MED437
KING SAUD UNIVERSITY

Immunology team - 437

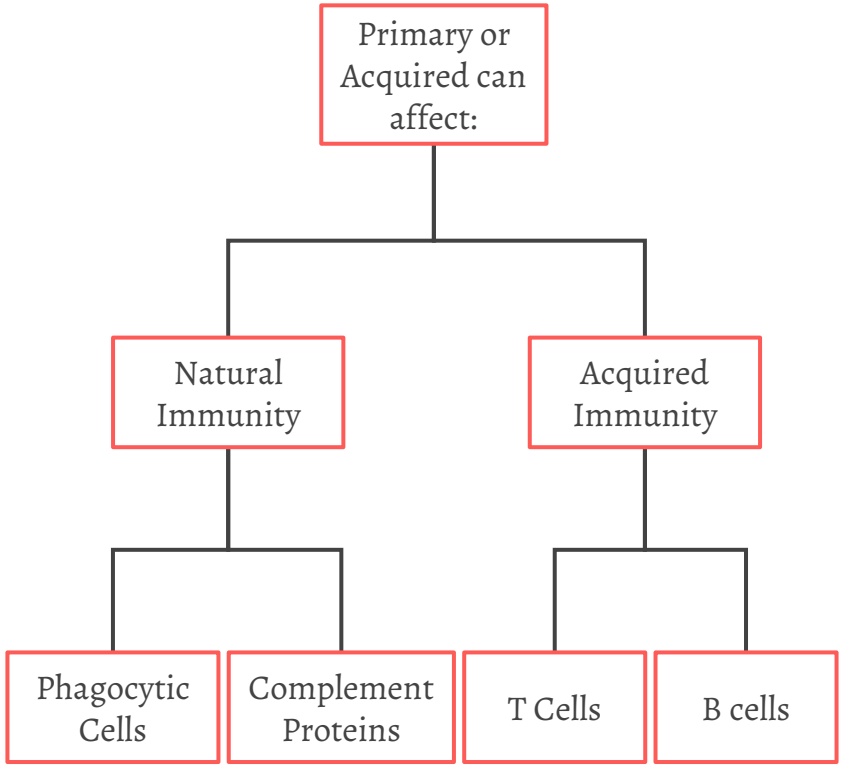
6- Immunodeficiency Disorders

Objectives :

- 1-Identify that immunodeficiency is due to a defect in the immune function.
- 2- Describe the classification of immunodeficiency.
- 3- Explain the presentations of different types of immunodeficiencies (e.g. Recurrent infection)
- 4- Understand the varieties of immune system deficiencies involving defects in :
  - T cells, B cells, phagocytes & complement.
- 5- Know the laboratory investigations for immunodeficiency disorders.

Definition: A state in which the ability of the immune system to fight infectious disease is compromised or entirely absent.

A person who has an immunodeficiency is said to be immuno-compromised.



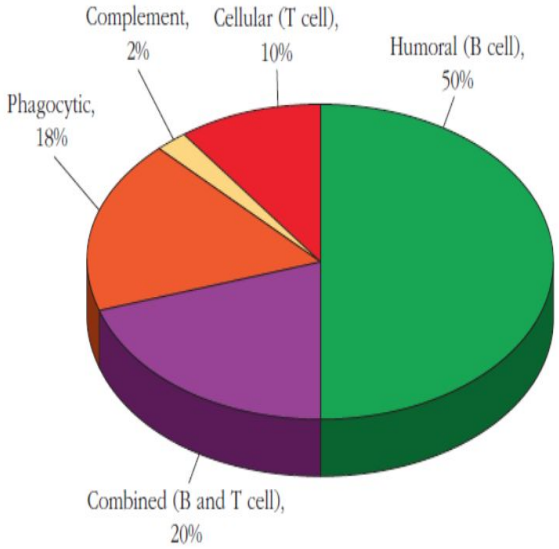
Immunodeficiency is considered to be present when infections are:

1. Frequent and severe.
2. Caused by opportunistic microbes.
3. Resistant to antimicrobial therapy.

Classification of ID (Immunodeficiency):

- **Primary (Congenital)**
  - Genetic Mutation :
    - 1- Monogenic (Single gene)
    - 2- Polygenic (Multiple genes)
- **Secondary (Acquired)**
  - Malnutrition
  - Viral and Bacterial infections (AIDS)
  - Immunosuppressive Therapy (Corticosteroids)
  - Excessive Proteins Loss (Burns, nephrotic syndrome)

