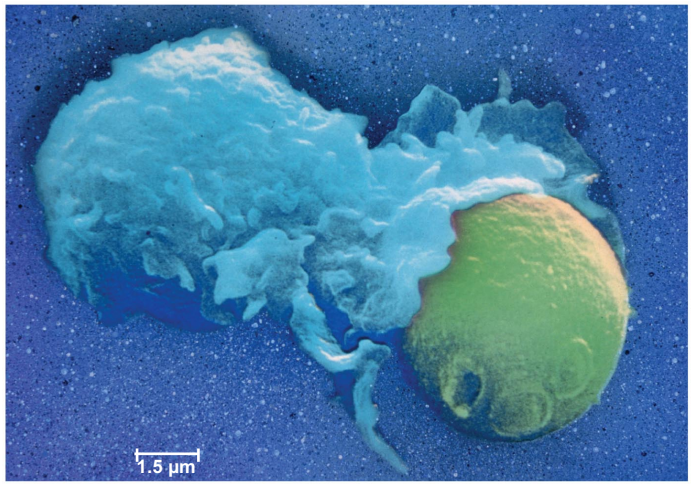
Overview: Reconnaissance, Recognition, and Response

- Barriers help an animal to defend itself from the many dangerous **pathogens** it may encounter.
- The **immune system** *recognizes* foreign bodies = *"not self"* and *responds* with the production of immune cells and proteins.
- Two major kinds of defense have evolved: ***innate immunity*** and ***acquired immunity***.

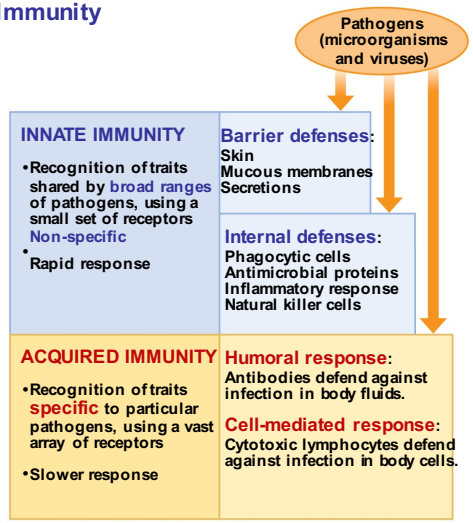
How do immune cells of animals recognize foreign cells?



- **Innate immunity** is present before any exposure to pathogens and is effective from the time of birth.
- It involves *nonspecific* responses to pathogens.
- Innate immunity consists of *external barriers* plus *internal cellular* and *chemical defenses*.

- **Acquired immunity** = adaptive immunity, develops *after exposure* to agents such as microbes, toxins, or other foreign substances.
- It involves a very specific response to pathogens.

Animal Immunity



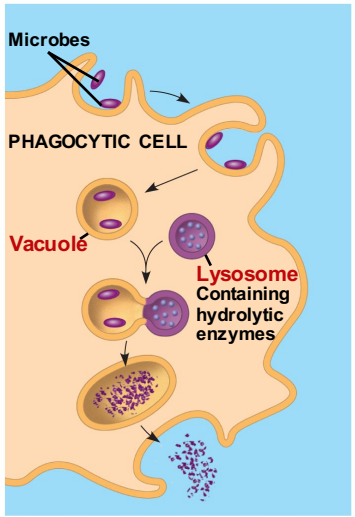
For Innate Immunity, recognition and response rely on shared traits of pathogens

- Both invertebrates and vertebrates depend on innate immunity to fight infection. Vertebrates also develop acquired immune defenses.
- The immune system recognizes bacteria and fungi by structures on their cell walls.
- An immune response varies with the class of pathogen encountered.

Innate Immunity of Invertebrates

- In insects, an exoskeleton made of chitin forms the first barrier to pathogens.
- The digestive system is protected by low pH and **lysozyme**, an enzyme that digests microbial 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 bacteria.

Phagocytosis



Innate Immunity Defenses of 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: the ***inflammatory response*** and ***natural killer cells***.

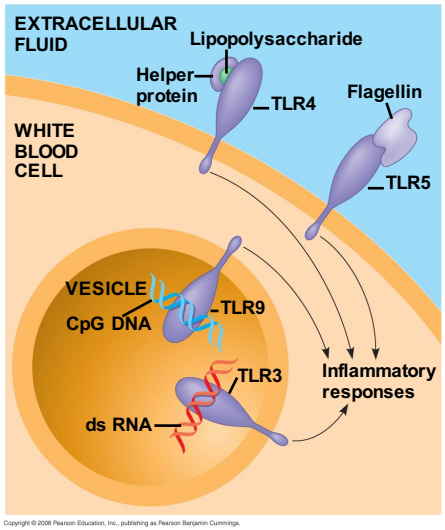
Barrier Defenses

- ***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 microbes.
- The ***low pH*** of skin and the digestive system prevents growth of microbes.

