

A vibrant, multi-colored scanning electron micrograph (SEM) of various microorganisms. The image features a large, textured orange structure at the top left, several bright green spherical cells, and a complex network of purple and blue branching structures at the bottom. Numerous small, pinkish rod-shaped bacteria are scattered throughout the scene.

PRESCOTT'S
MICROBIOLOGY

WILEY / SHERWOOD / WOOLVERTON

EIGHTH EDITION

Human Immunodeficiency Virus (HIV)

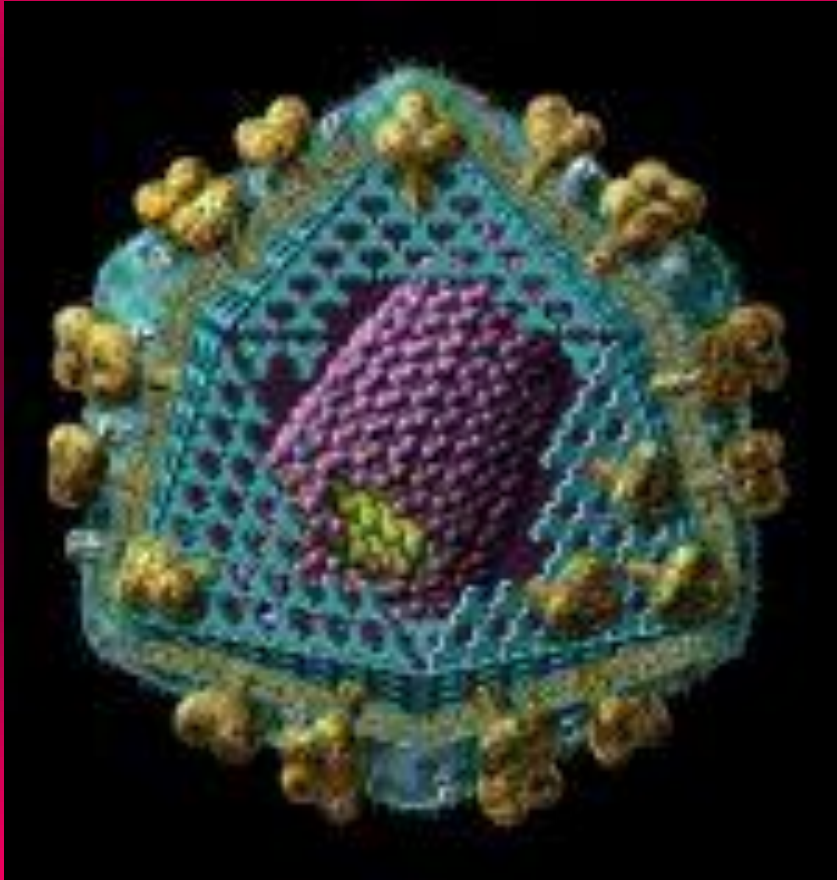
Chapter 37

Retroviridae

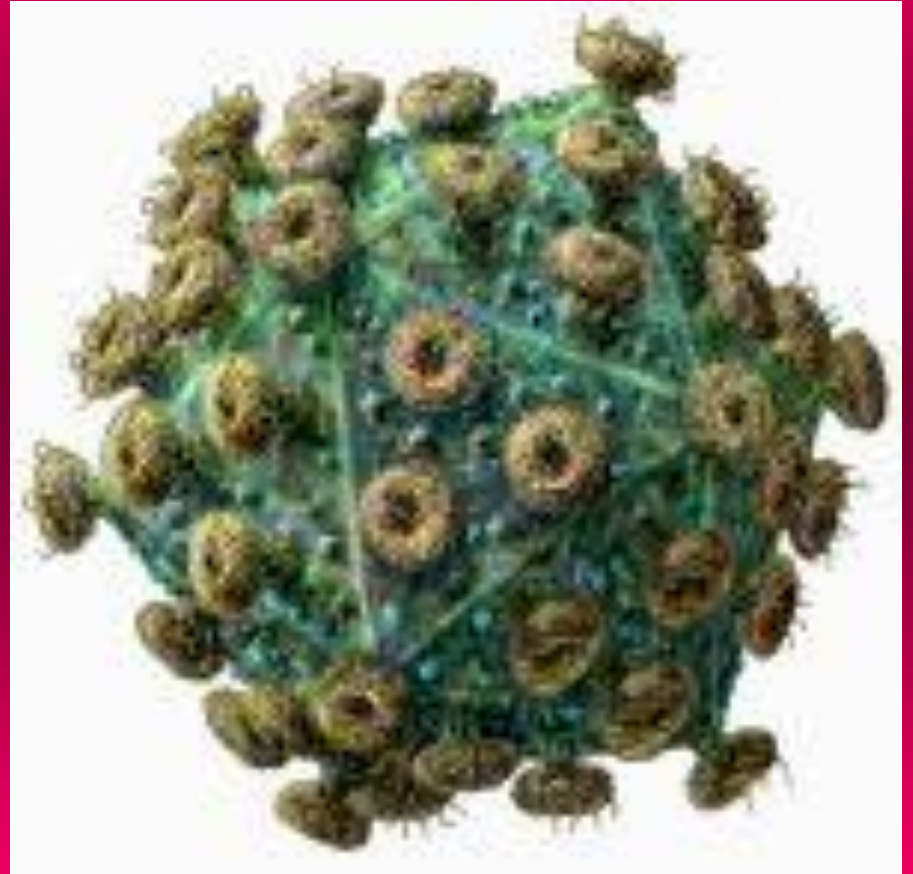
Retroviridae

- RNA
