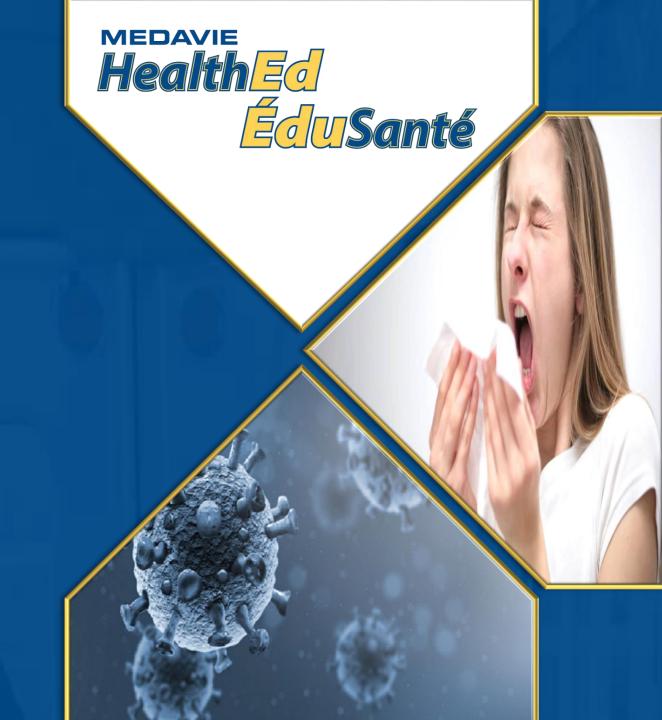
# **I**MMUNOLOGY

Primary Care Paramedicine

Module: 16

Section: 01





Immunology

## LYMPHATIC SYSTEM

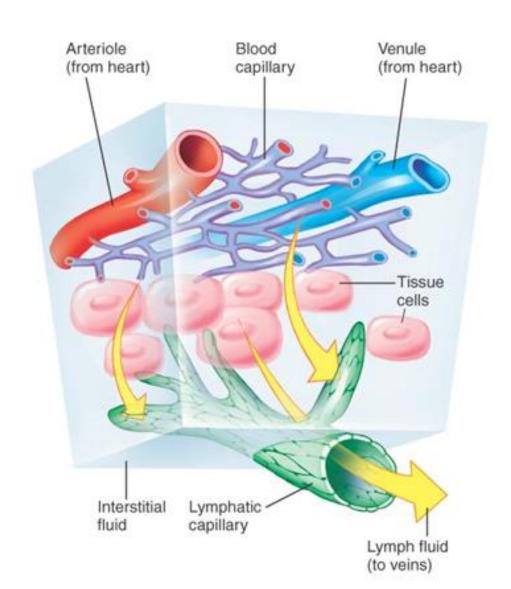


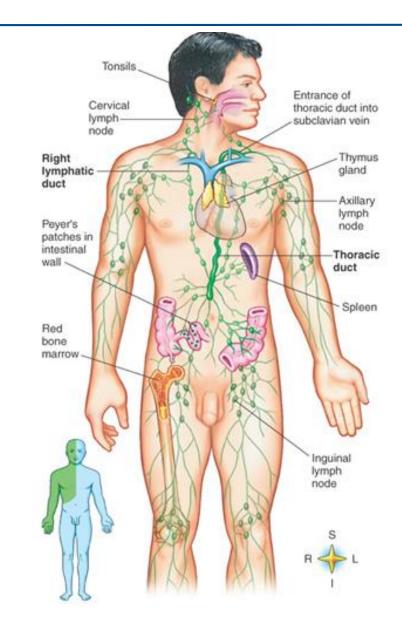


- Maintains fluid balance
- Immunity
- A specialized portion of the circulatory system
- Contains
  - Lymph (moving fluid)
  - Lymphatics (group of vessels)