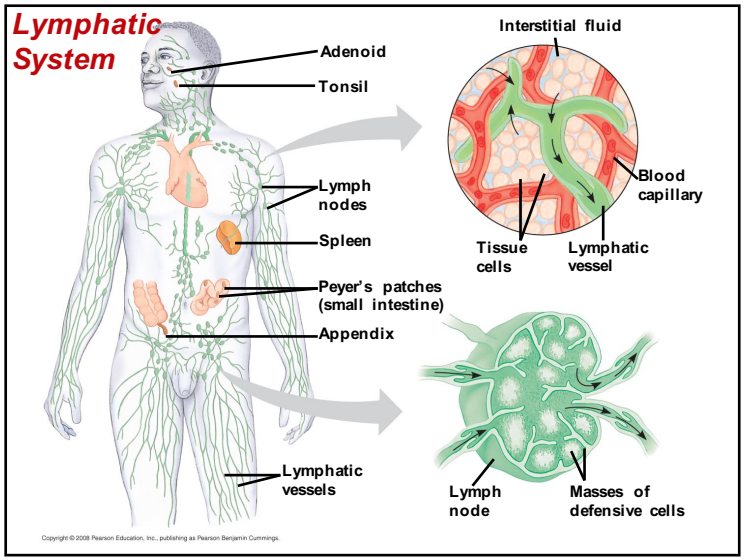
Cellular Innate Defenses

- *White blood cells* = ***leukocytes*** engulf pathogens in the body via *phagocytosis*.
- Groups of pathogens are recognized by **TLR**, **Toll-like receptors.**

TLR signaling



- 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 microbes.
  - **Macrophages** are part of the *lymphatic system* and are found throughout the body.
  - **Eosinophils** discharge *destructive enzymes*.
  - **Dendritic cells** stimulate development of *acquired immunity*.



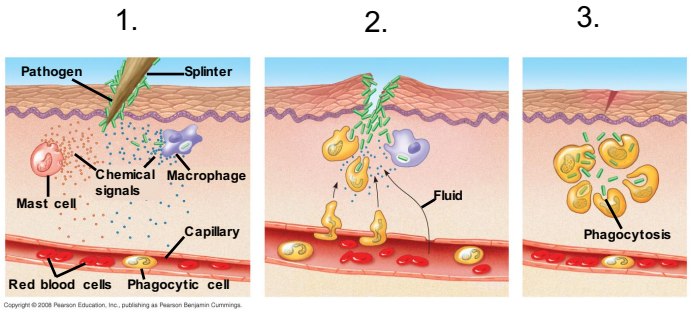
Antimicrobial Peptides and Proteins

- *Peptides* and *proteins* function in *innate defense* by *attacking microbes directly* or *impeding their reproduction*.
- ***Interferon*** proteins provide innate defense against *viruses* and help activate macrophages.
- About 30 proteins make up the ***complement system***, which causes *lysis* of invading cells and helps trigger inflammation.

Inflammatory Responses

- Following an injury, ***mast cells*** release ***histamine***, which promotes changes in *blood vessels*; this is part of the **inflammatory response.**
- These changes *increase local blood supply* and allow more phagocytes and antimicrobial proteins to enter tissues.
- *Pus* = a fluid rich in white blood cells, dead microbes, and cell debris, accumulates at the site of inflammation.

Major events in a local Inflammatory Response



- Inflammation can be either local or systemic (throughout the body).
- Fever is a systemic inflammatory response triggered by pyrogens released by macrophages, and toxins from pathogens.
- *Septic shock* is a life-threatening condition caused by an *overwhelming inflammatory response*.

Natural Killer Cells

- All body cells (except red blood cells) have a class I MHC protein on their surface.
- **MHC = Major Histocompatibility Complex** , part of the extracellular matrix.
- Class II MHC protein molecules are found on specialized cells
- Cancerous or infected cells no longer express this MHC protein; **natural killer (NK) cells** attack these damaged cells.

Innate Immune System Evasion by Pathogens

- Some pathogens avoid destruction by modifying their surface to prevent recognition or by resisting breakdown following phagocytosis.
- Tuberculosis (TB) is one such disease and kills more than a million people a year.

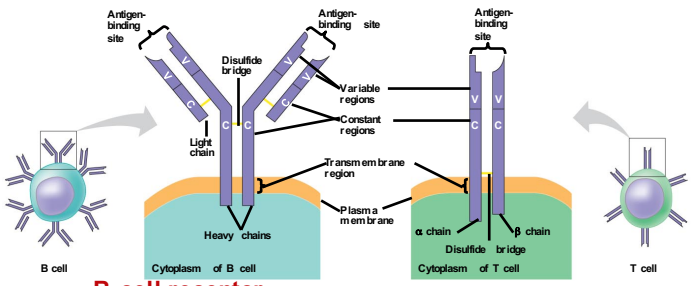
In Acquired Immunity, lymphocyte receptors provide pathogen-specific recognition

- White blood cells called ***lymphocytes*** recognize and respond to antigens, foreign molecules.
- Lymphocytes that *mature in* the *thymus* above the heart are called ***T cells***, and those that *mature in bone marrow* are called ***B cells***.
- Lymphocytes contribute to immunological memory, an enhanced response to a foreign molecule encountered previously.
- **Cytokines** are secreted by macrophages and dendritic cells to recruit and activate lymphocytes.

