



Color code:
Important in **red**
Extra in **blue**



Immunology
MED438

Antibody-Mediated Immunity



Objectives

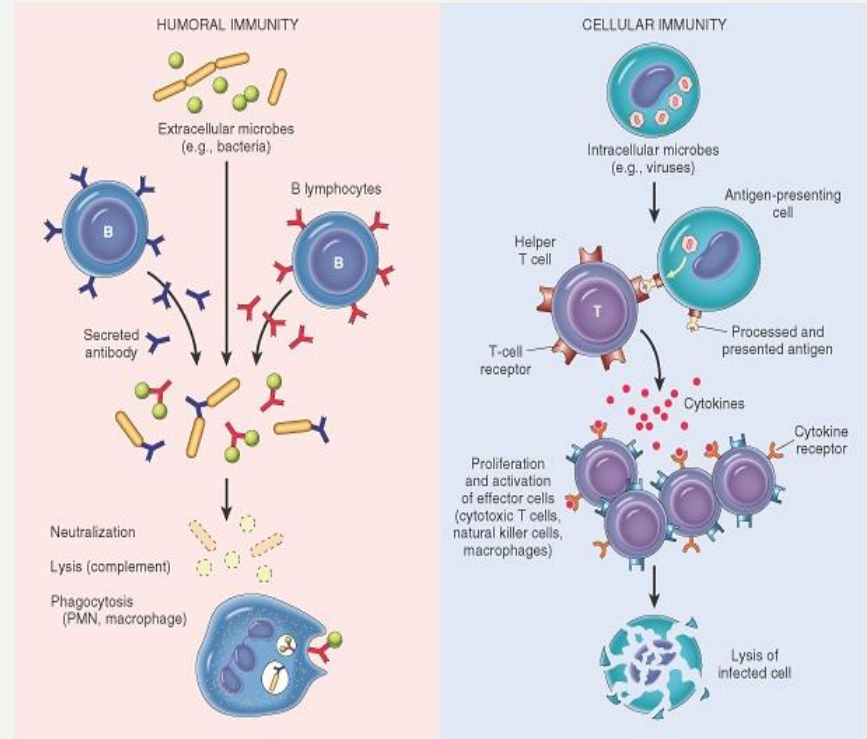
- To describe B-cells as the mediators of humoral immunity, (antibody-mediated immunity)
- To describe activation of B-cells which involve:
 - Antigen recognition
 - T-dependent & T-independent antigens
 - Requirement for T-helper cells
- To explain clonal selection, clonal expansion & generation of plasma cells & memory cells
- To describe primary & secondary immune responses
- To describe the structure & function of Immunoglobulins

Humoral Immunity

- The aspect of immunity mediated by antibody secretion.
- Named as such because it involves substances found in the **humours** (body fluids).

The nature of the antigen determines its type or response:

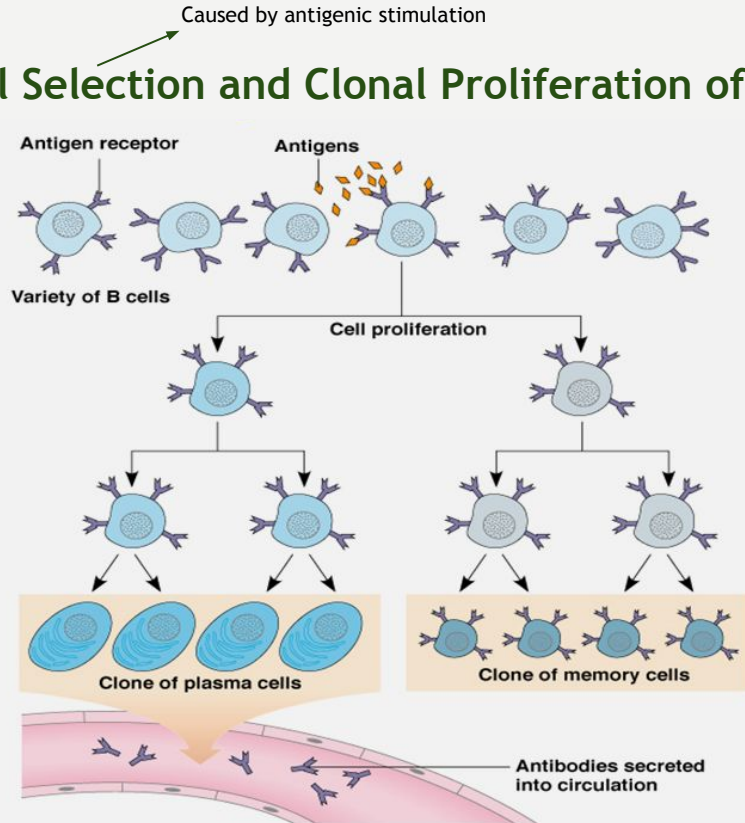
- Extracellular (mostly bacteria):
Humoral Immunity
- Intracellular (mostly viruses):
Cell-mediated immunity



