HIV/AIDS
21st Century Pandemic
History of HIV/AIDS

- It is now thought that HIV came from a similar virus found in chimpanzees - SIV.
- HIV probably entered the United States around 1970.
- CDC in 1981 noticed unusual clusters of Kaposi’s sarcoma in gay men in NY and San Francisco, which led to the disease to be called GRID (Gay Related Immune Deficiency).
- By 1982 the disease was apparent in heterosexuals and was renamed AIDS (Acquired Immune Deficiency).
- 1984- Scientists identify HIV (initially called HTLV-III or LAV) as the cause of AIDS.
- 1987- AZT is the first drug approved for treating AIDS.

http://www.avert.org/aids-timeline.htm
The Ryan White Comprehensive AIDS Resources Emergency (CARE) Act (Ryan White Care Act, Ryan White, Pub.L. 101-381, 104 Stat. 576, enacted August 18, 1990) was an Act of the U.S. Congress named in honor of Ryan White, an Indiana teenager who contracted AIDS through a tainted hemophilia treatment in 1984, and was expelled from school because of the disease. White became a well-known advocate for AIDS research and awareness, until his death on April 8, 1990.[1]

Prevalence

HIV Prevalence Estimate
- Prevalence is the number of people living with HIV/AIDS in a given year.
- At the end of 2003, an estimated 1,039,000 to 1,185,000 persons in the United States were living with HIV/AIDS, with 24%-27% undiagnosed and unaware of their HIV infection.¹

HIV Incidence Estimate
- Incidence is the number of new HIV infections that occur during a given year.
- In 2008, CDC estimated that approximately 56,300 people were newly infected with HIV in 2006 (the most recent year that data are available). Over half (53%) of these new infections occurred in gay and bisexual men. African American men and women were also strongly affected and were estimated to have an incidence rate than was 7 times greater than the incidence rate among whites.

http://www.cdc.gov/hiv/topics/surveillance/basic.htm#hivest
Eighty percent of Americans with HIV do not know they are infected.

Philip Emeagwali

One out of every 100 American men is HIV positive. The rate of infection has reached epidemic proportions in 40 developing nations.

Philip Emeagwali
Cases of HIV infection and AIDS in the United States and Dependent Areas, 2006

Sex of adults and adolescents with HIV/AIDS diagnosed during 2006

Transmission categories of adults and adolescents with HIV/AIDS diagnosed during 2006

http://www.cdc.gov/hiv/resources/factsheets/us.htm
Cases of HIV infection and AIDS in State of Louisiana - AIDS

http://www.cdc.gov/nchhstp/stateprofiles/Louisiana/Louisiana_Profile.htm
Estimated Prevalence Rates for Adults and Adolescents Living with HIV Infection (not AIDS), 2006—33 States and 5 U.S. Dependent Areas

Note. Data from 33 states and 5 U.S. dependent areas with confidential name-based HIV infection reporting since at least 2003. Data have been adjusted for reporting delays.
Estimated Number of AIDS Cases, Deaths, and Persons Living with AIDS, 1985–2006—United States and Dependent Areas

Note. Data have been adjusted for reporting delays.
EPIDEMIOLOGY

- Males > females
- Occurs in all ages and ethnic groups
- All areas of the country are affected
- About 2 million adults & 500,000 children in US are HIV positive (male 1:100; female 1:800)
- In some city inner areas, as many as 50% of males are HIV positive
- AIDS is now the second leading cause of death for all men aged 25-44 years
- Unintended injuries is #1 and heart disease is #3 for this age group
Risk Factors

Anyone of any age, race, sex or sexual orientation can be infected with HIV, but you're at greatest risk of HIV/AIDS if you:

- Have unprotected sex with multiple partners. You're at risk whether you're heterosexual, homosexual or bisexual. Unprotected sex means having sex without using a new latex or polyurethane condom every time.
- Have unprotected sex with someone who is HIV-positive.
- Have another sexually transmitted disease, such as syphilis, herpes, chlamydia, gonorrhea or bacterial vaginosis.
- Share needles during intravenous drug use.
- Received a blood transfusion or blood products before 1985.
- Have fewer copies of a gene called CCL3L1 that helps fight HIV infection.
- Newborns or nursing infants whose mothers tested positive for HIV but did not receive treatment also are at high risk.
Risk Factors

- Most dangerous sexual practice: anal intercourse
- Recent evidence that HIV can be transmitted by oral sex
- If the patient has AIDS today, most likely homo/bisexual man
- If recently became HIV positive, most likely IV drug abuser
- Fastest growing method of HIV transmission: heterosexual contact (esp. for blacks and hispanics)
- Heterosexual transmission is easier from men to women than from women to men
Risk Factors

