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, Phagocytic 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 CD40L 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)

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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.

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Immunopathogenesis of HIV-Infection. (continued)

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