THE IMMUNE RESPONSE

CHAPTER 19
2 TYPES OF IMMUNE RESPONSE

1) NON-SPECIFIC- aka “INNATE”

2) SPECIFIC- aka “ACQUIRED” OR “ADAPTIVE”
INNATE IMMUNITY

**PHYSICAL:**
Intact physical barriers- skin, mucous membranes

**CHEMICAL:**
Cytokines ➔ intercellular messengers
Histamine ➔ vasodilatation

**CELLULAR:**
The inflammatory reaction- neutrophils, monocytes, (macrophages) ➔ the phagocytic cells.
INNATE IMMUNITY

- Non-specific: occurs the same way regardless of the invading substance

- Occurs quickly. Goal is to control or contain the infection/invader/pathogen.

- Not typically successful by itself; “buys time” while specific immunity kicks in
SPECIFIC / ADAPTIVE IMMUNITY

- Occurs more slowly, after the inflammatory process.

- Is specific; directed at specific antigens on the foreign substance.

- Can “remember” the pathogen and mount a response more quickly w/ subsequent exposure.
SPECIFIC IMMUNITY

2 TYPES:

1) HUMORAL IMMUNITY - The B-Cells.

2) CELL-MEDIATED IMMUNITY - The T-Cells.

MORE LATER
ANTIGENS

- Substances foreign to the host that can stimulate an immune response.
- Most antigens are macro-molecules:
  - Proteins, polysaccharides.
  - Lipids, nucleic acids.
- Found on:
  - Bacteria, fungi, viruses, protozoa, parasites.
  - Pollen, poison ivy residue, insect venom.
  - Foreign RBC’s, transplanted organs.
THE MHC’s – Also known as HLA’s = HISTOCOMPATABILITY LOCUS ANTIGENS aka HUMAN LEUKOCYTE ANTIGENS.
HLA’s = The human MHC proteins.
Are the complex of molecules that determine “self” antigens from foreign.
Essential for correct cell-to-cell interactions among immune and body cells.
Class I and Class II.
**FUNCTION:** To bind with foreign antigens and to “present” them to the Cytotoxic T-Cells and the Helper T-Cells.
IMMUNE CELLS

1) LYMPHOCYTES

2) ACCESSORY OR ANTIGEN-PRESENTING CELLS – THE “APC’s”

3) EFFECTOR CELLS
IMMUNE CELLS

 Mature immune cells functionally fall into two types:

1) **REGULATORY CELLS**: orchestrate and control the immune response; Ex.: Helper T-Cells: activate other lymphocytes and phagocytes.

2) **EFFECCTOR CELLS**: eliminate the antigen; activated T lymphocytes, monocytes, other leukocytes.
LYMHOCYTES

- Specifically recognize and respond to foreign Antigens.
- **B CELLS:** originate in the bone marrow; mature in the bone marrow; develop into plasma cells, produce antibodies (humoral immunity).
- **T CELLS:** originate in the bone marrow; mature in the thymus; cell-mediated immunity; aid in antibody production.
- Both are “activated” by the recognition of the antigen by unique surface receptors.

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LYMHOCYTES

CD MOLECULES - “Clusters of Differentiation” – Additional membrane molecules on T and B cells; define functionally distinct subsets of cells:

CD4 Cells: Helper T-Cells- a regulatory cell.
CD8 Cells: Cytotoxic T-Cells- an effector cell.
ANTIGEN-PRESENTING CELLS

- THE “APC” CELLS.

- Macrophages and dendritic cells.

- Enlisted to ensure appropriate processing and presentation of the antigen.
MONOCYTES, MACROPHAGES, AND DENDRITIC CELLS

**MONOCYTES:**
- Derived in the bone marrow → migrate to tissues → become macrophages.
- Become activated to engulf and digest antigens that associate w/ their cell membranes.
- Contain an infection until Ab’s can be produced.
- Initiate adaptive immunity by producing cytokines: TNF (tumor necrosis factor), IL’s (interleukins) → activation of lymphocytes.
- Break down larger Ag’s → associate w/ Class II MHC → present to Helper T-Cells → removal of Ag-Ab complex, destroy viruses, tumor cells.
MONOCYTES, MACROPHAGES, AND DENDRITIC CELLS

DENDRITIC CELLS:

- Present processed Ag’s to T-Lymphocytes.
- Rich in Class II MHC.

