

# MIRACLE Academy

قال تعالى (يَرْفَعُ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ)

تفريغ المناة  
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لجان الدفعات

# Immunodeficiency Diseases

أمراض نقص المناعة

# Objectives

- Outlines different types of autoimmune deficiencies
- Differentiates primary and secondary autoimmune deficiencies
- Discuss the common characteristics and the major clinical diseases of
  1. B cell deficiency
  2. T cell deficiency
  3. Combined deficiency
  4. Phagocytic deficiency
  5. Compliment deficiency

# Introduction

- Deficiencies of host defense systems result in an immunologic imbalance that can lead to a susceptibility to infection, an autoimmune disease, or a predisposition to malignancies.

الناس المصابين بمرض نقص المناعة رح يعانون طوال عمرهم من **recurrent infections** يعني بيطلعو من مرضة وبيدخلو بمرضة في ناس بيتحملو وبيعيشو لأعمار طويلة وفي أطفال من عمر 3 شهور لما يصيبهم **infection** بيموتو ، وزمان كانوا يعملو للمصاب بهاد المرض **isolation** عن الهواء الجوي لحتى ما يتعرض لأي بكتيريا أو فيروس



# Types of immunodeficiency disorders:

## Primary: Causes in immune system component:

### a. According of component:

- Complements.
- Phagocytic.
- B cells.
- T Cells.

### b. According to the etiology:

- Congenital (X-linked disease)
- Acquired (AIDS)
- Embryogenesis (Digeorge syndrome).
- Idiopathic

## Secondary: Non Immunogenic causes:

- Prematurity. بيكون الجهاز المناعي لسا ما اكتمل نموه
- Mal nutrition. سواء المجاعة بالمعنى الحرفي اللي هو نقص تغذية أو سوء التغذية يعني تناول أطعمة غير مفيدة فلازم الواحد يأكله يركز على نوعية مش كمية.
- Hodgkin`s and others malignancy. سواء بسبب المرض نفسه أو الأدوية اللي بيستخدمها لعلاج ال cancer
- Injury, Burns, Splenectomy.
- Drugs. مثل ال corticosteroid واحنا بنعرف انه لما نستخدم ال inhaled corticosteroid لازم نعمل mouth washing لحتى نخفف من خطر الإصابة من fungal infection in the mouth

# 1. B-cell defect

- Recurrent infection by extracellular organisms, namely pyogenic and enteric bacteria, because patients are deficient in serum antibodies necessary for phagocytosis.
- Recurrent infections with encapsulated bacteria
- Chronic sinupulmonary (ears, sinuses, and respiratory tract) infections
- Sites of infection include the skin, sinuses, meninges, and the respiratory, urinary, and gastrointestinal tracts.

فإذا دكتور كان يبجي عنده عالعيادة طفل بشكل مستمر بسبب bacterial infection فهو بيروح وبيعمل فحص للantibodies عنده ويتأكد اذا في مشكلة مناعية أو لأ

# Bruton's Agammaglobulinemia

- Also known as X-linked agammaglobulinemia (XLA) or Bruton agammaglobulinemia
- Immunology:
  - No B cells or non functional B cells including defective signaling or defective BCR
  - Markedly low levels of Immunoglobulins
- Clinical:
  - Child clinically well for first 6 months of life
  - Recurrent upper/lower respiratory tract infections with encapsulated bacteria (*S. pneumoniae*) large type of bacteria that can't be engulfed by phagocytes
  - Sepsis, meningitis, skin infections
  - Short life span
- Treatment: IVIG, antibiotic therapy  
IV immunoglobulin

# IgA deficiency

- Immunology:
  - Most common humoral antibody deficiency
  - Isolated low IgA level
- Manifestation:
  - 50-80% asymptomatic
  - frequent infections of both the sinuses (paranasal sinuses) and the respiratory tract (lungs, airways, and bronchi)  
● Recurrent sinopulmonary infections most frequent manifestation
  - May have severe malabsorption (chronic diarrhea)
  - Increased risk of autoimmune disorders
- Treatment: Broad spectrum antibiotics

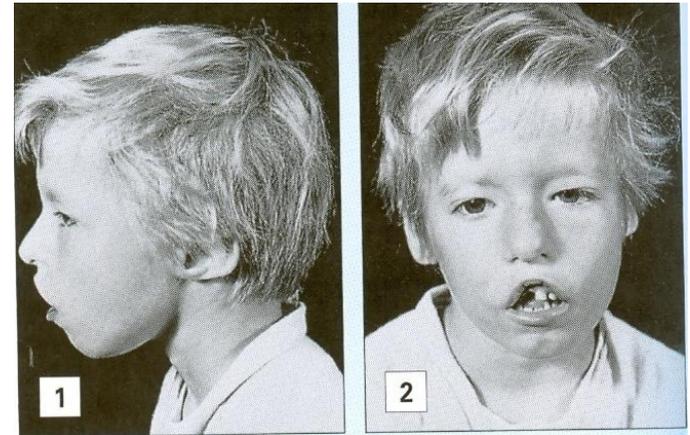
## 2. T-cell deficiency disorders

- Also known as cell-mediated (cellular) immunodeficiencies, result from **abnormalities in T-cell functions**. *humoral immunity* أو *cellular immunity* سواء دورها بال
- Antibody production is also likely to be affected in patients with severe T-cell abnormalities because T cells are important immunoregulators of B-cell differentiation and function.
- **Recurrent infections** --Causative agents are intracellular pathogens (e.g., herpesviruses, mycobacteria, fungi (Candida), and protozoa (Pneumocystis carinii, **Toxoplasma**)).

