BHARATHIDASAN UNIVERSITY

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Programme: M.Sc., Biomedical Science

Course Code: BM35C6
Course Title: Immunology

Unit-IV

Immune response to infectious agents & Hypersensitivity reactions

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Unit IV:

Immune response to infectious agents & hypersensitivity reactions. Overview on immunity to intracellular and extracellular pathogens-Bystander damage caused by the immune response to infection- evasion of immune responses by various infectious agents. Overview on hypersensitivity reactions – Gell and Coombs classification, IgE-mediated (Type I), antibody- mediated (Type II), immune complex- mediated (Type III) (Glomerulonephritis, extrinsic allergic alveolitis, serum sickness) and TDTH-mediated (Type IV) hypersensitivity

PRESENTATION: 1

Key concepts of Immunity

1. The immune system has evolved to serve two major functions:
   (1) Protect against the invading pathogens (or foreign substances)
   (2) Maintain tissue homeostasis (damaged cells or cancer).
   Meanwhile, microbes (outside) and tumors (inside) have evolved to survive in the host.

2. The immune system (in mammals) consists of (1) Innate immunity and (2) Adaptive immunity
   => An integrated system of host defense
   => Cells & molecules function cooperatively
   Antigen-presenting cells => Lymphocytes => Effector cells

3. Innate immunity is evolutionally the more conserved host defense system: (1) Existed in both Invertebrates & Vertebrates;
   (2) Provides the first line of defenses against infections,
   and (3) "Activates" and "Programs" adaptive immune responses

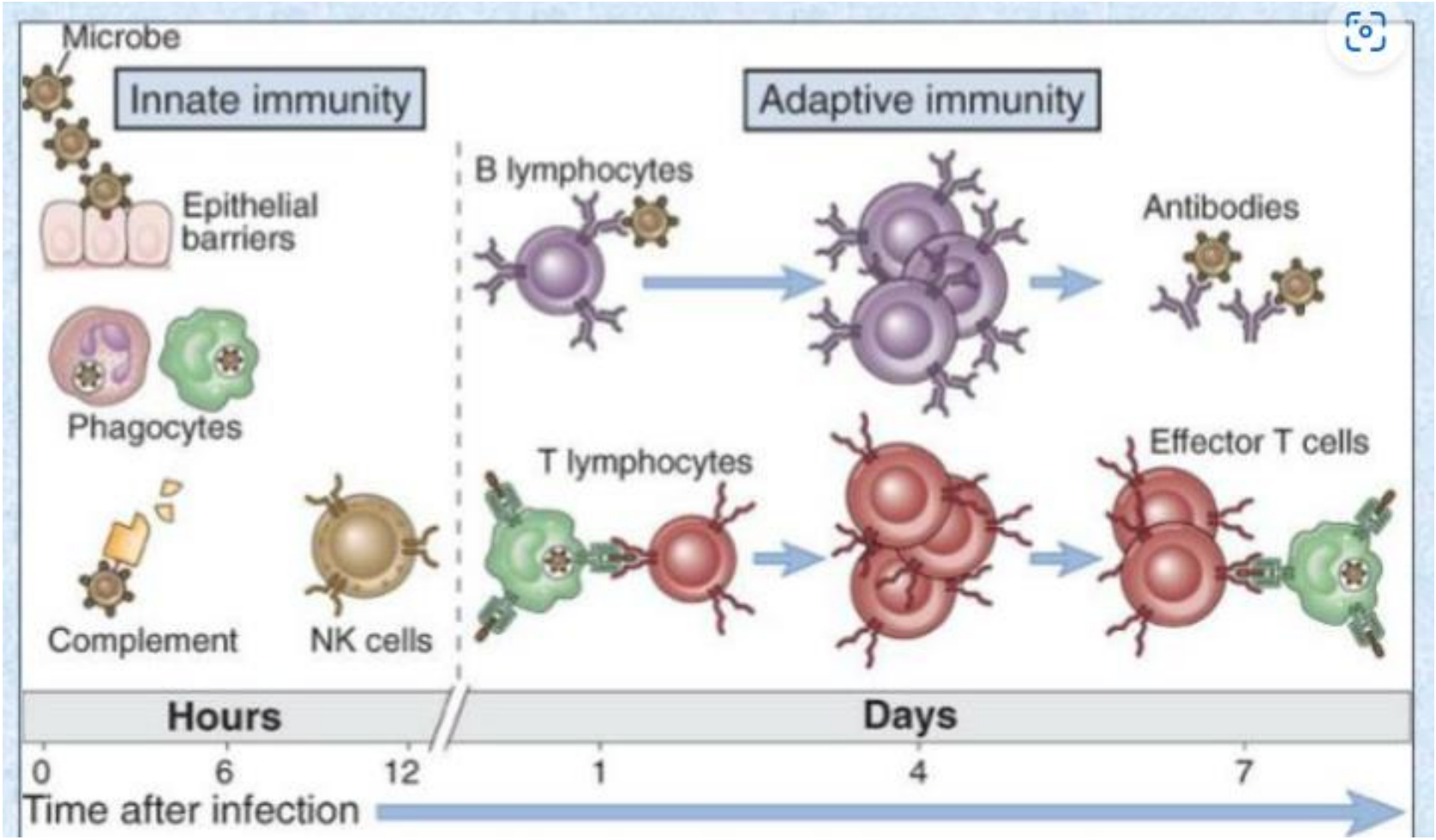
5. Adaptive immunity evolved later:
   - Existed only in Vertebrates
   - Provides the more potent and diverse defenses against infections

Better Understanding of Immunology
⇒ Help manipulate immune responses

6. ⇒ Solve the medical problems
   Hypersensitivity, & Autoimmune diseases.

