
بسم الله الرحمن الرحيم

14.06.2023

# Humoral Immunology

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**MBBS, M.Phil, Ph.D, CHPE**

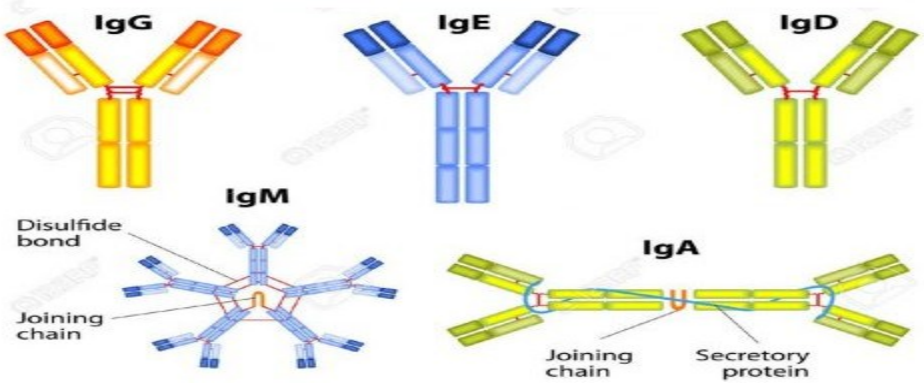
# Objectives

At the end of lecture, students of 3rd year should be able to

1. Describe humoral immunity.
2. Describe the role of B & T lymphocytes in immunity.
3. Describe the role of B lymphocytes in humoral immunity.
4. Explain how T cells regulate the immune system.
5. Differentiate between humoral and cell mediated immunity.

- Immune System
  - Innate System
    - Biochemical
      - Lysozyme
      - Complement
    - Physical Barrier
      - Skin
      - Mucosa
      - Phagocytes
  - Adaptive System
    - Immunoglobulins
      - IgG
      - IgM
      - IgA
      - IgD
      - IgE
    - Lymphocytes
      - T cells → B cells* (Activation)
        - Plasma cells

