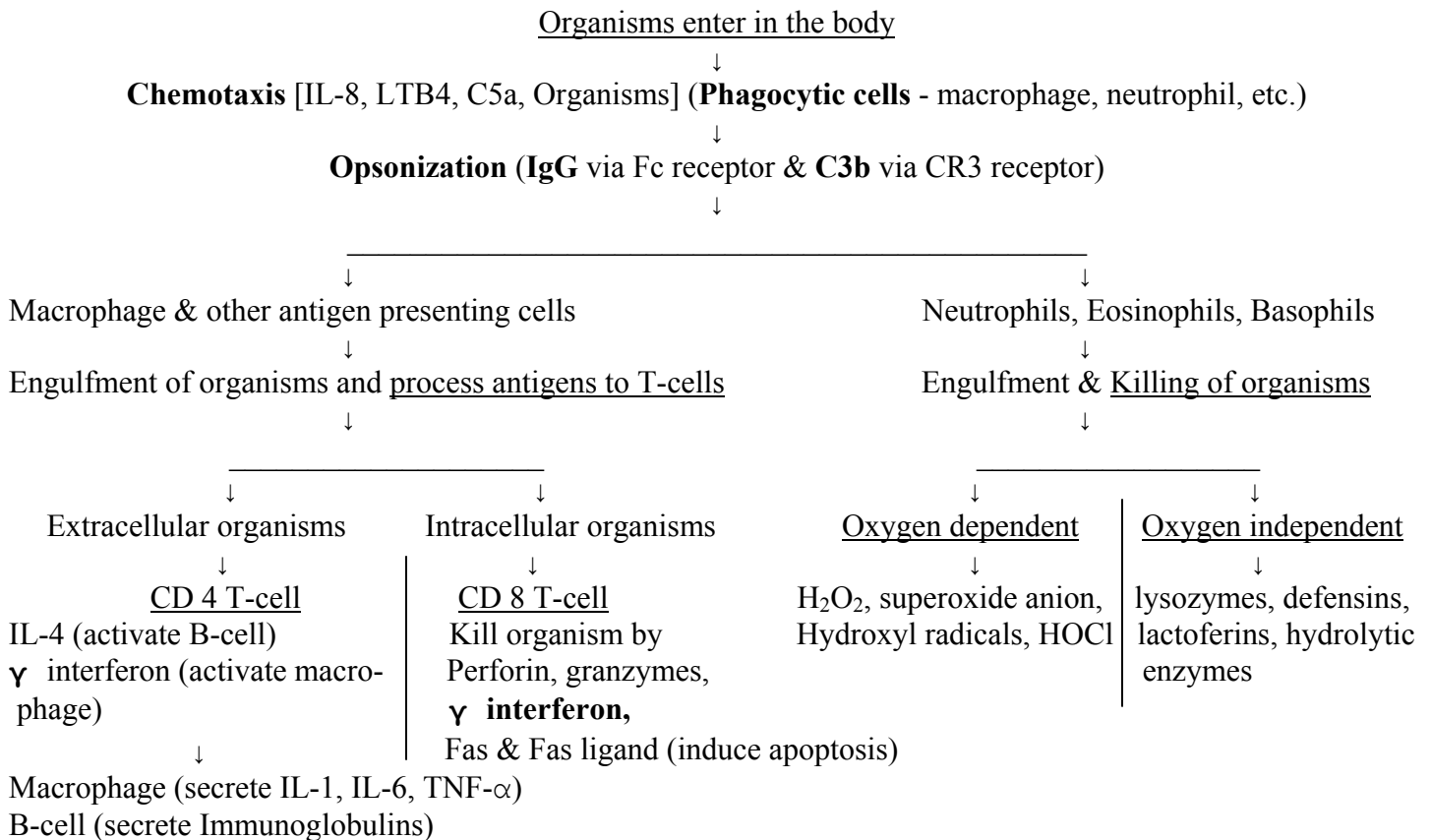


IMMUNOLOGY

## 1. What happen when organism enter to the body?



- When organism enter in the body, IL-8, LTB4, C5a and Organisms itself act as a chemotactic agents to attract phagocytic cells (macrophage, neutrophil, etc.) Meanwhile IgG via Fc receptor and C3b via CR3 receptor attach to organism and mark them for engulfing by phagocytic cells. Now depends upon phagocytic cell, organisms are either presented to T-cells or killed directly. Macrophage and other antigen presenting cells present organisms to T-cells whereas neutrophils, eosinophil kill them directly.
- **Macrophage** present extracellular organisms to CD 4 cells while intracellular organisms to CD 8.
- When organisms are presented to CD4 cells, they secrete IL-4 (which activate B-cells) & gamma interferon (which activate macrophage, now to kill organisms). Macrophage secrete IL-1, IL-6 and TNF-α (acute phase reactants) and B-cells (transform into plasma cells) secrete immunoglobulins to kill organisms [**B-cell mediated immunity**: Naïve mature B cells produce both IgM and IgD. After activation by antigen, these B cells proliferate and begin to produce high levels of IgM and IgD. If these activated B cells are also activated via their CD40 and IL-4 receptors (both modulated by T helper cells), they undergo antibody class switching to produce IgG, IgA or IgE antibodies. During class switching, the constant region portion of the antibody heavy chain is changed, but the variable region of the heavy chain stays the same. Since the variable region does **not** change, class switching does **not** affect antigen specificity. Instead, the antibody retains affinity for the same antigens, but can interact with different effector molecules.]

- **Concept:** IgM is the **only Ab** where there is **NO** class switching required. So If **thymus (T-cells)** is **not** involved, there is **no** class switching & **only IgM is produced**
