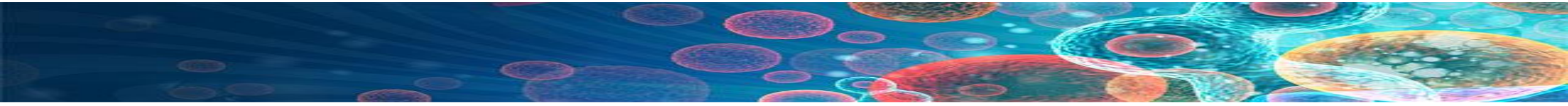
Immunodeficiency

Lecture 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 Immuno-deficiencies (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



Immune deficiency:

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

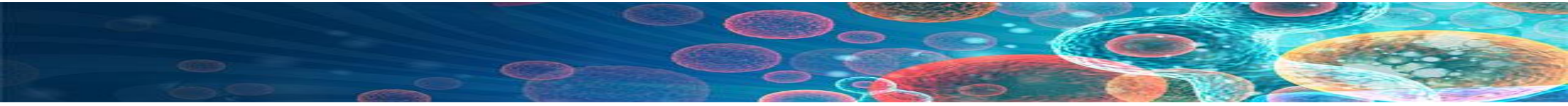
(A person who has an immunodeficiency is said to be immunocompromised).

Immunodeficiency is considered to be present when infections are:

1-Frequent and severe.

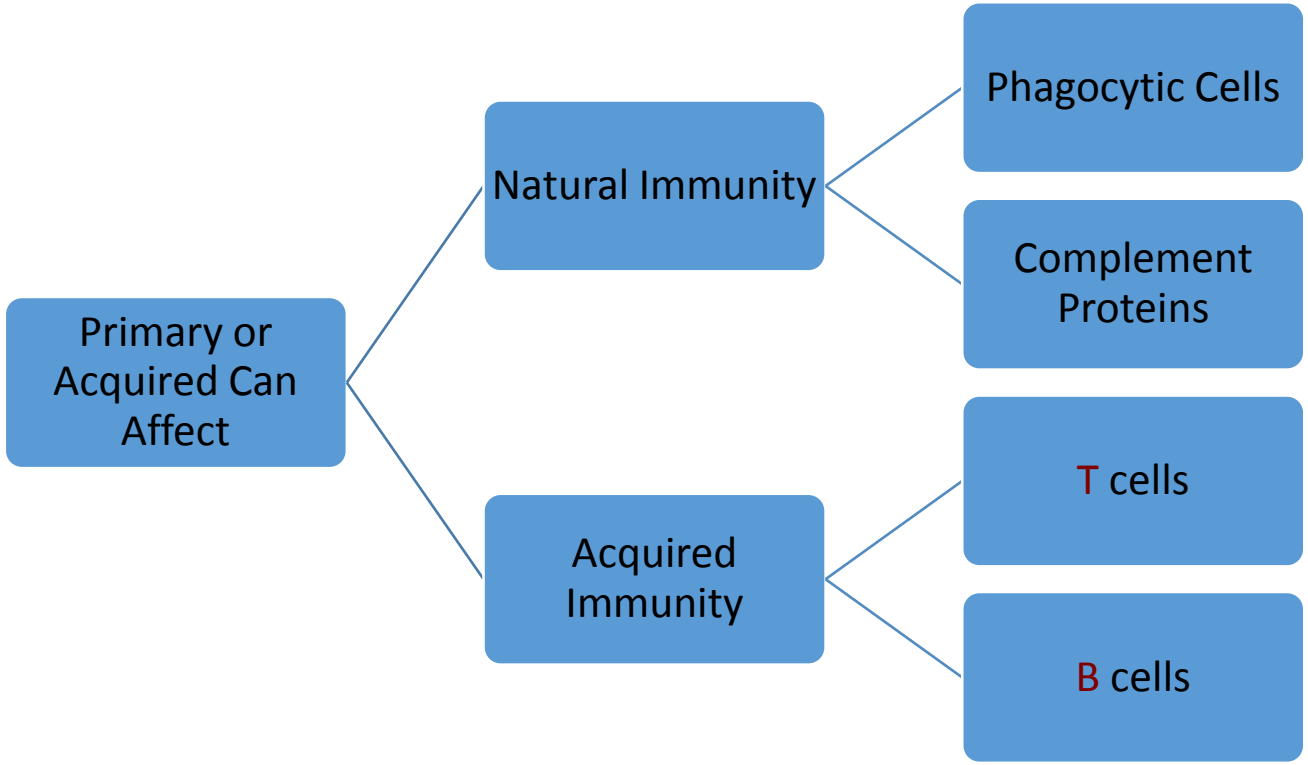
2-Caused by opportunistic microbes.