Distribution of Primary Immunodeficiencies

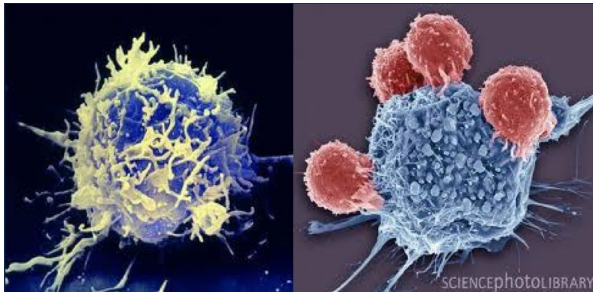


Pattern of infections and symptoms associated with primary immunodeficiencies

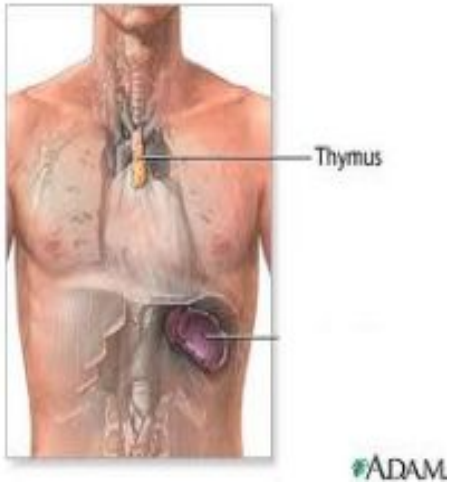
Disorder	Disease	
	OPPORTUNISTIC INFECTIONS	OTHER SYMPTOMS
Antibody	Sinopulmonary (pyogenic bacteria) Gastrointestinal (enterovirus, giardia)	Autoimmune disease (autoantibodies, inflammatory bowel disease)
Cell-mediated immunity	Pneumonia (pyogenic bacteria, *Pneumocystis carinii*, viruses) Gastrointestinal (viruses), mycoses of skin and mucous membranes (fungi)	
Complement	Sepsis and other blood-borne infections (streptococci, pneumococci, neisseria)	Autoimmune disease (systemic lupus erythematosus, glomerulonephritis)
Phagocytosis	Skin abscesses, reticuloendothelial infections (staphylococci, enteric bacteria, fungi, mycobacteria)	
Regulatory T cells	N/A	Autoimmune disease

T Cells defect

- **DiGeorge Syndrome (Congenital Thymic Aplasia)**



- **A congenital defect that is marked by:**
  - Absence or underdevelopment of the Thymus gland (hypoplasia)
  - Facial abnormalities
  - Hypoparathyroidism
  - Cardiovascular abnormalities



- **Features of DiGeorge syndrome:**
  - Children may present with tetany
  - In the complete form:
    - Extreme susceptibility to viral protozoal, and fungal infections
    - Profound depression of T-cell numbers
    - Absence of T-cell responses
- **Management of DiGeorge syndrome:**
  - fetal thymus tissue graft (14 weeks old).

B Cells defect
(Gammaglobulinaemias)

- **Patients with B-cell defects are subject to :**

Recurrent bacterial infections.

But

Display normal immunity to most viral and fungal infections.

Why ?

- **Diverse spectrum ranging from:**

1. Complete absence of B-cells
2. Complete absence of plasma cells
3. Low or absent immunoglobulins
4. Selective absence of certain immunoglobulins
5. Genetic Transmission
    a. Autosomal recessive
    b. X-linked disease:
        i. Females : carriers (normal)
        ii. Males : manifest the disease

X-linked agammaglobulinaemia (XLA) or Bruton's hypogammaglobulinaemia (Congenital disease)	Selective immunoglobulin deficiency (Congenital disease)	X- linked hyper-IgM Syndrome (Congenital disease)
★ The most common type, 80% - 90% ★ Defect in Bruton Tyrosine Kinase (BTK) The defect involves a block in maturation of pre-B- cells to mature B-cells in bone marrow **Features of XLA** • Reduced B-cell counts to 0.1% (normally 5-15 %) • Absence of Immunoglobulins • Affected children suffer from recurrent pyogenic bacterial infections	- IgA deficiency (1:700) - Most are asymptomatic : but may have increased incidence of respiratory tract infections (R.T.I). - Some have recurrent R.T.I and gastrointestinal tract symptoms.	**Characterized by:** 1. Low IgG, IgA & IgE. 2. Variable IgM levels most frequently high.

