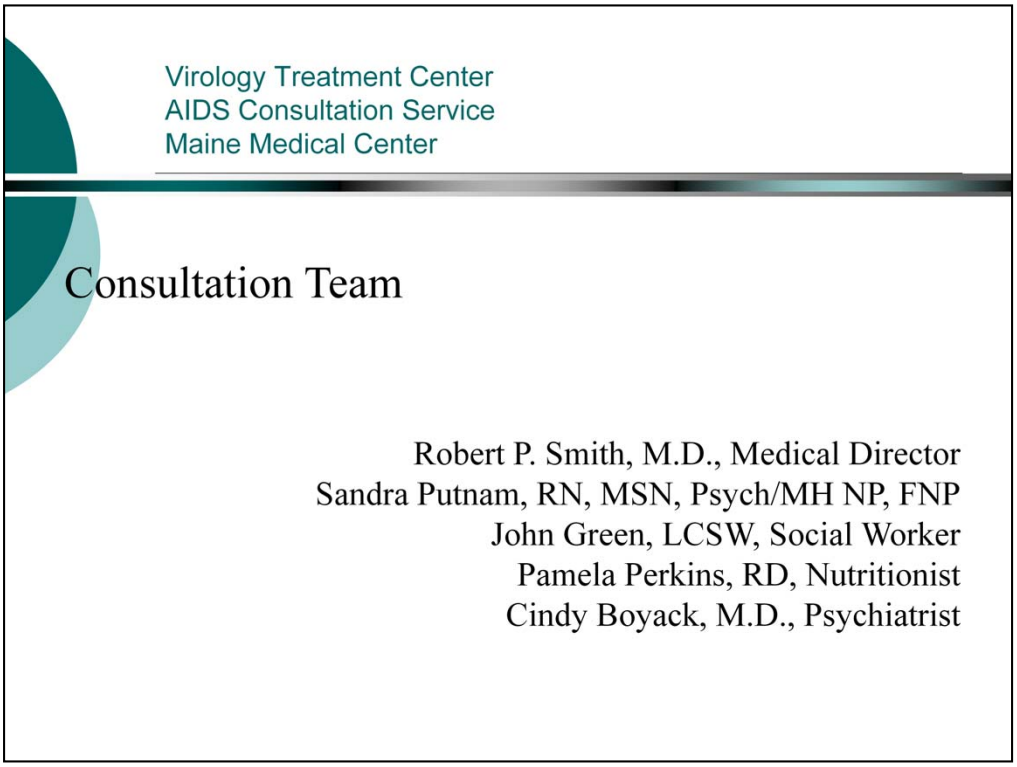


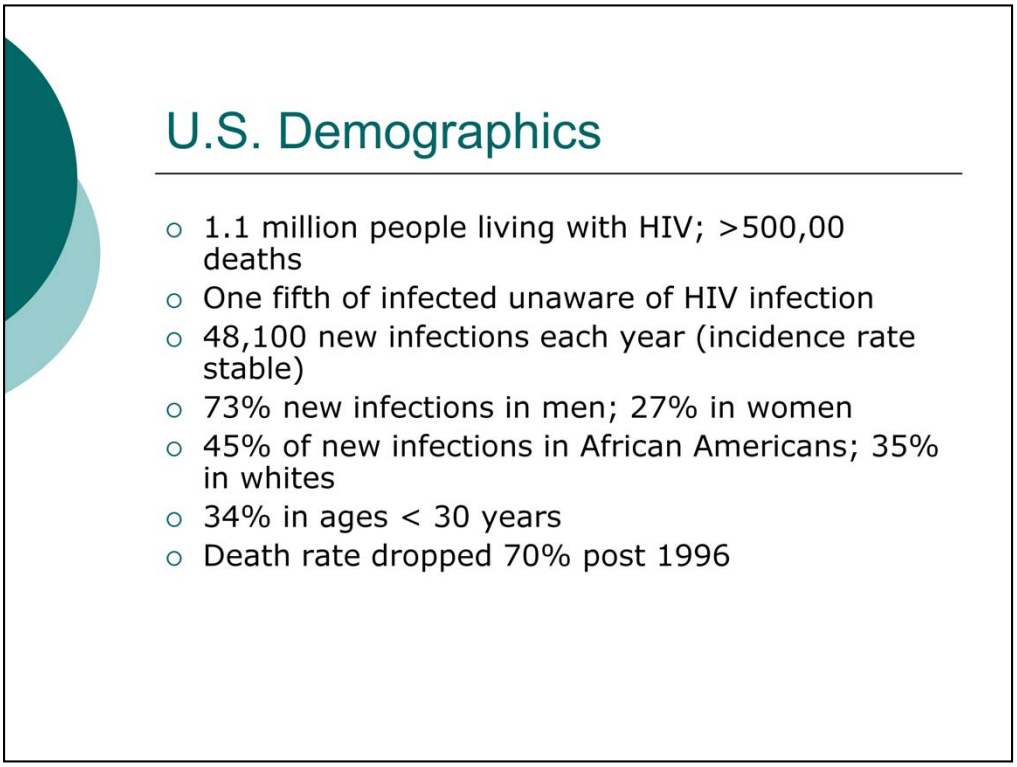
Presented November 8, 2012

HIV in 2012

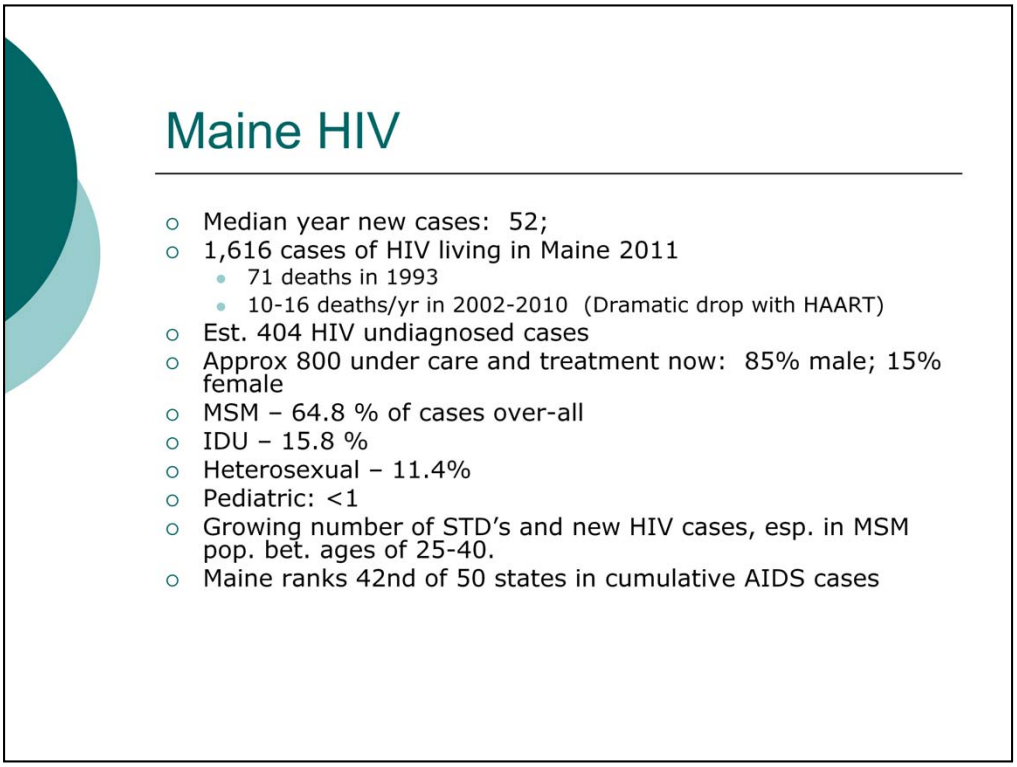
4th Decade in the Epidemic

World Pandemic

- >43 million people living with HIV or AIDS, 68% in sub-Saharan Africa
- Approximately 2 million deaths in 2010 (5500/day), 72% in sub-Saharan Africa
- 8000 new infections every day (95% in developing countries)
- Fifty percent of adults living with HIV are women
- HIV is a disease of young people in world, 45 % of new infections in ages 15 to 24
- 11-12 million orphans under age 18 in sub-Saharan Africa



People infected with HIV are living much longer today because of the combined use of 3 separate cocktails



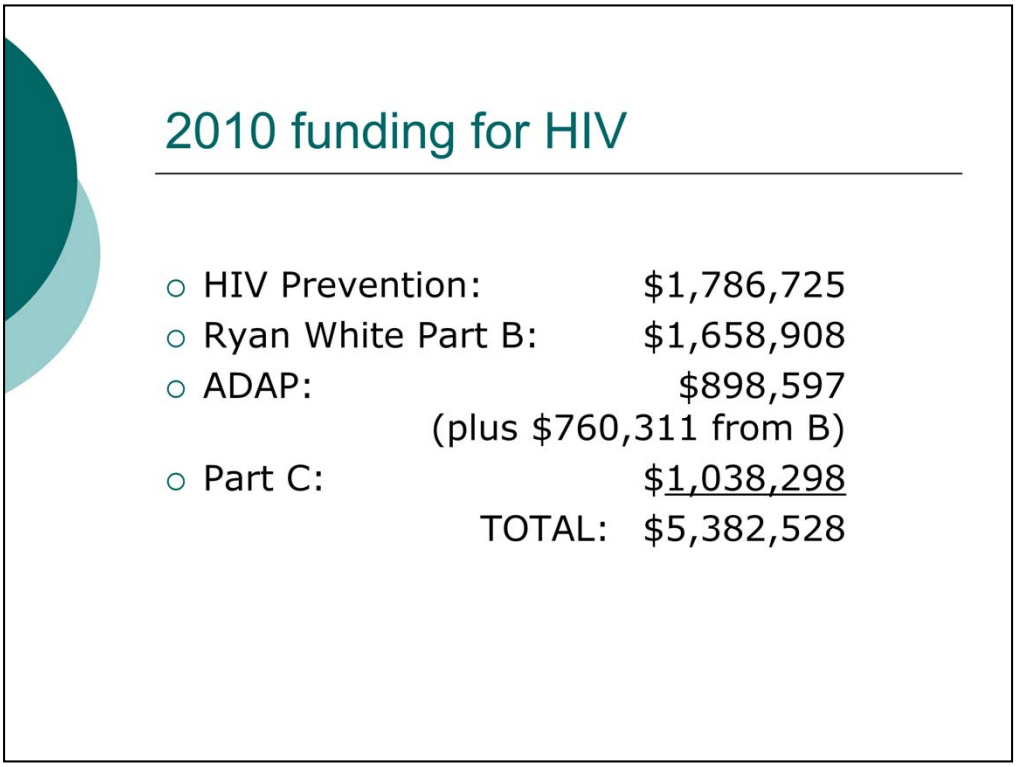
HAART = highly active antiretroviral therapy

