The Immune System

by

Dr. Carmen Rexach
Physiology
Mt San Antonio College
What is the immune system?

- defense system found in vertebrates
- Two categories
  - Nonspecific
  - specific
- provides protection from pathogens and cancer cells
- utilizes a variety of cell types and a variety of responses
- may induce a memory response
Nonspecific (Innate) Immunity

• basic resistance
• consists of anatomic and physiological defense barriers, specialized cells, and inflammation
• does not require specific recognition of the “enemy”
Examples of Innate Immunity

- Intact skin
- Secretions: saliva, lysozyme, sweat
- pH of the stomach
- Mucociliary escalator
- White blood cells
- Inflammatory response
- Interferons
- Complement
Immune System Cells

- **Nonspecific**
  - *Granular white blood cells*
    - neutrophils, basophils, eosinophils
  - **NK cells**
  - *Agranular white blood cells*
    - monocytes, macrophage

- **Specific**
  - B lymphocytes
  - T lymphocytes
Blood cell lineages
Monocytes/Macrophage

- **Monocytes**
  - Circulate in blood
  - Mildly phagocytic
  - Differentiate into macrophage in tissues when stimulated

- **Macrophage**
  - Free and fixed
  - Normal and inflammatory
  - A major link between nonspecific and specific
Neutrophils

- 50-60% of circulating leukocytes
- First line of defense against infectious agents
- First cells on scene in inflammatory response
- Pus
  - Myeloperoxidase and green color

Fig. 8 - Neutrophil
Basophils and Eosinophils

• **Basophils**
  - Smallest circulating granulocyte
  - Allergies and inflammatory response
  - Release histamine + other chemicals

• **Eosinophils**
  - Circulate and reside in tissues
  - Helminth infections and allergic responses
  - Hypersensitivity reactions
Mast cells

- Inflammatory and allergic response
- Stationary in connective tissue
- Contain granules, including histamine
NK cells

- Subset of lymphocytes
- Circulating cells
- Nonspecific cells attack virally infected cells and cancer cells
- Granules contain perforin and granzyme
Inflammatory response

- **Cardinal Signs**
  - Rubor
  - Dolor
  - Tumor
  - Calor

- **Effects**
  - Prevent intruder from spreading farther into body
  - Eliminates cellular debris and pathogens
  - Allows for the repair of damaged tissues
The Inflammatory Response

Blood platelets
Mast cells
Neutrophil
Cytokines signaling path to injury site
Cytokines
Initiate tissue repair
Macrophage
RBC
Blood vessel
Wound
Acute appendicitis
Complement

• Group of more than 20 plasma proteins circulating in an inactive form that can protect by:
  - chemotaxis
  - opsonization
  - activation of inflammation
  - cytolysis = MAC
Complement cascade

- **Classic pathway**
  - Antibody:antigen complexes
  - C reactive protein produced by liver during inflammation activates C1

- **Alternative pathway**
  - Pathogen surfaces
Fever

- Pyrogens secreted by other leukocytes and macrophage
- Resets hypothalamus
  - Increased temperature
  - Liver and spleen sequester zinc and Fe
  - Increased metabolic rate = increased body repair
Specific (Acquired) Immunity

- Specific recognition and selective elimination of pathogens and molecules
- Cellular and humoral
- May induce memory
- Involves distinction between self/nonself
- Systemic
What are antigens and haptens

- **Antigens** = substances that can elicit an immune response
  - Cell surface markers
  - Foreign antigens
  - Complete
    - Immunogenicity = ability to stimulate immune response
    - Reactivity = ability to react with immune effectors
  - Incomplete
    - **Haptens** = small molecules that cannot elicit an immune response independently, but can when bound to native proteins
    - Allergens are often incomplete
Haptens

Hapten molecules + Carrier molecule → Complete antigen

Copyright © 2004 Pearson Education, Inc., publishing as Benjamin Cummings.
APC's

- **Cell types**
  - Dendritic cells (CT)
  - Langerhans' cells (epidermis)
  - Macrophage
  - B lymphocytes

- **Location**
  - Systemic and localized
  - Ex) Lymph nodes
    - T cells = paracortical area
    - B cells, dendritic cells = germinal centers
Histocompatibility antigens

- Surface antigens found on all cells except RBC’s
- Coded by Chromosome #6
- Specific type determines what will bind
- Must be matched to minimize transplant problems
- HLA in humans, MHC in all animals
Class I vs. Class II MHC