داء القطط ينتقل للإنسان عن طريق ال*feces* تبع القطط  
بتمر بعدة *cycles* بتصيب الحويصلات الموجودة بال*lungs* وتسبب *sever pneumonia*

# DiGeorge Syndrome

- Immunology:
  - Poorly developed or functioning thymus
  - Depression of T cell numbers
  - Absence of T cell response
  - Humoral response to T independent antigens only
- Clinical: Overwhelming infections with viruses, fungi, bacteria
- Treatment: correct hypocalcemia, cardiac defects, fetal thymus transplant



## 3. Combined Deficiencies

- Immunological abnormalities are combined to B cells and T cells

# Sever Combined Immune Deficiency (SCID)

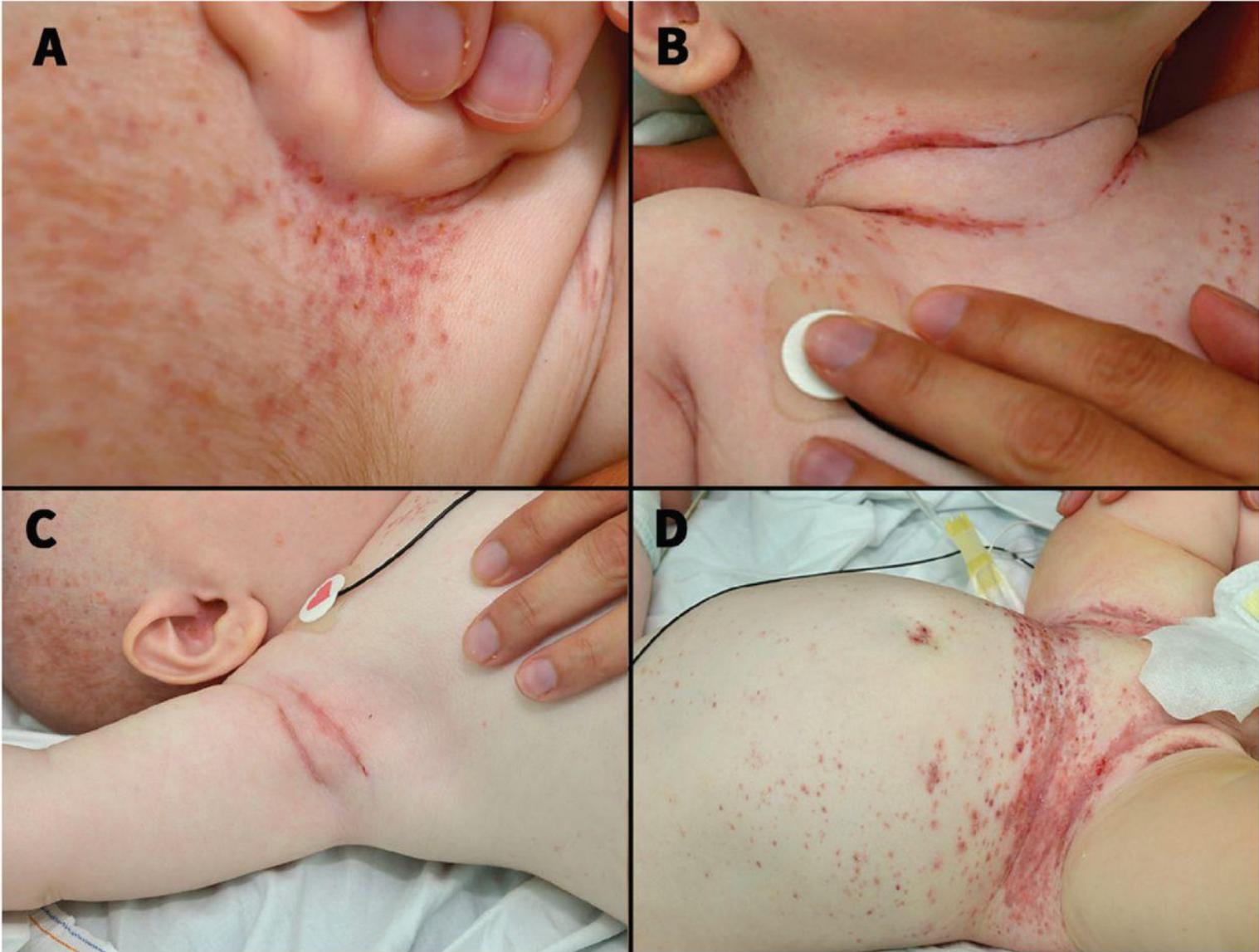
- Immunology:
  - Defects in stem cell maturation with various genetic defects
  - No TCR or defective TCR (T cell receptor )
  - Defective cell signaling
  - Defective IL 2
- Manifestations seen in first 3 months of life
  - Recurrent, severe bacterial, viral, fungal, and protozoan infections (usually respiratory infections)
  - Failure to thrive, diarrhea, dermatitis, candidiasis
  - Death at early age
- Treatment: isolation, treat underlying infections, bone marrow transplant



