IMMUNOLOGICAL DISORDERS

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Autoimmune Diseases

Brain
Multiple Sclerosis
Guillain-Barre Syndrome
Autism

Thyroid
Thyroiditis
Hashimoto's Disease
Graves' Disease

Blood
Leukemia
Lupus Erythematosus
Hemolytic Dysglycemia

Bones
Rheumatoid Arthritis
Ankylosing Spondylitis
Polymyalgia Rheumatica

GI Tract
Celiac's Disease
Crohn's Disease
Ulcerative Colitis
Diabetes Type I

Muscles
Muscular Dystrophy
Fibromyalgia

>100 Autoimmune Diseases

Nerves
Peripheral Neuropathy
Diabetic Neuropathy

Skin
Psoriasis
Vitiligo
Eczema
Scleroderma

Lung
Fibromyalgia
Wegener's Granulomatosis

DEFINITION

- Immunological disorders are diseases or conditions caused by a dysfunction of the immune system and include allergy, asthma, autoimmune diseases, autoinflammatory syndromes and immunological deficiency syndromes.

IMMUNODEFICIENCY DISORDERS

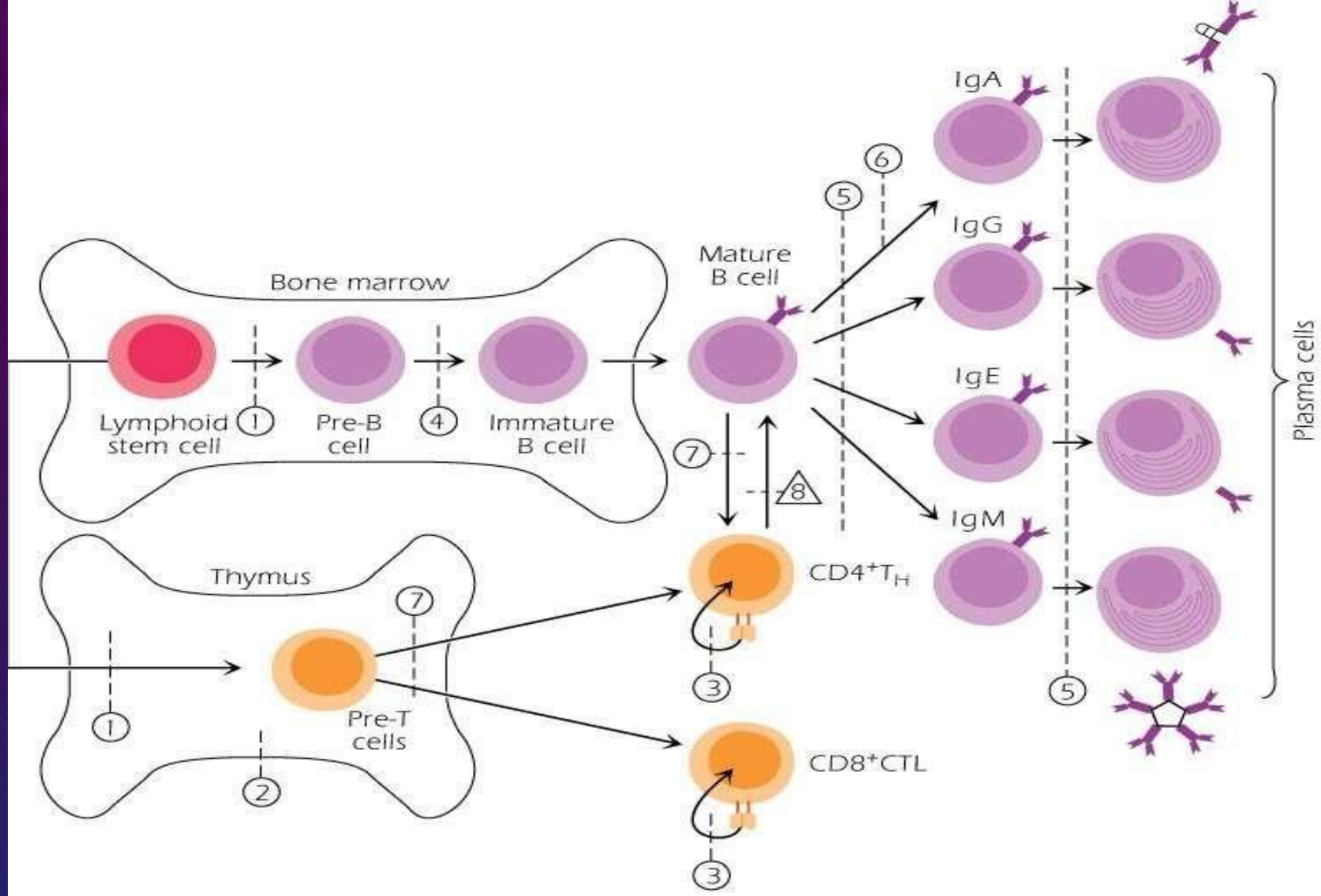
- **Immunodeficiency disorders associated with defect or impairment in immune function or induced through infections and various environmental factors.**

TYPES

- **Primary immunodeficiency disorders:-** Usually congenital, resulting from genetic defects in some components of the immune system.

- **Secondary immunodeficiency disorders:-**

As a result of other disease condition such as HIV infections, malnutrition, immunosuppression.