- Single Stranded
- Positive
- DNA Step in Replication
- Enveloped

Artist's Images of HIV



Cutaway Image

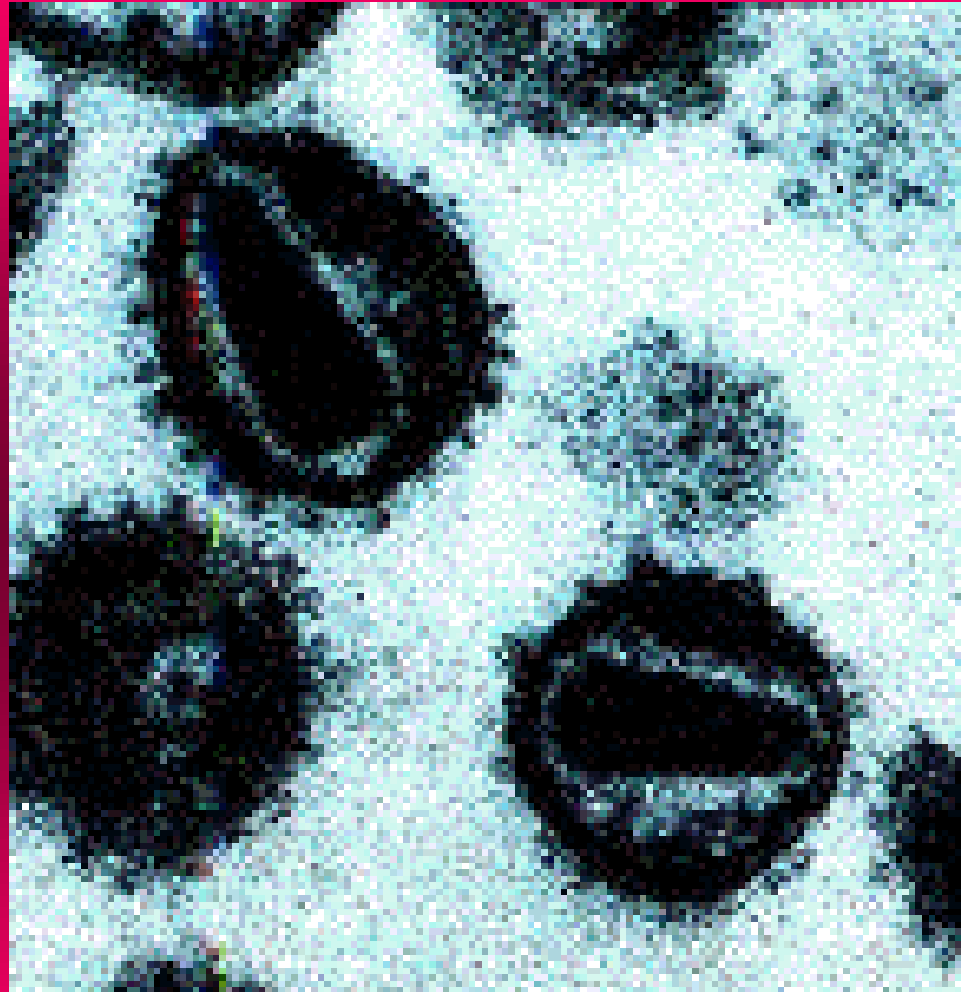


External Image

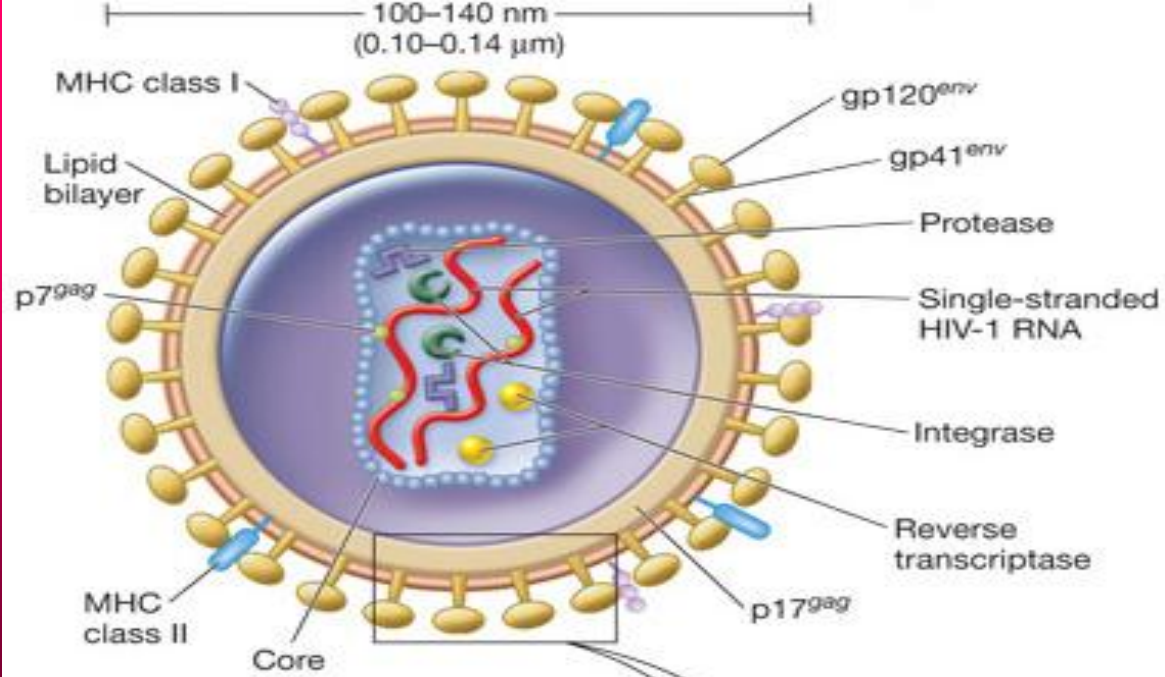
Acquired Immune Deficiency Syndrome (AIDS)

- **caused by human immunodeficiency virus (HIV)**
 - **occurs world wide, causing the great pandemic of the second half of the twentieth century**
 - **retrovirus**
 - **theories on origin of disease**
 - **HIV-1 evolved from chimp virus SIVcpz**
 - **use of human blood products in chimps infected animals with HIV-1 precursor that evolved into SIVcpz**

