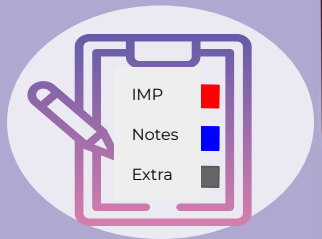
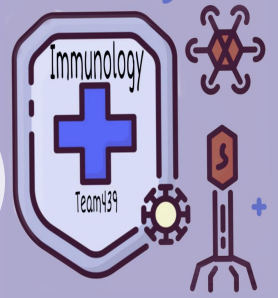
Immunodeficiency disorders

Revised & Approved by:
Shayma Abdullah Alghanoum
Yusuf Mohammad Alkatbi





Objectives

01

Identify that Immunodeficiency is due to a defect in the immune function.

02

Describe the difference classification of Immunodeficiency.

03

Explain the presentations of different types of Immuno-deficiencies (e.g. recurrent infections).

04

Understand the varieties of immune system deficiencies involving defects in :
- T cells, B cells, phagocytes and complement.

05

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 called immuno-compromised

Immunodeficiency is considered to be present when infections are:

- Frequent and severe
- Caused by opportunistic microbes bacteria, viruses, fungi
- Resistant to antimicrobial therapy. ability of a microbe to resist the effects of medication

A boy with congenital ID lived in a bubble for 12 years before he died

The HIV virus is the only virus that attacks the immune system directly, while other viruses attack the immune system indirectly.

Classification of Immunodeficiency (ID)

Secondary (Acquired)

- Malnutrition the body does not receive enough nutrients for proper function
- Viral and Bacterial Infections(aids)
- Excessive Proteins Loss e.g (Burns, nephrotic syndrome)
- Immunosuppressive Therapy
- (Corticosteroids) Treatment that lowers the activity of the body's immune system

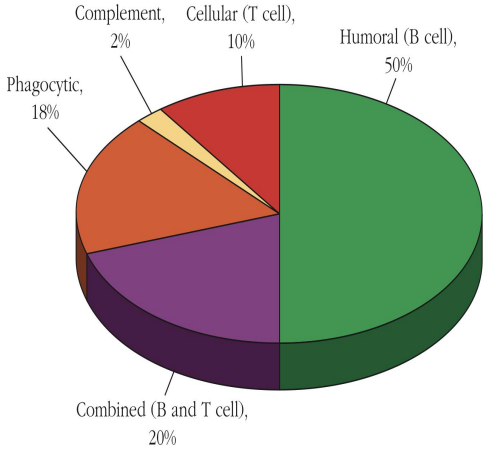
Primary (Congenital)

Genetic Mutation:

- Monogenic(Single gene)
- Polygenic (Multiple genes)

Distribution of Primary immunodeficiencies

*Antibody defects are more commonly seen



the effect of primary and secondary

Acquired Immunity

(adaptive) affected by secondary

- T-cells
- B-cells

Natural Immunity

(innate) affected by primary

- Phagocytic cells unable to engulf or kill the antigen
- Complement proteins

Pattern of infections and symptoms associated with primary immunodeficiencies

Disorder	Opportunistic infection	Other symptoms
Antibody	Sinopulmonary (pyogenic bacteria), Gastrointestinal(enterovirus,giardia)	Autoimmune disease (autoantibodies,inflammatory bowel disease)
Cell-mediated immunity	Pneumonia (pyogenic bacteria,pneumocystis carinii,virus) Gastrointestinal (viruses),mycoses of skin and mucous membranes(fungi)	N/A
Complement	Sepsis and other blood-borne infection(streptococci,pneumococci,Neisseria)	Autoimmune disease(systemic lupus erythematosus,glomerulonephritis)
Phagocytosis	Skin abscess, reticuloendothelial infections(staphylcocci,enteric bacteria,fungi,mycobacteria)	N/A
Regulatory T cells	N/A	Autoimmune disease

T-cell defects

DiGeorge Syndrome (Congenital Thymic Aplasia)

The most commonly and frequently seen abnormality.

