Pathogens, agents that cause disease, infect a wide range of animals, including humans.

The immune system recognizes foreign bodies and responds with the production of immune cells and proteins.

All animals have innate immunity, a defense active immediately upon infection.

Vertebrates also have adaptive immunity.

Innate Immunity

Innate immunity is found in all animals and plants.

In vertebrates, innate immunity is a first response to infections and also serves as the foundation of adaptive immunity.

In insects, an exoskeleton made of chitin forms the first barrier to pathogens.

The digestive system is protected by a chitin-based barrier and lysozyme, an enzyme that breaks down bacterial cell walls.

Hemocytes circulate within hemolymph and carry out phagocytosis, the ingestion and digestion of foreign substances including bacteria.

Hemocytes also secrete antimicrobial peptides that disrupt the plasma membranes of fungi and bacteria.

Innate Immunity - Vertebrates

The immune system of mammals is the best understood of the vertebrates.

Innate defenses include barrier defenses, phagocytosis, antimicrobial peptides.

Additional defenses are unique to vertebrates: natural killer cells, interferons, and the inflammatory response.

Barrier Defenses

Barrier defenses include the skin and mucous membranes of the respiratory, urinary, and reproductive tracts.
• Mucus traps and allows for the removal of microbes
• Many body fluids including saliva, mucus, and tears are hostile to many microbes
• The low pH of skin and the digestive system prevents growth of many bacteria
• A white blood cell engulfs a microbe, then fuses with a lysosome to destroy the microbe
• There are different types of phagocytic cells
  – **Neutrophils** engulf and destroy pathogens
  – **Macrophages** are found throughout the body
  – **Dendritic cells** stimulate development of adaptive immunity
  – **Eosinophils** discharge destructive enzymes
• Cellular innate defenses in vertebrates also involve **natural killer cells**
• These circulate through the body and detect abnormal cells
• They release chemicals leading to cell death, inhibiting the spread of virally infected or cancerous cells
• Many cellular innate defenses involve the lymphatic system
• **Antimicrobial Peptides & Proteins**
• Peptides and proteins function in innate defense by attacking pathogens or impeding their reproduction
• **Interferon** proteins provide innate defense, interfering with viruses and helping activate macrophages
• About 30 proteins make up the **complement system**, which causes lysis of invading cells and helps trigger inflammation
• **Inflammatory responses**
• The **inflammatory response**, such as pain and swelling, is brought about by molecules released upon injury of infection
• **Mast cells**, a type of connective tissue, release **histamine**, which triggers blood vessels to dilate and become more permeable
• Activated macrophages and neutrophils release **cytokines**, signaling molecules that enhance the immune response
  – *Pus*, a fluid rich in white blood cells, dead pathogens, and cell debris from damaged tissues
  – Inflammation can be either local or systemic (throughout the body)
• Fever is a systemic inflammatory response triggered by pyrogens released by macrophages and by toxins from pathogens
• **Septic shock** is a life-threatening condition caused by an overwhelming inflammatory response
• **Adaptive Immunity**
  • The adaptive response relies on two types of **lymphocytes**, or white blood cells
  • Lymphocytes that mature in the **thymus** above the heart are called **T cells**, and those that mature in bone marrow are called **B cells**
• **Antigens** are substances that can elicit a response from a B or T cell
  • Exposure to the pathogen activates B and T cells with **antigen receptors** specific for parts of that pathogen
  • The small accessible part of an antigen that binds to an antigen receptor is called an **epitope**
  • Binding of a B cell antigen receptor to an antigen is an early step in B cell activation
  • This gives rise to cells that secrete a soluble form of the protein called an **antibody** or **immunoglobulin (Ig)**
• Secreted antibodies are similar to B cell receptors but lack transmembrane regions that anchor receptors in the plasma membrane
• **T cells**
  • Each T cell receptor consists of two different polypeptide chains (called α and β)
  • The tips of the chain form a variable (V) region; the rest is a constant (C) region
  • T cell and B cell antigen receptors are functionally different
  • T cells bind to antigen fragments displayed or presented on a host cell
• These antigen fragments are bound to cell-surface proteins called MHC molecules

• **MHC (major histocompatibility complex)** molecules are host proteins that display the antigen fragments on the cell surface

• The adaptive immune system has four major characteristics
  – Diversity of lymphocytes and receptors
  – Self-tolerance; lack of reactivity against an animal’s own molecules
  – B and T cells proliferate after activation
  – Immunological memory