Maine HIV Stats

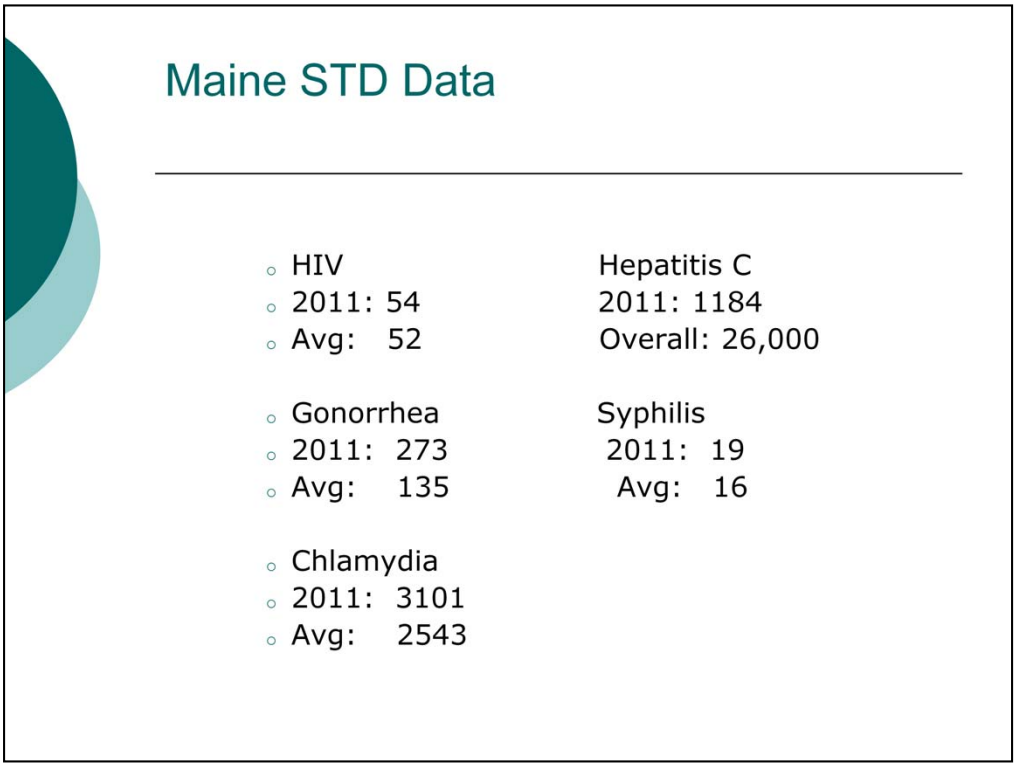
- 2010: New Diagnoses:
  - 51 % have AIDS diagnosis at time of + test
  - 49% have HIV diagnosis
  - HIV 9th leading cause of death
  - 84% male; 16% female
  - 78% of all diagnoses > 30 yrs old
  - 82% of new diagnoses >30
  - 0.2% of new cases 40-49 yrs old
  - 87.1% white; 10.7% black; 4.8% Spanish; 0.8% Native American; Asian 0.3%; unknown 1.1%

Maine HIV Distribution

- Maine by Region:
  - Cumberland county 562
  - York County 238
  - Western (ox, Frank, andros) 184
  - Central (somerset, Kenneb) 161
  - Mid Coast (Linc, Knox, Waldo, Sagadahoc) 114
  - Penquis (Pisc, Penob) 113



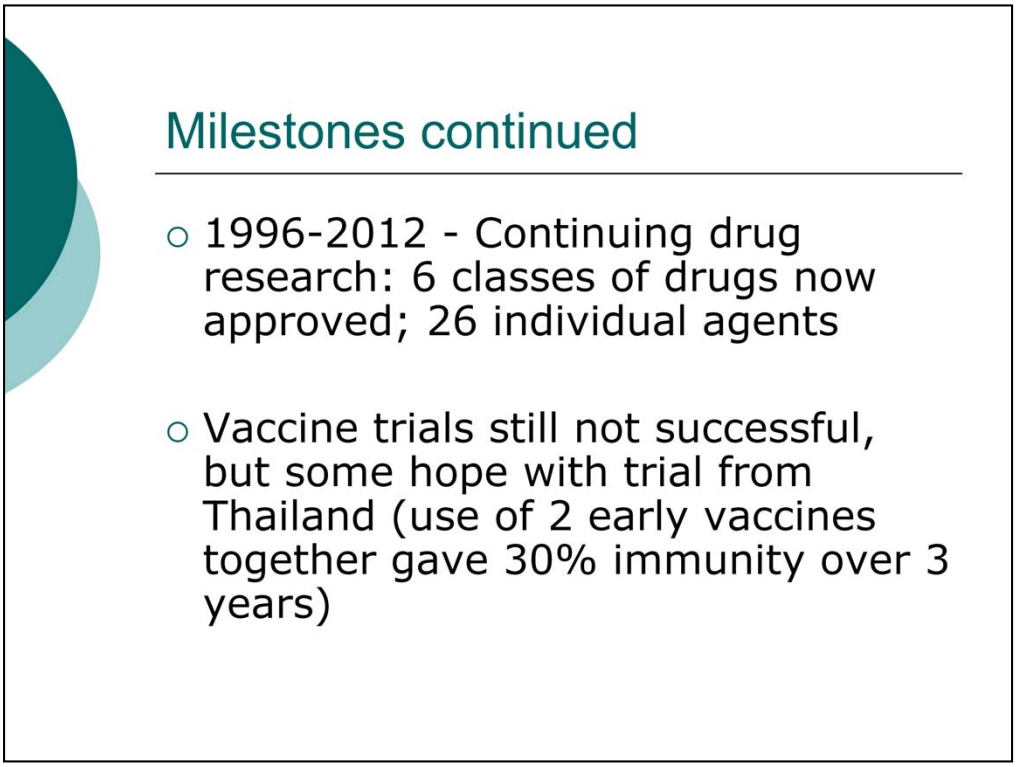
The US Centers for Disease Control (CDC) has been reducing funding to low incidence states like Maine (rank 42 out of 50 states for cumulative HIV cases)



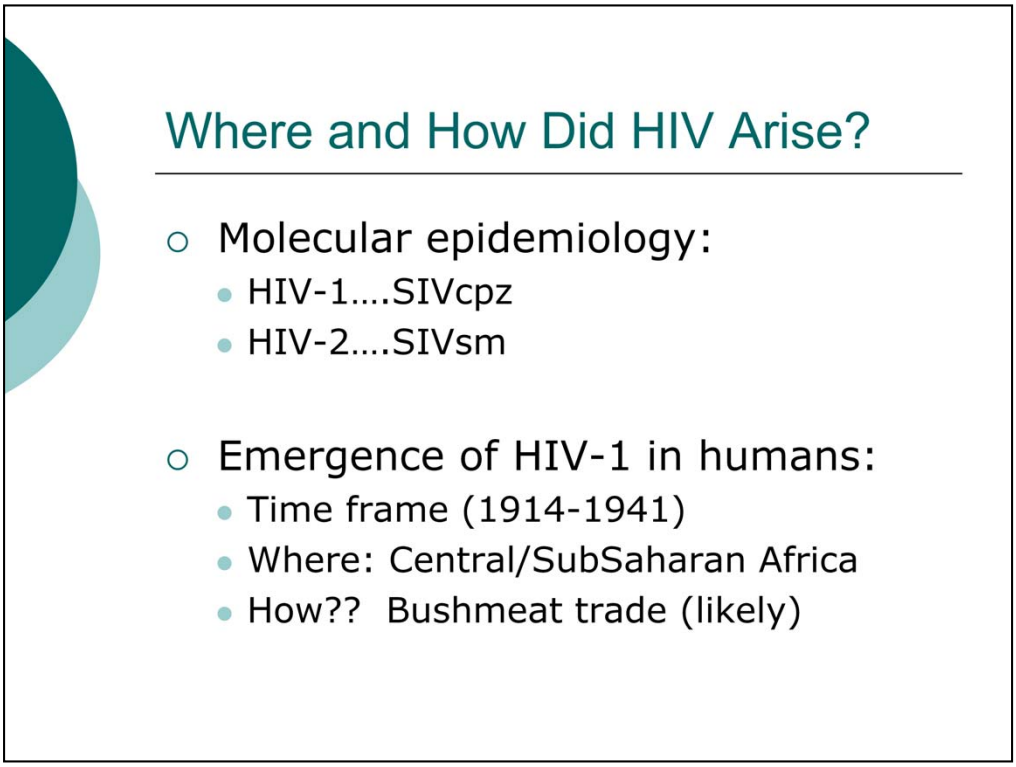
YTD = year to date Avg = average for the past 5 years

Milestones of HIV Treatment

- 1981 – first cases of AIDS reported
- 1985 – HIV antibody test
- 1987 – AZT approved (1st antiviral)
- 1987 - early 1990's: more antiviral (NRTI) agents (ie., DDI, D4T, 3TC); OI treatments improved
- 1996 – Vancouver Conference – PI's in combo: use of 3 drugs to treat HIV becomes standard of care: virus is controlled



HIV+ German patient given 2 bone marrow transplants for treatment of leukemia has no verifiable viral load for HIV



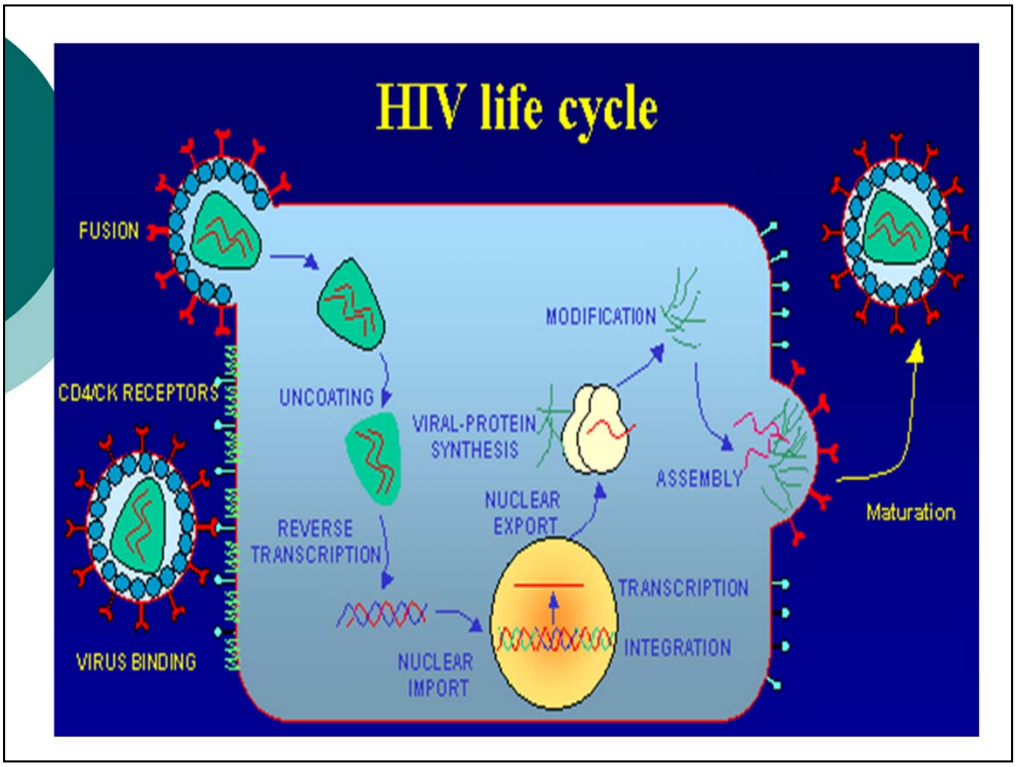
In 2005, scientists report that HIV most likely originated in the jungles of Africa in wild chimps. The virus was transferred to humans through monkey bites or eating meat and brains of infected chimps. Viruses that jump from one animal species to another usually are more destructive in the second species

HIV/AIDS:
What is the Difference?