# Wiskott Aldrich Syndrome

- Immunology:
  - X linked disorder (more common in females)
  - Affects platelet numbers/function
  - Affects T cell function
  - Lower amounts of IgM
  - characterized by eczema, thrombocytopenia (low platelet count), immune deficiency, and bloody diarrhea (secondary to the thrombocytopenia).
- Symptoms in infancy
  - Recurrent, severe infections
  - Eczema
  - Thrombocytopenia (petechiae)
- Treatment: manage bleeding/infections, BMT  
bone marrow transplantation

petechiae



## 4. Phagocyte disorders

- Clinical features: Affected individuals are prone to infections with low-grade bacteria such as *Staphylococcus aureus* and gram-negative enteric bacteria.

# Chronic Granulomatous Disease (CGD)

- Immunology:

- Non functional phagocytes
- Defective NADPH oxidase

هاد الانزيم بتستخدمه كريات الدم البيضاء لحتى تصنع hydrogen peroxide وتستخدمه لحتى تقضي على الـ bacteria أو الـ fungi

- 75% X-linked recessive, 25% autosomal recessive

- Manifestation:

- Severe, recurrent staph aureus infections of lymph nodes, skin, and lung

- Dx: Nitroblue tetrazolium (NBT) test

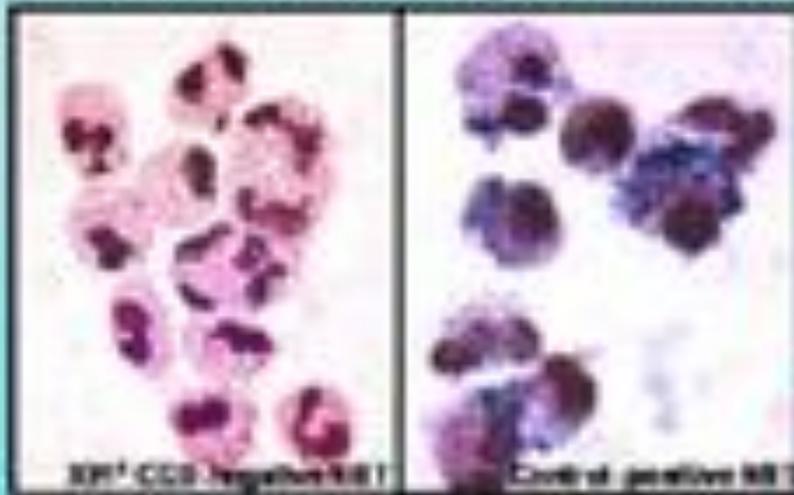
- Treatment: antimicrobial prophylaxis, IFN-gamma, BMT





## NBT test to diagnose CGD

negative NBT



positive NBT  
Negative for CGD

NBT reduction test

# 5. Complement Disorders

- Deficiency of early complement components (C1, C4, C2) results in a symptom complex resembling collagen vascular disorders (e.g., systemic lupus erythematosus (SLE)] and increased susceptibility to pyogenic infections.
- C3 deficiency results in severe pyogenic infections. Several patients have also had SLE and glomerulonephritis.
- Deficiency of late complement components (C5, C6, C7, C8) results in systemic Neisseria infections such as meningococcal sepsis and meningitis, and disseminated gonococcal infections.

مرض السيلان ينتقل عن طريق  
sexual intercourse

# Diagnosis of immunodeficiency disease

- laboratory investigation:
  - CBC: increase PMNL suspect phagocyte deficiency
  - Culture: to know the organism and choose the antibiotics.
  - ESR and CRP: inflammation markers for follow up.

## ESR (erythrocyte sedimentation rate )

بالعادة كريات الدم الحمراء بتكون محاطة بـ negative charge فبيصير بين الخلايا repulsion فما بيترسبو بسرعة ، بينما لما يصير فيه infection هي الـ negative charge إما بتضعف أو بتختفي فما يصير repulsion بين الخلايا فبيترسو بسرعة فكل ما كان الـ sedimentation rate أعلى فهاد indication انه عندي infection

## (C-reactive protein)

هاد بروتين بيتصنع بالـ liver لما يكون فيه acute inflammation

- Specific tests:

1. B-cells:

- Total Ig
- Selected IgA and IgG
- Antibodies for previous vaccination

2. T cells:

- Lymphocyte count.
- Delayed hypersensitivity reaction
- T cells and macrophage function test.

3. Phagocyte:

- Neutrophil count
- NBT test for screening.
- Macrophage function test

4. Complement: Total and specific complement count.