Antibodies

- Antibodies are immunoglobulins with **specific functions**.
- They bind to specific sites on antigen surfaces called **epitopes** and perform protective functions by different mechanisms.
Part of the antibody reacting with the epitope is called a **paratope**.
- There is a **specific** antibody for any **one** given type of antigen.

Clonal Selection and Clonal Proliferation of B Cells



Monoclonal antibodies are specific antibodies produced by a single clone of cells and are directed towards a specific target (can only bind to one epitope).

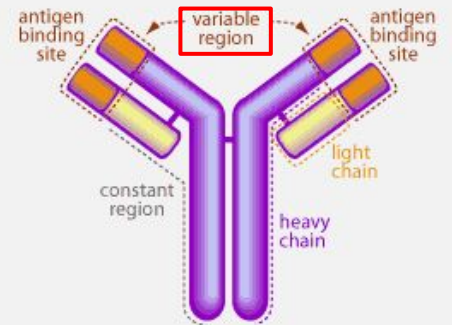
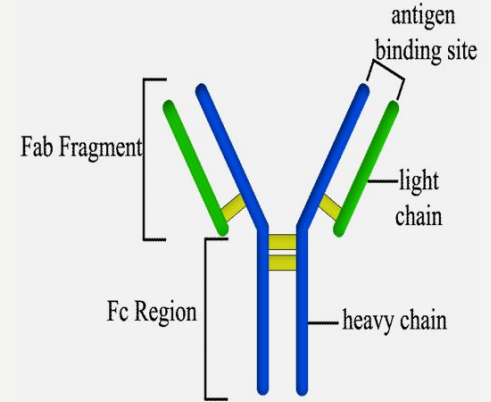
Antibodies

Antibody structure and functions:

- Made up of **four polypeptides chains**.
- Two longer and larger (**heavy**) chains and two shorter and smaller(**light**) chains.
- Has the shape of the letter “Y”.
- Variable region has the potential to bind with particular classes of antigens.

Single Specificity:

Once a raw antibody is stimulated to fit to a **specific** antigen, it can then react with **only** that antigen. (Can fit as precisely as a lock-and-key to an antigen)



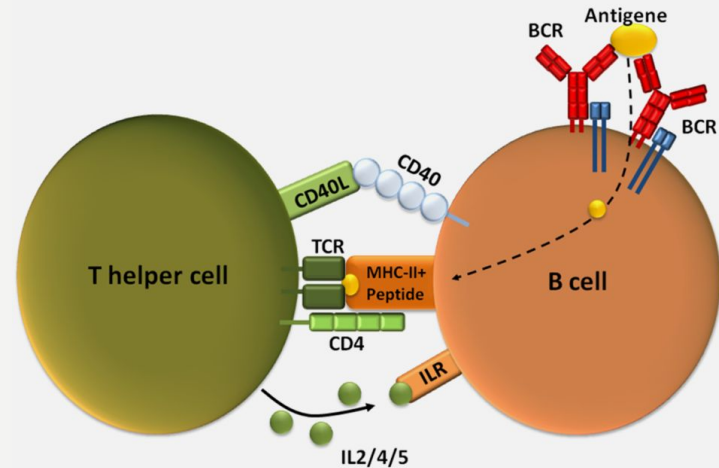
Activation of B Cells by Antigens

Types of Antigens:

T-dependent Antigens	T-independent Antigens
<ul style="list-style-type: none"> Antibody production by B-cells requires T-helper cells. (Th2) Antigen presenting cells recognize antigen & present it to T-helper cells T-helper cells stimulate B-cells specific for that antigen to become plasma cells (mature form of B cells) B cell can produce Ig (Ab) but cannot release until it matures T-dependant antigens are mainly proteins They develop immunological memory 	<ul style="list-style-type: none"> B-cells do not require T-helper cells to produce antibodies. Immune responses induce the production of IgM of low affinity (because they're newly produced) for the antigen and have no immunologic memory (no T cells). Antigens are mainly polysaccharides or lipopolysaccharides with repeating subunits (bacterial capsules)

