Fundamental Biology BI 1101

an interdisciplinary approach to introductory biology

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<text>



Learning outcomes

After this lecture, you should be able to:

- 1. Describe the functions of neutrophils.
- 2. Describe the nature of innate defenses in invertebrates and vertebrates.
- 3. Describe the steps of the inflammatory response and explain how they help to prevent the spread of disease.
- 4. Describe the specific nature of adaptive immune system responses.
- 5. Describe the development and functions of B lymphocytes and T lymphocytes.
- 6. Define and distinguish between the humoral immune response and the cell-mediated immune response.
- 7. Describe the nature of antigens. Explain how an antigen and an antibody interact.

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You should now be able to

- 6. Describe the specific structure of an antibody and relate its shape to its functions.
- 10. Describe the production and uses of monoclonal antibodies.
- 11. Describe the specific functions of helper T cells and how they interact with other cells.
- 12. Explain how cytotoxic T cells destroy infected body cells.
- 13. Explain how HIV infects cells, multiplies, and causes disease.
- 15. Explain how the immune system identifies the body's own molecules and how this system complicates organ transplantations.
- 16. Describe how the malfunction or failure of the immune system can cause disease.
- 17. Explain why allergies occur and what causes anaphylactic shock.

ANIMAL STRUCTURE & FUNCTION THE IMMUNE SYSTEM



- The human body's immune system
 - recognizes agents that cause disease and
 - attacks them.
- Many cells, tissues, and organs defend the body
- The immune system enables the body to recognize its own cells and to defend against infections, cancer, and foreign substances.

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The vertebrate immune system consists of a network of cells, defensive chemicals, and fluids that permeate the body

	Immune System
Tissue Types*	Examples of Locations/Functions
Epithelial	Thymus, spleen, and tonsils consist partly of epithelial tissue; lines lymphatic and blood vessels; lymphoid tissue lies beneath epithelial tissues of the digestive, respiratory, and urinary tracts, guarding potential points of entry for pathogens.
Connective	Lymphocytes, antibodies, and other immune system chemicals circulate in blood and lymph, which are connective tissues; bone marrow is connective tissue that produces lymphocytes; thymus, spleen, and lymph nodes consist partly of connective tissue.

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White Blood Cells Play Major Roles in the Immune System

Blood is critical to immune function.

- Plasma carries defensive proteins called antibodies. Infection-fighting white blood cells are suspended in blood plasma
- White blood cells :
 - neutrophils and eosinophils are white blood cells that function primarily as phagocytes, which are scavenger cells that travel in the bloodstream or wander through body tissues, engulfing bacteria and debris.
 - **Basophils** release chemical signals that trigger inflammation and allergies.
 - Mast cells, originate in red bone marrow but do not circulate in blood. They settle in tissues, especially those near the skin, digestive tract, and respiratory system.

- Lymphocytes include several types of white blood cells.
 - **B cells** mature in red bone marrow, then migrate to lymphoid tissues and into the blood.
 - **T cells** also originate in red bone marrow, but they mature in the **thymus** ("T" is for thymus).
 - The **natural killer cell**, attacks cancerous or virus-infected body cells.
- **Monocytes** give rise to **macrophages**, which also function as phagocytes. Some types of macrophages wander throughout the body; others remain in just one tissue.





Nature Reviews | Immunology

The Immune System has divided into two subdivision

- innate defenses/immunity → provide a broad defense against any infectious agent. Innate refers to the fact that these defenses are always present and ready to function
- adaptive immunity, the body's immune cells not only recognize specific parts of a pathogen, but they also "remember" previous encounters.

Innate defenses and adaptive immunity interact in highly coordinated ways to defend the body against pathogens.



Overview of Body Defenses. Innate defenses prevent bacteria, viruses, and other pathogens from entering the body, or they attack those that do breach the physical and chemical barriers. In the adaptive immune response, macrophages displaying antigens (molecules stripped from pathogens) stimulate helper T cells, which trigger both cell-mediated and humoral immunity.

INNATE IMMUNITY

All animals have innate immunity

- Nearly everything in the environment teems with **pathogens**, agents that cause disease.
- The immune system is the body's system of defenses against agents that cause disease.
- Innate immunity is a series of defenses that
 - act immediately upon infection and
 - are the same whether or not the pathogen has been encountered before.