- HIV: A viral infection causing gradual depletion of T4 lymphocytes (a key WBC) by using them for replication and in the process killing them
- AIDS: A diagnosis given when T4 count reaches 200 (normal is 1000), defined by CDC as point where Opportunistic Infections are likely to occur

How Does HIV Harm the Human Immune System?

- The Virus…….
  - It is a Pretty 'SMART' Virus: well packaged to replicate!
  - RNA genetic material: needs cell DNA to replicate



For more complete explanation go to: aidsinfo.nih/gov/contentfiles/HIVLifeCycle

The Irony……

- Our immune system tries to 'remember' HIV infection by scooping up pro-viral DNA
- BUT: These long-lived memory T-cells that hold pro-viral DNA live for 40-60 yrs.

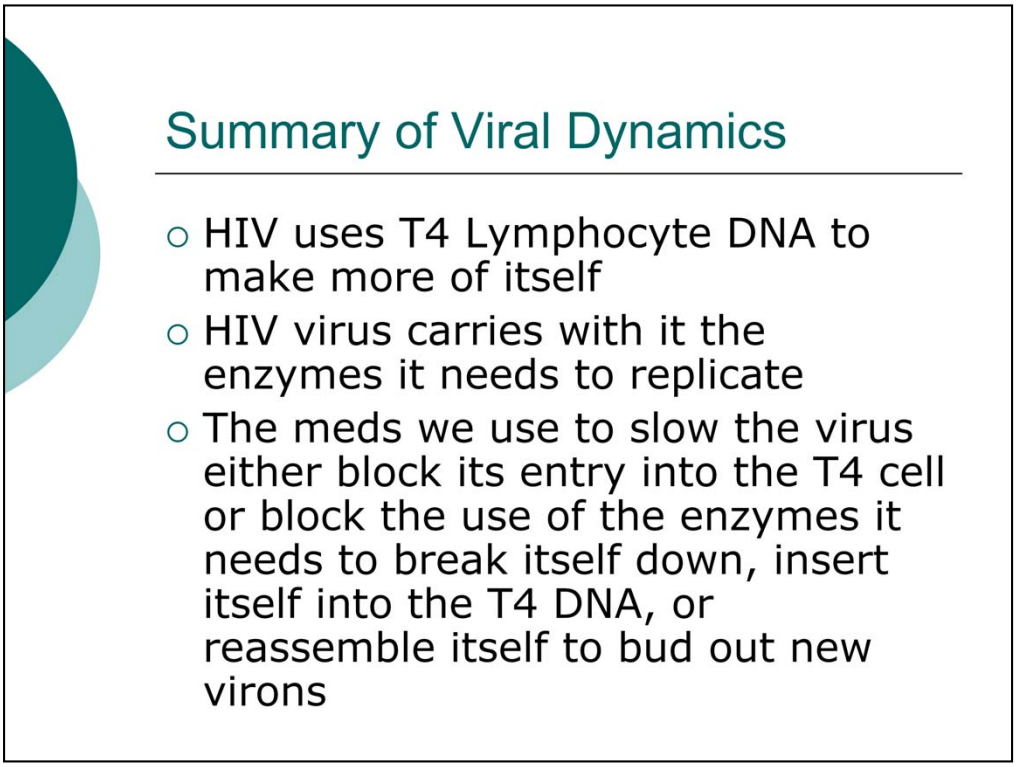
Viral Dynamics

VI

- Avg. total HIV viron production per day:

  10 billion RNA strands

- Avg. life span of infected T cell: 2.2 days
- Min. duration of HIV life cycle: 1.2 days
- Avg. HIV generation time: 2 days
- Memory T cells can live for 40-60 years



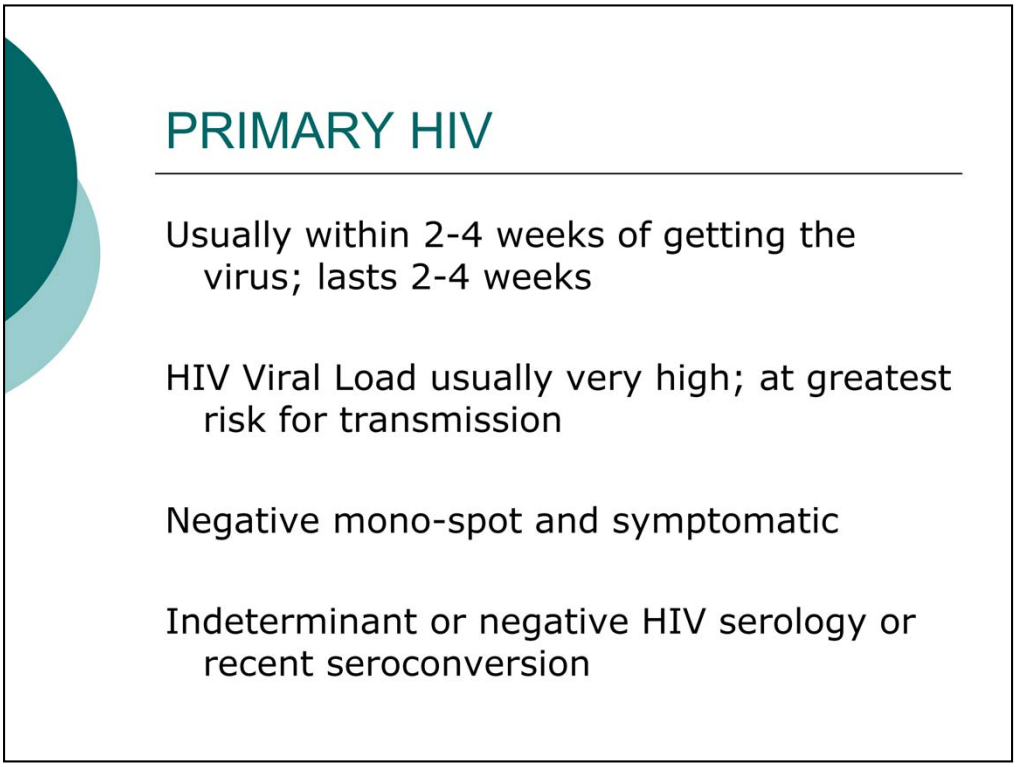
The essential piece of treatment is to keep HIV from replicating

Summary continued

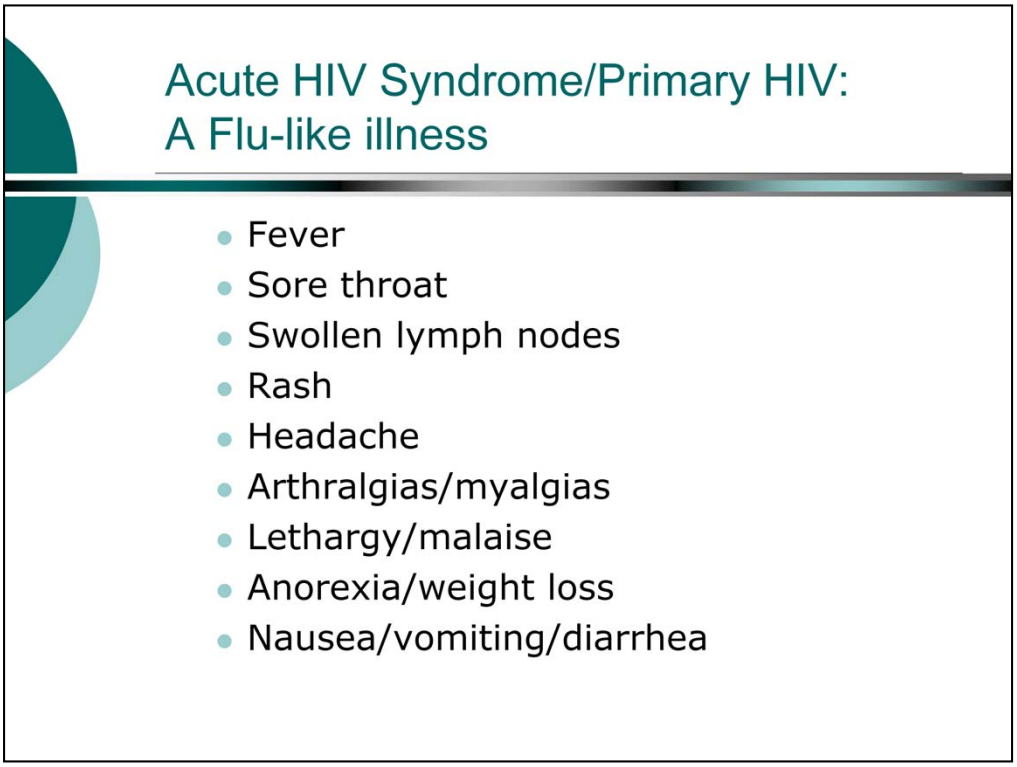
- In going through this replication process, the virus damages the T4 lymphocyte and it dies.
- The virus has amino acids on its surface which can mutate rapidly to provide resistance to drugs.
- Therefore, adequate drug levels are essential to keep replication from occurring

HIV: Death sentence or Chronic Disease?

- Nothing to 'cure' HIV yet
- But we can control viral replication by blocking how it works
- KEY: Keeping blood levels up: almost perfect adherence!!!



