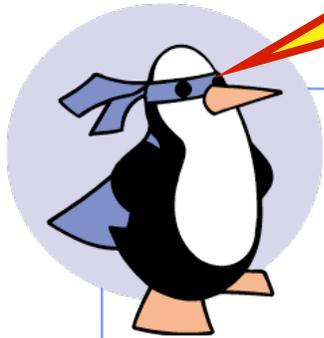
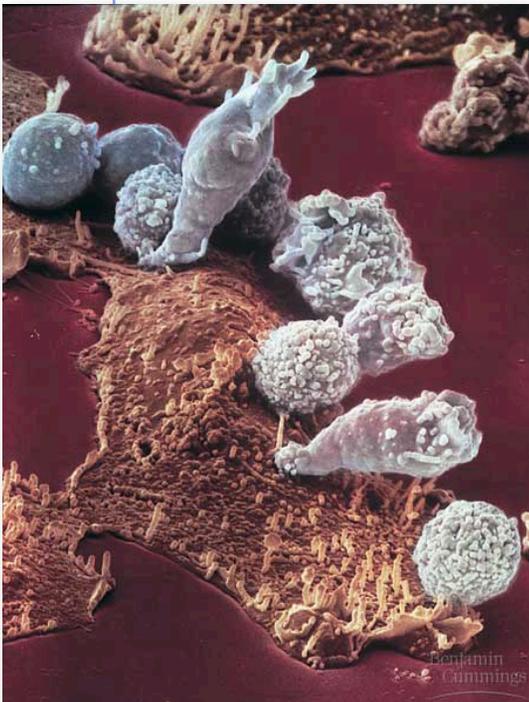


Fighting the
Enemy Within!

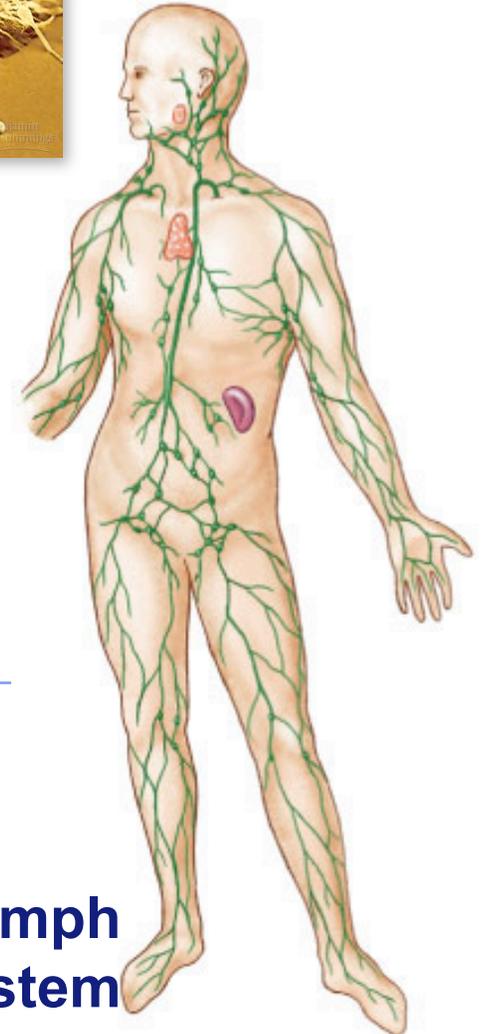


phagocytic
leukocyte

Cardio/Lymphatic/ Immune Systems



lymphocytes
attacking
cancer cell



lymph
system

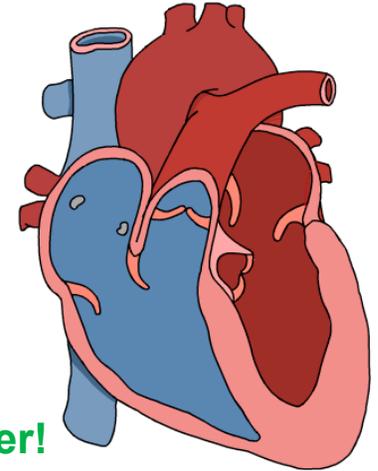
Vertebrate closed circulatory system

Called a cardiovascular system

- Length of human vessels = 2x earth's circumference
- 100,000km

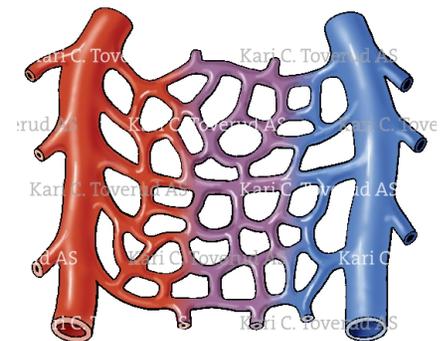
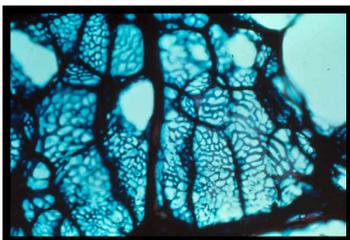
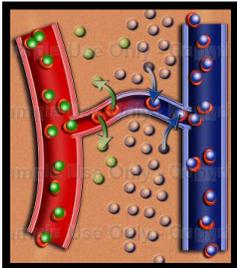
◆ Chambered heart

- **atrium** (*plural atria*) = receive blood of heart
- **ventricle** = pump blood out of heart
 - ◆ O₂ content is not relevant to the name of the chamber!

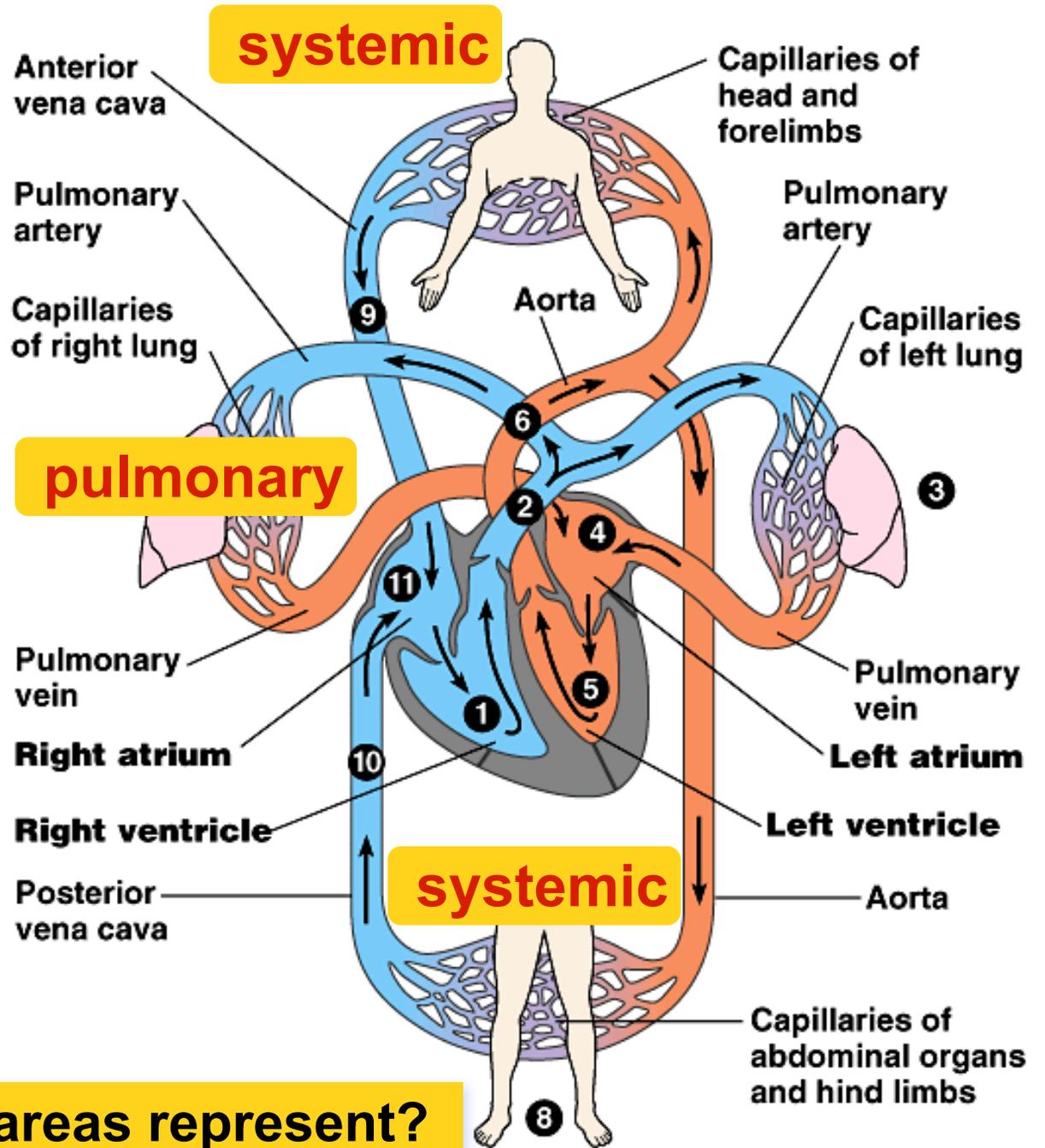
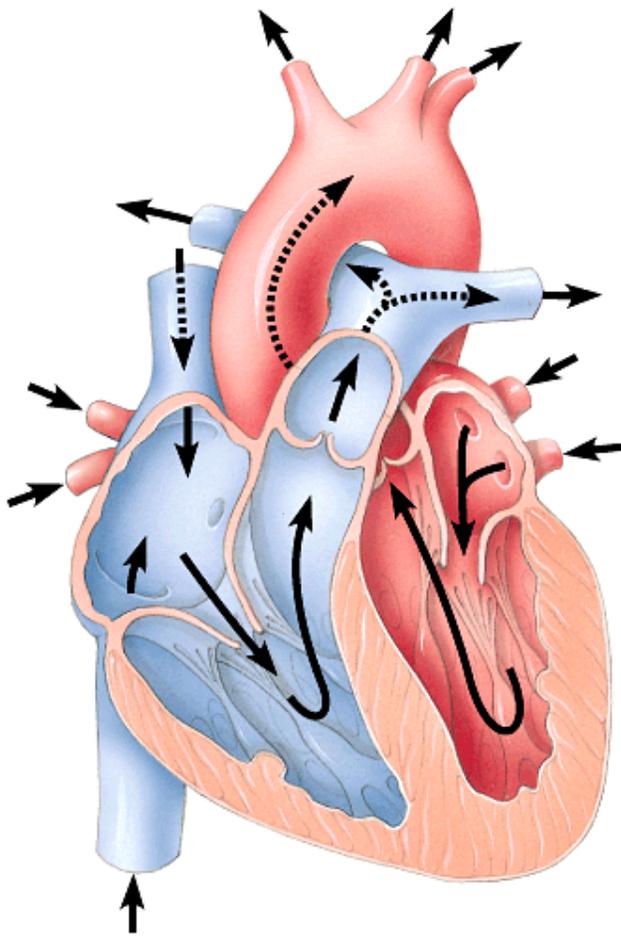


