

Immune Mechanisms in Response to Extracellular Pathogens

Sequential overview of innate and adaptive responses leading to pathogen clearance.

Entry and Recognition (Innate Phase)

- Pathogen enters via breaches in skin or mucosa.
- PRRs on epithelial cells, macrophages, dendritic cells detect PAMPs (e.g., LPS, peptidoglycan, β -glucans).
- Inflammatory cytokines (IL-1, IL-6, TNF- α) and chemokines are released.
- Results in recruitment of immune cells and local inflammation.

Complement System Activation

- Triggered by microbial surfaces or antibody binding.
- Pathways:
 - Alternative: spontaneous C3b deposition.
 - Lectin: mannose-binding lectin recognizes microbial carbohydrates.
 - Classical: antibody-antigen complexes.
- Functions:
 - Opsonization (C3b)
 - Chemotaxis (C5a)
 - Lysis (MAC: C5b–C9)

Recruitment of Inflammatory Cells

- Neutrophils are first to arrive; perform phagocytosis and degranulation.
- Macrophages follow to engulf opsonized microbes.
- Production of ROS, NO, and proteolytic enzymes.
- Cytokines (IL-1, TNF- α) increase vascular permeability; IL-8 recruits more neutrophils

Antigen Presentation and T Cell Activation

- Dendritic cells ingest pathogen and migrate to lymph nodes.
- Antigen presented on MHC class II to naïve CD4+ T cells.
- Co-stimulation (CD80/86 – CD28) and cytokine environment guide differentiation.

CD4+ T Helper Cell Polarization

- Th1: IFN- γ activates macrophages for intracellular killing.
- Th2: IL-4, IL-5 promote B-cell class switching to IgE; activate eosinophils.
- Th17: IL-17, IL-22 recruit neutrophils and strengthen mucosal barriers.

B Cell Activation and Antibody Production

- B cells recognize native antigen via surface Ig.
- With T cell help (CD40–CD40L and cytokines), they undergo:
 - Class switching
 - Affinity maturation
- Plasma cells secrete antibodies:
 - IgM (early, complement activation)
 - IgG (opsonization, neutralization)
 - IgA (mucosal defense)
 - IgE (parasite defense)

Antibody-Mediated Effector Functions

- Neutralization: Blocks pathogen binding or toxins.
- Opsonization: IgG enhances phagocytosis via Fc γ receptors.
- Complement activation: IgM/IgG initiate classical pathway.
- ADCC: NK cells kill antibody-coated targets.

Resolution of Inflammation

- Anti-inflammatory cytokines (IL-10, TGF- β) suppress responses.
- Apoptotic neutrophils are cleared by macrophages (efferocytosis).
- Tissue repair and restoration of homeostasis.

Immunological Memory

- Memory B and T cells persist after clearance.
- Provide rapid, robust response upon re- exposure.
- Basis for long-term immunity and vaccination.

Summary Table

Phase	Major Players	Mechanisms	Outcome
Innate	Complement, Neutrophils, Macrophages	Recognition, opsonization, phagocytosis	Initial control
Adaptive Activation	Dendritic cells, CD4+ T cells	Antigen presentation, cytokine signaling	Immune coordination
Effector	Th cells, B cells, Antibodies	Neutralization, opsonization, complement activation	Pathogen clearance
Resolution	Regulatory cytokines, macrophages	Inflammation control, tissue repair	Homeostasis
Memory	Memory B and T cells	Rapid recall response	Long-term protection

Key Takeaways

- Extracellular pathogens mainly evoke humoral and innate defenses.
- Complement and phagocytes provide early control.
- CD4+ T helper cells orchestrate adaptive immunity.
- Antibodies neutralize, opsonize, and activate complement.
- Memory formation ensures future protection.