A congenital defect is **characterized** by: Low T-cell amounts

- Absence or underdevelopment of the Thymus gland (hypoplasia)
  the Thymus is where the T- cells mature (lecture 1)
- Hypoparathyroidism causes **tetany** which is involuntary muscles constriction, Ca affected (hypocalcemia)
- Facial abnormalities
- Cardiovascular abnormalities

Features of DiGeorge syndrome:

Extreme susceptibility
to viral protozoal, and fungal infections

susceptibility is lack of ability to resist some antigen

Profound depression (decreased) of T-cell numbers

Absence of T-cell responses

Management of DiGeorge syndrome:

Fetal thymus tissue graft (14 weeks old)
graft: is the surgical transplant of living tissue
*438

B-cell defects (Gammaglobulinaemias)

patients with B-cell defects are subject to:

Recurrent bacterial infection **BUT** display normal immunity to most viral and fungal infections (Because the T cells are not affected. only B cells work in the case of bacterial infection and T cells work in cases of viral infections)

B-cell defects are **characterized** by:

- Complete absence of B cells or Plasma cells.
- Low or absent of immunoglobulins (Igs) or Selective absence of certain Igs.
-

It's genetically transmitted
(Autosomal recessive)
(X linked) making males show manifestation (express the disease) and females acting as normal carriers

X-linked agammaglobulinemia(**XLA**) or Burton's hypogammaglobulinemia

- the most common type (80%-90%)
- (Congenital) marked by a defect in burton tyrosine kinase (**BTK**) which blocks maturation of B cells in the bone marrow
- Reduces B-cell count to 0.1% (normal is 5%-15%)
- Absence of Immunoglobulins
- Affected Children Recurrent infections of pyogenic (pus producing) bacteria
- **Management**: Periodic IV Immunoglobulin injections

BTK is responsible for maturation of B cells into Plasma cells

X-linked **hyper IgM syndrom**

- Congenital
- High Levels of IgM IgM can be High, normal or low (Variable)
- Low levels of IgA, IgG, IgE (remember the word AGE)

- **Management**: Periodic IV Immunoglobulin injections

Because its X-linked, males are more affected Patients lack CD40-L (effect secondary)

Selective immunoglobulin deficiency (**IgA deficiency**)

- (Congenital) It's a deficiency in IgA (1:700)
- Asymptomatic (usually doesn't cause symptoms)
- can show recurrent Respiratory tract infections (R.T.I) and GIT infections

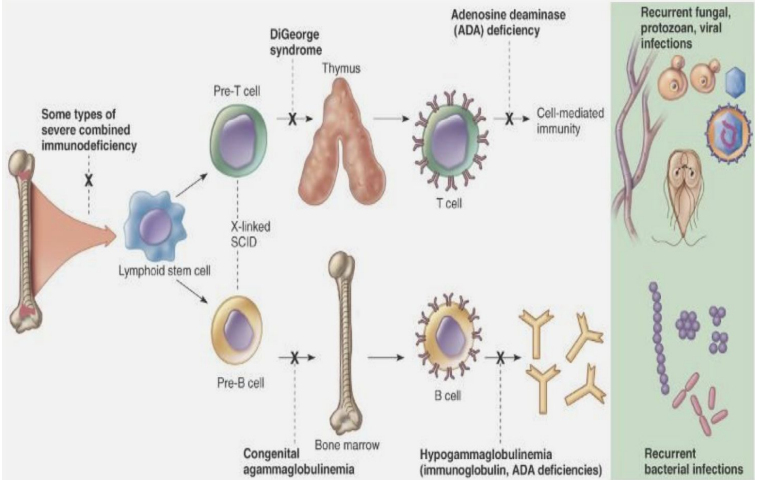
- **Management**: Periodic IV Immunoglobulin injections

Both T and B cell defects

almost complete absence of B&T cells functions

Severe Combined Immunodeficiency (SCID)