7. Normal immune responses can be obstacles in medical cases, e.g., organ transplantation

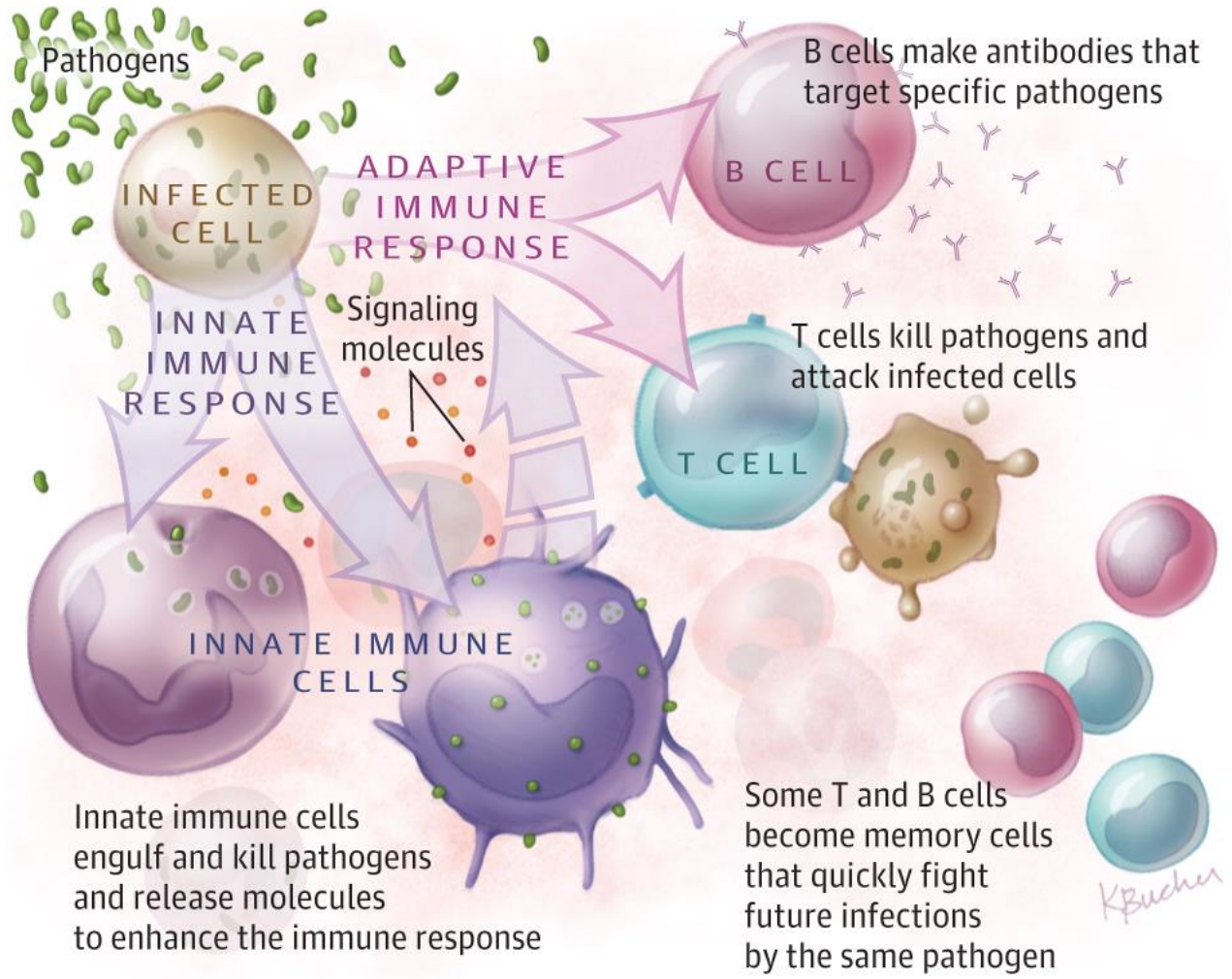
Overview of immune response



Immune Response to Infectious Agents

- The immune system plays a crucial role in defending the body against infectious agents, which can be broadly classified into intracellular and extracellular pathogens.
- The immune response involves a coordinated action of various cells and molecules to eliminate these pathogens.

The Immune Response



Immunity to Intracellular Pathogens

Intracellular pathogens (e.g., viruses, some bacteria like *Mycobacterium tuberculosis*, and protozoa like *Plasmodium spp*.) reside within host cells, making them less accessible to antibodies and other extracellular immune components.

