Adaptive Immunity

CCV
Microbiology
Ch. 16

1

Overview of Adaptive Immunity

- Adaptive immunity is the body's ability to recognize and defend itself against distinct invaders and their products
- Five attributes of adaptive immunity
  - Specificity
  - Inducibility
  - Clonality
  - Unresponsiveness to self (tolerance)
  - Memory

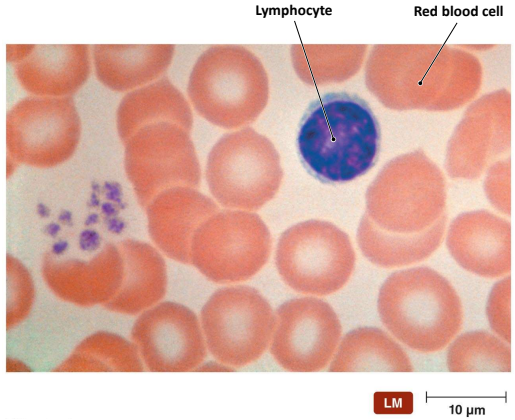
2

Overview of Adaptive Immunity

- Involves activity of lymphocytes
- Two main types of lymphocytes
  - B lymphocytes (B cells)
    - Mature in the bone marrow
  - T lymphocytes (T cells)
    - Mature in the thymus
- Two types of adaptive immune responses
  - Cell-mediated immune responses
  - Antibody immune responses

3

Figure 16.1 Lymphocytes play a central role in adaptive immunity.



4

Elements of Adaptive Immunity

- **The Tissues and Organs of the Lymphatic System**
  - Composed of lymphatic vessels and lymphatic cells, tissues, and organs
  - Screen the tissues of the body for foreign antigens

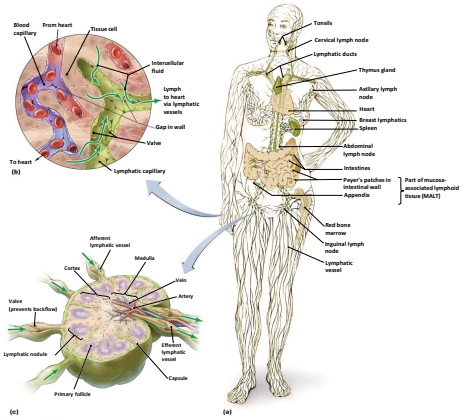
5

Elements of Adaptive Immunity

- **The Tissues and Organs of the Lymphatic System**
  - The lymphatic vessels and the flow of lymph
    - Lymphatic vessels
      - One-way system that conducts lymph from tissues and returns it to the circulatory system
    - Lymph
      - Liquid with composition similar to blood plasma
      - Arises from fluid leaked from blood vessels into surrounding tissues

6

Figure 16.2 The lymphatic system.



7

Elements of Adaptive Immunity

- **The Tissues and Organs of the Lymphatic System**
  - Lymphoid organs
    - Primary lymphoid organs
      - Red bone marrow
      - Thymus
    - Secondary lymphoid organs
      - Lymph nodes
      - Spleen
      - Tonsils
      - Mucosa-associated lymphoid tissue (MALT)

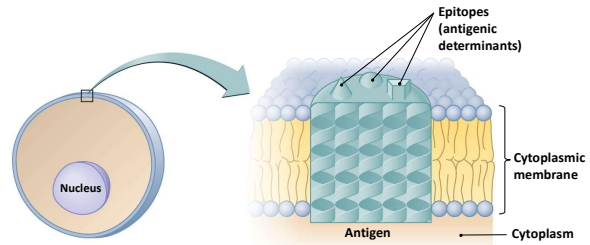
8

Elements of Adaptive Immunity

- **Antigens**
  - Properties of antigens
    - Molecules that the body recognizes as foreign and worthy of attack
    - Recognized by three-dimensional regions called *epitopes* on antigens
    - Large foreign macromolecules make the best antigens
    - Include various bacterial components as well as proteins of viruses, fungi, and protozoa
    - Food and dust can also contain antigenic particles

9

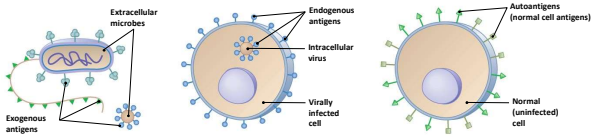
Figure 16.3a Antigens, molecules that provoke a specific immune response.