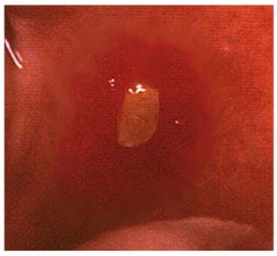
Mono-spot is a test for mononucleosis. Aperson presenting with fever and swollen glands is given this test. Seroconversion is the development of detectable specific antibodies to microorganisms in the blood serum as a result of infection. A person may not yet test positive for HIV but can still transmit the virus to others



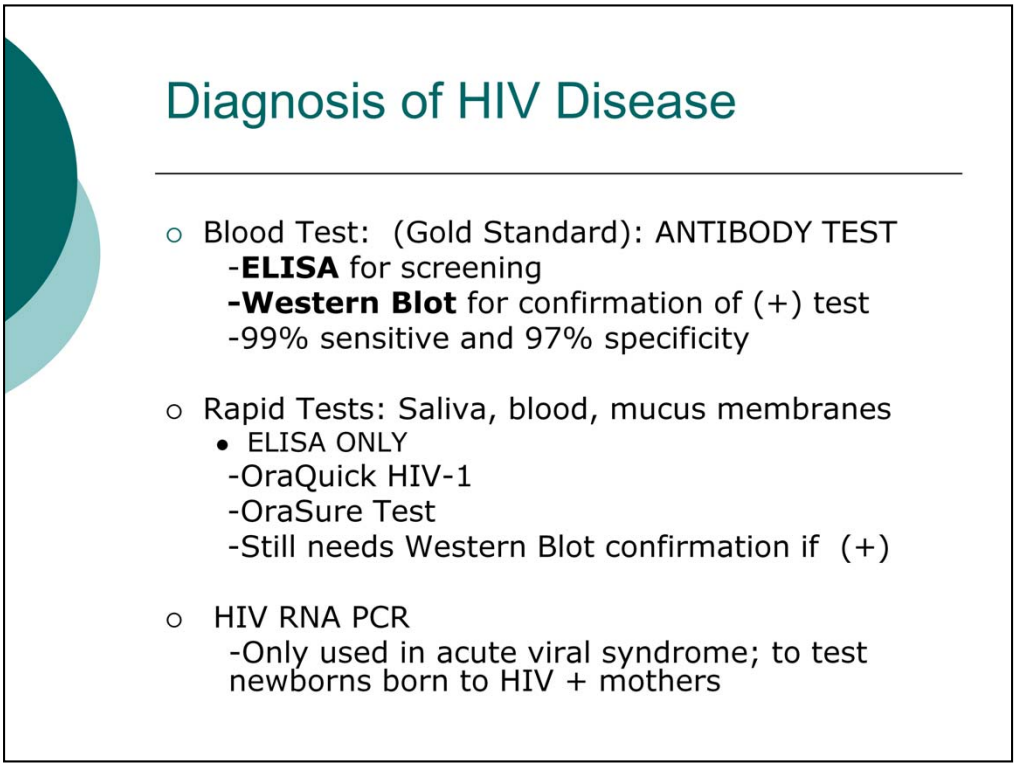
Arthralgia = joint pain myalgia = muscle pain

This is a picture of the skin rash which may occur during initial infection

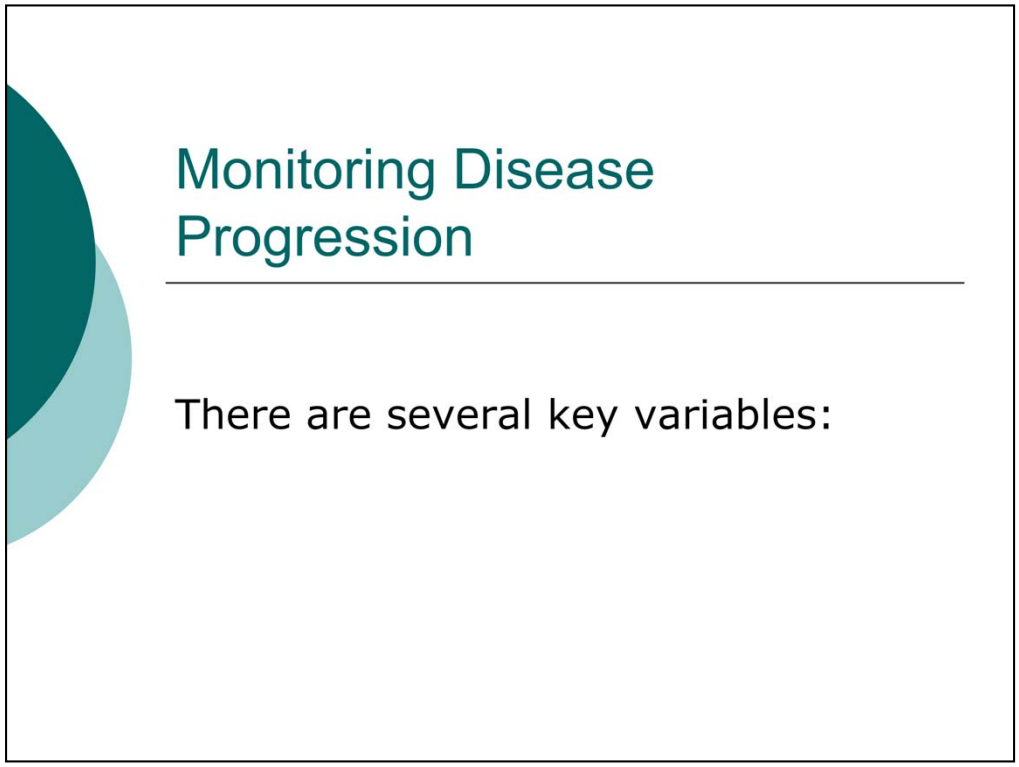
Thrush, apthus ulcers



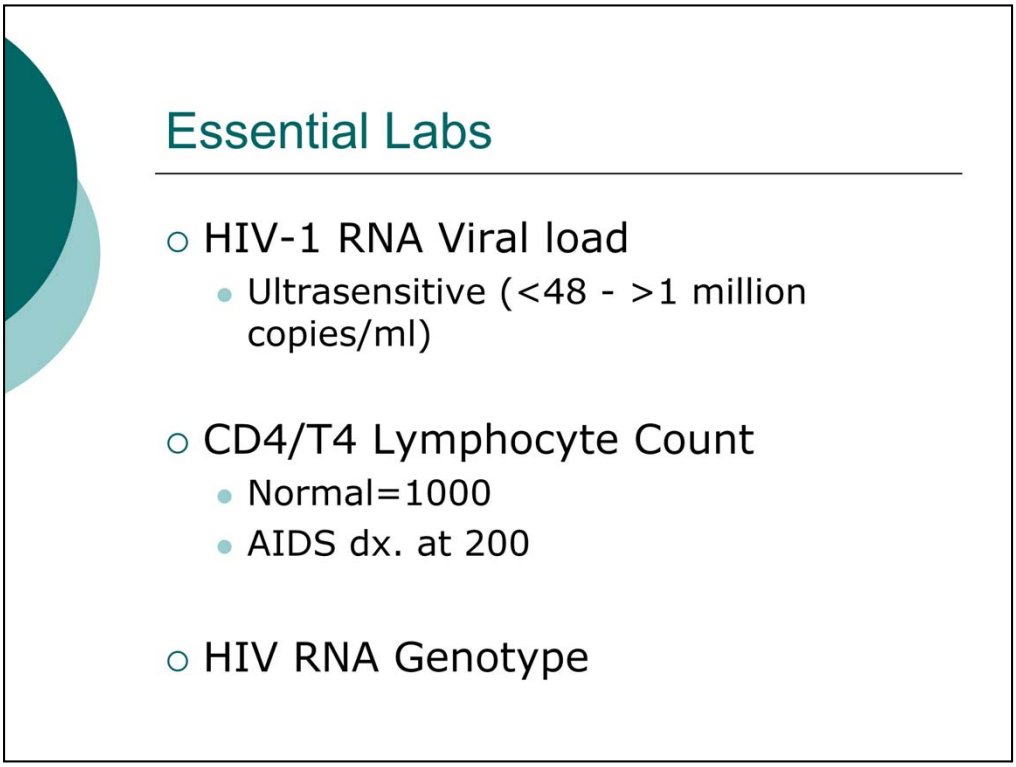
Thrush is a yeast infection in the mouth and apthus ulcers are also known as canker sores. Both can occur in a person with a weakened immune system



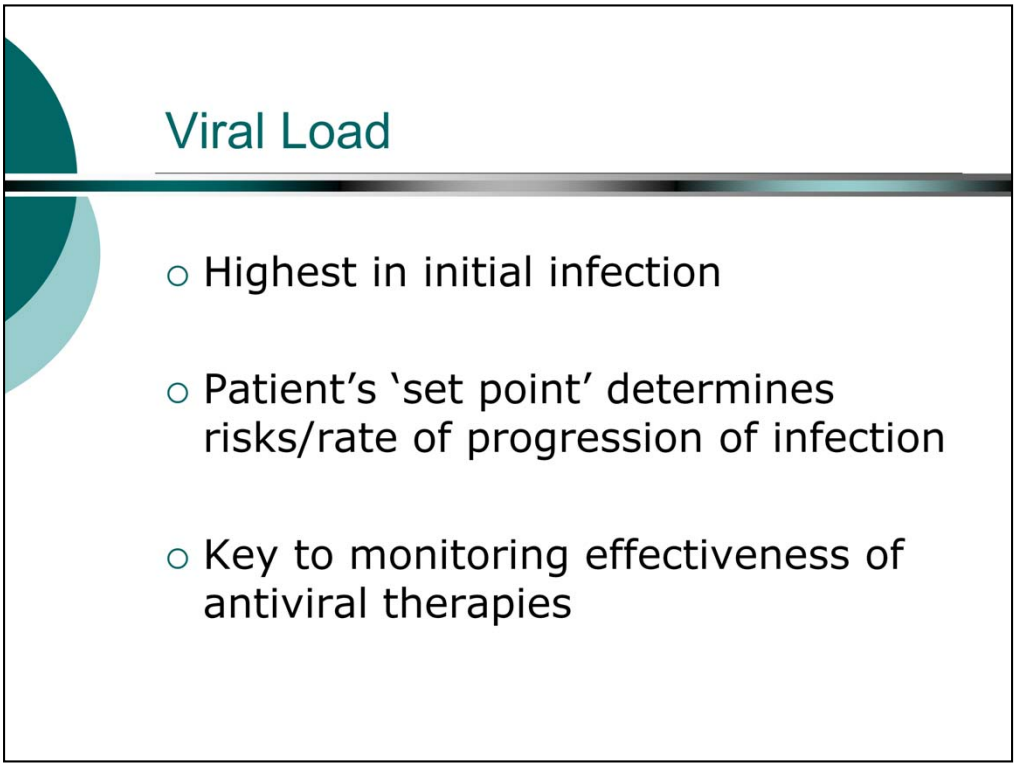
HIV+ pregnant women taking medication have a 1% chance of transmitting HIV to baby. If they are not only medication, the risk increases to 25%



