
# HLS

## MODIFIED NO. 9

## PHYSIOLOGY

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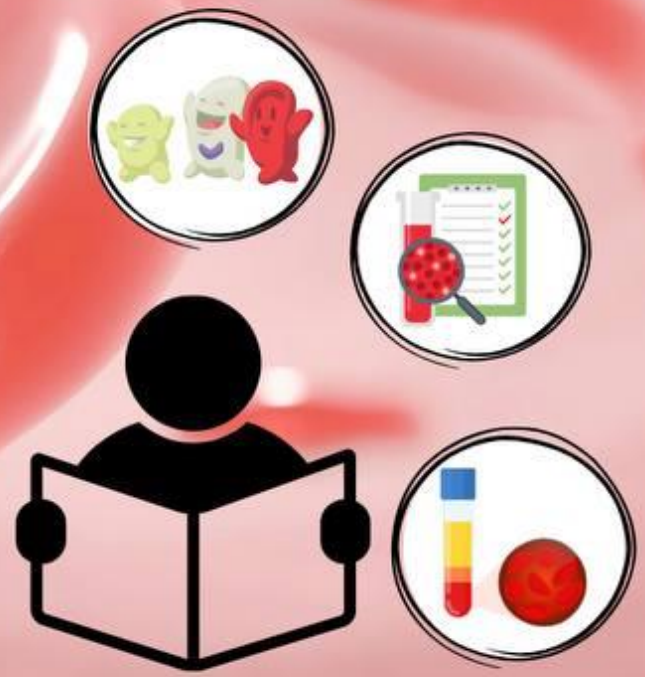

UNIT VI

Chapter 35:

# Resistance of the Body to Infection:

# II. Immunity and Allergy; Innate Immunity

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**Color code**

- Slides
- Doctor
- Additional info
- Important

# Immunity

| **Innate** | **Acquired = specific = adaptive** |
|---|---|
| **inborn ability to resist damaging organisms and toxins: skin, gastric acids, tissue neutrophils and macrophages complement, microbicidal and lytic chemicals in blood and blood cells** | **humoral → circulating antibodies**<br>**cellular → activated cells** |
| • Not specific, non-specialized<br>• It is fast , since neutrophils and microphages are first line of defense<br>• it has the ability to resist pathogens and toxins regardless of their type . Hydrogen peroxide/ hypochlorite destroys whatever pathogen or particle contacts with it<br>• It doesn't need a previous exposure to a pathogen to develop immunity against it<br>• Against pathogens that affect other species, for example; pathogens from dogs and pigs, also dogs have innate immunity against the human viruses and pathogens | It develops once we are exposed to the specific antigen (not established before the exposure to the pathogen)<br>Two types<br>1. humoral →circulating antibodies<br>Producing (molecules, chemicals) antibodies/ immunoglobulins which are able of specific binding to a certain sequence of the pathogen so it can get rid of it by different mechanisms (will be discussed in details later on) like neutralisation<br>2. Cellular →activated cells<br>whole cell attacks the pathogen ,damaging it or neutralizing it |

# Acquired Immunity

- **Antibodies or activated cells that specifically target and destroy invading organisms and toxins**
- **Powerful: can neutralize 100,000 x lethal dose of some toxins**
  - For example if we don't have acquired immunity ,very low dose of botulinum toxin will cause death however with acquired immunity we can afford having 100,000 of that toxic
- **Two types of acquired immunity:**
  - **Humoral ( B cell )**
  - **Cell-mediated ( T cell )**

# Antigen

- What is antigen? A trigger for immune system

- **A substance that can elicit an immune response**
- **Unique to each invading organism**

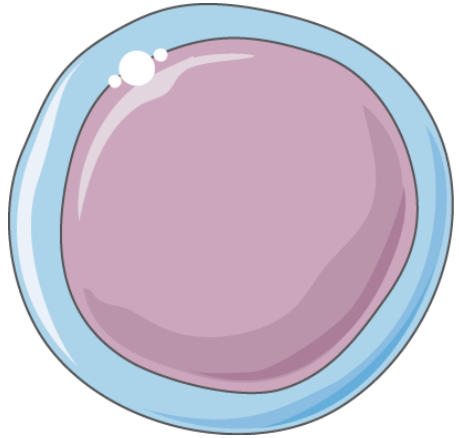
- Antigen structure or sequence is unique for each pathogen or organism we also have our own unique antigens for each cell in our bodies

