HIV INFECTION & AIDS

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HUMAN IMMUNE DEFICIENCY VIRUS

LEARNING OBJECTIVES

- Discuss the replicating cycle of HIV
- Describe entry, spread and pathogenesis of HIV infection
- Explain the role of T Helper cells in normal immune amplification and effects of low number of T Helper cells in HIV infection

• HIV-GENERAL DESCRIPTION

- ❑ Family Retroviridae
- ❑ Genus Lentivirus-Slow virus
- ❑ HIV-1 &2
- ❑ Enveloped RNA virus
- ❑ Envelop from host cell memb
- ❑ Only virus that has RNA dependent DNA polymerase- called reverse transcriptase
- ❑ Retrovirus

• HIV STRUCTURE

- ❑ Envelop
- ❑ Has gp120 (surface) & gp41 (transmembrane)
- ❑ Icosahedral p24 capsid protein
- ❑ 2 copies of single stranded RNA
- ❑ Essential enzymes

- Reverse transcriptase
- Integrase
- Protease

• HIV REPLICATION

• TRANSMISSION OF HIV

- ❑ Sexual route-MSM
- ❑ Transfer of infected blood
- ❑ Perinatal transmission ~50% in neonatal disease
- ❑ Post natal transmission-Breast milk
- ❑ Concurrent STI increase the transmission
- ❑ Uncircumcised-↑ transmission
- ❑ Saliva, tears-No transmission
- ❑ Not transmitted by casual contact

• TRANSMISSION OF HIV

- Transmission via blood transfusion much decreased
- Window period-antibodies not detected
- Check p 24 antigen in blood or HIV RNA
- Eclipse period-when HIV is inside tissue and not in blood lasts for few weeks

• PATHOGENESIS

- HIV enters through cuts/ abrasion
- Mucosal infection
- Macrophage ingest
- Migrate to local lymph nodes
- Dendritic cells in follicular region- form reservoir of HIV particle
- CD4 cells infected from dendritic cells in lymph nodes
- Gp120- binds CD4, CCR5, CXCR4 co-receptor

• PATHOGENESIS

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- ❑ Viremia
- ❑ Drop in CD 4 count
- ❑ Widely disseminated
- ❑ Lymphoid organs seeded
- ❑ Acute mononucleosis like syndrome
- ❑ Strong immune response against HIV
- ❑ Viremia drops, CD 4 count rebound

• PATHOGENESIS

- ❑ Immune system- cannot clear virus
- ❑ Latency period for 10 years
- ❑ CD 4 count dropping slowly
- ❑ 10 billion HIV particles are produced and destroyed each day
- ❑ Rapid production of HIV viroin
- ❑ High error rates in HIV
- ❑ Immune system collapses

• PATHOGENESIS

- Cytotoxic T cell response effective
- HIV induces down-regulation of MHC-1 molecules
- Up-regulates FasL on target cell
- Dendritic cells maturation effected
- Limited antigen presentation

• PATHOGENESIS

- Ultimately immune system cannot keep pace
- It fails
  - Low CD4 Count
  - CD 8 cells become non responsive due to high mutation & ↓ help from CD 4
    - High virus load in blood
    - Opportunistic infections
    - Ultimately death

• ROLE OF T HELPER CELLS

- Helper T Cells activated by
- APC that present exogenous antigen

- Virally infected cells that present endogenous made antigen
  - CD4+ cells activate
- Themselves & increase numbers
- Memory cells CD4+ & CD8+
- Macrophages & Neutrophils
- Cytotoxic T cells
- B cells
- NK cells

- **ROLE OF T HELPER CELLS**
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- Activated macrophages, CD8+ cells further activate CD4+ cells
- It is central in the immune response regulation
- Immune response is amplified
- Cytokines like Interleukins control the differentiation
- The adequate number of CD4+ cells is crucial in immune amplification

- **HIV & T HELPER CELLS**
- **HIV & IMMUNE DEFICIENCY**

Mechanism of immune suppression in HIV

- ❑ Direct lysis of CD4+ cells
- ❑ Virus induces apoptosis in CD4+ cells
- ❑ CD8+ cells attack CD4+ cells
- ❑ T cells replenishment impaired by stem cell infection
- ❑ Defect in antigen presentation due to infection of dendritic cells
- ❑ Immunosuppressive viral coated molecules (e.g. gp120, gp41)