## Constant region of the heavy chain determines the isotype



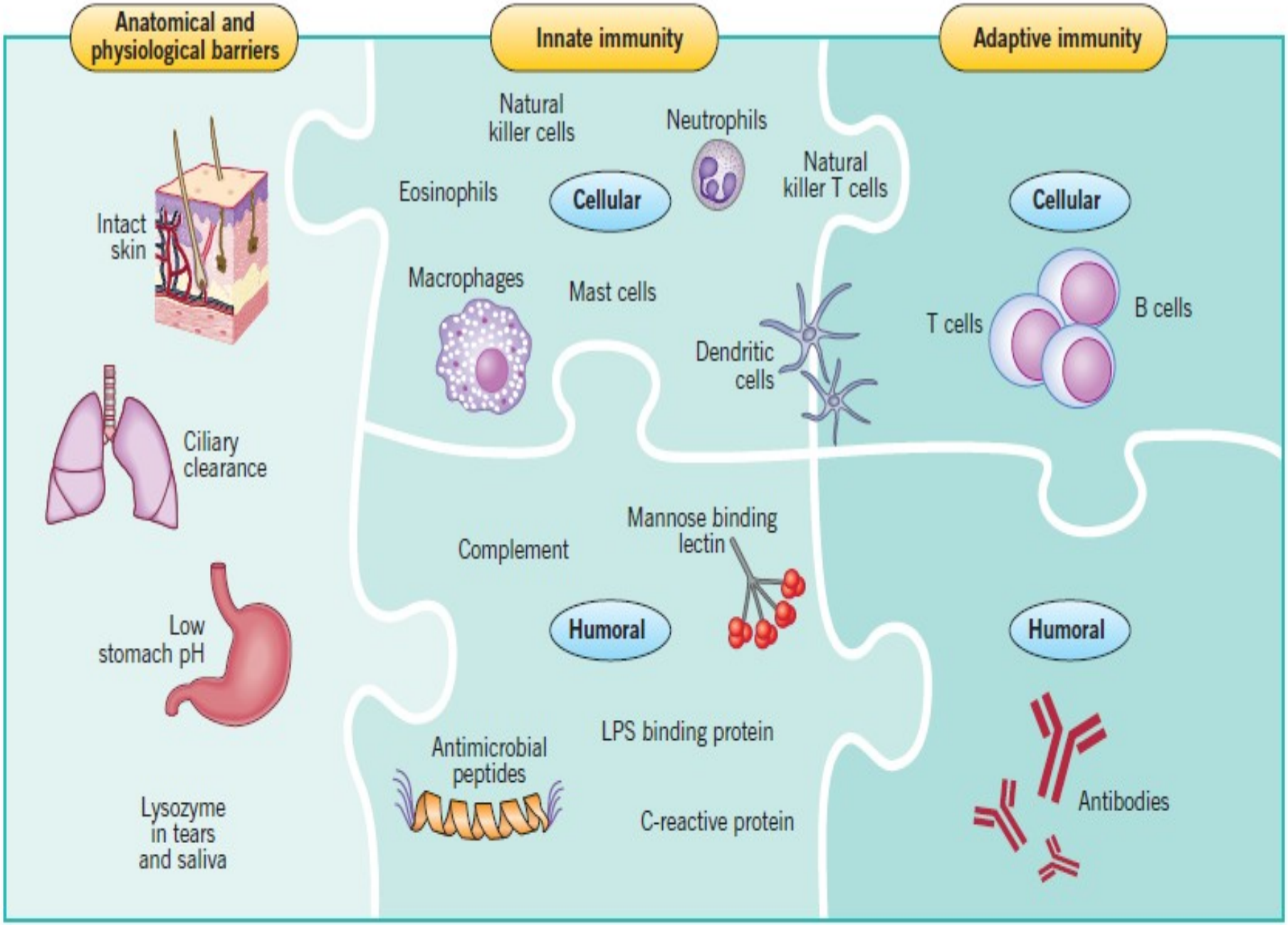
# HUMORAL IMMUNITY

- **Humoral immunity** is the antibody-mediated defense against foreign - antigens.
- It is mediated by macromolecules - including secreted antibodies, complement proteins, and certain antimicrobial peptides - located in extracellular fluids.
- Humoral immunity is named so because it involves substances found in the humors, or body fluids.

# Humoral Immunity

Humoral immunity is the principal defense against extracellular microbes, bacterial toxins and viruses e.g.

- It is directed primarily against exotoxin-mediated infections by *Clostridium tetani*, *Vibrio cholera*, and *Corynebacterium diphtheria*, extracellular pyogenic bacteria *(Staph, Streptococci),* infections by polysaccharide capsules containing bacteria (e.g., pneumococci, meningococci, *Haemophilus influenzae*), and certain viral infections i.e. HBV.


Anatomical and physiological barriers
Innate immunity
Adaptive immunity
Intact skin
Ciliary clearance
Low stomach pH
Lysozyme in tears and saliva
Natural killer cells
Neutrophils
Eosinophils
Cellular
Natural killer T cells
Macrophages
Mast cells
Dendritic cells
Complement
Mannose binding lectin
Humoral
Antimicrobial peptides
LPS binding protein
C-reactive protein
Cellular
T cells
B cells
Humoral
Antibodies

# MAIN FUNCTIONS OF HUMORAL IMMUNITY

- Defense against infection (opsonize bacteria, neutralize toxins and viruses).
- Allergy (hypersensitivity) (e.g., hay fever, anaphylactic shock)
- Autoimmunity

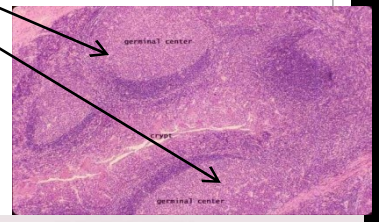
# Cells of humoral immune system

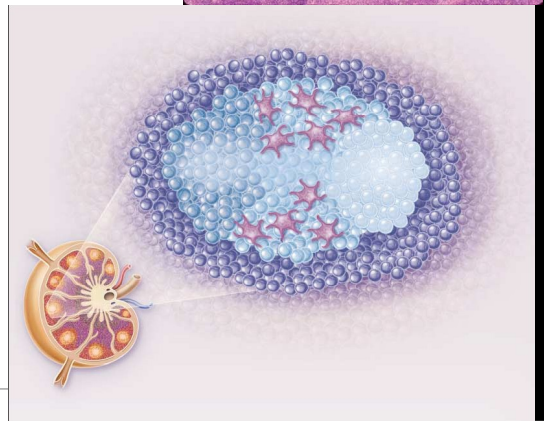
B cells and T cells are the main component of the humoral immunity.

- They have specific receptors,
- Each cell’s receptors recognize only one antigen
- lymphocytes can recognize thousands of antigens,
  - one antigen / clone
  - There are many cells of each clone in blood stream or lymph nodes

# B cells

- constitute 10 – 20% of circulating lymphocytes
- form lymphoid follicles in the superficial cortex of lymph nodes
- Organized in lymphoid follicles in the white pulp of spleen and tonsils.
- When activated, stain pale & occupy Germinal centers.
- They are the ancestor of plasma cells.
- produce antibodies,
- Act as antigen-presenting cells.
- produce a variety of cytokines to modify the immune response.