◆ Blood vessels

- **arteries** = carry blood **away** from heart to capillaries
 - ◆ In organs arteries branch into smaller diameter **arterioles**
 - Arterioles deliver blood to capillaries
- **veins** = return blood **to** heart from capillaries
 - ◆ Capillaries converge into larger diameter **venules**
- **capillaries** = thin wall, porous walls
 - ◆ exchange / diffusion between blood & interstitial fluids
 - **capillary beds** = networks of capillaries that infiltrate each tissue passing blood within small distance of every cell

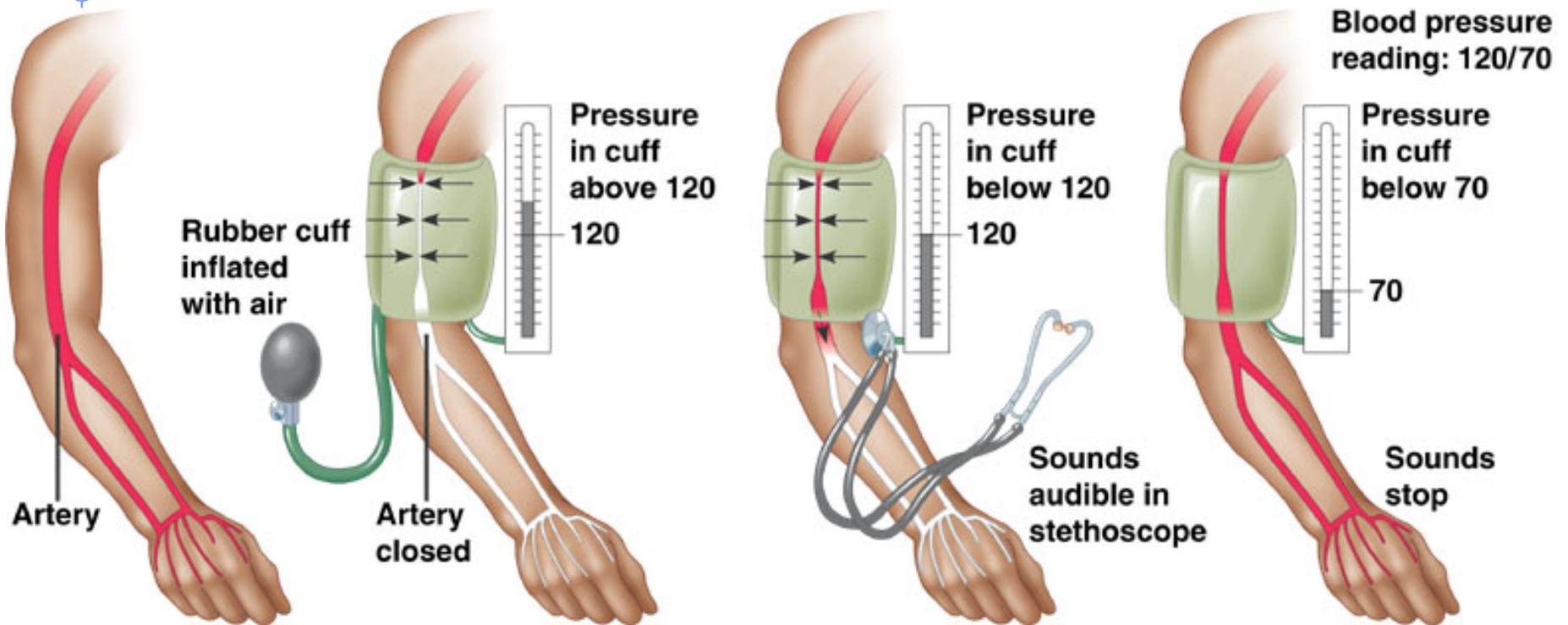


Mammalian circulation



What do blue vs. red areas represent?

Measurement of blood pressure



■ High Blood Pressure (hypertension)

- ◆ if top number (**systolic** pumping - **ventricle contracting**) > 150
- ◆ if bottom number (**diastolic** filling - **atria and ventricle relaxed**) > 90

Blood vessels

arteries

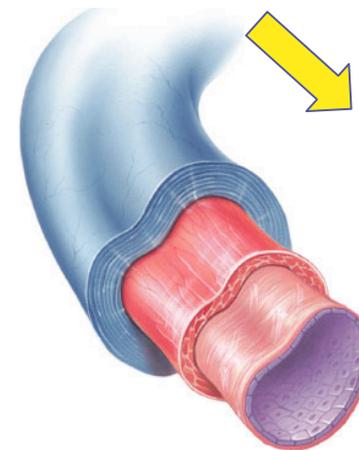


arterioles

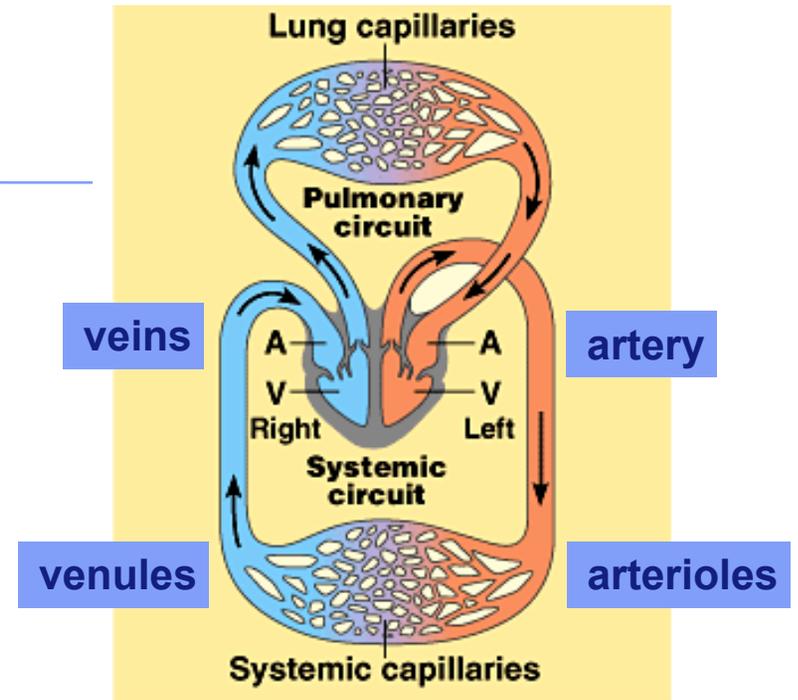


capillaries

venules



veins



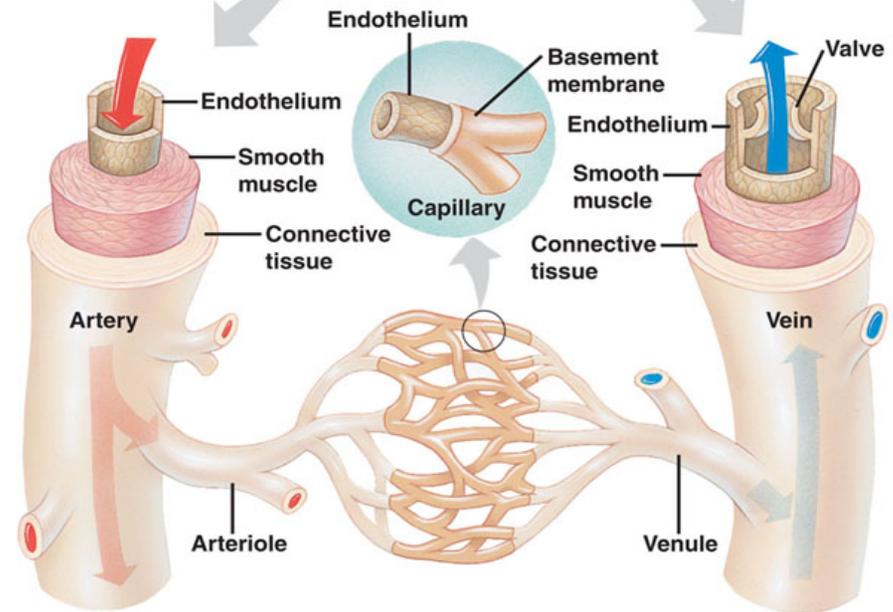
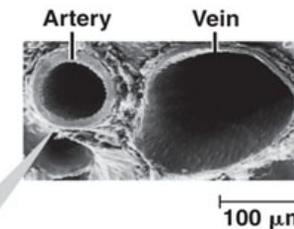
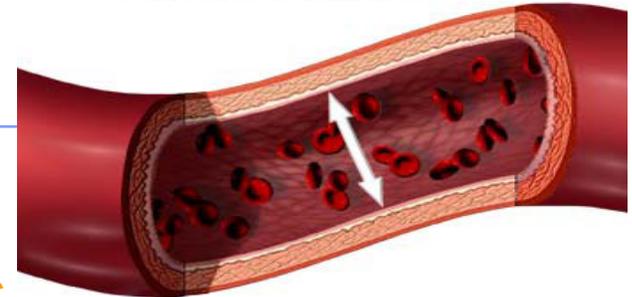
Arteries: Built for high pressure flow

- Both walls of arteries and veins have 2 layers of tissue surrounding endothelium
 - Outer layer of **connective tissue** with elastic fibers
 - Allow for stretch and recoil
 - Middle layer of **smooth muscle** with elastic fibers

Arteries

- thicker walls** (3x veins)
 - Provide strength for high pressure pumping of blood
- narrower diameter**
- elasticity**
 - elastic recoil helps maintain blood pressure even when heart is relaxed
- Nervous system and hormones act on smooth muscles** [can constrict vs dilate artery]

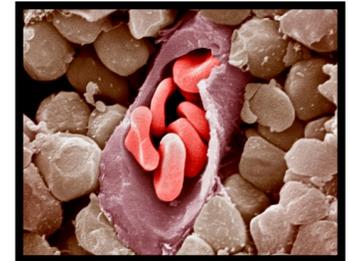
Blood pressure is the measurement of force applied to artery walls



