Immunodeficiencies

Definition and Complexity of the Immune System

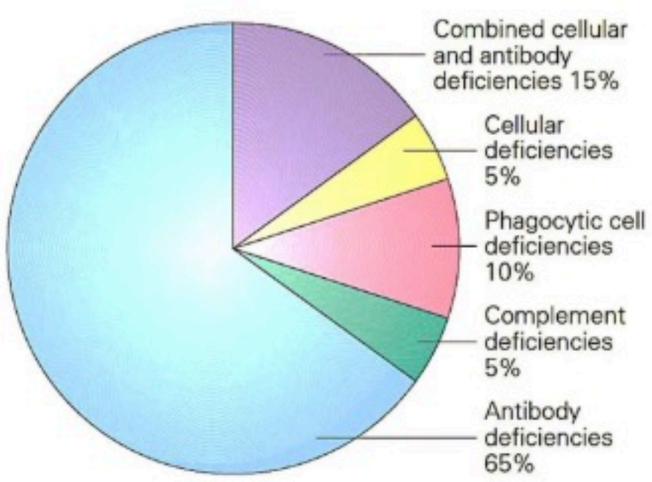
Immunodeficiencies occur when a component of the immune system is defective, which can involve a multitude of components due to the immune system's complexity. Mutations or genetic defects can lead to various immune deficiencies, affecting different parts of the immune response.

Immunocompromised States

Individuals with weakened immune systems are termed immunocompromised. This condition can be genetic or acquired, such as through immunosuppressive drugs.

Types and Prevalence of Immunodeficiency Diseases

There are over 100 immunodeficiency diseases, broadly categorized into combined cellular and antibody deficiencies, with SID being a severe form affecting both B and T cells. The majority of these deficiencies are antibody-related, with symptoms varying based on the specific defect in immune pathways.



Impact of Defects in Immune Pathways

Defects can occur at different points in immune pathways, such as thymic maturation affecting T cells or isotype switching affecting antibody production. The severity of immunodeficiency depends on the defect's location and nature within these pathways.

Role of Immunodeficiencies in Immunology Research

Studying immunodeficiencies has significantly advanced immunology by helping to understand gene functions and immune mechanisms. Modern techniques like CRISPR allow for creating genetic defects in animal models to study immune responses, which can then be correlated with human conditions.

Categories of Immunodeficiencies

Immunodeficiencies are mainly divided into primary and acquired types:

1. **Primary Immunodeficiency Disorders (PID):** Inherited genetic mutations causing immune failure, often X-linked or autosomal recessive. More than 60% affect males due to X-linkage.
2. **Secondary (Acquired) Immunodeficiencies:** Develop due to external factors like infections (e.g., HIV), cancer, autoimmune diseases, or immunosuppressive treatments.

Examples of Acquired Immunodeficiencies

- **HIV/AIDS:** Depletes CD4 T cells, impairing immune response and increasing susceptibility to infections and cancers like EBV-related B cell lymphoma.
- **Cancer and Viral Infections:** Certain viruses infect immune cells, leading to immune suppression and malignancies.
- **Immunosuppressive Drugs:** Used in autoimmune diseases or post-transplant, these drugs reduce immune function, increasing vulnerability.

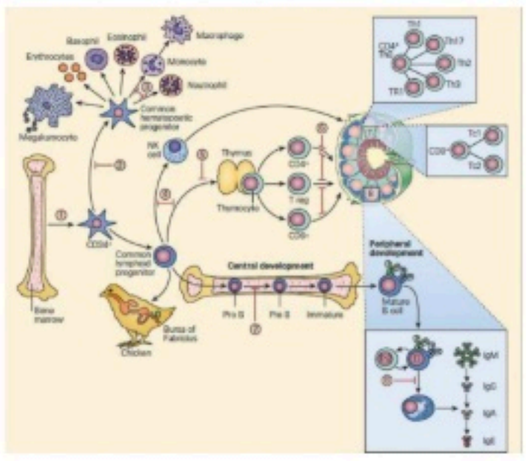
Diagnosis of Immunodeficiencies

Most primary immunodeficiencies manifest early in life with recurrent infections, including opportunistic pathogens, as well as allergy, autoimmunity, cancer. Diagnostic tests include measuring serum antibody levels and lymphocyte counts, which help identify immune deficiencies.

Treatment Strategies

Treatment varies depending on the defect:

- **Immunoglobulin Replacement:** Regular infusions of IgG or IgA are common, especially for antibody deficiencies, and are lifelong.
- **Enzyme Replacement Therapy:** For example, ADA deficiency was the first condition treated with genetically engineered enzyme replacement.
- **Bone Marrow Transplant:** The definitive treatment for severe combined immunodeficiency (SID), aiming to restore immune function entirely.



- Phagocytic cell deficiencies
- Complement deficiencies
- B cell deficiencies
- T cell-mediated deficiencies
- Combined cellular and antibody deficiencies (severe combined immunodeficiencies [SCID])