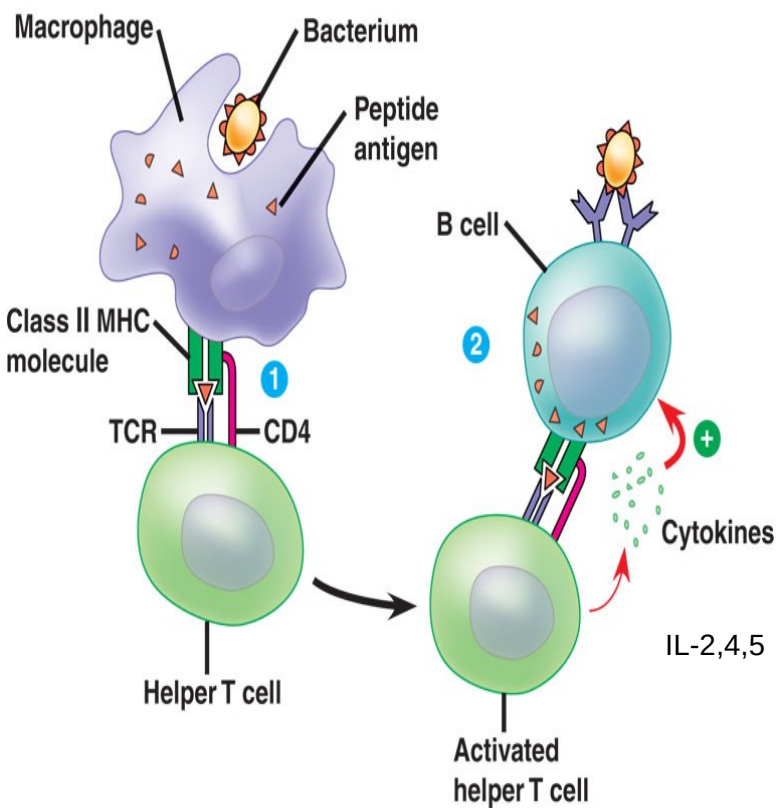



# HUMORAL IMMUNITY

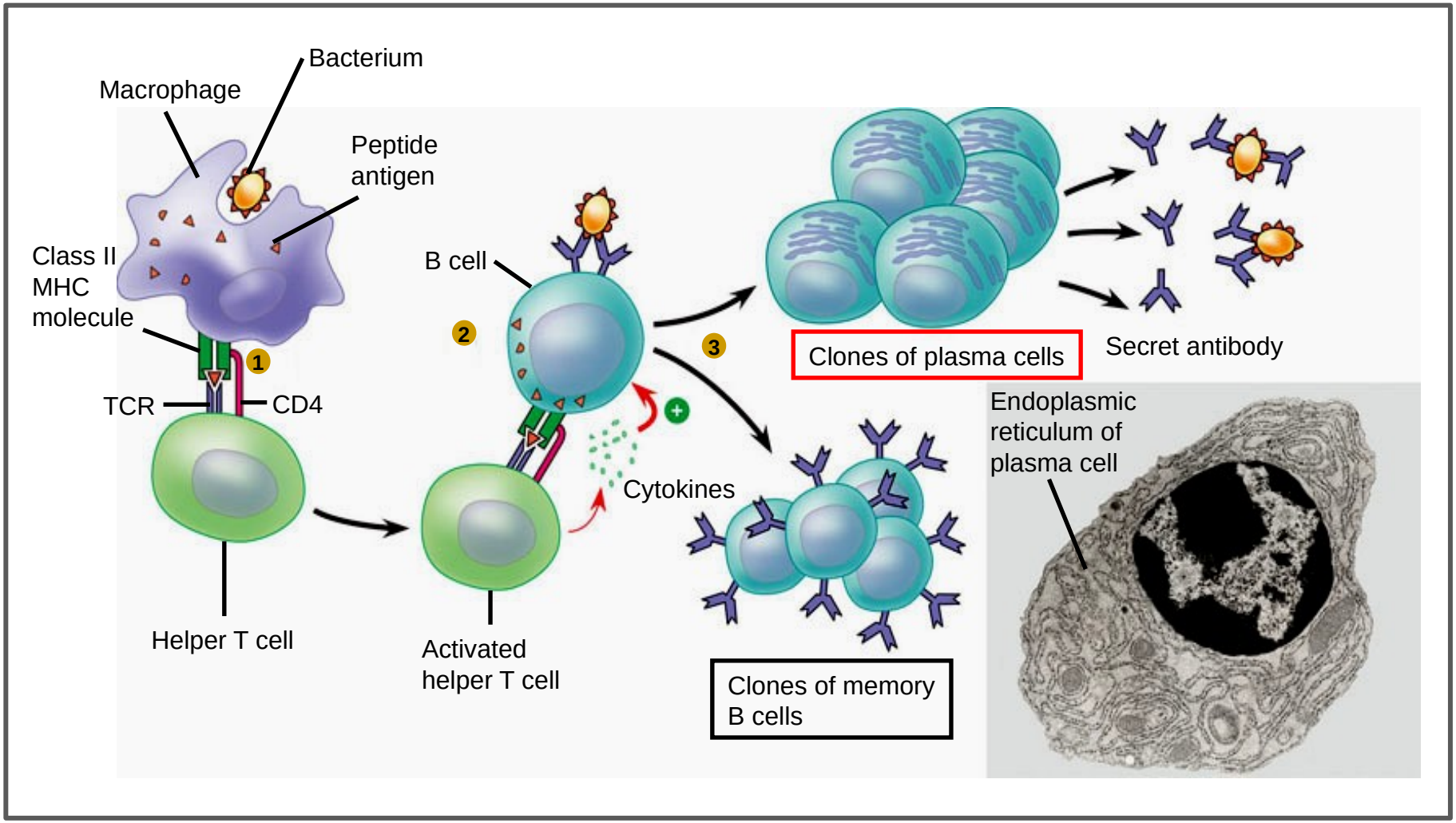
Activation of B cell through $T_H$ cells