AP Biology

- Control amount of blood flow to capillaries

Capillaries: Built for exchange

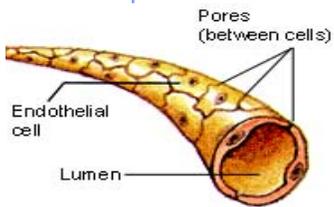


All blood vessels contain a central lumen or cavity

- ◆ **Lined with a single layer of endothelial cells**
 - Minimizes resistance

Capillaries

- ◆ **very thin walls**
 - Lack 2 outer wall layers of arteries & veins (no muscle or connective tissue)
 - ◆ Have only **endothelium** attached to **basal lamina**
 - enhances exchange across capillary



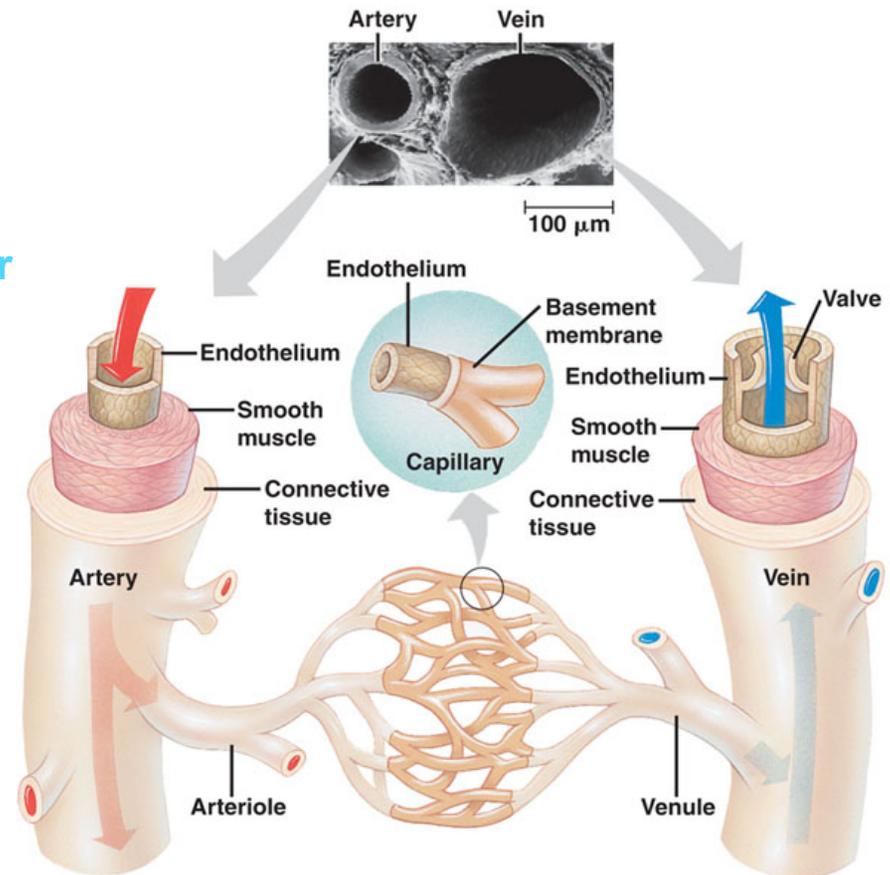
◆ **Diffusion through membrane**

- exchange O_2 & CO_2 between blood & interstitial fluid

◆ **Diffusion through openings**

- Sugars, salts, urea

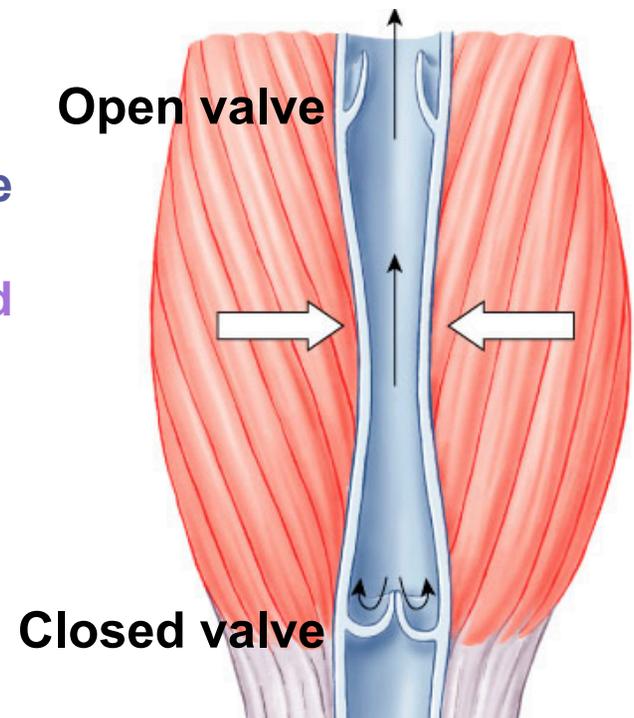
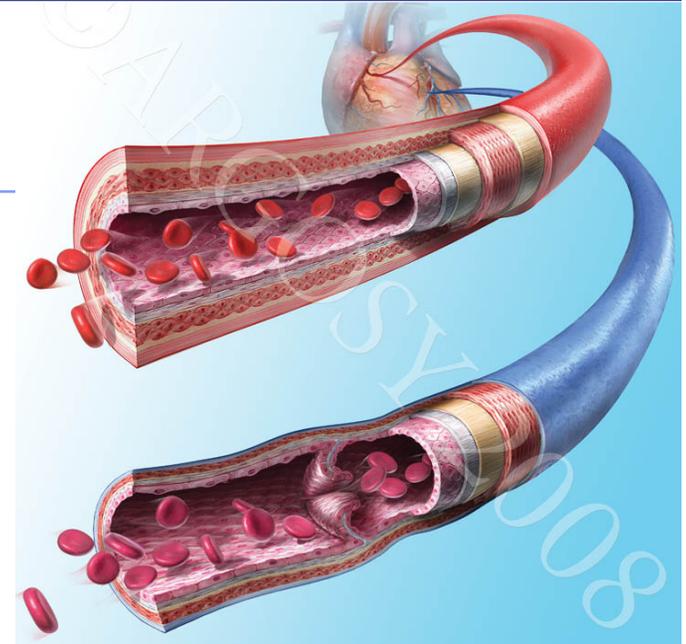
◆ **Some substances carried across endothelium by endocytosis and exocytosis**



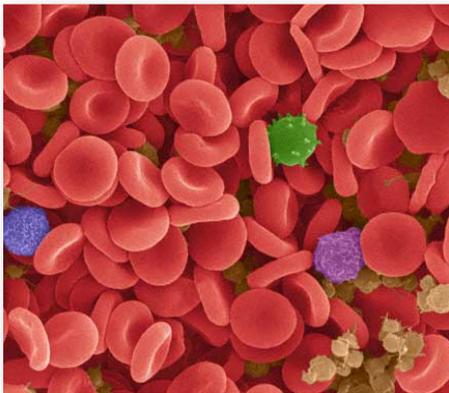
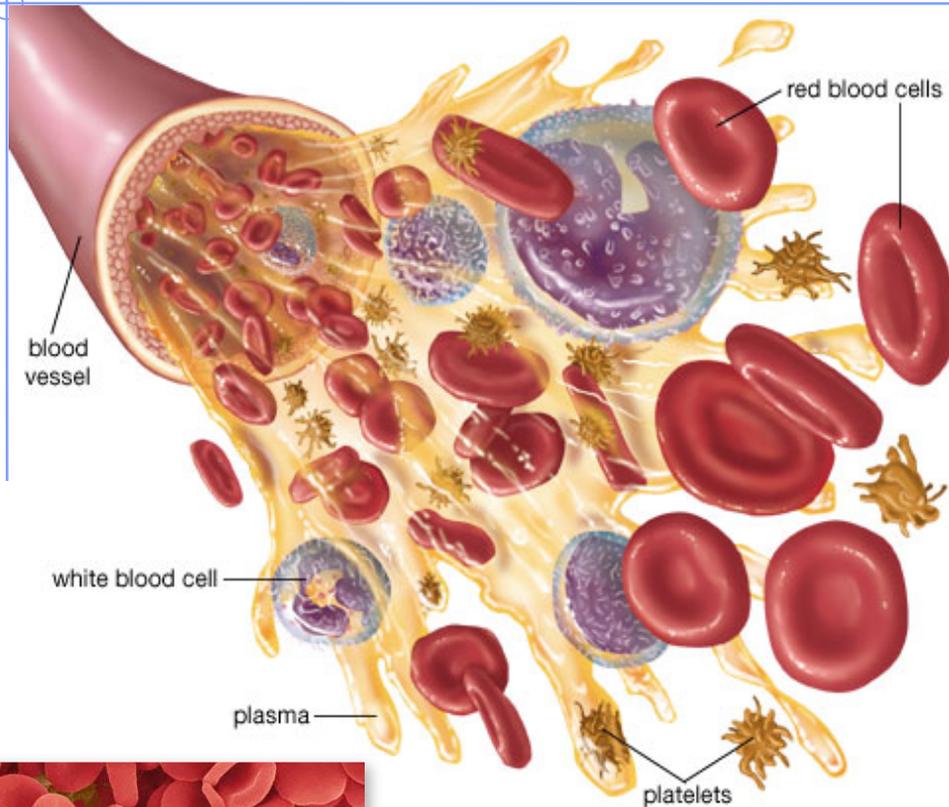
Veins: Built for low pressure flow

■ Veins

- ◆ Also has connective tissue and smooth muscle layers
- ◆ thinner-walled
- ◆ wider diameter
 - blood travels back to heart at low velocity & pressure
 - ◆ distant from heart
 - ◆ blood must flow by skeletal muscle contractions when we move
 - Skeletal muscles squeeze blood through veins
- ◆ valves
 - in larger veins **one-way valves** allow blood to flow only toward heart (**unidirectional flow**)



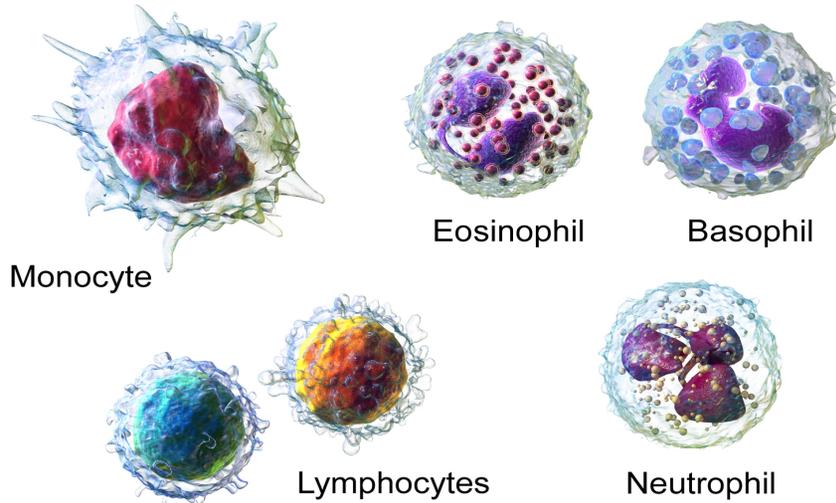
In circulation...