- When organisms are presented to **CD8 cells**, they kill organisms directly by perforins, granzymes, **gamma interferon** and Fas & Fas ligand (which induce apoptosis). [**Cell mediated immunity, T-cell mediated immunity**]
- When **Neutrophils** engulf organism, they kill them directly. Killing occurs through two pathway, oxygen dependent and oxygen independent.
- **Oxygen Dependent:** Killing occurs by producing H<sub>2</sub>O<sub>2</sub>, superoxide anion, Hydroxyl radicals, HOCl. This involve **NADPH oxidase** [produce superoxide anion] & **Myeloperoxidase** enzymes [produce HOCl]
- **Oxygen Independent:** Killing occur by lysozymes, defensins, lactoferins, hydrolytic enzymes
- **Concept:** Oxygen independent killing is still working in patient with NADPH oxidase [Chronic Granulomatous Disease] and Myeloperoxidase disease
- **Concept:** In Myeloperoxidase deficiency, H<sub>2</sub>O<sub>2</sub> is still produce so organisms which lack catalase enzyme can be still killed by neutrophils. [**Example: Streptococci** are still **killed** but **not staphylococci** which produce catalase]

## 2. Important CD markers on different cells

CD Markers	Different Cells	Functions
▪ CD 3	▪ All T-cells	▪ TCR associated signal transduction molecule ▪ TCR = T-cell receptor
▪ CD 2	▪ All T-cells	▪ Adherence to other cells, bind to LFA-3 ▪ LFA-3 = Lymphocyte Function associated Antigen
▪ CD 4	▪ Helper T-cells	▪ Interaction with MHC class 2 cells
▪ <b>CD 28</b>	▪ Helper T-cells ▪ Most CD 8 cells	▪ Co-stimulatory molecule needed for activation of T-cells ▪ Binds on B-cells, Macrophage, Dendritic cells
▪ <b>CD 40 ligand</b>	▪ Activated Helper T-cells	▪ Binds to CD 40 on B-cells ▪ <b>Essential for class switching (from IgM to IgG, IgA or IgE)</b>
▪ CD 14	▪ Macrophage	
▪ CD 16, CD 56, CD 2	▪ NK cells ▪ Lymphokine Activated Killer (LAK)	▪ <b>NO</b> CD 3,4,8,19 on NK cells
▪ CD 19, CD 20, <b>CD 21, CD 40</b>	▪ B-cells	▪ <b>CD 40:</b> Require for class switching ▪ <b>CD 21:</b> Serve as receptor for EBV (Ebstein-Bar Virus)
▪ CD 15, CD 30	▪ Reed – Sternberg Cells	