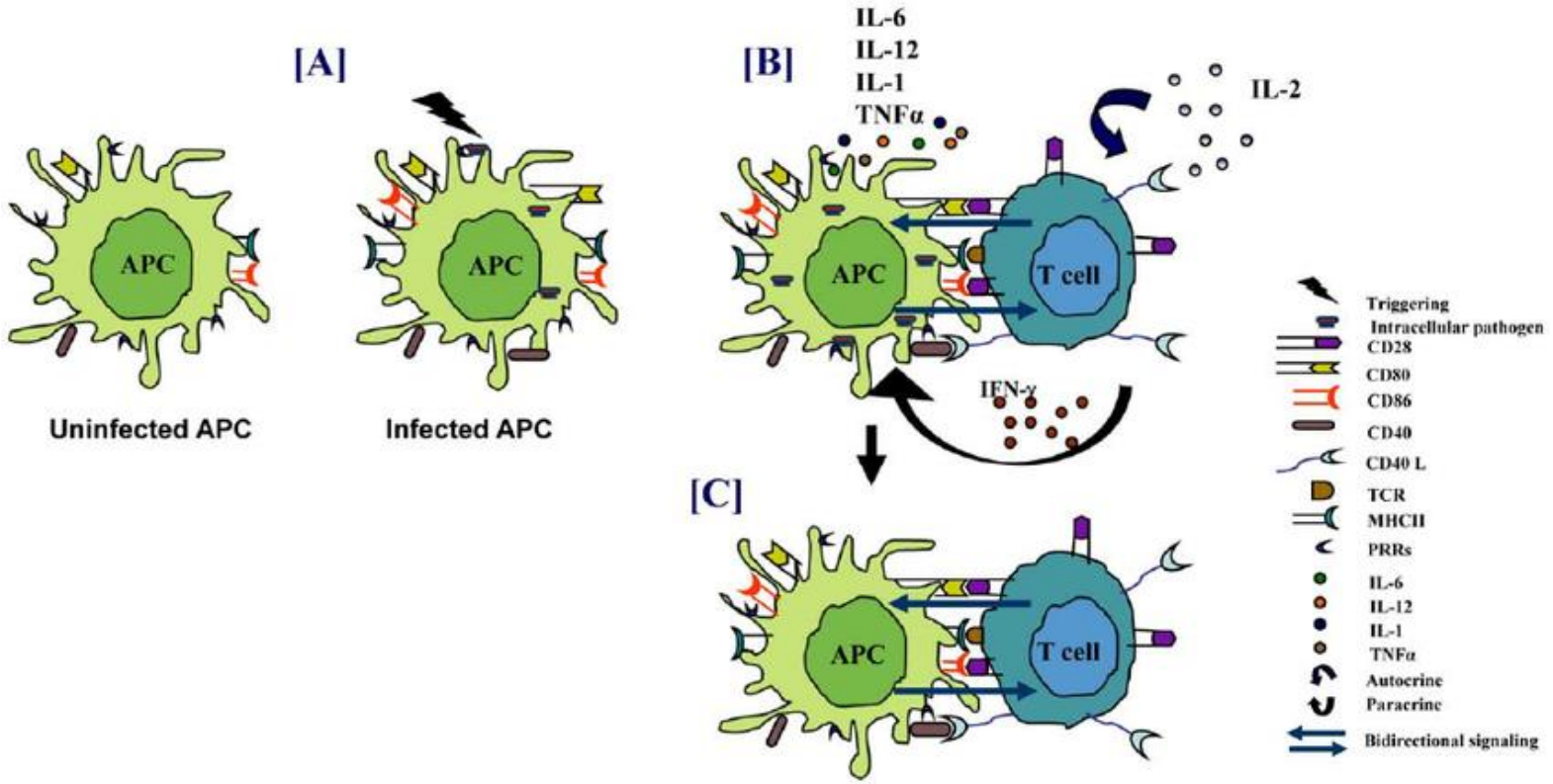
1. Innate Immune Response:

- **Natural Killer (NK) Cells:** Recognize and kill infected cells by detecting the absence of MHC class I molecules or the presence of stress-induced ligands.
- **Macrophages and Dendritic Cells:** Engulf infected cells and present antigens to T cells, initiating the adaptive response.

2. Adaptive Immune Response:

- **Cytotoxic T Lymphocytes (CTLs):** CD8+ T cells recognize and kill infected cells displaying pathogen-derived peptides on MHC class I molecules.
- **Th1 Response:** CD4+ T helper cells (Th1) release interferon-gamma (IFN-γ) to activate macrophages, enhancing their ability to kill intracellular pathogens.

Immunity to Intracellular Pathogens



Immune response against intracellular pathogens. (A) PRRs of APCs sense pathogens that result in the activation of APCs. (B) This leads to enhanced antigen presentation, upregulation of costimulatory molecules, and secretion of proinflammatory cytokines that promote the activation of T cells. The activated T cells help eliminate pathogens. (C) Engagement of costimulatory molecules on APCs by T cells also results in ‘‘bidirectional signaling’’ that activates APCs to restrict the growth of pathogens.