# Lymphatic System









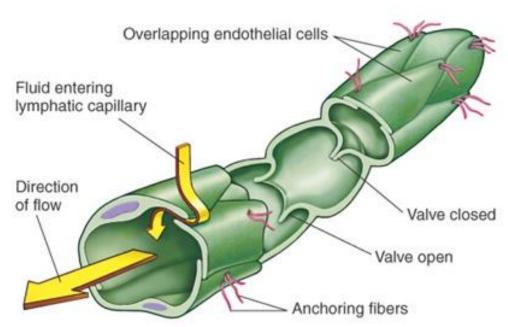
## Lymph

- Clear, watery fluid
- Results from fluid exiting circulation (c. 3000 ml daily)
- Is similar to interstitial fluid (is isotonic to)
  - Usual contains more proteins
- Most comes from the liver and small intestines (more then ½)



## Lymphatic System

- Lymphatic Vessels
  - Originate as lymphatic capillaries
  - Lie side by side of the blood capillaries
    - Thinner
    - Have more valves
    - Have nodes
  - Continues to merge to form major ducts
    - Right lymphatic duct
      - Upper right quadrant of body
    - Thoracic duct
      - Rest of body







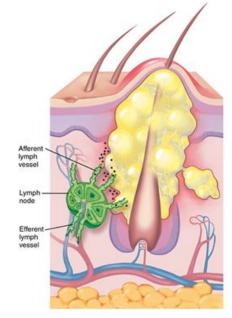
- Function of vessels
  - Permit particulate matter (which cannot be absorbed into capillary)
     to be removed from interstitial space

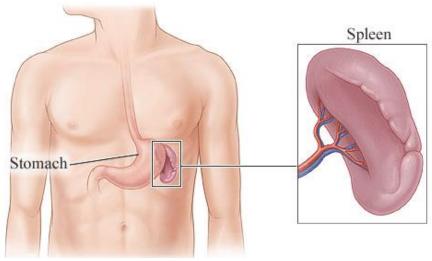
- Movement of fluid
  - Is uphill
  - Usually attributed to muscular movement



# Lymphatic System

- Lymph nodes
  - Have several lymph vessels entering into this "cellular hub"
    - One vessel leaving
  - Function
    - Defense
      - Filtration
      - Phagocytosis
    - Hematopiesis
      - Site of maturation of some cells
- Spleen
  - Large lymphoid organ
    - Monitors blood for infection
    - Filters out old erythrocytes and platelets







- A system that uses many mechanisms to ensure the integrity and survival of the internal environment.
- Two major categories:
  - Non-specific "innate" immunity
    - Ancient general defense system against common pattern elements found in pathogens
    - Able to attack the threat as soon as it is present
    - No memory
  - Specific "adaptive" immunity
    - Recognizes specific pathogens and remembers them
    - Slow to recognize targets and overcome the threat (especially first time exposure)





- The work of the system is completed by cells or substances created by cells
- Primary Type:

### Non-specific Immunity

- Neutrophils
- Monocytes
- Macrophages
- Natural Killer (NK) Cells

### **Specific Immunity**

- Lymphocytes
  - T-Cells
  - B-Cells



# Non-Specific Immunity

- Species resistance
  - Genetic characteristics to protect the body from certain pathogens
- Mechanical and chemical barriers
  - Skin and mucosa
    - A continuous wall that separates the internal environment from the external environment
  - Secretions
    - Sebum, mucus and enzymes chemically inhibit the activity of pathogens
- Inflammation
  - Isolates pathogens and stimulates the speedy arrival of large numbers of immune cells



## Non-Specific Immunity

## Phagocytosis

- Neutrophils
  - Granular leukocytes that are usually the first phagocytic cell to arrive due to the inflammatory response
- Macrophages
  - Monocytes that have enlarged to become phagocytic cells (may be called by other names when found in specific tissues)
- Dendritic Cells
  - Important bridge between innate and adaptive immune responses
  - Phagocytose pathogens in the tissues and carry them to lymph nodes for identification by T cells
- Natural Killer (NK) Cells
  - A group of lymphocytes that kill different types of cancer cells and virus infected cells