Management of immunoglobulin deficiencies:

Periodic intravenous immunoglobulins (IVIG) reduces infectious complications

Severe Combined Immunodeficiency (SCID)
(Congenital disease)

Causes of SCID

Enzyme deficiencies:

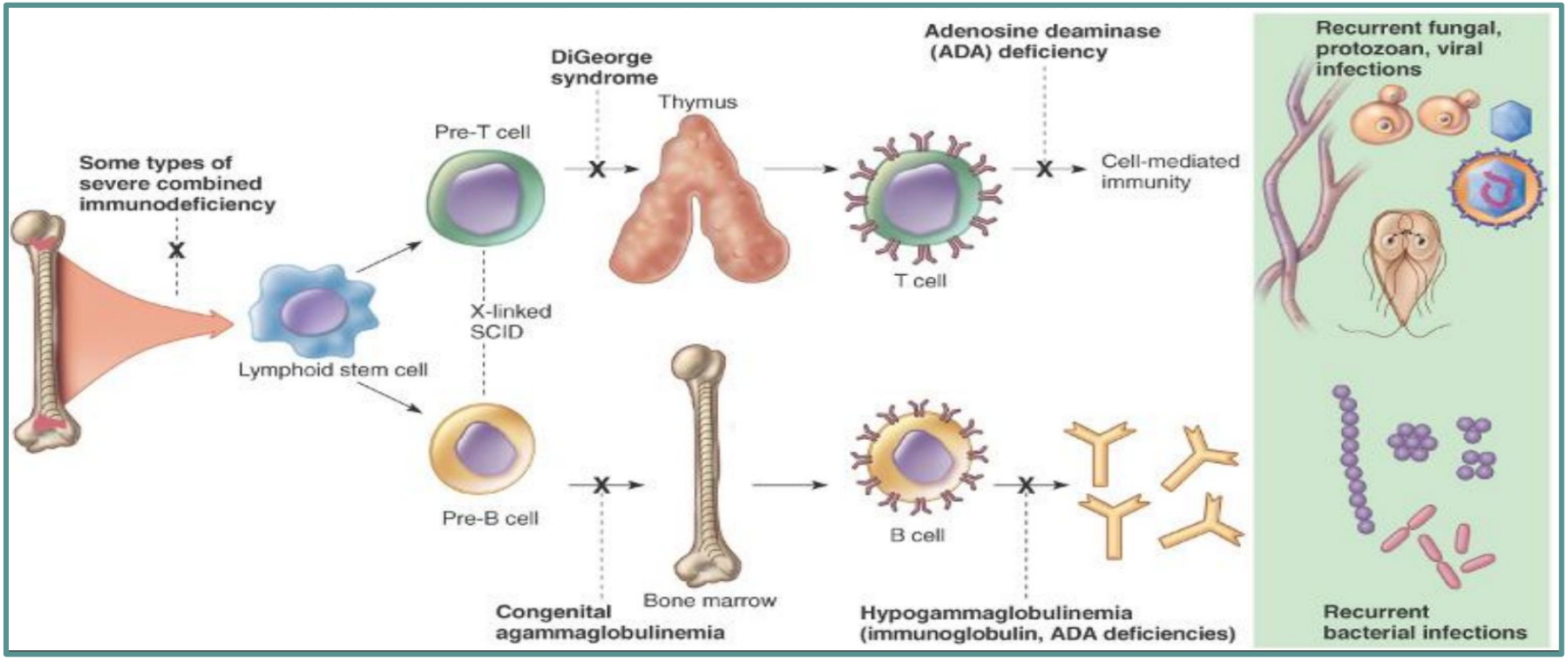
1. ADA (adenosine deaminase) deficiency
2. PNP (purine phosphorylase) deficiency Toxic metabolites accumulate in T and B cells

Management of SCID

1. Infusion of purified enzymes
2. Gene therapy

Features of SCID

Increased susceptibility to :viral, fungal, bacterial protozoal infections (starting at 3 months of age)



Leukocyte Defects

Quantitative Defect
Congenital agranulocytosis

Defect in the gene inducing G-CSF (granulocyte colony stimulating factor).