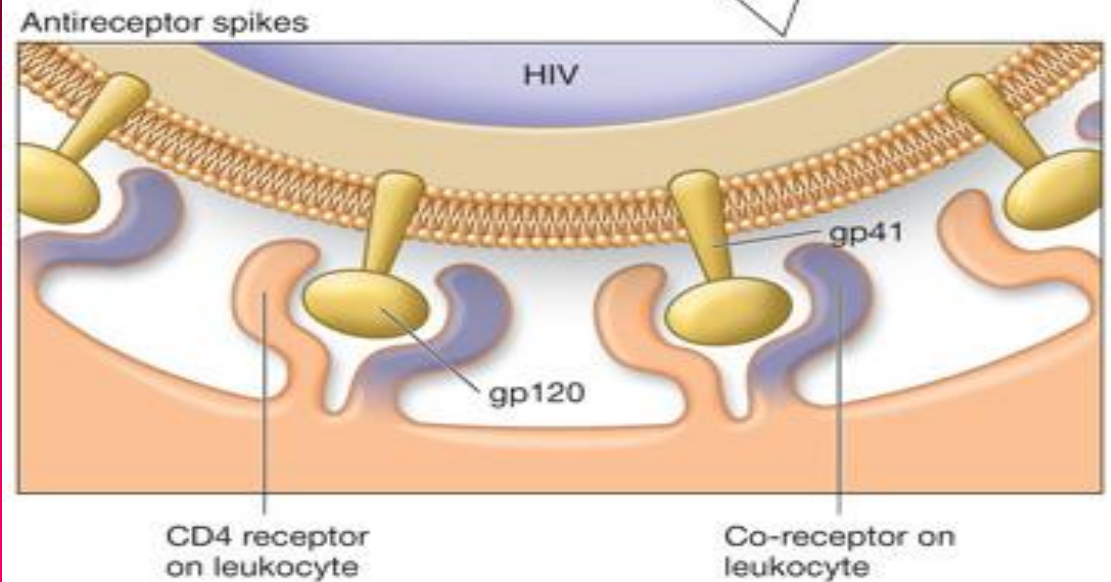
HIV



HIV video



(a) HIV virion



(b) HIV attachment to host cell