• Class I
  - all cells except RBC’s
  - binds CD8
  - usually intracellular pathogens
    • actively pumped from cytoplasm to ER
    • loaded into binding cleft and expressed on surface

• Class II
  - only on macrophage and B lymphocytes
  - binds CD4
  - extracellular antigens
Innate immunity is critical to adaptive immune response.
Specific immune response

Begins with non-specific response

Macrophage

Invader

Antigen presentation

T

Only recognizes presented antigen

B

Recognizes:
- antigen directly presented
- antigen can also present antigen
T lymphocytes

- Specific cells for specific antigens
- Only recognize presented antigen
- Three types
  - helper T cells ($T_H$)
  - killer T cells ($T_C$)
  - suppressor T cells ($T_S$)
T cell stimulation

Antigen-Presenting Cell (APC)

B7 → "Signal Two"

CD28 → T cell

Histocompatibility molecule peptide

T cell receptor

"Signal One"

One method of the "co-stimulation" needed to activate T cells. If the T cell fails to receive "signal two", it dies by apoptosis. (B7 comes in two forms: B7-1 [CD80] and B7-2 [CD86].)
Clonal Expansion of T cells

The activated T cell increases in size and divides by mitosis. A clone of competent T cells is produced. T cells differentiate, becoming various types of T cells.
B lymphocytes

- Each cell recognizes a specific antigen
- Recognition results in clonal expansion
- Stimulated B lymphocytes become plasma cells
- Produce antibodies specific to antigen
Immunoglobulins (Antibodies)

- Function
  - Primary response
  - Secondary response

- Five types
  - IgM: seen in a primary response
  - IgG: seen in greatest quantities in secondary response
  - IgA: secretory antibody
  - IgE: allergic reactions and parasitic worms
  - IgD: cell surface marker

Generalized structure
Immunoglobulin structure
Active Immunity

• Primary vs. secondary response
• Immunity results from prior exposure to antigen
  - actually get disease
  - clinical immunization
• clonal expansion + memory
Passive immunity

• Direct transfer of antibodies from one animal to another
  - maternal IgA/IgG
    • Transplacental
    • breast milk
  - Erythroblastosis foetalis
    • RhoGAM
      - Serum containing anti-Rh+ antibodies at 28 weeks and 72 hours post partum
      - Causes agglutination of any fetal blood cells, removing them and preventing activation of immune response
      - Must be repeated for all subsequent pregnancies
Clonal selection hypothesis

- Each lymphocyte progenitor gives rise to many lymphocytes during development
- Many that are self-reactive are eliminated early in development = tolerance to self antigens
- Mature lymphocytes blast when they encounter antigen = clonal expansion
- Each clone has the same antigen specificity
Clonal selection
Allergic Response & Hypersensitivity Reactions

- **Type I**: (2-30 min)
  - asthma, hay fever, hives, eczema
- **Type II**: (5-8 hrs)
  - erythroblastosis foetalis, blood transfusions
- **Type III**: (2-8 hrs)
  - serum sickness, rheumatoid arthritis, SLE
- **Type IV**: (24-72 hrs)
  - contact dermatitis, graft rejection
Autoimmunity

• When the immune system fails to recognize “self”
• Examples of autoimmune diseases
  - Myasthenia gravis (ACh receptors)
  - Multiple sclerosis (white matter)
  - Rheumatoid arthritis (connective tissue)
  - IDDM (pancreatic $\beta$ cells)
  - SLE (DNA, nuclear protein)
Rheumatoid arthritis

- Affects women more than men
- Genetic link to HLA-DR4, DQ & DP
- RF’s & the formation of immune complexes
Myasthenia gravis

Auto-antibodies block Acetylcholine receptors
Immune complex disease

- Ag:ab complexes not attached to other cells activate the complement cascade
  - SLE
    - production of antibodies against DNA and nuclear proteins
    - increased immune complex formation
    - glomerulonephritis & many other systemic manifestations
    - treated with corticosteroids
SLE

- Pleural effusions
- Heart problems
- Lupus nephritis
- Arthritis
- Butterfly rash

Symptoms of systemic lupus erythematosus may vary widely with the individual.

Raynaud's phenomenon
Lupus
Tolerance

• Ability of immune system to distinguish self from nonself
• Clonal deletion vs. clonal anergy
• High level tolerance vs. low level tolerance
  - Baboon marrow transplant
AIDS activist Jeff Getty dead at 49

Jeff Getty, a prominent AIDS activist who in 1995 received the first bone-marrow transplant from a baboon to treat the disease, has died. He was 49.