Definitions & Basic Concepts

- **Immunology**: The study of the immune system and host defense mechanisms against infection.
- **Immunity**: Resistance to infectious diseases.
- **Immune System**: A collection of tissues, cells, and molecules that provide resistance to infections.
- **Immune Response**: The body's coordinated reaction to foreign invaders.
- **Historical Perspective**: Immunity observed since the Athens plague (430 BC), where recovered individuals resisted reinfection.

Types of Individuals in Immunity

- **Immune Individual**: Has encountered a microbe, responded actively, and developed resistance.
- **Naïve Individual**: Has not been exposed to microbe.

Functions of the Immune System

1. **Defense**: Protects against infections.
2. **Homeostasis**: Maintains immune balance.
3. **Surveillance**: Identifies and removes abnormal cells.

Immune System Dysfunctions

Hyperfunction: Causes allergies and autoimmune diseases.
Hypofunction: Leads to immunodeficiency and increased susceptibility to infections.

Organs of the Immune System

- **Primary (Central) Lymphoid Organs**:

Bone Marrow: Produces blood cells, including B and T lymphocytes.
Thymus: Matures T cells.

- **Secondary (Peripheral) Lymphoid Organs**:

Lymph nodes, spleen, mucosal-associated lymphoid tissues (MALTs), gut-associated lymphoid tissues (GALTs)

Cells of the Immune System

1. **Specific Immunity** (Adaptive Immunity):

B cells: Produce antibodies.
T cells: Recognize and remove infected cells.

2. **Non-Specific Immunity** (Innate Immunity):

Natural Killer Cells (NK cells): Attack virus-infected and cancer cells.
Granulocytes: Includes neutrophils (phagocytes), basophils (allergy response), and eosinophils (parasite response).
Monocytes/Macrophages: Engulf pathogens and aid in immune response.
Dendritic Cells: Present antigens to activate T cells.

Secretory Products of Immune Cells

✓ **Non-Specific Immunity**: Cytokines, CRP, hydrogen peroxide, complement proteins, allergic mediators, etc.
✓ **Specific Immunity**: Lymphokines (e.g., IL-2, IL-4) and antibodies.

Types of Immunity

1. **Innate Immunity**: First-line defense, immediate response
2. **Adaptive Immunity**: Develops over time and provides long-lasting protection.

Features of Adaptive Immunity

✓ **Self-Recognition**: Distinguishes between self and non-self.
✓ **Specificity**: Recognizes and targets specific pathogens.
✓ **Diversity**: Can recognize millions of antigens.
✓ **Memory**: Remembers past infections for a faster secondary response.
✓ **Self-Elimination**: Immune response declines after antigen removal.

Phases of Immune Response

➢ **Recognition of Antigen**
➢ **Activation of Lymphocytes**
➢ **Elimination of Antigen (Effector Phase)**
➢ **Memory Formation**

Innate Immunity

- **Characteristics**:
  - ➢ Present before exposure to microbes, non-specific, no memory.
  - ➢ Destroys most microbes within minutes or hours.
  - ➢ Recognizes shared microbial structures via Pattern Recognition Receptors (PRRs), like Toll-like receptors (TLRs).
- **Components**:
  - **First Line of Defense**:

✓ **Physical barriers:** Skin, mucus membranes, nasal hairs, coughing/sneezing reflex, blinking, tears.
✓ **Chemical barriers:** Acidic secretions, stomach HCl, lysozyme in saliva/tears, vaginal acidity.
✓ **Biological barriers:** Normal flora that compete with pathogens.

  - **Second Line of Defense**:
    - **Cells**:

Neutrophils: Phagocytosis and inflammation.
Macrophages: Phagocytosis and antigen presentation.
Natural Killer (NK) cells: Destroy virus-infected and tumor cells via perforin and granzyme.
Eosinophils: Combat parasites and inflammation.
Basophils/Mast cells: Involved in allergic responses.

    - **Soluble Factors**:

✓ Acute phase proteins (C-reactive protein, fibrin).
✓ Complement system (enhances pathogen destruction).
✓ Cytokines (TNF-α, IL-1, IL-6, IFNs).

    - **Inflammatory Response**:

✓ Triggered by tissue damage/pathogens.
✓ Chemical mediators (histamine, cytokines) cause vasodilation, fluid influx, and phagocyte migration.