Figure 37.8

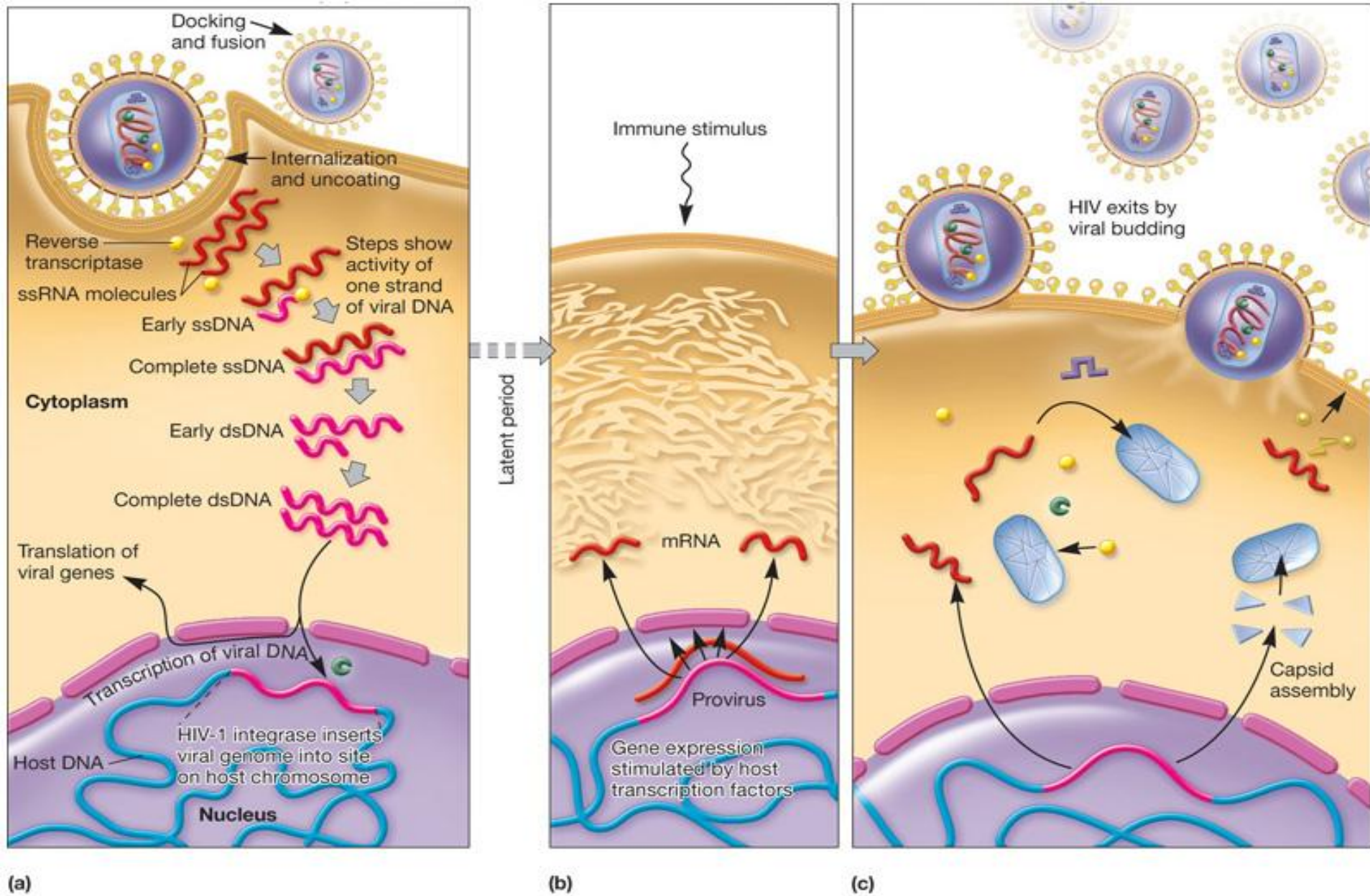
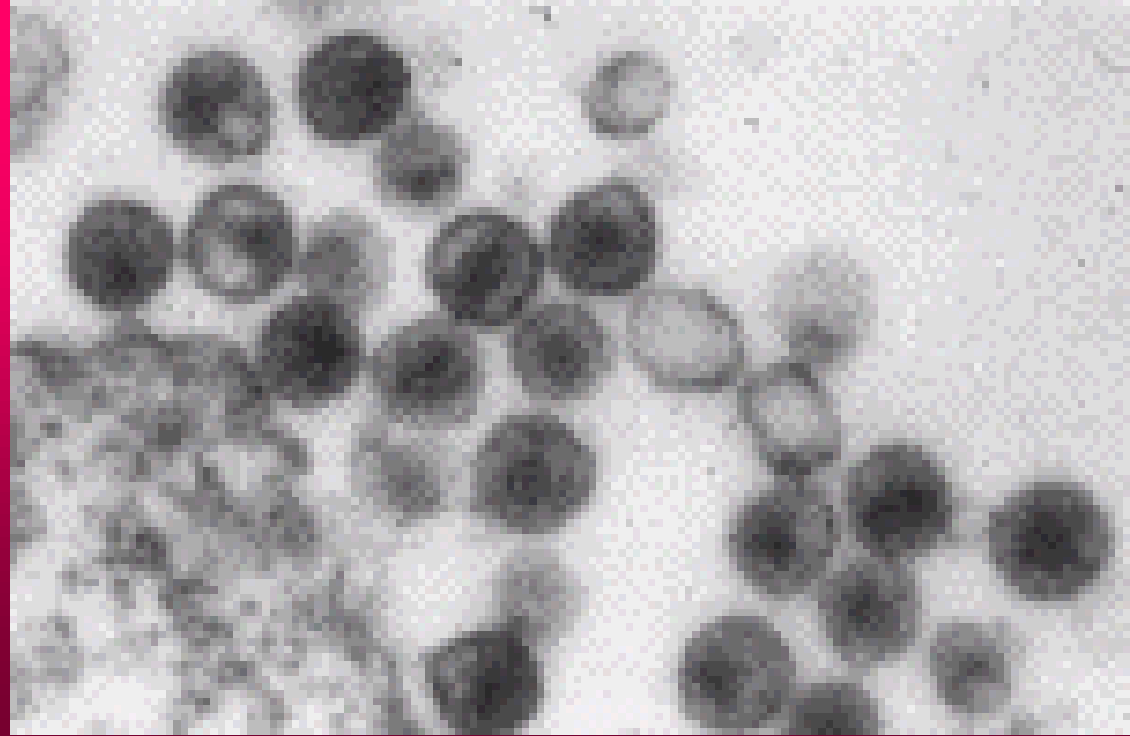


