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### General Principles of Virology

- Viral replication
  - > A virus cannot replicate on its own.
  - > It must attach to and enter a host cell.
  - > It then uses the host cell's energy to synthesize protein, DNA, and RNA.

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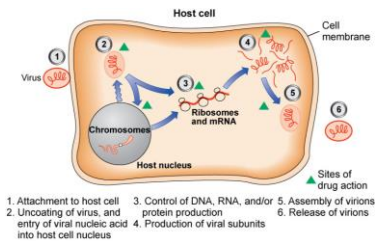
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### Virus replication



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## General Principles of Virology (Cont.)

- Viruses are difficult to kill because they live inside the cells.
  - Any drug that kills a virus may also kill cells.

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### Case Study



(iStockphoto/Thinkstock)

- A.O. is a 20-year old Hispanic male college student who comes to the student health center complaining of pain on urination.
- His urine test is positive for *Neisseria gonorrhoea*.
- What should you do?

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### Case Study



(iStockphoto/Thinkstock)

- A.O. informs you he has been sexually active since age 15 with both males and females.
- He has had intercourse with 3 people in the last month and doesn't use protection.

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### Case Study



- A.O. tells you he drinks at weekend parties and has smoked pot but “not recently.”
- He reports no regular use of injection drugs, tobacco, or anabolic steroids but that sometimes he gets so drunk he doesn’t remember.
- How would you rate his risk and why?
- What would you teach A.O?

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### Case Study



- A.O. says he will not be abstinent but is willing to use a condom during contact sex.

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### Case Study



- As you talk to A.O. about barrier methods of protection, he begins to look away and seems to lose interest.
- He finally says, “I don’t know if I can do this.”
- What are some cultural considerations that may be a factor here?

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### Case Study



- A.O. tells you he “really cares” about one of his partners.
- What do you tell him about informing his previous sexual partners about his gonorrhea?
- What should he tell them about the HIV infection if he tests positive?

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### Diagnostic Studies

- Most useful screening tests detect HIV-specific antibodies and/or antigens
  - May take several weeks to detect antibodies (*window period*)
  - Performed using blood or saliva
  - Combination (4<sup>th</sup> generation) tests can detect HIV earlier

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### Case Study continued

- A.O. HIV RNA viral level was positive for the virus
- CD4 Lymphocyte count was 583 mm/3
- Zidovudine was started and to follow up with PCP in 1 week.

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### What is HIV?

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### Transmission of HIV

- HIV can be transmitted through contact with certain body fluids
  - Blood, semen, vaginal secretions, and breast milk
- HIV is not spread through casual contact

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### Pathophysiology of HIV

- HIV is a ribonucleic acid virus
  - Called retroviruses because they replicate in a "backward" manner going from RNA to DNA
  - CD<sub>4</sub>+T cell is the target cell for HIV
    - Type of lymphocyte
    - HIV binds to the cell through fusion

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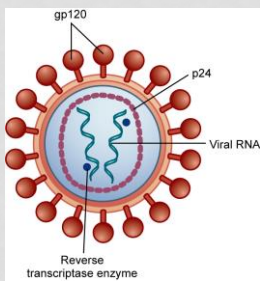
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### Components of HIV



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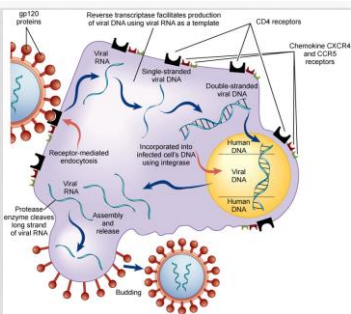
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### HIV Proteins Bind to Cell



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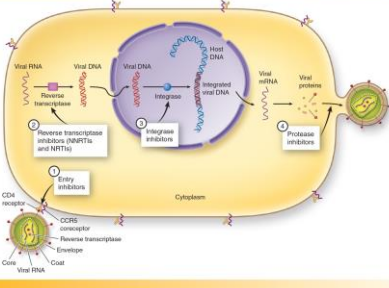
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### PHARMACOTHERAPY ILLUSTRATED