Immunity to Extracellular Pathogens

Extracellular pathogens (e.g., bacteria like *Streptococcus pneumoniae*, fungi, and parasites like *Helminths*) live outside cells, in tissues or blood, and are directly accessible to antibodies and complement.

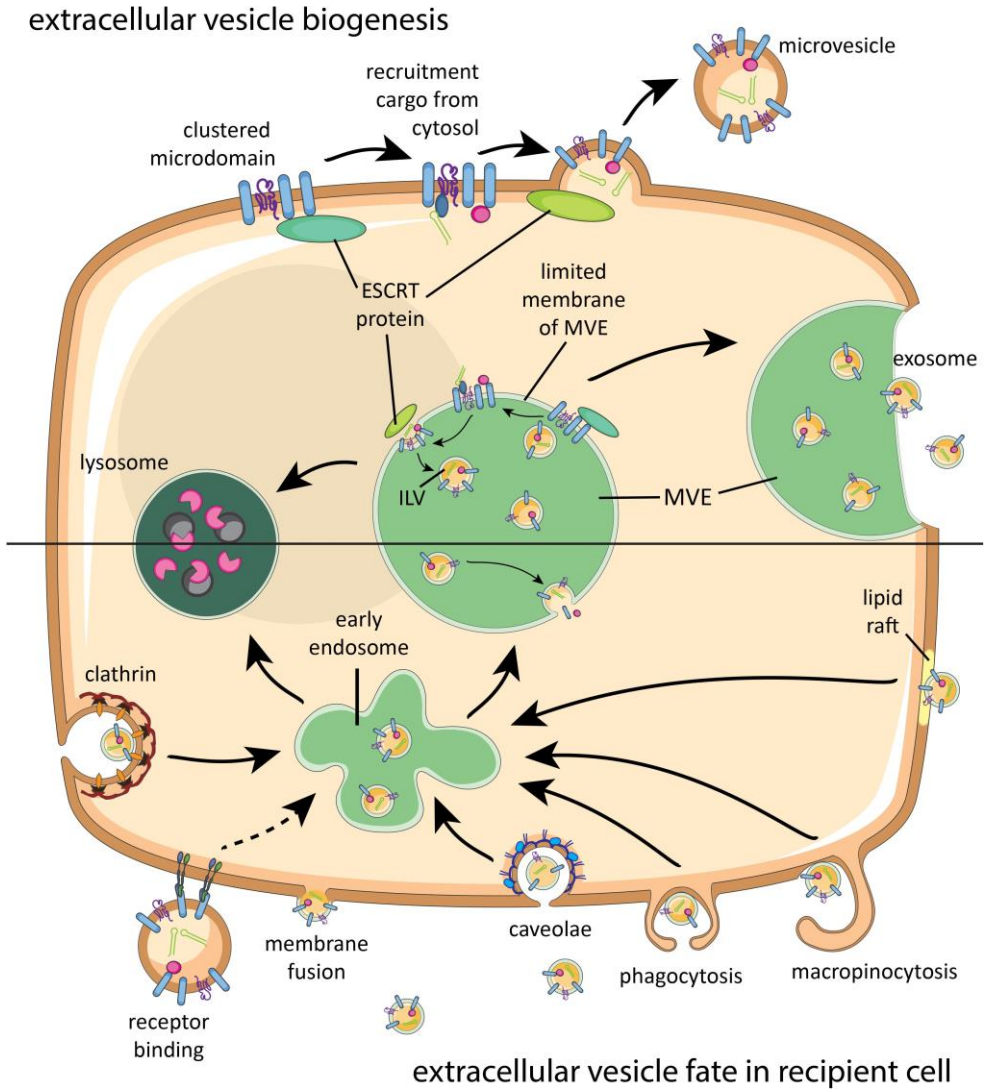
1. Innate Immune Response:

- **Complement System:** Activates through classical, alternative, or lectin pathways, leading to opsonization, inflammation, and lysis of pathogens.
- **Phagocytes:** Neutrophils and macrophages engulf and destroy pathogens.