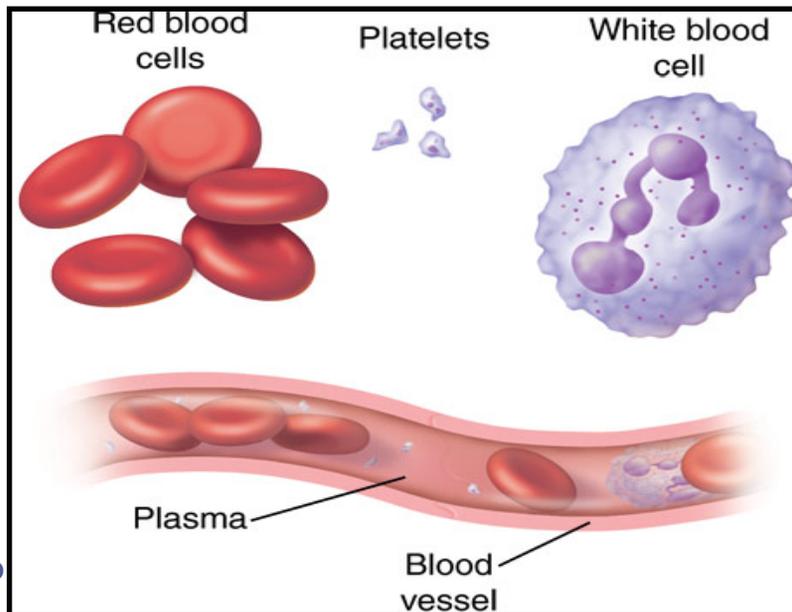
■ What needs to be transported

- ◆ nutrients & fuels
 - Absorbed from digestive system
- ◆ respiratory gases
 - O₂ & CO₂ from & to gas exchange systems
 - ◆ Lungs & gills
- ◆ intracellular waste
 - waste products from cells
 - ◆ water, salts, nitrogenous wastes (urea in humans)
- ◆ protective agents
 - immune defenses
 - ◆ white blood cells & antibodies
 - blood clotting agents
- ◆ regulatory molecules
 - hormones

Cellular Elements in Blood



White Blood Cells



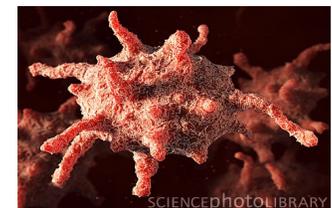
AP

Leukocytes

- Five major types of white blood cells
- ◆ **Function in fighting infections**
 - Some are phagocytic
 - Some like T and B cells mount immune responses against foreign substances
- ◆ Leukocytes, unlike erythrocytes, patrol interstitial fluid and lymph fluid as well as the blood

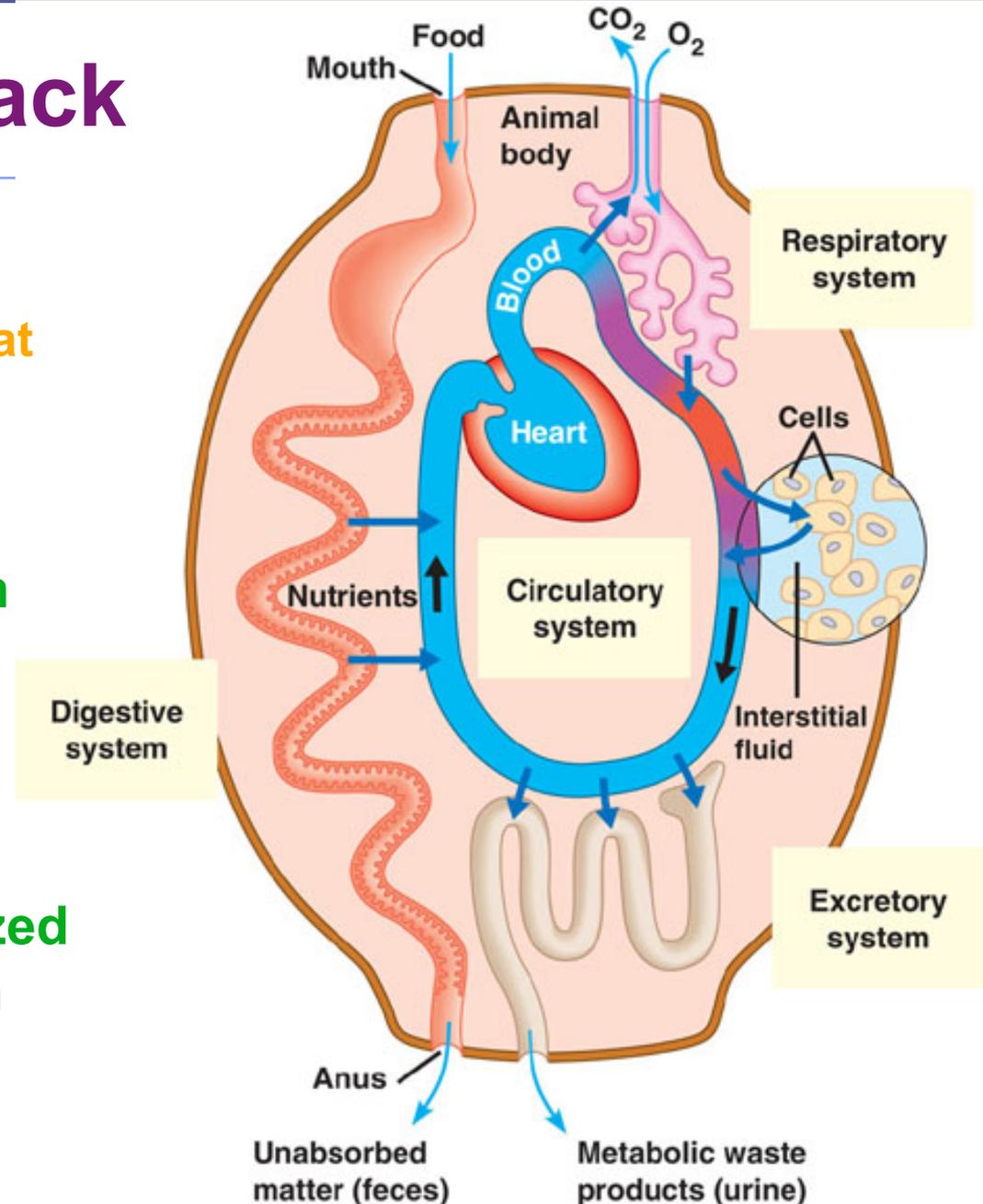
Platelets

- ◆ **Pinched-off cytoplasmic fragments of special bone marrow cells**
 - Lack nuclei
- ◆ **Function in blood clotting**



Avenues of attack

- **Pathogens**
 - Infectious agents that cause disease
- **Points of entry**
 - ◆ digestive system
 - ◆ respiratory system
 - ◆ urogenital tract
 - ◆ eye ducts
 - ◆ break in skin
- **Routes of attack**
 - ◆ may remain localized
 - ◆ circulatory system
 - ◆ lymph system



Why an immune system?

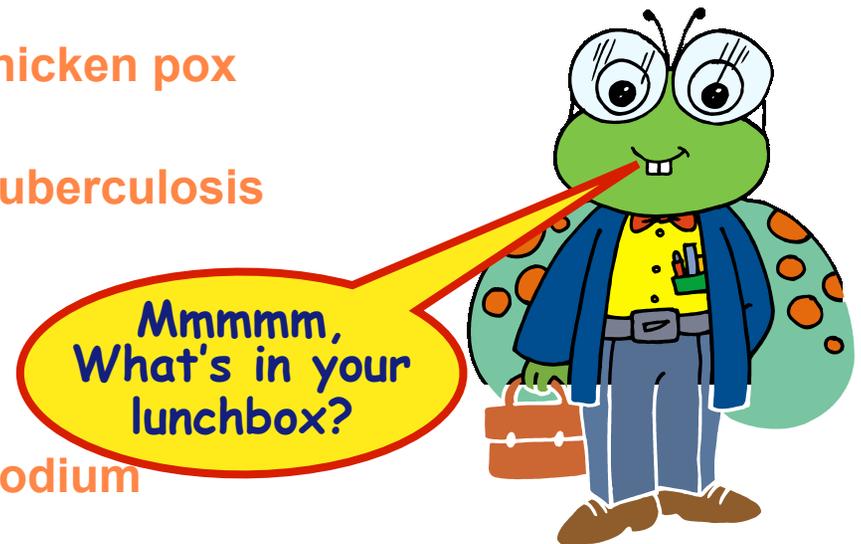
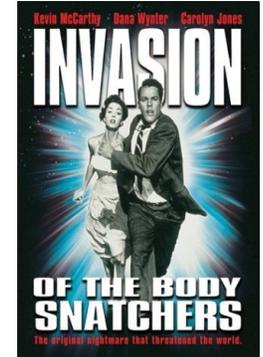
■ Attack from outside

- ◆ lots of organisms want you for lunch!
- ◆ animals are a tasty nutrient- & vitamin-packed meal
 - cells are packages of macromolecules
- ◆ animals must defend themselves against invaders (pathogens)
 - viruses
 - ◆ HIV, flu, cold, measles, chicken pox
 - bacteria
 - ◆ pneumonia, meningitis, tuberculosis
Lyme disease
 - fungi
 - ◆ yeast ("Athlete's foot" ...)
 - protists
 - ◆ amoeba, malaria's plasmodium