B Cell activation is a two signal process:

- 1- MHC Class II-peptide binds to the TCR and Co-receptor
 - 2- CD40 Ligand binds with CD40
- CD40 helps in maturation of B cells into plasma cells

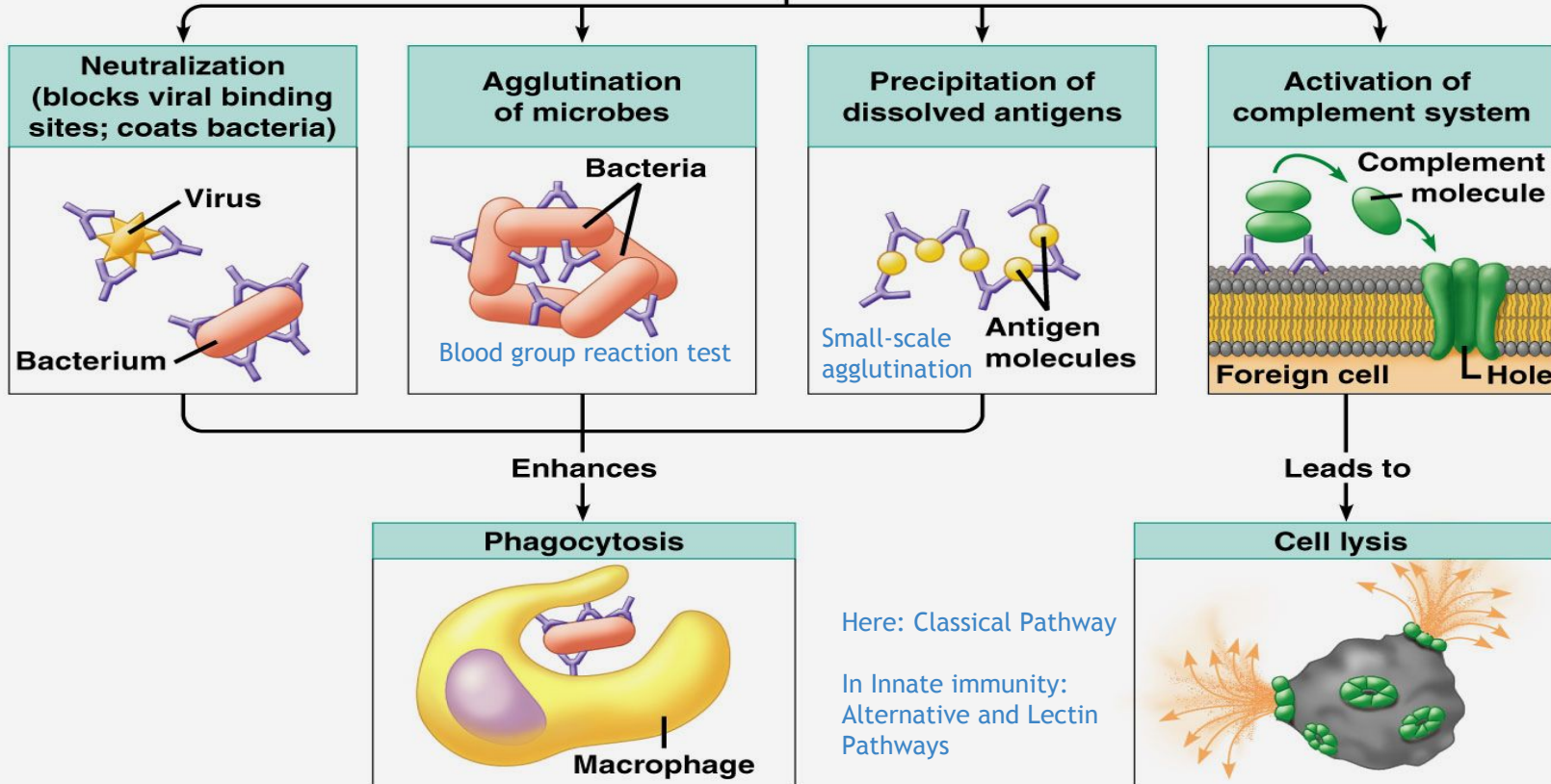


Th2 is only in humoral immunity and can produce IL-2, IL-4, and IL-5.
(only produced by Th2)

Naive T cell: never encountered an antigen. Once it does, it will only recognize that specific antigen (B cells too).