### Interferon

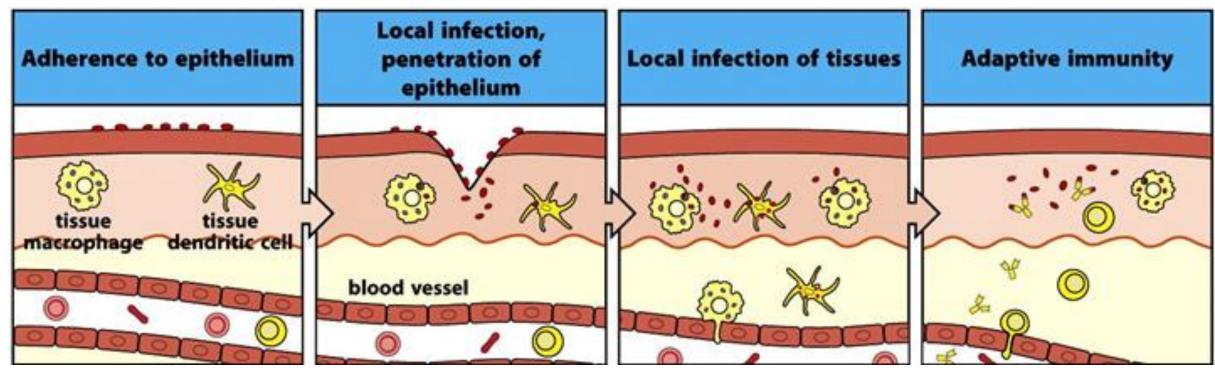
 Protein produced by cells after they become infected by a virus which inhibits further spread of the viral infection

## Complement

 Plasma proteins that produce a cascade of chemical reactions that cause lysis of foreign cells



## Immune System



**Physical Barriers** 

Innate non-specific Immunity

Adaptive specific Immunity





- Attack specific agents the body recognizes as "non-self"
- Adapts to pathogens and has a memory for future exposures
- Controlled by lymphocytes (a class of WBC)
- Lymphocytes are produced throughout life in the red bone marrow from the hematopoietic stem cells
- Develop into two major classes
  - B lymphocytes (B Cells)
    - Produce antibodies (antibody-mediated immunity)
  - T lymphocytes (T Cells)
    - Kill infected human cells or activate other cells to kill pathogens (cell-mediated immunity)



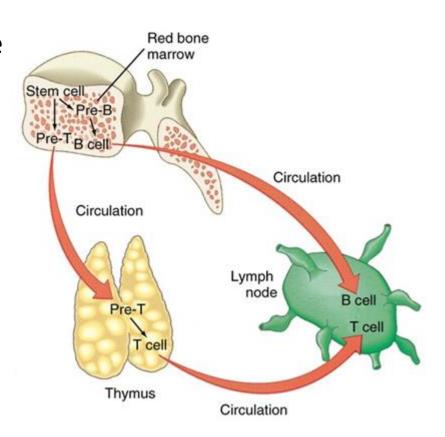
# Antibody-Mediated Immunity

#### Inactive B Cells

- Produced in the yolk sac, then the red marrow or the fetal liver
- Circulated to the lymph nodes and spleen

#### Activate B Cells

- When an inactive B cell encounters a specific antigen
- This binding triggers a series of mitotic divisions producing clones of B cells
- The clones can differentiate into plasma cells and secrete antibodies
- Others remain in the lymphatic system as memory cells and will become plasma cells if introduced to the antigen at another time

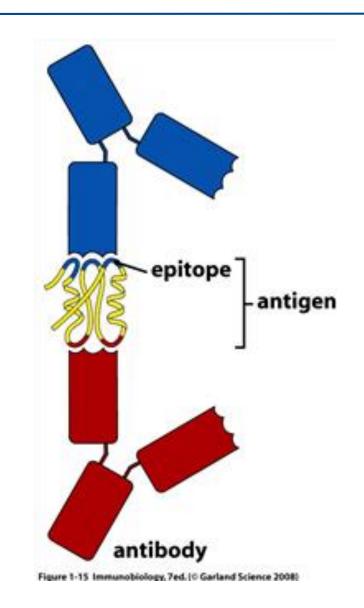




# Antibody-Mediated Immunity

## Antigen

- A substance that introduced to the body that induces the formation of antibodies
- Usually proteins located in the membranes of microorganisms or the outer coats of viruses
- Antigenic Determinants
  - Variously shaped, small regions on the surface of the antigen molecule (epitope)
  - Each kind of antigen has specific and uniquely shaped epitopes