## 3. Important antigen receptors on different cells

- **TCR:**  $\gamma\delta$  [T-cells in Skin & Mucosal surface],  $\alpha\beta$  [T-cells at other sites]
- **BCR:** Ig M, Ig D
- **MHC-1:**  $\alpha$  1,2,3  $\beta$ <sub>2</sub>
- **MHC-2:**  $\alpha\beta$

4. Receptors through which signal transduction occur in B & T cells
  - B-cells –  $\alpha$ ,  $\beta$ , CD 19,20,21
  - T-cells – CD 3
  
5. **Human leukocyte antigens and different classes:**
  - The human leukocyte antigen system (HLA) is the name of the **major histocompatibility complex (MHC)** in humans. It is **located on chromosome 6**. Two different classes.
  - HLA class 1 [MHC-1]: HLA-A, HLA-B, HLA-C
  - HLA class 2 [MHC-2]: HLA-DP, HLA-DQ, HLA-DR

\* **Location of MHC-1 & MHC-2 antigens:**

  - MHC-1: All nucleated cells & platelets (**NO** MHC on RBC)
  - MHC-2: Antigen Presenting cells (Dendritic cells, langerhans cells, activated macrophage, B-cells, activated T-cells & activated endothelial cells)

\* **Importance:**

  - MHC-1 is necessary for antigen recognition by CD8+ T-cells
  - MHC-2 is necessary for antigen recognition by CD4+ T-cells

\* **Difference:**

  - MHC-1: React with **ENDOGENOUSLY** produce peptides by virus, intracellular bacteria, intracellular parasites and tumor cells
  - MHC-2: React with **EXOGENOUSLY PROCESSED** antigens

\* **Handling of organisms:**

  - MHC-1: It works with intracellular organisms *so after reacting with endogenously processed antigen*,  $\beta_2$  microglobulin transports MHC class-1 molecules to the cell surface where it can be recognized by CD 8 T-cells and organisms are then killed by CD8 T-cells
  - MHC-2: It works with Extracellular organisms so once organisms engulfed, MHC class-2 molecule *fuse with vacuole containing exogenously processed antigen*, invariant chain is released and MHC-2-peptide complex is then transported to the cell surface where it can be recognized by CD 4 T-cells. **Invariant chain** prevents interaction b/w endogenously produced peptide and MHC-2 molecules intracellularly
  
6. How does ADCC [Antibody Dependent Cellular Cytotoxicity] and NK cells mediated cytotoxicity differed?
  - ADCC: **IgG** + NK cells → use CD 16 molecule (Fc receptor) to identify target cells.
  - NK cells mediated cytotoxicity: use CD 56 (**No** antibody involve Ex.- **lysis of infected RBC**)
  
7. **Complement system:**
  - **Classical Pathway**: activated by antigen-Ab reaction (IgG & IgM, IgM most efficient) [start point C1] [C1 - C4 - C2 - C3] [C4bC2a is C3-convertase] [C4bC2aC3b (C5-convertase) splits C5 into C5a & C5b which then form C5b,6,7,8,9]
  - **Alternative Pathway**: C3 hydrolyze *spontaneously* in our body into C3a & C3b. If there is a pathogenic membrane surface nearby, C3b binds to it. If not, both C3a & C3b rejoin. Upon binding with a cellular membrane, C3b is bound by factor B to form C3bB. This complex in presence of factor D will be cleaved into Ba and Bb. Bb will remain covalently bonded to C3b to form C3bBb which is the alternative pathway C3-convertase. Alternative pathway is also activated by simple presence of

organism in body (LPS of cell wall of gram (-) bacteria), it *doesn't require antibody*. [**start point C3b**]  
[C3b splits C5 into C5a & C5b which then form C5b,6,7,8,9]

