MZO-008: Immunology
Guess Paper-1

Q1. What are the various primary and secondary lymphoid organs? Explain each one of them in detail.

Ans. The immune system protects the body from infectious agents, cancer cells, and foreign substances. A major structural framework of this system is the *lymphoid organs*, which support production, maturation, activation, and proliferation of immune cells. These organs are broadly classified into **primary (central) lymphoid organs** and **secondary (peripheral) lymphoid organs**. Each plays a unique role in ensuring proper development and functioning of the immune system.

Primary Lymphoid Organs

Primary lymphoid organs are responsible for the **development and maturation of lymphocytes**. They provide an environment where immature lymphocytes differentiate into immunocompetent cells capable of recognizing antigens.

1. Bone Marrow

Bone marrow is the soft, vascular tissue located inside bones, especially in flat bones like the pelvis, ribs, and sternum. It is the major **site of hematopoiesis**—the formation of all blood cells including erythrocytes, platelets, and leukocytes.

• All lymphocytes (B and T cells) originate in bone marrow from hematopoietic stem cells.
• **B lymphocytes mature in the bone marrow**. During this process, B cells rearrange immunoglobulin genes, gain antigen-specific receptors (B-cell receptors), and undergo selection to remove self-reactive clones.
• After maturation, B cells migrate through the bloodstream to secondary lymphoid organs where they encounter antigens.

Bone marrow also acts as a reservoir for memory B cells and plasma cells after immune activation. Any defect in bone marrow, such as leukemia or aplastic anemia, impairs overall immunity.

2. Thymus

The thymus is a bilobed organ located behind the sternum above the heart. It is the site of **T lymphocyte (T cell) maturation**.

• Immature T cells, produced in the bone marrow, migrate to the thymus to complete development.
• Inside the thymus, they undergo a unique process of **positive and negative selection**:
  - *Positive selection* ensures that T cells can recognize self–MHC molecules.
  - *Negative selection* eliminates T cells that strongly react with self-antigens to prevent autoimmune disorders.

The thymus is most active during childhood and adolescence. After puberty, it gradually shrinks (a process called involution), but it remains functionally important throughout life.

Secondary Lymphoid Organs

Secondary lymphoid organs are the sites where **mature lymphocytes encounter antigens**, become activated, proliferate, and differentiate into effector and memory cells. They act as meeting points between immune cells and pathogens.

1. Lymph Nodes

Lymph nodes are small, bean-shaped structures distributed throughout the lymphatic system. They filter lymph fluid and monitor it for pathogens.

• Lymph nodes contain B cell–rich follicles in the cortex and T cell–rich paracortex.
• Antigen-presenting cells (APCs) such as dendritic cells bring antigens to lymph nodes and present them to T cells.
• B cells undergo activation, clonal expansion, and antibody production in the *germinal centers*.

Swelling of lymph nodes during infection is due to rapid immune cell proliferation.

2. Spleen

The spleen is located in the upper left abdomen and filters **blood** rather than lymph.

• It is divided into *white pulp* (immune cell activation) and *red pulp* (removal of damaged RBCs).
• White pulp contains T and B cell zones similar to lymph nodes.
• The spleen is essential for defending against blood-borne pathogens like bacteria and viruses.

Splenectomy increases susceptibility to infections, especially encapsulated bacteria.

3. Mucosa-Associated Lymphoid Tissue (MALT)

MALT consists of immune tissues along mucosal surfaces including the gastrointestinal, respiratory, and genitourinary tracts—regions most exposed to pathogens.

Forms of MALT include:

- GALT (gut-associated lymphoid tissue) – e.g., Peyer's patches in the small intestine
- BALT (bronchus-associated lymphoid tissue)
- Tonsils and adenoids
- Appendix

MALT contains clusters of B and T cells that generate rapid immune responses against pathogens entering through mucosal surfaces.

Summary

Category	Organs	Primary Function
Primary Lymphoid Organs	Bone marrow, Thymus	Lymphocyte development and maturation
Secondary Lymphoid Organs	Lymph nodes, Spleen, MALT	Antigen encounter, activation, proliferation of immune cells

Together, these organs maintain a continuous cycle of immune surveillance, lymphocyte development, and memory formation, ensuring long-term protection against pathogens.

Q2. What are the various components of the Innate immune system?

