HIV 101

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Outline

- What is HIV?
- History of HIV/AIDS
- Epidemiology
- HIV Basics
- Drug Primer
- Hot Topics

What is HIV?

- HIV = Human immunodeficiency virus
  - HIV-1: pandemic virus affecting 33 million people worldwide
  - HIV-2: mostly confined to heterosexual persons in western Africa, asymptomatic infection more common, virus is less likely to be transmitted and viral loads are lower

HIV and AIDS: Definitions

- All individuals who are infected with the HUMAN IMMUNODEFICIENCY VIRUS have "HIV"
- AIDS is the most advanced form of this viral illness, and an AIDS diagnosis ("full blown AIDS") requires specific set of criteria:
  - CD4 count < 200
  - Develop certain opportunistic infections or cancer

History of HIV

- 1933: humans acquired a common ancestor of HIV through natural cross-species transmission, likely in West Africa
- 1959: oldest HIV-1 infection in the world
- 1980-81: unusual cluster of cases of rare infections in patients in Los Angeles, San Francisco and New York
  - Outbreak of Kaposi's sarcoma in homosexual men in same 3 cities
- 1983: identification of retrovirus

Medical Response to HIV

- 1985: development of HIV-1 blood test
- 1987: introduction of antiretroviral therapy
- 1996: introduction of HAART (highly-active antiretroviral therapy)
- 2006: FDA approves "one pill once-a-day" cocktail
- 2009: first vaccine trial with positive results

Epidemiology

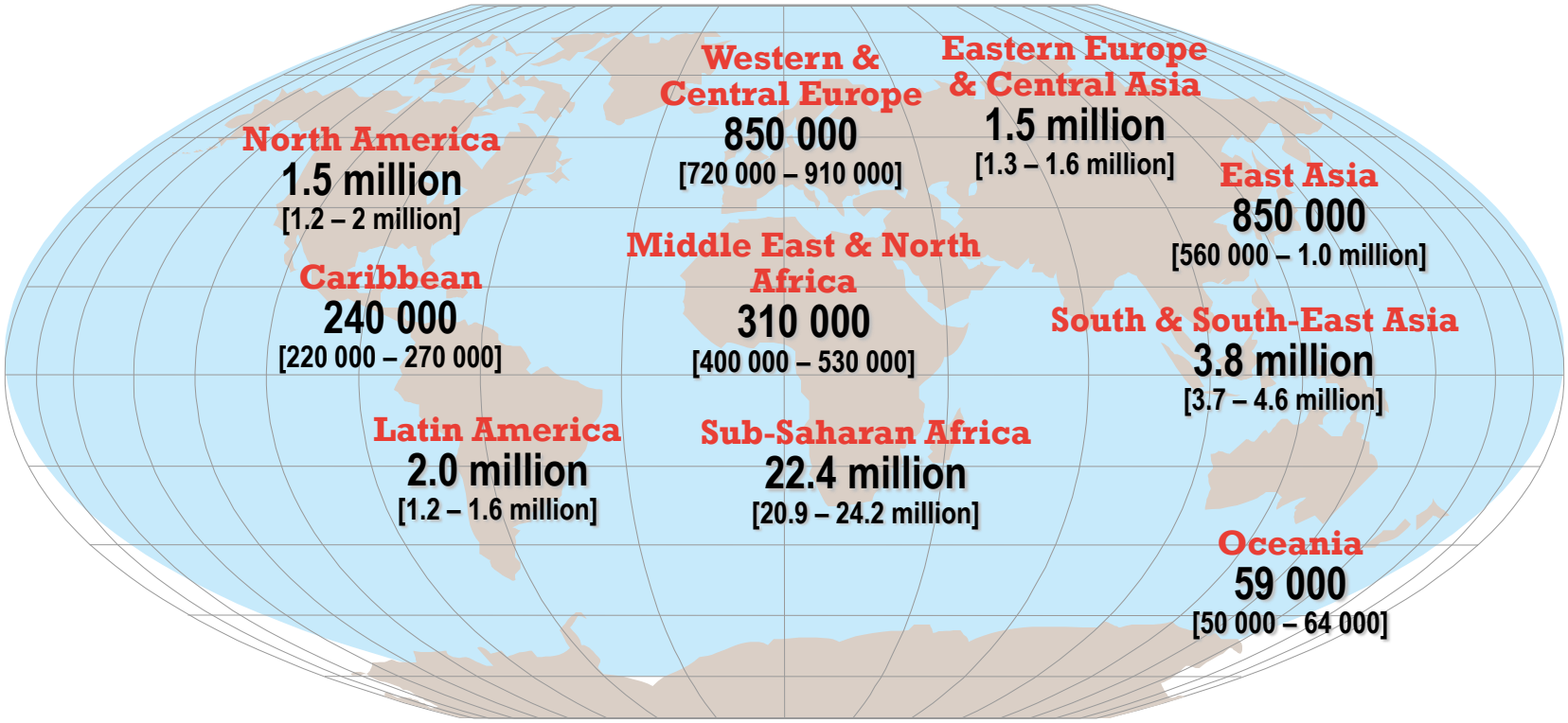
"Branch of medical science that deals with the incidence, distribution and control of a disease in a population"