• Generation of B & T cell diversity

• By combining variable elements, the immune system assembles a diverse variety of antigen receptors

• The immunoglobulin (Ig) gene encodes one chain of the B cell receptor

• Many different chains can be produced from the same gene by rearrangement of the DNA

• Rearranged DNA is transcribed and translated and the antigen receptor formed

• Immunological Memory

• Immunological memory is responsible for long-term protections against diseases, due to either a prior infection or vaccination

• The first exposure to a specific antigen represents the **primary immune response**

• During this time, selected B and T cells give rise to their effector forms

• In the **secondary immune response**, memory cells facilitate a faster, more efficient response

• Two branches of acquired immunity

• Acquired immunity has two branches: the humoral immune response and the cell-mediated immune response
• In the **humoral immune response** antibodies help neutralize or eliminate toxins and pathogens in the blood and lymph

• In the **cell-mediated immune response** specialized T cells destroy affected host cells

• A type of T cell called a **helper T cell** triggers both the humoral and cell-mediated immune responses

• Signals from helper T cells initiate production of antibodies that neutralize pathogens and activate T cells that kill infected cells

• **Antigen-presenting cells** have class I and class II MHC molecules on their surfaces

• **Cytotoxic T Cells**

• **Cytotoxic T cells** are the effector cells in the cell-mediated immune response

• Cytotoxic T cells recognize fragments of foreign proteins produced by infected cells and possess an accessory protein that binds to class I MHC molecules

• The activated cytotoxic T cell secretes proteins that disrupt the membranes of target cells and trigger apoptosis

• **Antibody function**

• Antibodies do not kill pathogens; instead they mark pathogens for destruction

• In neutralization, antibodies bind to viral surface proteins preventing infection of a host cell

• Antibodies may also bind to toxins in body fluids and prevent them from entering body cells

• B cells can express five different forms (or classes) of immunoglobulin (Ig) with similar antigen-binding specificity but different heavy chain C regions
  
  – IgD: Membrane bound
  – IgM: First soluble class produced
  – IgG: Second soluble class; most abundant
  – IgA and IgE: Remaining soluble classes

• **Active & Passive immunization**
• **Active immunity** develops naturally when memory cells form clones in response to an infection

• It can also develop following immunization, also called vaccination

• In immunization, a nonpathogenic form of a microbe or part of a microbe elicits an immune response to an immunological memory

• **Passive immunity** provides immediate, short-term protection

• It is conferred naturally when IgG crosses the placenta from mother to fetus or when IgA passes from mother to infant in breast milk

• It can be conferred artificially by injecting antibodies into a nonimmune person

• Immune Rejection

• Cells transferred from one person to another can be attacked by immune defenses

• This complicates blood transfusions or the transplant of tissues or organs

• Blood Groups

• Antigens on red blood cells determine whether a person has blood type A (A antigen), B (B antigen), AB (both A and B antigens), or O (neither antigen)

• Antibodies to nonself blood types exist in the body

• Transfusion with incompatible blood leads to destruction of the transfused cells

• Recipient-donor combinations can be fatal or safe

• Allergies

• Allergies are exaggerated (hypersensitive) responses to antigens called allergens

• In localized allergies such as hay fever, IgE antibodies produced after first exposure to an allergen attach to receptors on mast cells

• Autoimmune diseases

• In individuals with autoimmune diseases, the immune system loses tolerance for self and turns against certain molecules of the body
• Autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, insulin-dependent diabetes mellitus, and multiple sclerosis

• Exercise and Immunity
  • Moderate exercise improves immune system function
  • Psychological stress has been shown to disrupt immune system regulation by altering the interactions of the hormonal, nervous, and immune systems
  • Sufficient rest is also important for immunity

• HIV – autoimmune disease
  • Human immunodeficiency virus (HIV) infects helper T cells
  • The loss of helper T cells impairs both the humoral and cell-mediated immune responses and leads to AIDS
  • HIV eludes the immune system because of antigenic variation and an ability to remain latent while integrated into host DNA
  • People with AIDS are highly susceptible to opportunistic infections and cancers that take advantage of an immune system in collapse
  • The spread of HIV is a worldwide problem
  • The best approach for slowing this spread is education about practices that transmit the virus

• Cancer & Immunity
  • The frequency of certain cancers increases when adaptive immunity is impaired
  • 20% of all human cancers involve viruses
  • The immune system can act as a defense against viruses that cause cancer and cancer cells that harbor viruses
  • In 2006, a vaccine was released that acts against human papillomavirus (HPV), a virus associated with cervical cancer