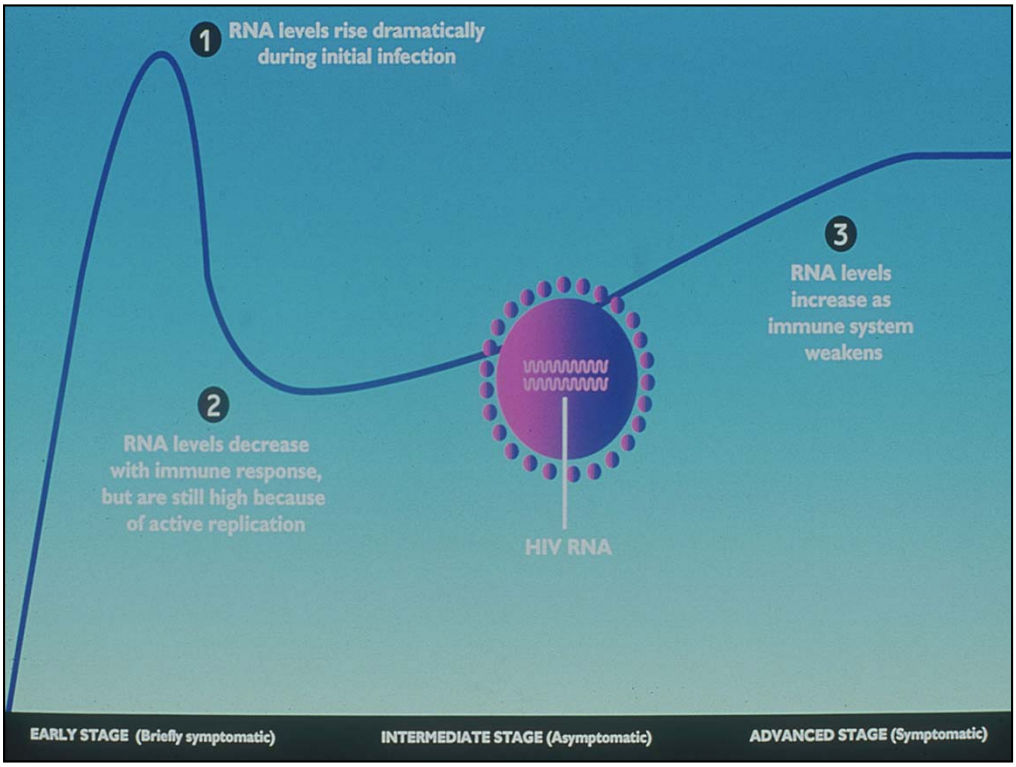
Variables include viral load, T4 Lymphocyte count, and HIV RNA genotype (HIV 1 is most virulent and originated with chimps; HIV 2 is much less common and not as destructive and comes from a type of monkey called a sooty mangabey



The viral load test measures the amount of HIV in the blood and shows how actively the virus is reproducing in the body. There are 9 different HIV subtypes and each responds differntly to medication



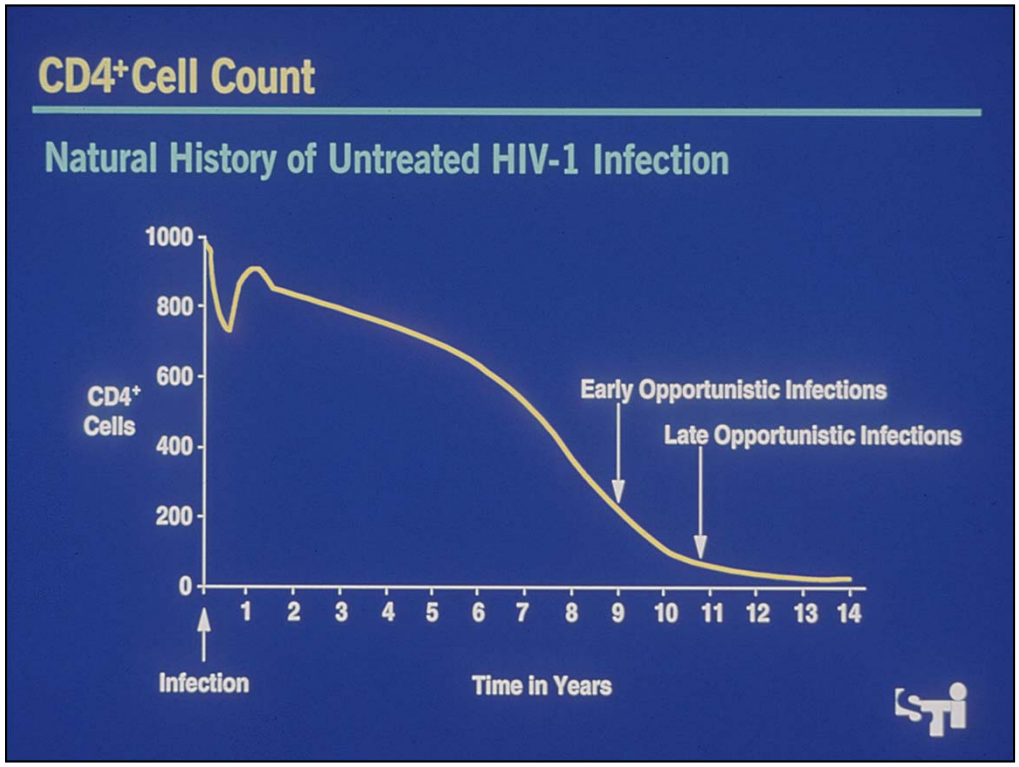
Viral load greater than 100,000 in initial diagnosis indicates a greater likelihood of developing AIDS within 5 years



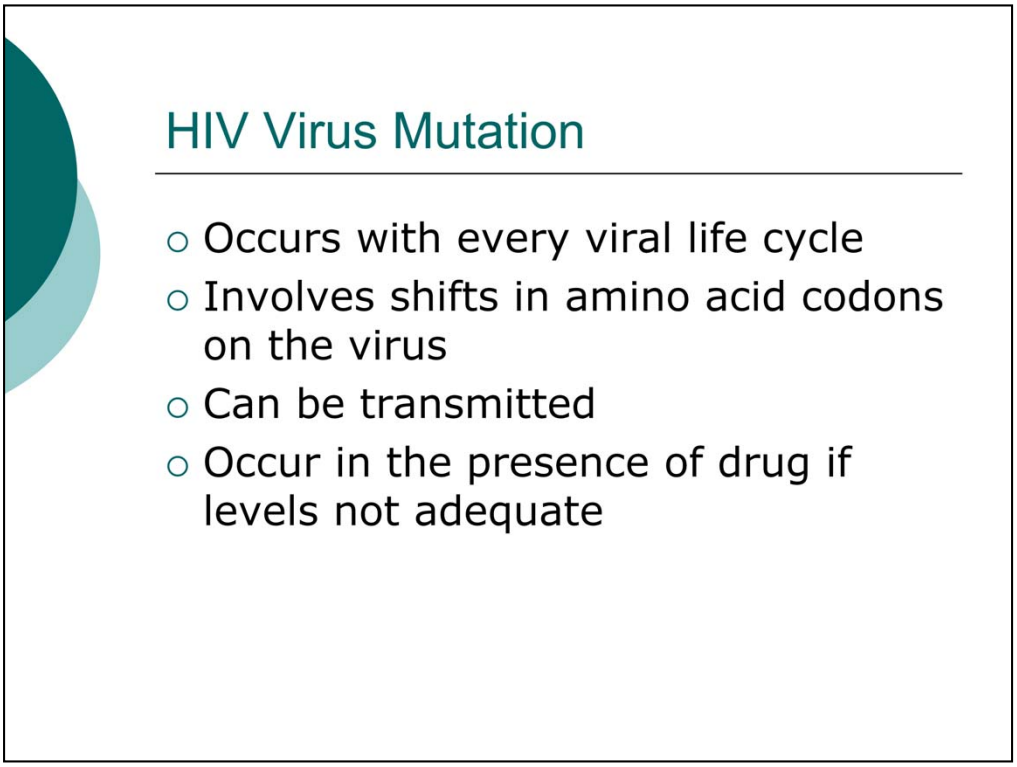
A person is very infectious in the early stage

T4 Lymphocyte Count

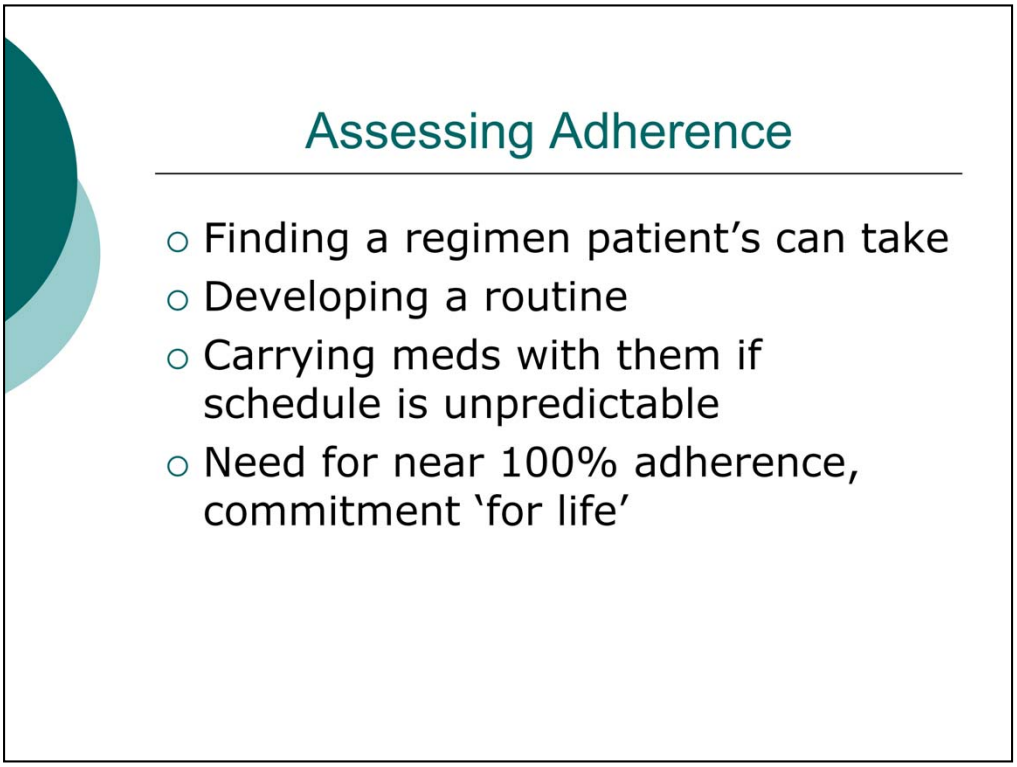
- Normal Count approx. 1000
- On average, with HIV lose approx. 50-100 cells a year (production vs. destruction)



In Maine, people diagnosed as HIV+ typically progress to AIDS within a few years, which means that they have had undiagnosed HIV for a number of years



This mutation is why development of a vaccine has not happened to date



In order for HIV to not progress, patients must strictly follow a treatment medication regimen. Missing just a single dose can result in mutation of the virus, making the original medication no longer work