Acquired Immunity = Active Immunity: *Specific*

- B cells and T cells have receptor proteins that can bind to foreign molecules.
- Each individual lymphocyte is specialized to recognize a **specific** type of molecule.
- An **antigen** is any foreign molecule to which a lymphocyte responds.
- A single B cell or T cell has about 100,000 identical **antigen receptors**.

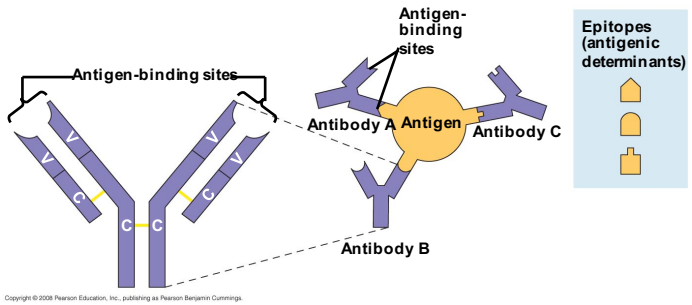
Antigen receptors on lymphocytes



B cell receptor **T cell receptor**

- All antigen receptors on a single lymphocyte recognize the same ***epitope***, or *antigenic determinant*, on an antigen.
- B cells give rise to **plasma cells**, which secrete proteins called **antibodies** or **immunoglobulins**.

Epitopes = antigen determinants



The Antigen Receptors of B Cells and T Cells

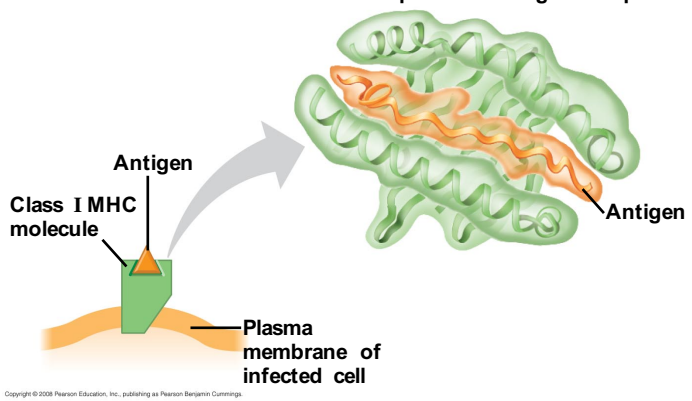
- **B cell receptors** bind to **specific**, intact antigens.
- The B cell receptor consists of two identical **heavy chains** and two identical **light chains.**
- The tips of the chains form a *constant (C) region*, and each chain contains a *variable (V) region*, so named because its amino acid sequence varies extensively from one B cell to another.
- *Secreted **antibodies**, or **immunoglobulins**, are structurally similar to B cell receptors* but lack transmembrane regions that anchor receptors in the plasma membrane.

- Each **T cell receptor** consists of two different polypeptide chains. The tips of the chain form a variable (V) region; the rest is a constant (C) region.
- *T cells can bind to an antigen that is free or on the surface of a pathogen*.
- T cells bind to *antigen fragments presented on a host cell*. These antigen fragments are *bound to cell-surface proteins called MHC* molecules.
- **MHC** molecules are so named because they are encoded by a family of genes (many unique / specific) called the **Major Histocompatibility Complex.**

The Role of the MHC

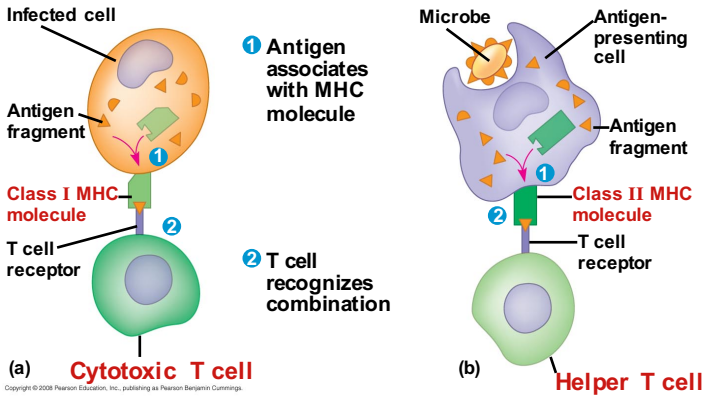
- In infected cells, *MHC molecules* bind and transport antigen fragments to the cell surface, a process called ***antigen presentation*.**
- A nearby *T cell can then detect* the antigen fragment displayed on the cell's surface.
- Depending on their source, peptide antigens are handled by different classes of MHC molecules.