All animals have innate immunity

- Invertebrates rely solely on innate immunity, which may consist of
 - an exoskeleton,
 - low pH,

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- the enzyme lysozyme, and
- immune cells capable of phagocytosis, cellular ingestion and digestion of foreign substances.
- Vertebrates have innate and adaptive immunity.

Innate immunity (24.1–3) The response is the same whether or not the pathogen has been previously encountered		Adaptive immunity (24.4–15) Found only in vertebrates; previous exposure to the pathogen enhances the immune response
External barriers (24.1)	Internal defenses (24.1–2)	
 Skin/ exoskeleton Acidic environment Secretions Mucous membranes Hairs Cilia 	 Phagocytic cells NK cells Defensive proteins Inflammatory response (24.2) 	 Antibodies (24.8–10) Lymphocytes (24.11–13)
	The lymphatic system (24.3)	

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All animals have innate immunity

- Vertebrate innate immunity includes
 - barriers such as skin and mucous membranes,
 - interferons, proteins produced by virus-infected cells, that help to limit the cell-to-cell spread of viruses,
 - neutrophils (phagocytic cells),

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- macrophages, large phagocytic cells that wander through the interstitial fluid,
- natural killer cells that attack cancer cells and virusinfected cells, and
- a complement system, a group of about 30 kinds of proteins that can act with other defense mechanisms.



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How Complement Kills. Complement proteins combine to riddle a bacterium's cell membrane with holes. The bacterial cell quickly dies.

Inflammation mobilizes the innate immune response

- Tissue damage triggers the **inflammatory response**, a major component of our innate immunity, which can
 - disinfect and clean infected tissues and
 - limit the spread of infection to surrounding tissues.
- Bacterial infections can bring about an overwhelming systemic inflammatory response leading to septic shock, characterized by
 - very high fever and
 - low blood pressure.



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The lymphatic system becomes a crucial battleground during infection

• The lymphatic system is

- involved in innate and adaptive immunity and
- consists of a network of
 - lymphatic vessels,
 - · lymph nodes, and
 - lymph.
- Lymphatic vessels
 - collect fluid from body tissues and
 - return it as **lymph** to the blood.
- Lymph organs
 - include the spleen and lymph nodes and
 - are packed with white blood cells that fight infections.

The lymphatic system becomes a crucial battleground during infection

- As lymph circulates through lymphatic organs it
 - collects
 - microbes,
 - parts of microbes, and
 - · microbial toxins, and
 - transports them to lymphatic organs where
 - macrophages in lymphatic organs engulf the invaders and
 - lymphocytes may mount an adaptive immune response.



ADAPTIVE IMMUNITY

The adaptive immune response counters specific invaders

- Our immune system responds to foreign molecules called **antigens**, which elicit the adaptive immune response.
- The adaptive immune system
 - is found only in the vertebrates,
 - reacts to specific pathogens, and
 - "remembers" an invader.

The adaptive immune response counters specific invaders

- Infection or vaccination triggers active immunity.
- Vaccination, or immunization, exposes the immune system to a vaccine,
 - a harmless variant or
 - part of a disease-causing microbe.
- We can temporarily acquire **passive immunity** by receiving premade antibodies.

Figure 24.4



Lymphocytes mount a dual defense

Lymphocytes

- are white blood cells that spend most of their time in the tissues and organs of the lymphatic system,
- are responsible for adaptive immunity, and
- originate from stem cells in the bone marrow.
 - B lymphocytes or **B cells** continue developing in bone marrow.
 - T lymphocytes or **T cells** develop further in the thymus.

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Lymphocytes mount a dual defense

- B cells
 - participate in the humoral immune response and
 - secrete antibodies into the blood and lymph.
- T cells
 - participate in the cell-mediated immune response,
 - attack cells infected with bacteria or viruses, and
 - promote phagocytosis by other white blood cells and by stimulating B cells to produce antibodies.



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Lymphocytes mount a dual defense

- Millions of kinds of B cells and T cells
 - each with different antigen receptors, capable of binding one specific type of antigen,
 - wait in the lymphatic system,
 - · where they may respond to invaders.