(a) Epitopes (antigenic determinants)

10

Figure 16.3b-d Antigens, molecules that provoke a specific immune response.



(b) Exogenous antigens (c) Endogenous antigens (d) Autoantigens

11

Elements of Adaptive Immunity

- **T Lymphocytes (T Cells) and Preparation for an Adaptive Immune Response**
  - T cells act primarily against cells that harbor intracellular pathogens
  - Some T cells act against body cells that produce abnormal cell-surface proteins
  - Circulate in the lymph and blood
  - Migrate to the lymph nodes, spleen, and Peyer's patches
  - Have T cell receptors (TCRs) on their cytoplasmic membrane

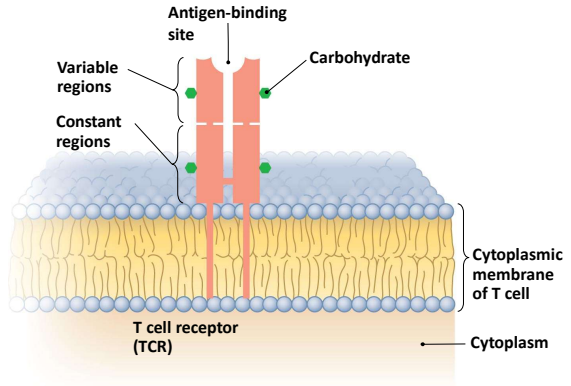
12

Elements of Adaptive Immunity

- **T Lymphocytes (T Cells) and Preparation for an Adaptive Immune Response**
  - Specificity of the T cell receptor (TCR)
    - Each cell's TCR has a specific antigen-binding site
    - TCRs do not recognize epitopes directly
    - TCRs bind only epitopes associated with an MHC protein

13

Figure 16.4 A T cell receptor (TCR).



14

Preparation for an Adaptive Immune Response

- **T Lymphocytes (T Cells) and Preparation for an Adaptive Immune Response**
  - **The Roles of the Major Histocompatibility Complex and Antigen-Presenting Cells**
    - Group of antigens first identified in graft patients
    - Important in determining compatibility of tissues for tissue grafting
    - Major histocompatibility antigens are glycoproteins found in the membranes of most cells of vertebrate animals
    - Hold and position antigenic determinants for presentation to T cells

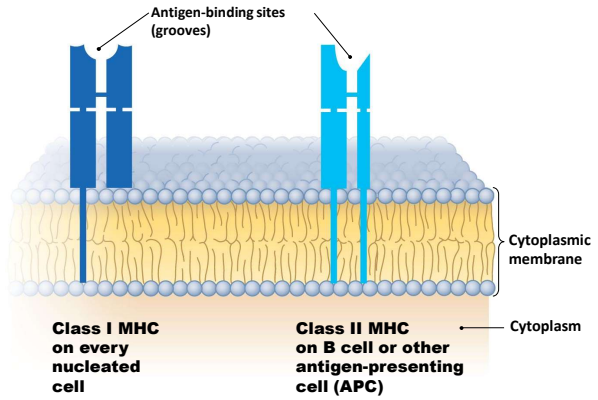
15

Preparation for an Adaptive Immune Response

- **T Lymphocytes (T Cells) and Preparation for an Adaptive Immune Response**
  - **The Roles of the Major Histocompatibility Complex and Antigen-Presenting Cells**
  - Antigens bind in the antigen-binding groove of MHC molecules
  - Two classes of MHC proteins
    - MHC class I
      - Present on all cells except red blood cells
    - MHC class II
      - Present on antigen-presenting cells (APCs)
        - Include B cells, macrophages, and dendritic cells

