Specific Immunity – Adaptive Line of Defense

- The production of specific antibodies by a dual system of B and T lymphocytes in response to an encounter with a foreign molecule, called an antigen.
- Two features that characterize specific immunity:
  - Specificity – antibodies produced, function only against the antigen that they were produced in response to.
  - Memory – lymphocytes are programmed to "recall" their first encounter with an antigen and respond rapidly to subsequent encounters.

Classifying Immunities

- Active immunity – results when a person is challenged with antigen that stimulates production of antibodies; creates memory, takes time and is lasting.
- Passive immunity – preformed antibodies are donated to an individual; does not create memory, acts immediately, and is short term.
- Natural immunity – acquired as part of normal life experiences.
- Artificial immunity – acquired through a medical procedure such as a vaccine.

Immunities - Continued

- Natural active immunity – acquired upon infection and recovery.
- Natural passive immunity – acquired by a child through placenta and breast milk.
- Artificial active immunity – acquired through inoculation with a selected Ag.
- Artificial passive immunity – administration of immune serum or globulin.

Overview of Specific Immune Responses

- Separate but related activities of the specific immune response:
  - Development and differentiation of the immune system.
  - Lymphocytes and antigens.
  - The challenge of B and T lymphocytes by antigens.
  - B lymphocytes and the production and activities of antibodies.
  - T lymphocyte responses.

Introductory Concepts

- Cell receptors or markers confer specificity and identity.
- Major functions of receptors are:
  1. to perceive & attach to non-self or foreign molecules.
  2. to promote the recognition of self molecules.
  3. to receive & transmit chemical messages among other cells of the system.
  4. to aid in cellular development.
Major Histocompatibility Complex (MHC)
- Receptors found on all cells except RBCs
- Also known as human leukocyte antigen (HLA)
- Plays a role in recognition of self by the immune system and in rejection of foreign tissue

Functions of MHC Proteins
- Class I – markers that display unique characteristics of self molecules & regulation of immune reactions
  - Required for T lymphocytes to function
- Class II – receptors that recognize & react with foreign antigens. Located primarily on macrophages & B cells
  - Involved in presenting antigen to T cells
- Class III – secreted complement components, C2 and C4

Lymphocyte Receptors
- Lymphocyte's role in surveillance and recognition is a function of their receptors
- B-cell receptors – bind free antigens
- T-cell receptors – bind processed antigens

Clonal Selection Theory
- Lymphocytes use 500 genes to produce a tremendous variety of specific receptors
- Undifferentiated lymphocytes undergo genetic recombination while they proliferate in the embryo, forming a billion different clones with the ability to react with a huge variety of antigens

Clonal Selection - Continued
- Lymphocyte specificity is preprogrammed, existing in the genetic makeup before an antigen has ever been seen
- Each genetically different type of lymphocyte expresses a single specificity
- First introduction of each type of antigen into the immune system selects a genetically distinct lymphocyte and causes it to divide and produce a population of cells that react to the antigen
Characteristics of the Specific B cell Receptor: Immunoglobulins

- Large glycoproteins that serve as specific receptors of B cells
- Composed of 4 polypeptide chains
  - 2 identical heavy chains
  - 2 identical light chains
- Y shaped
- Variable regions
- Constant regions

Development of Receptors

- Immunoglobulin genes lie on 3 different chromosomes
- An undifferentiated lymphocyte has 150 different genes for the variable region of light chains and 250 for the variable region and diversity region of the heavy chain
- During development, recombination causes only the selected V and D genes to be active in the mature cell

B Cell Receptors

- Once synthesized, immunoglobulin is transported to cell membrane & inserted there to act as a receptor
- First receptor on most B cells is a small form of IgM; mature B cells carry IgD receptors
T cell receptors

- Formed by genetic recombination, having variable and constant regions
- 2 parallel polypeptide chains
- Small, without humoral functions (don't circulate)