Antigen Presentation by an MHC molecule



- **Class I MHC molecules** are found on almost *all nucleated cells* of the body.
- They display peptide antigens to **cytotoxic T cells.**
- **Class II MHC molecules** are found on *specialized cells*: macrophages, B cells, and activated T cells…

Interaction of T cells with Antigen-Presenting Cells



- **Class II MHC molecules** are located mainly on dendritic cells, macrophages, and B cells.
- Dendritic cells, macrophages, and B cells are **antigen-presenting cells** that display antigens on their surface to cytotoxic T cells and **helper T cells.**

Lymphocyte Development

- The ***acquired immune system*** has three important properties:
  - *Receptor Diversity*
  - *Lack of reactivity against host cells*
  - *Immunological Memory*

Generation of Lymphocyte Diversity by Gene Rearrangement

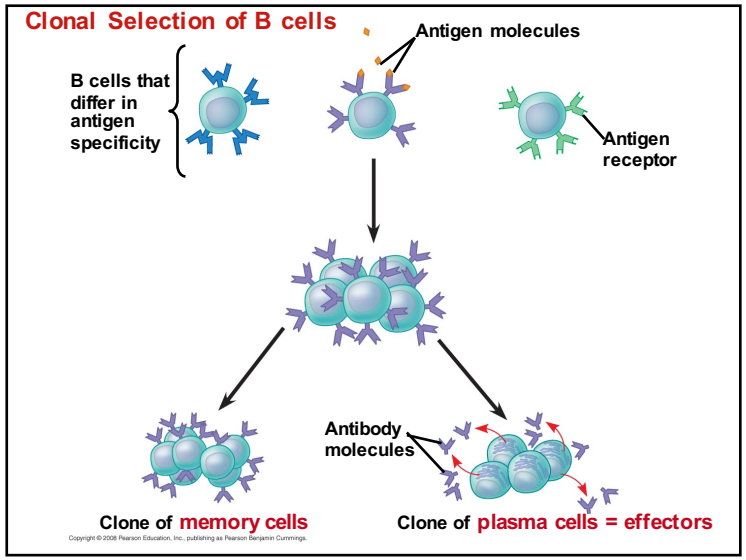
- Differences in the *variable region* account for *specificity of antigen receptors*.
- The *immunoglobulin* (*Ig*) gene encodes one chain of the B cell receptor.
- Many *different chains* can be produced from the same Ig chain gene by rearrangement of the DNA.
- *Rearranged DNA* is transcribed and translated and the antigen receptor formed.

Origin of Self-Tolerance

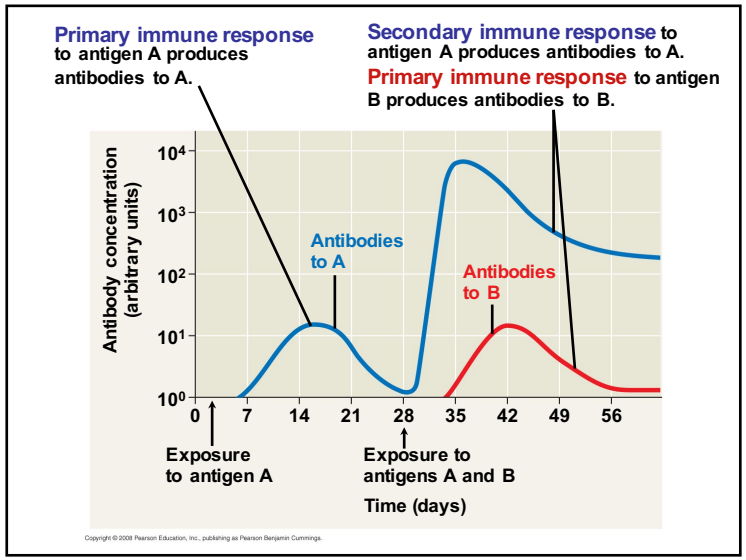
- Antigen receptors are generated by random rearrangement of DNA.
- As lymphocytes mature in bone marrow or the thymus, they are tested for self-reactivity.
- *Lymphocytes with receptors specific for the body's own molecules are destroyed* by apoptosis, or rendered nonfunctional.

Amplifying Lymphocytes by Clonal Selection

- In the body there are few lymphocytes with antigen receptors for any particular epitope.
- The binding of a mature lymphocyte to an antigen induces the lymphocyte to divide rapidly.
- This proliferation of lymphocytes is called **clonal selection**.
- Two types of clones are produced: short-lived activated **effector cells** *(fight current battle)* and long-lived **memory cells**… *for future attacks by same pathogen*.