- **Properties of antigens:**
- **Usually proteins or large polysaccharides**
- **Most are large (MW > 8,000) and have recurring molecular groups on their surfaces,** **both polysaccharides and proteins have recurrent sequence of units like sugars or amino acids (respectively) which is unique for each antigen**
- **The molecular structures that are specifically recognized in acquired immunity are called "epitopes"**

- Epitopes are the sequence of either polysaccharides or proteins that can elicit an immune response (recognised by immune system hence comes the selectivity and specificity of the adaptive immunity)

# Lymphocytes

- B &T CELLS



- **Mediate acquired immunity**

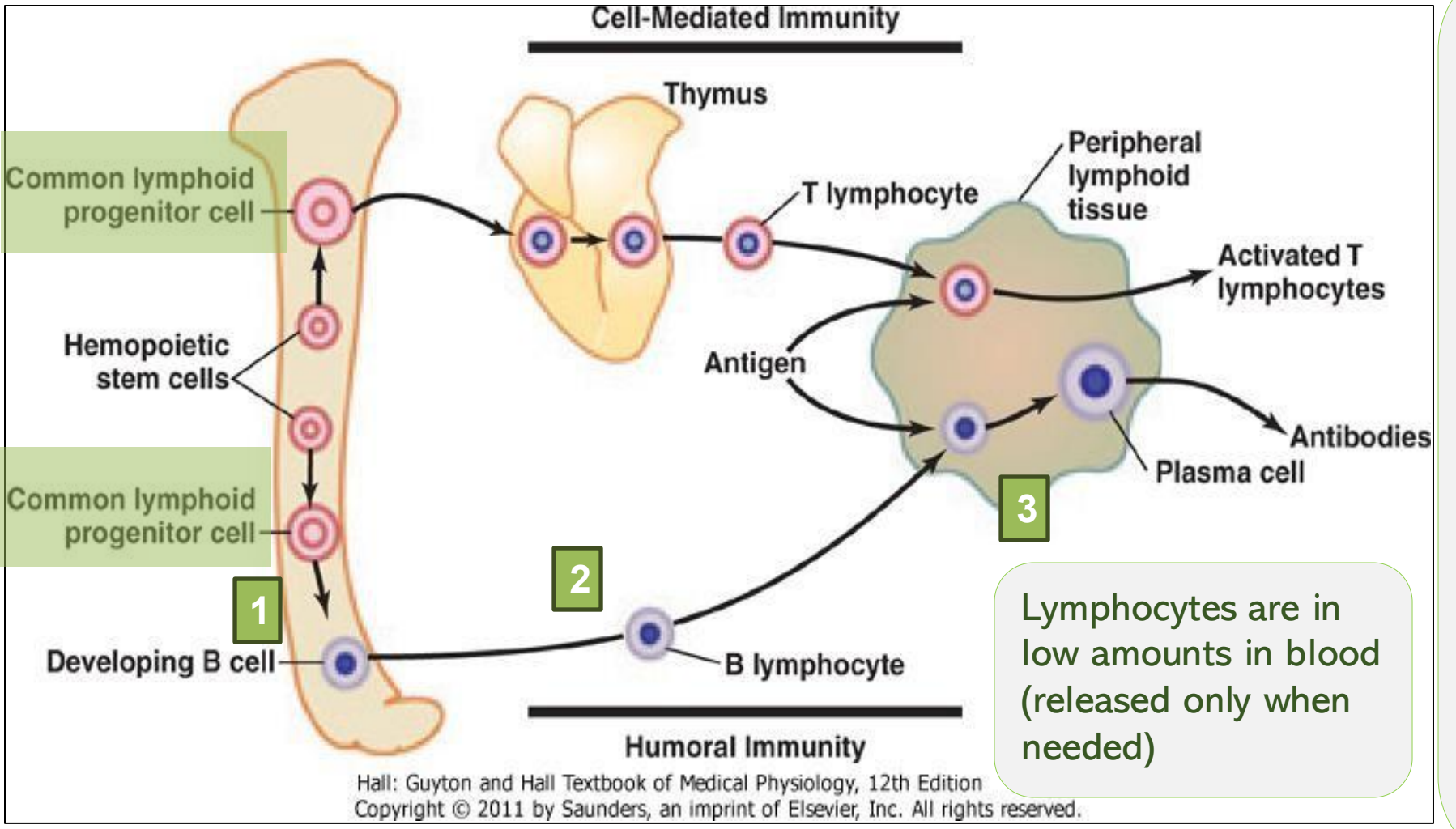
- After birth lymphocytes originate from bone marrow from Pluripotent hematopoietic stem cells then they are directed toward lymphoid organs and tissues