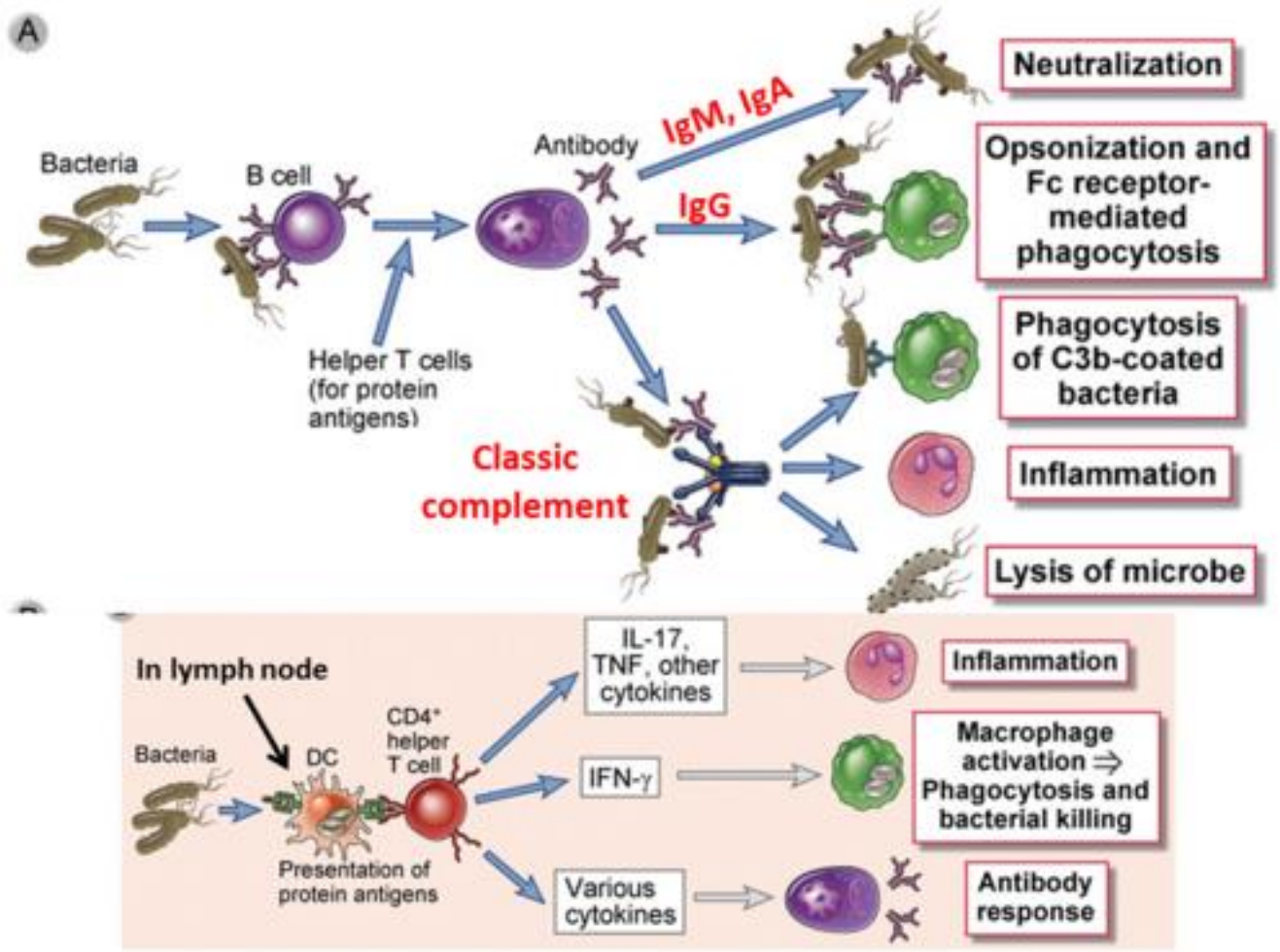
2. Adaptive Immune Response:

- **Humoral Immunity:** B cells produce antibodies that neutralize pathogens, opsonize them for phagocytosis, and activate the complement system.
- **Th2 Response:** CD4+ T helper cells (Th2) promote B cell activation and antibody production, especially IgE, which is involved in responses to parasites and allergic reactions.