Protective functions of antibodies

Binding of antibodies to antigens inactivates antigens by

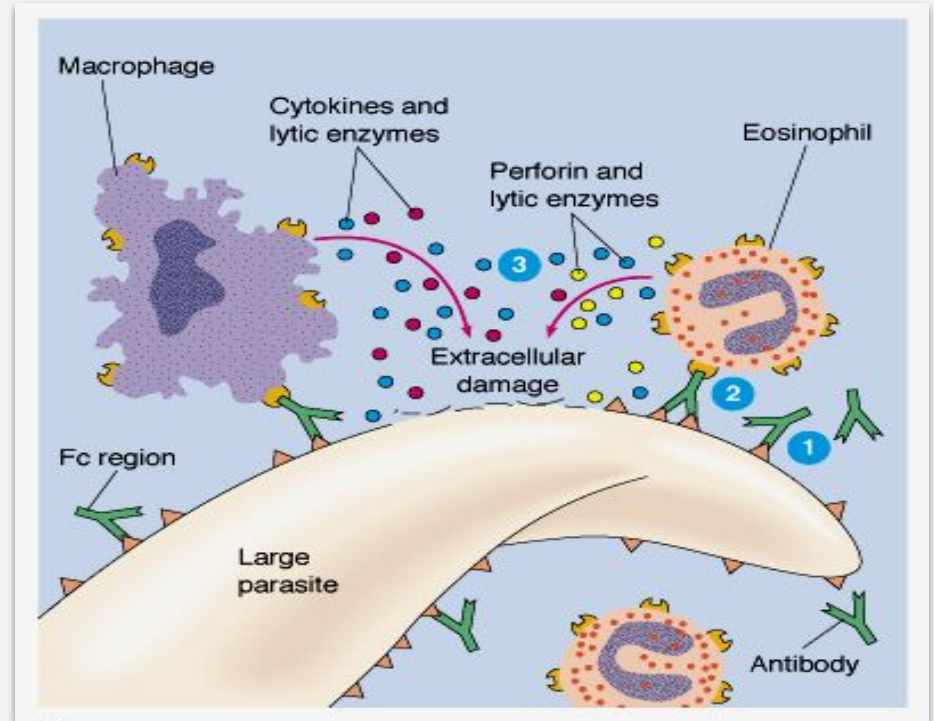


Functions of Antibodies

1

Antibody dependent cell-mediated cytotoxicity

- Antibodies coat infecting cell (large parasite usually) - FC region facing outwards.
- NK (lysing ability), Macrophage, neutrophils, and eosinophils **have receptors** for FC region of antibody.
- Secretion of lytic enzymes to destroy parasite.



Frustrated Phagocytosis:

Failure of phagocytic cells to dislodge antigens (small yellow triangles in the picture) from parasite surface causes them to release lytic enzymes instead.

Functions of Antibodies

2 Opsonization and phagocytosis

Antibodies **coat** infecting cells and facilitate their phagocytosis by cells possessing **Fc** Receptors.

3 Complement activation

Classical pathway, after binding to antigen
IgM > IgG3 > IgG1 > IgG2 (activation ability)


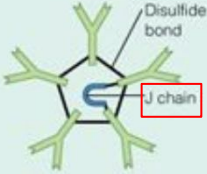




4 Transplacental transfer


The mother transfers **IgG** to the fetus through the placenta.

Only IgG is able to cross the placenta because it is the smallest and the most abundant antibody. This applies for RH factor and NOT blood groups (IgM).

Antibody isotype	Relative capacity to fix complement
IgM	+++
IgD	-
IgG1	++
IgG2	+
IgG3	+++
IgG4	-
IgA1	+
IgA2	+
IgE	-

