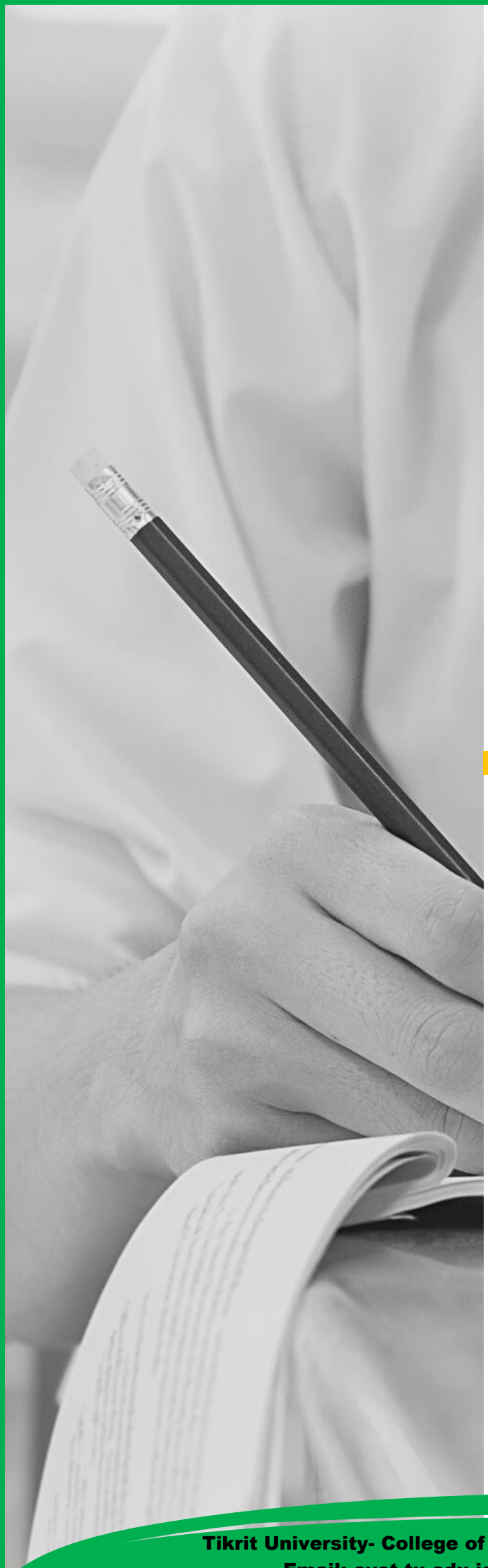

Tikrit University
College of Veterinary Medicine

Lecture 9: Humoral Immunity and the Immune Response

Subject name: Immunology (Theoretical)
Subject year: Third Stage / 3rd Year
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Lecturers link

Humoral Immunity and the Immune Response

1. Introduction to Humoral Immunity

Humoral immunity—also known as **antibody-mediated immunity**—is the arm of adaptive immunity that targets **extracellular pathogens**, such as bacteria, toxins, and viruses circulating outside cells.

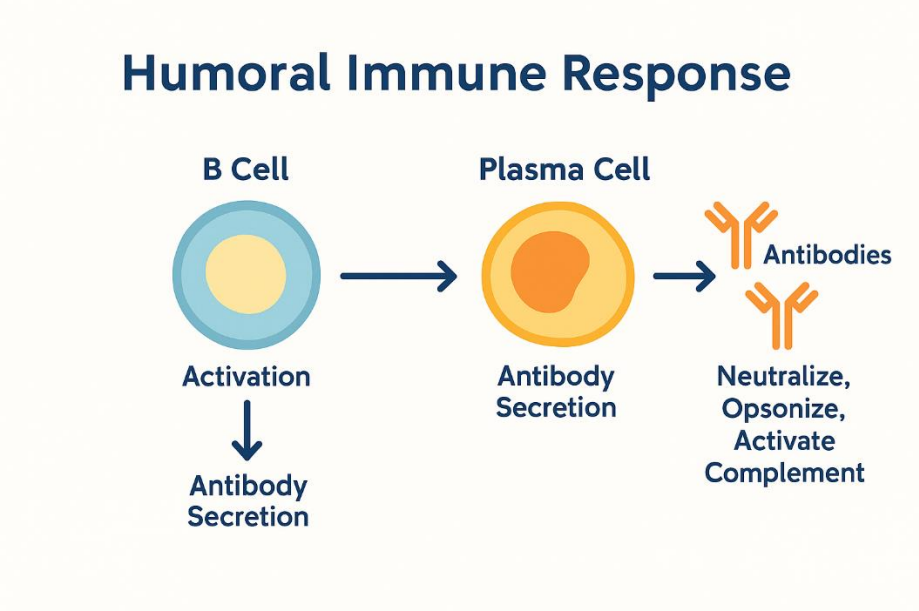
The process requires cooperation between:

- **B lymphocytes (B cells)**
- **Helper T cells (Th cells)**
- **Cytokines**, which guide B-cell proliferation and antibody production

Once activated, B cells differentiate into:

- **Plasma cells** → secrete antibodies
- **Memory B cells** → enable faster, stronger responses upon re-exposure

Humoral immunity(antibodies) is essential for neutralization, opsonization, activation of complement, and long-term protection.