Figure 37.9

HIV replication

HIV



HIV

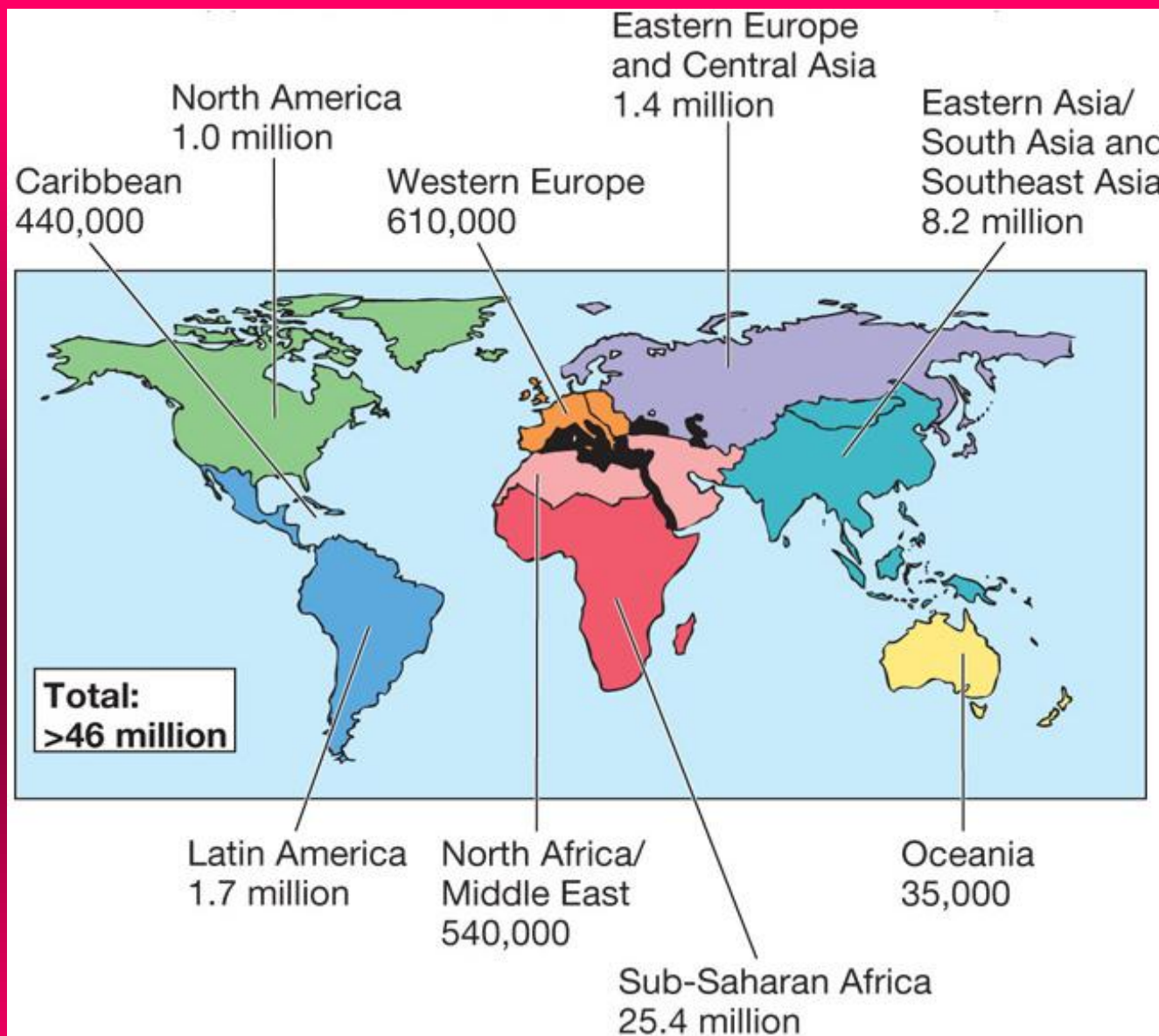


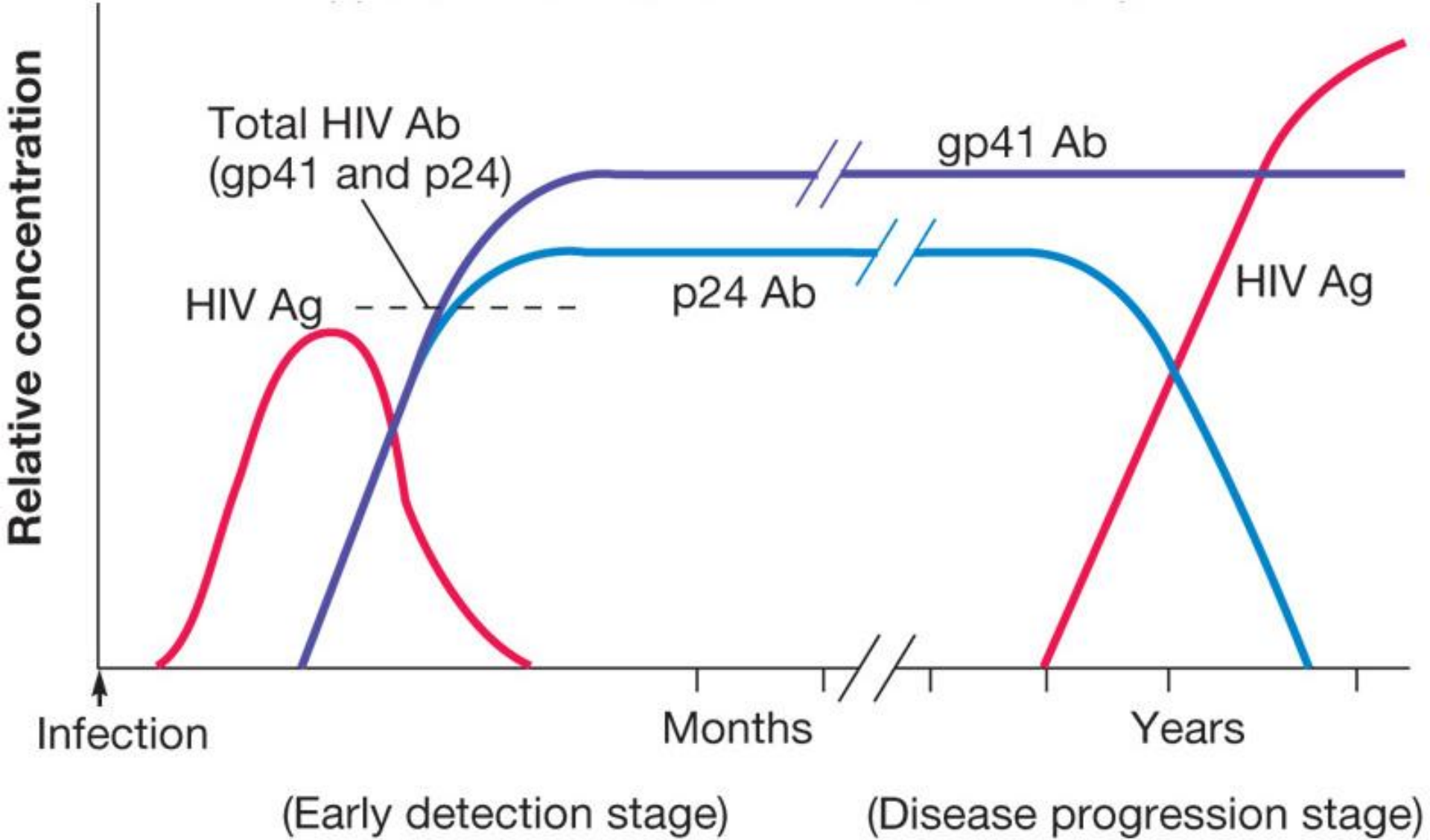
Figure 37.7

Transmission

- **acquired and can be passed from person to person**
 - **when infected blood, semen or vaginal secretions come in contact with uninfected person's broken skin or mucous membranes**

Groups Most at Risk

- **in descending order**
 - **men who have sex with other men**
 - **intravenous drug users**
 - **heterosexuals who have intercourse with drug users and prostitutes**
 - **children born of infected mothers, as well as their breast-fed infants**
 - **transfusion patients and transplant recipients**



Serological changes during infection

Figure 37.11

HIV pathogenesis

- once inside host, HIV gp120 envelope protein binds to host CD4⁺ glycoprotein plasma membrane receptor on CD4⁺ cells
- after entry into host cells, viral RNA is reverse transcribed into DNA, then second strand of DNA is synthesized to produce **proviral DNA**
 - integrates into host cell's DNA as a provirus which can remain latent or, alternatively, can direct synthesis of viral RNA → synthesis of new viral particles