■ Attack from inside

- ◆ cancers = abnormal body cells

- Immune system = a system used by animals to try to avoid or limit infections



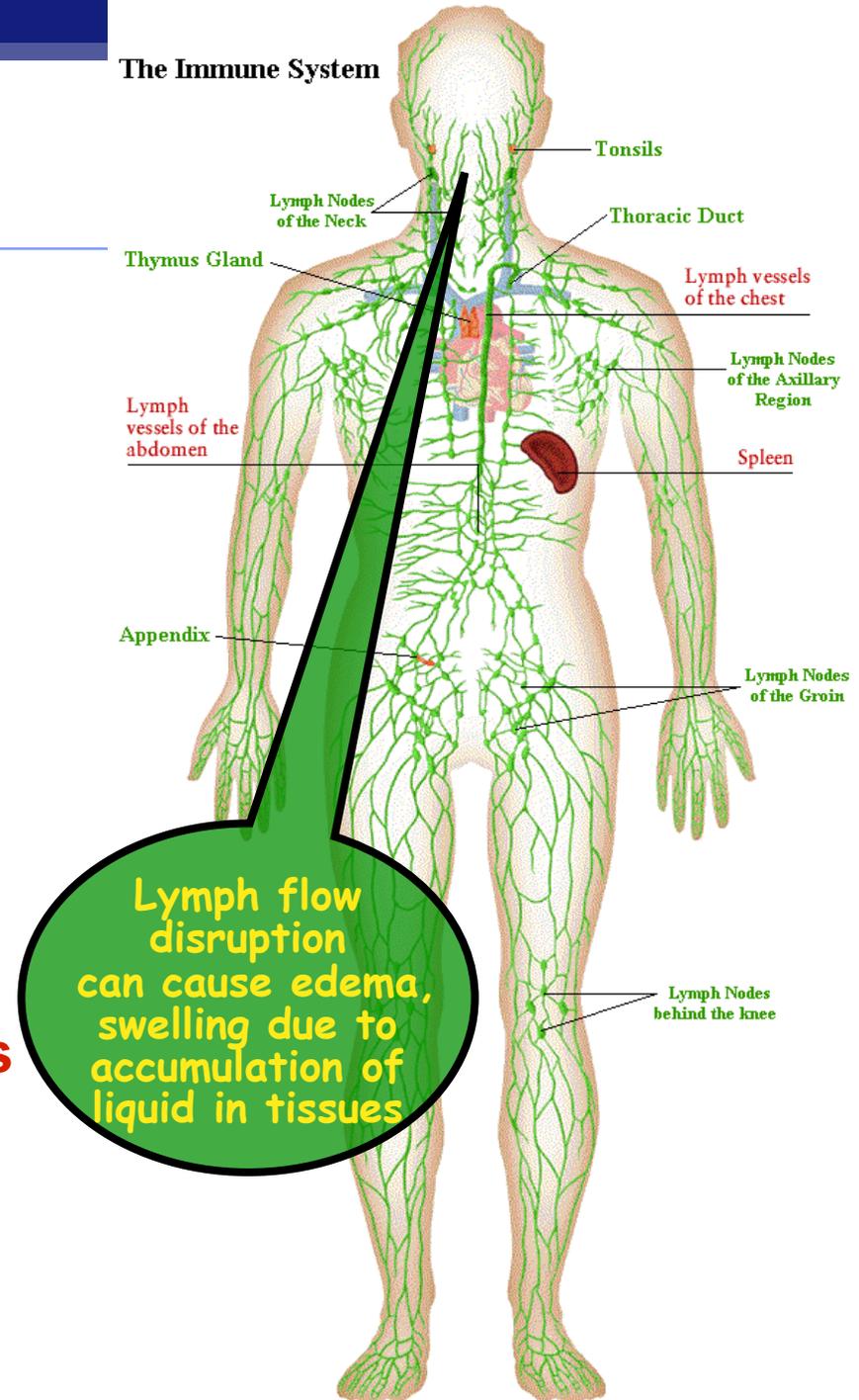
Lymphatic system

Parallel circulatory system

- ◆ **collects interstitial fluid & proteins lost from capillaries**
 - Returns “lymph” to blood
 - ◆ Empties into vena cava (cardiovascular vein in base of neck)
 - Maintains volume & protein concentration of blood
- ◆ **transports white blood cells**
 - defend against infection
- ◆ **Vessels have valves like veins**
 - Small contractions of vessels & movement of skeletal muscles helps lymph flow

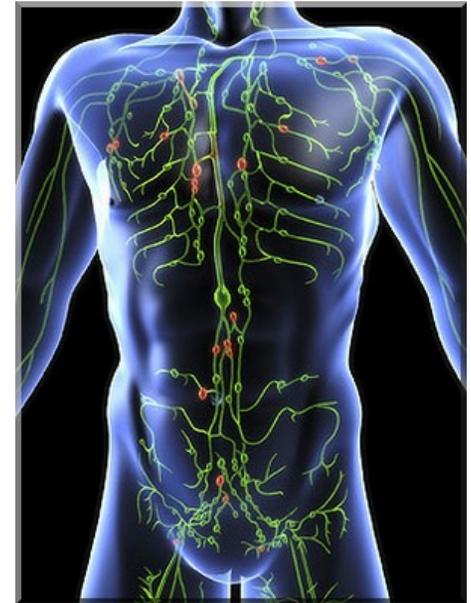
AP Biology

The Immune System



Lymphatic System Overview

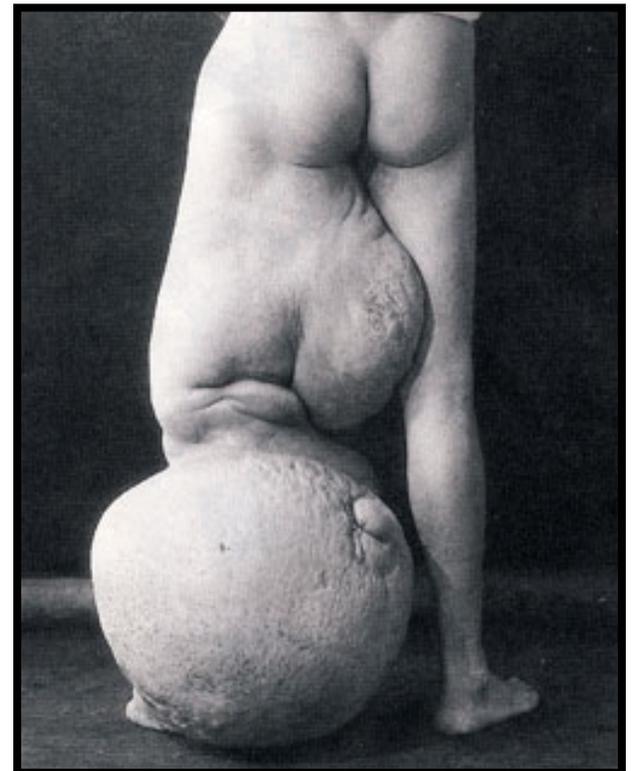
- The lymphatic system is an extensive drainage network that helps...
 1. **keep bodily fluid levels in balance**
 2. **defends the body against infections**
- It is made up of a network of **lymphatic vessels**
 - ◆ Filled with **lymph**, a clear, watery fluid that contains protein molecules, salts, glucose, urea, and immune system cells throughout the body.
 - When lymph surrounds cells and is outside the lymphatic vessels we call it **INTERSTITIAL FLUID**.

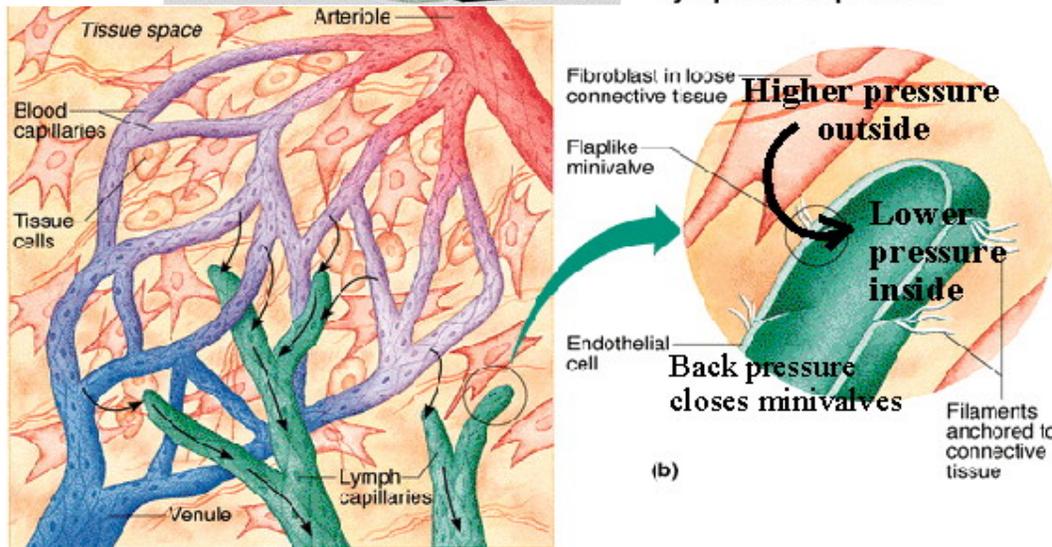
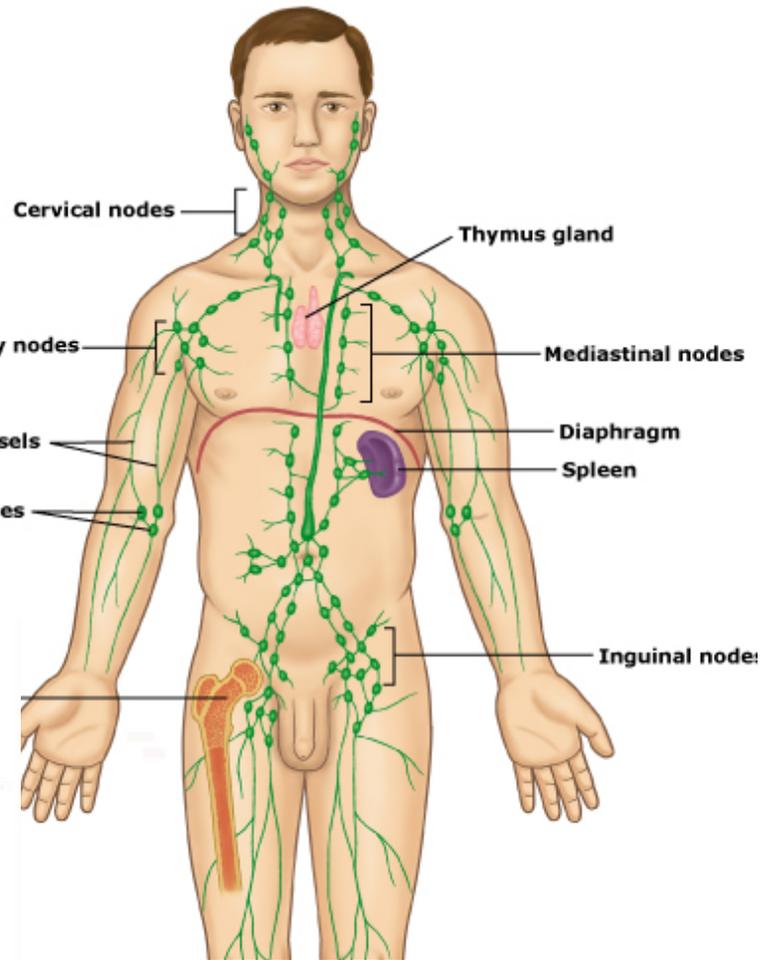
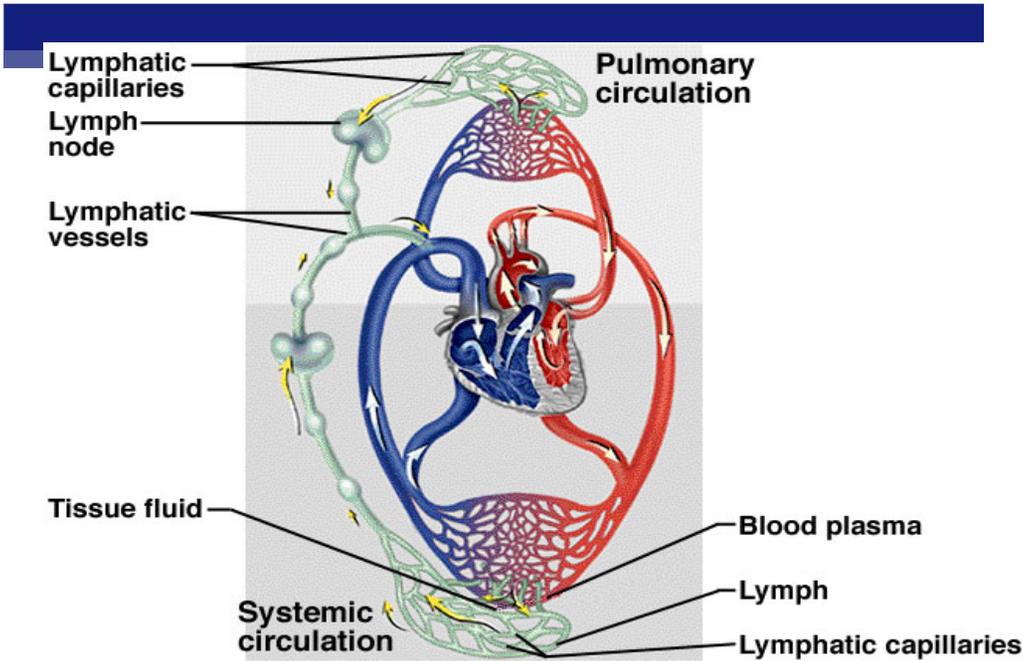