- **Develop in lymphoid tissues**
  - **Tonsils / adenoids,** They have resident macrophages and lymphocytes which filters the antigens that enters our body through **respiratory system** and preventing them from entering the circulation
  - **Peyer's patches (GI),** Deals with **ingested** antigens
  - **lymph nodes,** If any pathogen succeeded in entering the body they will face resident macrophages in **tissues** and also be taken to lymph nodes that work as checkpoints where lymphocytes will deal with them
  - **Spleen,thymus, marrow,** if the pathogen succeeded in entering **blood circulation** other lymphoid tissues like spleen liver and bone marrow will deal with it
- **Are strategically positioned** in lymphoid tissues

# Two types of lymphocytes

T cell :*Common **lymphoid** progenitor cells go to thymus to complete the development. T cells processing lasts from one month before birth to 6 months after birth

When common lymphoid progenitor cells are formed in the BM, they will either be committed to form B cells and continue their maturation in BM, or if committed to form T cells they will travel to the thymus to complete their maturation





Lymphocytes are in low amounts in blood (released only when needed)

- **B** cells

1. The development is continued in the bone marrow

2. Then released to reside in lymphoid tissues for further development and differentiation when exposed to certain antigens however cells stay in bone marrow and released when needed

3. When b cells get activated they produce large cells known as plasma cells which synthesis antibodies

# Maturation of T cells in the Thymus _Preprocessing of T cells

-Some self antigen can be recognized by T cells or B cells
-we can deal with this problem during the preprocessing in **Thymus** Where all self antigens will be presented to already developed clones of T cells and self reactive clones will be deleted preventing **the development of autoimmune disease**

**Expansion in the number of T cells**

Rapid expansion

Each clone is specific for a single antigen

Self-reactive clones are deleted (up to G0%)

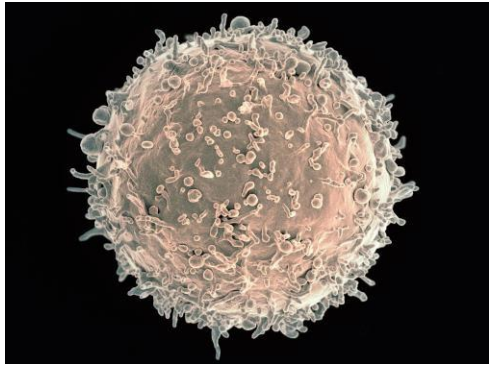
Migrate to peripheral lymphoid organs

Much of the above occurs just before and shortly after birth

-T progenitor cells have few hundreds of genes responsible for the identification of millions of antigens .
-How come few genes produce thousands of clones where each clone has its own specific identity to recognize specific antigen!
-This is due to **the combination of the single units of genes with different arrangement each time (permutations).**
**-The number of these Genes are even more in B cells than T cells cells**

-If Thymus is removed before birth or pre-processing the T cells will **not** be able to **recognize** antigens including the **self and foreign antigens** so pathogen can invade body without being recognized.
- If a transplant takes place **before** the pre-processing begin later on, the lymphocyte immunity will recognize the **transplanted** organ as **self** and will **not attack** it