Worldwide Burden of Disease

- >7000 new infections daily
- 97% in low and middle income countries
- 1000 in children < 15 years old
- 6200 in adults > 15 years old
  - 51% women
  - 41% young people (ages 15-24)

UNAIDS 2010 Global Report at http://www.unaids.org

Adults and Children Living with HIV, 2009



Total: 33.3 million (31.4 – 35.3 million)

UNAIDS 2010 Global Report at http://www.unaids.org

HIV/AIDS in the U.S.A.

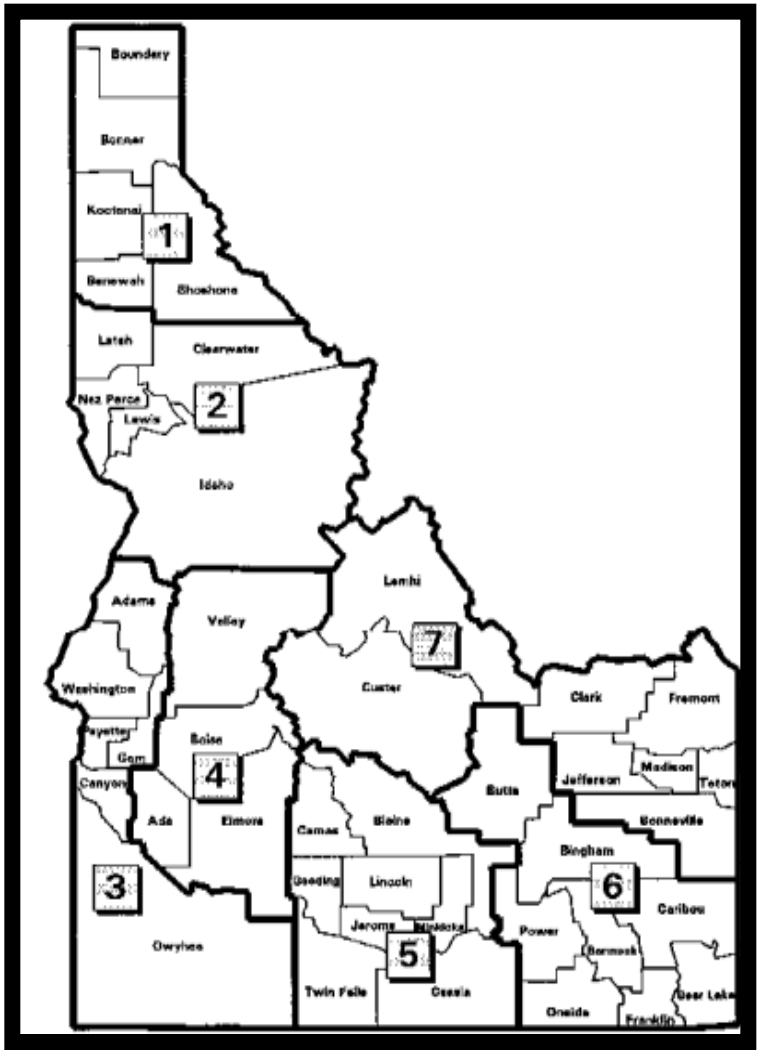
- 1.1 million HIV+ people in USA as of 9/2006
- 21% of HIV+ individuals are unaware of status
  - People unaware of status are responsible for transmission of > 50% of new infections and and are 3.5x more likely to transmit infection to others
- 15% increase in new diagnoses 2004-07
- 56,000 new infections in 2006