- Contact of antigen presenting cells activate helper T cells

  - Cytokines (protein signals) are released
  - B cells are activated and differentiated into plasma cells
    - Cell binding produces greater response



- B cells divide (and form clones of cells)
- Plasma cells release thousands of antibody per second for a few days and then die. Memory cells are saved for future.



- Certain antigens (e.g., bacterial polysaccharides) can activate B cells directly, without the help of T cells, and are called **T-cell–independent antigens.** In this, **only IgM is produced** by B cells.
- Interleukins 4 and 5 from helper T cell and CD40L-CD40 interaction are required for the B cell to “class switch” immunoglobulins to produce IgG, IgA, and IgE.

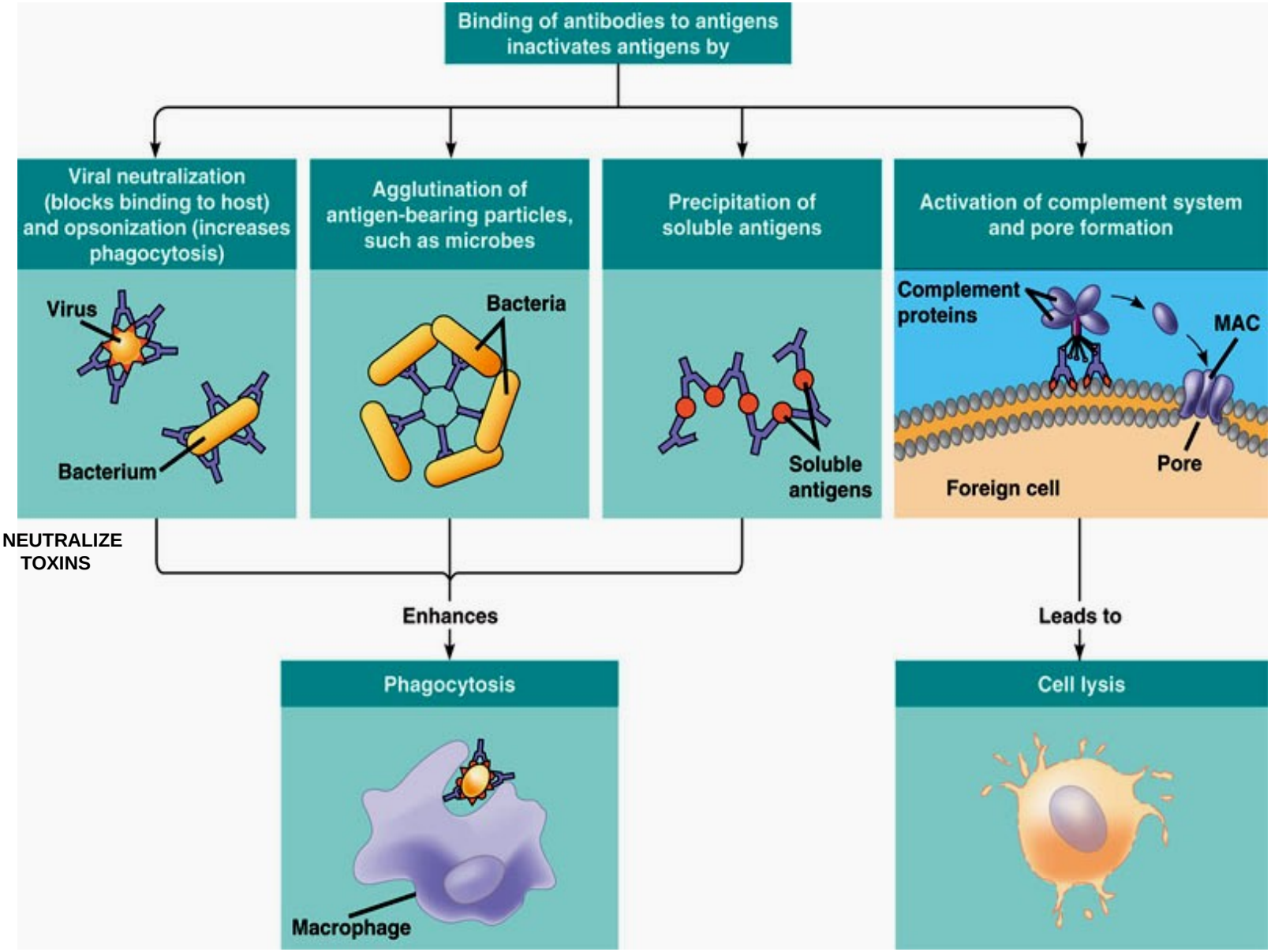
  TGF-beta

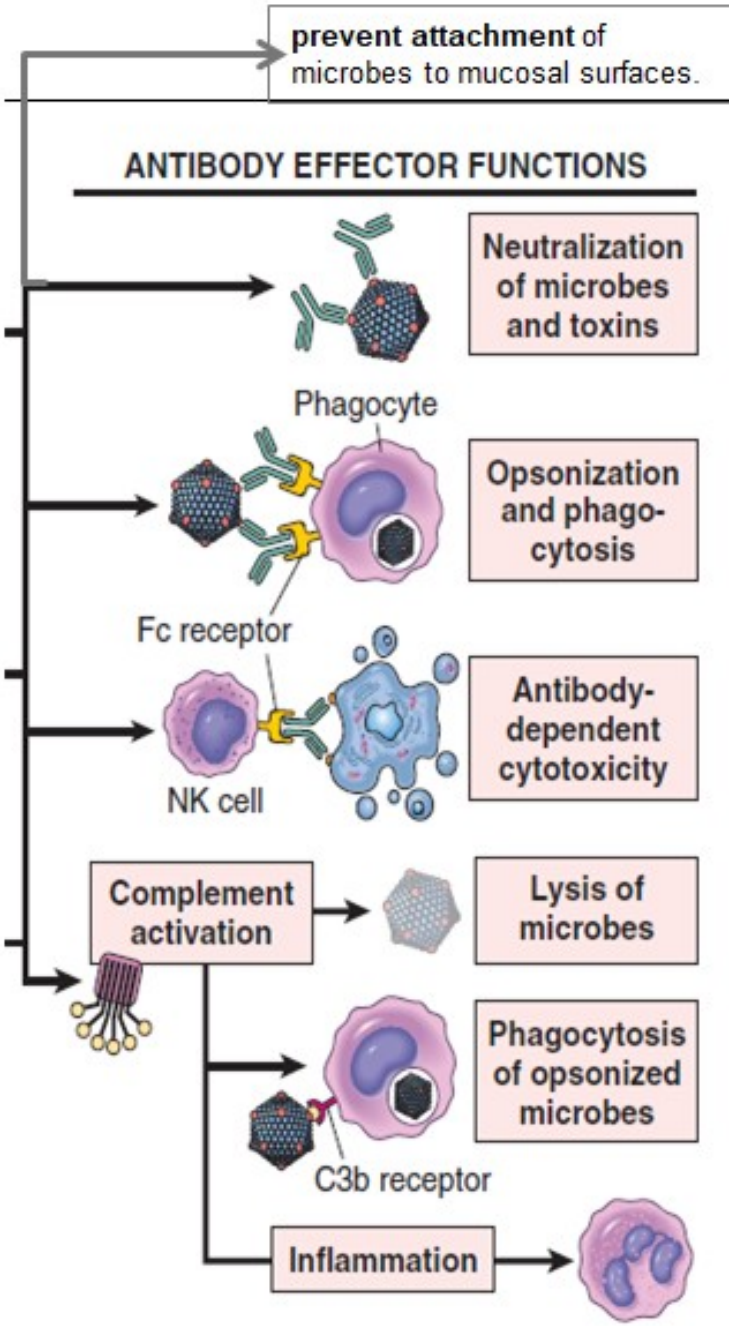
  IFN-gamma IL-4
- The T-cell–dependent response generates **memory B cells**, whereas the T-cell–independent response **does not**; therefore, a secondary antibody response does not occur in the latter.

# EFFECTOR MECHANISMS OF HUMORAL IMMUNITY

**Antibodies** may initiate different mechanisms to combat microbes,

- promote phagocytosis,
- bind to cells and trigger release of inflammatory mediators,
- Enter mucosal organs to provide defense against ingested and inhaled microbes
- IgG crosses the placenta to induce immunity against infections of the newborn.
- The risk of pyogenic infections increases if IgG levels drops below 400 mg/dl (N= 100-1500 mg/dl).