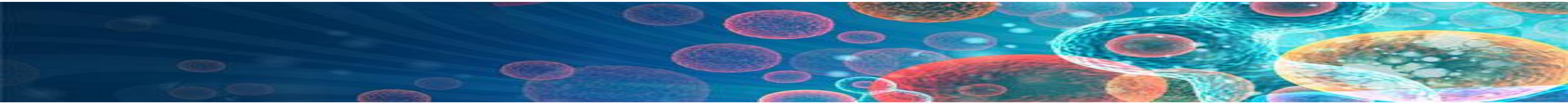
3-Resistant to antimicrobial therapy.



Classification of ID :

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


Primary or Acquired Can Affect
Natural Immunity
Acquired Immunity
Phagocytic Cells
Complement Proteins
T cells
B cells



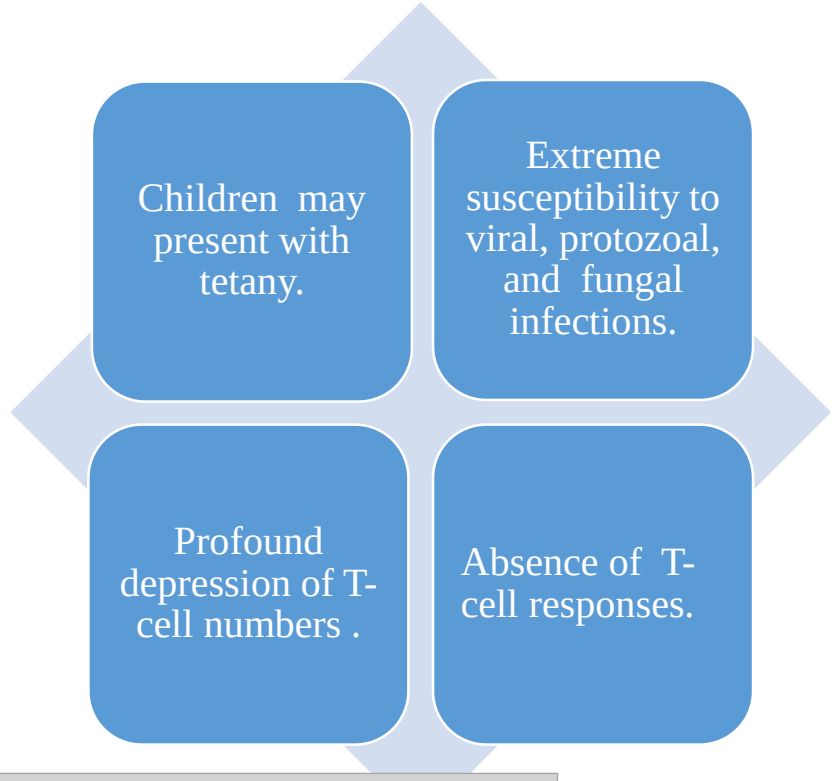
T-cell defects

DiGeorge Syndrome (Congenital Thymic Aplasia)

A congenital defect that is marked by:

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

Features of DiGeorge syndrome



Management of **DiGeorge** syndrome

Fetal thymus tissue graft (14 weeks old)