Lymphatic System Jobs in more Depth

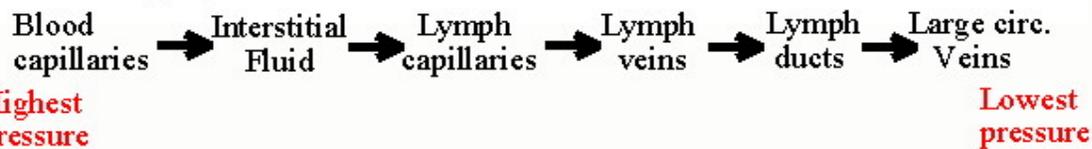
1. To collect extra lymph fluid from body tissues and return it to the blood.
 - ◆ Crucial = water, proteins, and other substances continuously leak out of tiny blood capillaries into tissues.
 - ◆ If the lymphatic system didn't drain excess fluid the lymph fluid would build up in the body's tissues causing swelling
 - Swelling is called **EDEMA**

Elephantiasis is a condition of extreme edema that occurs when lymph vessels become blocked by filarial worms.





Lymphokinetic Motion and Pressure Gradient



THE LYMPATHIC SYSTEM

Includes your spleen, thymus, bone marrow, lymph nodes and lymph channels, as well as your tonsils and adenoids.

Lymphatic System Jobs in more Depth

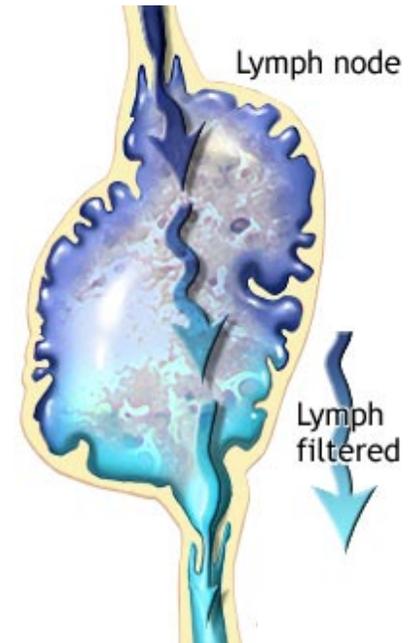
2. The lymphatic system also helps defend the body against germs like viruses, bacteria, and fungi that can cause illnesses.

- ◆ **Lymph nodes** = small masses of tissue located along the network of lymph vessels that **filter** out germs.

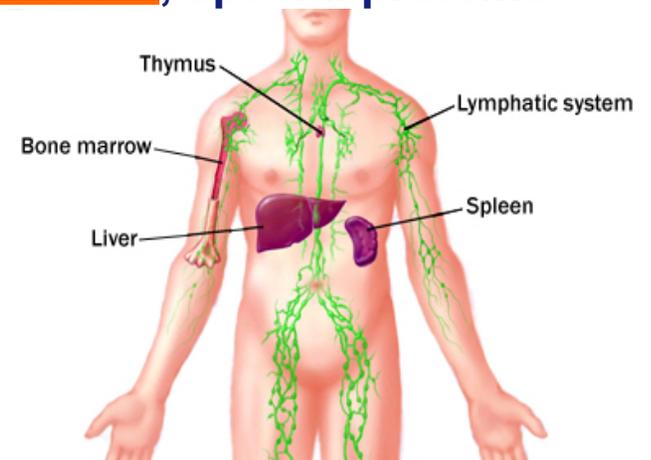
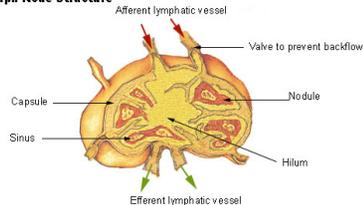
- The nodes house **lymphocytes**, a type of white blood cell (WBC).

Some of those lymphocytes make **antibodies**, special proteins that fight infections

- The **spleen clears worn out red blood cells** and **houses lymphocytes** and **macrophages** (another WBC type) that engulf and destroy foreign bodies from the bloodstream.



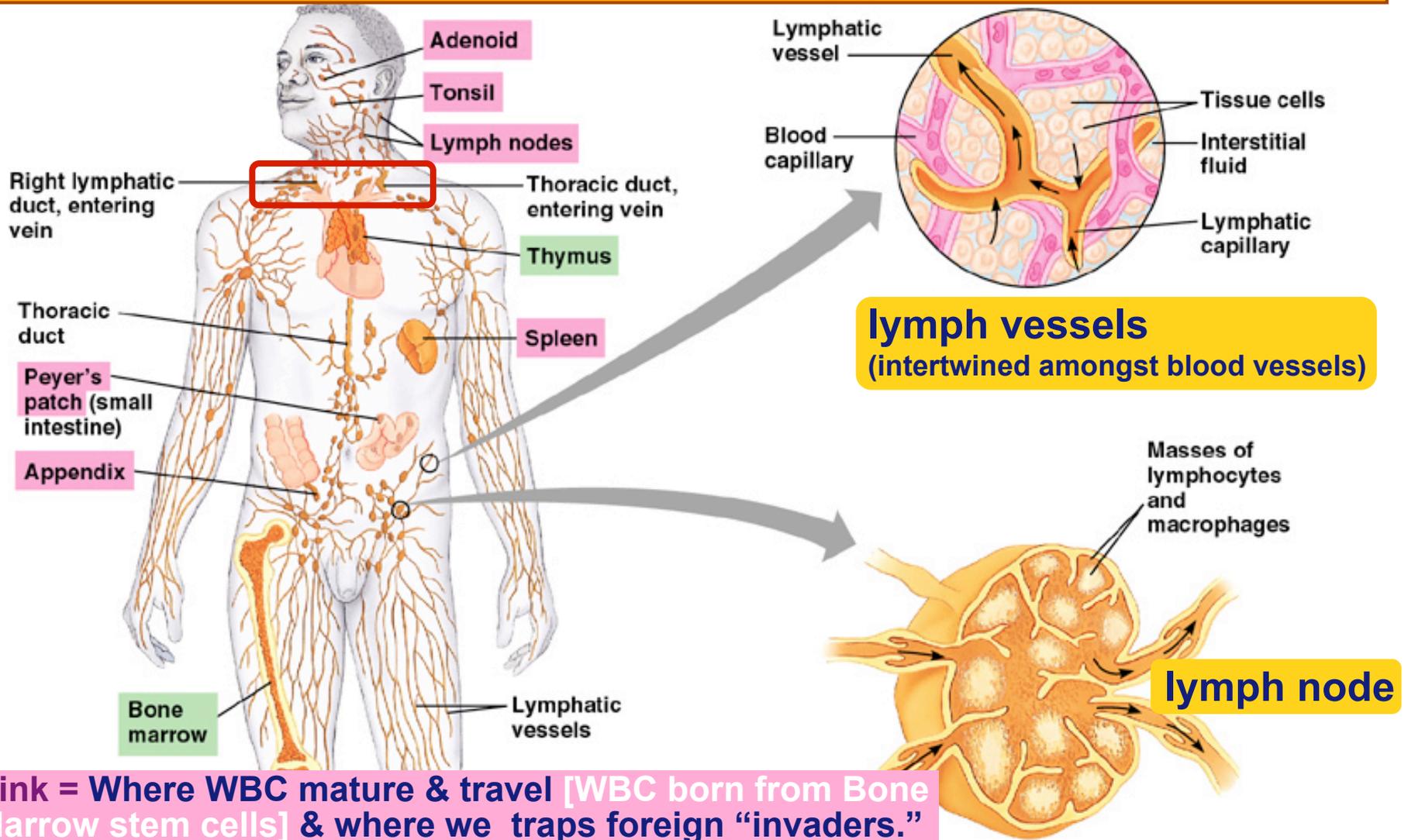
Lymph Node Structure



Lymph system

= Traps foreign invader, distributes body fluid, & filters out dead RBC

Lymph vessels collect the interstitial fluid and then return it to the bloodstream by emptying through the **LYMPHATIC DUCTS** it into large **SUBCLAVIAN VEINS** in the upper chest, near the neck.



