* **HIV INFECTION & AIDS**
* Assist Professor Microbiology
* Dr. Syed Yousaf Kazmi
* **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)