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AIDS

It is a disease caused by the retrovirus Human Immuno Deficiency Virus (HIV) and characterized by immunosuppression that leads to opportunistic infections, secondary neoplasms and neurologic manifestations.

Epidemeiology:

- Acquired immune deficiency syndrome was first identified in 1981 in a small group of gay men in the San francisco area who presented with unusual opportunistic infections.
- In 1983, the human immunodeficiency virus (HIV) responsible for AIDs was first isolated.
- Today, according to the U.S. centers for disease control over 36 million people are living with HIV infection.
- It is estimated that nearly 22 million people have died since the epidemic began. In the year 2000 alone, it was estimated that 3 million people died from AIDs.
- Women are increasingly at risk for HIV infection, currently 47% of adults infected worldwide with HIV are women.
- The developing world is especially hard hit by the HIV epidemic. It is estimated that 95%. of people with HIV infection now live in developing countries

Etiology:

The HIV matrix proteins, lie between the envelope and core The viral core, contains the viral capsule protein p24 which surrounds two ~~sigs~~ single stands of HIV RNA and the enzymes needed for HIV replication, such as reverse transcriptase, protease, ribonuclease and integrase, out of

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the nine virus genes, there are three, namely gag, pol an env, that contain the information needed to make structu proteins for new virus particles.

Revers

Body fluids and HIV:

Four fluids, if infected, can transmit HIV.

- Blood
- Semen
- Vaginal Secretions.
- Breast milk.

Four fluids that can't transmit HIV.

- Spit / saliva.
- Pee / Urine
- Sweat
- Tears.

HIV entry to T cell

HIV is a retrovirus.

The genome of retrovirus is made of RNA, 160 and each virus has two single chains of RNA,

For replication, the virus needs a host cell, and the RNA must first be transcribed into DNA, which is done with the enzyme reverse transcriptase.

HIV Life cycle:

1. Binding and Fusion:

HIV begins its life cycle when it binds to a CD4 receptor and one of two co-receptors on the surface of a CD4 +T-lymphocyte. The virus then fuses with the host cells. After fusion, the virus releases RNA its genetic material, into the host cell.

Revense Transcription:

An HIV enzyme called revense transeriptase converts the single standed HIV RNA to double stananded HIV DNA.

3. Integration:

The newly formed HIV DNA entens the host cell's nucleus, where an HIV enzyme called integrase 'hides' the HIV DNA within the host cell's own DNA. The integrated HIV DNA is called provirus. The provirus may remain inactive for several yeans, producing few or no new copies of HIV.

4. Transeription:

When the host cell receives a signal to become active the provirus uses a host enzyme called RNA polymenase to create copies of the HIV genomic material, as well as shorter stands of RNA called messenger RNA. The m-RNA is used as a blueprint to make long chains of HIV proteins.

5. Assembly:

An HIV enzyme called pratease cuts the long chains of HIV proteins into smaller individual proteins. As the smaller HIV proteins come together with copies of HIV's RNA genetic material, a new paticle is assembled.

6. Budding:

The newly assembled virus pushes out from the host cell. During budding the new virus steals pant of the cells outen envelope. This envelope which acts as a covening is studded with proteins / sugan combinations called HIV gulycoproteins. These HIV gulycoproteins are necessany

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for the virus to bind CD4 and co-receptors. The new copies of HIV can now move.

Pathophysiology:

- HIV belongs to a class of viruses called retroviruses, which carry their genetic information in ribonucleic acid rather than deoxyribonucleic acid.
- HIV infects a limited number of cell types in the body including a subset of lymphocytes called CD4+ T helper cells and macrophages 162.
- The CD4+ T cells are necessary for normal immune function. Among other functions, the CD4+ T cell recognizes foreign antigen and infected cells and helps activate antibody-producing B lymphocytes.
- The CD4+ T cells also orchestrate cell-mediated immunity in which cytotoxic CD8+ T cells and natural killer cells directly destroy viral infected cells and foregin antigens.
- phagocytic monocytes and macrophages are also activated by CD4+ T cells.
- Through the action of reverse transcriptase, HIV produces DNA from its viral RNA. Transcription is often poor, leading to mutations, and some such mutations make HIV resistant to antiviral drugs.
- The viral DNA enters the nucleus of the cell and is incorporated into the host cell's DNA, where it is transcribed into ~~more~~ more viral RNA.
- If the host cell reproduces, it duplicates the HIV DNA along with its own and passes it on to the daughter cells.

If activated, the host cell carries this information and, if activated replicates the virus.

- Viral enzymes, proteases, arrange the structural components and RNA into viral particles that move out to the periphery of the host cell, where the virus buds and emerges from the host cell.
- Thus, the virus is now to travel and infect other cells.
- HIV replication may lead to cell death or it may become latent.

What is the 'window period?"

- The time period between a person's exposure and actual infection with HIV and until antibodies are detectable in the body.
- After three months there are usually enough antibodies to show on an AIDS test.
- Nearly all people (99%) develop antibodies by three months.