- Risk of acquiring for men is greater if contact occurs during menstruation
- Uncircumcised men are more likely to be seropositive and contract HIV during sex
- HIV transmission rates:
  - Risk from single sexual encounter with man who is not a member of a risk group: 1 in 5 million
  - Risk from single encounter with man who is a member of a high risk group: 1 in 20 to 1 in 2
  - Needle-stick (with HIV-positive blood): 1 in 100 to 1 in 1000 (average 1 in 250)
  - Seroconversion from blood transfusion: 2 of 3
Risk Factors

If mother is HIV positive, 100% of children will test positive at birth

- About 20% of these will remain HIV positive after 1 year
- Breast feeding increases transmission rate
- AZT (zidovudine/Azidothymidine) reduces risk by half (to about 10%). AZT + c-section reduces transmission rate to 5%
- Nevirapine: If given during labor to mother and to child after birth, cuts rate to 10%
HIV does not make people dangerous to know, so you can shake their hands and give them a hug: Heaven knows they need it.

Princess Diana
Prevention

There's no vaccine to prevent HIV infection and no cure for AIDS. But it's possible to protect yourself and others from infection. That means educating yourself about HIV and avoiding any behavior that allows HIV-infected fluids — blood, semen, vaginal secretions and breast milk — into your body.

If you're HIV-negative
- Educate yourself and others.
- Know the HIV status of any sexual partner.
- Use a new latex or polyurethane condom every time you have sex.
- Consider male circumcision.
- Use a clean needle.
- Be cautious about blood products in certain countries.
- Get regular screening tests.
- Don't become complacent.

http://www.mayoclinic.com/health/hiv-aids/DS00005/DSECTION=prevention
Prevention

If you're HIV-positive
- Follow safe-sex practices.
- Tell your sexual partners you have HIV.
- If your partner is pregnant, tell her you have HIV.
- Tell others who need to know.
- Don't share needles or syringes.
- Don't donate blood or organs.
- Don't share razor blades or toothbrushes.
- If you're pregnant, get medical care right away.

http://www.mayoclinic.com/health/hiv-aids/DS00005/DSECTION=prevention
Prevention by Common Sense

ABC rule
- Abstinence
- Be faithful (one partner)
- Condom
Causative agent: Human Immuno-deficiency Virus

**Organization of the HIV-1 Virion**

- gp120
- gp41
- Lipid Membrane
- Reverse Transcriptase
- RNA
  - Capsid
  - Matrix
Structure of HIV virus

- Enveloped RNA retrovirus
- Spherical 120 nm in diameter; envelope proteins make the spikes on the membrane.
- Enveloped truncated conical capsid
- Electron dense core
- Two copies of the single stranded (+) RNA
- Has enzymes: Reverse transcriptase, Integrase & Protease
- Has gag, pol and env structural genes
- Has LTR (long terminal repeats) rev and neg regulatory genes
T-cell count from HIV To full blown AIDS
HIV disease progression

PROGRESSION OF HIV DISEASE

- Acute retroviral syndrome
- Oral or esophageal candidiasis
- Oral or pharyngeal candidiasis
- Kaposi’s sarcoma
- Tuberculosis
- Herpes zoster (Shingles)
- Vaginal candidiasis
- Pneumocystis
- Cryptococcus
- Histiocytosis
- Resistant candidiasis
- CMV disease
- MAC disease

CD4 cell/ml vs. time from transmission in years
HIV life cycle

- HIV infects CD-4 positive cells
  - CD4+ T-cell lymphocytes
  - Macrophages
  - Lymph node follicular dendritic cells
  - Langerhans cells
- Binding to CD4 by gp120
- Entry into cell by fusion requires gp41 and coreceptors
  - CCR5 (Beta chemokine receptor)
HIV life cycle

- CXCR4 (alpha chemokine receptor)
- Envelope lost and RNA uncoated
- DNA made from RNA using reverse transcriptase
- DNA and Integrase migrate to nucleus forming a provirus by integrating viral DNA to host DNA
HIV life cycle

• Rate of viral replication regulated by the activity of regulatory proteins (tat/rev, nef, etc)
• Co-infections (e.g., mycobacterial) stimulate the HIV-infected cells to produce more virus
• Transcription and translation produces necessary polyprotiens which are cleaved by the HIV protease
• Assembly
• Maturation/release of virus
Modes of transmission

- Sexual contact
  - Homosexuals (MSM), & Heterosexuals

- Parenteral transmission
  - IVDA, Hemophiliacs, accidental needle sticks

- Vertical transmission
  - From mother to child during delivery (MTCT)
Stages of HIV