2009 AIDS Epidemic Update. Found at http://www.unaids.org

HIV/AIDS Surveillance Report, 2006. Vol. 18. Atlanta: US Department of Health and Human Services, CDC; 2008. Found at http://www.cdc.gov/hiv

HIV in Idaho – Prevalence as of 9/2010

*Presumed additional 20-25% undiagnosed



District	HIV	AIDS
1	65	83
2	40	42
3	68	91
4	273	256
5	56	61
6	73	61
7	51	52
Total	626	646

HIV/AIDS = 1272

Found at: http://www.healthandwelfare.idaho.gov

Failing our Women and Minorities

- Blacks: 12% of US population but 46% of people living with HIV AND make up 45% of new HIV diagnoses each year
  - Black men: 6x risk of white men, 3x risk of Latino men
  - Black women: 15x risk of white women, 4x risk of Latino women
- Hispanics/Latinos: 15% of US population but 17% of people living with HIV AND make up 17% of new diagnoses
  - Hispanic men: 3x risk of white men
  - Hispanic women: 15x risk of white women

UNAIDS 2010 Global Report at http://www.unaids.org

Failing our Youth

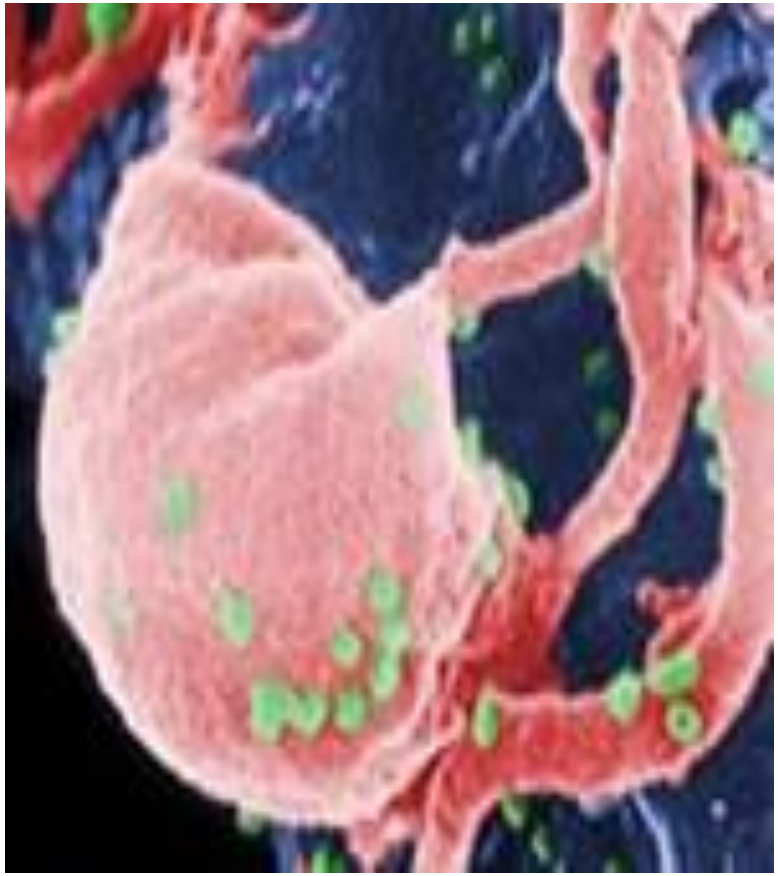
- 62% of diagnoses 2001-4 were in age group 13-24
- MSM (men who have sex with men) youth most at risk
  - MSM is the only risk group in the US in which new infections have been increasing since the early 1990s