Development of the Dual Lymphocyte System

- Starting in the embryonic & fetal stages, stem cells in the yolk sac, liver, and bone marrow release immature lymphocytes into the circulation
- These undifferentiated cells must mature to be able to react to antigen

T cell Maturation

- Maturation is directed by the thymus and its hormones
- 7 classes of T-cell receptors, called the CD cluster (cluster of differentiation)
- Mature T cells migrate to lymphoid organs

B cell Maturation

- This is directed by bone marrow sites that harbor stromal cells, which nurture the lymphocyte stem cells & provide hormonal signals
- Millions of distinct B cells develop & home to specific sites in the lymph nodes, spleen, and GALT where they come into contact with antigens throughout life

Antigen (Ag)

- A substance that provokes an immune response
- Foreign cells & large complex molecules over 10,000 MW are most antigenic
- Foreign molecules less than 1,000 MW are not antigenic unless attached to a larger carrier
- Antigenic determinant or epitope – small molecular group that is recognized by lymphocytes. An antigen has many antigenic determinants
**B cell Activation & Antibody Production**

- Once B cells process the Ag, they interact with T helper cells and are stimulated by growth and differentiation factors; they enter the cell cycle in preparation for mitosis and clonal expansion.
- Divisions give rise to plasma cells that secrete antibodies and memory cells that can react to the same antigen later.

**Nature of Antibodies**

- Immunoglobulins
- A large Y-shaped protein
- Consists of 4 polypeptide chains
- Contains 2 identical fragments (Fab) with ends that bind to specific antigen

**Ag-Ab reactions**

- Opsonization – Coating of foreign materials by Ab’s preparatory to phagocytosis
- Neutralization – Ab coating inactivates virus
- Agglutination – Ab’s complexing particles together
- Complement fixation
Ag Exposure and Response

- Primary response – after first exposure to an Ag, the immune system produces IgM and a gradual increase in Ab titer
- Secondary response – after second contact with the same Ag, immune system produces a more rapid, stronger response due to memory cells

T cells & Cell Mediated Immunity

- T cells act directly against Ag and foreign cells
- T cells secrete cytokines that act on other cells
- Sensitized T cells proliferate into long-lasting memory T cells

Types of T cells

1. T helper cells (CD4 or T₄) most prevalent type of T cell; regulate immune reaction to antigens, including other T and B cells; also involved in activating macrophages and improving opsonization; differentiate into T helper 1 (Th1) cells or T helper 2 (Th2) cells
2. Cytotoxic T cells (CD8 or T₈) destroy foreign or abnormal cells by secreting perforins that lyse cells
3. Natural killer cells – lack specificity; circulate through the spleen, blood, and lungs

Antigen Processing and Presentation to Lymphocytes

- T-cell dependent antigens must be processed by phagocytes called antigen presenting cells (APC)
- APCs modify the antigen so it is more immunogenic and recognizable; then the Ag is moved to the APC surface and bound to MHC receptor
- Antigen presentation involves a direct collaboration among an APC, a T helper cell and an antigen-specific B or T cell
  - Interleukin-1 is secreted by APC to activate Th cells
  - Interleukin-2 is produced by Th cells to activate B and other T cells
Vaccines

Provide an antigenic stimulus that does not cause disease but can produce long lasting, protective immunity

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<thead>
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<th>TABLE 15.4</th>
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<tr>
<td><strong>Checklist of Requirements for an Effective Vaccine</strong></td>
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<tr>
<td>• It should have a low level of adverse side effects or toxicity and not cause serious harm.</td>
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<td>• It should protect against exposure to natural, wild forms of pathogens.</td>
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<tr>
<td>• It should stimulate both humoral (B-cell) response and cell-mediated (T-cell) response.</td>
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<td>• It should have long-term, lasting effects (produce memory).</td>
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<td>• It should not require numerous doses or boosters.</td>
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<td>• It should be inexpensive, have a relatively long shelf life, and be easy to administer.</td>
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