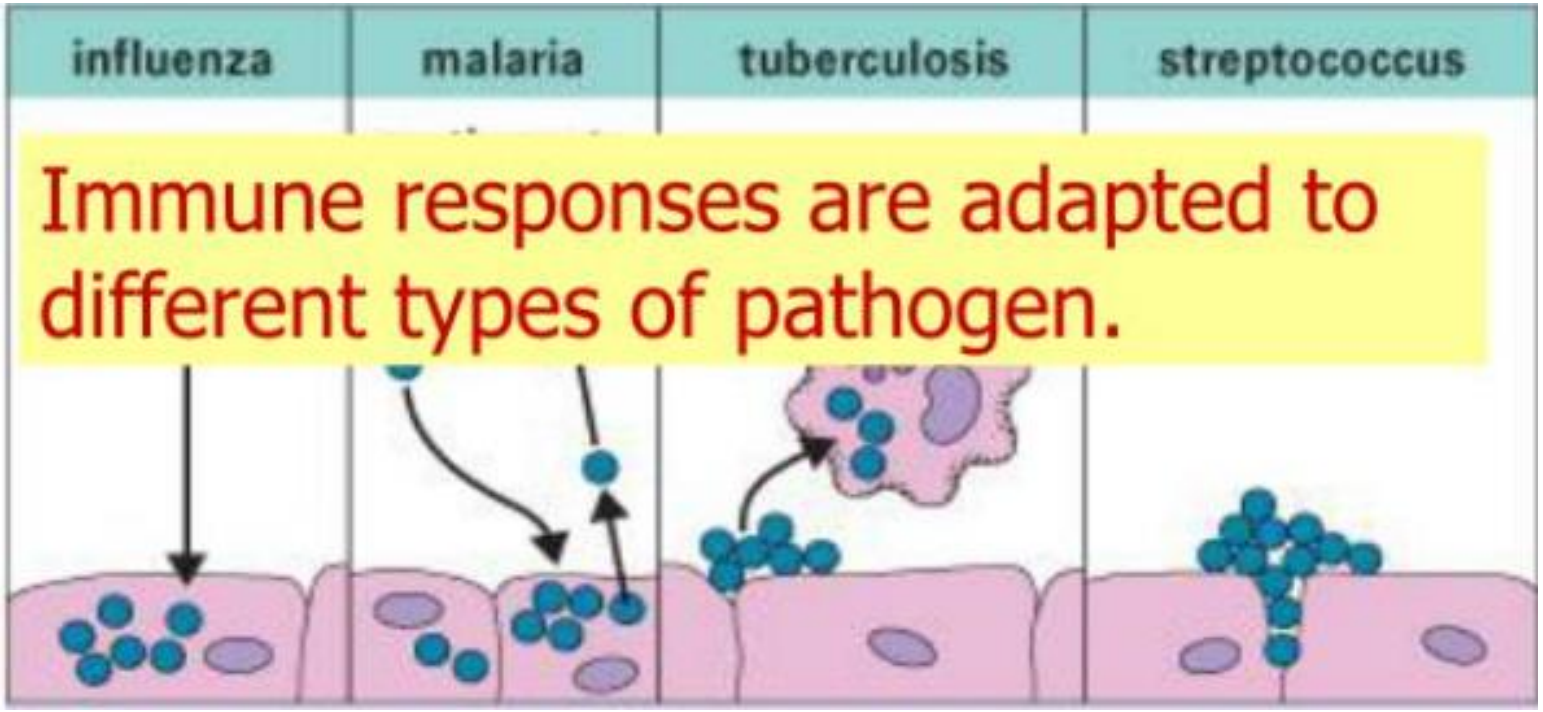
Immunity to Extracellular Pathogens



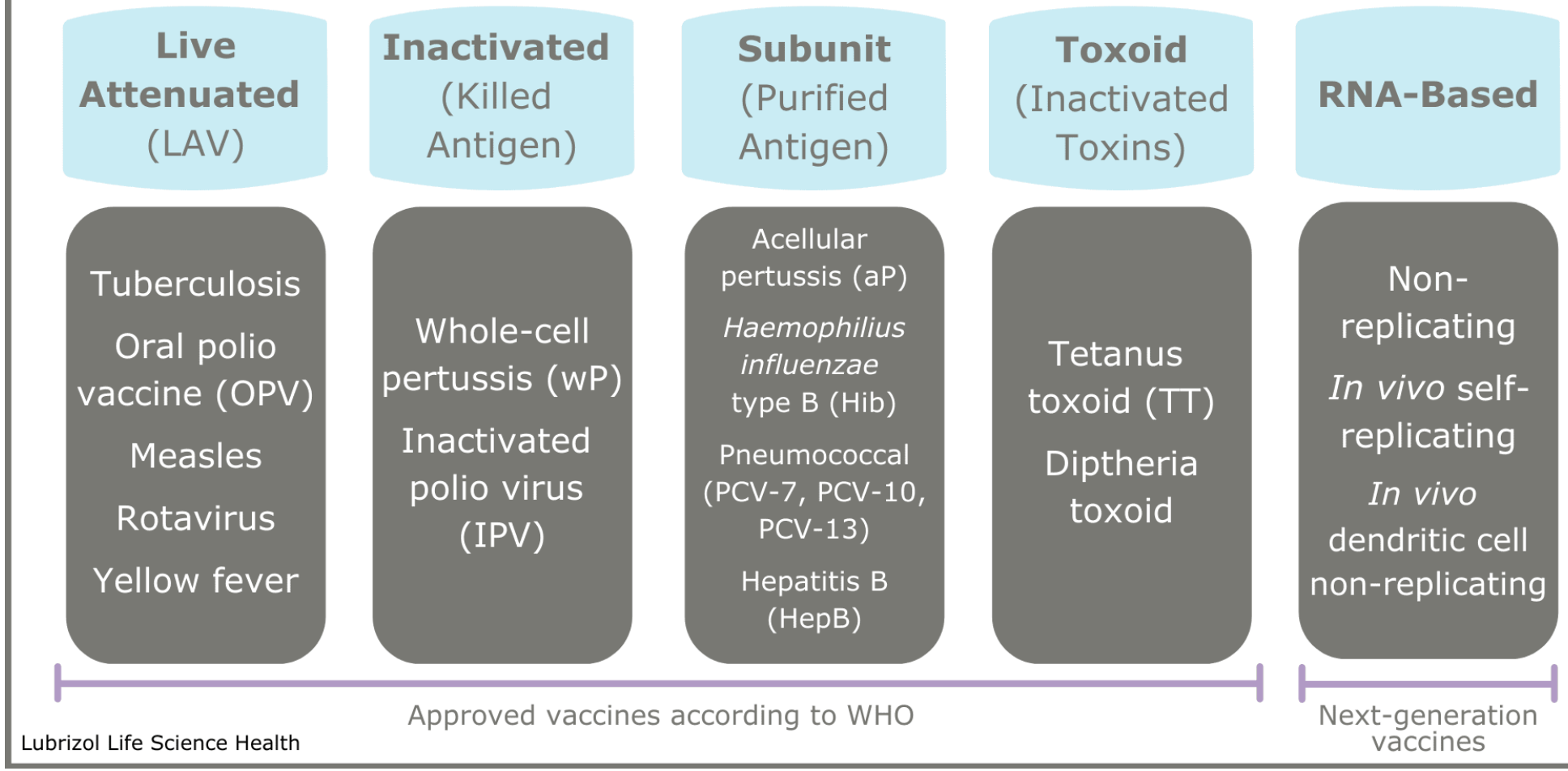
Extracellular and intracellular microbe immunity