Ans. The innate immune system is the body's **first line of defense** against infection. Unlike the adaptive system, it acts immediately, does not require prior exposure, and lacks antigen specificity. Its function is to prevent pathogen entry, rapidly neutralize invading organisms, and trigger mechanisms that activate the adaptive immune system.

The innate immune system is composed of multiple layers of protection: **physical barriers, chemical barriers, cellular defenses, humoral factors, and inflammatory responses**.

1. Physical and Mechanical Barriers

These barriers prevent pathogen entry into the body.

- **Skin** acts as a tough physical shield.
- **Mucous membranes** trap microbes in the respiratory and digestive tracts.
- **Cilia** in the respiratory tract push trapped microbes upward for expulsion.
- **Tears, saliva, urine flow, and coughing reflexes** mechanically wash away pathogens.

Any damage to these barriers—burns, wounds, catheterization—dramatically increases infection risk.

2. Chemical Barriers

These chemicals create hostile environments for pathogens.

- **Stomach acid** destroys ingested microbes.
- **Lysozyme** (in tears, saliva) breaks down bacterial cell walls.
- **Sebum and sweat** create antimicrobial surface acidity.
- **Interferons** inhibit viral replication.

Together, chemical defenses reduce microbial survival even before cellular immunity is activated.

3. Cellular Components

These include specialized white blood cells that destroy pathogens.

- **Neutrophils** – first responders that kill microbes via phagocytosis and release of antimicrobial molecules.
- **Macrophages** – long-lived phagocytes that engulf microbes and present antigens to T cells, linking innate and adaptive immunity.
- **Dendritic cells** – main antigen-presenting cells that trigger adaptive responses.
- **Natural Killer (NK) cells** – destroy virus-infected and cancer cells without needing antigen recognition.
- **Eosinophils and Basophils** – defend against parasitic infections and mediate allergic reactions.

4. Complement System

This system is a network of plasma proteins that enhances pathogen clearance by:

- forming membrane attack complexes (MAC) to lyse microbes
- tagging pathogens for phagocytosis (opsonization)
- promoting inflammation

The complement system bridges innate and adaptive immunity.

5. Pattern Recognition Receptors (PRRs)

Innate cells use PRRs to detect pathogens through conserved structures called **PAMPs (pathogen-associated molecular patterns)**.

• **Toll-like receptors (TLRs)** detect bacterial cell walls, viral RNA, and fungal molecules.
• Activation of PRRs triggers cytokine release and immune cell recruitment.

6. Cytokines and Inflammatory Mediators

Cytokines such as interleukins, interferons, and TNF-α coordinate immune cell activity. Inflammation results in heat, redness, swelling, and pain—signals that direct immune cells to infection sites.

7. Inflammation

The inflammatory response localizes infection and promotes healing.
• Blood vessels dilate to increase immune cell flow
• Capillaries become permeable to allow phagocyte movement
• Neutrophils and macrophages eliminate pathogens and remove debris
While protective, excessive inflammation can cause tissue damage.

8. Fever

Fever is an innate defense mechanism caused by pyrogens. Elevated temperature inhibits microbial growth and enhances immune efficiency.
The innate immune system is a highly coordinated network that prevents infection through immediate, non-specific mechanisms. It not only protects the body during early infection but also shapes and activates adaptive immune responses for long-term protection.

Q3. What are the three different ways of complement system activation?

Ans. The complement system is composed of more than 30 proteins circulating in the blood in inactive form. Upon activation, these proteins form a cascade that enhances immune defense by opsonization, inflammation, and pathogen lysis. Complement activation can occur through **three major pathways**: the **classical pathway, lectin pathway, and alternative pathway**. Though they differ in initiation mechanisms, all converge on the activation of C3 protein and eventually generate the **membrane attack complex (MAC)**, which lyses pathogens.

1. Classical Pathway

The classical pathway is triggered when antibodies bind to antigens on microbial surfaces.

Initiation:

• Antibodies (IgG or IgM) bind to antigens → activates the C1 complex.
• Activated C1 cleaves C4 and C2, forming **C4b2a**, known as **C3 convertase**. **Outcome:**
• C3 convertase cleaves C3 into C3a and C3b.
• C3b leads to opsonization and forms **C5 convertase**, resulting in MAC formation.

