Ch 24: The Immune System

3 Major Functions

1. Protection from disease causing invaders (= ?)
2. Removal of dead /damaged tissues & cells
3. Recognition & removal of abnormal cells

Immunologic “mistakes:”
1. Incorrect responses: autoimmunity
2. Overactive responses: allergy
3. Lack of response: immune deficiency

History: First effective immunization

Developed by
John Gallagher, MS, DVM
Terminology

- Pathogen, allergen
- Antigen, antigenic determinant
- Antibody (Ab), immuno-globulin, γ-globulin
- Allergen
- Opsonins: proteins that coat pathogens that make them targets for immune cells
  - May be complement, Ab, others
- Nonspecific (innate) vs. specific (acquired) Immunity
- Active vs. passive Immunity
- Cellular vs. humoral Immunity
Pathogens:

- Bacteria (Staph, Strep)
- Viruses (Herpes)
- Fungi, yeasts (Coccidioidomycosis)
- Parasites (malaria, trypanosomiasis)
- Toxins (EtOH)
Bacteria

- True cells
  - Cell wall (usually)
  - Capsule
- Selfreplicate
  - Most can reproduce outside host cells
- Susceptible to AB

Escherichia coli
Viruses

- Not a true cell
  - DNA or RNA with capsule of protein
- Intracellular replication only
  - Grow in tissue culture
- Not susceptible to AB
  - There are a few antiviral drugs

HIV (see Emerging Concept, p 779)
The Immune Response, introduction

• If physical and chemical barriers fail, the Immune System responds with detection, identification, destruction.
  – Sometimes overwhelmed
• Antibodies (Ab) recognize and then bind to antigens (Ag)
• Lots of cytokine communication
The Immune Response: Keep pathogens out & destroy those that break defense

1. **Innate (= nonspecific):**
   - Present at Birth
   - Nonspecific
   - Hinders pathogen and toxin entry and dispersion through body.
     - E.g. skin.
   - Strengthens specific immune system

2. **Acquired (= specific):**
   - Inactivation of a specific pathogen
   - Requires previous exposure
   - Humoral vs. CMI
Anatomy of Immune System

Lymph system + Immune cells
6 basic groups of Leukocytes:

1. Eosinophils
2. Basophils (blood); Mast cells (tissue)
3. Neutrophils
4. Monocytes (blood), macrophages (tissue)
5. Dendritic cells
6. Lymphocytes (plasma, helper, cytotoxic & NK)
Antigen Presenting Cells (APCs)

- Note foreign protein on their surfaces
- Macrophages, dendritic cells, lymphocytes

[Diagram showing the process of antigen presentation by macrophages.]
1) Innate Immunity – Barriers, Phagocytosis & Inflammation

- Physical & chemical **barriers keep pathogens out**
  - skin, mm – stomach acid, lysozyme

- **Phagocytosis:** Patrolling & stationary leukocytes (macrophages, neutrophils, NK cells) attack and destroy pathogens/foreign molecules nonspecifically
  - Phagocytes may be aided by opsonins (Usually an Ab)
  - NK cells use antiviral interferons

- **Inflammatory response** initiated via secretion of cytokines (e.g. histamine)

![Image](https://via.placeholder.com/150)

Fig 24-6
Inflammation

- An innate protective mechanism activated by cytokines in response to tissue damage
- Acute Phase: Release of several proteins
  - Prevent further damage
  - Mast Cell degranulation
- Histamine (from mast cells) is vasodilator
- Other cytokines:
  - Interleukin: for MP
  - Bradykinin: pain mediation
  - Complement: Damages invaders

Uterine inflammation
Inflammatory Reaction

Histamine released by mast cells dilates capillaries to bring blood to the scene.

Tissue cells release bradykinins, which cause free nerve endings to alert the nervous system.

Neutrophils and monocytes squeeze through the capillary wall and begin to phagocytize microbes.

Monocytes become aggressive macrophages, which quickly phagocytize microbes and stimulate the immune response.
Some factors in Inflammation

• Acute Phase Proteins
  • Prevent further damage
• Histamine
  • Present in mast cells
  • Vasodilation
• Interleukins
• Cytokines
• Complement
  • Cascade of proteins
  • Chemotaxins, cytokines, etc.
2) Acquired (Specific) Immunity p 787

- Antigen (pathogen) specific
- Overlaps with innate immunity
- 1° cell type involved: lymphocyte
- Is systemic (= whole body involved)
- Has memory
- Two branches:
  - Humoral
  - Cell-mediated
**Active vs. Passive Immunity**

**Active:** protection via introduction of antigen into responsive host  
- naturally acquired via infection  
- “unnaturally” acquired via ?

**Passive:** protection via transfer of antibodies or immune cells into non-immune host  
- Naturally: fetus receives mother’s antibodies via placenta  
- “unnaturally” via injection of immune serum after exposure  
  *(snake bite, Rh- mother with Rh+ child)*
2 Branches of Acquired Immune System:

1. Humoral or antibody mediated (B-cells)
2. Cellular or cell mediated (T-cells)

Three major types of lymphocytes: B, T & NK
Lymphocytes
Antigen-Specific Responses

**B lymphocytes** activated $\Rightarrow$ become:
- **Plasma cells**: antibodies – attack that antigen
- **Memory cells**: $2^{\text{nd}}$ immune response to same antigen

**T lymphocytes** activated $\Rightarrow$ direct attack

NK (Natural Killer) cells attack virus-infected cells and tumor cells
1° cell: Naive Lymphocyte

Compare to Fig 24-10

Memory cells  Effector (plasma) cells
Immune Memory

- From B-Lymphocyte clones
  - Plasma Cells manufacture Ab
  - Memory Cells wait for the next exposure
Antibodies = Immunoglobulins = Ig = $\gamma$ globulins (origin of name)

Heterogenous group of molecules: 5 subclasses

Fig 24-12
5 subclasses of Igs:

1. IgG: main Ab (75%) in serum; + main Ab during 2\textsuperscript{o} response
2. IgA: main Ab is external secretions
3. IgE: main Ab in allergic reactions
4. IgM: Ab on virgin B-cells; + main Ab during 1\textsuperscript{o} response
5. IgD: Ab on virgin B-cells
2° immune response: stronger & more rapid

Importance of Immunizations!!