HIV pathogenesis

- involves depletion of T cells, possibly by:
 - disruption of plasma membrane permeability
 - destruction by immune system cells due to presence of gp120 in membrane
 - syncytia formation
 - integration and transposition of HIV provirus
 - apoptosis
- may cause disruption of balance between different T cell populations
- may destroy or disable dendritic cells
- HIV mutates rapidly, so that it evades immune system

apoptosis

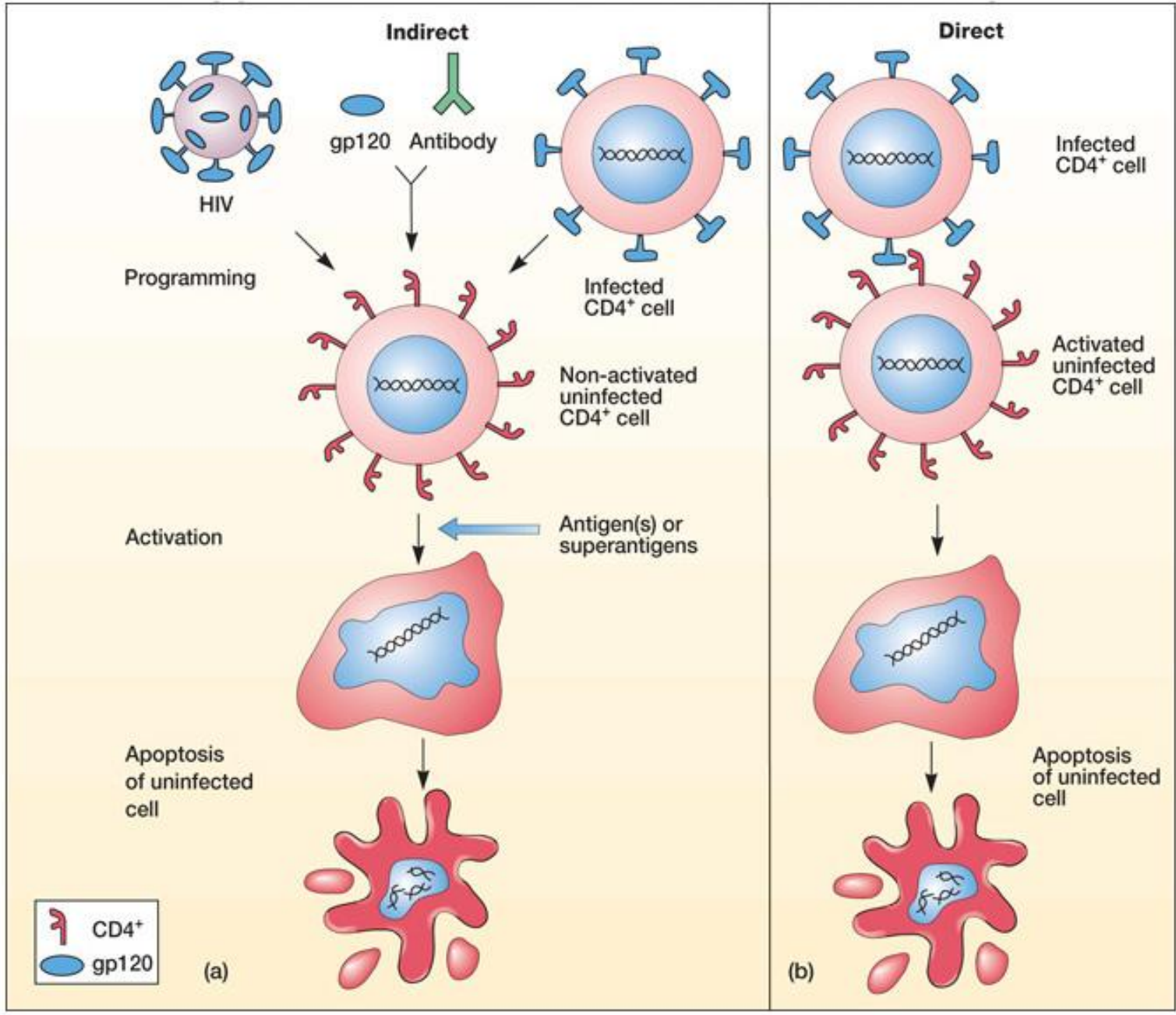


Figure 37.12

Clinical manifestations

- four types of pathological changes
 - AIDS-related complex (ARC)
 - AIDS
 - central nervous system disease
 - AIDS-related cancers

ARC

- fever, malaise, headaches, macular rash, weight loss, lymph node enlargement, oral candidiasis, and presence of antibodies to HIV
- occurs in first few months after infection; lasts 1 to 3 weeks
- can develop to full-blown AIDS

AIDS

- progressive destruction of CD4+ cells leads to collapse of immune system
- patient susceptible to opportunistic infections

Course of Disease

- **some patients rapidly develop clinical AIDS; die within 2-3 years**
- **some patients remain relatively healthy for at least 10 years post infection**
- **in majority of patients HIV infection progresses to AIDS in 8-10 years**

CDC Classification System for Stages of HIV-Related Conditions

- **acute**
 - 2-8 weeks after infection
 - most individuals experience a brief illness called acute retroviral syndrome
 - rapid multiplication and dissemination of virus throughout body
 - stimulation of immune response
- **asymptomatic**
 - may last from 6 months to 10 or more years
 - levels of detectable HIV in blood decrease, although viral replication continues
 - effects on immune functions may occur