- Category A (A1-A3: > 500 to <200 CD4+ T cells/µl): Acute and asymptomatic HIV infection + persistent generalized lymphadenopathy
- Category B (B1-B3: 500 to <200 CD4+ T cells/µl): Symptomatic but not conditions in C
- Category C (C1-C3: 500 to <200 CD4+ T cells/µl): AIDS defining conditions
- AIDS: A3, B3, or C1-3
- Acute phase has high level of viral production and mononucleosis-like Sx: fever, sore throat, rash, malaise, lymphadenopathy, diarrhea, etc.
Signs and symptoms

- List of symptoms of HIV/AIDS:
- **Early infection:**
  - more common to develop a brief flu-like illness two to four weeks after becoming infected. Signs and symptoms may include:
  - Fever
  - Headache
  - Sore throat
Signs and symptoms

• Swollen lymph glands
• Rash

**Later infection:**
• may remain symptom-free for eight or nine years or more
• you may develop mild infections or chronic symptoms such as:
• Swollen lymph nodes — often one of the first signs of HIV infection
• Diarrhea
- Weight loss
- Fever
- Cough and shortness of breath
- **Latest phase of infection**: (AIDS):
- HIV-antibody test plus at least one of the following:
- The development of an opportunistic infection — an infection that occurs when your immune system is impaired — such as Pneumocystis carinii pneumonia (PCP)
A CD4 lymphocyte count of 200 or less — a normal count ranges from 800 to 1,200
The signs and symptoms of some of these infections may include:
- Soaking night sweats
- Shaking chills or fever higher than 100 F (38 C) for several weeks
- Dry cough and shortness of breath
- Chronic diarrhea
• Persistent white spots or unusual lesions on your tongue or in your mouth
• Headaches
• Blurred and distorted vision
• Weight loss
• You may also begin to experience signs and symptoms of later stage HIV infection itself, such as:
  • Persistent, unexplained fatigue
  • Soaking night sweats
• Shaking chills or fever higher than 100 F (38 C) for several weeks
• Swelling of lymph nodes for more than three months
• Chronic diarrhea
• Persistent headaches
• If you're infected with HIV, you're also more likely to develop certain cancers, especially Kaposi's sarcoma, cervical cancer and lymphoma
• **Symptoms of HIV in children:**  
  Children who are HIV-positive may experience:  
  • Difficulty gaining weight  
  • Difficulty growing normally  
  • Problems walking  
  • Delayed mental development  
  • Severe forms of common childhood illnesses such as ear infections (otitis media), pneumonia and tonsillitis
• **AIDS defining conditions:**
  • Encephalopathy, HIV-related
  • Pneumonia, recurrent (leading cause of death)
ELISA (Enzyme Linked Immuno-Sorbent Assay): Done to detect HIV antibodies in patient’s serum (antigens used are p24, p17, gp160, gp120, and gp41).

Anti-p24 is the first reliably detected antibody but declines as viral titres rise in late infection.

Envelope antibodies rise more slowly but stay high at the end.

Env antigens show major antigenic variation.

ELISA for p24 useful early.
Western blot for antibodies specific to HIV
Immunoelectrofluorescence
HIV DNA PCR (Polymerase Chain Reaction):
- Qualitative to detect HIV infection in newborns of mothers are HIV+
- Quantitative HIV DNA PCR to determine viral load to assess treatment
Culture for HIV (with antigen detection in culture):

- HIV infection in newborns whose mothers are HIV+

- To assess drug resistance
I recommend the same therapies for all humans with HIV. There is no reason to believe that physiologic responses to therapy will vary across lines of class, culture, race or nationality.

Paul Farmer
Treatment

- HAART: Highly Affective Anti-Retro Viral Therapy: Physicians consider 200 to 350 CD4 cells/mm³ as the range to consider starting HAART (Highly Active Antiretroviral Therapy).
- HAART combines two types of antiretroviral drugs
- RTI’s (Reverse Transcriptase Inhibitors): Zidovudine (AZT/ZDV), Didanosine (DDI), Zalcitabine (DDC), Stavudine (D4T), Lamivudine (3TC)
- NNRTI’s (Non-Nucleoside RTI’S) : Delavirdine, Nevirapine, Efavirenz
- Protease Inhibitors: Indinavir, Ritonavir
For needle stick:
- ZDV+3TC 1 month, but in high risk (high viral RNA copies) a combination of ZDV+3TC+Indinavir

Pregnancy:
- ZDV full dose, trimester 2 and 3+ 6 weeks to neonate reduces vertical transmission by 80%
- ZDV restricted to intrapartum period/NEVIRAPINE-1 dose at onset of delivery+one dose to neonate
- Symptomatic tx and antibiotics/antivirals/glucocorticoids/thalidomide/antifungals/metronidazole for bacterial, viral, autoimmune, fungal and parasitic infections.
References