- Congenital
- Causes Increased susceptibility to viral, bacterial, protozoal and fungal. (Because both T and B cells are affected) (starting at 3 months of age)
- **Caused by enzyme deficiency**:
  - ADA (Adenosine DeAminase) deficiency (important in DNA synthesis) → 438
  - PNP (Purine Phosphorylase) deficiency (important in detoxifying cell metabolites) → 438
- **Management**:
  - Gene therapy
  - Infusion of purified enzymes
  - Bone marrow transplant



Leukocyte deficit
Affects innate immunity

Quantitative defects (Related to numbers)

Congenital Agranulocytosis
- **Defect in the gene inducing G-CSF** (Granulocyte colony stimulating factor) important for producing granulocytes (play a major role in bacterial infections)
- **Features (can cause) :** pneumonia and abscesses, otitis media (ear infection)

Qualitative defects (related to function)

Defects in Chemotaxis

Leukocyte Adhesion Deficiency
Defect in the adhesion molecules responsible for leukocyte migration to sites of infection

Defects in Intracellular killing

Chronic Granulomatous Disease (CGD)
- **Defect in the oxidative complex** responsible for producing superoxide radicals
- Neutrophils lack the "Respiratory burst (Rapid release of ROS) upon phagocytosis
- Characterized by recurrent life threatening bacterial and fungal infection and granuloma formation
- Repeated pyogenic infections and abscesses in multiple parts of the body

Complement Deficiency

team438
(slightly edited)

Deficiency in	Components	Definicey leads to:
classical pathway	C1 C2 C4	Immune-complex disease
Alternative pathway	Factor D Factor B	Infection with pyogenic bacteria and neisseria Spp. No immune-complex disease
MB-lectin pathway	MBL MASP 1 MASP 2 C2 C4	Bacterial infections (mainly in childhood)
C3b deposition	C3	Infection with pyogenic bacteria and neisseria Spp. sometimes immune-complex disease
Membrane attack complex components	C5 to C9	Infection with Neisseria Spp. Only

Laboratory diagnosis of Immunodeficiencies

- Complete **Blood Count** (CBC): Total & Differential information about cell count for each blood cell type
- Evaluation of **Antibody Levels** and response to antigens
- T and B cells count (**Flow Cytometry**)
- Measurement of **Complement proteins** and function (CH50)
- Assessment of **Phagocytosis and respiratory burst** (Oxygen Radicals)

Take Home Messages:

- Immunodeficiency may be congenital or acquired
- it can involve any component of immune system such as cells, antibodies, complement etc.
- most common presentation of immunodeficiency is recurrent infection that may be fetal due to delay in diagnosis and lack of appropriate therapy

Quiz

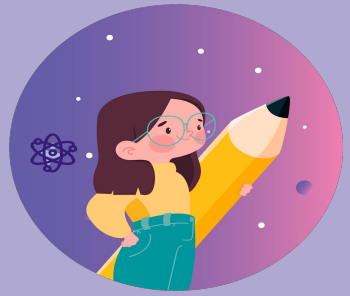
Question 1: Digeorge syndrome is a congenital defect that is marked by:
A - B-cell absence B- Hyperparathyroidism C- Bacterial infection D- none
Question 2:Burton's hypogammaglobulinemia is marked by
A -Deficiency in ADA B-Deficiency in IgA C- High levels of IgM D- Defect in BTK
Question 3: Which of the following is caused by a defect in the gene inducing G-CSF
A -Congenital Agranulocytosis B- Leukocyte adhesion deficiency C- Chronic granulomatous disease D- A&C
Question 4: A deficiency in which of the following may lead to immune-complex disease
A - MB-lectin pathway B- C3b deposition C- Membrane attack complex components D- Alternative pathway

4: B
3: A
2: D
1: D

team leaders

Hessah Fahad Alalyan

Faisal alotaibi



- Asma Alamri
- Fatimah Almeather
- Nourah Almasaad
- Renad AlOsaimi
- Sara Alrashidi
- Sarah Alqahtani
- Shatha Aldhohair
- Yara Alzahrani

- Abdulaziz alamri
- Abdulaziz alrabiah
- Hamad Almousa
- Homoud Algadheb
- Mohammed albabtain
- Salih Alqarni
- Osama Mobeirek

Immunologyteam439@gmail.com

editing file
click here