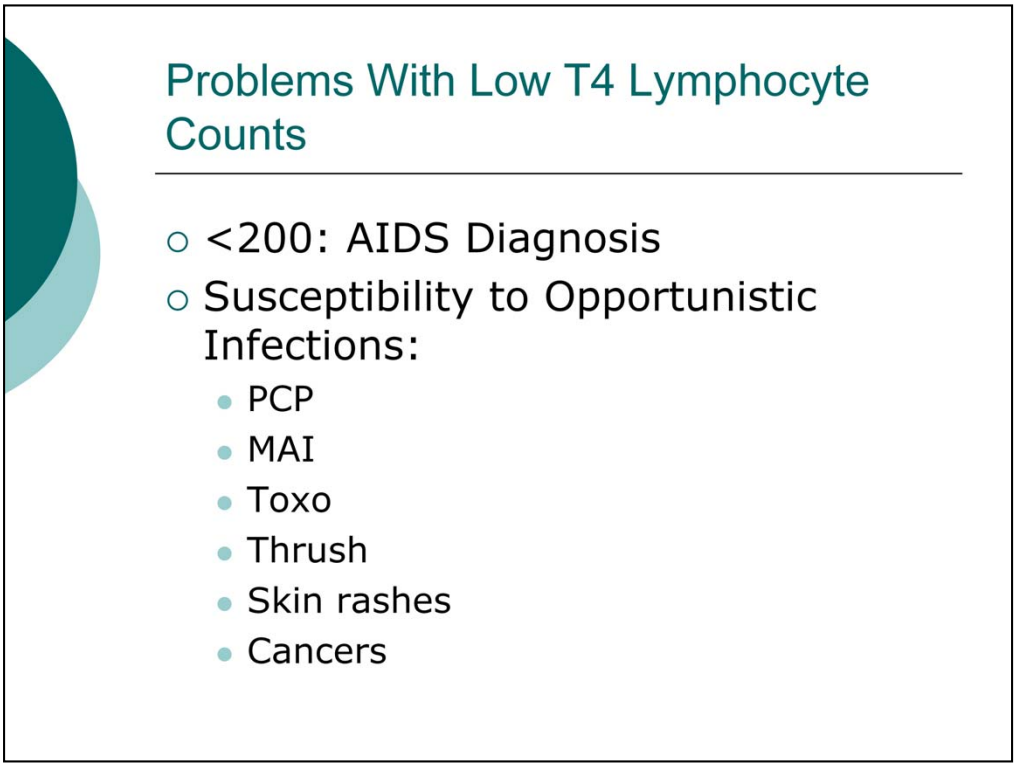
Goals of Treatment: Viral Suppression

- Viral Suppression
- Preserve /improve immune function: Increase in T4 cell count/strengthen immune function
- Delay/abort disease progression

No Cure: Just Viral Suppression: Then Improved Immune Function

- All the drugs control viral replication:
  - They DO NOT KILL HIV
- By suppressing virus, allows immune system to recover, make naïve T4 lymphocytes

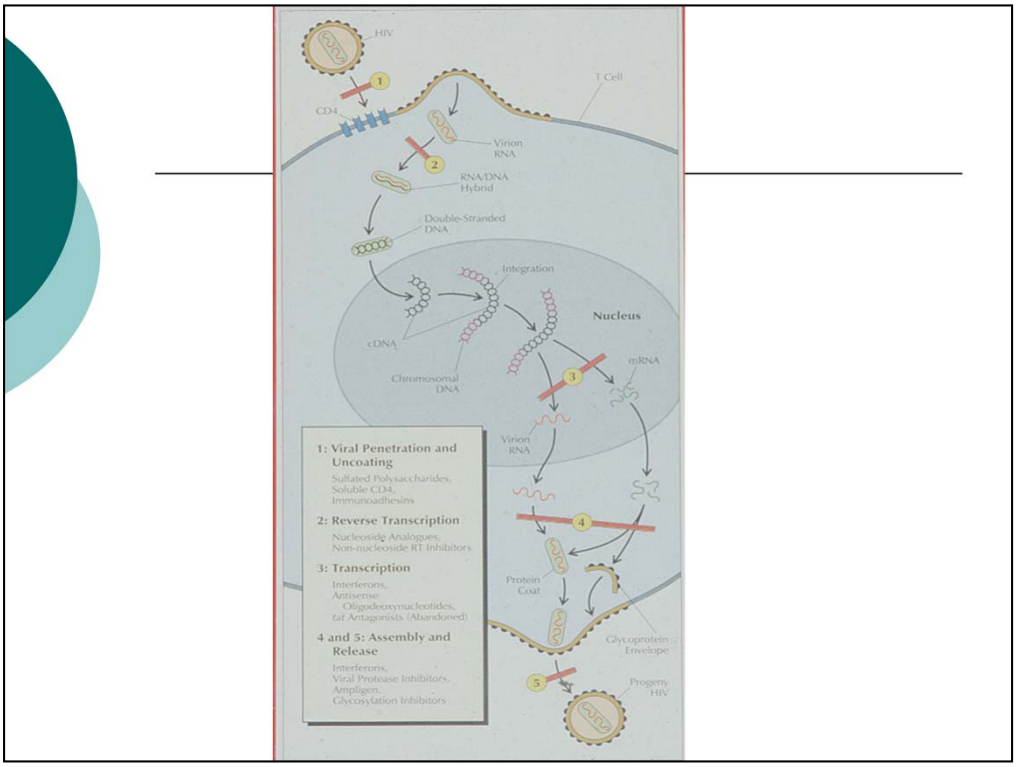
  But ONLY if drugs taken exactly right
- EVERY DAY, EVERY DOSE



PCP = pneumocystis pneumonia (caused by fungus) MAI = atypical mycobacterial infection (such as encephalitis) Toxo = toxoplasmosis (protozoal disease) Karposi's sarcoma is a type of cancer

The Antiviral Medications

Where and How They Work

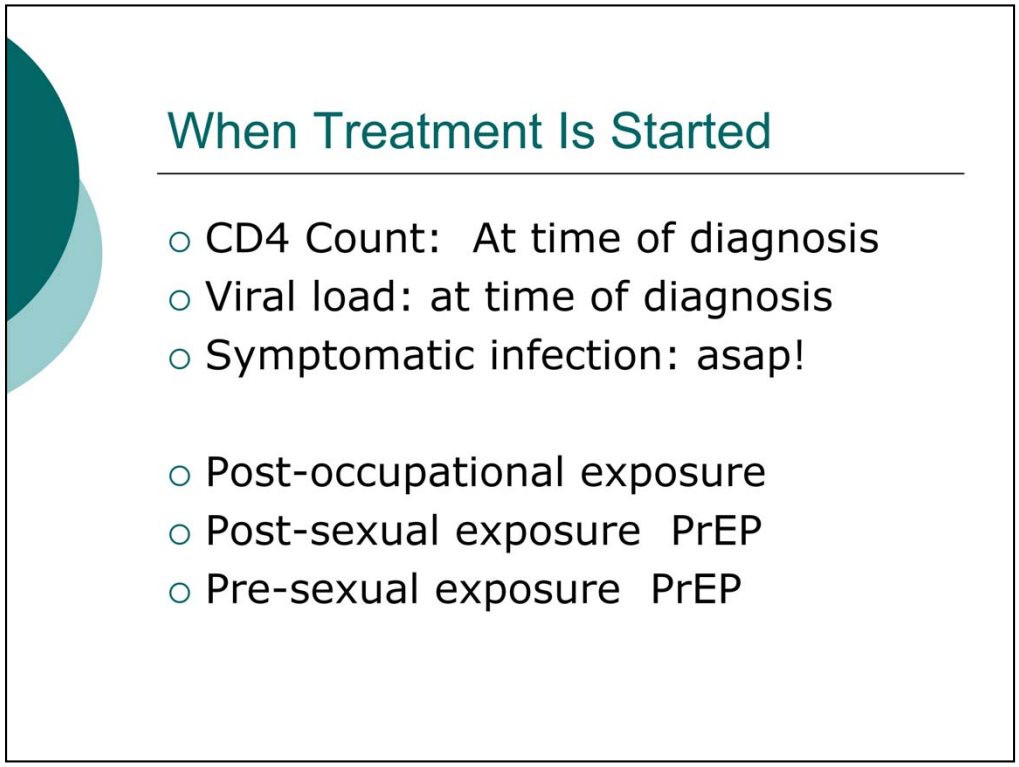

HIV
T Cell
CD4
Virion RNA
RNA/DNA Hybrid
Double-Stranded DNA
Integration
Nucleus
cDNA
Chromosomal DNA
mRNA
Virion RNA
Protein Coat
Glycoprotein Envelope
Progeny HIV
1: Viral Penetration and Uncoating
Sulfated Polysaccharides, Soluble CD4, Immunoadhesins
2: Reverse Transcription
Nucleoside Analogues, Non-nucleoside RT Inhibitors
3: Transcription
Interferons, Antisense Oligodeoxynucleotides, tat Antagonists (Abandoned)
4 and 5: Assembly and Release
Interferons, Viral Protease Inhibitors, Ampligen, Glycosylation Inhibitors

Classes of HIV Antiviral Drugs

- Reverse Transcriptase Inhibitors: RTIs
  - Nucleoside analogs/Nucleotide analogs
  - Non-nucleoside analogs

Antiviral Drugs cont'd

- Protease Inhibitors
- Fusion Inhibitors
- Entry Inhibitors
- Integrase Inhibitors



PrEP stands for Pre-Exposure Prophlaxis, a new HIV prevention method in which people who do not have HIV take a daily pill to reduce their risk of becoming infected

What Meds to Take?

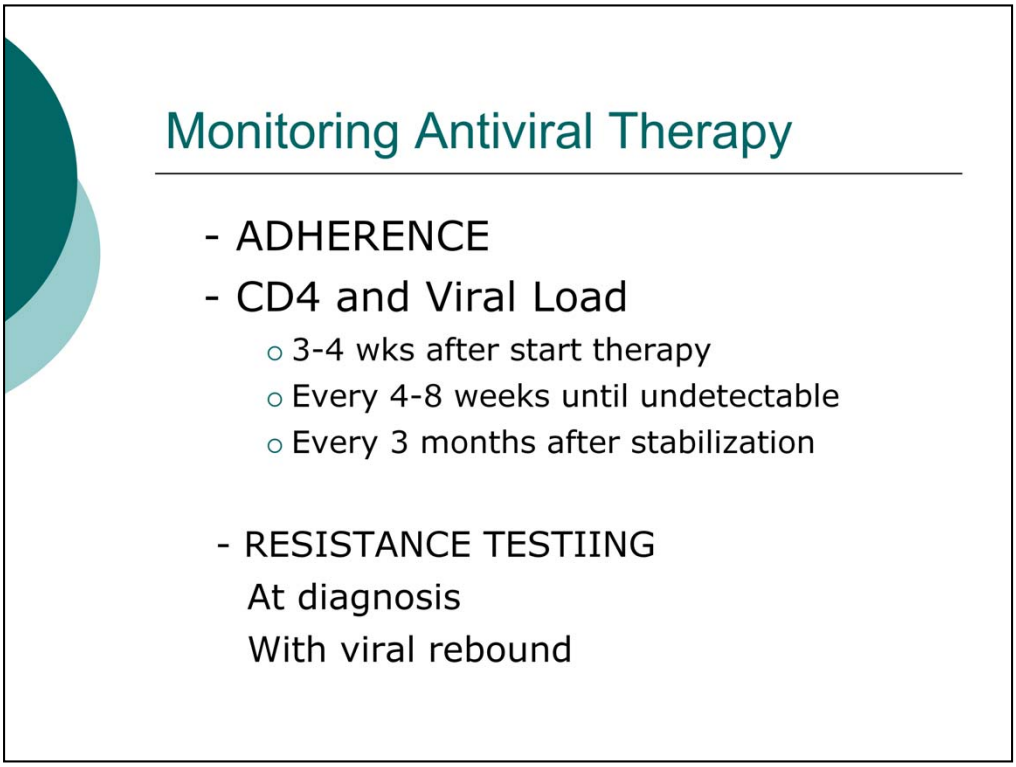
- STANDARD of CARE:
  - 3 antivirals at all times
  - Use of at least 2 classes