Features:
1) Pneumonia
2) Otitis media
3) Abscesses

Qualitative Defect
Congenital diseases

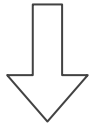
A. Defect in chemotaxis
Leukocyte adhesion deficiency (LAD)

Defect: in the adhesion molecules responsible of leukocyte trafficking and migration to sites of infection.

B. Defect in intracellular Killing
Chronic granulomatous disease

Defect:in the oxidative complex responsible for producing superoxide radicals.

Chronic granulomatous disease (CGD)
(Congenital disease)

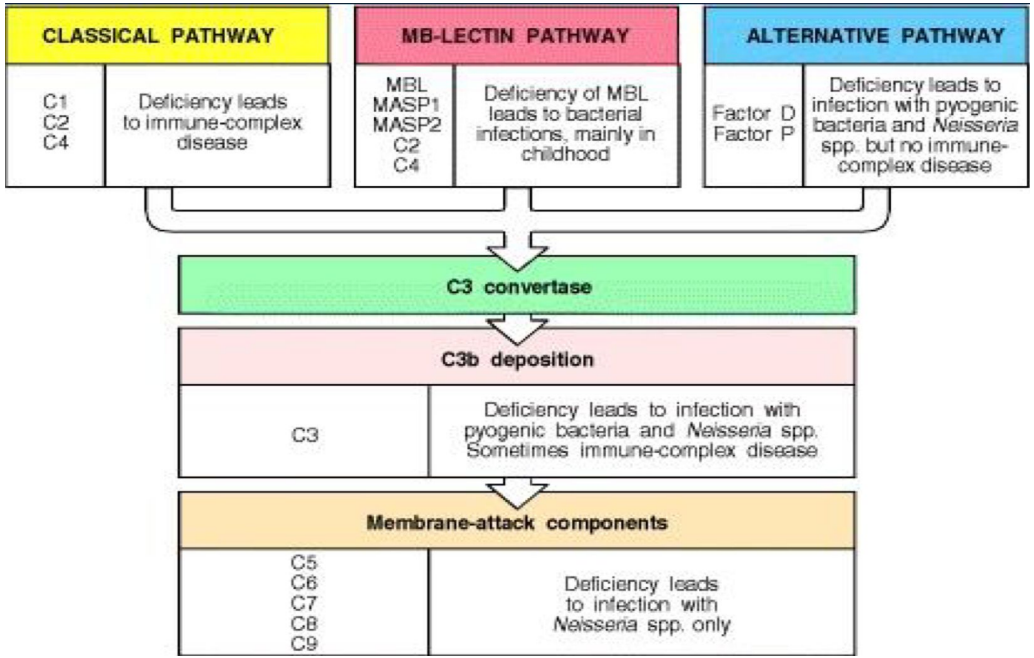


Neutrophils lack the "respiratory burst" upon phagocytosis.

Characterized by recurrent life-threatening bacterial and fungal
infections and granuloma formation

Complement Deficiency

Deficiency of all complement components have been described C1-C9.



Laboratory diagnosis of ID

1. Complete **blood count** : total & differential.

2. Evaluation of **antibody levels** and response to antigens.

3. T and B cells **counts** (Flowcytometry).

4. Measurement of **complement proteins** and function (CH_{50}).

5. Assessment of **phagocytosis and respiratory burst** (oxygen radicals).

MCQ

1-A person who has an immunodeficiency is said to be
A- Humoral Immunity
B- cell mediated immunity
C-immuno-compromised
D-Immune complex

2-Immunodeficiency is considered to be present when infections are:
A- Frequent and severe
B- Caused by opportunistic microbes
C-Resistant to antimicrobial therapy
D-all above

3- Immunodeficiency may be congenital or acquired
A- T
B- F

4- in the classification of immunodeficiency Genetic Mutatio is a
A- acquired
B- congenital
C- both A&B
D-neither AorB

5-DiGeorge Syndrome is happening because
A- absence or depression T cell number
B- absence of B cells
C- absence of plasma cells
D- absence of immunoglobulin

6- which of the following features describe X-linked agammaglobulinaemia
A- IgA deficiency
B- Low IgG, IgA & IgE
C- Enzyme deficiencies
D- Absence of Immunoglobulins

Answers
1-C
2-D
3-A
4-B
5-A
6-D

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