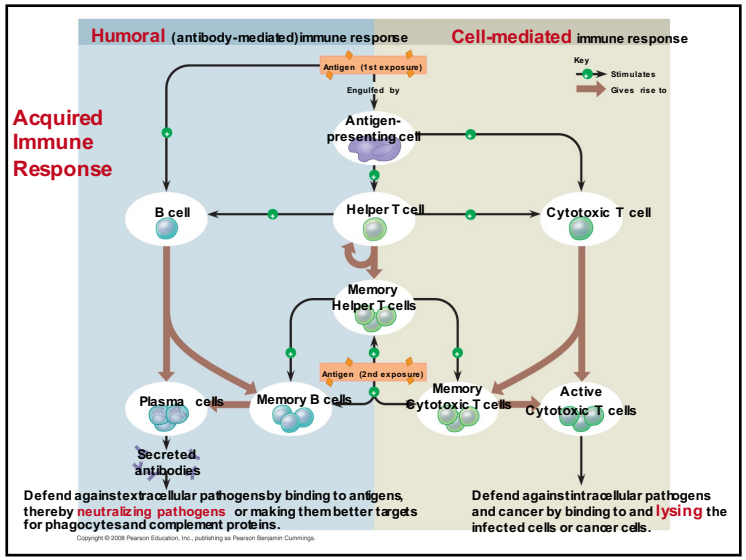


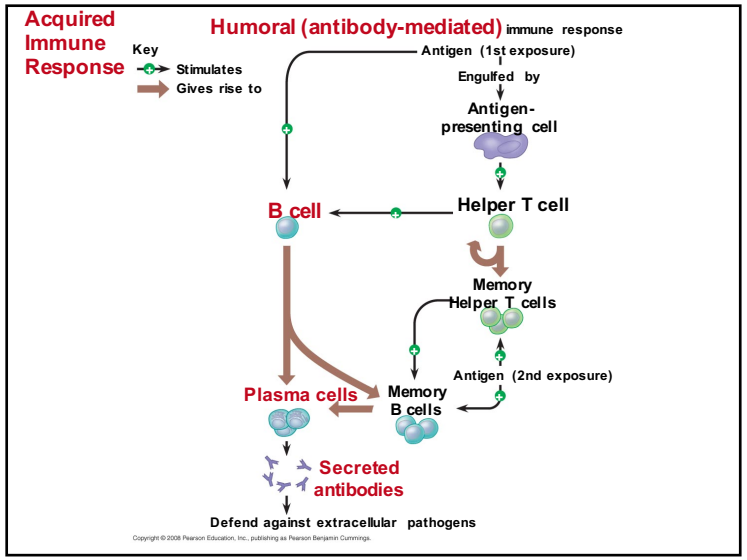
- The first exposure to a specific antigen represents the **primary immune response.**
- During this time, effector B cells = **plasma cells** are generated, and T cells are activated to their effector forms.
- In the **secondary immune response** = memory cells facilitate a *faster*, more efficient response.

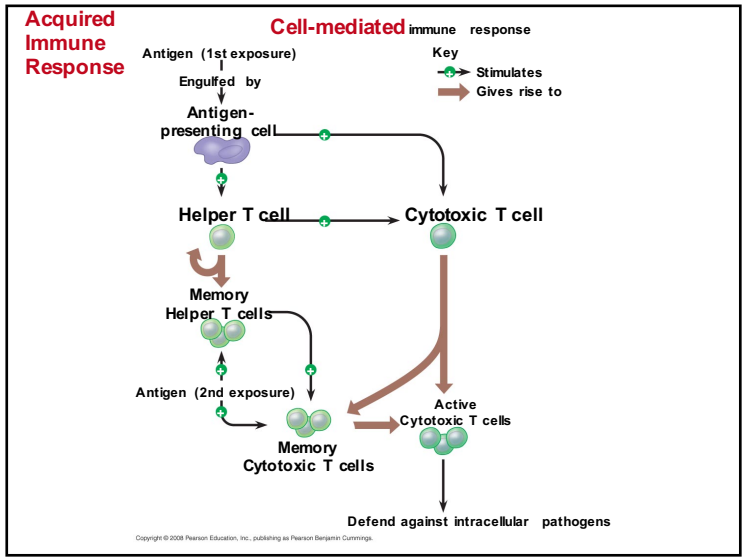


Acquired immunity defends against infection of body cells and fluids

- Acquired immunity has two branches: the humoral immune response and the cell-mediated immune response.
- **Humoral immune response** involves activation and clonal selection of ***B cells***, resulting in production of secreted ***antibodies***.
- **Cell-mediated immune response** involves activation and clonal selection of ***cytotoxic T*** cells.
- *Helper T cells aid both responses*.