#### 36.1 Replication of HIV



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### Consequences of Integrase

1. Newly formed double-stranded DNA is infected with HIV because all genetic material is replicated during cell division
2. Viral DNA in genome directs cell to make new HIV

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### Continued

- 5 years later A.O. comes to the clinic with a temperature 103, non-productive cough and dyspnea which has progressively worsened over the last week.
- NKDA
- The patient said he was placed on Zidovudine but stopped taking it after 6 months and has not followed up with HCP.

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### Assessment

- He has anorexia and lost 40 pounds over 3 months
- He is pale, diaphoretic, and in acute respiratory distress
- He is alert and oriented x3
- Pulse 96, RR 30, 110/70
- Lungs reveal bi-base crackles 2/3 of the way up to the posterior lung field.
- ABD. Non-tender, no enlargement of spleen or liver

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### Question

- Why do you think A.O. stopped taking his medicine?
- What would be important for the nurse to assess?
- What went wrong with his care at the time of diagnosis?
- How has this impacted A.O. now?

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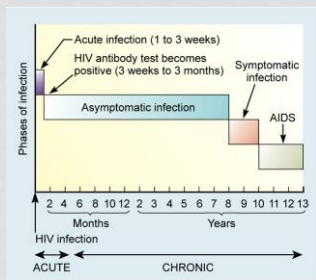
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### Timeline for Untreated HIV Infection



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### Drug Therapy

- Main goals
  - Decrease viral load
  - Maintain/increase CD<sub>4</sub>+T counts
  - Prevent HIV-related symptoms and opportunistic diseases
  - Delay disease progression
  - Prevent HIV transmission

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### Continued

- Dr sent the patient to be admitted to hospital.
- CXR, ABGS were ordered
- Sputum specimen per respiratory
- CBC , CMP, CD<sub>4</sub> and HIV RNA level was ordered stat.
- What should the nurse be worried about?

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### Medication orders

- Dr. ordered trimethoprim/Sulfamethoxazole IV
- And prednisone 40 mg by mouth twice a day
- Why are these ordered?
- What about prophylaxis?

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### *Pneumocystis jiroveci* Pneumonia



(From the Centers for Disease Control and Prevention. Courtesy Jonathan W.M. Gold, MD, New York.)

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### LABS

- CD4 183 mm/3
- HIV RNA LEVEL 234,000 COPIES/ML
- Induced sputum pneumocystis jrovecii

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### Pathophysiology of HIV

- Immune problems start when CD4+ T cell counts drop to < 500 cells/μL
  - Severe problems develop when < 200 CD4+ T cells/μL
  - Normal range is 800 to 1200 cells/μL
- Insufficient immune response allows for opportunistic diseases

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### CD4 Count

- **CD4-** Cells are also called **T-cells**- they alert the immune system to invading bacteria and viruses.
- **Infection lowers CD4 counts**; the lower the count means the more weakened the immune system and predicts the likelihood of opportunistic disease.
- A normal CD4 count ranges from **800-1200 cells/mm3**
- A **count less than 200 cells/mm3** qualifies an **AIDS diagnosis**
- Current **treatment guidelines recommend that therapy** should be initiated in everyone living with HIV at any CD4 cell count.

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## Viral load

- **Viral load**- is the best gauge of the level of HIV in body. According to the U.S. Department of Health and Human Services (HRSA) the lowest levels of detectable viral load are about 40-75 copies/mL.
- **Low viral load**- lower amount of HIV activity
- Is determined by **measuring the amount of HIV RNA** in the **blood**. The **HIV RNA level is an estimate of how rapidly the virus is replicating** and is considered a more accurate predictor of clinical outcome than CD4 counts.
- These tests are performed **every 3-6 months** to assess the **degree of effectiveness of antiretroviral therapy**
- The **GOAL** of antiretroviral therapy is to **reduce plasma HIV RNA to less than 75 copies /mL**
- **A viral load of less than 50 copies/ml is undetectable and a primary goal of antiretroviral therapy.**\*\*\*\*

