

# Immunodeficiency disorders

**Immunology Unit**

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**Reference**  
**Kuby Immunology 7<sup>th</sup>**  
**Edition 2013**  
**Chapter 18 Pages 593-624**

# Objectives

- Identify that Immunodeficiency is due to a defect in the immune function.
- Describe the classification of Immunodeficiency.
- Explain the presentations of different types of Immunodeficiencies (e.g. recurrent infections).
- Understand the varieties of immune system deficiencies involving defects in :
  - T cells, B cells, phagocytes and complement.
- 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**

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

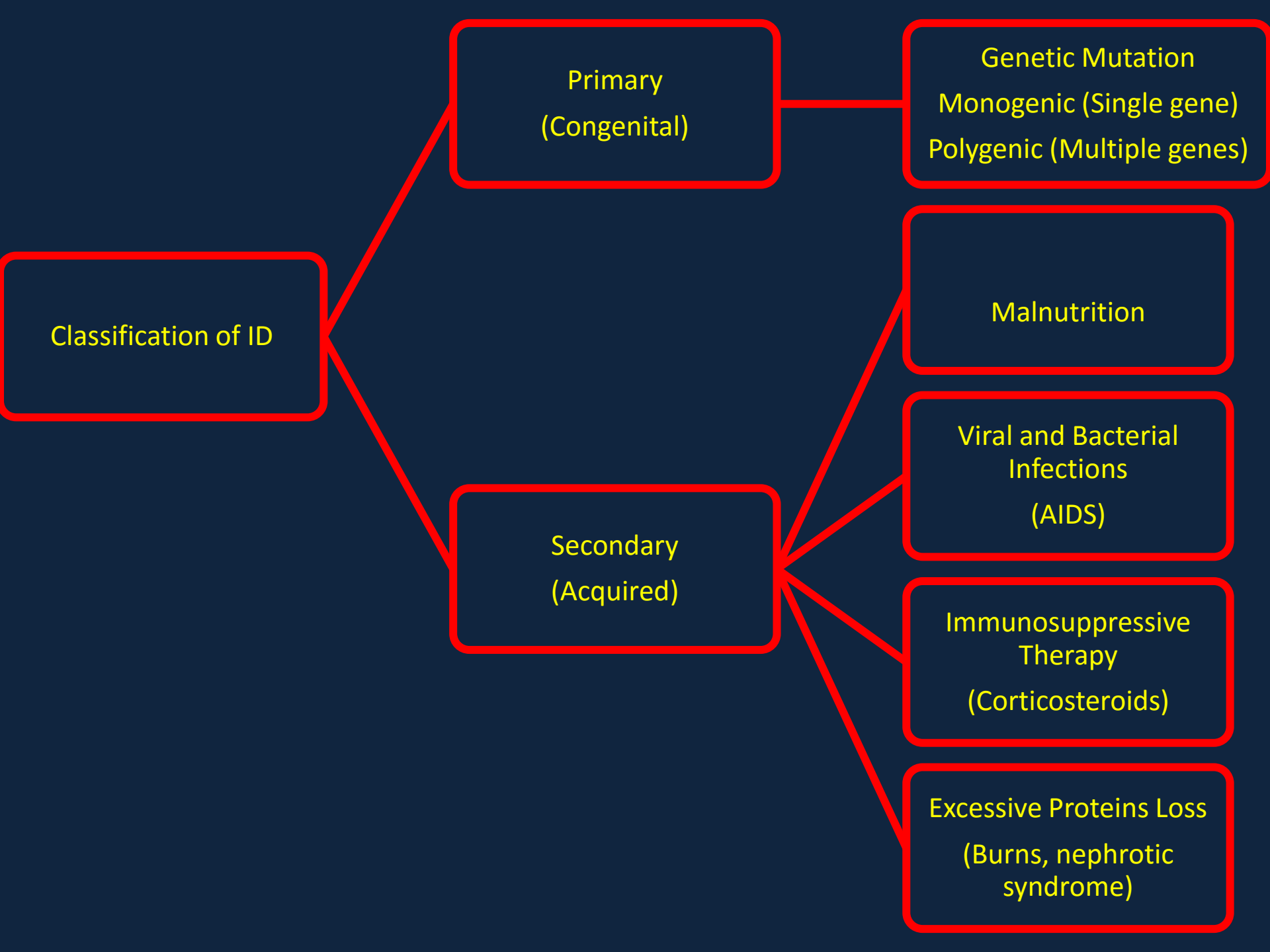


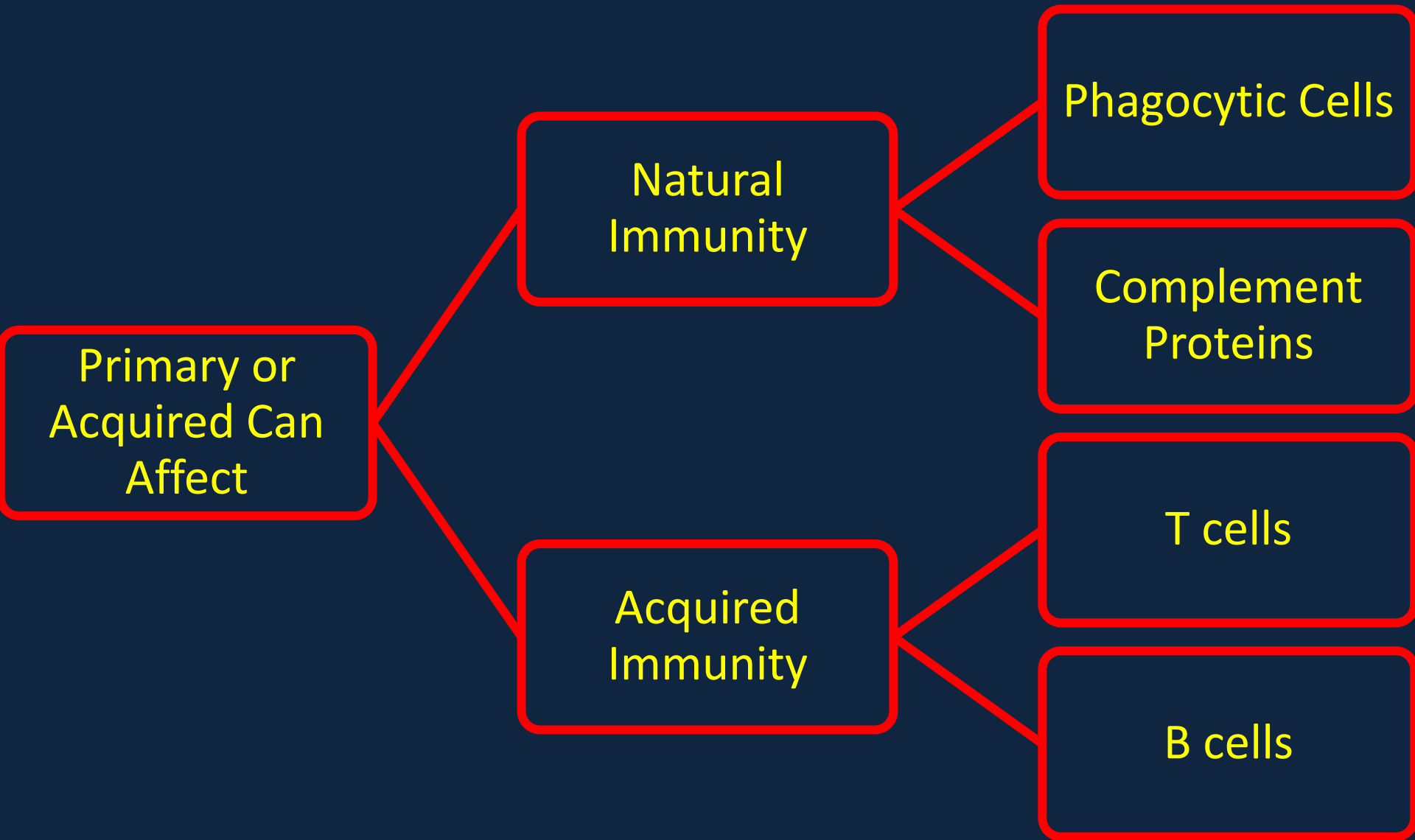
Immunodeficiency is considered to be present when infections are:

Frequent and severe

Caused by opportunistic microbes

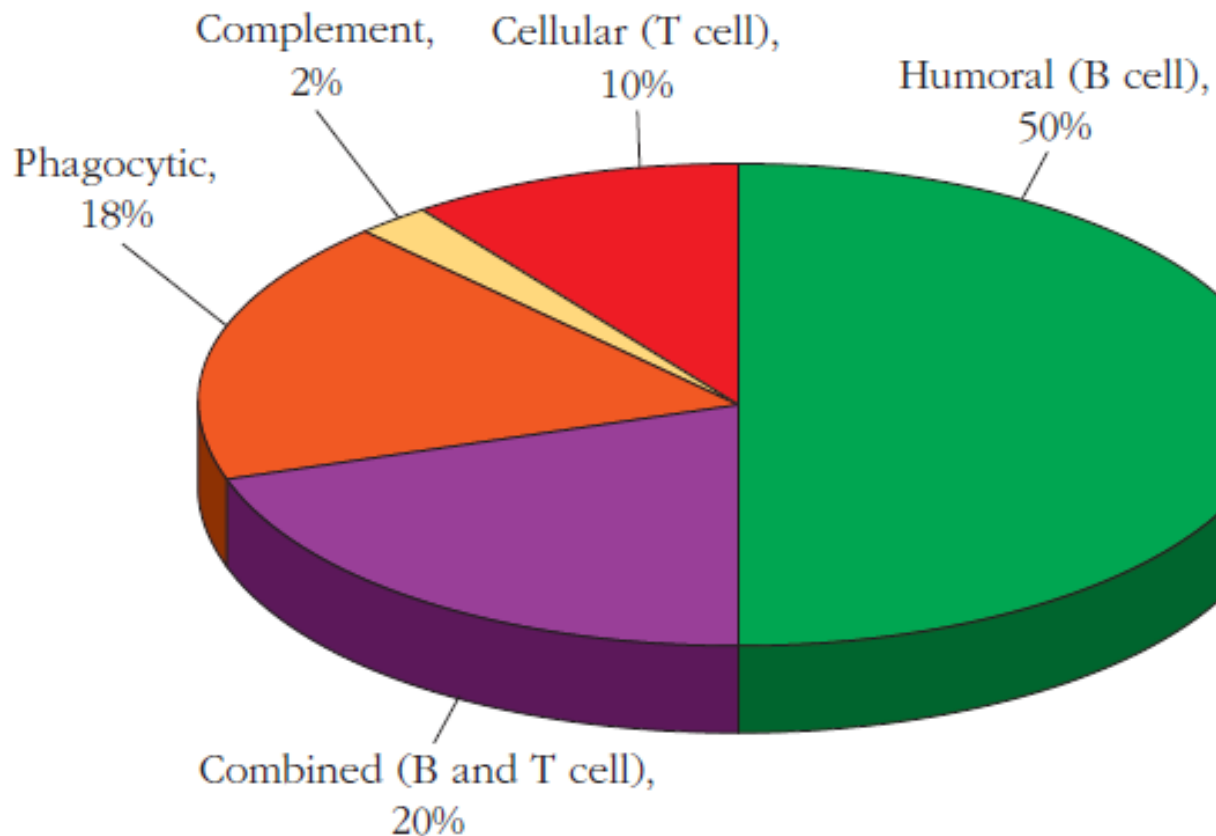
Resistant to antimicrobial therapy







# Distribution of Primary immunodeficiencies

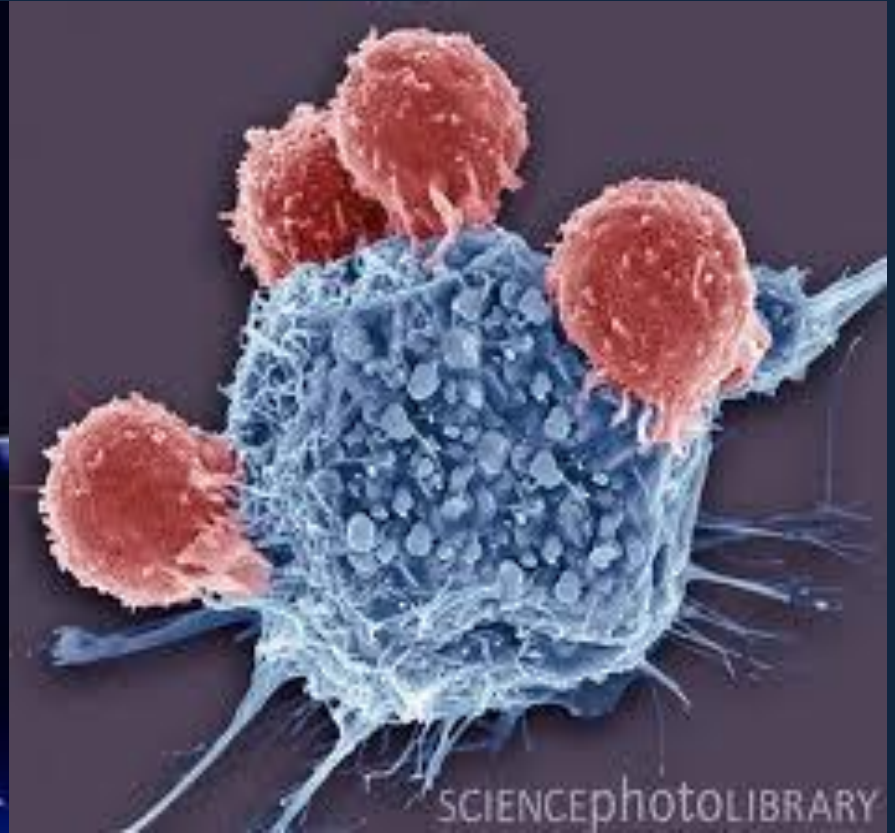
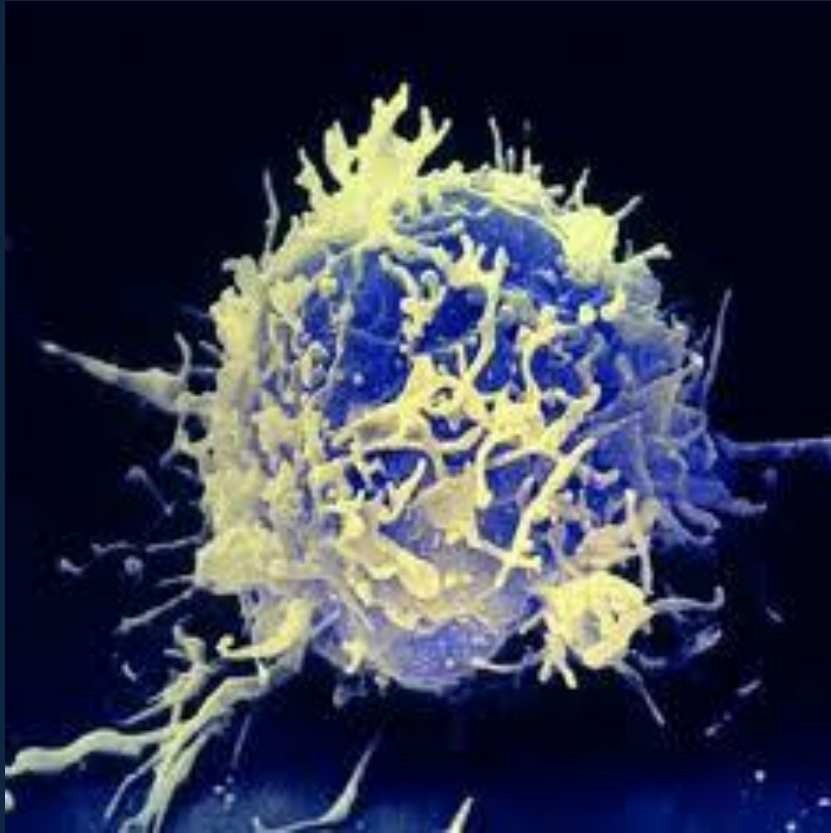


# Pattern of infections and symptoms associated with primary immunodeficiencies

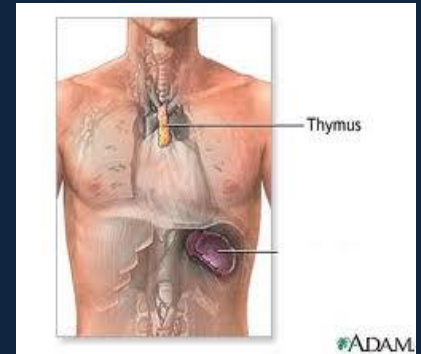
Disorder	Disease	
	OPPORTUNISTIC INFECTIONS	OTHER SYMPTOMS
Antibody	Sinopulmonary (pyogenic bacteria) Gastrointestinal (enterovirus, giardia)	Autoimmune disease (autoantibodies, inflammatory bowel disease)
Cell-mediated immunity	Pneumonia (pyogenic bacteria, <i>Pneumocystis carinii</i> , viruses) Gastrointestinal (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

Source: Adapted from H. M. Lederman, 2000, *The clinical presentation of primary immunodeficiency diseases*, Clinical Focus on Primary Immune Deficiencies. Towson, MD: Immune Deficiency Foundation 2(1):1.