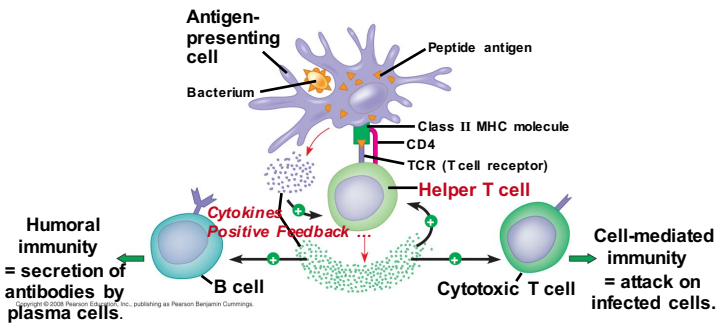




Helper T Cells: Respond to Nearly All Antigens

- A ***surface protein*** called ***CD4*** binds the class II MHC molecule.
- This *binding* keeps the *helper T cell* joined to the *antigen-presenting cell* while activation occurs.
- Activated helper T cells *secrete cytokines* that stimulate other lymphocytes.
- ***Positive Feedback in the Immune System enhances the process until some endpoint or maximum rate is reached.***

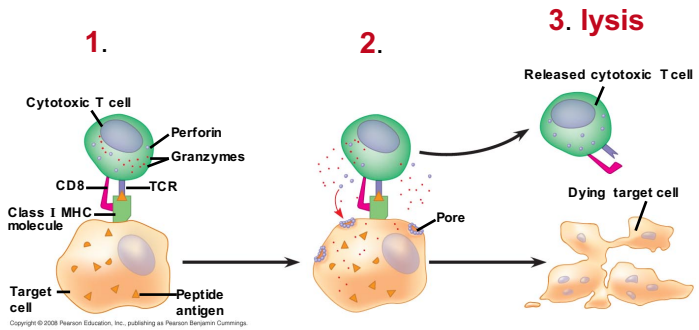
The central role of helper T cells in humoral and cell-mediated immune responses



Cytotoxic T Cells: A Response to Infected Cells

- Cytotoxic T cells are the effector cells in cell-mediated immune response.
- Cytotoxic T cells make **CD8**, a surface protein that greatly enhances interaction between a target cell and a cytotoxic T cell.
- Binding to a class I MHC complex on an infected cell activates a cytotoxic T cell and makes it an active killer.
- The *activated cytotoxic T cell secretes proteins that destroy the infected target cell*.

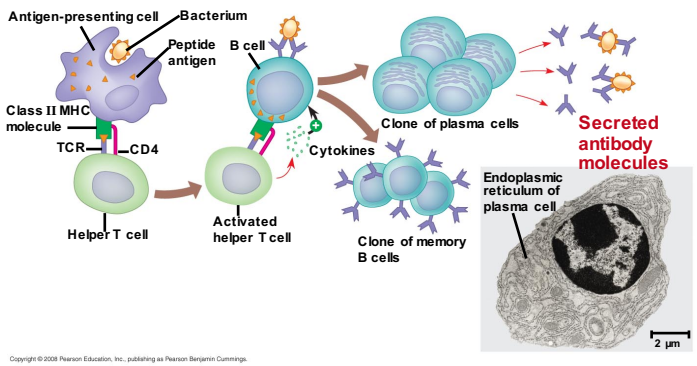
The killing action of cytotoxic T cells



B Cells: A Response to Extracellular Pathogens

- The humoral response is characterized by secretion of antibodies by B cells.
- Activation of B cells is aided by cytokines and antigen binding to helper T cells.
- *Clonal selection of B cells generates antibody-secreting plasma cells, the effector cells of humoral immunity.* ***Positive Feedback ...***

B cell activation in the humoral immune response

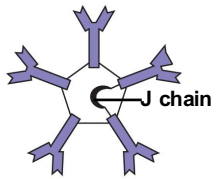


Antibody Classes

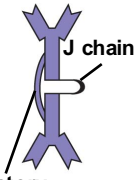
- The ***five major classes of antibodies***, or immunoglobulins, differ in distribution and function.
- *Polyclonal antibodies* are the products of many different clones of B cells following exposure to a microbial antigen.
- *Monoclonal antibodies* are prepared from a single clone of B cells grown in culture.

The five antibody, or immunoglobulin (Ig), classes

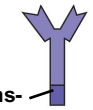
Class of Immuno-globulin (Antibody)	Distribution	Function
IgM (pentamer) 	First Ig class produced after initial exposure to antigen; then its concentration in the blood declines	Promotes neutralization and cross-linking of antigens; very effective in complement system activation
IgG (monomer) 	Most abundant Ig class in blood also present in tissue fluids	Promotes opsonization, neutralization, and cross-linking of antigens; less effective in activation of complement system than IgM Only Ig class that crosses placenta, thus conferring passive immunity on fetus
IgA (dimer) 	Present in secretions such as tears, saliva, mucus, and breast milk	Provides localized defense of mucous membranes by cross-linking and neutralization of antigens Presence in breast milk confers passive immunity on nursing infant
IgE (monomer) 	Present in blood at low concentrations	Triggers release from mast cells and basophils of histamine and other chemicals that cause allergic reactions
IgD (monomer) 	Present primarily on surface of B cells that have not been exposed to antigens	Acts as antigen receptor in the antigen-stimulated proliferation and differentiation of B cells (clonal selection)