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### Clinical Manifestations and Complications

- **Asymptomatic Infection**
  - Left untreated, a diagnosis of AIDS is made about 10 years after initial HIV infection
  - Symptoms are generally absent or vague
  - High risk behaviors may continue

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### Clinical Manifestations and Complications

- **Symptomatic Infection**
  - CD4+ T cells decline closer to 200 cells/ $\mu$ L
  - Symptoms become worse
  - HIV advances to a more active stage

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What is this? The nurse assess A.O and observes this?



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What is this?



From: Freeman-Konig, MD. Color atlas of AIDS. Philadelphia, 1989. Saunders. Copyright © 2017, Elsevier Inc. All Rights Reserved.

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What is this?



For information on this and other conditions, visit our website at www.elsevier.com/locate/9780323750000. Copyright © 2017, Elsevier Inc. All Rights Reserved.

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## Clinical Manifestations and Complications

- **AIDS**
  - Diagnostic criteria is established by CDC
  - Immune system severely compromised
    - Infections
    - Malignancies
    - Wasting
    - HIV-related cognitive changes

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## Laboratory Studies

HIV progression is monitored by

1. **CD4+ T-cell counts**
  - CD4+ T-cell count provides a marker of immune function
2. **Viral load**
  - The lower the viral load the less active the disease

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## Diagnostic Studies

- **Abnormal blood tests are common**
  - Caused by HIV, opportunistic diseases, or complications of therapy
    - Decreased WBC counts
    - Low platelet counts
    - Anemia is associated with ART
    - Altered liver function

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### Diagnostic Studies

- Resistance tests can help determine if a patient is resistant to ART
- Assays help HCPs know which medications may be effective
  - Genotype assay
  - Phenotype assay

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### Safety Alert

- Drug interactions
  - Herbal therapies
    - St. John's wort
  - Commonly used drugs
  - OTC drugs
    - Antacids, proton pump inhibitors, supplements

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### Drug Therapy

- Opportunistic diseases complicate management of HIV infection
  - Prevention is key
  - Onset can be delayed with adequate measures
  - Effective management has significantly increased life expectancy

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### Reducing the Risk of Transmission to Health Care Providers

- Standard precautions
- Hand hygiene
- Post exposure prophylaxis
  - Antiretroviral medications within 72 hours of exposure
  - 2 to 3 drugs prescribed for 28 days

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### Nursing Management Planning

- Goals for care are aimed at
  - Compliance with drug regimens
  - Adopting a healthy lifestyle
  - Keep current with vaccines
  - Beneficial relationships
  - Spiritual well-being in regard to life and death
  - Coping with the disease and its treatment

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### Health Promotion

- Prevention of HIV
  - Decreasing risk: Work
    - Adhere to precautions and safety measures to avoid exposure
    - Report all exposures for timely treatment and counseling
    - Post-exposure prophylaxis with combination ART can significantly decrease risk of infection

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### Acute Exacerbations

- HIV infection
  - Has no cure
  - Continues for life
  - Causes physical disability
  - Impairs social, emotional, economic, and spiritual wellbeing
  - Ultimately leads to death

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### Disease and Drug Side Effects

- Common physical problems
  - Anxiety, fear, depression
  - Diarrhea
  - Peripheral neuropathy
  - Pain
  - Nausea/vomiting
  - Fatigue
  - Rash
  - Headache
  - Difficulty sleeping

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### Metabolic Disorders that occurs as part of the disease and medications for HIV

- Lipodystrophy
- Hyperlipidemia
- Insulin resistance
- Hyperglycemia
- Bone disease
- Lactic acidosis
- Renal disease
- Cardiovascular disease

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## Lipodystrophy



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## Pharmacology for treatment of HIV-AIDS