HIV Rises Among Young Gay Men. *New York Times* 14 January 2008: Editorial. Web 3 April 2010.

2009 AIDS Epidemic Update at http://www.unaids.org

HIV Basics

HIV Basics

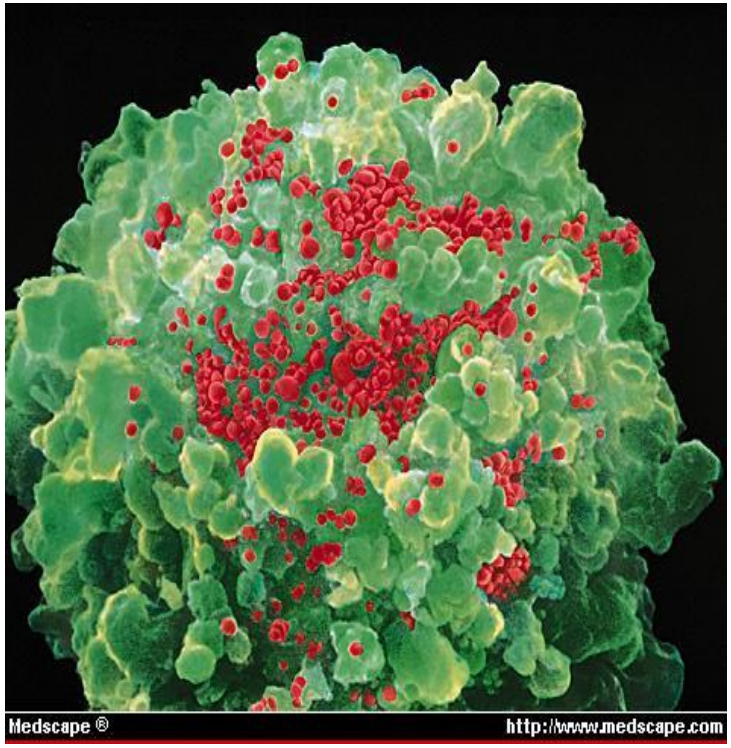


http://commons.wikimedia.org/wiki/File:HIV-budding-Color.jpg

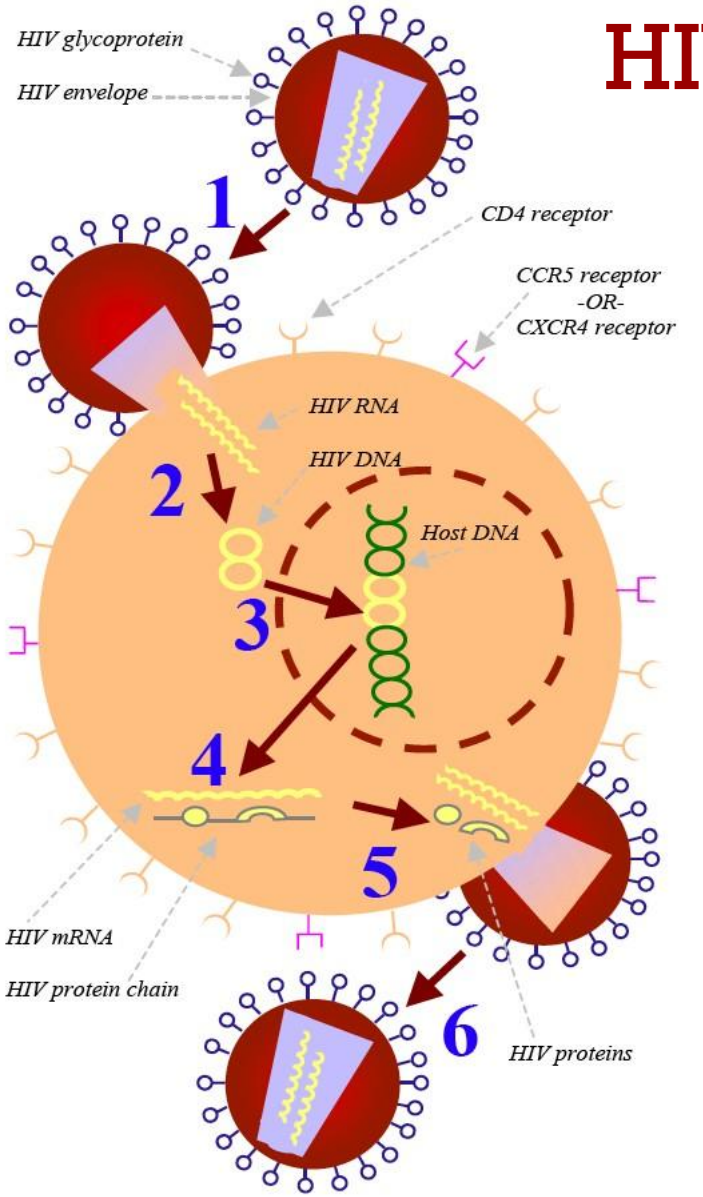
- HIV destroys specific subset of white blood cells called CD4 cells
- The CD4 cell is the "quarterback" of the immune system (coordinates both B cell and cell-mediated immunity)
- HIV reproduces rapidly in CD4 cells (billions made per day)
- Gradual destruction of CD4 cells over 8-10 years on average
- Body eventually cannot fight off opportunistic infections (OIs) and/or cancers

HIV Basics

- HIV enters the bloodstream and migrates to lymph node system over 3-5 days
- Primary HIV infection is often mistaken for "the flu"
- "Window period" between infection and time when the body develops antibodies
- Most people will test positive by 3 months after infection
- May be symptomatic for > 10 years



HIV Life Cycle



1. Binding and Fusion
2. Reverse Transcription
3. Integration
4. Transcription
5. Assembly
6. Budding

www.thebody.com

How HIV is commonly spread

- Unprotected sexual intercourse (vaginal, oral, anal)
- Multiple sexual partners
- Concurrent other sexually transmitted infections
- Sharing needles and other drug equipment
- Mother-to-child transmission during pregnancy, delivery or breastfeeding

www.cdc.gov

Less common modes of HIV transmission

- Occupational exposure (i.e. needlestick) – no cases since 2006
- Blood and organ transfusion – extremely rare due to current testing practices in USA
- Bite from HIV-infected person – rare cases of transmission with severe bite trauma
- Contact between broken skin or mucus membranes and HIV-contaminated blood/fluid – very rare case reports
- Tatooing/body piercing – theoretical risk, no cases

www.cdc.gov

How HIV is NOT spread

- Air, water, insects
- Saliva, tears, sweat, spitting
- Casual contact (i.e. shaking hands, sharing dishes)
- Kissing (unless HIV-infected partner has bleeding gums or open mouth sores)
- Vomit, stool, urine, mucus/phlegm

www.cdc.gov

How do HIV tests work?