Binding of antibodies to antigens inactivates antigens by
Viral neutralization (blocks binding to host) and opsonization (increases phagocytosis)
Agglutination of antigen-bearing particles, such as microbes
Precipitation of soluble antigens
Activation of complement system and pore formation
Virus
Bacterium
Bacteria
Soluble antigens
Complement proteins
MAC
Pore
Foreign cell
& NEUTRALIZE TOXINS
Enhances
Leads to
Phagocytosis
Cell lysis
Macrophage


prevent attachment of microbes to mucosal surfaces.
ANTIBODY EFFECTOR FUNCTIONS
Neutralization of microbes and toxins
Phagocyte
Opsonization and phago-cytosis
Fc receptor
Antibody-dependent cytotoxicity
NK cell
Complement activation
Lysis of microbes
Phagocytosis of opsonized microbes
C3b receptor
Inflammation

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# 5 Types of Antibodies

Antibodies or immunoglobulins (Ig) are Y-shaped proteins that recognize unique markers (antigens) on pathogens.

**IgA**

Secreted into mucous, saliva, tears, colostrum. Tags pathogens for destruction.

**IgD**

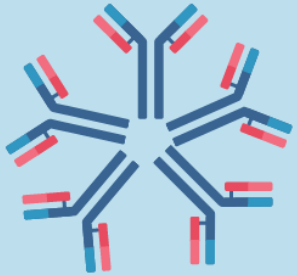
B-cell receptor. Stimulates release of IgM.

**IgE**

Binds to mast cells and basophils. Allergy and antiparasitic activity.

**IgG**

Binds to phagocytes. Main blood antibody for secondary responses. Crosses placenta.



**IgM**

Fixes complement. Main antibody of primary responses. B-cell receptor. Immune system memory.

# T cells

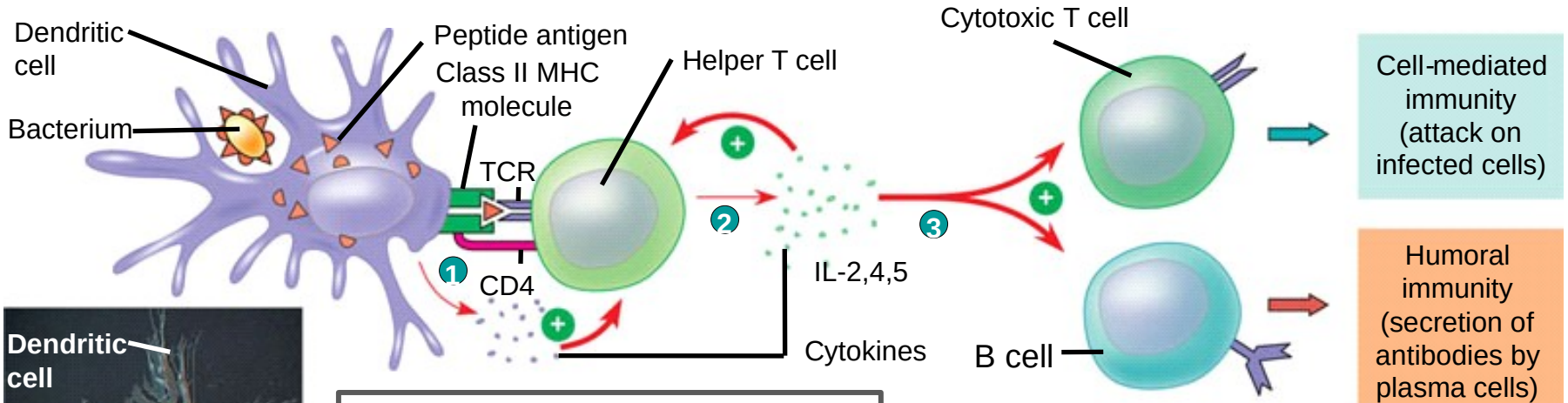
T-cells form the main component (70-80%) of the total lymphocytes in adults. These have T-cell receptors (TCR) on their surface.