CDC Classification System for Stages of HIV-Related Conditions

- chronic symptomatic
 - formerly called AIDS-related complex or ARC
 - can last for months to years
 - viral replication continues
 - numbers of CD4⁺ cells in blood significantly decrease
 - results in patients developing a variety of illnesses often caused by opportunistic pathogens

CD4⁺ T Cell Depletion by HIV

- possible mechanisms
 - direct cytopathic effects of HIV on T cells
 - formation of syncytia
 - immune-mediated destruction of HIV-infected cells
 - effects of viral products (e.g., gp120) on uninfected cells

Other Mechanisms for CD4 + T Cell Depletion by HIV

- free gp120 proteins released from infected cells may bind to CD4 on uninfected cells inducing them to undergo apoptosis
- immune system components may contribute to continuing destruction of virus-infected CD4+ cells
- HIV may inhibit or destroy dendritic cells
- rapid mutation rate of virus may overwhelm immune system
- may alter immune system integrity by disrupting balance between various T cell phenotypes

Back to CDC Classification System for Stages of HIV-Related Conditions

- **AIDS – fourth and last stage**
 - immune system no longer able to defend against virus
- **definition of AIDS**
 - all HIV-infected individuals who has fewer than 200 CD4⁺ T cells/microliter of blood or a CD4⁺ cell percentage of lymphocytes of less than 14

Table 37.3

Disease Processes Associated with AIDS

Candidiasis of bronchi, trachea, or lungs
Candidiasis, esophageal
Cervical cancer, invasive
Coccidioidomycosis, disseminated or extrapulmonary
Cryptosporidiosis, chronic intestinal (>1 month's duration)
<i>Cyclospora</i> , diarrheal disease
Cytomegalovirus disease (other than liver, spleen, or lymph nodes)
Cytomegalovirus retinitis (with loss of vision)
Encephalopathy, HIV-related
Herpes simplex: chronic ulcer(s) (>1 month's duration); or bronchitis, pneumonitis, or esophagitis
Histoplasmosis, disseminated or extrapulmonary
Isosporiasis, chronic intestinal (>1 month's duration)
Kaposi's sarcoma
Lymphoma, Burkitt's (or equivalent term)
Lymphoma, immunoblastic (or equivalent term)
Lymphoma, primary, of brain
<i>Mycobacterium avium</i> complex or <i>M. kansasii</i>
<i>Mycobacterium tuberculosis</i> , any site
<i>Mycobacterium</i> , other species or unidentified species
<i>Pneumocystis pneumonia</i>
Pneumonia, recurrent
Progressive multifocal leukoencephalopathy
<i>Salmonella</i> septicemia, recurrent
Toxoplasmosis of brain
Wasting syndrome due to AIDS

Source: Data from MMWR 41 (No. RR17). 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults.

Table 37.3

Central nervous system disease caused by HIV

- **headaches, fever, subtle cognitive changes, abnormal reflexes, and ataxia**
- **dementia and severe sensory and motor changes observed in advanced cases**
- **autoimmune neuropathies, cerebrovascular disease, and brain tumors are common**

AIDS-related cancers

- **Kaposi's sarcoma**
 - **caused by human herpesvirus 8**
- **carcinoma of mouth and rectum**
- **B-cell lymphomas**

AIDS Associated Diseases

Thrush

Candida albicans

Karposi's sarcoma

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(a)



(b)

Diagnosis

- **viral isolation and culture**
- **assays for reverse transcriptase activity or viral antigens**
- **most commonly done by detection of specific anti-HIV antibodies in the blood**
 - **routine screening tests use ELISA assays which have many false positive results which are retested using western blot technique**
- **most sensitive test uses polymerase chain reaction**

Treatment

- **no cure for AIDS**
- **treatment directed at reducing viral load, disease symptoms, and treating disease and malignancies**
- **most successful treatment involves a combination of drugs**

Treatment

Antivirals used

- **nucleoside reverse transcriptase inhibitors, e.g., AZT**
- **nonnucleoside reverse transcriptase inhibitors, e.g., delavirdine**
- **protease inhibitors, e.g., indinavir**
- **fusion inhibitors (FIs) – prevent entry of HIV into cells, e.g., enfuvirtide**

Prevention and control

- **achieved primarily through education**
- **barrier protection from blood and body fluids**
- **not sharing intravenous needs or syringes**
- **continued screening of blood and blood products**

Vaccine

- **not available**
- **ideal vaccine**
 - **would stimulate the production of neutralizing antibodies which would bind to virus preventing it from entering host cells**
 - **promote formation of cytotoxic T cells capable of destroying cells infected with virus**
- **problems with development of vaccine**
 - **envelope proteins of virus continually change their antigenic properties**

Long Term Nonprogressors

- **HIV-infected people who**
 - maintain CD⁺ T cell counts of at least 600 cells/ μ l of blood
 - have <5,000 copies of HIV RNA/ml of blood
 - have remained this way for > 10 years after documented infection
- **explanations of phenomena**
 - effective immune response to relatively conserved proteins
 - initial infection was with attenuated strain
 - predisposing genetic differences