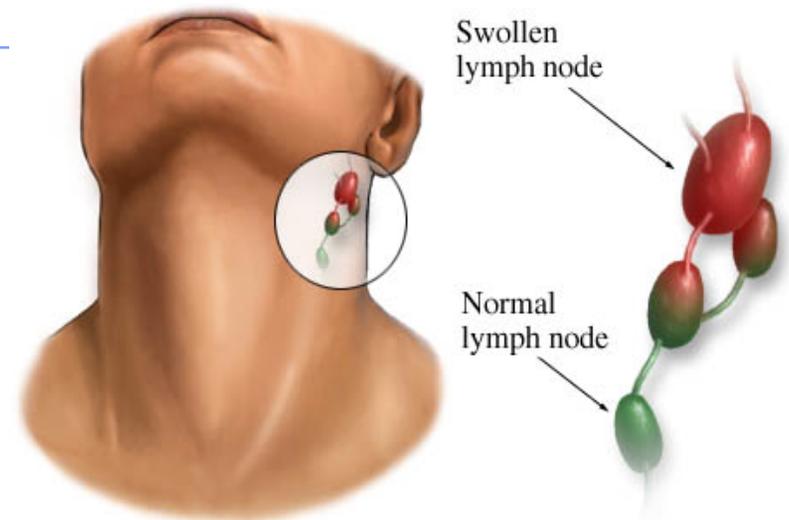
lymph vessels
(intertwined amongst blood vessels)

lymph node

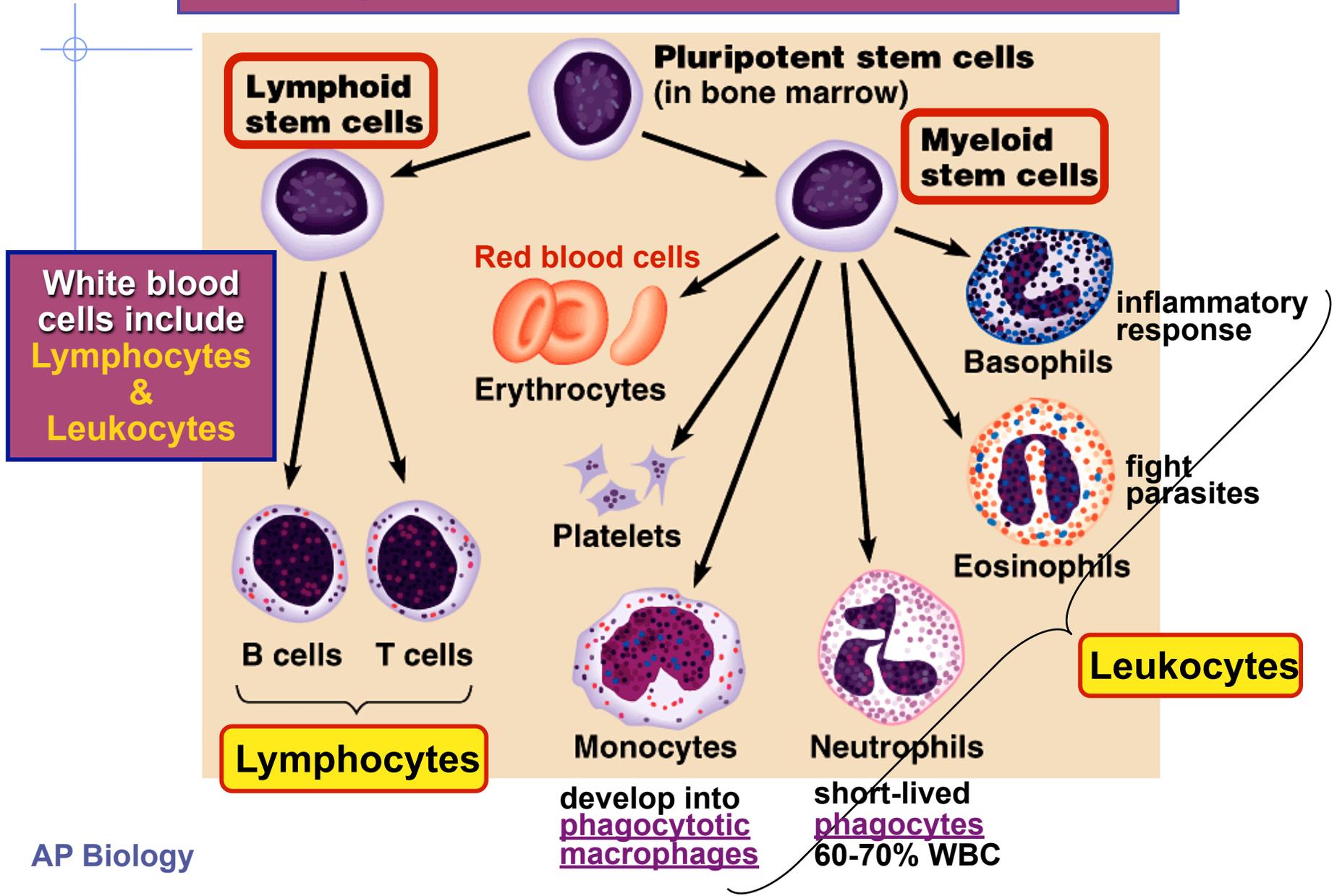
Pink = Where WBC mature & travel [WBC born from Bone Marrow stem cells] & where we traps foreign "invaders."

When you have an infection, nodes swell.

- When a person has an infection, pathogens collect in the lymph nodes.
 - ◆ If the throat is infected, for example, the lymph nodes of the neck may swell because its white blood cells start multiplying via mitosis.
 - That's why doctors check for swollen lymph nodes ("glands") in the neck
- Most of the lymph nodes are found in clusters in the neck, armpit, and groin area.
 - ◆ Nodes are also located along the lymphatic pathways in the chest, abdomen, and pelvis
 - ◆ Lymphatic tissue is also found around major organs and in and around the gastrointestinal tract.



Development of Red & White blood cells



Lines of Defense

1st line

◆ Non-specific barriers

- Broad & external defense
“walls & moats”
- skin & mucous membranes



2nd line

◆ Non-specific patrols

- Broad & internal defense
“patrolling soldiers”
- leukocytes = phagocytic WBC
Macrophages & neutrophils
- Inflammatory response
- Natural Killer Cells
- Specialized proteins
Complement system & interferon



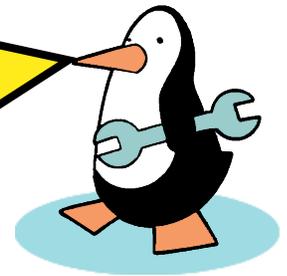
3rd line

Specific immune system

- Specific & acquired immunity
“elite trained units”
- lymphocytes & antibodies
B cells & T cells



Bacteria & insects inherit resistance.
Vertebrates acquire immunity.



Official Terminology

■ Innate Immunity (1st & 2nd Line) - in almost all animals

- ◆ Recognition of traits shared by broad ranges of pathogens
 - Uses a small set of receptors for particles only present on foreign microbes and not in the body
- ◆ Rapid Response
- ◆ Same response whether pathogen encountered for the first time or the third or fifth or tenth....

1. External Barrier defenses

- * Physical Barriers stop or trap microbes:

Skin or shell
Mucous membranes

- * Chemical Barriers may kill microbes:

Enzymes
Secretions
pH



2. Internal Defenses

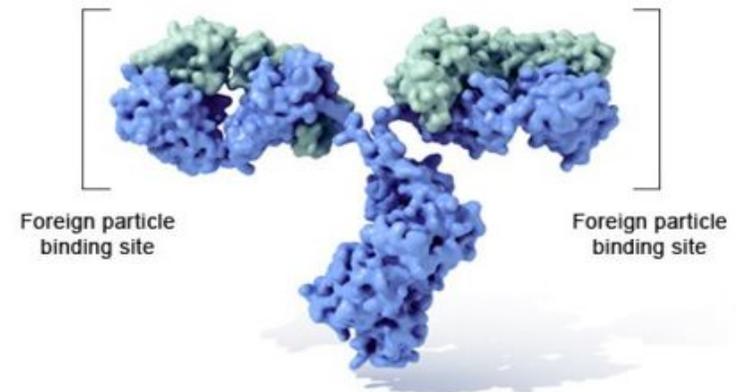
- * Phagocytotic cells
- * Antimicrobial peptides
- * Inflammatory Response (unique to vertebrates)
- * Natural Killer cells (unique to vertebrates)

Official Terminology

Acquired Immunity (3rd Line) - Unique to vertebrates

- ◆ Recognition by lymphocytes (certain WBCs) of traits specific to particular pathogens
 - Using a vast array of receptors
- ◆ Slower Response than 1st & 2nd line (*animal does use 1st & 2nd line too*)
- ◆ Can be “active” or “passive”
 - Humoral Response
 - ◆ Secretion of antibodies - defend against infectious particles in body fluids and on the outside of the animal’s body cells
 - Can be active (made by the infected) or passive (obtained from an outside source but not the animal itself)
 - Cell-mediated Response
 - ◆ Cytotoxic lymphocyte cells defend against infections inside the animal’s body cells themselves

Immunoglobulin G (IgG)



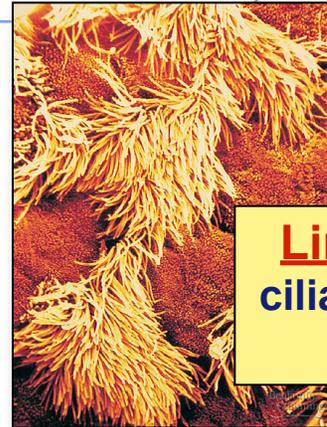
1st line: Non-specific External Defenses