2. Humoral vs. Cellular Immunity

Humoral Immunity

- Mediated by **B cells** and **antibodies**
- Targets pathogens **outside cells**
- Antibodies neutralize toxins, prevent adhesion, activate complement, and enhance phagocytosis

Cellular Immunity

- Mediated by **T lymphocytes**
- Targets **intracellular pathogens** (viruses, intracellular bacteria)
- Cytotoxic T cells (CTLs) kill infected cells
- Helper T cells release cytokines that regulate immune responses

Both branches form the two major components of **adaptive immunity**.

3. TH1 vs TH2 Differentiation

Helper T cells differentiate into **TH1 or TH2** based on cytokines present during activation.

TH1 Pathway

- Driven by: **IL-12**, IFN-γ
- Promotes: **cell-mediated immunity**
- Effective against **intracellular pathogens**

TH2 Pathway

- Driven by: **IL-4**
- Leads to:
    - Strong **humoral response**
    - Activation and differentiation of B cells
    - Protection against **extracellular bacteria and parasites**
    - Allergy-related responses

TH2 cells secrete IL-4, IL-5, IL-9, IL-10, IL-13 → these cytokines instruct B cells to proliferate and become antibody-secreting plasma cells.

4. Primary Humoral Immune Response

The **primary response** occurs when a **naïve B cell** encounters an antigen for the first time.

Process

1. Antigen binds to B-cell receptor (BCR).(IgM,IgD)

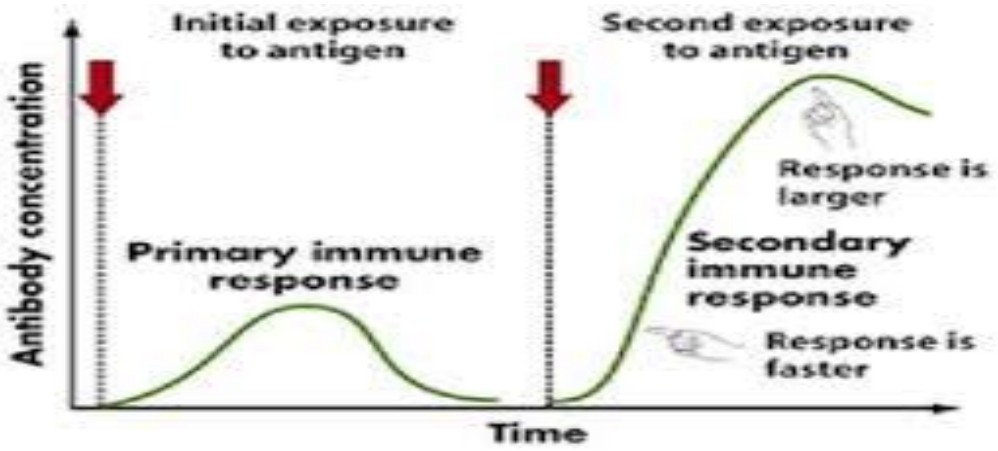
2. B cell internalizes and presents antigen to helper T cells.
3. TH cells release cytokines (e.g., IL-4, IL-21,IL-5).
4. B cells proliferate and differentiate into plasma cells.
5. Plasma cells secrete antibodies.

Characteristics of Primary Response

- **Slow onset** (IgM appears around days 4–7)
- **Low affinity antibodies**
- IgM titers initially **higher than IgG**
- Some plasma cells migrate to bone marrow → long-term antibody production
- Memory B cells are generated

Important Notes

- IgM appears **first** because it requires **no isotype switching(a biological process where a B cell changes its antibody production from one class to another, such as from IgM to IgG, while keeping the antigen specificity the same**
- IgG appears **later**, after class switching
-



5. Secondary Humoral Immune Response

This response occurs when the same antigen is encountered again.

Characteristics

- **Rapid and powerful**
- Dominated by **high-affinity IgG (or IgA/IgE depending on antigen)**
- Memory B cells proliferate much faster than naïve B cells
- Produces **greater quantities** of antibodies

Why Is the Secondary Response Stronger?

1. Memory B cells respond more efficiently.
2. They have **higher-affinity BCRs** due to affinity maturation.(**affinity maturation** is an immune process that creates **high-affinity B-cell receptors (BCRs)** through a cycle of **somatic hypermutation**(Somatic hypermutation (SHM) is a process in B cells that introduces high-frequency mutations in the variable regions of immunoglobulin (antibody) genes to create high-affinity antibodies) and selection for better antigen binding.
3. They migrate faster to lymphoid follicles.

4. They express more adhesion and costimulatory molecules.
5. Their plasma cell progeny already produce **isotype-switched antibodies**.