Intracellular and extracellular pathogens



Types of Vaccines



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Bystander Damage Caused by the Immune Response to Infection

Bystander damage is a result of the immune response to infection when cells or tissues are injured by the immune reaction.

Bystander effect:

The immune response to infection can expose auto-antigens to the immune response. This can happen when T cells recognize the auto-antigens or when B cells respond to mitogens generated by tissue damage or virus infection.

Bystander immune cytolysis:

This is when an immune response to an antigen destroys autologous blood cells. This can happen when autoantibodies temporarily develop.

Bystander T cell activation:

This is when T cells are activated without recognizing an antigen. This can happen during a viral infection when cytokines like interleukin-18- 18, interleukin-15, and type I interferons induce bystander activation. Bystander- Bystander-activated T cells can impact the immune response and cause host injury.

Inflammatory environment:

The inflammatory environment created by the immune response can damage self-tissue. This can happen when the immune system responds to invading pathogens.

Features

1. Collateral Damage:

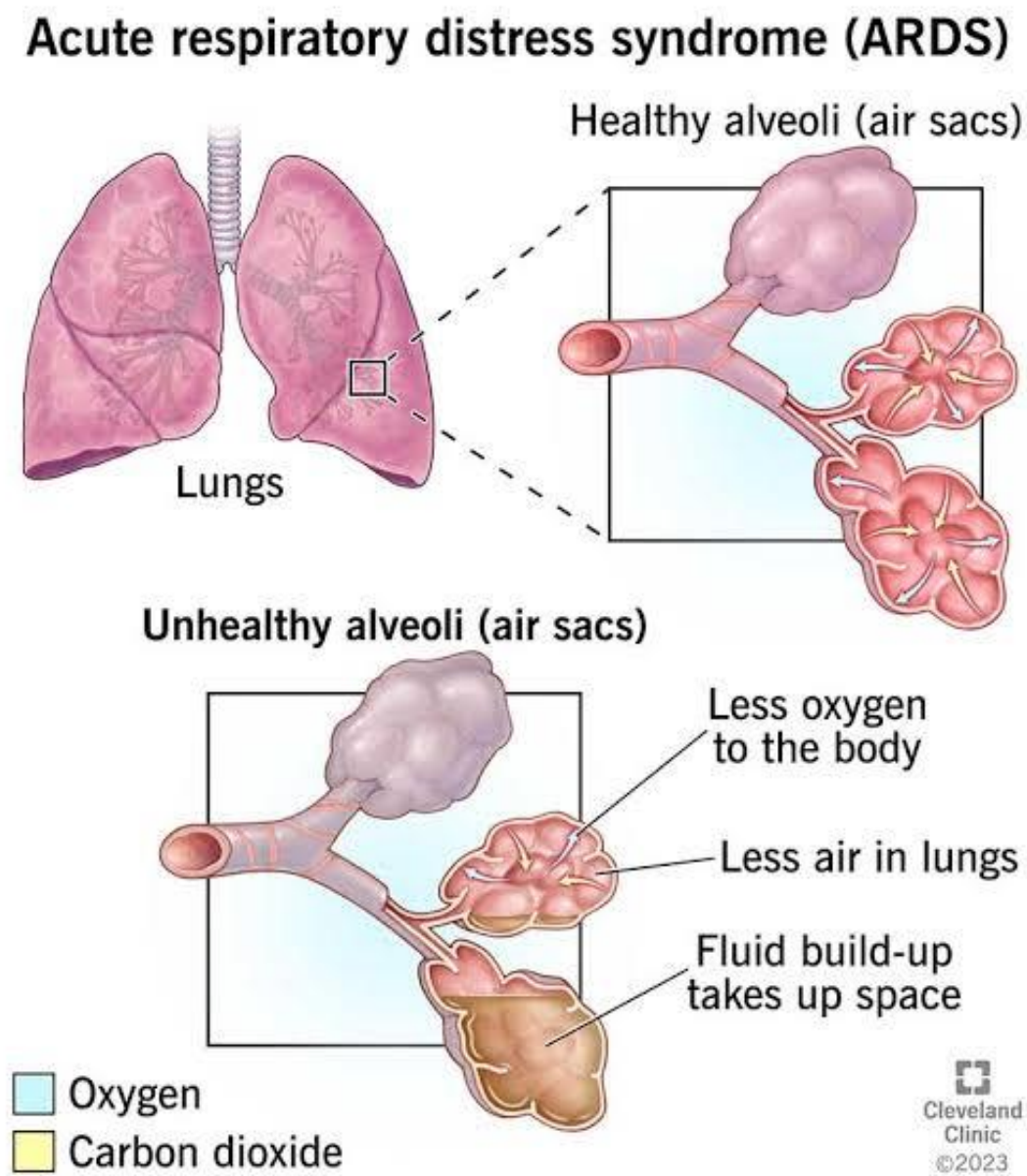
- During infection, the immune response can inadvertently cause damage to host tissues. This "bystander damage" occurs when immune cells and molecules target not only pathogens but also surrounding tissues.