▪ **Important Products of Complement Pathways:** C3a,C4a,C5a; C3b and C5b6789

\* **Function of complement system:**

- C3b – Opsonization of pathogen
- C3a,C4a,C5a – Play role in Chemotaxis
- C5b,6,7,8,9 – Membrane attack complex – kill pathogen

\* **How to determine complements are working:**

- ↓C2/C4 – classical pathway is working
- ↓Factor B – alternate pathway is working
- ↓C3 – both pathways are working

- C3-convertase can be inhibited by Decay accelerating factor (DAF)
- C5a and C3a are known to trigger mast cell degranulation
- The inhibition of C1-complex is controlled by C1-inhibitor (C1 esterase). [C1-esterase also inhibits proteinases of the fibrinolytic, clotting, and kinin pathways. The kinin-kallikrein system makes bradykinin. Deficiency of C1-inhibitors leads to activation of plasma kallikrein which produce bradykinin which is a potent vasodilator responsible for angioedema.]

8. Important points to remember about **different immunoglobulins:**

- **IgG:** Main Ab in Secondary immune response – highest concentration in the body – **only Ab** that can **cross placenta** – remain up to 4-6-months in the newborn – capable of **Opsonization**
- **IgM:** Main Ab in Primary immune response – **largest Ab** in the body, has five Fc regions (circulates as a pentamer) – presence on IgM in newborn suggest recent infection – **first Ab to appear** in the serum **after exposure to antigen** – effective in complement fixation – Isohemagglutinins, rheumatoid factors, and heterophile antibodies are all IgM
- **IgA:** present in secretions [**Breast milk (colostrum)**, GI secretions, saliva, tears] – deficiency of IgA causes **repetitive upper respiratory tract infections, transfusion reaction**
- **IgD:** functions as a cell surface antigen receptor on **undifferentiated B cells**.
- **IgE:** involved in **allergic response and immediate type of HS** (type-1) – Fc region of IgE binds to basophils and mast cells – binding of antigen to two IgE molecules leads to mast cells degranulation and release of leukotrienes, Histamines, eosinophils, hemotactic factors and Heparin – IgE is also involved in killing of parasites [IgE + eosinophils mediated cytotoxic reaction – type-2 HS].

9. What is the difference b/w papain & pepsin?

- **Papain:** If Ab reacts with papain & then Ag is added – Ag will be unaffected
- **Pepsin:** If Ab reacts with pepsin & then Ag is added – Ag will agglutinate / precipitate

10. **Antigen Specificity:** Variable region of both heavy & light chain. **Class switching doesn't affect Variable region of both heavy & light chain** therefore class switching doesn't affect specificity of antibody to that antigen

11. What are Allotype & Idiotype?

- **Allotype:** A genetically determined difference in molecule b/w two members of the **SAME SPECIES**
- **Idiotype:** The individual, unique differences b/w antibodies of different antigen-binding specificities

12. **Important interleukins, other immune system cells & their functions:**

- IL-4 – class switch to **IgE**
- IL-5 – class switch to IgA & ↑**Eosinophils**
- Macrophage – IL-1, IL-6, IL-8, TNF- $\alpha$
- **IL-10** – Downregulate CMI (cell mediated immunity), Th1 [helper T-cell 1]
- **$\gamma$  interferon** – Downregulate Th2
- **Th1 – Delayed Type Hypersensitivity (DTH)** (type-IV HS)
- Th2 – Antibody mediated immunity
- IL-1 – Pyrogenic (**fever inducing**)
- IL-6 – Stimulate Acute phase proteins
- IL-3 – Stimulate Bone marrow stem cells (granulocyte & monocytes)
- IL-7 – Stimulate Pre-B & Pre-T cells (lymphoid cell development)
- IL-2 – stimulate B-cells to produce antibody and self stimulation of T-cells. IL-2 is produced by Th1, NK and Tc

