HIV / AIDS

Acquired Immunodeficiency Syndrome (_____)

- 1981: In United States, cluster of *Pneumocystis* and Kaposi's sarcoma in young homosexual men discovered. The men showed loss of immune function.
- 1983: HIV discovered by Luc Montagnier, Pasteur Institute, Paris, France

The Origin of AIDS

- Crossed the species barrier into humans in Africa in the 1930s.
- Patient who died in 1959 in Congo is the oldest known case.
- Spread in Africa as a result of urbanization.
- Spread world-wide through modern transportation and unsafe sexual practices.
- Norwegian sailor who died in 1976 is the first known case in Western world.

- Controversial, especially since believed to originate in Africa
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- probably no more than 50 yrs existent as we know it?
- 3 possible origins:
- 1. man-made, biological warfare creation
- 2. originated in animal, then crossed over to humans (probably from monkeys)
- 3. has existed in small human pops. (with or without causing disease) for long time but due to right conditions (?) has escaped to larger pops.
- whatever origin, studies of SIV suggest HIV evolved over last 100 yrs
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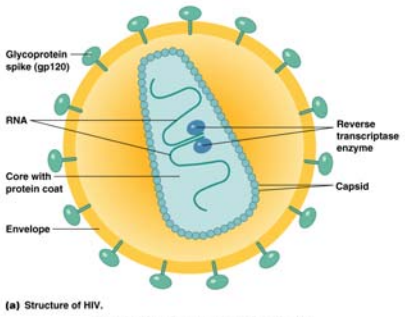
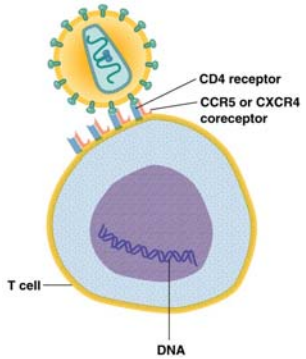
Characteristics of HIV



- lipid membrane envelope (protein spikes gp 160)
- 2 copies of its RNA genome - consisting of at least 9 genes
- proteins: reverse transcriptase – (_____) copies RNA → DNA
- integrase - (_____) inserts HIV DNA into host chromosome
- protease -
- HIV genetically similar SIV (simian immunodeficiency virus)

Life Cycle



- attachment - gp160 attaches to T-helper cell (T4, CD4 cell) via CD4 cell surface receptor + either CCR5, or CXCR4 (fusin -membrane fusion and penetration)
- uncoating
- ssRNA →
- dsDNA → nucleus, circularizes and integrates into host chromosome =
- viral transcription and protein synthesis
- assembly - core proteins cleaved, RNA packaged into virions
- release - budding, takes part of cell membrane →
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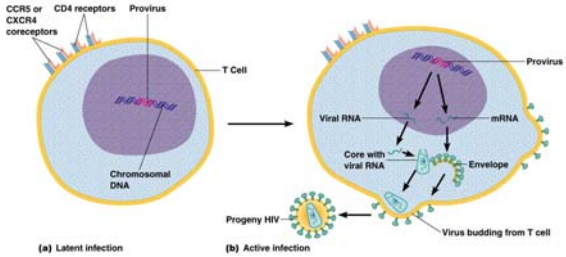

- upon integration, host cell infected for its life

- HIV can hide in lymph nodes where it can continuously infect T cells without exposing itself to bloodstream
- HIV infects T4 lymphocytes, monocytes and macrophages – all have CD4 receptors (other cell types are also infected)

- monocytes and macrophages serve as HIV reservoirs
- T4 cell depletion → immune system suppression/deficiency
- host vulnerable to opportunistic infections, cancers—T4 helper cell no can no longer stimulate macrophages, cytotoxic T cells, or B cells
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- Host Abs are produced against HIV but Abs do not confer resistance. Why?
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- HIV doesn't have to re-enter bloodstream
- HIV's mutation rate constantly producing new antigenic variants

Implications of High HIV Replication Rate

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- HIV can undergo up to 5000 replication cycles (generations) over 10 years producing up to 10^{13}

- every mutation that can occur does occur

- immune system cannot keep up
- mono-drug therapy won't work because potentially resistant mutants will exist for any drug used, therefore, multi-drug (combination) therapy required
- antigenic variation makes vaccine development difficult, regardless, a vaccine must generate an immune response that can stop HIV before it enters a cell

The Stages of HIV Infection

- Category A: Asymptomatic or persistent lymphadenopathy (_____)
- Category B: Persistent *Candida albicans* infections
- Category C: Clinical AIDS. CMV, TB, *Pneumocystis*, toxoplasmosis, and Kaposi's sarcoma

HIV Transmission

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- HIV survives less than 1.5 days inside a cell (it completes its life cycle in that time)
- Infected body fluids transmit HIV via
  - Unprotected sexual intercourse (_____)
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  - Transplacental infection of fetus
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  - Organ transplants & blood transfusions
  - Artificial insemination

Transmission and Susceptibility

- HIV does not discriminate among age, race, gender or socioeconomic status—all are susceptible – almost
- originally it was believed that no one was immune
- in fact, there appears to be a small population of humans naturally resistant to HIV infection
- these people have mutation in gene that codes for CCR5 receptor

- homozygous mutants currently are completely resistant to the strain of HIV in US and Europe
- heterozygotes are less susceptible, progression is slower
- so far mutant gene found only in whites of European descent
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- Why would such a mutation exist in the first place?

AIDS Worldwide

- United States, Canada, western Europe, Australia, northern Africa, and South America
  - Injecting drug use and male-to-male sexual contact.
- Sub-Saharan Africa
  -
- Eastern Europe, Middles East, and Asia
  - Injecting drug use, heterosexual contact.

Clades

- HIV-1 is the most common. It has 11 clades:
  - 90% of U.S. infections caused by clade B.
  - Clade C predominates in sub-Saharan African.
  - Clades B, C, and E are in south and southeast Asia.

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- Clade = a group of organisms comprising a single common ancestor and all the descendants of that ancestor

Prevention of AIDS

- HIV/AIDS is entirely preventable.

- How?

- Use of condoms and sterile needles.
- Health care workers use Universal Precautions
  - Wear gloves, gowns, masks, and goggles.
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  - Risk of infection from infected needle-stick injury is 0.3%.

Vaccine Difficulties

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- Clades
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- Infected cells not susceptible to cytotoxic T cells
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- Latent viruses

Chemotherapy

- Nucleotide reverse transcriptase inhibitors.
- Non-nucleoside reverse transcriptase inhibitors.
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Study Objectives

1. HIV was discovered by whom and when?

2. Describe the 3 possible origins of HIV and which one is most likely?

3. Define: pandemic

4. What 3 proteins does HIV bring with it and what are their functions?

5. In general, describe the life cycle of HIV.

6. What are the primary cell types infected with HIV? Why are these cells susceptible to infection?

7. How is HIV transmitted and is anyone resistant?

8. How can HIV be prevented?

9. How can HIV be treated?