Class of Immuno-globulin (Antibody)	Distribution	Function
IgM (pentamer) 	First Ig class produced after initial exposure to antigen; then its concentration in the blood declines	Promotes neutralization and cross-linking of antigens; very effective in complement system activation

Class of Immunoglobulin (Antibody)	Distribution	Function
IgG (monomer) 	Most abundant Ig class in blood; also present in tissue fluids	Promotes opsonization, neutralization, and cross-linking of antigens; less effective in activation of complement system than IgM Only Ig class that crosses placenta, thus conferring passive immunity on fetus

Class of Immunoglobulin (Antibody)	Distribution	Function
IgA (dimer) 	Present in secretions such as tears, saliva, mucus, and breast milk	Provides localized defense of mucous membranes by cross-linking and neutralization of antigens Presence in breast milk confers passive immunity on nursing infant

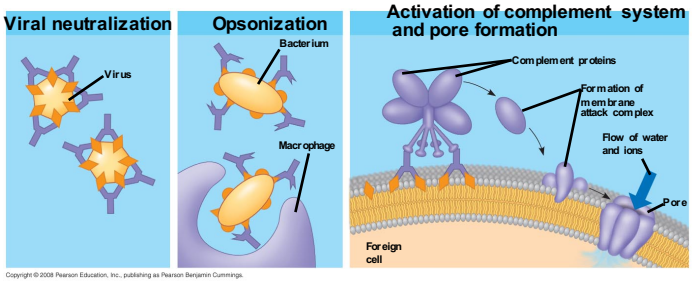
Class of Immunoglobulin (Antibody)	Distribution	Function
IgE (monomer) 	Present in blood at low concentrations	Triggers release from mast cells and basophils of histamine and other chemicals that cause allergic reactions

Class of Immunoglobulin (Antibody)	Distribution	Function
IgD (monomer) 	Present primarily on surface of B cells that have not been exposed to antigens	Acts as antigen receptor in the antigen-stimulated proliferation and differentiation of B cells (clonal selection)

The Role of Antibodies in Immunity

- ***Neutralization*** *occurs when a pathogen can no longer infect a host because it is bound to an antibody*.
- *Opsonization* occurs when antibodies bound to antigens *increase phagocytosis*.
- Antibodies together with proteins of the complement system generate a *membrane attack complex* and *cell lysis*.

Antibody-mediated mechanisms of antigen disposal



Active Immunization

- ***Active immunity*** develops naturally in *response to an infection*.
- It can *also* develop following/ *from* **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

- ***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 *also* be conferred *artificially by injecting antibodies* into a nonimmune person.

Passive immunization of an infant occurs during breast-feeding

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.
- MHC molecules are different among genetically nonidentical individuals.
- Differences in MHC molecules stimulate rejection of tissue grafts and organ transplants.

- Chances of *successful transplantation* increase if *donor and recipient MHC tissue types* are *well matched*.
- Immunosuppressive drugs facilitate transplantation.
- Lymphocytes in bone marrow transplants may cause the donor tissue to reject the recipient.

Blood Groups

- *Antigens on red blood cells surface* 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.

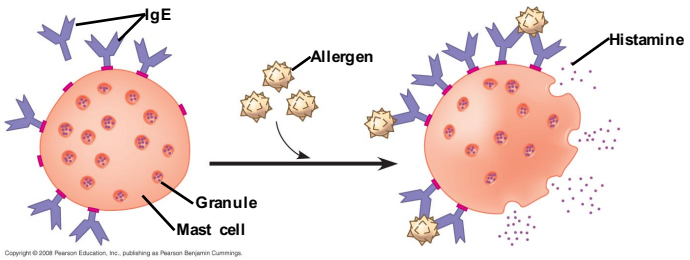
Disruption in immune system function can elicit or exacerbate disease

- Some pathogens have evolved to diminish the effectiveness of host immune responses.
- If the delicate balance of the immune system is disrupted, effects range from minor to often fatal.

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.

Mast cells, IgE, and the allergic response

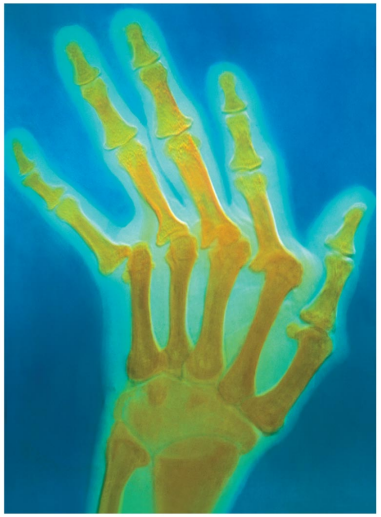


- The next time the allergen enters the body, it binds to mast cell–associated IgE molecules.
- *Mast cells release histamine and other mediators that cause vascular changes leading to typical allergy symptoms*.
- An acute allergic response can lead to anaphylactic shock, a life-threatening reaction that can occur within seconds of allergen exposure.