13. Important points to remember about **Hypersensitivities & their examples:**

- **Type I Hypersensitivity reaction (HS):** Anaphylaxis [**bee stung**, severe allergic reaction due to peanut]; mast cells and Basophils degranulation (release of Histamines) – Bronchospasm, vasodilation, etc – **Tx:** Epinephrine [SC, 1:1,000] [prevents mast cell degranulation by increasing cyclic AMP levels; relax smooth muscle of respiratory tract]
- **Type II HS: Antibody to receptor** [eg. Myasthenia gravis, Good-Pasture's, Grave's disease] and **Cytotoxic reaction** [Ab binds to antigen which activate complements causing cell destruction, eg. IgG + complement mediated platelet destruction in **ITP**, IgE + eosinophils and complements mediated cytotoxic lysis of filaria, complement mediated lysis of RBCs, **Rheumatic fever**, **Erythroblastosis fetalis**]
- **Type III HS:** deposition of circulating Immune complexes in different tissues and then activate complement system which produce damage [eg. Vasculitis, **Rheumatoid arthritis**, **SLE**, Arthus reaction] [Blockage of C3b by Ab helps in patient with disease due to Type-3 HS]
- **Type IV HS:** CD4 cells mediated HS [eg. **Tuberculosis**, **poison Ivy**, **latex gloves**]

- \* Which *HS reaction* is responsible for symptoms of nematodes infection and destruction of filaria?
- In **Nematodes infection**, larva migrates to lung and produce cough, wheezing, etc. These symptoms are due to **Type-1 HS** reaction
- In **Filarial Infection**, destruction of microfilaria is **IgE dependent Cytotoxicity (Type-2 HS)**
- \* How does destruction of Toxoplasma occur?
- Usually IgE involved in parasite destruction but Toxoplasma is intracellular parasite and IgE is **not** involved in its destruction. *Th1, Tc, NK, ADCC involve in killing of Toxoplasma*

#### 14. Different types of graft:

- Allograft – transplant b/w different genetic make-up within the same species
- **Isograft** – transplant b/w genetically identical (monozygotic twins)
- Autograft – transplant from one site to another on the same individual
- Xenograft – transplant across species barriers (transplant a heart from baboon to human)

15. **Graft-vs-Host Disease:** when immunocompetent tissue (fresh whole blood, thymus, bone marrow) is transplanted into an immunocompromised host

- **Important point:** T-cells from transplant tissue attack host tissues. (*Type-4 Hypersensitivity(HS) reaction*)

#### 16. Different type of rejections:

- **Hyperacute Rejection: Mins. To Hrs.** – preformed antidonor antibody. (*Type-2 HS*)
- **Acute Rejection: Days to Weeks** – primary activation of T-cells. (*Type-4 HS*)
- **Chronic Rejection: Months to Years** – causes unclear. (*Type-4 HS*)
- **Accelerated Rejection: Days (3-5)** – reactivation of sensitized T-cells. Ex. If 1 kidney is rejected, then you transplant another kidney. If it is rejected second time, then it rejects faster than first time.

#### 17. Important HLA association with different diseases:

- HLA-A3 – Hemochromatosis
- HLA-B27 – Ankylosing Spondylitis
- HLA-DR2 – Multiple Sclerosis, Goodpasture, Narcolepsy, Hay fever
- HLA-DR2,DR3 – SLE
- HLA-DR3 – Celiac Sprue, Dermatitis herpatiformis
- HLA-DR3,DR4 – Type-1 DM
- HLA-DR4 – Rheumatoid Arthritis(RA), Pemphigus Vulgaris
- HLA-DR5 – Pernicious Anemia, Juvenile RA
- HLA-DR7 – Steroid-responsive Nephrotic Syndrome