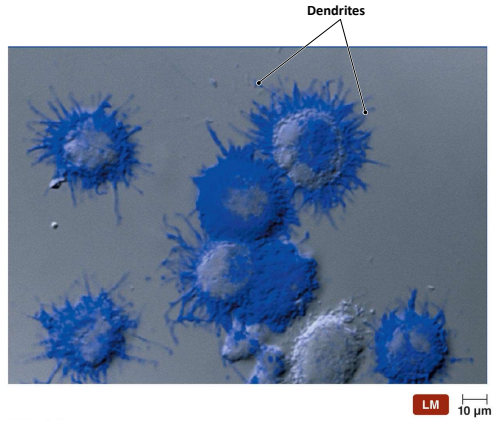
16

Figure 16.5 The two classes of major histocompatibility complex (MHC) proteins.



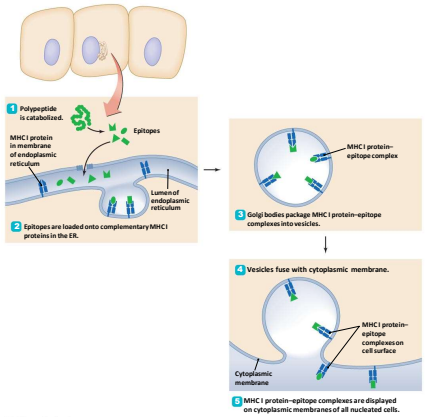
17

Figure 16.6 Dendritic cells.



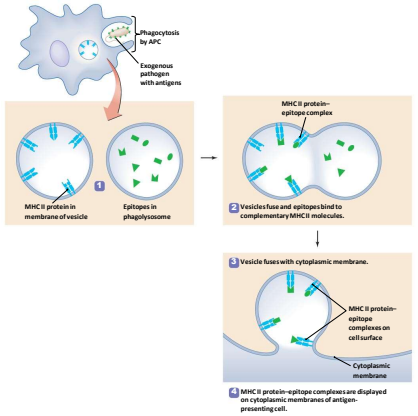
18

Figure 16.7 The processing of T-dependent endogenous antigens.



19

Figure 16.8 The processing of T-dependent exogenous antigens.



20

Elements of Adaptive Immunity

- **T Lymphocytes (T Cells) and Preparation for an Adaptive Immune Response**
  - Types of T lymphocytes
    - Based on surface glycoproteins and characteristic functions
      - Cytotoxic T lymphocyte
        - Directly kills other cells
      - Helper T lymphocyte
        - Helps regulate B cells and cytotoxic T cells
        - Includes type 1 and type 2 helper T cells
      - Regulatory T lymphocyte
        - Represses adaptive immune responses

21

TABLE 16.1 Characteristics of T Lymphocytes

Lymphocyte	Site of Maturation	Representative Cell-Surface Glycoproteins	Selected Secretions
Helper T cell type 1 (Th1)	Thymus	CD4, CCR5, and distinctive TCR	Interleukin 2, IFN-γ
Helper T cell type 2 (Th2)	Thymus	CD4, CCR3, CCR4, and distinctive TCR	Interleukin 4
Cytotoxic T cell (Tc)	Thymus	CD8, CD95L, and distinctive TCR	Perforin, granzyme
Regulatory T cell (Tr)	Thymus	CD4, CD25, and distinctive TCR	Cytokines, such as interleukin 10

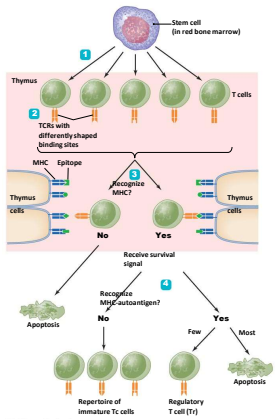
22

Elements of Adaptive Immunity

- **T Lymphocytes (T Cells) and Preparation for an Adaptive Immune Response**
  - Clonal deletion
    - Vital that immune responses not be directed against autoantigens
    - Body eliminates self-reactive lymphocytes
    - Lymphocytes that react to autoantigens undergo apoptosis

23

Figure 16.9 Clonal deletion of T cells.