Summary of Immunoglobulin Classes

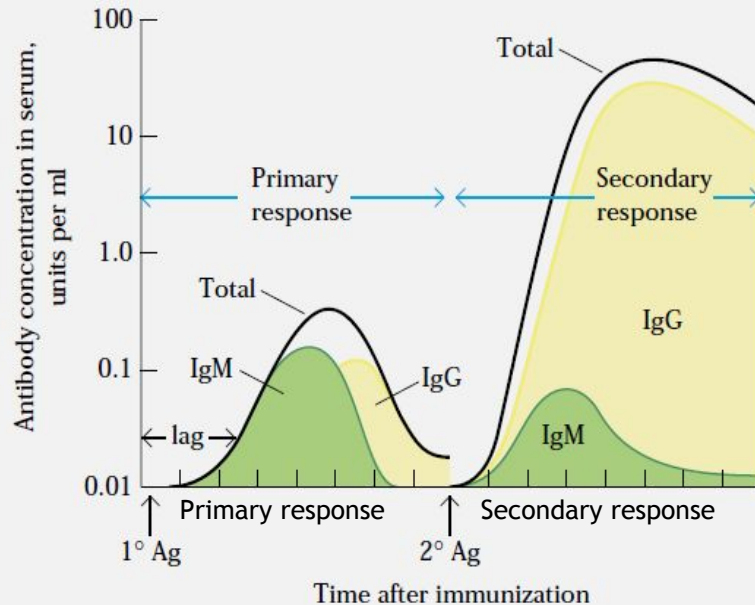
Characteristics	IgG	IgM	IgA	IgD	IgE
	(4 subclasses) 	 Disulfide bond J chain	(2 subclasses)  J chain Secretory component		
Structure	Monomer	Pentamer	Dimer (with secretory component)	Monomer	Monomer
	Longest half-life				Shortest half-life
Percentage of total serum antibody	80%	5–10%	10–15%*	0.2%	0.002%
Location	Blood, lymph, intestine	Blood, lymph, B cell surface (as monomer)	Secretions (tears, saliva, mucus, intestine, milk), blood, lymph	B cell surface, blood, lymph	Bound to mast and basophil cells throughout body, blood
Complement fixation	Yes classical	Yes	No 	No	No
Placental transfer	Yes	No	No	No	No
Known functions	Enhances phagocytosis; neutralizes toxins and viruses; protects fetus and newborn	Especially effective against microorganisms and agglutinating antigens; first antibodies produced in response to initial infection	Localized protection on mucosal surfaces	Serum function not known; presence on B cells functions in initiation of immune response	Allergic reactions; possibly lysis of parasitic worms

*Percentage in serum only; if mucous membranes and body secretions are included, percentage is much higher.
 May be yes via alternate pathway.

Primary & Secondary Immune Responses

- **Primary immune response:** Initial encounter with antigen produce
- **Secondary immune response:** Subsequent encounter with same antigen produces

Concentration & type of antibody in primary & secondary immune responses.



This graph is an example of why we receive multiple vaccinations against diseases (Hepatitis B).

It shows the efficacy differences between the initial and the second vaccinations, with the latter being much more effective.

A detailed comparison is shown in the next slide.

Comparison Between Primary & Secondary Responses (refer to previous graph)

Property	Primary response	Secondary response
Responding B cell	Naive B cell	Memory B cell
Lag period following antigen administration	4-7 days	1-3 days
Time of peak response	7-10 days	3-5 days
Magnitude of peak antibody response	Varies depending on antigen	100-1000 times higher than primary
Predominant Isotype	IgM	IgG
Antigens	Thymus dependent/Independent	Thymus Independent
Antibody affinity	Lower	Higher

Take Home Messages

- B cells can be activated by antigen to produce antibodies either with the assistance of helper T cells or directly by the antigen itself
- Antibodies are made up of two heavy and two light amino acid chains and have a shape of letter “Y”
- Different types of antibodies are located at various sites to provide protection by agglutination, precipitation, complement fixation etc.
- Secondary humoral immune response is swift and a stronger immune response mediated by IgG class of antibodies because of the memory cells.

Quiz:

1. Antigens get bound to specific sites on antibody surfaces called

- a) epimers
- b) paratopes
- c) epitopes
- d) parachutes

2. Which cell is able to release antibodies?

- a) Mast cell
- b) B cell
- c) T cell
- d) Plasma cell

3. Which of the following helps in B cell maturation?

- a) IL-4
- b) CD40
- c) IgD
- d) All of the above

4. The antibody that has the highest complement activation is:

- a) IgG3
- b) IgG2
- c) IgM
- d) IgG1

5. Which of the following antibodies is least found in our bodies?

- a) IgA
- b) IgD
- c) IgE
- d) IgM

6. Which of the antibodies is the first to be released in a primary immune response?

- a) IgM
- b) IgG
- c) IgD
- d) IgA

Team Leaders:

Sedra Elsirawani

Ibrahim Aldakhil

Team Members:

1. Noura Alturki
 2. Lama Alzamil
 3. Shahad Althaqeb
 4. Leena Alnassar
 5. Joud Aljebreen
 6. Renad Alkanaa
 7. Shahad Bin Selayem
 8. Sara Alflaj
1. Alwaleed Alsaleh
 2. Muhannad Makkawi
 3. Abdullah Basamh
 4. Hashem Halabi
 5. Amjad Albaroudi
 6. Abdulrahman Alhawas
 7. Mohammed Alhuqbani



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