Key feature: This pathway links the **adaptive immune system** to complement activation because it requires antibodies.

2. Lectin Pathway

The lectin pathway resembles the classical pathway but is **antibody-independent**.

Initiation:

• Mannose-binding lectin (MBL), a plasma protein, binds to mannose residues on microbial cell walls.
• MBL-associated serine proteases (MASPs) activate C4 and C2, forming **C4b2a (C3 convertase)**.

Outcome:

• Similar to the classical pathway—C3 convertase activates C3 and drives MAC formation.

Key feature: This pathway is part of the **innate immune system** and detects pathogens based on carbohydrate signatures.

3. Alternative Pathway

The alternative pathway continuously samples microbial surfaces and amplifies complement activation.

Initiation:

• C3 undergoes spontaneous hydrolysis in blood, generating C3b.
• C3b binds to pathogen surfaces (because host cells regulate C3b deposition and are protected).
• With factors B, D, and properdin, it forms **C3bBb (C3 convertase)**.

Outcome:

• C3 convertase further activates C3 and amplifies the response.
• C5 convertase leads to MAC assembly and cell lysis.

Key feature: This pathway does **not require antibodies** and is important during early infections.

Convergence of All Pathways

Regardless of the activation route:

Classical →
Lectin → **All create C3 convertase → C3 activation → C5 activation → MAC → Pathogen lysis**
Alternative →

MAC (composed of C5b, C6, C7, C8, C9) inserts into microbial membranes, creating pores that lead to osmotic imbalance and cell death.

The complement system enhances immune efficiency by linking innate and adaptive immunity. The **classical pathway** depends on antibody–antigen complexes, the **lectin pathway** recognizes carbohydrate molecules on microbes, and the **alternative pathway** activates spontaneously on pathogen surfaces. Together they ensure rapid pathogen elimination, promote inflammation, and enhance phagocytosis—making complement activation a central mechanism of host defense.

Q4. What is hematopoiesis, and where does it occur in the body?

Ans. Hematopoiesis is the process through which all blood cells are developed from hematopoietic stem cells (HSCs). This complex physiological process is crucial for maintaining the body's blood cell populations, which include red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes). Hematopoiesis plays a vital role in transporting oxygen, protecting against infections, and aiding in clotting mechanisms.

Origin and Development of Hematopoiesis

Hematopoiesis occurs primarily in the bone marrow, the soft tissue found within the cavities of bones, particularly in the pelvis, vertebrae, ribs, and sternum in adults. However, throughout different stages of development, the site of hematopoiesis shifts. In the early embryonic stage, blood cell production starts in the yolk sac. As development progresses, hematopoiesis transitions to the liver and spleen around the second trimester of gestation. By the time of birth, the bone marrow becomes the predominant site for the production of blood cells.

The Hematopoietic Stem Cells

The fundamental units of hematopoiesis are hematopoietic stem cells, which are multipotent cells capable of giving rise to all the various blood cell types. These stem cells reside in the bone marrow and have the unique ability to self-renew, preserving the stem cell pool, and to differentiate into specific lineages of blood cells. They express markers such as CD34 and do not exhibit a specific function as they require stimulation to differentiate.

Microenvironment and Regulatory Signals

The bone marrow microenvironment, often referred to as the 'niche,' plays a crucial role in hematopoiesis. This niche comprises various cells, including stromal cells, adipocytes, endothelial cells, and extracellular matrix components, which provide structural support and produce key signaling molecules. The interaction between stem cells and their niche influences their proliferation and differentiation.

Growth factors and cytokines significantly influence hematopoiesis. These signaling molecules dictate the fate of HSCs and their progeny, determining which cell types are produced and in what quantities. Tightly regulated, these processes ensure the proper response to physiological demands, such as during infection, injury, or increased physical activity.

Types of Hematopoiesis: Primitive and Definitive

Hematopoiesis can be categorized into two types based on the developmental stage: primitive and definitive hematopoiesis. Primitive hematopoiesis occurs during early embryonic development and primarily generates erythrocytes. Definitive hematopoiesis begins later in development and continues throughout life, producing all blood cell types, starting from HSCs in the bone marrow.

Conclusion

Hematopoiesis is a dynamic and tightly regulated process essential for life. It ensures a consistent supply of blood cells, critical for various physiological functions. Understanding this process provides essential insights into health and disease, especially in conditions such as anemia, leukemia, and other hematological disorders.

