Immunodeficiency

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Origins of Immunodeficiency

- Primary or Congenital
  - Inherited genetic defects in immune cell development or function, or inherited deficiency in a particular immune molecule
- Secondary or acquired
  - A loss of previously functional immunity due to infection, toxicity, radiation, splenectomy, aging, malnutrition, etc.

Infectious Consequences of Immunodeficiency

- Antibody deficiency, Phagocyte deficiencies, or Complement protein deficiencies are associated with recurrent infections with extracellular pyogenic bacteria (pneumonia, otitis media, skin infections)
- Deficiency in Cell-mediated immunity is associated with recurrent or chronic viral, fungal, or protozoal diseases.
B cell Deficiencies

- **Congenital hypogammaglobulinemia**
  - Symptoms at 9 mo. to 2 yr of age
  - Treat with intravenous immunoglobulin (IVIG)
- **Hyper IgM**: defective CD-40L expression
- **Selective IgA deficiency**
  - Occurs in 1:600-1:800 people
  - Possible connection with increased sinopulmonary infections and allergies

T Cell Deficiencies

- **Congenital Thymic aplasia**
- **Chronic Mucocutaneous Candidiasis**
### Severe Combined Immunodeficiency

- **X-linked SCID**: Defect in IL-2 receptor
- **Swiss-Type SCID**: Adenosine deaminase deficiency
- **Bare Lymphocyte syndrome**: Absence of MHC Class II gene products

### Phagocyte Deficiencies

- **Chronic Granulomatous Disease**: NADPH oxidase defect
- **Chediak -Higashi Syndrome**: Abnormal lysosome formation
- **Leukocyte Adhesion Deficiency**: Absence of leukocyte adhesion molecules

### Complement Deficiencies

- **Single component deficiencies**: Example: C3 deficiency
- **Hereditary Angioedema**: C1 Inhibitor deficiency
- **C5,C6,C7,C8, or C9 deficiency**: Recurrent bacterial meningitis due defective membrane attack complex

### Causes of Acquired Immunodeficiency

- Cancer (immunoproliferative diseases)
- Cytotoxic drugs or radiation
- Malnutrition
- Splenectomy
- Immunosuppressive therapies
- Stress/emotions
- Aging (thymic atrophy)
- Infection
Immunopathogenesis of HIV-Infection

- HIV infects and ultimately destroys CD4+, CCR5+, or CXCR4+ T cells, monocytes, & dendritic cells.
- **Primary HIV Infection**: A vigorous immune response to HIV controls the primary infection. (clonal Cytotoxic T cells, suppressive chemokines, poorly neutralizing antibody)

Immunopathogenesis of HIV-Infection. (continued)

- **Chronic Asymptomatic Phase**: Viral trapping & replication in lymphoid tissues, high rate turnover of virus and CD4 T cells, loss of CD4 functional help to CTL and antibody responses, destruction of lymph tissue, viral mutation and escape from recognition, exhaustion or viral inhibition of CD4 T cell renewal.

Immunopathogenesis of HIV-Infection. (continued)

- **Overt AIDS**: CD4 count declines, viral load increases, opportunistic infections.

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From Abbas, Lichtman, & Pillai: Cellular and Molecular Immunology. W.B. Saunders, 1999, Fig. 20-6a
Mechanisms of CD4+ T cell depletion-
Dysfunction

- Accumulation of unintegrated viral DNA
- Loss of plasma membrane integrity due to viral budding
- Elimination of infected cells by HIV-specific immune effectors
- Syncytium formation
- Autoimmunity

Mechanisms of CD4+ T cell depletion-
Dysfunction(continued)

- Superantigenic stimulation
- Apoptosis
- Infection of stem cells and interference with lymphopoiesis