



iv. Natural and Acquired immunity, cell-mediated immunity and toxicity and cytokines

Immunity refers to the body's protective strategies against infections or abnormal cells. It is broadly segmented into **natural (innate)** vs. **acquired (adaptive)** immunity, with **cell-mediated** mechanisms playing a crucial role in eliminating intracellular pathogens and malignant cells. **Cytokines**, as signaling molecules, orchestrate immune cell communication and direct inflammatory responses. Below is a comprehensive discussion on each aspect, connecting modern immunological details with occasional Ayurvedic correlates where relevant.

Natural (Innate) vs. Acquired (Adaptive) Immunity

Natural or Innate Immunity

- Definition**
 - The **first-line, non-specific** defense present at birth, unaffected by prior exposure to pathogens.
 - Components: **physical barriers** (skin, mucous membranes), **physiological** (acidic pH in stomach), **cellular** (neutrophils, macrophages, NK cells), **soluble factors** (complement, acute-phase proteins).
- Key Features**
 - Immediate response:** Reacts within minutes/hours, recognizes **PAMPs** (Pathogen-Associated Molecular Patterns) using **PRRs** (Pattern Recognition Receptors).
 - No memory:** Repeated infections with the same microbe do not significantly enhance innate reaction.
 - Limited specificity:** Innate cells and molecules target broad microbial signatures.
- Ayurvedic Corollary**
 - Concept of *vyādhikṣamatva* (natural resistance) including external defenses (skin, secretions) and doṣa-balancing approach.
 - Examples: Consistent daily routine (*dinacharyā*) to keep kapha in check, ensuring robust natural defense.

Acquired or Adaptive Immunity

- Definition**
 - Antigen-specific** immunity developed after exposure to pathogens or via immunization.
 - Divided into **humoral** (B-cell/antibody-mediated) and **cell-mediated** (T-cell mediated) arms.
- Key Features**
 - Specificity:** Receptors (TCR, BCR) tailored to unique epitopes.
 - Memory:** Reinfections produce faster, more robust secondary responses.
 - Diversity:** Vast repertoire from somatic recombination (VDJ or VJ gene rearrangements).
- Sub-Types**
 - Active immunity:** Achieved by natural infection or vaccination (long-lasting).
 - Passive immunity:** Transfer of IgG across placenta, colostrum (breast milk), or administered immunoglobulins (short-lived, no memory).

Cell-Mediated Immunity (CMI)

Overview

- Definition**
 - The adaptive immune response is primarily driven by **T lymphocytes** (CD4+, CD8+, other subsets), orchestrating the direct **destruction** of infected or altered cells and regulating other immune components.
- Principal Effectors**
 - CD8+ Cytotoxic T Cells (CTLs):** Kill virally infected or tumor cells by releasing perforin/granzymes or inducing Fas-mediated apoptosis.
 - CD4+ T Helper Cells:** Secrete cytokines to activate macrophages (Th1 response), help B cells produce antibodies (Th2), or modulate responses (Treg, Th17).
 - NK Cells:** Innate-like lymphocytes bridging innate and adaptive immunity, attack cells with downregulated MHC I.

Mechanisms and Relevance

- 1. Antigen Presentation**
 - T cells recognize peptides in **MHC** context (Class I for CD8+, Class II for CD4+).
 - APCs (dendritic cells, macrophages) are essential for T-cell priming.
- 2. Elimination of Intracellular Pathogens**
 - Viruses replicating inside cytoplasm or bacteria like *Mycobacterium tuberculosis* within phagosomes require T-cell (CD4+ Th1) activation of macrophages or direct cytotoxic approach from CD8+ T cells.
- 3. Translational Impact**
 - Vaccines harness cell-mediated immunity for robust, long-term protection (e.g., BCG for TB, cellular immunity crucial).
 - Immunotherapies (CAR T-cells) exploit T-cell specificity against tumors.

Cytokines

Definition and Classification

- 1. Definition**
 - **Cytokines** are low-molecular-weight proteins/peptides produced by immune cells (and others) that mediate **communication, growth, differentiation, and effector** functions.
- 2. Major Families**
 - **Interleukins (IL)**: IL-1, IL-2, IL-6, etc., regulating leukocyte interactions.
 - **Interferons (IFN)**: IFN- α , IFN- β (type I), IFN- γ (type II) with antiviral, immunoregulatory roles.
 - **Tumor Necrosis Factors (TNFs)**: E.g., TNF- α involved in inflammation, cell death pathways.
 - **Chemokines**: Direct leukocyte migration (e.g., IL-8, RANTES).
 - **Colony-Stimulating Factors (CSFs)**: Stimulate marrow production of granulocytes, macrophages, etc.

Functions and Signaling

- 1. Immune Regulation**
 - Orchestrate T/B cell proliferation (IL-2 for T cells), macrophage activation (IFN- γ), or neutrophil mobilization (G-CSF).
 - Anti-inflammatory (IL-10, TGF- β) vs. pro-inflammatory (TNF- α , IL-1 β).
- 2. Mechanisms**
 - Bind specific cytokine receptors, triggering JAK-STAT or other signaling cascades.
 - High specificity, short half-lives, often function in local microenvironments (paracrine).
- 3. Clinical Applications**
 - Cytokine therapy (e.g., IFN- α for some cancers, IL-2 in immunotherapy).
 - Cytokine inhibitors (anti-TNF for rheumatoid arthritis, IL-6 inhibitors) in autoimmune or inflammatory diseases.

Integrated Understanding and Clinical Implications

- 1. Immune Responses**
 - **Natural** (innate) immunity confers rapid, broad protection. **Acquired** (adaptive) immunity invests in specificity and memory.
 - **Cell-mediated** T-cell functions are crucial against intracellular microbes and malignant cells, while **B cells** and antibodies address extracellular pathogens.
- 2. Cytokine Modulation**
 - Dysregulated cytokine production can cause hyperinflammatory states (cytokine storm) or immunodeficiency.
 - Therapeutic manipulation of cytokines or their receptors is central to treating autoimmunity (e.g., RA, IBD) or boosting anticancer immunity.
- 3. Ayurvedic Correlations**
 - While not referencing “cytokines,” Ayurveda acknowledges the concept of “*agni*” and balanced “*ojas*” for robust immune functioning.



- Approaches to reduce “*amavisha*” (toxic buildup) or *doṣa* aggravation might parallel controlling excessive inflammatory cytokines.

Future Prospects

1. Personalized Immunity

- Incorporating genetic screenings (HLA or TCR repertoire) plus *doṣa*-based constitutional analysis might refine preventive or therapeutic strategies.

2. Cytokine-Based Therapies

- Emerging biologics (IL-17 inhibitors, IL-23 blockers) for psoriasis, advanced cytokine gene therapies, or targeted nanomedicine.

3. Holistic Integration

- Cross-disciplinary research bridging advanced immunology with Ayurveda’s immunomodulatory approaches (herbal *rasāyanas*, stress management) for synergy in chronic inflammatory or autoimmune diseases.

Conclusion

Natural and acquired immunity constitute the **pillars** of host defense, with innate defenses providing **immediate** coverage and adaptive systems ensuring **specific, long-term** protection. **Cell-mediated immunity** (T-cell-driven) is indispensable for tackling intracellular pathogens and tumor cells, while **cytokines** serve as the **communication hub** across immune cells—fine-tuning responses to pathogens or self-antigens. Recognizing these fundamentals is key to **immunodiagnostics, vaccine design, immunotherapies**, and an integrative approach weaving modern immunology with classical prophylactic or rejuvenative principles.