?

- Retrovirus- carries genetic makeup on RNA, not DNA
- Lentivirus-long time between infection and symptoms; may be 15-20 years before major symptoms
- Latency-Provirus; Another virus can turn the virus on and into a virus factory
- Antigenic drift-constantly changes; “moving target” to produce vaccine

HIV Differences

- Attaches to CD4 receptors and inserts its RNA into cell
- Once inside cell, RNA activity converts to DNA by reverse transcriptase, infecting host genetic activity
- Becomes a live virus factory
- Cell must be alive to be a virus factory
- Hides from immune system inside cell, changes AG

AIDS Infection Process

- **First infection-Acute Retroviral Syndrome**
  - Often assumed to be "the flu" and is forgotten
  - Occurs 1-3 weeks after initial viral infection
    - May have persistent swollen glands, red patchy rash, fever, sore throat, HA
  - Person gradually feels better
  - HIV AG may be present
  - May have no AB for testing but be highly contagious-testing worthless

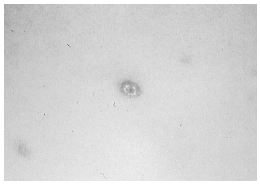
Asymptomatic HIV Positive

- Usually has AB

  Highly contagious
  - Looks and feels healthy
  - AB test usually positive 3-6 weeks post infection
  - Symptoms may take 8-12 years
  - Gradual decrease in CD4 count

Symptomatic HIV Positive

- **Full blown AIDS**
  - Allergies may improve; TB test may be a false negative-WHY?
- If very immune suppressed may not test positive!
- Weight loss (wasting), fever, lymphadenopathy, multiple cutaneous nodules, brain lesions



Advanced HIV Disease (AIDS)

- Immune system gradually destroyed-**No Seroconversion! PPD negative, allergies improve!**
- CD4 count decreases, increased opportunistic infections

OI

- Opportunistic infections-Pneumocystitis carinii pneumonia (leading cause of death), cryptococcus meningitis, parasitic and viral infections, lymphomas, Kaposi's Sarcoma, Mycobacterium avium, CMV, toxoplasmosis, histoplasmosis, coccidiomycosis, syphilis, HIV encephalitis, etc.
- OI not AIDS defining-thrush, oral hairy leukoplakia, multidermatomal herpes zoster

Pediatric Considerations

- Without treatment-50% risk of transmission from mother to fetus
- Wide variety of manifestations
- Failure to thrive, lymphadenopathy, thrush, fever, delayed development
- No Kaposi's Sarcoma, but pronounced bacterial infections

Health Care Worker (HCW) Risks

- HCW risks
  - Workers' needle stick injuries
    - Blood in open cut or mucous membrane
- 1 case of patients infected by HCW
  - 1 dentist infected 6 patients

HIV and Immune System

- Attacks CD4 cells-T_H and T_{DH}
- Does not attack CD8 cells-T_C and T_S
- Flips immune system ratio from 2:1 CD4:CD8 to 2:1 CD8:CD4
- Therefore, immune system is always in an "off position"

Macrophage Role

- Attaches to CD4 receptors on macrophages, but macrophages not destroyed
- Macrophages act as reservoirs carrying HIV throughout body
- Macrophages leave circulation in brain and infect brain tissue

HIV and B Cell Role

- B cells (AB prod. cells) help ferry HIV delivering it to T cells
  - B cells not reservoirs; can't house replicating virus; B cell amount decreases w/ HIV decrease.
  - HIV docks on B cell at CD21-a B surface protein that binds w/complement to tag microbes for destruction, signaling AB production
  - Signals B cell AB production, making uncontrolled amounts of AB (NIAD, 8/29/00)