24

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Found primarily in the spleen, lymph nodes, and MALT
  - Small percentage of B cells circulate in the blood
  - Major function is the secretion of antibodies

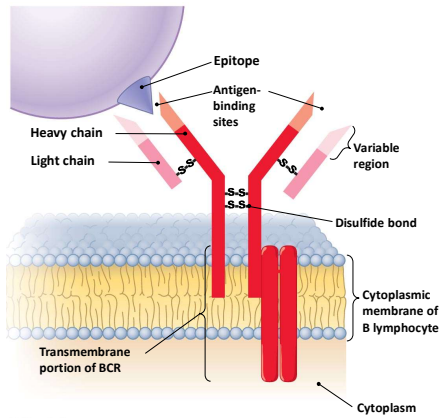
25

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Specificity of the B cell receptor (BCR)
    - Each B lymphocyte has multiple copies of the B cell receptor (BCR)
    - Each B cell generates a single BCR
    - Two variable regions of the BCR form the antigen-binding sites
    - Each BCR recognizes only one epitope
    - The entire repertoire of an individual's BCRs is capable of recognizing millions of different epitopes

26

Figure 16.10 B cell receptor (BCR).



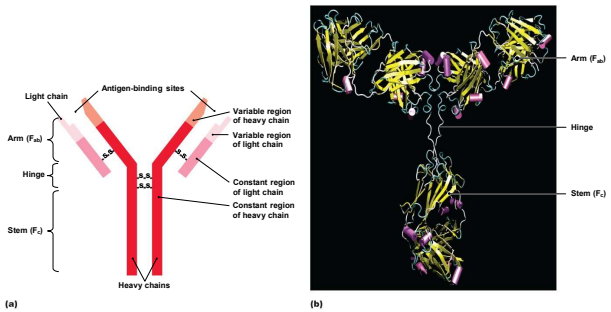
27

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Specificity and antibody structure
    - Antibodies are immunoglobulins similar to BCRs
    - Secreted by activated B cells called *plasma cells*
    - Have antigen-binding sites and antigen specificity identical to the BCR of the activated B cell

28

Figure 16.11 Basic antibody structure.



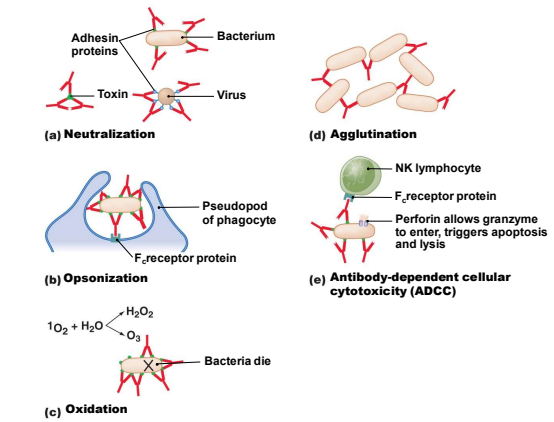
29

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Antibody function
    - Antigen-binding sites are complementary to epitopes
    - Antibodies function in several ways
      - Activation of complement and inflammation
      - Neutralization
      - Opsonization
      - Killing by oxidation
      - Agglutination
      - Antibody-dependent cellular cytotoxicity (ADCC)

30

Figure 16.12 Five functions of antibodies.