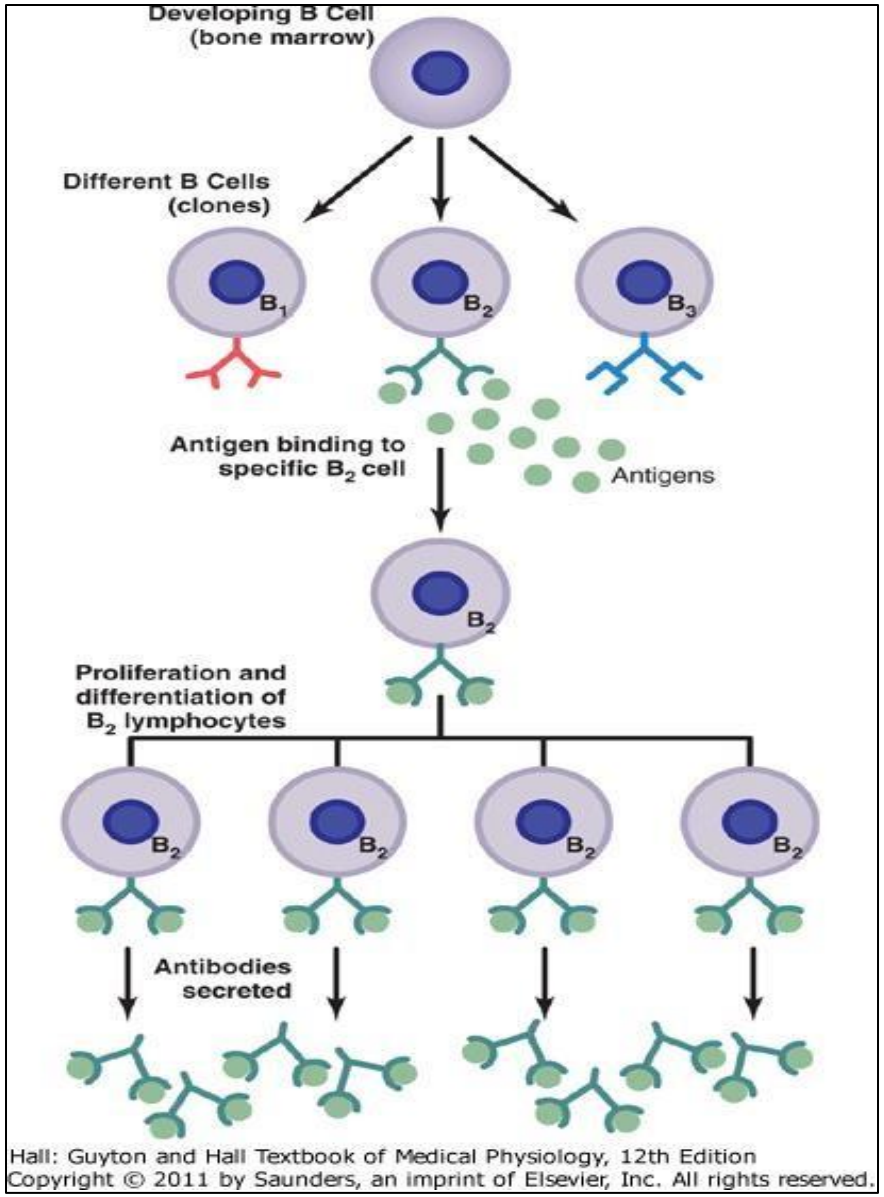
# B cell Development



B cells are similar to T cells in terms of developing specific immunity to a certain antigen

- **Initial growth and differentiation in the liver (fetal) and bone marrow (after birth)**
- **Migrate to the peripheral lymphoid organs**
- **Each clone is specific for a single antigen**
- **Clonal development provides almost limitless antibody specificity.** B cell clones are even more variable than T cells
- **Secreted antibodies destroy or neutralize molecules or organisms bearing their cognate antigen**