#### 18. Important syndromes / diseases due to deficiency of different immune components:

- **Phagocyte Dysfunction (CGD, Chediak-Higashi Syndrome)** – *Extracellular Bacteria* (Staph. Aureus) + *Fungi* (Aspergillosis) [CGD – negative NBT (nitro-blue tetrazolium test)]
- **T-Cells Deficiency (DiGeorge Syndrome)** – *Intracellular Organisms* (Virus, **Candida**, TB) but **NOT** Extracellular; **3<sup>rd</sup>&4<sup>th</sup> pouch defect**, **absent thymus**; **Hypocalcaemia** due to **absent parathyroid glands**
- **B-cells Deficiency (Bruton's Agammaglobulinemia)** – *Extracellular Pyogenic Bacteria* but **NOT** intracellular
- **SCID (severe combined immune deficiency)** – *Bacteria, Virus, Fungus (extracellular + intracellular)*; **Adenosine Deaminase deficiency**; Neutrophils - ↑ or N, **B&T cells** - ↓↓↓
- **Bruton's Agammaglobulinemia** – *tyrosine kinase deficiency* – arrest of B-cell maturation – virtually **absent B-cell** but pre-B cells present and **low circulating immunoglobulins**
- **Wiskott-Aldrich Syndrome** – *deletion of T & B cells* – Eczema, **Thrombocytopenia** and **Low IgM**, association with *Non-Hodgkin Lymphoma*
- **Bruton's Agammaglobulinemia & Wiskott-Aldrich Syndrome** are the only **X-linked recessive** immune deficiency syndromes. [Both have **LOW** circulating immunoglobulins but Wiskott-Aldrich has low T cells too]

- Hereditary Angioedema – **C1 esterase deficiency**
- **C3 deficiency** – Pyogenic Bacteria
- **C1, C4 or C2 deficiency** – Opsonization not efficient
- **C5-8 deficiency** – Neisseria Infections
- **Paroxysmal Nocturnal Hemoglobinuria (PNH):** Defect in molecule anchoring decay accelerating factor (DAF) which normally degrade C3&C5 convertase on hematopoietic cell membranes therefore in the absence of DAF, complement mediated Intravascular lysis of RBC occur (Hemoglobinuria) [**Clue:** Red urine in the morning]
- ↑IgM but **deficient IgG & IgA** – CD40 ligand deficiency on activated T-cells
- **How to assess different Immunodeficiency Syndromes in exam:** look at the organisms in question

If recurrent infection with only Staph Aureus then you are most probably dealing with **phagocyte dysfunction** [CGD & Chediak-Higashi syndrome] **or C3 deficiency**. If you find word **neutrophil inclusions** in questions then go with **Chediak-Higashi** but if you find word **negative NBT** (Nitro-blue tetrazolium) test in question then go with **CGD** (chronic granulomatous disease).

If **no** Staph Aureus infection in question but **infection with intracellular (virus, TB, Candida)** organisms **&/or** sign & symptoms of **hypocalcemia** (tetany) then go with **DiGeorge Syndrome**.

**If Intracellular (Virus, TB) + Extracellular (staph, Aspergillosis) organisms** then go with **SCID**

If **Low immunoglobulins** then **either Bruton's or Wiskott-Aldrich**. If **low IgM, Thrombocytopenia & Eczema** present then go with **Wiskott-Aldrich**

If staph (Extracellular) infection & ask about which complement then **C3 deficiency**

If **deficient Opsonization** (recurrent **encapsulated** organism infection) and ask about which complement then go with **C1, C4 or C2 deficiency**. But if they ask **which complement is responsible for opsonization**, then remember it is **C3b**.

If disseminated **Neisseria infection (meningococcal and gonococcal)** then go with **C5-8 deficiency**

### Important Clinical Scenarios

1. A 9-month-old child is hospitalized for a **severe yeast infection** that does not respond to therapy. The patient has a history of **multiple, acute pyogenic infections**. A differential WBC count shows 90% neutrophils, 2% lymphocytes, and 3% monocytes. A bone marrow biopsy contains **no plasma cells or lymphocytes**. A chest x-ray reveals the **absence of a thymic shadow**. These findings are most consistent with

- Wiskott-Aldrich syndrome
- chronic granulomatous disease
- severe combined immunodeficiency**
- DiGeorge Syndrome
- Waldenström's macroglobulinemia

2. A 7-month-old boy baby is evaluated because of **repeated infections with encapsulated bacteria**. Serum studies demonstrate **very low levels of all immunoglobulin**. Which of the following is the most likely diagnosis in this patient?