31

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Classes of antibodies
    - Threats confronting the immune system are variable
    - Antibody class involved in the immune response varies
      - Type of antigen
      - Portal of entry
      - Antibody function needed
    - Five different classes of antibodies

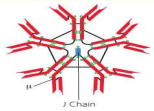
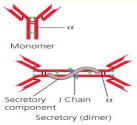
32

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Classes of antibodies
    - IgM – first antibody produced
    - IgG – most common and longest-lasting antibody
    - IgA – associated with body secretions
    - IgE – involved in response to parasitic infections and allergies
    - IgD – exact function is not known

33

TABLE 16.2 Characteristics of the Five Classes of Antibodies

	IgM	IgG	IgA	IgE	IgD
					
Structure, number of binding sites	Pentamer, 10	Monomer, 2	Monomer, 2 Dimer, 4	Monomer, 2	Monomer, 2
Type of heavy chain	Mu (μ)	Gamma (γ)	Alpha (α)	Epsilon (ε)	Delta (δ)
Functions	Monomer can act as BCR; pentamer acts in complement activation, neutralization, agglutination	Complement activation, neutralization, opsonization, production of hydrogen peroxide, agglutination, and antibody-dependent cellular toxicity (ADCC); crosses placenta to protect fetus	Neutralization and agglutination; dimer is secretory antibody	Triggers release of antiparasitic molecules from eosinophils and of histamines from basophils and mast cells (allergic reactions)	Unknown, but perhaps acts as BCR
Locations	Serum, B cell surface	Serum, mast cell surfaces	Monomer: serum Dimer: mucous membrane secretions (e.g., tears, saliva, mucus); milk	Serum, mast cell surfaces	B cell surface
Approximate half-life (time it takes for concentration to reduce by half) in blood	10 days	20 days	6 days	2 days	3 days
Percentage of serum antibodies	5–10%	80%	10–15%	<1%	<0.05%
Size (mass in kilodaltons)	970	150	Monomer: 160 Dimer: 385	188	184

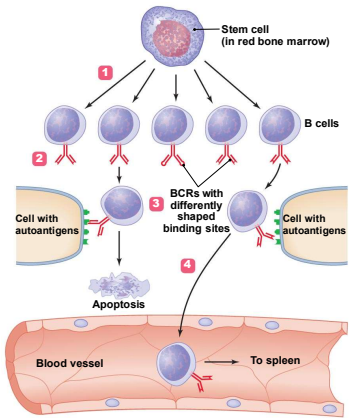
34

Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Clonal deletion of B cells
    - Occurs in the bone marrow
    - Similar to deletion of T cells
    - Self-reactive B cells may become inactive or change their BCR

35

Figure 16.13 Clonal deletion of B cells.



36

Elements of Adaptive Immunity

- **Immune Response Cytokines**
  - Soluble regulatory proteins that act as intercellular signals
  - Cytokines secreted by various leukocytes
  - Cytokine network
    - Complex web of signals among cells of the immune system

37

Elements of Adaptive Immunity

- **Immune System Cytokines**
  - Interleukins (ILs)
    - Signal among leukocytes
  - Interferons (IFNs)
    - Antiviral proteins that may act as cytokines
  - Growth factors
    - Proteins that stimulate stem cells to divide
  - Tumor necrosis factor (TNF)
    - Secreted by macrophages and T cells to kill tumor cells and regulate immune responses and inflammation
  - Chemokines
    - Chemotactic cytokines that signal leukocytes to move

38

Cell-Mediated Immune Responses

- Respond to intracellular pathogens and abnormal body cells
- Common intracellular pathogens are viruses
- The response is also effective against cancer cells, intracellular protozoa, and intracellular bacteria

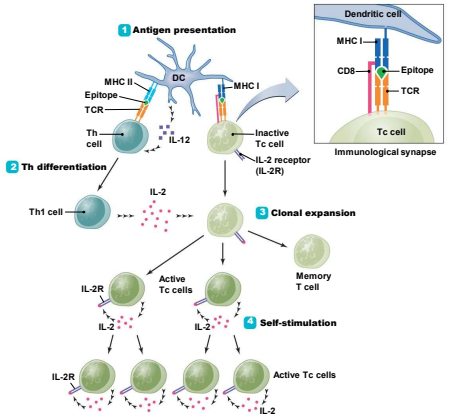
39

Cell-Mediated Immune Responses

- **Activation of Cytotoxic T Cell Clones and Their Functions**
  - Adaptive immune responses initiated in lymphoid organs
  - Steps involved in activation of cytotoxic T cells
    - Antigen presentation
    - Helper T cell differentiation
    - Clonal expansion
    - Self-stimulation

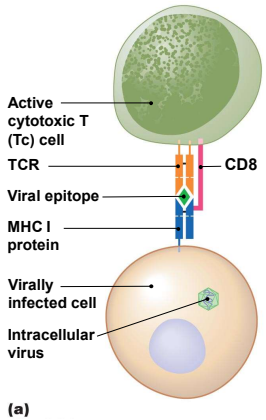
40

Figure 16.14 Activation of a clone of cytotoxic T (Tc) cells.