These recognize foreign cells from native cells.
B LYMPHOCYTES

✿ HUMORAL IMMUNITY.
✿ ANTIBODIES.
✿ ELIMINATION OF BACTERIAL INVADERS.
✿ NEUTRALIZATION OF BACTERIAL TOXINS.
✿ PREVENTION OF VIRAL INFECTIONS.
✿ IMMEDIATE ALLERGIC RESPONSES.
B LYMPHOCYTES

IDENTIFIED BY:

1) PRESENCE OF MEMBRANE IMMUNOGLOBULIN - ANTIGEN RECEPTORS.
2) CLASS II MHC PROTEINS.
3) COMPLEMENT RECEPTORS.
4) SPECIFIC CD MOLECULES.
B LYMHPHOCYTES

PRODUCTION / MATURATION OF B-CELLS:

- Originate & mature in the bone marrow.
- Enter the circulation.
- Go to peripheral lymphoid tissues – lymph nodes, spleen, tonsils, Peyer’s patches.
- In peripheral tissues → stimulated to respond to specific antigens.
B LYMPHOCYTES

PRODUCTION OF ANTIBODIES:

fillable: Lots of stuff happens – see text.

(fillable: Ag’s bind to membrane receptor → cytokines produced.

(fillable: Cytokines trigger multiplication and maturation of Ag-activated B-Cells → Plasma Cells → Ab’s → Ag-Ab complex → removed by other immune effector cells and molecules.)
IMMUNOGLOBULINS

✿

ANTIBODIES - 5 CLASSES:

1) IgG.
2) IgA.
3) IgM.
4) IgD.
5) IgE.

Each has a different role.
IgG

- Most abundant.
- Only one that crosses the placenta.
- Protects against bacteria, toxins, and viruses.
- Activates the Complement System.

IgG - Rises during acute phase, remains elevated until / beyond resolution.
“Secretory” Immunoglobulin.

- Found in: Saliva, tears, colostrum, Resp. tract, GI tract, prostatic & vaginal secretions.
- Defends against local infections in these mucosal tissues.
- Prevents attachment of micro-organisms to these epithelial cells.
“M” = Macromolecule.

Can not cross the placenta.

1st Antibody type made by the newborn.

Presence of IgM in the newborn is diagnostic of congenital infection – ie in utero.

IgM- rises and falls during the acute phase of infection.
Serves as an antigen receptor for initiating the differentiation of B-Cells.
IgE

- Found in: Inflammation, allergies, parasitic infections.

- Binds to Mast Cells or Basophils.

- Triggers release of histamine and other mediators of inflammation and allergy.
T LYMPHOCYTES

- CELL-MEDIATED IMMUNITY.
- RESPOND TO CELL-ASSOCIATED ANTIGENS

FUNCTIONS:
1) Activation of other T and B Cells.
2) Rejection of foreign tissue.
3) Delayed hypersensitivity.
**T LYMPHOCYTES**

**PRODUCTION / MATURATION OF T-CELLS:**
- Originate in the bone marrow.
- Mature in the Thymus.
- Develop a unique T-Cell antigen receptor (TCR) – recognizes processed antigen peptide (MHC).
- TCR – MHC Complex is stabilized by CD4 (Helper T-Cell) or CD8 (Cytotoxic T-Cell).
T LYMPHOCYTES

- Go to peripheral lymphoid tissue \( \rightarrow \) encounters Ag \( \rightarrow \) differentiates into Memory T-Cells and Effector T-Cells.
HELPER T-CELLS – CD4

- Master regulator of the immune system.

- Secrete cytokines (Interferons, Interleukins) that influence the function of nearly all other cells of the immune system.

- The type of cytokine that is produced will determine whether a humoral or cell-mediated response will occur.
CYTOTOXIC T-CELLS – CD8

After activation → destroy target cells by releasing cytotoxic enzymes, cytokines, “pore-forming” molecules, and by triggering programmed cell death (apoptosis).

Pore-forming molecules- allow Ab’s and other substances into the cell to control viruses and bacteria.
NATURAL KILLER T-CELLS - NK

Do not need to recognize an Ag to become activated.

Primarily programmed for immune surveillance for cancerous cells and viruses.

Kill after contact w/ a target cell.
LYMPHOID ORGANS

✿ **CENTRAL:**
✿ Bone Marrow, Thymus.
✿ Immune cell production and maturation.

