Immunodeficiency

(2 of 2)

Ali Al Khader, M.D.
Faculty of Medicine
Al-Balqa’ Applied University
Email: ali.alkhader@bau.edu.jo
Acquired (secondary) immunodeficiencies

• More common

• Many causes such as therapy, cancer, sarcoidosis, malnutrition, infection & renal disease

• The most common of which is therapy-related
AIDS, epidemiology

• AIDS was first described in the United States

• Largest number is in Africa

• Major routes of transmission:
  - Sexual contact
  - Parenteral inoculation
  - From infected mothers to their newborns
  - 10%...unknown risk factors
AIDS, 5 major risk groups

- Men who have sex with men...the largest group
  ...now declining, less than 50% of new cases

- Heterosexual contacts of members of other high-risk groups
  ...The largest group with new infections in Africa & Asia

- IV drug abusers

- Recipients of blood and blood components

- Hemophiliacs, especially those who received large amounts of factor VIII or IX concentrates before 1985

*1%: in children
  ...90% by vertical transmission
AIDS, epidemiology, cont’d

• Sexually transmitted diseases increase risk of infection

• Measures to decrease transmission by blood products transfusion:
  - antibody screening
  - antigen screening
  - heat treatment of clotting factor concentrates
  - nucleic acid testing

• In gonorrhea, chlamydia and chorioamnionitis:
  in inflammatory cells carrying the virus
AIDS, epidemiology, cont’d

• Needle stick injury....

Visit https://web.stanford.edu/group/parasites/ParaSites2006/Leish_vaccine/Links%20and%20References.html for references.
AIDS, etiology

- HIV
  - ...of lentivirus family
- HIV-1 and HIV-2
  - More common

- Infectious particle: 2 RNA strands within a protein core surrounded by a lipid envelope derived from infected host cells but containing viral proteins
AIDS, etiology...cont’d

• Life cycle:
  Infection of cells $\rightarrow$ production of viral DNA $\rightarrow$ its integration into host genome $\rightarrow$ expression of viral genes $\rightarrow$ production of viral particles

• Major envelope glycoprotein: gp120

  Binds to CD4, CXCR4, or CCR5
AIDS, etiology...cont’d
AIDS, pathogenesis

• It infects mainly CD4+ T cells...progressive destruction of these cells
  
  May also infect macrophages and dendritic cells

• Latent ↦ reactivation ↦ progressive destruction of cells...
  AIDS development over many years
AIDS, pathogenesis...cont’d
Clinical features of HIV infection

• Early after HIV infection: mild acute illness
  Fever and malaise due to initial viremia ...see slide #15

• The illness subsides within a few days...enters the clinical latency period
  ...during this latency:  -progressive loss of CD4+ T cells in lymphoid tissues
  -progressive destruction of lymphoid tissue architecture

• Eventually: the blood CD4+ T cell count begins to decline
Clinical features of HIV infection, cont’d

• When the count < 200 cells/mm³...AIDS (susceptibility to infections)

• If not given treatment:
  - infections by intracellular microbes ➔ viruses
    - Pneumocystis jiroveci
    - atypical mycobacteria
  - infections by extracellular bacteria ➔ defective helper T cell-dependent antibody responses

  ...also defective CTL function against viruses
Clinical features of HIV infection, cont’d

- susceptibility to cancers caused by oncogenic viruses
  - B cell lymphomas
  - Kaposi sarcoma

- patients with advanced AIDS: wasting syndrome (cachexia)

- dementia...infection of microglial cells (macrophages)
Clinical features of HIV infection, cont’d

- Infected patients produce antibodies & CTLs against HIV Ags early in disease
  - Limit the early acute HIV syndrome...but do not prevent progression

  - The virus rapidly mutates the region of gp120
  - CTLs are not much effective because the virus
  - Expression of MHC I in infected cells

  Immune responses against HIV may paradoxically ↑ the spread
  ...Ab-coated viral particles may gain entry through Fc receptors on FDCs & macrophages in lymphoid organs

  Even if CTLs are able to kill infected cells, phagocytes may become infected when they clear the dead cells
The elite controllers

- They are long-term nonprogressors
- They control the infection without therapy
- Some...deletion of CCR5 gene
- Certain HLA alleles...HLA-B57 & HLA-B27
Therapy

- HAART = highly active antiretroviral therapy

...by blocking the activity of viral reverse transcriptase, protease, and integrase

but

- The virus can undergo mutations
- Reservoirs of latent virus are not eradicated by these drugs
Thank You