# Antibody-Mediated Immunity

- Antibodies
  - Plasma proteins (Immunoglobulins) secreted by B cells
- Combining sites
  - Two small concave regions on the surface of the antibody
  - Like epitopes, have specific and unique shapes
  - Shaped to allow the epitope of the antigen fit into it and thereby bind to form a antigen-antibody complex
- Clone
  - The genetic descendant of a cell
- Complement
  - A group of proteins that work together to destroy foreign cells, can be activated by antibodies

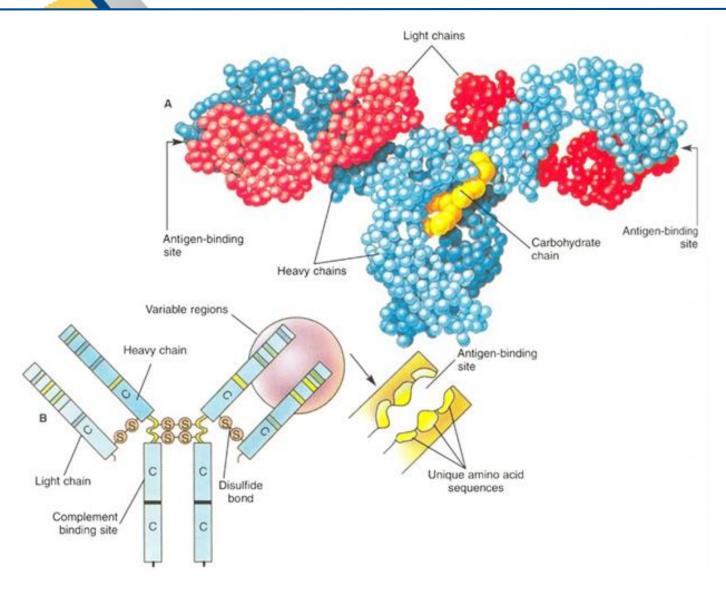




- Proteins of the Immunoglobulin family
- Large molecules composed of long chains of amino acids (polypeptides)
- Consists of four polypeptide chains
  - 2 Heavy
    - Twice as long and heavy
    - Has one variable and three constant regions
  - 2 Light
    - Has one variable and one constant region
- Formed to give a Y shape appearance
- Disulfide bonds join the 2 heavy chains to each other and their adjacent light chain
- Antigen-binding sites are located at the top of the variable regions
- Complement binding sites found in the constant regions

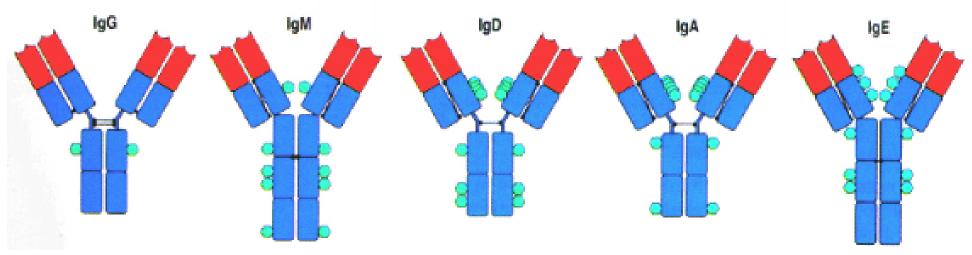


## **Antibodies**





## **Antibody Classes**



- IgM
  - Produced by immature B cells and inserted into plasma membranes
  - Predominate antibody produced after initial contact with an antigen
- IgG
  - Most abundant circulating antibody (75%)
  - Predominate in a secondary exposure
  - Cross the placenta barrier to provide natural passive immunity
- IgA
  - Found in the mucous membranes, in saliva, tears, and breastmilk