- HIV test looks for HIV antibodies
  - "Window period" between time of infection and body's production of antibodies
  - During "window period" (2-8 weeks), HIV test will be negative but individual is at high risk for transmitting infection to others
  - 97% of people mount antibody response by 3 month mark
- Blood test or oral swab, similar sensitivity
- Positive antibody test needs confirmation by Western blot (which confirms that antibodies detected are actually due to HIV and not a cross-reaction with another antibody type)

A note on "False Positives"

- HIV antibody test may be positive in situations where the patient does NOT have HIV infection
  - Certain autoimmune diseases, multiple pregnancies, hemodialysis, blood transfusions, certain vaccinations
  - In these cases, follow-up Western blot will be negative
- In a "low prevalence" state such as Idaho, high rate of false positives
  - If you put 1000 people in a room, 1 will have HIV (TRUE POSITIVE).
  - However, test will pick up 1 in every 100 people…so out of 1000, you will have 9 FALSE POSITIVES for 1 TRUE POSITIVE

How to prevent HIV

- Know your status → treatment improves survival and decreases rate of transmission to partners and babies
- Abstinence or mutual monogamy with uninfected partner
- Limit number of sexual partners
- Correct and consistent condom use
- Get tested for STDs regularly
- Male circumcision
- Do not inject drugs
- Seek medical care right away if you think you have been exposed to HIV

Prevention of mother-to-child transmission of HIV (PMCT)

- Untreated HIV+ moms have 30% chance of passing on HIV to newborn babies
- Can reduce risk of transmission to < 2% if:
  - Mom gets treatment during pregnancy, labor and delivery
  - Baby gets postpartum treatment x 6 weeks
  - Mom avoids breastfeeding

www.cdc.gov

Drug Basics

Goals of therapy

- Restore and improve immune system function
- Decrease viral transmission to others
- Decrease rates of cardiovascular diseases, cancers, and other HIV-associated illnesses