3. Phagocytosis (Microbe Engulfment and Destruction)

1. **Chemotaxis:** Attraction of phagocytes via IL-8 and C5a.
2. **Adherence:** Phagocyte binds pathogen via receptors (TLRs, mannose receptors).
3. **Ingestion:** Phagocyte engulfs pathogen, forming a phagosome.
4. **Digestion:** Phagosome merges with lysosome, destroying the microbe via oxygen-dependent and independent mechanisms.

4. Antigen Presentation (Link to Adaptive Immunity)

Antigen-Presenting Cells (APCs): Dendritic cells, macrophages, and B cells.
Major Histocompatibility Complex (MHC) Pathways:

MHC Class I: Presents intracellular (endogenous) antigens to CD8+ T cells.
MHC Class II: Presents extracellular (exogenous) antigens to CD4+ T cells.

Humoral Immune

Activation of B Cells & Antibody Production

- **T-Dependent Antigens** (proteins) require **T-helper (TH) cells** for B-cell activation.
- **T-Independent Antigens** (polysaccharides, lipids) activate B cells directly.
- **B Cell Activation Steps:**

1. **Recognition**: Naive B cells encounter antigens and bind via **IgM-IgD** receptors.
2. **Antigen Processing & Presentation**: B cells present the antigen on **MHC-II** to **TH cells**.
3. **Co-stimulation**: B7-CD28 and **CD40-CD40L** interactions occur between B and TH cells.
4. **Cytokine Release & Differentiation**: TH cells secrete **IL-4, IL-5, IL-6, IL-13, TNF-β**, promoting B cell proliferation and **class switching** from **IgM to IgG, IgA, or IgE**.
5. **Memory B Cells Formation**: Some B cells become **memory cells**, ensuring a **rapid secondary response** upon re-exposure.

Structure of Antibodies (Immunoglobulins, Ig)

✓ Consist of **two heavy chains** and **two light chains** linked by **disulfide bonds**.
✓ **Fab region**: Contains antigen-binding sites (variable regions **VH & VL**).
✓ **Fc region**: Determines antibody function (e.g., IgG crosses the placenta).

Hypervariable Regions: Form **paratope**, which binds to the antigen's **epitope**

Types of Immunoglobulins (Isotypes)

1. **IgG**

✓ Most abundant (75%), long **half-life (23 days)**.
✓ Involved in **secondary immune response, opsonization, ADCC, and complement activation**.
✓ Crosses the **placenta**, providing **neonatal immunity**.

2. **IgA**

✓ Found in **mucosal secretions** (saliva, tears, milk).
✓ Provides **local immunity** by preventing microbial adherence.

3. **IgM**

✓ **First antibody produced** in primary response.
✓ Exists as a **pentamer**, strong in **agglutination and complement activation**.

Functions of Antibodies

❖ **Agglutination**: Clumps microbes to prevent spread.
❖ **Neutralization**: Blocks toxins and viruses from binding to cells.
❖ **Opsonization**: Enhances phagocytosis.
❖ **Complement Activation**: Triggers **lysis** of pathogens.
❖ **Antibody-Dependent Cellular Cytotoxicity (ADCC)**: Kills antibody-coated **tumor or virus-infected cells** via **NK cells, macrophages, and neutrophils**.

Differences Between T-Dependent & T-Independent Responses

Feature	T-Dependent	T-Independent
Antigen Type	Proteins	Polysaccharides Lipids
TH Cell Involvement	Required	Not required
Antibody Classes Produced	**IgG, IgA, IgE, IgM**	**IgM only**
Memory B Cells	Yes	No

Types of Immunity and Vaccines

1. Immunity Overview

Specific (Acquired) Immunity: Protects against specific pathogens.
Types of Acquired Immunity:
Passive: From mother or antiserum.
Active: From infection or vaccine.
Modes of Acquisition:
Natural: Mother or infection.
Artificial: Antiserum or vaccine.

2. Vaccines and Protective Immunity

A vaccine is a biological preparation provides **active, acquired specific immunity** to a disease.
Duration of Immunity:
Long-term (e.g., MMR vaccine).
Short-term (e.g., cholera vaccine, lasting ~6 months).

3. Types of Vaccines

Inactivated (Killed) Vaccines
Pathogen is inactivated via heat, chemicals, or UV (e.g., Salk polio, cholera).
Pros: Safe, stimulates immunity.
Cons: Requires boosters, only induces humoral immunity, costly.

Attenuated (Weakened) Vaccines
Pathogen is grown under conditions that reduce virulence (e.g., Sabin polio, MMR).
Pros: Stronger immune response, requires fewer doses, induces mucosal immunity.
Cons: Risk of reversion to virulent form, unsafe for immunosuppressed individuals.