Problems With HIV Antivirals

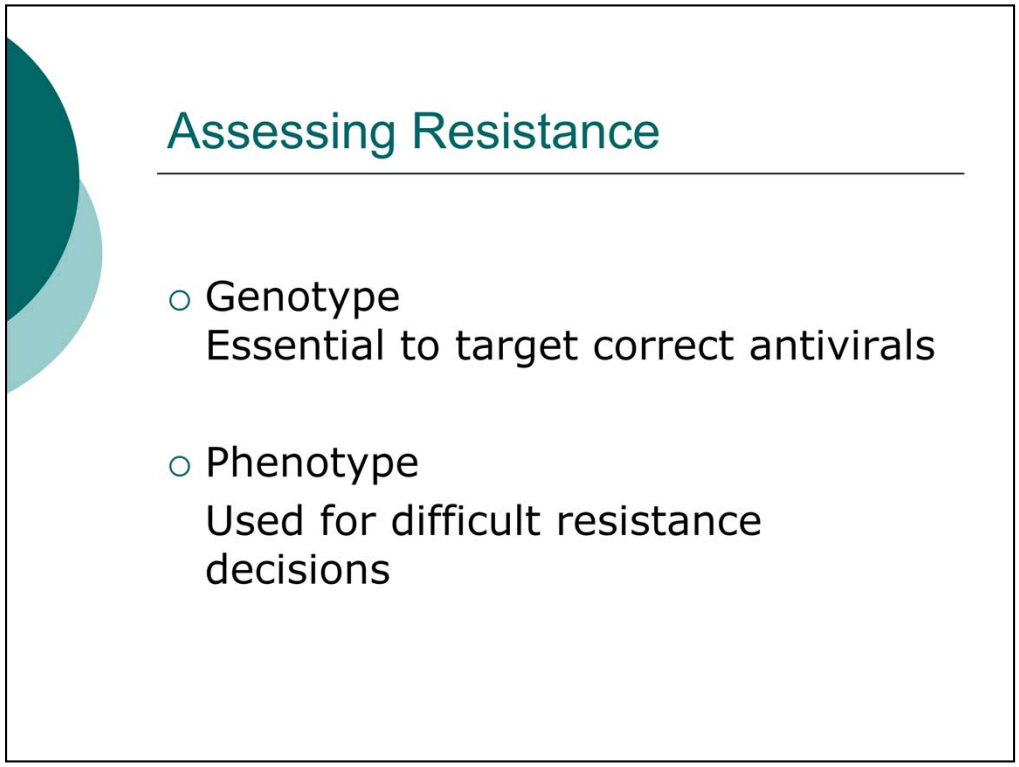
Drug/drug interactions (Cytochrome P-450 interactions)

Multiple drug **side effects/toxicities**: vary from person to person

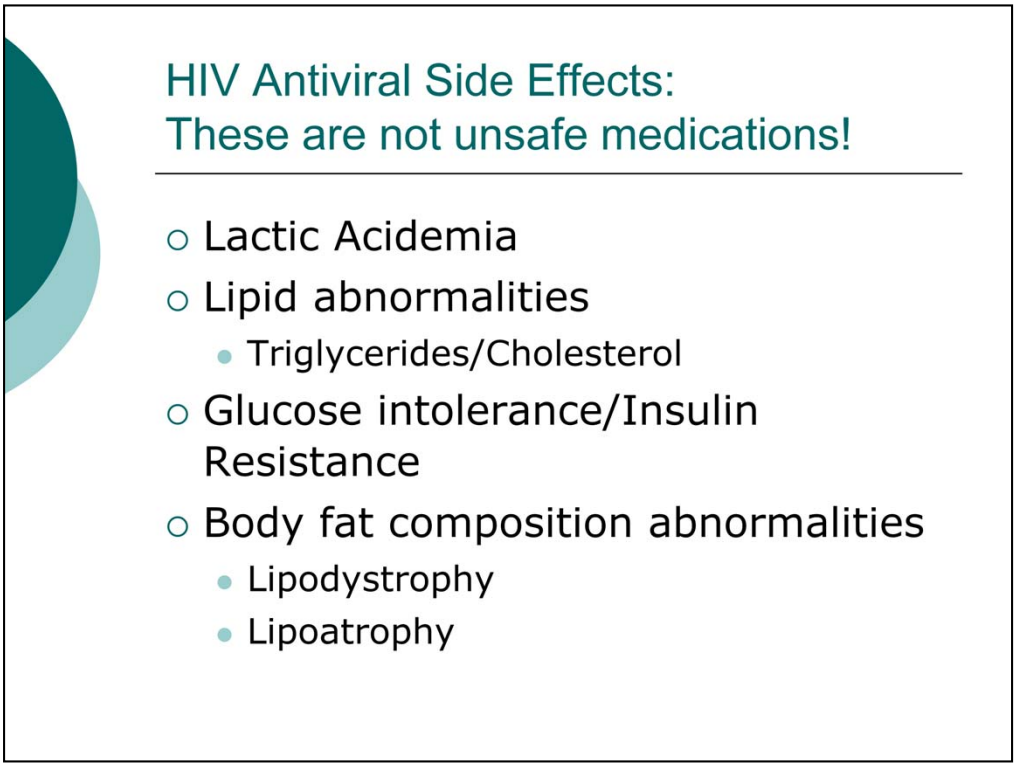
Need for nearly **perfect adherence for years, ? lifetime**



HIV is"resistent" to a drug if it keeps multiplying rapidly while you are taking the drug. Resistence testing helps health care providers make better treatment decisions for their patients

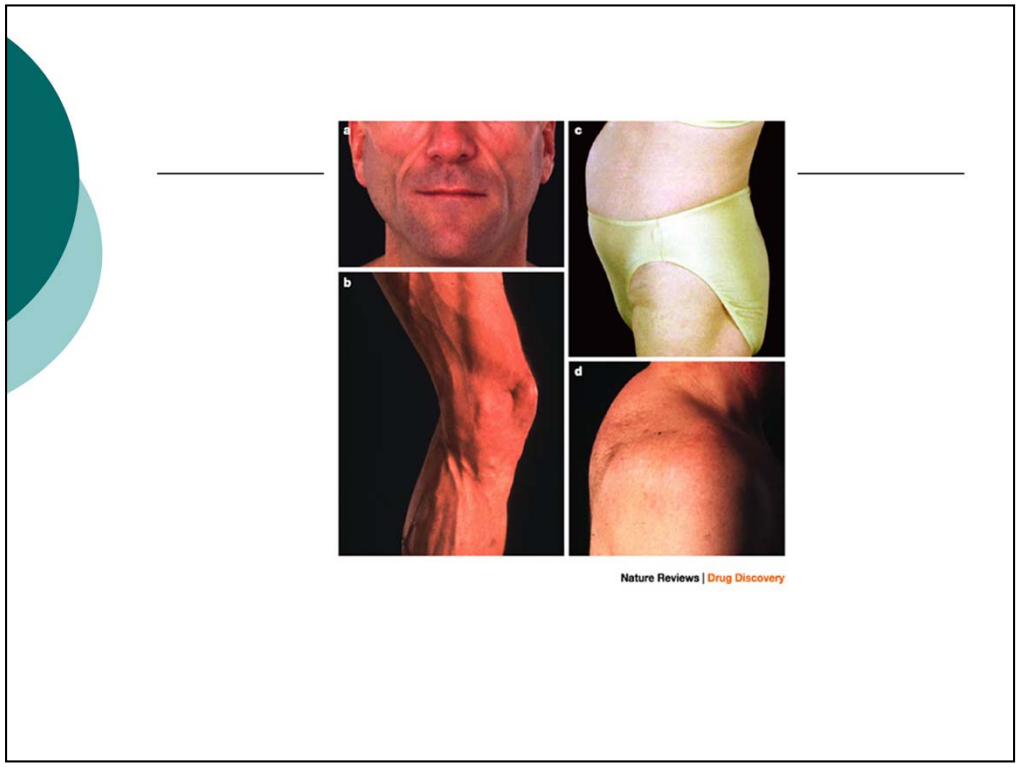


Genotype = genetic makeup of a cell Phenotype = outward, physical manifestation of the organism

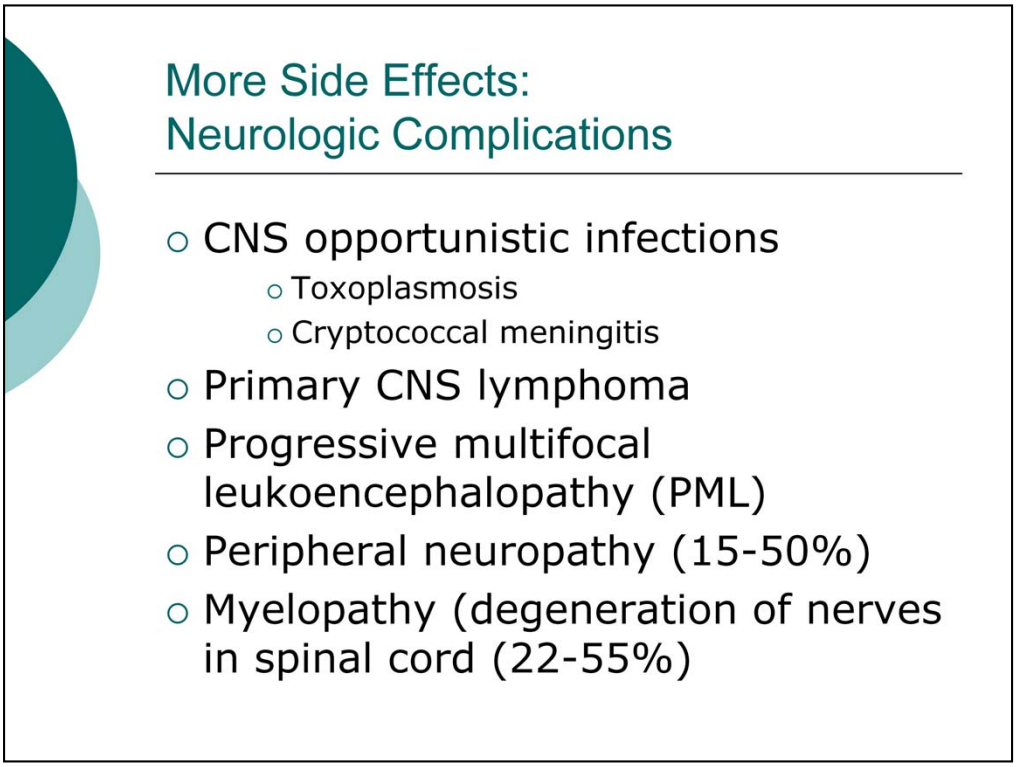


Lactic acidemia is too muc lactic acid in the blood. Lipoatrophy involves fat redistribution. The next slide shows a picture of an individual with “buffalo hump” fat deposits in the upper back. Lypodystropy is fat loss in the face, buttocks, arms, and legs