Antigens have specific regions where antibodies bind to them

- Antigens
 - are molecules that elicit the adaptive immune response,
 - usually do not belong to the host animal, and
 - are proteins or large polysaccharides on the surfaces of viruses or foreign cells.
- Antigenic determinants are specific regions on an antigen where antibodies bind.
 - An antigen usually has several different determinants.
 - The antigen-binding site of an antibody and an antigenic determinant have complementary shapes.



Clonal selection gatherings defensive forces against specific antigens

- When an antigen enters the body it activates only a small subset of lymphocytes that have complementary receptors.
- In **clonal selection**, the selected lymphocyte cells
 - multiply into clones of short-lived **effector cells**, specialized for defending against the antigen that triggered the response, and
 - multiply into **memory cells**, which confer long-term immunity.
 - **Plasma cells** are the effector cells produced during clonal selection of B cells.



Clonal selection gatherings defensive forces against specific antigens

- The clonal selection of B cells occurs in two responses.
 - In the primary immune response, clonal selection produces
 - effector cells and
 - **memory cells** that may confer lifelong immunity.
 - In the secondary immune response, memory cells are activated by a second exposure to the same antigen.

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Clonal selection gatherings defensive forces against specific antigens

- Primary vs. secondary immune responses
 - The primary immune response
 - occurs upon first exposure to an antigen and
 - is slower than the secondary immune response.
 - The secondary immune response
 - · occurs upon second exposure to an antigen and
 - is faster and stronger than the primary immune response.



Antibodies are the weapons of the humoral immune response

- Antibodies are secreted
 - by plasma (effector) B cells,
 - into the blood and lymph.



Antibodies are the weapons of the humoral immune response

An antibody molecule

- · is Y-shaped and
- has two antigen-binding sites specific to the antigenic determinants that elicited its secretion.



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Antibody Class	Location	Sample Functions
lgA ⋟⊭⊯	Lining of digestive, respiratory, and urogenital tracts; also in milk, saliva, and tears	Protects points of entry into the body
IgD	B cell membranes	Antigen receptor; regulates B cell activation
	Tonsils, skin, mucous membranes	Stimulates mast cells and basophils to release histamine in inflammatory and allergic responses
IgG	Circulate in blood plasma; can cross placenta to confer immunity on fetus	Predominant antibody secreted in secondary immune response
IgM	B cell membranes; circulate in blood plasma	Antigen receptor; predominant antibody secreted in primary immune response

Antibodies mark antigens for elimination

- Antibodies promote antigen elimination through several mechanisms:
 - 1. neutralization, binding to surface proteins on a virus or bacterium and blocking its ability to infect a host,
 - 2. agglutination, using both binding sites of an antibody to join invading cells together into a clump,
 - 3. precipitation, similar to agglutination, except that the antibody molecules link dissolved antigen molecules together, and
 - 4. activation of the complement system by antigen-antibody complexes.



Ways to Acquire Immunity:

Туре	Description	Examples
Passive immunity	One individual acquires antibodies from another individual.	 Fetus acquires antibodies from mother via placenta or milk.
		 Dog bite victim receives injections of antibodies to rabies virus.
		• Snake bite victim receives intravenous antivenom (antibodies to snake venom).
Active immunity	Individual produces antibodies to an antigen.	 Having chickenpox confers future immunity to that disease ("natural" active immunity).
		 Influenza vaccine triggers production of memory cells specific to antigens in the vaccine ("artificial" active immunity).

Monoclonal antibodies are powerful tools in the lab and clinic

· Monoclonal antibodies (mAb) are

- identical antibodies
- produced by cells that are all descendants of a single, hybrid cell.
- To make the hybrid cell with desirable properties, two cells are fused.
 - 1. A cancerous tumor cell, able to multiply indefinitely, is fused to
 - 2. a normal antibody-producing B cell, which is producing the desired antibody.

Monoclonal antibodies are powerful tools in the lab and clinic

- · Monoclonal antibodies are useful in
 - research,
 - diagnosis (such as home pregnancy tests), and
 - treatment of certain cancers.