- **Major role of CD4+ cells** is to help B cells make antibody (**"helper T cells").**
  - **Th1 → activate CTL (IL2),**
  - **Th2→ B-cell helper (IL4, 5)**
- **The major role of CD8+ T cells** is to recognize and lyse infected target cells ( **"cytotoxic T cells"** or CTL)

# T cell perform regulatory & effector functions

- **Regulatory functions are**
  - IL4 is **B cell growth factor** while IL5 is B cell **differentiating** factor
  - IL4 & IL5 activate B cells  Immunoglobulin production
  - IL2 is **T cell growth factor** and activates CD4, CD8 T cells,
  - Gamma interferon activates macrophages to initiate delayed hypersensitivity reaction against intracellular microbes (i.e. *Mycobacterium tuberculosis.*
- **Effector functions are carried out by Tc cells**
  - Kill virus infected cells, tumor cells & allograft

1 After a dendritic cell engulfs and degrades a bacterium, it displays bacterial antigen fragments (peptides) complexed with a class II MHC molecule on the cell surface. A specific helper T cell binds to the displayed complex via its TCR. This interaction promotes secretion of cytokines by the dendritic cells





2 Proliferation of the T cell, stimulated by cytokines from both the dendritic cell and the T cell itself, gives rise to a clone of activated helper T cells (not shown), all with receptors for the same MHC–antigen complex.

3 The cells in this clone secrete other cytokines that help activate B cells and cytotoxic T cells.

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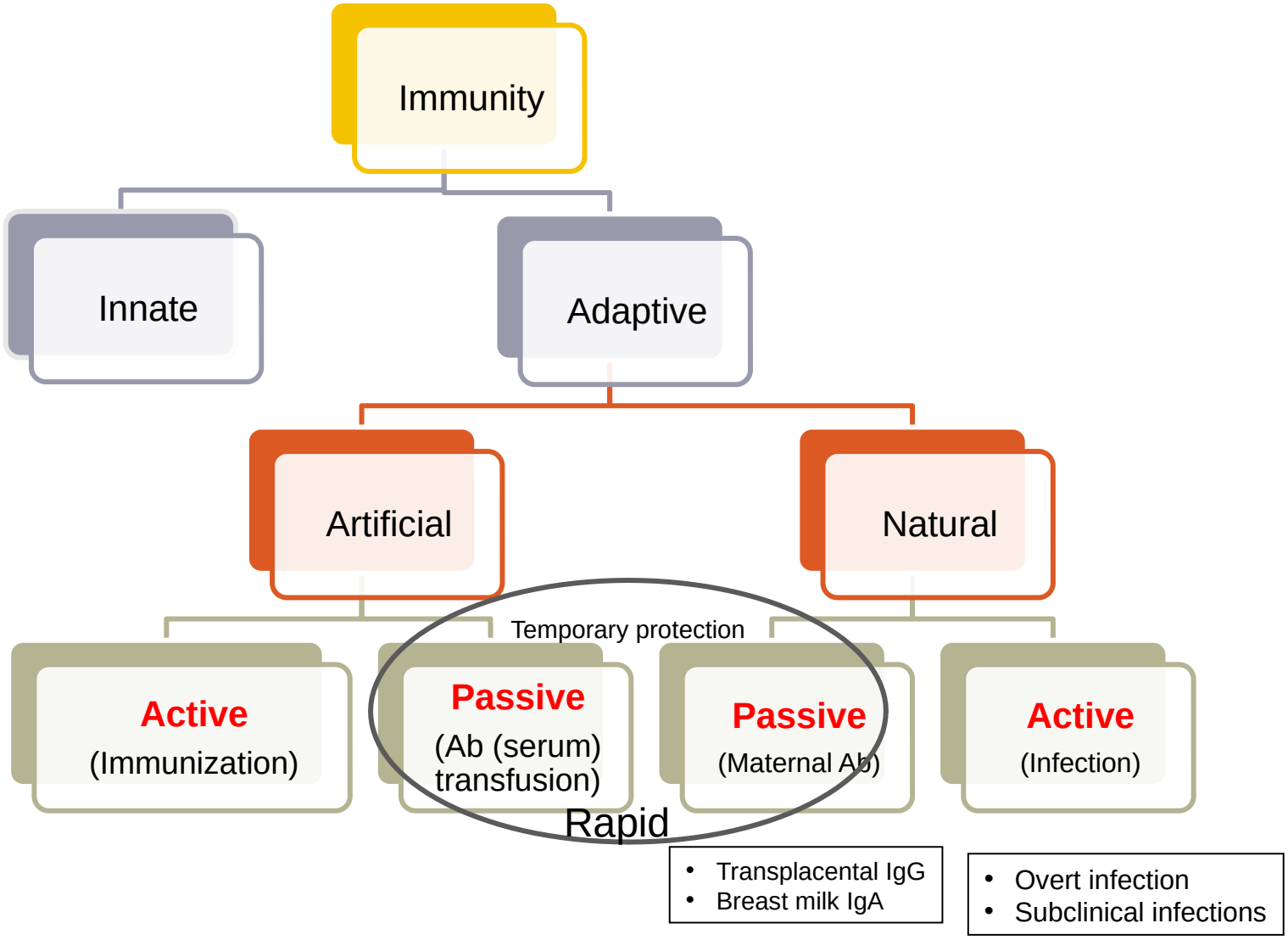
- Remarkable diversity (can respond to millions of Ag)
- Long memory (memory B & T cells are produced  can respond after many years after initial exposure)
- Exhibit specificity (show activity against the specific Ag)

# INDUCTION OF ANTIBODIES

- Antibodies can be
  - induced actively in the host or
  - acquired passively (for immediate defense i.e. post-exposure).
- Passive immunity is used to neutralize toxins of diphtheria, tetanus, and botulism by antitoxins. Passive immunity neutralizes viruses early in the incubation period (i.e. rabies and hepatitis A and B viruses).


