WHERE CLASSICAL WISDOM MEETS INTELLIGENT LEARNING

iii. Antigen antibody reactions

iii. Antigen antibody reactions, Innate immune cells, Pathogen-associated molecular pattern (PAMP), Pathogen recognition receptors (PRR) and Complement system

Immunity relies on (1) specific recognition by antigen-antibody (adaptive) mechanisms, (2) innate immune cells rapidly neutralizing threats, (3) pathogen pattern recognition via PAMPs binding to PRRs, and (4) the complement cascade bridging innate and adaptive responses. Below is an in-depth discussion of each component, weaving modern immunological science with occasional Ayurvedic parallels (where relevant).

Antigen-Antibody Reactions

Fundamental Principles

1. Antigen Definition

 Molecules (proteins, polysaccharides) recognized by B or T cells. B cells bind native antigens directly, forming antigen-antibody complexes.

2. Antibody Structure

- o Y-shaped immunoglobulins with variable (V) regions forming the antigen-binding site.
- Ig classes (IgG, IgM, IgA, IgE, IgD) differ in structure and effector functions (complement activation, opsonization, etc.).

Binding and Biophysics

1. Non-Covalent Interactions

- o Electrostatic, hydrogen bonding, hydrophobic, and Van der Waals forces drive antigen-antibody specificity.
- High-affinity binding → stable immune complexes, enabling opsonization or neutralization.

2. Valency and Avidity

 Multiple antigen-binding sites (e.g., IgM pentamer) increase avidity, potentially compensating for lower affinity.

Examples of Antigen-Antibody Outcomes

1. Agglutination

o Clumping of cells/particles coated with antigen by multivalent antibodies, facilitating phagocytic clearance.

2. Precipitation

Soluble antigens forming insoluble complexes, removed by macrophages.

3. Neutralization

• Prevent pathogens/toxins from binding host receptors.

4. Complement Activation

Classical pathway triggered by IgG/IgM-antigen complexes.

Innate Immune Cells

Key Innate Cell Types

1. Neutrophils

 Rapid responders, specialized in phagocytosing and killing bacteria/fungi, forming NETs (neutrophil extracellular traps).

2. Macrophages / Monocytes

o Tissue-resident or recruited, phagocytose pathogens, produce cytokines, present antigens to T cells.

3. Dendritic Cells

• Professional antigen-presenting cells (APCs), bridging innate and adaptive immunity. Capture antigens in periphery, migrate to lymph nodes, prime T cells.

4. Natural Killer (NK) Cells

 $\circ~$ Lymphocytes that kill virus-infected or tumor cells lacking MHC I expression.

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5. Eosinophils / Basophils

o Combat parasitic infections, mediate allergic inflammation.

6. Mast Cells

• Reside in tissues, release histamine, key in anaphylaxis/allergies.

Innate Immunity Hallmarks

- Rapid Response: Does not require prior sensitization.
- Broad Recognition: Via pattern recognition receptors (PRRs) that detect generic microbial signatures (PAMPs).

PAMP and PRR (Pathogen-Associated Molecular Patterns and Pattern Recognition Receptors)

PAMPs

1 Definition

• **Conserved** molecular motifs found on groups of microbes, e.g., LPS (lipopolysaccharide) in Gram-negative bacteria, peptidoglycan in Gram-positive, dsRNA in viruses.

2. Function

• Alert the innate immune system to "non-self" invasion, prompting rapid inflammatory or phagocytic responses.

PRRs

1. Receptors

- Pattern Recognition Receptors on innate cells (macrophages, dendritic cells, neutrophils) that bind PAMPs.
- Examples: Toll-like Receptors (TLRs), NOD-like receptors (NLRs), RIG-I-like receptors (RLRs), C-type lectin receptors.

2. Signaling and Immune Activation

- PRR ligation triggers transcription factors (NF-κB, IRFs) that upregulate cytokines, chemokines, costimulatory molecules.
- o Facilitates recruitment of additional immune cells, bridging to adaptive immunity.

Clinical/Pharmaceutical Relevance

- TLR agonists can **boost vaccine efficacy** (adjuvants).
- Targeting PAMP-PRR pathways can modulate inflammation in autoimmune disease or reduce sepsis severity.

Complement System

Overview

1. Definition

∘ ~30 plasma proteins forming a cascade to opsonize, lyse pathogens, and recruit inflammatory cells.

2. Pathways

- Classical: Triggered by antigen-antibody complexes (IgG, IgM).
- o Alternative: Spontaneous hydrolysis of C3, stabilized on pathogen surfaces lacking complement inhibitors.
- \circ **Lectin**: Mannose-binding lectin (MBL) recognizes mannose residues on microbes \rightarrow complement activation.

Effector Functions

1. Opsonization (C3b)

 Coats pathogens, facilitating phagocytosis by complement receptor-bearing cells (macrophages, neutrophils).

2. Chemotaxis (C5a)

 $\circ\,$ A potent chemoattractant, draws neutrophils/monocytes to infection sites.

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3. Membrane Attack Complex (MAC: C5b-C9)

o Creates pores in pathogen membranes → cell lysis, especially effective against Gram-negative bacteria.

Regulation and Pathology

1. Regulatory Proteins

• Factor H, Factor I, C1-inhibitor prevent over-activation or host cell damage.

2. Deficiencies

- C3 deficiency → severe recurrent infections.
- C1 inhibitor deficiency → hereditary angioedema.

3. Clinical Utility

o Complement levels (CH50, C3, C4) used to diagnose autoimmune conditions (SLE) or immunodeficiencies.

Integrative Insights and Ayurvedic Analogies

1. **İmmune Surakshā** (Protection)

- Ayurveda posits *vyādhikṣamatva* (immunity) reliant on balanced doṣas, robust digestion (agni), and mental well-being.
- The interplay of PAMP recognition or complement cascades can be analogized to the body's protective *tejas* or "intelligence" scanning for "foreignness."

2. Phytotherapeutics

• Some Ayurvedic herbs (e.g., *Guduchi*, *Tulsi*) may modulate innate immunity or complement function, though bridging trials remain ongoing.

Conclusion

The immune system's ability to detect pathogens and mount appropriate responses relies on:

- 1. Antigen-antibody interactions specifying humoral immunity.
- 2. Innate immune cells (macrophages, neutrophils, dendritic cells, NK cells) orchestrating immediate defenses.
- 3. PAMP-PRR recognition bridging non-self detection and robust inflammatory or phagocytic activity.
- 4. **Complement** acting as a potent effector mechanism—opsonizing, recruiting, and lysing pathogens.

Interdisciplinary synergy of **biophysical** understanding (antigen-antibody binding), **molecular** immunology (PRRs, complement cascade), and classical prophylaxis or rasāyanas in Ayurveda can yield **comprehensive** strategies to combat infections and enhance **immunological resilience**—underpinning both fundamental research and translational therapies.

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