Helper T cells stimulate the humoral and cellmediated immune responses

- In the cell-mediated immune response, an **antigenpresenting cell** displays
 - a foreign antigen (a nonself molecule) and
 - one of the body's own self proteins
 - to a helper T cell.
- The helper T cell's receptors
 - recognize the self-nonself complexes and
 - the interaction activates the helper T cells.
- The helper T cell can then activate
 - cytotoxic T cells, which attack body cells that are infected with pathogens, and
 - B cells.



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Cytotoxic T cells destroy infected body cells

- Cytotoxic T cells
 - are the only T cells that kill infected cells,
 - bind to infected body cells, and
 - destroy them.
- Cytotoxic T cells also play a role in protecting the body against the spread of some cancers.





Figure 33.7 Cytotoxic T Cells. (a) An activated cytotoxic T cell binds to a cancer cell (step 1) and injects a protein that pokes holes in the cancer cell's membrane (step 2). The cancer cell dies (step 3), leaving behind debris that macrophages clear away. (b) A small cytotoxic T cell attacks a large cancer cell above it.

CONNECTION: HIV destroys helper T cells, compromising the body's defenses

AIDS (acquired immunodeficiency syndrome), results from infection by HIV, the human immunodeficiency virus.

- Since 1981 AIDS has killed more than 27 million people, and more than 33 million people live today with HIV.
- In 2008,
 - 2.7 million people were newly infected with HIV, and
 - over 2 million died, including 300,000 children under age 15.
- Most AIDS infections and deaths occur in nonindustrialized nations of southern Asia and sub-Saharan Africa.

CONNECTION: HIV destroys helper T cells, compromising the body's defenses

- The AIDS virus usually attacks helper T cells, impairing the
 - cell-mediated immune response and
 - humoral immune response, and
 - opening the way for **opportunistic infections**.

CONNECTION: HIV destroys helper T cells, compromising the body's defenses

- AIDS patients typically die from
 - opportunistic infections and
 - cancers
 - that would normally be resisted by a person with a healthy immune system.
- Until there is a vaccine or a cure, the best way to stop AIDS is to educate people about how the virus is transmitted.



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EVOLUTION CONNECTION: The rapid evolution of HIV complicates AIDS treatment

- HIV mutates very quickly.
- New strains are resistant to AIDS drugs.
- Drug-resistant strains now infect new patients.



The immune system depends on our molecular fingerprints

- The immune system normally reacts
 - only against nonself substances and
 - not against self.
- Transplanted organs may be rejected because the transplanted cells lack the unique "fingerprint" of the patient's self proteins, called major histocompatibility complex (MHC) molecules.
- Donors are used that most closely match the patient's tissues.
- Transplants between identical twins do not typically have this problem.

DISORDERS OF THE IMMUNE SYSTEM

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Malfunction or failure of the immune system causes disease

- Autoimmune diseases occur when the immune system turns against the body's own molecules.
- Examples of autoimmune diseases include
 - lupus,
 - rheumatoid arthritis,
 - insulin-dependent diabetes mellitus
 - multiple sclerosis.



Malfunction or failure of the immune system causes disease

- Immunodeficiency diseases occur when an immune response is
 - defective or
 - absent.
- The immune system may be weakened by
 - physical stress or
 - emotional stress.
 - Students are more likely to be sick during a week of exams.

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Allergies are overreactions to certain environmental antigens

- Allergies are hypersensitive (exaggerated) responses to otherwise harmless antigens in our surroundings.
- Antigens that cause allergies are called **allergens**.

Allergies are overreactions to certain environmental antigens

- Allergic reactions typically occur
 - very rapidly and
 - in response to tiny amounts of an allergen.
- Allergic reactions can occur in many parts of the body, including
 - nasal passages,
 - bronchi, and
 - skin.

Allergies are overreactions to certain environmental antigens

- The symptoms of an allergy result from a twostage reaction.
 - 1. The first stage, called sensitization, occurs when a person is first exposed to an allergen.
 - 2. The second stage begins when the person is exposed to the same allergen later.
 - The allergen binds to mast cells.
 - Mast cells release histamine, causing irritation, itchy skin, and tears.





Later exposure to the same allergen

Allergies are overreactions to certain environmental antigens

Antihistamines

- interfere with histamine's action,
- provide temporary relief, but
- often make people drowsy.

Anaphylactic shock

- is an extreme life-threatening allergic reaction and
- can be treated with injections of epinephrine.

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