- a) Wiskott-Aldrich syndrome
- b) DiGeorge syndrome
- c) Bruton's agammaglobulinemia**
- d) Chronic granulomatous disease

[Understand the concept in questions 1 and 2. In **SCID**, there is deficiency of *both B & T cells* so you will get **no** plasma cells and **no** lymphocytes on bone marrow biopsy and patient will get infection from *both intracellular and extracellular organism*. In **Bruton's agammaglobulinemia**, *only B cells* are deficient (B cells do not mature in Bruton's) so only antibody mediated defense is **not** working so patient will get recurrent infection from *extracellular, encapsulated infection*]

**3.** A 5-yo boy comes to the office for c/o intense **itching**. His past medical history is significant for **recurrent bacterial and viral infection**. An **uncle had similar problems**. Physical examination is remarkable for multiple petechial lesions on the skin and mucous membranes. Lab results are remarkable for **increased IgE and low platelets**. Which of the following is the most likely diagnosis?

- a) Wiskott-Aldrich syndrome**
- b) Ataxia telangiectasia
- c) DiGeorge syndrome
- d) Atopic dermatitis

**4.** A 5-yo boy comes to the office with c/o productive cough. Past history is significant for **recurrent fungal infections**. He didn't show reaction to PPD. CXR showed active TB lesion. Evaluation of his serum electrolytes reveals **hypocalcemia**. Which of the following is the most likely diagnosis?

- a) Wiskott-Aldrich syndrome
- b) DiGeorge syndrome**
- c) Bruton's agammaglobulinemia
- d) Chronic granulomatous disease

**5.** A 5-yo boy is brought to the office for **recurrent boils** on his body. Her mother denies any history of eczema or typical childhood illnesses such as measles or chicken pox. Lab results show normal CBC, immunoglobulin levels, B cell & T cell counts, complement levels, serum calcium and parathyroid hormone level. **The NBT (nitro blue tetrazolium) test is negative**. Which of the following is the most likely diagnoses?

- a) Wiskott-Aldrich syndrome
- b) Chronic granulomatous disease**
- c) DiGeorge syndrome
- d) SCID (severe combined immunodeficiency disease)

**6.** A 30-yo male patient is being evaluated for **recurrent infections with encapsulated bacterial organisms**. Lab study shows normal immunoglobulin levels and NBT test positive. Which of the following is the correct diagnosis?

- a) Selective IgA deficiency
- b) C3 deficiency**
- c) X-linked hypogammaglobulinemia
- d) Wiskott-Aldrich syndrome

**7.** A 30-yo male patient is being evaluated for **recurrent infections with encapsulated bacterial organisms**. Lab study shows normal immunoglobulin levels and NBT test positive. Which of the following is the correct diagnosis?

- a) Selective IgA deficiency
- b) **C1, C4 or C2 deficiency**
- c) X-linked hypogammaglobulinemia
- d) Wiskott-Aldrich syndrome

**8.** A 23-yo college student presents with the wrist pain and knee pain. On examination, you found red line along the tendons of the forearm muscles. She had **two similar previous episodes. She just had her menstrual period during the previous week.** These symptoms are most likely due to deficiency of

- a) C1 esterase inhibitor
- b) C3
- c) **C5-C8**
- d) C1, C4 or C2

**9.** A 20-yo woman brought to the ER with profuse internal bleeding due to car accident. She underwent abdominal surgery and required blood transfusion. She is transfused with **appropriate blood group match with her blood group.** But as the transfusion begins, she rapidly becomes hypotensive and **developed anaphylaxis.** Review of system shows **h/o recurrent sinusitis.** Which of the following is the most likely reason for developing these symptoms?