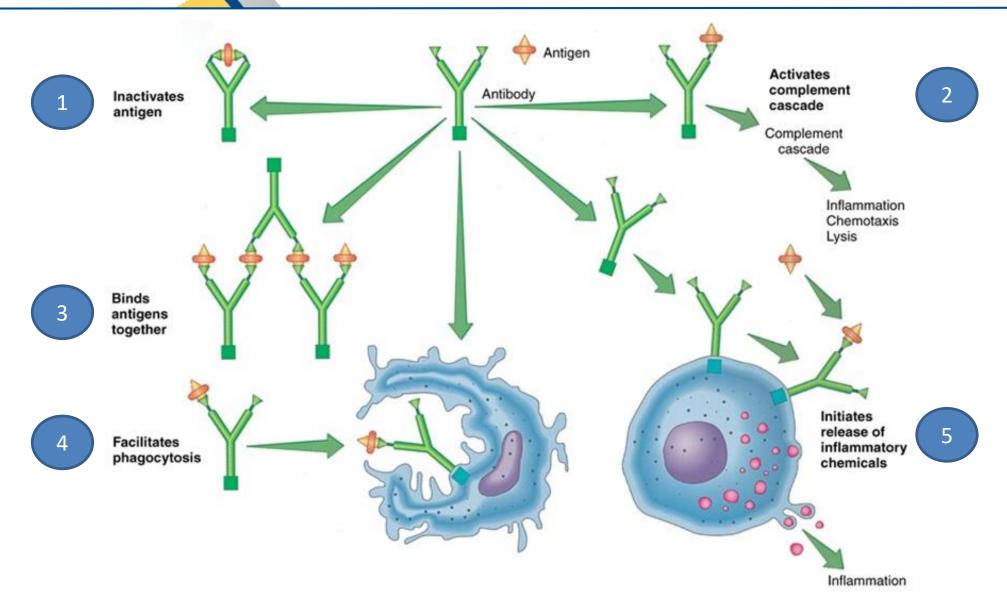
- IgE
  - Minor in amount
  - Can produce major effects (allergies)
- IgD
  - Found in blood in small amounts (unknown function)



- Function to produce antibody-mediated immunity (humoral immunity)
- Antigen-Antibody reactions
  - Antibodies distinguish self-antigen and nonself-antigens at the binding site
  - This binding causes 5 main outcomes:
    - Transforms toxins into nontoxic substances
    - Exposes the complement-binding sites initiating the complement reaction
    - Agglutinates antigens (clumps) for phagocytic disposal
    - Facilitates phagocytosis (provides a handle for the white blood cells)
    - Initiates release of inflammatory chemicals

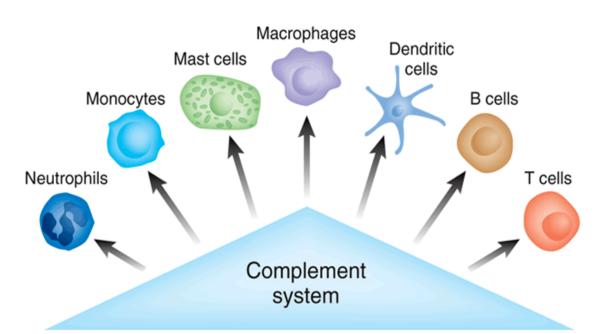


## Antibodies





## Antibodies



#### Innate immunity

Opsonization
Lysis of pathogens
Chemotaxis
Inflammation
Cell activation

#### Disposal system

Clearance of immune complexes and apoptotic cells

#### Adaptive immunity

Augmentation of antibody response
Promotion of T-cell response
Elimination of self-reactive B cells
Enhancement of immunologic memory

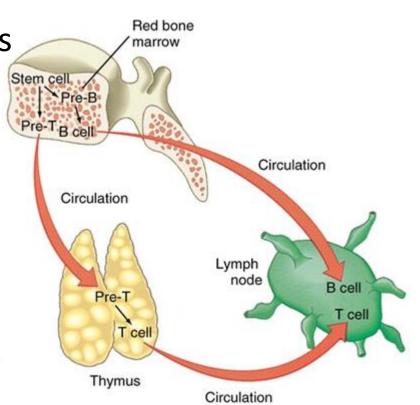
#### Complement

- Component of blood plasma
- Are inactive enzymes that are activated in a definitive sequence to catalyst a series of reactions
  - The reactions are produced as proteins react with the complement-binding site
  - Molecules produce by the reactions assemble on the surface of the foreign cell to form a donut-shaped structure
  - Water and ions are diffused into the cell and cause cytolysis
- Various complement proteins may produce other reactions
  - Vasodilatation in the invaded area
  - Attract Neutrophils and enhance phagocytosis



## Cell-Mediated Immunity

- T cells are lymphocytes that have passed through the thymus gland where they learn to distinguish between self and foreign antigens
- Pre-T cells are released from bone marrow
- Pre-T cells develop into thymocytes in the thymus
- Thymocytes are rapidly reproduced (can divide 3
  - 4 times a day)
- Once released into the blood from the thymus they locate in areas of the lymph nodes and spleen (T-dependant zones)
- Now they are T cells