# B cell proliferation in response to antigen





Once B lymphocytes are processed in the bone marrow, we will have millions of clones. The clones that have been presented with certain antigens in the lymphoid organs will be activated. This activation involves proliferation and differentiation into plasma cells and secretion of immunoglobulins. The amount of antibodies produced is tremendous. It approximates to about 2000 antibodies per cell/sec

# Immunologic Specificity

- **Each B or T cell clone is specific for a single epitope of a single antigen**
- **The genes for B cell receptors (immuno-globulins) and T cell receptors have hundreds of “gene segments” that are used in varying combinations**
- **Permutations (arrangements) of these cassettes allow specificity for millions of distinct epitopes. Therefore,**

Immunoglobulins produced by B cells are equivalent and similar in function to T cell receptors on T cells. The sequence of genes that results in the production of a certain antibody (in B cells) or T cell receptor (in T cells) cannot be found in the progenitor cells because these antibodies are a result of the randomization of arrangement of different segments of genes, giving us millions of different combination probabilities each forming a unique epitope.

# Lymphocyte Activation

Macrophages produce IL-1 stimulating T helper cells, then T cells further activate macrophages by certain lymphokines

## Macrophages in lymphoid organs…

- ingest antigen and present antigenic peptides to "helper" T cells
- Secrete IL-1, other cytokines that promote lymphocyte growth and differentiation

## Helper T cells produce additional cytokines that stimulate B and T cell proliferation and differentiation

## Both B and T cells require antigenic stimulation to proliferate

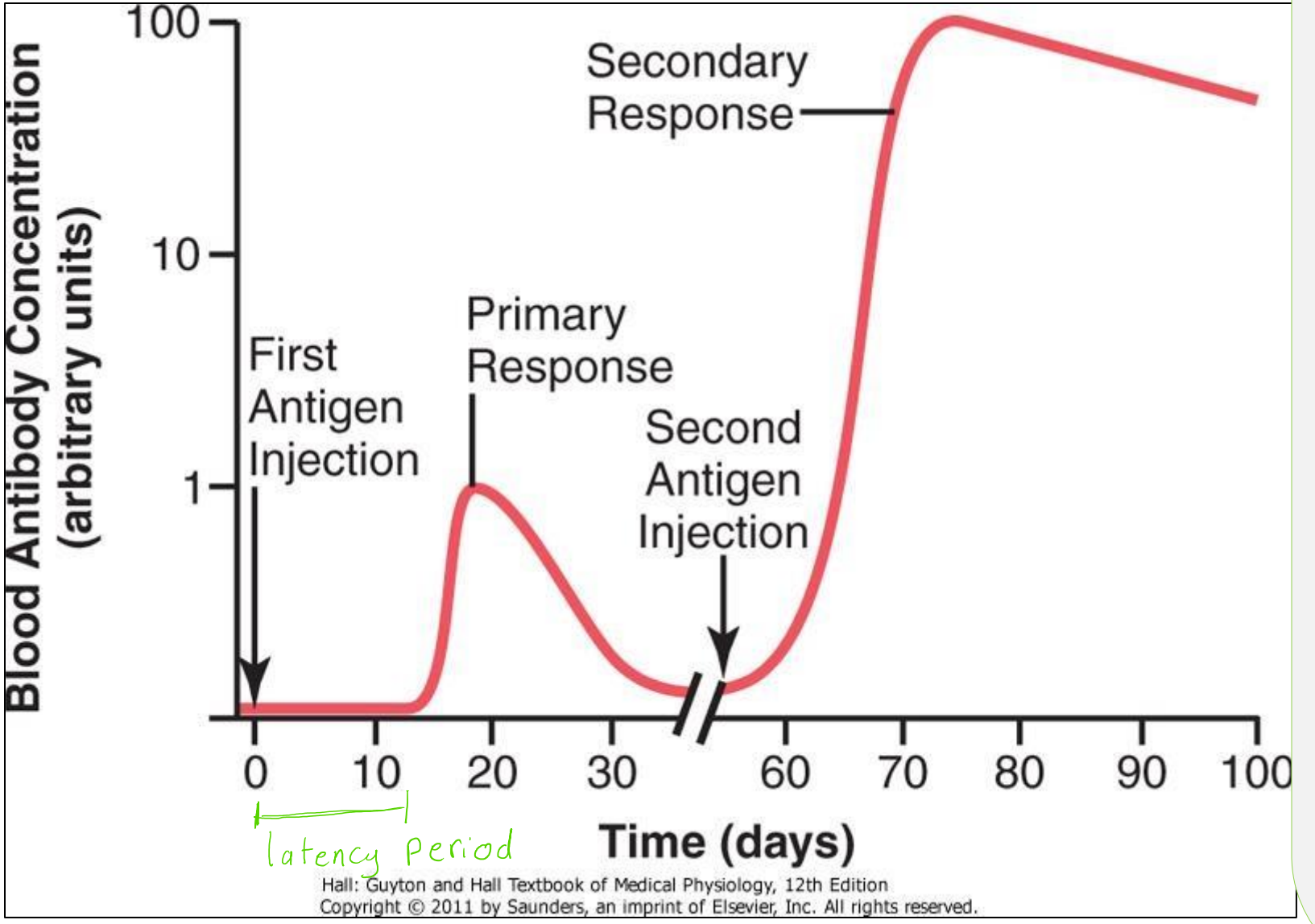
-**T helper** cells are important not only for the T cell-mediated immunity, but for the function of the whole immune system (including T and B cells). For example, we need lymphokines from T helper cells to even stimulate the **proliferation of monocytes** in bone marrow. **If we lacked T helper cells our whole immune system will be paralyzed.**