Compare to Fig 24–11
Antibody = “work against foreign body”

1° Ab function: bind Ag to B lymphocyte and initiate production of additional antibodies (usually IgM)

Other Ab functions: bind to pathogens and target them for destruction (via several different mechanisms!)
Antibody Functions - Mechanisms of Antibody Action
N.B. All extracellular!

Fig 24-13 p 791

- Activates complement
- Triggers mast cell degranulation
- Activates antibody-dependent cellular activity
- Causes antigen clumping and inactivation of bacterial toxins
- Antigen binds to antibody
- Antibody binding site
- Activates B lymphocytes
- Memory cells
- Plasma cells
- Secrete antibodies
- Activates opsonins
- Bacterial toxins
- Enhanced phagocytosis

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Review:

**cellular** vs. **humoral immunity**

**T lymphocytes**

1. cytotoxic (killer)
2. helper
3. Memory
4. Direct attack of infected cells necessary

**B lymphocytes**

1. Become plasma cells
2. memory cells
**T cells - CTLs**

Have specific receptors on cell membrane (TCR)

TCR cannot bind free Ag. Ag must be presented by APC

Ag presentation together with APC form the **Major Histocompatibility Complex (MHC)**

*Fig 24-15*
Importance of MHC molecules

- **MHC class I**: found on surface of all nucleated cells – used to present peptides from *intracellular* invaders
  - E.g., viruses
  - Cytotoxic T-cells kill the cell

- **MHC class II**: found on surface of macrophages, dendritic cells, and B-cells
  - The APC

- High number of MHC alleles in population (Transplant rejection in case of incompatible MHC)
Cytotoxic T-lymphocytes (CTLs)

Attack and destroy cells with MHC I – Ag complex

2 mechanisms of destruction:
- Perforins and granzymes
- Fas (death) receptor activation

Apoptosis
Immune Response Pathways

1) Defense against extracellular bacteria
2) Defense against Viral Infections
3) Allergic Response
4) Organ & Tissue Transplants
1) Defense against extracellular bacteria:

- Complement activation
  - Mast cell degranulation and inflammation
  - Chemotaxins
  - Opsonins
- Phagocytes ingest bacteria
  - Enhanced by opsonization
- Inflammation $\Rightarrow$ recruitment of phagocytes, B & T lymphocytes
- Acquired response $\Rightarrow$ antibodies (opsonins and neutralization), CTLs ... if needed
2) Defense against Viral Infections

Remember: virus replication is intracellular and thus not exposed to circulating Ab

1. Circulating antibodies inactivate or target extracellular virus (opsonization, neutralization)

2. Intracellular defense mechanisms needed once virus has entered cell: CTL major defender (also some NK cells)

3. Activated Mφ ⇒ inflammatory cytokines; α-interferons (induce host cells to produce antiviral proteins)
3) Allergic Response

Inflammatory immune responses to non-pathogenic antigens

Symptoms range from mild tissue damage to fatal

1. **Immediate Hypersensitivity (ITH):** Hay fever, cat allergies . . . Ab mediated (IgE!), may take minutes

2. **Delayed Hypersensitivity (DTH):** poison oak . . . due to T-cell abnormality, may take days
Allergies cont.

- What is an allergen?
  - May be almost anything: pollen, metals, organic or inorganic, etc., etc.

- Strong genetic component

- Allergies in response to ingestion, inhalation, injection, skin contact

- Sensitization phase (= 1° immune response) followed by 2° immune response on subsequent exposures
Anaphylaxis

Most severe IgE mediated allergic reaction

Massive histamine release within minutes

⇒ Hives, bronchoconstriction and widespread vasodilation
⇒ shock
4) Organ & Tissue Transplants

- MHC (= HLA (Human leukocyte Ag)) are the 1º tissue antigens
  - If donor and recipient HLA match, less rejection
- Establishment of “self tolerance” during T cell development
  - Failure = Autoimmunity
- ABO (and Rh) blood typing (AA, AO, BB, BO, AB, OO)
- Blood transfusion problems due to antibodies in plasma → Transfusion reaction with hemolysis and possible kidney damage
Autoimmune diseases

- Immune surveillance recognizes abnormal cells
  - Cancer cells
- Important function of IS: Self-tolerance through clonal deletion
- Failure of self tolerance: autoimmunity

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>ANTIBODIES PRODUCED AGAINST</th>
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<tbody>
<tr>
<td>Graves’ disease (hyperthyroidism)</td>
<td>Thyroid-stimulating hormone receptor on the thyroid cells</td>
</tr>
<tr>
<td>Insulin-dependent diabetes mellitus</td>
<td>Pancreatic beta cell antigens</td>
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<tr>
<td>Multiple sclerosis</td>
<td>Myelin of CNS neurons</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>Acetylcholine receptor of motor endplate</td>
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Immunology is a fast-moving area

- PsychoNeuroImmunology Research deals with neuro-endocrine-immune interactions
- Stress alters immune system function