✿ **PERIPHERAL:**
✿ Lymph nodes, spleen, tonsils, appendix, Peyer’s patches, and mucosal lymphoid tissue in the resp. and GI tracts.
LYMPH NODES

1) Removal of foreign material from the lymph.

2) Center for the proliferation and response of immune cells.
THE SPLEEN

- Filters Ag’s from the blood.
- Responds to systemic infection.
- Sequence of activation events similar to the lymph nodes also occurs in the spleen.
CYTOKINES

- Made by and act on immune cells.
- Intercellular signaling molecules.
- Regulate neighboring cells.
- Made primarily by activated T-Cells and Macrophages.
- Produced in a “Cascade.”
- Some antagonize (inhibit) groups of previously-produced cytokines.
FUNCTIONAL GROUPS OF CYTOKINES

1) IL-1, IL-6, IL-8, TNF, IFN-δ - Mediate inflammation, produce fever, attract and activate phagocytes.

2) IL-3, GSF (granulocyte-stimulating factor), CSF (colony-stimulating factor): maturing factors for the production of WBC’s and RBC’s.

3) MOST IL’s AND INF’s: facilitate adaptive immunity by communicating among B-Cells, T-Cells, Macrophages, and others.
IL-1, IL-6, TNF: the major mediators of the early inflammatory response.

Produced by macrophages, dendritic cells, epithelial cells.

They cause:
- Production of acute phase proteins by the liver.
- Mobilization of neutrophils.
- Fever.
- Adhesion of molecules to vascular endothelium.
Also involved: Interferons – see text.

TNF: Can be manipulated pharmacologically to control chronic inflammation associated with Rheumatoid Arthritis and Inflammatory Bowel Disease.
IL-2, IL-4, IL-5, IFN δ:

- Activate immune cells in adaptive immunity to undergo proliferation and differentiation.
- Ensure their appropriate development into effector and memory cells.
CSF – Colony Stimulating Factors:
Stimulate pleuripotential stem cells or progenitor or precursor cells → platelets, RBC’s, Lymphocytes, Neutrophils, Monocytes, Eosinophils, Basophils, Dendritic cells.
ACTIVE VS. PASSIVE IMMUNITY

**ACTIVE:**
By having the disease.
By immunization.

**PASSIVE:**
Transferred from another source (maternal-fetal, pooled immunoglobulins).
ACTIVE IMMUNITY

**NATURAL ACTIVE**- Having the disease.

**ARTIFICIAL ACTIVE**- Having the vaccine.

- Depends on an immune response to the Ag.
- Long-lasting.
- Slow to develop, but quick to react w/ subsequent exposure.
PASSIVE IMMUNITY

- **NATURAL PASSIVE** - Mother to fetus. IgG.

- **ARTIFICIAL PASSIVE** - Pooled antibodies against a specific disease.
IN SUMMARY

**HUMORAL IMMUNITY:** Protection via B Lymphocytes → Plasma Cells → Ab’s → interact w/ circulating and cell wall Ag’s.

**CELL-MEDIATED IMMUNITY:** Protection via Cytotoxic T Lymphocytes, which protect vs. virus-infected or cancer cells.
THE COMPLEMENT SYSTEM

- A primary effector system.
- Innate and adaptive immunity.
- **Results in:**
  - Enhanced phagocytosis.
  - Enhanced inflammatory response.
  - Lysis of foreign cells.
  - Chemotaxis - attracts WBC’s to the area.
COMPLEMENT

- Inactive protein precursors, mainly proteolytic enzymes.
- Requires proper, sequential activation.

- 3 Pathways for activation:
  1) Classic Pathway.
  2) Alternate Pathway.
  3) Lectin-mediated Pathway.
TRANSFER OF IMMUNITY FROM MOTHER TO INFANT

✿ IgG: Crosses the placenta → protects the newborn from infection in the 1st few mos.
✿ IgG: Effective vs. most micro-organisms.

✿ IgA: Transferred in the colostrum during breastfeeding.
✿ IgA: Provides local protection in the GI Tract, less diarrheal illness.
Decrease in both cellular and humoral immunity.

1) ↑ susceptibility to infection.
2) ↑ auto-immune and immune complex disorders.
3) ↑ cancer.
4) ↓ success of vaccination.
5) ↓ size of thymus, ↓ T-Cell activation.