# T-cell defects



# DiGeorge Syndrome (Congenital Thymic Aplasia)



A congenital defect that is marked by:

- Absence or underdevelopment of the Thymus gland (hypoplasia)
- Hypoparathyroidism
- Facial abnormalities
- Cardiovascular abnormalities

# Features of DiGeorge syndrome

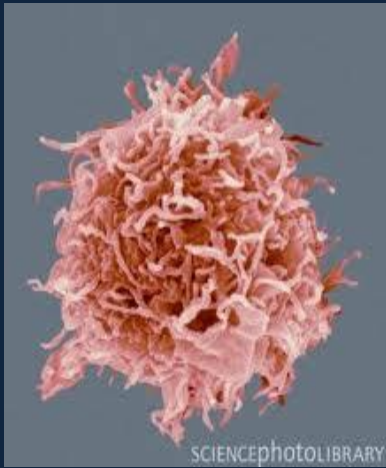
Children may present with tetany

## 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-cell defects

(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:

- Complete absence of B-cells
- Complete absence of plasma cells
- Low or absent immunoglobulins
- Selective absence of certain immunoglobulins
- Genetic Transmission
  - Autosomal recessive
  - X-linked disease:
    - Females : carriers (**normal**)
    - Males : **manifest** the disease

# X-linked agammaglobulinaemia (XLA) or Bruton's hypogammaglobulinaemia (Congenital disease)

The most common type, 80 to 90 percent

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 percent  
(normally 5-15 percent)
- Absence of Immunoglobulins
- Affected children suffer from recurrent pyogenic bacterial infections

# Selective immunoglobulin deficiency (Congenital disease)

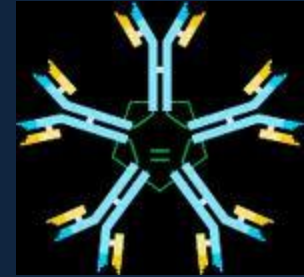
IgA deficiency (1:700)

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

# X-linked hyper-IgM Syndrome (Congenital disease)

Characterized by:



- Low IgG, IgA & IgE
- Variable IgM levels most frequently high

# Management of immunoglobulin deficiencies:

\*Periodic intravenous immunoglobulin (IVIG) reduces infectious complications

# Severe Combined Immunodeficiency (SCID) (Congenital disease)

## Causes of SCID:

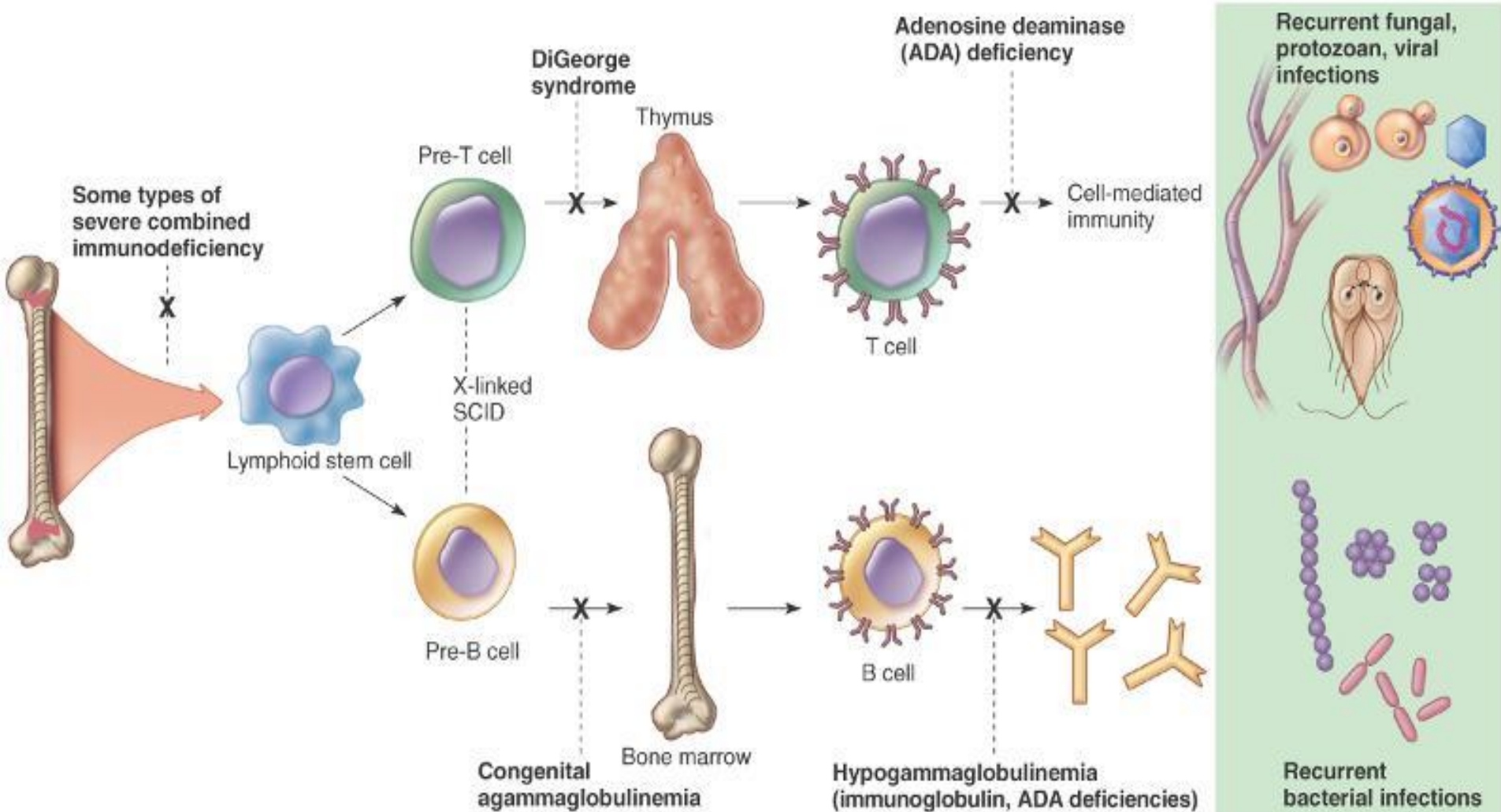
### Enzyme deficiencies:

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

# Features of SCID

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

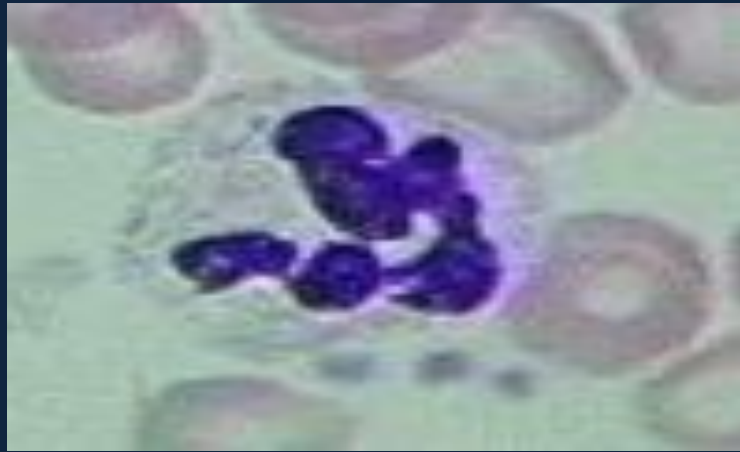
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# Management of SCID

1. Infusion of purified enzymes
2. Gene therapy



## Leukocyte defects

Quantitative

Qualitative

# Quantitative Defects

Congenital agranulocytosis:

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

Features:

Pneumonia, otitis media, abscesses

# Qualitative Defects (Congenital disease)

## A. Defect in chemotaxis

Leukocyte adhesion deficiency (LAD)

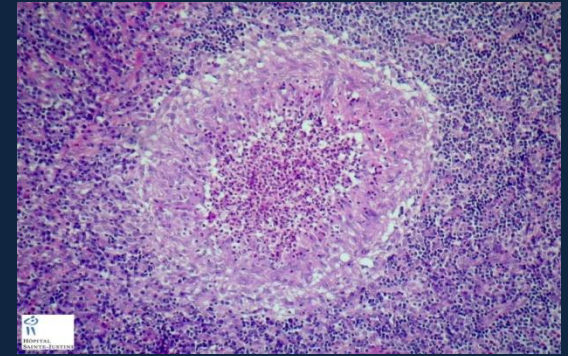
Defect: in the adhesion molecules responsible of leukocyte trafficking and migration to sites of infection