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.

X-ray of a hand deformed by rheumatoid arthritis



Exertion, Stress, and the Immune System

- Moderate exercise improves immune system function.
- Psychological stress has been shown to disrupt hormonal, nervous, and immune systems.

Immunodeficiency Diseases

- Inborn **immunodeficiency** results from hereditary or developmental defects that prevent proper functioning of innate, humoral, and/or cell-mediated defenses.
- Acquired immunodeficiency results from exposure to chemical and biological agents.
- **Acquired immunodeficiency syndrome (AIDS)** is caused by a virus.

Acquired Immune System Evasion by Pathogens

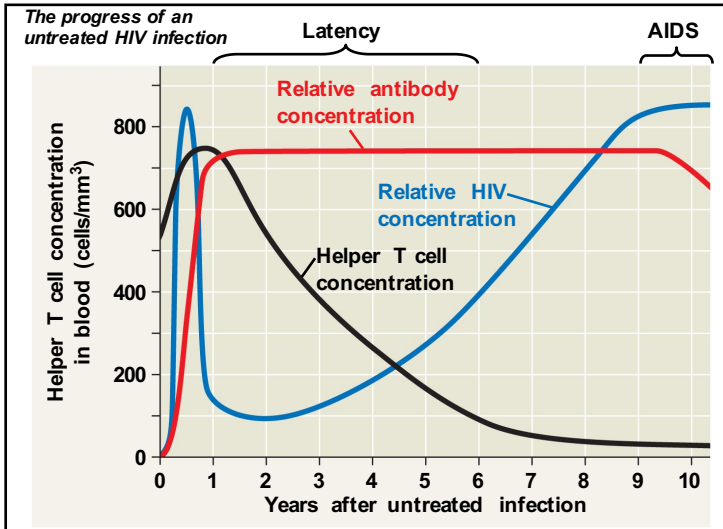
- Pathogens have evolved mechanisms to attack immune responses.
- Through antigenic variation, some pathogens are able to change epitope expression and prevent recognition.
- The human influenza virus mutates rapidly, and new flu vaccines must be made each year.
- Human viruses occasionally exchange genes with the viruses of domesticated animals.
- This poses a danger as human immune systems are unable to recognize the new viral strain.

Latency

- Some viruses may remain in a host in an inactive state called latency.
- Herpes simplex viruses can be present in a human host without causing symptoms.

Attack on the Immune System: HIV

- *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.*

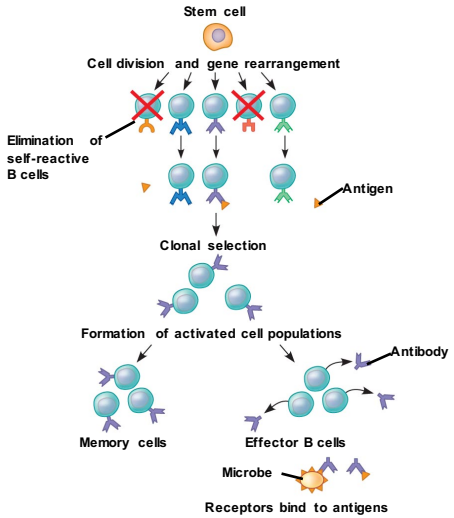


- People with AIDS are highly susceptible to opportunistic infections and cancers that take advantage of an immune system in collapse.
- The spread of HIV is a worldwide problem.
- The best approach for slowing this spread is education about practices that transmit the virus.

Cancer and Immunity

- The frequency of certain cancers increases when the immune response is impaired.
- Two suggested explanations are
  - Immune system normally suppresses cancerous cells
  - Increased inflammation increases the risk of cancer

Review



You should now be able to:

1. Distinguish between innate and acquired immunity.
2. Name and describe four types of phagocytic cells.
3. Describe the inflammation response.

4. Distinguish between the following pairs of terms: antigens and antibodies; antigen and epitope; B lymphocytes and T lymphocytes; antibodies and B cell receptors; primary and secondary immune responses; humoral and cell-mediated response; active and passive immunity.
5. Explain how B lymphocytes and T lymphocytes recognize specific antigens.
6. Explain why the antigen receptors of lymphocytes are tested for self-reactivity.

7. Describe clonal selection and distinguish between effector cells and memory cells.
8. Describe the cellular basis for immunological memory.
9. Explain how a single antigen can provoke a robust humoral response.
10. Compare the processes of neutralization and opsonization.

11. Describe the role of MHC in the rejection of tissue transplants.
12. Describe an allergic reaction, including the roles of IgE, mast cells, and histamine.
13. Describe some of the mechanisms that pathogens have evolved to thwart the immune response of their hosts.
14. List strategies that can reduce the risk of HIV transmission.