41

Figure 16.15a A cell-mediated immune response.



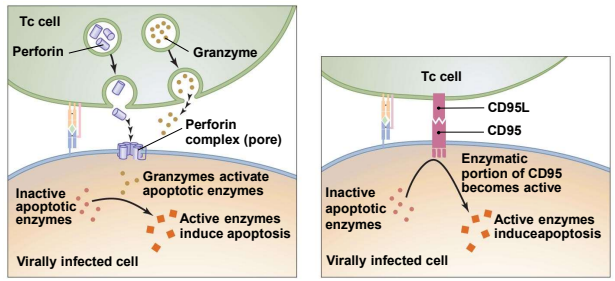
42

Cell-Mediated Immune Responses

- **Activation of Cytotoxic T Cell Clones and Their Functions**
  - Cytotoxic T cells kills their targets by two pathways
    - Perforin-granzyme pathway
      - Involves synthesis of killing proteins
    - CD95 pathway
      - Mediated by a glycoprotein on the body's cells

43

Figure 16.15b-c A cell-mediated immune response.



44

Cell-Mediated Immune Responses

- **Memory T Cells**
  - Some activated T cells become memory T cells
  - Persist for months or years in lymphoid tissues
  - Immediately functional upon subsequent contacts with epitope-MHC complex specific to its TCR
  - Memory response is more effective than the primary response

45

Cell-Mediated Immune Responses

- **T Cell Regulation**
  - Regulation needed to prevent T cell response to autoantigens
  - T cells require additional signals from an antigen-presenting cell
    - Interaction of the T cell and antigen-presenting cell stimulates the T cell to respond to the antigen
  - Regulatory T cells also moderate cytotoxic T cell activity

46

Antibody Immune Responses

- Antibody immune responses mounted against exogenous pathogens and toxins
- Activates only in response to specific pathogens

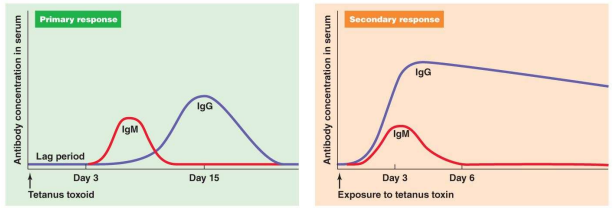
47

Antibody Immune Responses

- **Memory B Cells and the Establishment of Immunological Memory**
  - Memory B cells
    - Produced by B cell proliferation but do not secrete antibodies
    - Have BCRs complementary to the epitope that triggered their production
    - Long-lived cells that persist in the lymphoid tissue
    - Initiates antibody production if antigen is encountered again

48

Figure 16.19 The production of primary and secondary antibody immune responses.



49

Types of Acquired Immunity

- Specific immunity acquired during an individual's life
- Two types
  - Naturally acquired
    - Response against antigens encountered in daily life
  - Artificially acquired
    - Response to antigens introduced via a vaccine
- Distinguished as either active or passive

50

TABLE 16.4 A Comparison of the Types of Acquired Immunity

	Active	Passive
Naturally acquired	 The body responds to antigens that enter naturally, such as during infections.	 Antibodies are transferred from mother to offspring, either across the placenta (IgG) or in breast milk (secretory IgA).
Artificially acquired	 Health care workers introduce antigens in vaccines; the body responds with antibody or cell-mediated immune responses, including the production of memory cells.	 Health care workers give patients antisera or antitoxins, which are preformed antibodies obtained from immune individuals or animals.

51