## B. Defect in intracellular Killing

Chronic granulomatous disease:

Defect: in the oxidative complex responsible for producing superoxide radicals

# Chronic granulomatous disease (CGD) (Congenital disease)

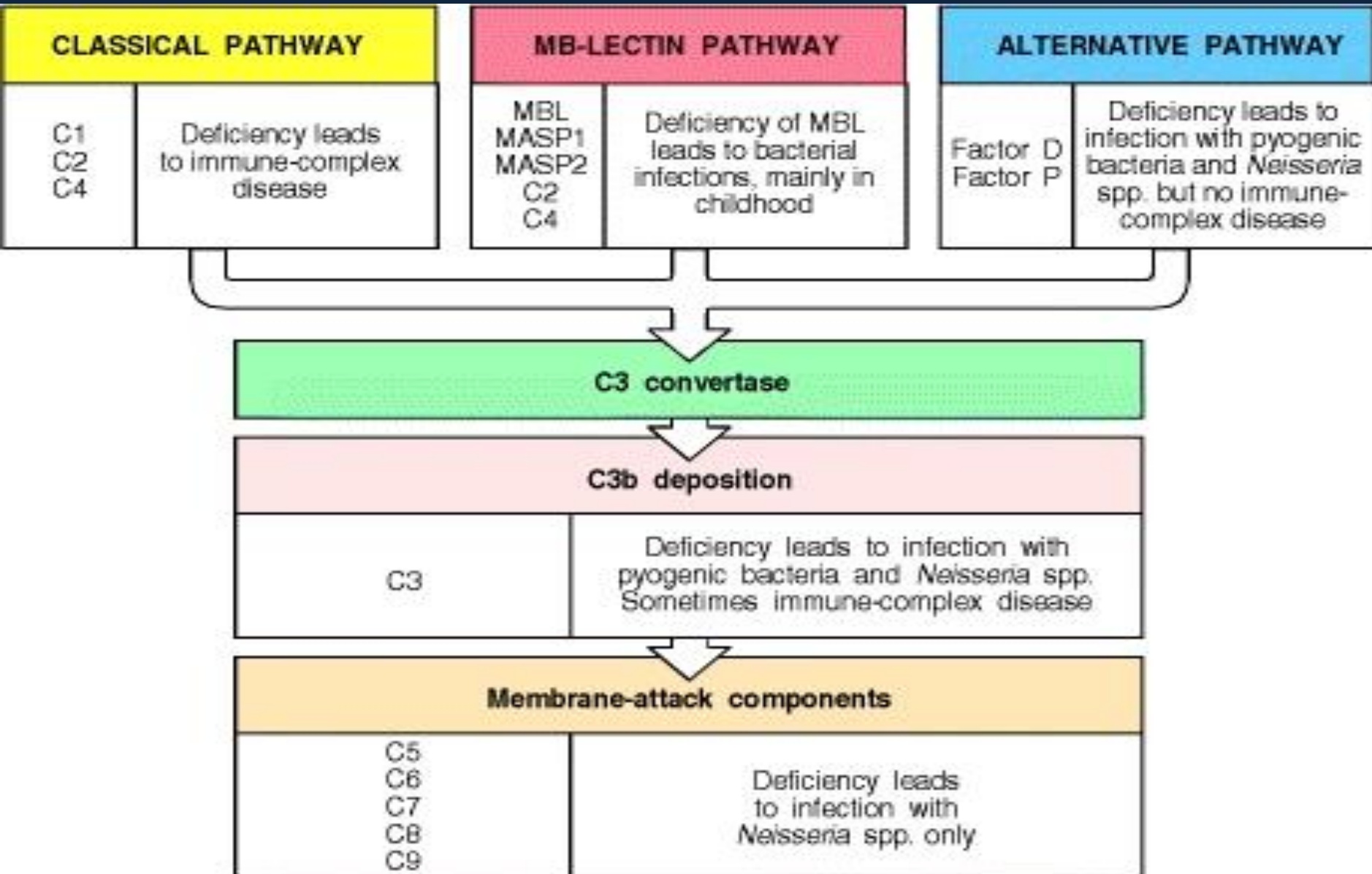


Neutrophils lack the "respiratory burst" upon phagocytosis

- 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<sub>50</sub>)
5. Assessment of **phagocytosis and respiratory burst** (oxygen radicals)



# Take Home Message

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