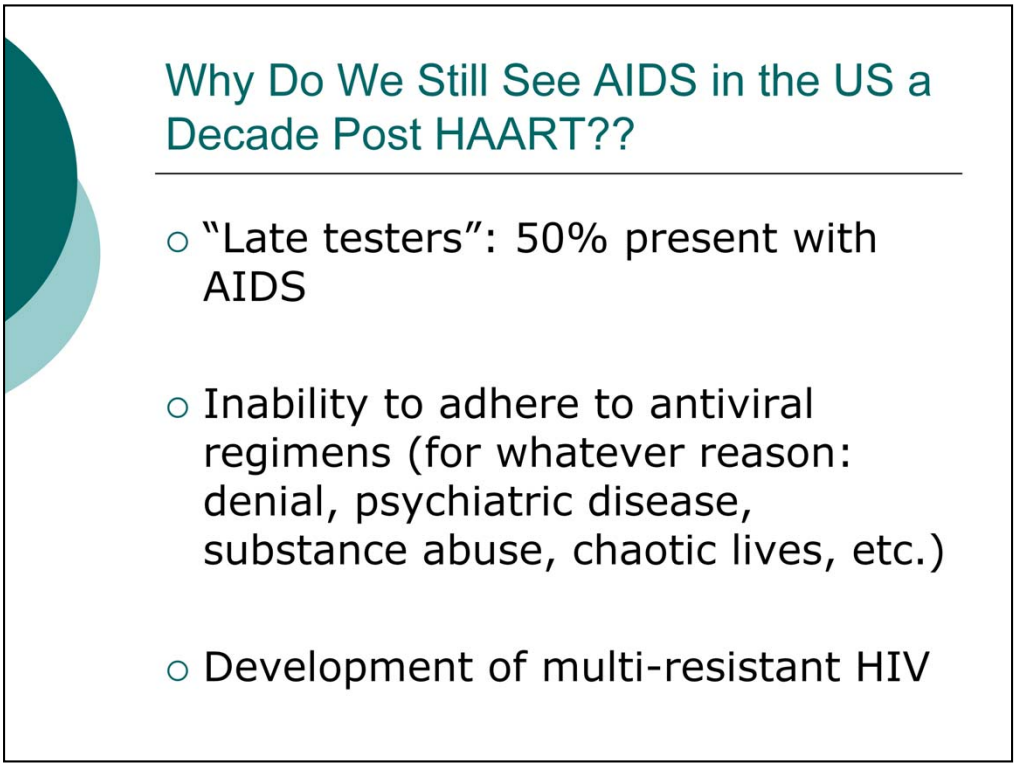
“Buffalo hump” fatty deposits



This slide also illustrates fat redistribution



CNS = central nervous system PML = viral disease characterized by progressive damage or inflammation of the white matter of the brain



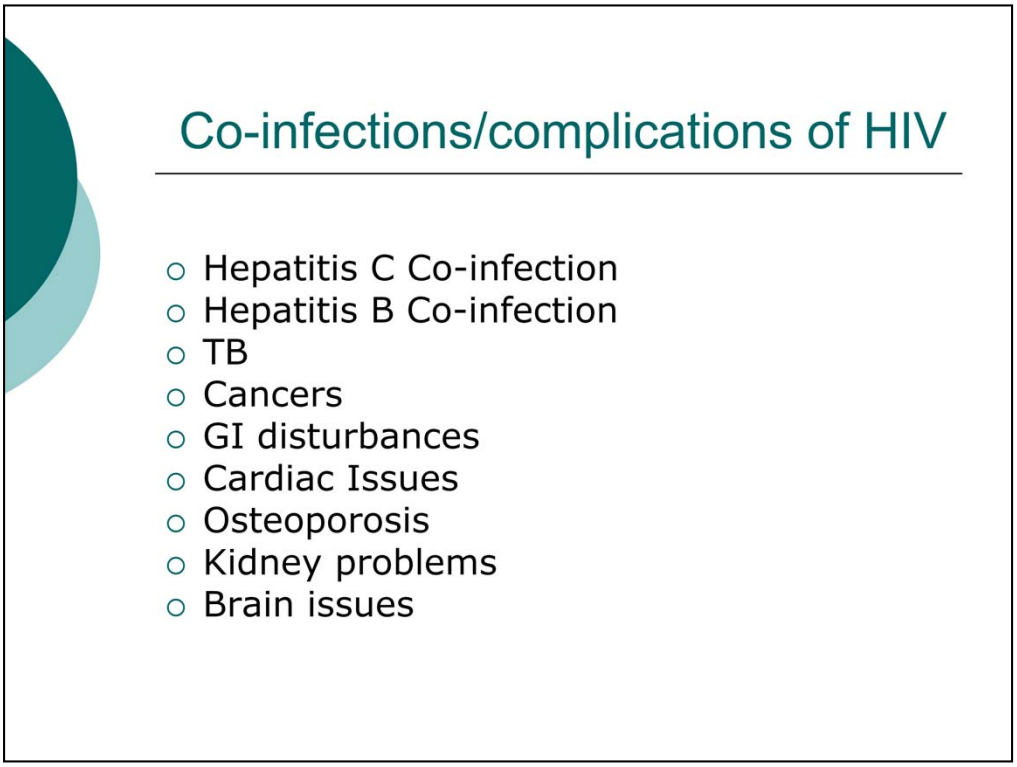
HAART = highly active antiretroviral therapy HAART involves taking 3-4 different classes of antiretroviral drugs

New Testing Guidelines

- CDC New Testing Guidelines:
  - Routine testing adults ages 13-64
  - Annual testing in those at risk
  - "Opt out" provision: implied consent vs. written informed consent
- Rapid Diagnostic Tests: 4 approved
  - "Point of care"
  - Home testing now available in drug stores: results in 30 minutes

Continuing HIV Treatment Challenges 2012

- Antivirals must be continued indefinitely
- Must be adhered to at a high level
- Requires 3 active agents
- Significant side effects may occur
- Drug interactions are common
- Drug resistance can occur if don't adhere
- Co-infections are common and complicate treatment
- Early start of therapy: first regimen is key
- Antivirals used as prevention (Truvada)
- Many new drugs: now 4 different 'start' choices



TB = tuberculosis

Biggest Challenge

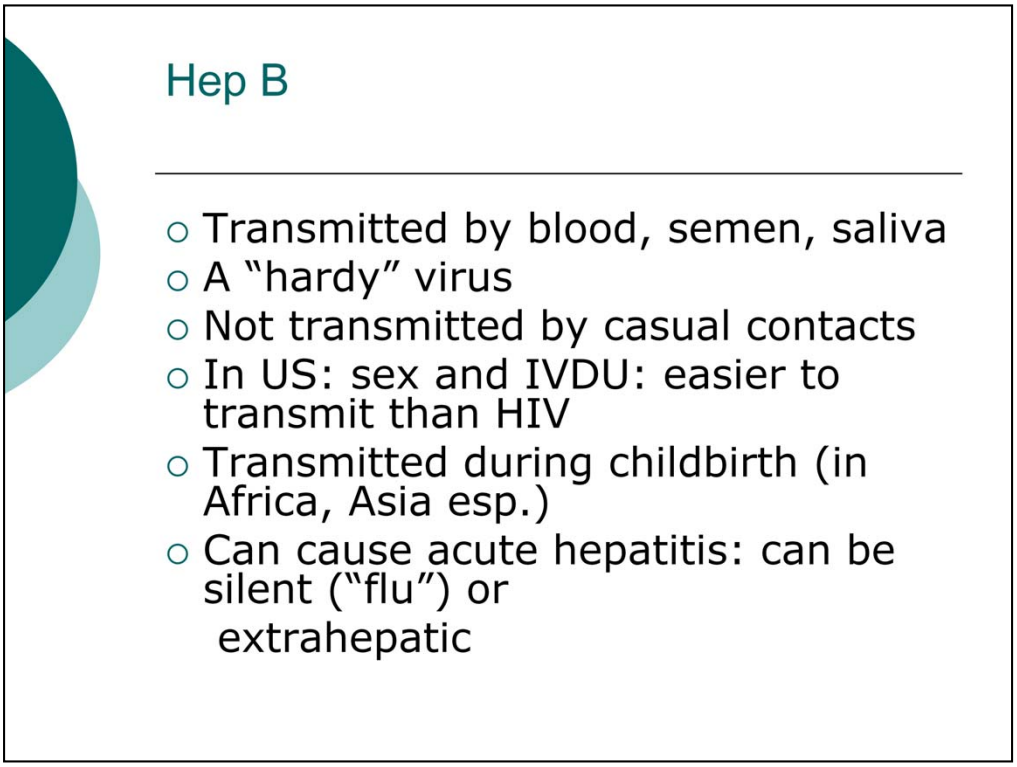
- Belief that YOU are NOT at Risk
- Therefore, NOT GETTING TESTED
- GOAL: Everyone be "Safe"
- GET TESTED

Hepatitis

- A: Virus that causes liver inflammation and damage;
  - Preventable by vaccine
- B: Virus that causes liver inflammation and damage; can last for life. Cause scarring of liver, liver cancer, liver failure, death
  - Preventable by vaccine
- C: Virus that causes inflammation of liver; identified in 1989 (before called non-A non-B)
  - NO vaccine for this

Hep A

- "Infectious" Hepatitis: very contagious
- Causes acute hepatitis
- Liver repairs itself within 6 months
- Does not cause chronic liver disease
- Can be fatal, esp in older adults
- Transmitted through person to person contact via fecal-oral route



Extrahepatic = happening outside the liver

Hep B cont'd

- Can resolve on own
- Can be chronic (failure to clear): silent
- 2% increase/year in probability will develop cirrhosis
- Increased risk of liver cancer
- Treatment can get DNA to undetectable levels

Hepatitis C

- RNA virus; after exposure, 10-20% clear the infection; rest develop chronic hep. C
- Prevalence 1.6% (4 million); 3.2 with chronic HCV
- Greatest risk factor: IVDU
- Progresses to cirrhosis 5%-25%; to liver failure 1%-7%; cause of 50% of liver cancer cases
- Co-infection with HIV: 3x rate of progression to cirrhosis, liver failure, and carcinoma
- Treatment depends on genotype, amount of inflammation and scarring
- Current treatment meds look like HIV med evolution 15 years ago

HIV, STD's, Hepatitis are Here To Stay…..

PREVENTION
of Transmission
is the ONLY WAY !!!!
Get Tested; Be Safe
Get Vaccinated; No IVDU