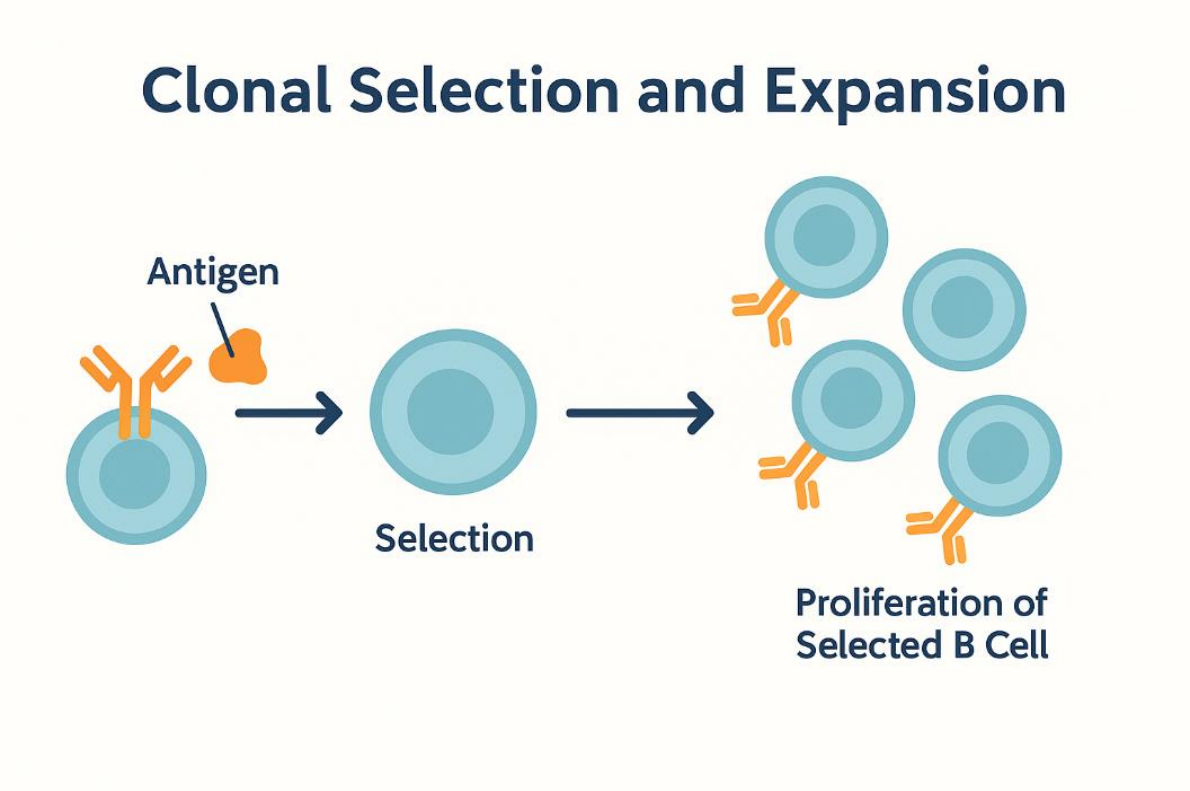
6. Clonal Selection and Expansion

Only B cells with receptors specific to an antigen are selected for activation.

Steps:

1. Antigen binds to a B cell with matching BCR
2. The B cell proliferates (clonal expansion)
3. Plasma cells and memory B cells are produced
4. Antibodies secreted by plasma cells have **the same specificity** as the original BCR

This ensures precise targeting of antigens.



7. IgM in the Primary Response

- IgM is the **first and dominant antibody** in primary responses
- Secreted as **pentameric IgM (sIgM)**
- Has **10 Fab sites**, but steric hindrance usually limits simultaneous binding to ~5
- Despite low affinity, pentameric structure gives **high avidity** (**IgM has low affinity per binding site, but because it is a pentamer (5 units), it binds antigens strongly overall → high avidity**
- Especially effective in **activating complement**
- High IgM levels in adults indicate **recent or new exposure**
- IgM pentamer "casts a broad net" by binding related epitopes (cross-reactivity)

8. Why IgM < IgG in Later Responses?

- IgG dominates because it appears after **isotype switching**
- IgG has **higher affinity** due to somatic hypermutation
- IgG diffuses better through tissues
- IgG activates complement efficiently
- IgG production increases dramatically in secondary and tertiary responses

9. Affinity vs. Avidity

Affinity

- Strength of **one** antigen-antibody interaction
- Depends on:
    - Shape compatibility

- Chemical interactions
- Hydrogen bonds, electrostatic forces, hydrophobic interactions

Avidity

- The **overall binding strength** of an antibody with multiple binding sites
- Depends on:
  - Affinity
  - Valency (number of binding sites)
  - Structural arrangement

IgM has **low affinity but high avidity** due to its pentameric structure.

10. Activation of Memory B Cells

Secondary activation is more efficient because:

1. Memory B cells migrate rapidly to lymphoid follicles
2. They express high-affinity BCRs
3. They are more numerous
4. They act as APCs for memory T cells
5. Their progeny immediately produce **high-affinity, isotype-switched antibodies**

This explains the **speed and strength** of secondary response

Activation of Memory B Cells