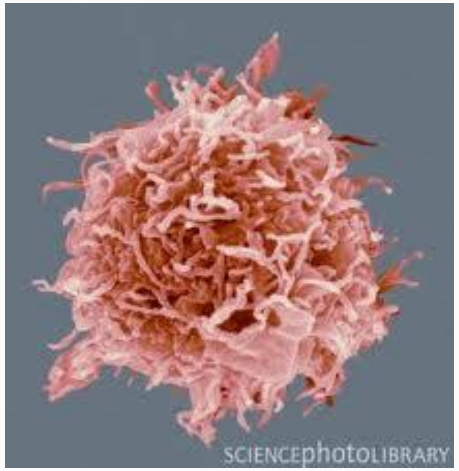
B-cell defects (Gammaglobulinaemias) :

Patients with B-cell defects are subject to:

Recurrent **bacterial** infections, but display the normal immunity to most **viral and fungal** infections.

-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**



-X-linked disease:

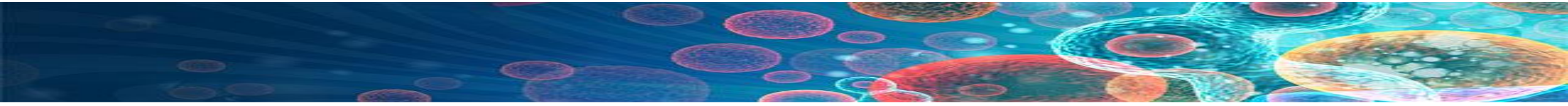
Females : carriers (normal)

Males : manifest the disease

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

(Congenital disease) → The most common type. (80-90%) → CAUSE: Defect in Bruton Tyrosine Kinase (BTK)

The defect involves a block in maturation of pre- B- cells to mature B-cells in bone marrow.

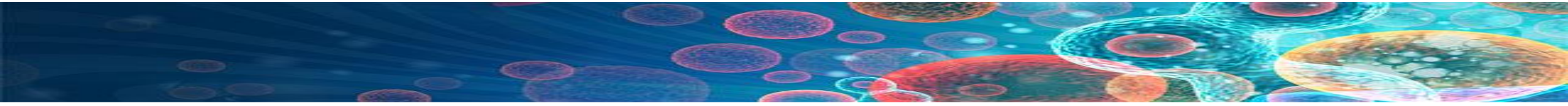


Features of XLA

Reduced B-cell counts to 0.1%
(normally 5-15 %)

Absence of Immunoglobulins

Affected children suffer from recurrent pyogenic bacterial infections



Selective immunoglobulin deficiency

(Congenital disease)

IgA deficiency.

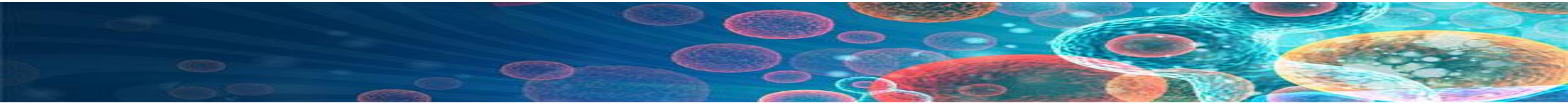
(1:700) ← Ratio

Some have recurrent R.T.I and gastrointestinal tract symptoms

Most are asymptomatic ← (without symptoms)

But may have increased incidence of respiratory tract infections (R.T.I)

Recurrent: متكرر



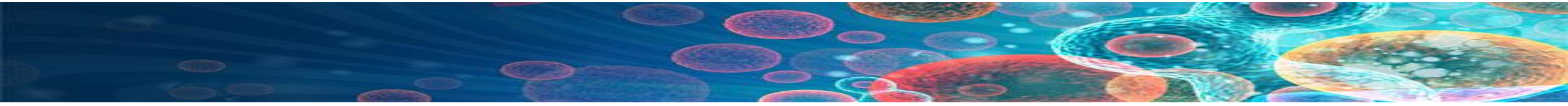
X- linked hyper-IgM Syndrome

(Congenital disease)