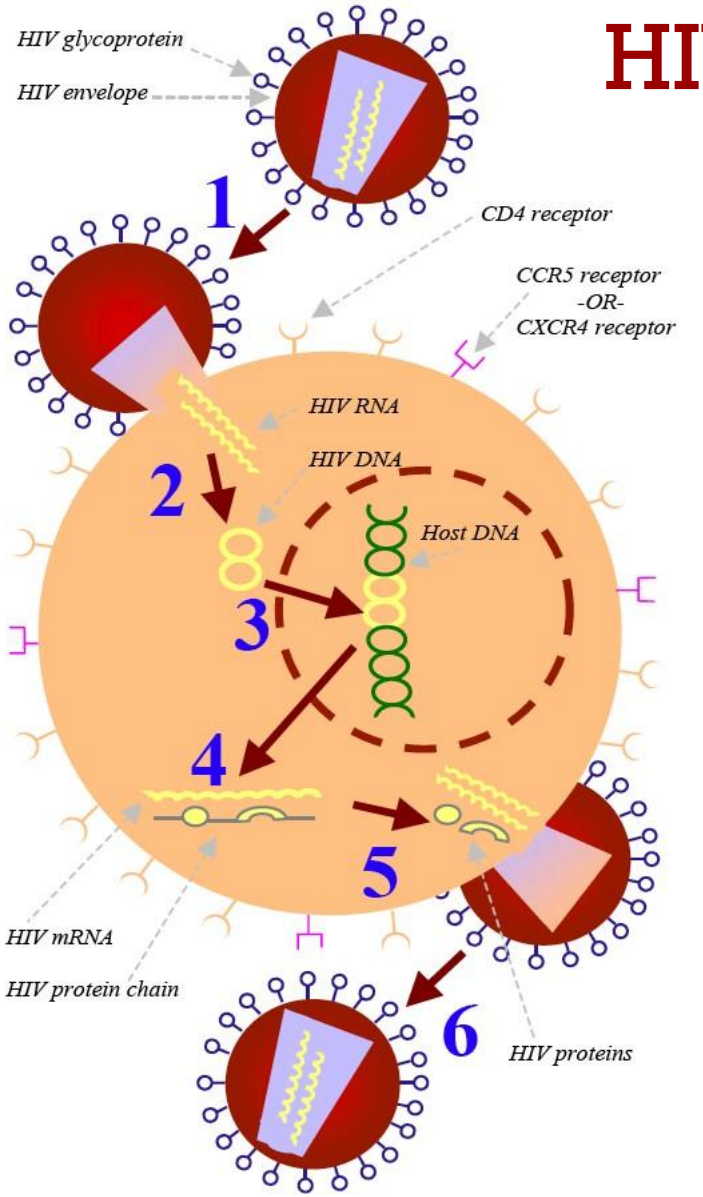
Drug Basics

- HAART = Highly Active Antiretroviral Therapy
- Introduced in 1996, forever changed course of this disease
- Decision to start medication is based on patient's current CD4 count, other medical problems, readiness
  - Current guidelines recommend treatment if CD4 < 500
- Patients take minimum of 3-drug combination, LIFELONG
- Occasionally other antibiotics are given to prevent development of other opportunistic infections

Drug Basics

- Antiretroviral regimens usually include THREE different medications from TWO different classes
  - "Backbone": usually two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)
  - "Base": protease inhibitor (PI), non-nucleoside reverse transcriptase inhibitor (NNRTI), integrase inhibitor (INSTI), entry inhibitor
- 2006: One-pill-once-a-day (Atripla)

HIV Life Cycle



1. Binding and Fusion
   - Fusion inhibitors, entry inhibitors
2. Reverse Transcription
   - Reverse transcriptase inhibitors
3. Integration
   - Integrase inhibitors
4. Transcription
5. Assembly
6. Budding and Maturation
   - Protease inhibitors

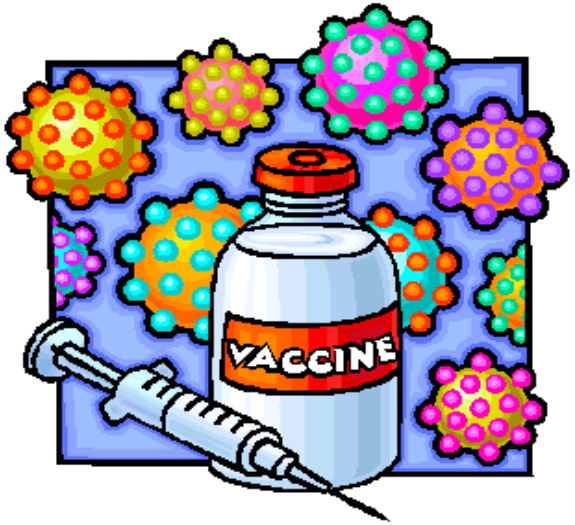
www.thebody.com

Side Effects

- GI side effects
- Anemia
- Bone problems
- Wasting/lipoatrophy/lipodystrophy
- Immune reconstitution syndrome
- Insomnia
- Pancreatitis
- Hypersensitivity reaction
- High cholesterol
- Heart disease
- Neuropathy
- Liver problems
- Kidney problems

Hot Topics in Research

Vaccine Trials



- Hundreds of vaccine trials in past 30 years
- FIRST vaccine trial with positive results – December 2009
  - Study done among 16,000 volunteers in Thailand
  - Up to 30% vaccine efficacy

Rerks-Ngarm S et al. Vaccination with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. *N Engl J Med*. 2009; 361 (23): 2209-20.

Microbicide

- Trial with nearly 900 HIV-negative women in Africa
- Using gel before and after sexual intercourse reduced rate of HIV acquisition by > 30%
- Crucial intervention for empowerment of women, who often lack control of sexuality

Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010 Sept 3; 329: 1168-74.

Pre-Exposure Prophylaxis (prEP)

- HIV negative high-risk individuals take antiretroviral medication daily to reduce chance of infection
- Has only been proven effective in gay and bisexual men, and in transgender women who have sex with men (not yet proven in heterosexuals or IV drug users)
- prEP cannot be the first or only line of defense, must be used in combination with condoms, risk reduction strategies and frequent HIV testing

www.cdc.gov/hiv/prep

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