- T cells have antigen receptor sites (T cell receptors) on their membrane
- Dendritic cells phagocytose pathogens in the tissues and present antigens to the T cell receptor on the T cell
- Binding activates (sensitizes) the T cell causing it to divide and produce clone cells (activated T cells)
- These T cells will be either:
  - Cytotoxic T cell
    - Kills infected or cancerous human cells on contact
  - Helper T cell
    - Helps B cells make antibodies and helps innate cells kill pathogens



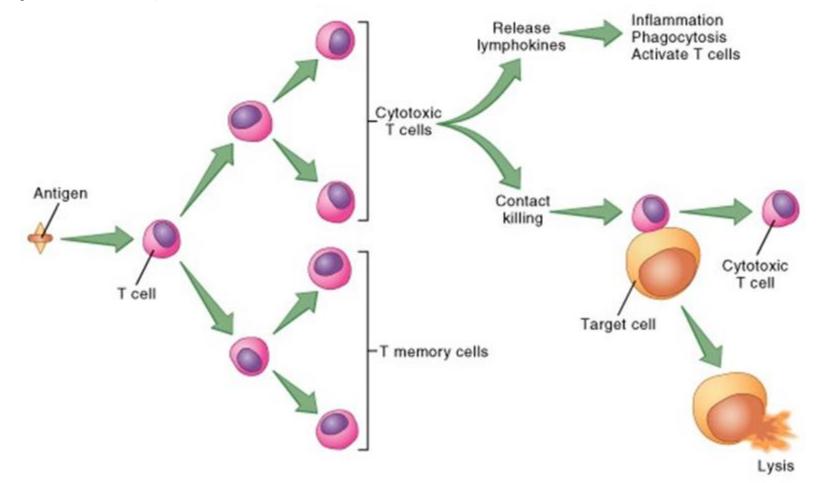


- T cells do not directly kill bacteria or viruses
  - Killer T cells kill virus infected human cells or cancer cells
  - Helper T cells help macrophages phagocytose bacteria
  - Helper T cells help B cells make antibodies to target bacteria or viruses for disposal





Killer (cytotoxic) T cells in action:





# Specific Immunity - Memory

- Some memory lymphocytes of each type (cytotoxic T cells, helper T cells, and B cells) can be saved for future encounters with the same pathogen
- This provides a memory for both:
  - Cell-mediated immunity
    - Memory Helper T cells
    - Memory Killer T cells
  - Antibody-mediated immunity
    - Memory B cells
- Innate immune cells (neutrophils, macrophages, and dendritic cells) don't have memory
- Immunologic memory is the principle that makes vaccination possible



# Specific Immunity

#### **Inherited Immunity**

Also known as Inborn Immunity

#### **Acquired Immunity**

- Natural (Exposure to the causative agent is not deliberate)
  - Active (exposure)
    - Exposure to infection (measles) and produces immunity
  - Passive (exposure)
    - Received from mother through the placenta barrier or through breast milk
- Artificial (Exposure is deliberate)
  - Active (exposure)
    - Vaccinations
  - Passive (exposure)
    - Antibodies that are produced by another immune system (e.g. Anti-venoms are typically horse or sheep antibodies that neutralize the venom toxins)



## Canadian Pediatric Society Routine Vaccine Schedule for healthy children and adolescents

Age:	Vaccines							
	DTaP/IPV	Hib Haemophilus influenza type b vaccine	MMR	HBV	dTap	VZV	PCV-7	MenC- conjugate
At 2 months	X	X		X			X (@ 2/3 mos)	X (@ 2/3 mos)
At 4 months	X	X		X			X (@ 4/5 mos)	X (@ 4/5 mos)
At 6 months	X	X		X			X (@ 6/7 mos)	X (@ 6/7 mos)
At 12 months			X			X	X (@12-15 mos)	
At 18 months	X	X	and X	or				
At age 4-6 years	X		or X	X 3 doses				
Teenage years				@ 0, 1 & 6 mos	dTap at 14-16 years			
Adult years				at any age	dT every 10 years			