HIV and the Immune System:

- A person can be HIV infected and not have AIDS if the person's immune system is intact.
- often this period is from 8-10 years.
- Has no symptoms, person is a carrier.
- After this period, the immune system begins to lose the fight.
- At this point the person has AIDS.

Stage in an HIV infection →

HIV Negative → (HIV infection) → Seroconversion illness → HIV Positive → As symptomatic

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- The typical clinical course of HIV is defined by three stages, which usually occur during a period of 8 to 12 years.
- The three stages are the primary infection or the acute clinical syndrome, chronic asymptomatic phase or latency and overt AIDS.

1. Acute illness stage:

- Generally occurs several weeks after infection with the virus.
- Manifestations include acute-onset fever, headache, malaise lymphadenopathy, sore throat and skin rash.
- Symptoms usually subside within several weeks and the patient becomes asymtomatic.
- During the acute illness phase there is a transient reduction in circulating CD4+ and CD8+ lymphocytes.

2. Asymptomatic Stage:

- Following the acute illness stage, most patients go into a prolonged period where there are no symptoms of the infection.
- patients generally remain in relatively good health for 5 to 10 years.
- This asymptomatic period may be highly variable in duration.
- Duration this period there is slow but persistent destruction of immune cells, particularly CD4+ lymphocytes.
- Toward the end of this period, circulating levels of CD4+ lymphocytes decline significantly.
- levels of CD8+ lymphocytes may also show moderate decrease.

Symptomatic or AIDS stage:

- When circulating levels of CD4+ lymphocytes fall below a critical level the infected individual becomes symptomatic.
- A number of symptoms faling under the heading of AIDS related complex (ARC) may occur.
- These symptoms include fever night sweats, diarrhea and opportunistic infections.
- 'opportunistic' organism are those that take advantage of the patients weakened immune status to infect his or her system Infections with many of these organism are unique to AIDs or immunocompromised patients.

HIV in children:

- In children, HIV infection has a mean incubation time of 17 months.
- Signs and Symptoms resemble those in adults, except for findings related to sexually transmitted diseases.
- Children have a high incidence of opportunistic bacterial infections otitis media sp sepsis, chronic salivary gland enlargement lymphoid interstitial pneumonia, Mycobacterium Ovium complex function, and pneumonias including Pneumocystis Carinii.

Epidemiology of HIV infection:

- The HIV virus is a blood-borne pathogen that is transmitted via contact with contaminated body fluids.
- Unprotected sexul intercourse with an infected individual currently accounts for the vast maronity of new HIV infections.
- The virus may also be spread through contaminated blood products as well as through sharing of contaminated needles.

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- Transmission of the HIV virus from infected mothers to their fetuses currently accounts for approximately 10% of all HIV infections.
- Because the HIV virus appears in breast milk, breastfeeding is not recommended in HIV infected mothers.
- The HIV virus may also be detected in trace amounts in the saliva of infected individuals, however, there is no current evidence that the virus can be transmitted by casual contact.

Laboratory diagnosis of HIV:

- ELISA is used to detect HIV antibodies.
- A positive ELISA must be confirmed by western blot or immunofluorescence assay to detect specific HIV proteins.
- HIV core protein p^{24} is the most abundant protein produced by HIV.
- Anti-p24 is the first reliably detected antibody but declines as viral titres rise in late infection.
- Other HIV proteins such as p55, p40, gp 120, and gp 41 may also be part of the analysis.
- Although not used to diagnose HIV infection, measurement of CD4+ lymphocyte levels and viral load are often useful indexes of the disease progression as well as the effectiveness of antiretroviral therapy.

Rationale for treatment of HIV:

- Prevent viral replication in infected cells by inhibiting HIV reverse transcriptase or protease enzymes.

⑤ Treat opportunistic infections when they arise and prophylactically.

⑥ Provide nutritional, medical and emotional support for patients with a chronic illness.

Treatment of HIV:

① The most effective way to limit the occurrence of HIV infection is through proper prevention.

HIV Drug therapy:

Currently available antiretroviral drugs for the treatment of HIV fall into three categories.

1) Nucleoside reverse transcriptase inhibitors.
2) Non-nucleoside reverse transcriptase inhibitors.
3) Protease inhibitors.

considerable research is currently being conducted on developing an HIV vaccine that would protect individuals from HIV infections even after exposure to the virus.

Nucleoside reverse transcriptase inhibitors.

Ex- Zidovudine (AZT), didanosine.

Non-nucleoside reverse transcriptase inhibitors

Ex- nevirapine, efavirenz.

Protease inhibitors.

Ex- Saquinavir, ritonavir.

Treatment of HIV:

① current recommendations include the use of two nucleosides plus one protease inhibitor, or two nucleosides and one nonnucleoside to help inhibit the production of

resistant mutant strains.

⊙ The drugs include –

⊙ protease inhibitors to block replication of virus particle formed through the action of viral protease.

⊙ Nucleoside reverse-transcriptase inhibitors to interfere with the copying of viral RNA into DNA by the enzyme reverse transcriptase.

⊙ Non nucleoside reverse transcriptase inhibitors to interfere with the action of reverse transcriptase.