Key:

1. Severe combined immunodeficiency syndrome
2. Congenital thymic aplasia (DiGeorge Syndrome)
3. T cell signaling deficiency
4. X-linked agammaglobulinemia (Bruton's)
5. Common variable immunodeficiency disease (various forms)
6. Selective IgA deficiency
7. Bare lymphocyte syndrome
8. Hyper IgM sysndrome

MANIFESTATIONS:

- Disorders are manifested at different levels including :
  - B cell, T cell, phagocytic cells and complement system.
  - Most prominent manifestations: dermatological conditions such as eczema and cutaneous infections.

SYMPTOMS:

- Recurrent respiratory infections.
- Persistent bacterial infections →sinusitis, otitis and bronchitis.
- Increased susceptibility to opportunistic infections (OIs) and recurrent fungal yeast infections.
- Skin and mucous membrane infections.
- Resistant thrush, oral ulcers and conjunctivitis.
- Diarrhoea and malabsorption.
- Failure to thrive and delayed or incomplete recovery from illness.

CLASSIFICATION OF PRIMARY IDDS

Primary B cell immunodeficiency:

X-linked Agammaglobulinaemia (Bruton,s disease)
Selective IgA deficiency

Primary T cell immunodeficiency:

Di George syndrome
Ataxia – telangiectasia
Wiskott – Aldrich syndrome
Acquired immunodeficiency
Chemotaxis deficiency
Chronic granulomatous disease
Chediak – Higashi syndrome
Leukocyte adhesion deficiency

Complement system deficiency

ETIOLOGY

- Etiology associated with
  - Genetic defects of missing enzymes.
  - Specific development impairment (pre-B-cell failure).
  - Infections, malnutrition and drugs

PRIMARY B CELL IMMUNODEFICIENCY

- Common variable immunodeficiency associated with
  - Mature B cells failure to differentiation into mature plasma secreting cells (antibody forming cells).

X-LINKED AGAMMAGLOBULINAEMIA (XLA)/BRUTON'S DISEASE:

- Deficiency of B cell tyrosine kinase causing failure in the development of pre-B cell maturation to B cells.
- Majority of XLA patients show:
  - Profound hypogammaglobulinaemia involving all immunoglobulin classes with <1% B cells in normal peripheral blood.

CLINICAL PRESENTATIONS OF BRUTONS DISEASE:

- Increased susceptibility to encapsulated recurrent pyogenic bacteria (*S. pneumonia*, and p*seudomonas* species).
- Skin infections (group A streptococci and *S. aureus*).
- Persistent viral or parasitic infections.

SELECTIVE IGA DEFICIENCY (IGA D)

- Patients with IgA deficiency have:
  - IgA levels < 5mg/dL with normal levels of other Igs and
  - 50% have chronic otitis, sinusitis or pneumonia.

- IgA committed B lymphocytes:
  - Fail to mature into IgA-secreting plasma cells caused by intrinsic B cell defect.

- **Patients of IgA deficiency are susceptible to:**
  - Allergic conjunctivitis, urticaria and asthma.
  - Autoimmune and neurological disorders.
  - Various gastrointestinal diseases (food allergy).
  - recurrent sinopulmonary infections.

SEVERE COMBINED IMMUNODEFICIENCY DISEASE (SCID)

Disorder characterized by:

- Deficiency in both B and T lymphocyte functions with markedly low IgG, IgA and IgE levels.

- SCID associated with:
  - Children failure to thrive.
  - chronic respiratory infections.
  - Gastrointestinal and/or cutaneous infections particularly recurrent viral, bacterial, fungal and protozoan infections in 6 month's infant.

- SCID manifests early with:
  - Persistent and recurrent diarrhoea, otitis, thrush and respiratory infections in the first few months of life.
- T cell defects associated with:
  - Candidiasis, CMV infection, measles and varicella leading to life threatening pneumonia, meningitis and sepsis.
- **SCID managed through Ig infusion, stem cell transplantation and gene replacement.**

T CELL IMMUNODEFICIENCY DISEASES

- **T cell congenital disorders display:**
  - Little or no cell mediated immunity and may involve B cell deficiencies.

- **Patients particularly susceptible to:**
  - Repeated fungal (*Candida*) infection.
  - Protozoan and viral infections.

PRIMARY T CELL IMMUNODEFIENCY INCLUDES:

- Di-George syndrome
- Wiskott-Aldrich syndrome
- Cartilage hair hypoplasi,
- Ataxia - telangiectasia
- Defective expression of class II MHC molecules
- Defective expression of CD3-T cell receptor (TCR) complex

DI GEORGE SYNDROME (THYMIC APLASIA)

Congenital disorder characterized by:

- Lack of embryonic development or underdevelopment of the 3rd and 4th pharyngeal pouches.
- Thymic hypoplasia, hypothyroidism and congenital heart disease.
- Patients susceptible to uncontrolled opportunistic infections.
  - Impaired in cellular mechanisms.
  - Profound lymphopenia (T cell <1200µL).

ATAXIA TELANGIECTASIA (AT)

Autosomal recessive progressive neurodegenerative childhood disorder associated with:

- Lack of coordination (cerebella ataxia) and dilation of facial blood vessels (telangiectasis) and slurred speech.
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- Patients have defective mechanisms of DNA repair and are predisposed to leukaemias and lymphomas.
- Extremely sensitive to radiation exposure and susceptible to chronic respiratory infections.

Wiskott-Aldrich Syndrome (WAS)

An X-linked recessive disorder associated with thyrombocytopenia and eczema.

- Patients have
  - Elevated IgA and IgE
  - Low IgM

Variable T cell dysfunctionsT cell dysfunction manifested by:

- Severe herpex virus and *Pneumocystis carinii* infections
- Increased lymphomas and autoimmune diseases.
- Recurrent pyogenic bacterial infections.
- Usually affecting ears, sinuses and lungs.


Thank you