Subunit Vaccines
Contain purified antigens instead of whole organisms.
Pros: Safe for immunosuppressed individuals, fewer side effects.
Cons: May not induce strong immunity; requires adjuvants (e.g., aluminum salts).

Conjugate Vaccines
Weak antigens combined with strong carriers to enhance immune response.
Used for **Haemophilus influenzae B (HiB), Streptococcus pneumoniae, Neisseria meningitidis**.

Toxoid Vaccines Made from inactivated bacterial toxins (e.g., tetanus, diphtheria).

Peptide Vaccines Synthetic peptides that stimulate immunity with minimal side effects.

Viral Vector Vaccines
Uses harmless viruses to deliver genetic material of pathogen
Pros: Cheaper than subunit vaccines.
Examples: AstraZeneca, Johnson & Johnson COVID-19 vaccines.

Recombinant Vaccines
Uses recombinant DNA technology (e.g., Hepatitis B vaccine).
Pros: Safe and eliminates harmful antigens.
Cons: High production cost.

DNA Vaccines
Injects DNA encoding the antigen to stimulate immune response.
Pros: Safe, induces both humoral and cellular immunity.

Rickettsiae

- **Classification:** Although classified as bacteria, they share viral traits as **obligate intracellular parasites**, requiring host cells to survive.

- **Characteristics:**

✓ Visible under a light microscope when stained with **Giemsa or Macchiavello stain**.
✓ Have **DNA and RNA**, replicate **by binary fission**.
✓ Their **cell wall resembles Gram-negative rods** but stains poorly.
✓ Sensitive to **chloramphenicol** and **tetracycline**.
✓ Best isolated in **yolk sac of embryonated eggs**, **mice**, or **guinea pigs**.

- **Groups, Diseases, and Vectors:**

Group	Organism	Disease	Reservoir	Vector	Proteus Antigen
Typhus	R. prowazekii	Epidemic typhus (worldwide)	Humans	Body louse	OX19
	R. typhi	Endemic typhus (worldwide)	Rats	Rat flea	OX19
Spotted Fever	R. rickettsii	Rocky Mountain Spotted Fever	Dogs & Rodents	Tick	OX19, OX2
	R. akari	Rickettsial pox (USA)	Mice	Mite	----
Orienta	O. tsutsugamushi	Scrub typhus (Japan, Asia)	Rodents	Mite	OXK

- **Transmission:**

✓ Transmitted via **arthropod vectors** (e.g., **ticks, lice, fleas**).
✓ Infection occurs through **bites or contaminated skin scratches**.
✓ Most rickettsial diseases are **zoonotic**, except **epidemic typhus**, which occurs only in humans.

- **Pathogenesis:**

✓ Causes **vasculitis**, damaging **endothelial cells** in small blood vessels.
✓ Leads to **rash, edema, hemorrhage**.
✓ Endotoxin may contribute to the disease.

- **Clinical Findings & Epidemiology:**

○ **Epidemic Typhus (R. prowazekii):**

✓ Associated with **wars, poverty, unsanitary conditions**.
✓ Found in **Africa and South America**.
✓ Symptoms: **Fever, chills, headache, rash (spares face, palms, soles)**.
✓ **Complications:** Myocarditis, delirium, death if untreated.
✓ **Brill-Zinsser Disease:** Latent R. prowazekii infection that reactivates under **immunosuppression**.

○ **Endemic Typhus (R. typhi):**

✓ Milder form of epidemic typhus with low mortality.
✓ **Reservoir:** Rats, transmitted by fleas.

- **Diagnosis:**

❖ **Serologic Tests:**

Indirect immunofluorescence, Complement fixation, Weil-Felix test (cross-reacts with **Proteus OX-19, OX-2, OX-K**).

❖ **PCR on blood/skin biopsy**.
❖ **Isolation** via yolk sac inoculation in embryonated eggs, guinea pigs, or tissue culture.

- **Control & Treatment:**

➢ **Vector control** to stop transmission.
➢ **Prophylaxis** with tetracycline/chloramphenicol in epidemics.
➢ **Vaccines:**
Killed vaccine (Cox vaccine): 3 doses subcutaneously. **Live attenuated vaccine** (R. prowazekii strain E).
➢ **Treatment: Tetracycline or chloramphenicol**.