Q5. What are the different types of immune system cells produced during hematopoiesis?

Ans. Hematopoiesis gives rise to a diverse array of immune system cells, which play critical roles in the body's defense mechanisms. These cells can broadly be categorized into three main groups: lymphoid cells, myeloid cells, and antigen-presenting cells. Each of these groups further comprises specialized cell types with unique functions tailored to combat infections and maintain homeostasis.

Lymphoid Cells

1. **B Cells**: B lymphocytes or B cells are responsible for producing antibodies, which neutralize pathogens and facilitate their clearance from the body. They develop in the bone marrow and migrate to secondary lymphoid organs like the spleen and lymph nodes.
2. **T Cells**: T lymphocytes include several subtypes, primarily helper T cells (CD4+) and cytotoxic T cells (CD8+). T helper cells assist other immune cells, while cytotoxic T cells directly target and destroy infected or cancerous cells. T cells originate in the bone marrow but mature in the thymus.
3. **Natural Killer (NK) Cells**: NK cells are a critical component of the innate immune system. They can recognize and kill virus-infected cells or tumor cells without prior sensitization. They play a role in the early response to viral infections.

Myeloid Cells

1. **Granulocytes**: These include neutrophils, eosinophils, and basophils. Neutrophils are the most abundant and are typically the first responders to infections. Eosinophils deal with parasitic infections and allergic responses, while basophils release histamine and play a role in allergic reactions.
2. **Monocytes**: These cells circulate in the bloodstream and migrate to tissues, where they differentiate into macrophages and dendritic cells. Macrophages are pivotal in phagocytosing pathogens and dead cells, while dendritic cells are crucial for antigen presentation to T cells.
3. **Platelets**: While not immune cells in the traditional sense, platelets are essential for wound healing and inflammatory responses. They participate in clotting processes that prevent excessive blood loss and can modulate immune responses.

Antigen-Presenting Cells (APCs)

Cells such as macrophages, dendritic cells, and B cells can act as APCs, bridging the innate and adaptive immune systems. They capture antigens and present them on their surface in conjunction with major histocompatibility complex (MHC) molecules to T cells. This process is vital for the activation of T cells and the subsequent immune response.

Importance of Hematopoietic Lineages in Disease

The proper functioning of these immune cells is essential for maintaining health. Dysregulation in hematopoiesis can lead to various disorders. For instance, an overproduction of certain leukocytes can lead to leukemia, while a deficiency can result in immunodeficiency disorders. Understanding the types and functions of immune cells derived from hematopoiesis is crucial for developing treatments for these diseases.

Through hematopoiesis, the body generates a complex array of immune cells, each with distinct roles in host defense. The orchestration of these cells ensures a robust and adaptive response to pathogens and cancer, emphasizing the importance of this process in health and disease.

Q6. What is the role of B and T cells in the immune system?

Ans. B cells and T cells are integral components of the adaptive immune system. Their specific roles are pivotal in combating pathogens, establishing immunological memory, and ensuring a robust and tailored immune response when faced with diverse threats.

B Cells: Guardians of Humoral Immunity

B cells originate in the bone marrow and are primarily responsible for humoral immunity, which involves the production of antibodies. Upon encountering an antigen, B cells undergo activation, proliferation, and differentiation into effector cells, known as plasma cells. These plasma cells secrete large quantities of antibodies, which can neutralize pathogens and mark them for destruction.

1. **Antibody Production**: The antibodies, or immunoglobulins, produced by B cells can bind to specific antigens, preventing pathogens from entering or damaging host cells. There are different classes of antibodies (IgM, IgG, IgA, IgE, and IgD), each serving unique functions, such as neutralizing toxins, opsonizing pathogens for phagocytosis, or triggering an inflammatory response.
2. **Memory B Cells**: After an initial encounter with an antigen, some B cells differentiate into memory B cells. These cells persist long term and enable a rapid and more effective response upon re-encountering the same antigen, which is crucial for vaccine efficacy.
3. **Role in Autoimmunity**: While necessary for fighting infections, dysregulation in B cell activity can lead to autoimmunity, wherein the immune system mistakenly targets the body's own tissues.

T Cells: Orchestrators of Cellular Immunity

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