- a) DiGeorge syndrome
- b) **Selective IgA deficiency**
- c) Wiskott-Aldrich syndrome

19. “Clue” to diagnose leukocyte adhesion defect

- Delayed separation of placental cord in newborn – **Leukocyte Adhesion Defect**

20. How does CD8 & CD4 T-cells differentiate in thymus?

- **In thymus,** cells with **LOW** affinity for MHC-1 molecule differentiate into CD 8 T-cells. (no affinity/high affinity cells are eliminated) Cells with **LOW** affinity for MHC-2 molecule differentiate into CD 4 T-cells

21. What are first & last events in maturation of B-cells?

- **1<sup>st</sup> event in Pre B-cells** – gene rearrangement of heavy chain
- **Last event in mature B-cells** – **IgM & IgD molecule on the surface of B-cells**

22. What is normal ratio for T-cells to B-cells?

- **T-cells to B-cells** ratio in the body – **Three to One**

**23. Primary & Secondary Immune Responses:**

- **Primary Immune response** – when antigen presented to our immune system **first** time – IgM
- **Secondary Immune response** – when same antigen presented to our immune system **second** time – IgG

**24. Active and Passive Immunities:**

- **Natural Active Immunity** – Chickenpox
- **Natural Passive Immunity** – Mother IgG protects her baby
- **Acquired Active Immunity** – Chickenpox vaccine
- **Acquired Passive Immunity** – Hepatitis B immunoglobulins

25. How does Superantigen work?
- **Superantigen binds to  $\beta$  chain of TCR & MHC-II molecule of APC (antigen presenting cells) stimulating T-cell activation**
26. What is responsible for killing of pathogen intra-macrophage?
- **$\gamma$  interferon**
27. Which T-cells are involved in T-cells mediated cytotoxicity & Type-4 HS?
- **T-cell mediated cytotoxicity – CD8 cells**
  - **Type-4 HS – CD4 cells**
28. How does destruction occur in TB?
- **TB** → macrophage → Th → secrete IL-2 & activate macrophage via  $\gamma$  interferon to become epitheloid cells & multinucleated giant cell → epitheloid cells secrete IL-1 & TNF- $\alpha$  (acute phase response), macrophage release large number of inflammatory mediators which are responsible for tissue damage → Fibrosis. So in TB damage occur by immune system (DTH), but **NO** endotoxin/exotoxin
29. What do we check in HIV screening & confirmatory test?
- We **check antibodies** in patient, **NOT** antigen
30. When do we consider western blot test positive?
- The **HIV Western blot** is considered **positive** when the patient demonstrates the **presence of antibody to at least two of three important HIV antigens**, which are gp120, gp41, and p24.
31. **Important autoantibodies in different diseases:**

<b>Autoantibodies</b>	<b>Disease</b>
Anti-acetylcholine receptor	Myasthenia gravis
Anti-basement membrane	Goodpasture syndrome
Anticentromere	CREST syndrome
Antiendomysial & Antigliadin	Celiac disease
Anti-insulin, Anti-islet cell	Type-1 DM
Anti-intrinsic factor, Anti-parietal cell	Pernicious anemia
Antimicrosomal	Hashimoto's thyroiditis
Antimitochondrial	Primary billiary cirrhosis
<b>p-ANCA</b>	<b>Polyarteritis nadosa (microscopic polyangitis)</b>
c-ANCA	Wegener's granulomatosis
Antiribonucleoprotein	Mixed connective tissue disease
Anti-TSH receptor	Grave's disease
Anti-Scl-70	Scleroderma
Anti-SS-A, Anti-SS-B	Sjogren syndrome
Anti-smith, Anti-ds-DNA, ANA (antinuclear antibody)	Systemic Lupus Erythematosus (SLE)
Anti-histone antibody	Drug induced lupus

**GOOD LUCK**