Characterized by

Markedly elevated
IgM

Low
IgG, IgA & IgE

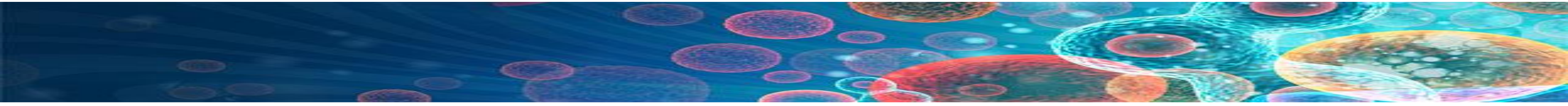


Management of immunoglobulin deficiencies:

- Periodic intravenous immunoglobulin (IVIG) reduces infectious complications.

Remember:
Immunoglobulin = antibodies

video



Severe Combined Immunodeficiency (SCID) (Congenital disease):

Causes of SCID:-

- Enzyme deficiencies:

1. ADA (adenosine deaminase) deficiency.

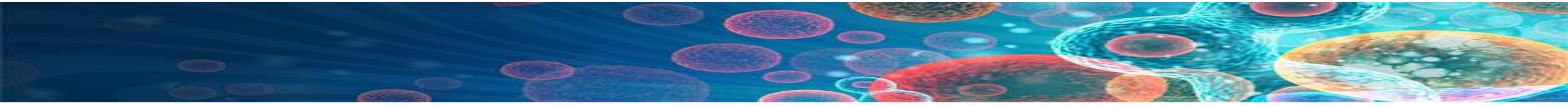
2.PNP (purine phosphorylase) deficienc
Toxic metabolites accumulate in T and B cells.

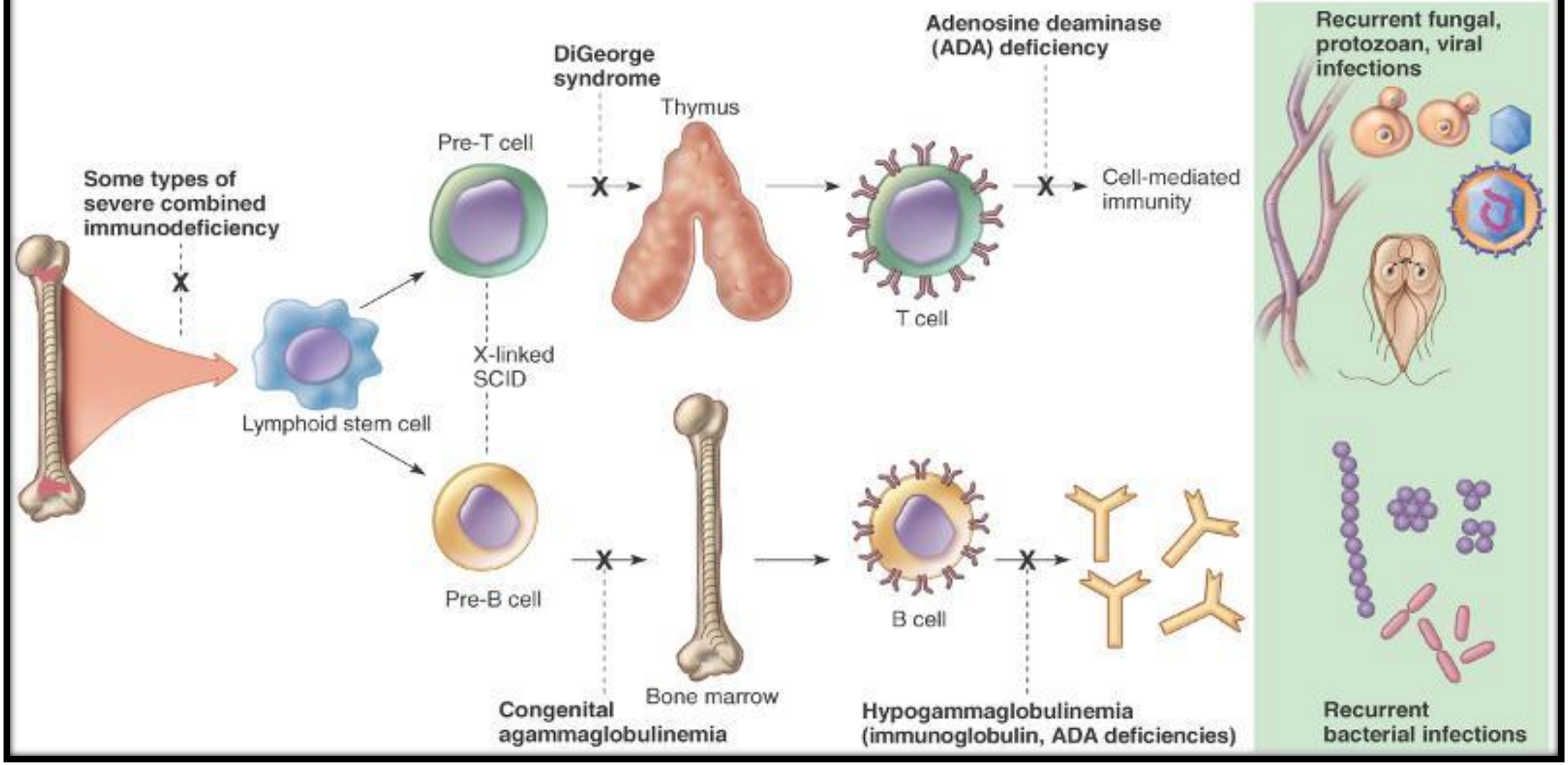
Features of SCID:

Increased susceptibility to :

- Viral.
- Fungal.
- bacterial.
- protozoal infections.

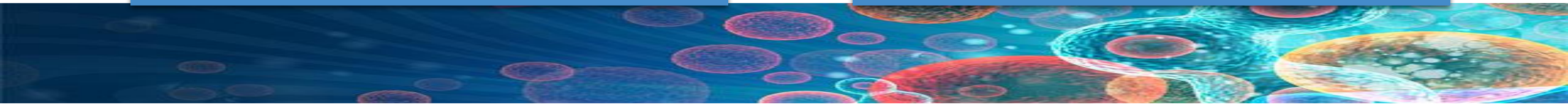
(starting at 3 months of age)

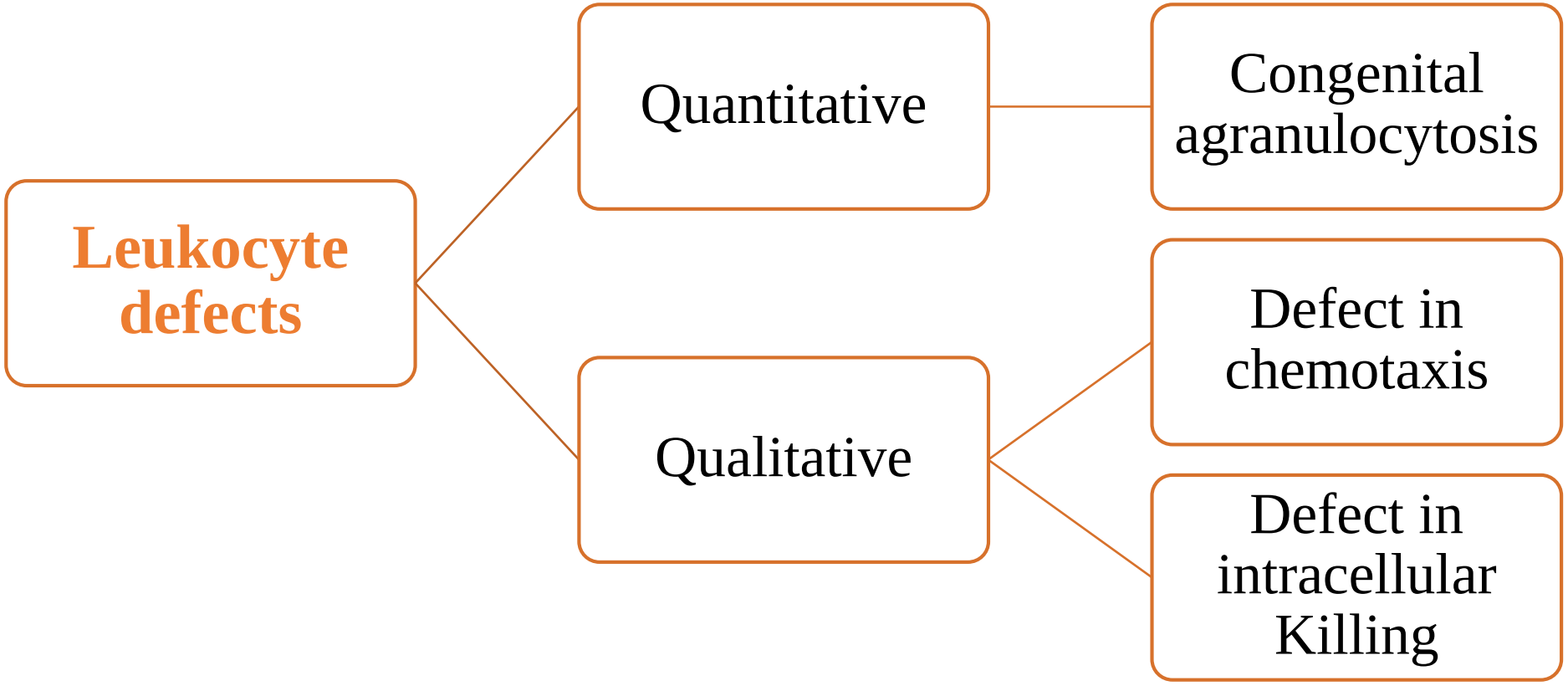


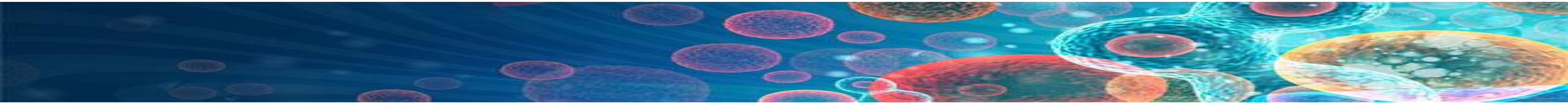


Management of SCID:

- Infusion of purified enzymes.
- Gene therapy.




Leukocyte defects
Quantitative
Congenital agranulocytosis
Qualitative
Defect in chemotaxis
Defect in intracellular Killing



* Quantitative Defects:

For example : Congenital agranulocytosis , which is caused by a defect in the G-CSF (granulocyte colony stimulating factor) .

Features: Pneumonia, otitis media, abscesses .

* Qualitative Defects (Congenital disease) :

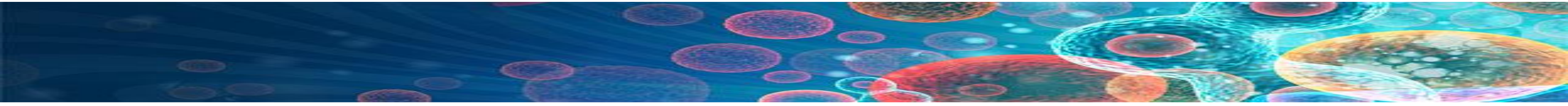
- Defect in chemotaxis

e.g. Leukocyte adhesion deficiency (LAD).