2. Mechanisms of Bystander Damage:

- **Cytokine Storm:** Excessive production of pro-inflammatory cytokines (e.g., IL-1, IL-6, TNF-α) can lead to systemic inflammation and tissue damage.
- **Autoimmunity:** Persistent infection may trigger an autoimmune response where the immune system mistakenly attacks host tissues.
- **Granuloma Formation:** Infections like tuberculosis cause granulomas, where immune cells surround pathogens but also damage lung tissue.

3. Clinical Manifestations:

- **Acute Respiratory Distress Syndrome (ARDS):** Severe lung inflammation caused by overactive immune responses, often seen in viral infections like influenza and COVID-19.
- **Sepsis:** Systemic inflammatory response to infection leading to organ dysfunction and death.


Acute respiratory distress syndrome (ARDS)
Healthy alveoli (air sacs)
Lungs
Unhealthy alveoli (air sacs)
Less oxygen to the body
Less air in lungs
Fluid build-up takes up space
Oxygen
Carbon dioxide
Cleveland Clinic
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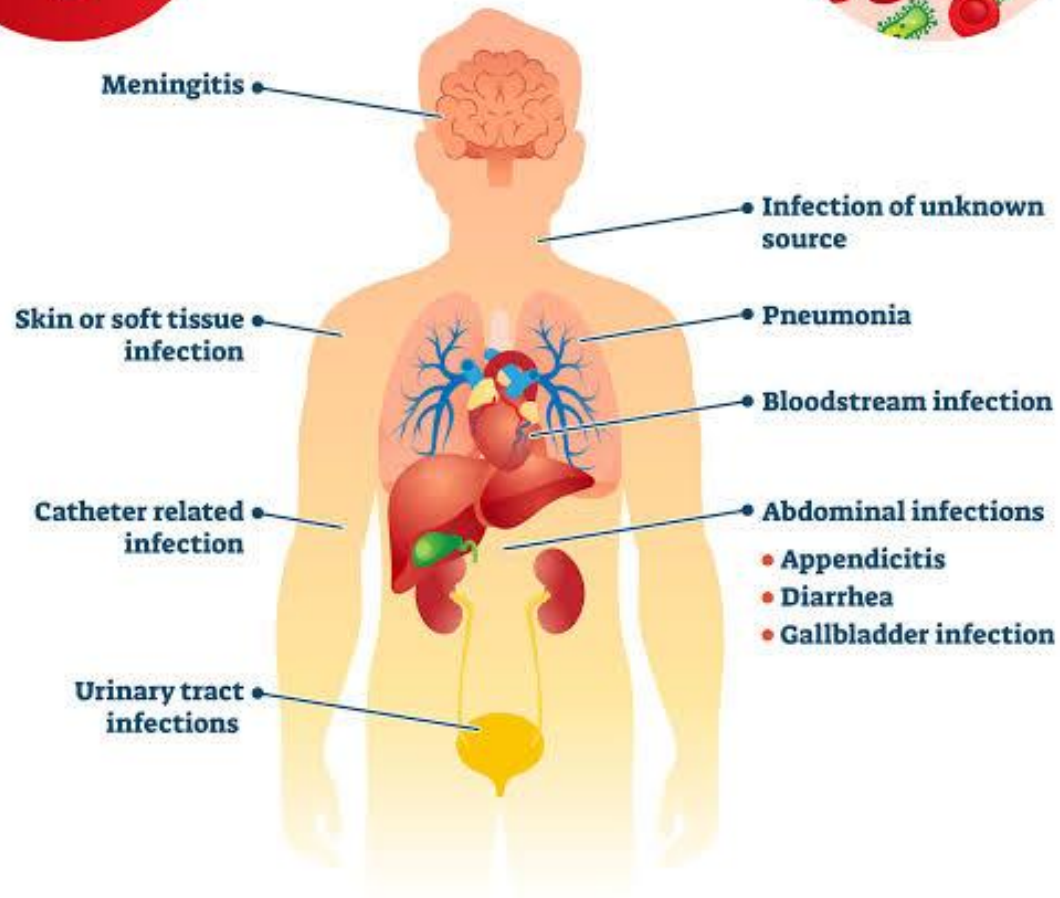
SEPSIS

Sepsis is a potentially life-threatening condition caused by the body's response to an infection



ACKNOWLEDGEMENT

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- Thanks are due to all the original contributors and entities whose pictures were used to create this presentation.