Immunity
Innate
Adaptive
Artificial
Natural
Temporary protection
Active
(Immunization)
Passive
(Ab (serum) transfusion)
Passive
(Maternal Ab)
Active
(Infection)
Rapid
• Transplacental IgG
• Breast milk IgA
• Overt infection
• Subclinical infections

# ANTIBODIES IN THE FETUS

- Antibodies in the fetus are primarily IgG acquired by transfer of maternal IgG across the placenta.
- Some antibodies can be made by the fetus if infection occurs, such as in congenital syphilis.
- Newborn infants can make IgG (and others isotypes, as IgM and IgA) to certain ‘protein antigens’. For example, the vaccine against hepatitis B that contains hepatitis B surface antigen is effective when given to newborns.
- After birth, maternal IgG declines and protection by maternal IgG is lost by 3 to 6 months.

# RESPONSE TO MULTIPLE ANTIGENS ADMINISTERED SIMULTANEOUSLY

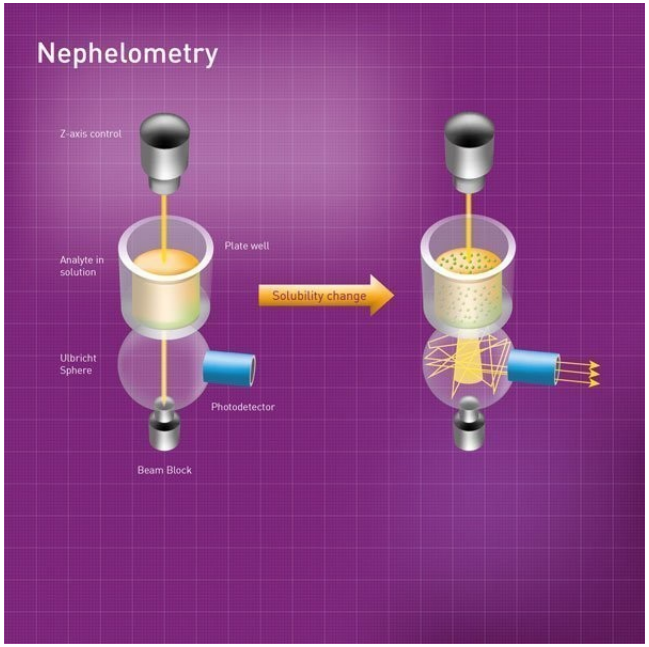
- When two or more antigens are administered at the same time, the host reacts by producing antibodies to all of them.
- Combined immunization is widely used (e.g., diphtheria, tetanus, and pertussis [DTP] vaccine or the measles, mumps, rubella [MMR] vaccine).

# Humoral vs Cell Mediated Immunity

| | Humoral Immunity | Cell Mediated Immunity |
|---|---|---|
| DEFINITION | An adaptative immunity that mediates by antibodies produced by B lymphocytes. | An adaptative immunity that mediates by cytotoxic T lymphocytes and TH cells without involvement of antibodies. |
| CELL TYPE | B lymphocytes | T lymphocytes |
| MODE OF ACTION | Antibodies travel through blood circulation. | Direct cell to cell contact or secrete cytokines. |
| ANTIBODY DETECTION | Done by antibodies | Done by receptors located on the cell surfaces |
| MECHANISM | Antibody-mediated immunity | Cell mediated immunity |
| ANTIBODY PRODUCTION | Yes | No |
| PURPOSE | Primary defense against extracellular pathogens | Primary defense against intracellular pathogens |
| IMMUNOLOGICAL SURVEILLANCE | Does not provide | Provides |
| IMMUNITY AGAINST CANCER | Since it cannot eliminate tumour cells, cannot develop immunity against cancers. | Develops immunity against cancers. |

# TESTS FOR EVALUATION OF HUMORAL IMMUNITY

- Evaluation of humoral immunity consists primarily of measuring the amount of each of the three important immunoglobulins (i.e., IgG, IgM, and IgA) in the patient's serum.
- This is usually done by **nephelometry**.
- Immunoelectrophoresis can also provide valuable information.



# THANK YOU