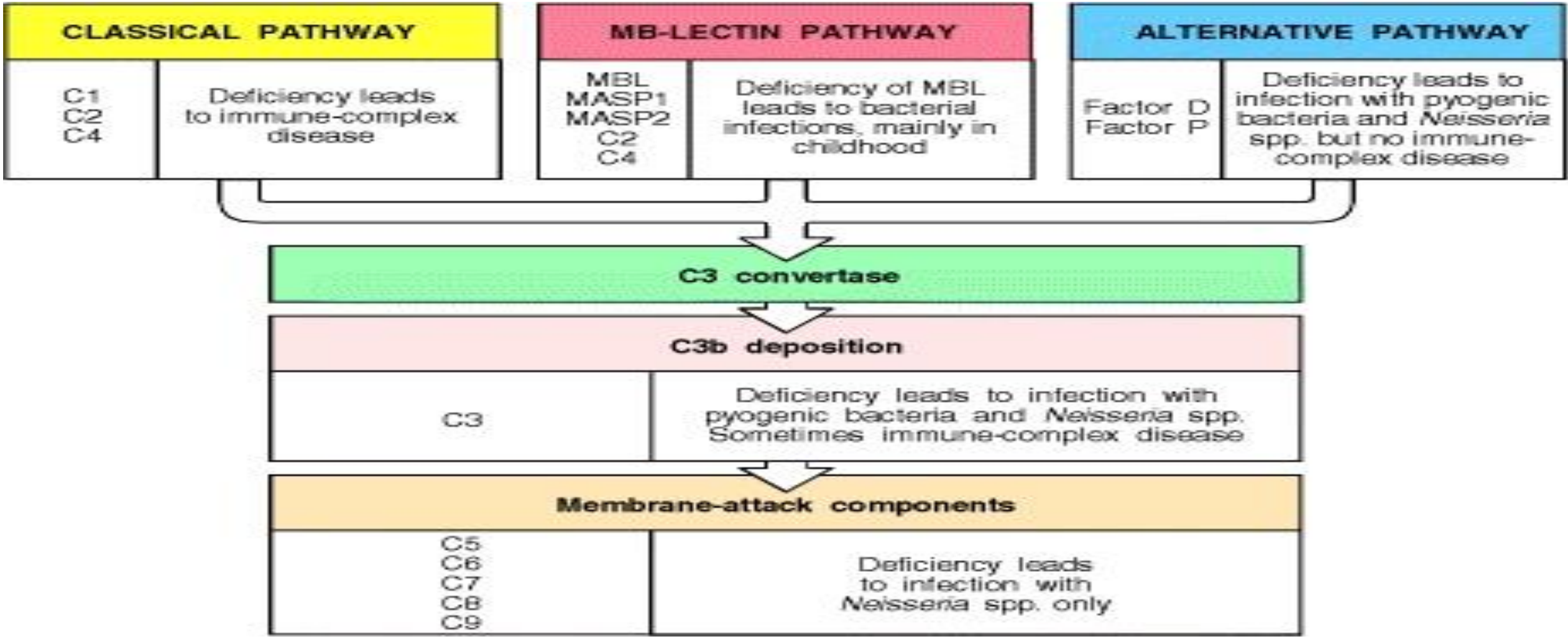
- Defect in intracellular Killing :

e.g. Chronic granulomatous disease (CGD): ⇒ YouTube

- Defect in the oxidative complex responsible for producing superoxide radicals.
- Neutrophils lack the "respiratory burst" upon phagocytosis
- Characterized by recurrent life-threatening bacterial and fungal infections and granuloma formation.