Coxiella burnetii (Q Fever)

Differences from Rickettsia:

- Forms a **spore-like resistant stage**.
- Causes **no rash**.
- **Not transmitted by arthropod bites**.
- Exists in **two phases:**
  - ❖ **Phase I:** Virulent, isolated from patients.
  - ❖ **Phase II:** Non-virulent, obtained after repeated culture passages.
- Grows in **cytoplasmic vacuoles** instead of free cytoplasm.

- **Q Fever:**

○ **Zoonotic disease**; **reservoirs** include **cattle, sheep, camels, birds, and ticks**.

- **Transmission:**

Airborne (main route): Inhalation of infected animal aerosols (placenta, feces, urine).
Ingestion: Drinking infected milk.

- **Acute vs. Chronic Q Fever:**

Feature	Acute Q Fever	Chronic Q Fever
Duration	< 6 months	> 6 months
Symptoms	Atypical pneumonia, hepatitis	Endocarditis, prolonged fever
Risk Factors	None	Immunocompromised, pregnant, heart valve defects
Serology	**Phase II antibody**	**Phase I antibody**
Treatment	Tetracycline (few days)	Tetracycline (months) + combination therapy

- **Diagnosis:**

- **Serology (IFA test preferred)** – detects **phase I and II antibodies**.
- **IgG anti-phase II > 200** → Acute Q fever.
- **Anti-phase I antibodies** → Chronic Q fever.
- **Fluorescent antibody stain** for detection.

- **Prevention & Treatment:**

- **Doxycycline** is the treatment of choice.
- **Vaccine** for high-risk workers (e.g., veterinarians, farmers).
- **Pasteurization of milk** to prevent transmission.

Herpes Viruses

❖ A family of viruses that cause lifelong latent infections with periodic reactivation.
❖ Can be treated with antiviral drugs.
❖ Classified into three groups:
  ○ **Alpha herpesviruses (Neurotropic viruses):** HSV-1, HSV-2, Varicella-Zoster virus (VZV).
  ○ **Beta herpesviruses (Salivary gland inclusion viruses):** Cytomegalovirus (CMV), HHV-6, HHV-7.
  ○ **Gamma herpesviruses (Lymphotropic viruses):**Epstein-Barr virus (EBV),HHV-8

- **General Characteristics:**

  ○ Large, enveloped, double-stranded DNA viruses with a cubical capsid.
  ○ Replicate in the nucleus, with an envelope derived from the nuclear membrane.
  ○ Sensitive to heat and produce intranuclear inclusion bodies.

Epstein-Barr Virus (EBV)

Causes **infectious mononucleosis (glandular fever)**, usually asymptomatic in early infections.

➢ **Transmission:** Through infected saliva (also called the "kissing disease").
➢ **Pathogenesis:**
- Infects the **oropharynx** and spreads to the blood, infecting **B lymphocytes**.
- **Cytotoxic T lymphocytes** attack infected B cells, forming **atypical lymphocytes** in blood smears.
- Remains **latent** in B lymphocytes.

➢ **Diagnosis:**
❖ **Hematology:** Leukocytosis with atypical lymphocytes.
❖ **Serology:**
  - Heterophil antibody tests (Monospot, Paul-Bunnel).
  - EBV-specific antibodies: **VCA-IgM (acute infection), VCA-IgG (lifelong), EA, EBNA**.
❖ **Other Tests:** Virus isolation (difficult), DNA hybridization (most sensitive).

➢ **Associated Diseases:**
- Burkitt lymphoma, Hodgkin's lymphoma, Nasopharyngeal carcinoma.
- **Hairy leukoplakia** in immunocompromised patients.

Parvovirus B19

- **General Features:**

  ○ Small, non-enveloped, single-stranded DNA virus.

  ○ Targets **erythroid precursor cells**.

- **Transmission:**

  ○ Respiratory route, transplacental, and via blood transfusion.

- **Diseases Caused:**

1. **Erythema infectiosum (Fifth disease):** Characterized by a **slapped cheek rash**.
2. **Transient aplastic crisis** in sickle cell disease patients.
3. **Hydrops fetalis** in pregnant women, leading to fetal death.

- **Pathogenesis:**

  ○ Infects **erythroblasts** in the bone marrow (causing anemia).

  ○ Infects **endothelial cells**, contributing to rashes.

  ○ **Immune complexes** also play a role in disease progression.

- **Diagnosis:**

  ○ PCR and hybridization for viral DNA.

  ○ Detection of viral antigens.

  ○ Serology (IgM/IgG).

- **Note:** The virus is difficult to culture.