- One thing to note is that **T cells need the antigen to be presented to them on MHC's** by antigen-presenting cells (APC's).
- Meanwhile, **B lymphocytes can directly recognize antigens**.

# Antibody Production

- B cells bind intact antigen
- T cells bind presented antigenic peptides
- B cells proliferate (with T cell help), developing lymphoblasts and plasmablasts. If T helper cells were removed, the amount of antibodies in our blood will be significantly lower than normal.
- Up to 500 antigen-specific progeny in 4 days, each producing as many as 2,000 Ig molecules/sec
- These immunoglobulins can persist for many weeks, if antigenic stimulation persists

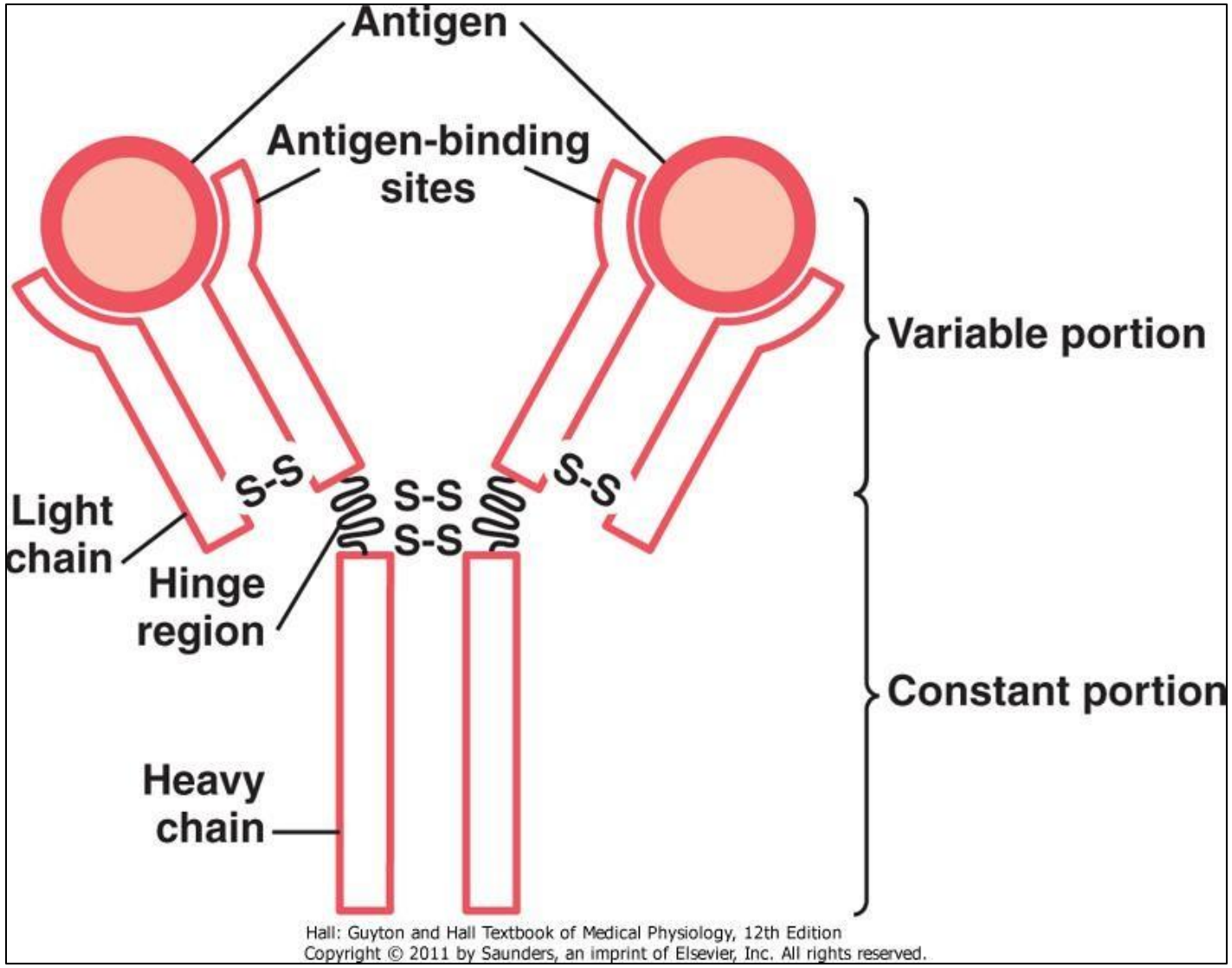
# Memory B cells and secondary responses





- When B cells recognize an antigen and elicit an immune response some of these B cells will differentiate into memory B cells.
- These **memory B** cells will easily recognize the antigen the next time they encounter it. Thus, the immune response will be **faster**, **more severe**, and **longer** than the first time the body encounters the antigen.
- That is why **immunization** is important and effective. It allows the body to generate memory B cells before actually experiencing the disease (so it would be more efficient if we got the disease later on).
- Notice from the graph that the **latency period** after the **second** antigen injection is **shorter** and the blood **antibody** concentration is **higher**.