- **HAART( Highly active antiretroviral therapy)**
- **Goal: Reduce the plasma HIV RNA to its lowest possible level.**
- **HIV is harbored in locations other than the blood, such as lymph nodes.** Therefore, elimination of virus from the blood is not a cure.
- **Simultaneous use of drugs from several classes reduces the probability that HIV will become resistant to treatment.**
- **Antiretroviral therapy must be continued for a lifetime.**

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## Pharmacology and Pharm. Classifications

- **Nucleoside Reverse Transcriptase Inhibitors-** Blocks activity of enzyme reverse transcriptase. **Abacavir**
- **Nonnucleoside Reverse Transcriptase Inhibitors**  
**Efavirenz**
- **Protease Inhibitors-** Inhibits protease retroviral enzyme.  
**Darunavir**
- **Entry inhibitors/ HIV Fusion Inhibitors** (includes fusion inhibitors and CCR5 antagonists) Suppresses the fusion process whereby a virion is attached to the outer membrane of a host T cell before entry into the cell and subsequent viral replication (**Enfuvirtide**)
- **Integrase inhibitors- New class** Inhibits integrase enzyme-preventing integration of proviral gene into human DNA.  
Raltegravir

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### Nucleotide Reverse Transcriptase Inhibitors- Abacair

- Adverse effects
- Lactic Acidosis
- Hepatomegaly with Steatosis
- Hypersensitivity Reactions (5-8%) usually develop first 6 weeks of tx can be fatal. Genetic variation HLA-B\*570 strongly associated with reaction,. If they have the genetic variation- SHOULD NOT TAKE THE DRUG
- MI- Screen pt for CAD
- Other: fatigue, headache lipodystrophy

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### NON-NUCLEOSIDE REVERSE INHIBITORS -EFAVIRENZ

- Only NNRTI as a preferred agent for treating HIV
- Has a long half life and can be given daily
- Crosses blood brain barrier, can reduce HIV levels in CNS
- Main drawbacks: Teratogenicity (fetal malfunctions) and CNS adverse effects
- CNS (50%): Dizziness, insomnia, drowsiness, vivid dreams
- Rash+ can be mild to severe desquamation
- Can also cause liver damage

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### Protease Inhibitor Darunavir

Adverse Effects:

- Hyperglycemia/Diabetes
- Lipodystrophy
- Hyperlipidemia
- Increased bleeding with pts with hemophilia
- Liver damage
- Decreased cardiac conduction

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### Integrase Strand Inhibitors- Raltegravir

- Adverse effects:
- Generally well tolerated
- Most common is elevated liver enzymes (10%)
- Elevated pancreatic enzymes ( 4-5%)
- Rarely skin hypersensitivity reactions but Steven-Johnson Syndrome can occur
- Teach patient to report any measles like rash with blisters

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### HIV FUSION INHIBITORS- ENFUVIRTIDE

- OR Entry blockers
- Only Entry blocker approved by FDA
- Dosing requires twice daily (subq)
- Expensive
- Adverse effects:
- Injection- Site Reactions
- Pnumonia
- Hypersensitivity Reactions

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### CCR5 ANTAGONIST MARAVIROC

- CCR5- is a co-receptor that some strains of HIV must bind with to enter CD4 cells.
- Binds with CCR5 and blocks viral entry
- Used to treat patients 16 years and older
- Adverse effects:
- Cough
- Dizziness
- Pyrexia
- Rash
- Abd. Pain
- Musculoskeletal symptoms
- URI
- Liver injury

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### Lifespan

- Antiretroviral therapy is recommended for all HIV pregnant woman to lower viral load and prevent perinatal transmission,
- Look for Category B Drugs
- Breast feeding should be avoided-danger of transmitting virus to infant.

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### Nursing Implications

- Before beginning therapy, thoroughly assess underlying disease and medical history, including allergies.
- Assess baseline vital signs and nutritional status.
- Assess for contraindications, conditions that may indicate cautious use, and potential drug interactions.

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