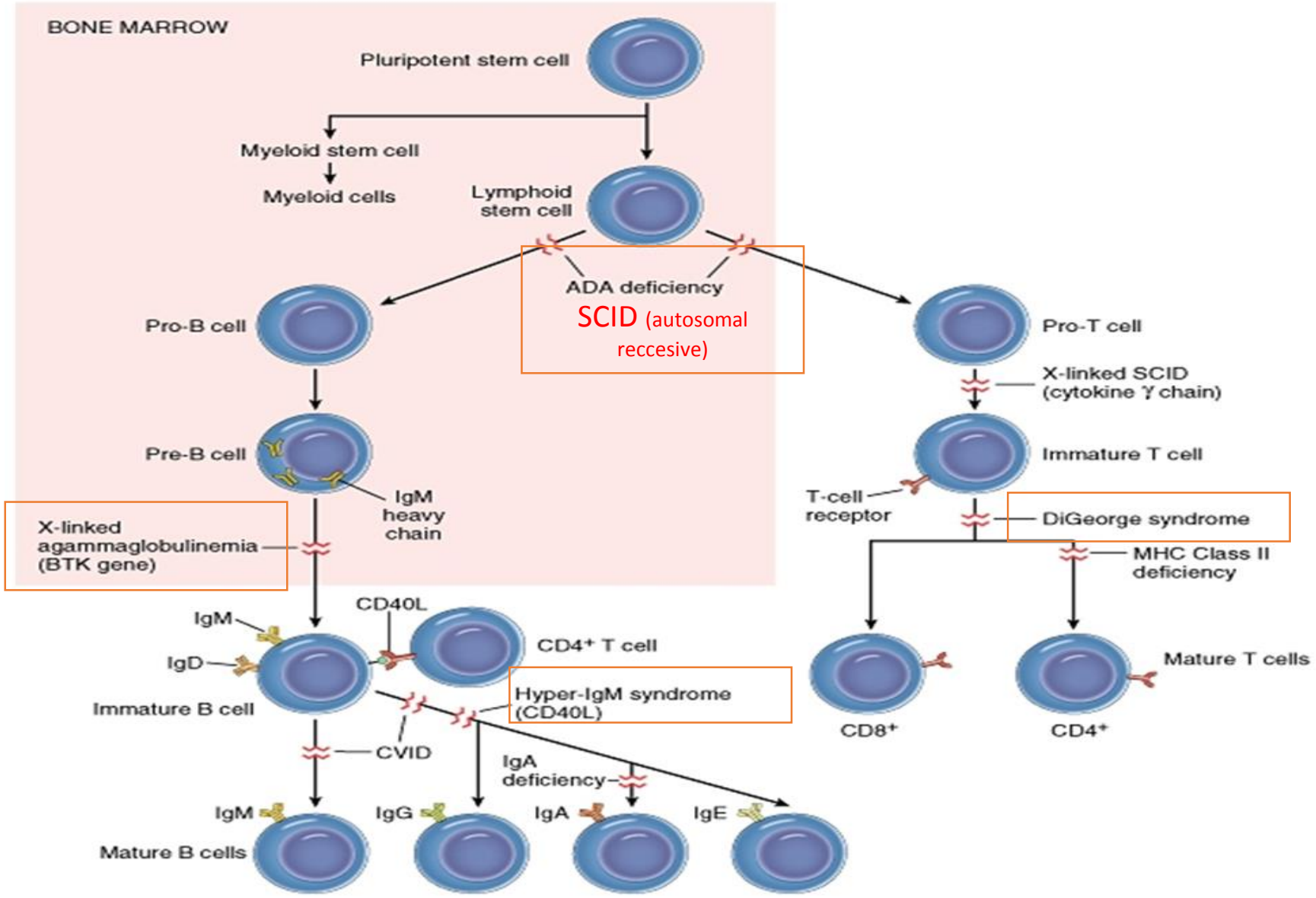


Deficiency of all complement components have been described C1-C9



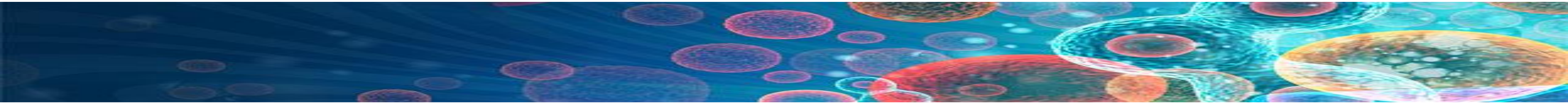
Laboratory diagnosis of ID

- Complete blood count : total & differential
- Evaluation of antibody levels and response to antigens
- T and B cells counts (Flowcytometry)
- Measurement of complement proteins and function (CH_{50})
- Assessment of phagocytosis and respiratory burst (oxygen radicals)



Summary

- 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.



Thank you!

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