# Structure of Immunoglobulins




This is the structure of immunoglobulins. There is a light chain and a heavy chain. There is a constant portion and a variable portion. The constant portion differs only between different types of immunoglobulins, which gives these immunoglobulins some of their particular characteristics. The variable portion gives the immunoglobulins their antigen binding specificity

# Antibody Specificity

- **Each antibody has a steric configuration specific to its antigen**
- **Multiple prosthetic groups of each antigen interact with complementary structures of the antibody, through…**
  - **hydrophobic bonding**
  - **hydrogen bonding**
  - **ionic interactions**
  - **van der Waals forces**
- **Antibodies are at least bivalent** **but can have more than one pair of antigen-binding sites, like IgM which has 5.**

# Antibody classes (isotypes)

- **IgM (important in primary response), earliest produced, five pairs of heavy chains and light chains)**
- **IgG (75% of all immunoglobulins)**
- **IgA (mostly in mucus membranes and body fluids)**
- **IgD**
- **IgE (critically involved in allergic reactions)**

  - **Immunoglobulins make up about 20% of all plasma proteins**

قال تعالى: (وما كان الله ليعذبهم وأنت فيهم وما كان الله معذبهم وهم يستغفرون)

| VERSIONS | SLIDE # | BEFORE CORRECTION | AFTER CORRECTION |
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| V1→ V2 | | | |
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امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!