■ Barriers

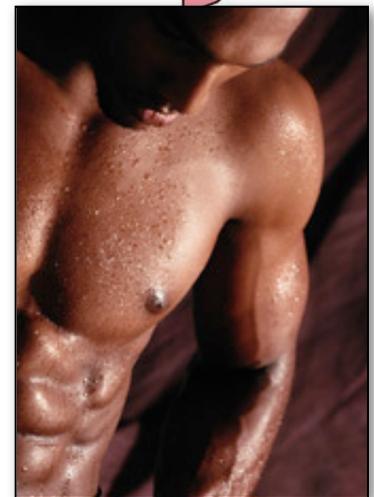
- Skin epithelial tissue blocks entry

■ Traps

- Some mucous membranes produce mucus = viscous fluid that traps particles
- Some mucous membranes like in the trachea contain cilia = sweep mucus away
- Hair & earwax prevent pathogen growth
- Salvia & tears bathe exposed epithelia



Lining of trachea:
ciliated cells & mucus
secreting cells



1st line: Non-specific External defense

■ Elimination Events

- coughing, sneezing, urination, diarrhea help remove pathogens from body



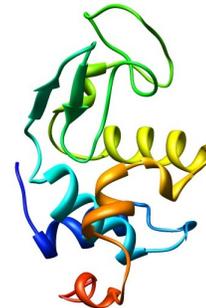
■ Unfavorable pH

- stomach acid, sweat, oil, urine keep pH of skin or organs lumen acidic

■ Lysozyme enzyme

- Digests bacterial cell walls

Found in tears, saliva & sweat



2nd line: Non-specific Internal Patrols/Defenses

■ Patrolling cells & proteins

- ◆ attack pathogens, but don't "remember" the pathogen to help with future infections

1. Leukocytes

- ◆ phagocytic white blood cells
- ◆ **Dendritic cells, macrophages, neutrophils, natural killer cells**

2. Interferon

- **Proteins released by cells infected with viruses that help non-infected cells avoid infection**

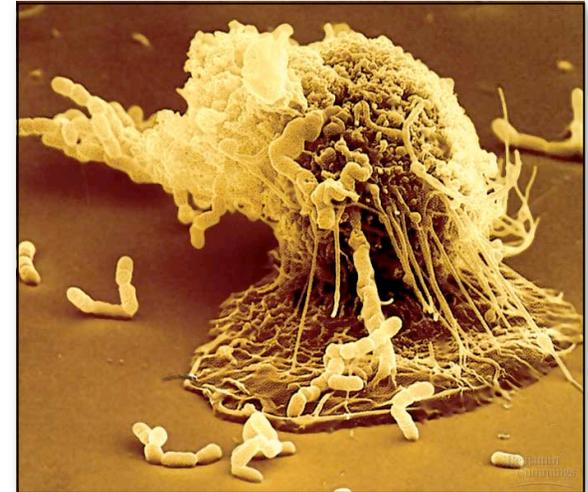
3. complement system

- ◆ **proteins that destroy foreign cells**

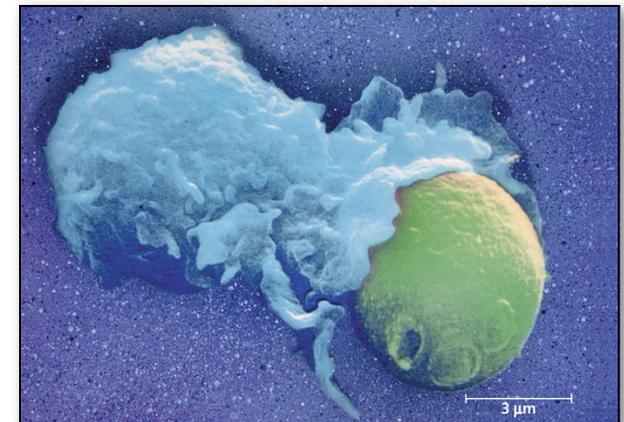
4. inflammatory response

- ◆ **increase in body temp.**
- ◆ **increase capillary permeability**
- ◆ **attract macrophages**

bacteria



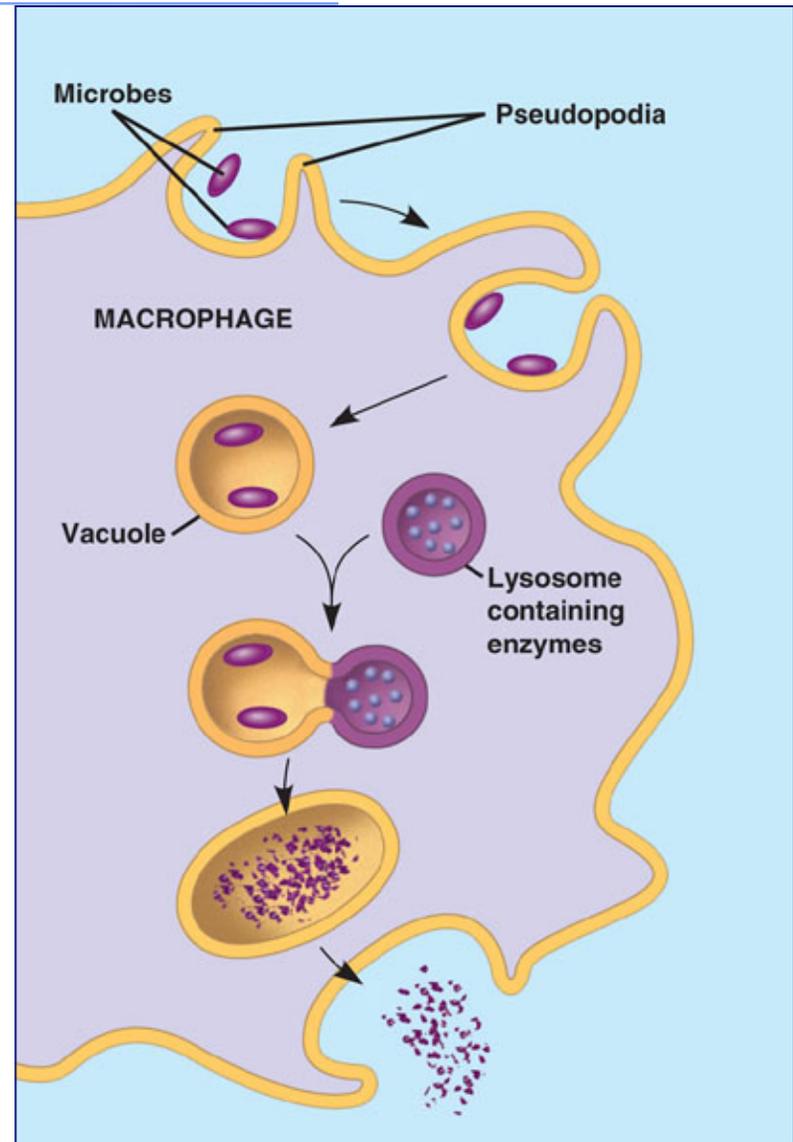
macrophage



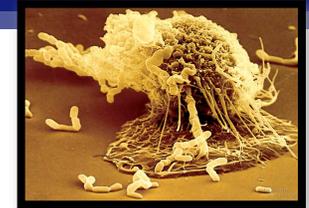
yeast

Cellular Innate defenses

- **Phagocytotic leukocytes**
(Types of white Blood Cells)
 - ◆ Cells recognize microbes using receptors = **Toll-Like Receptors or TLR**
 - Recognize fragments of molecules (often on outer surface of microbes) that are characteristic of sets of pathogens
 - ◆ Enter infected tissue and engulf & ingest microbes
 - Vacuole with particle fuses with **lysosome** to be digested



Phagocytotic Leukocytes (WBC)



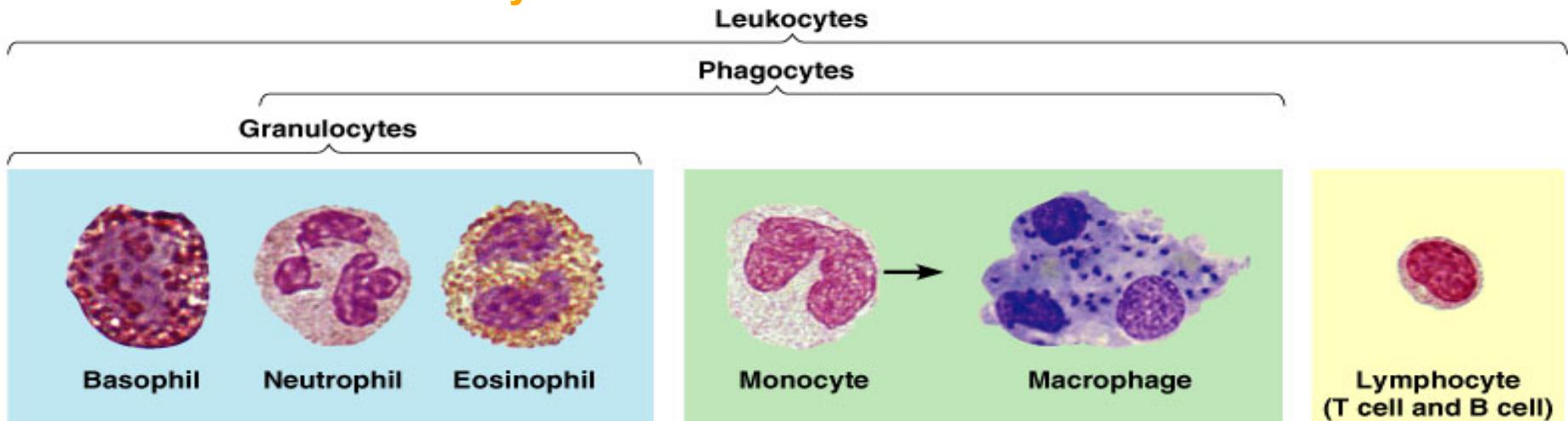
■ Neutrophils

- Attracted by chemical signals released by damaged cells
- most abundant WBC (~70%) in mammals
- ~ 3 day lifespan
 - ◆ Engulf invader and use chemicals (similar to to kill pathogen - neutrophil killed too



■ Macrophages

- “Big Eater”, long-lived
- Very effective in phagocytotic defense
 - ◆ May migrate throughout body, many in interstitial fluid
 - ◆ Others permanently reside in organs like spleen, lymph nodes etc..
 - Engulf invader and use lysozyme & joining food vesicle with lysosome to kills invader



Secreting Leukocytes - Destroying cells gone bad!

■ Natural Killer Cells

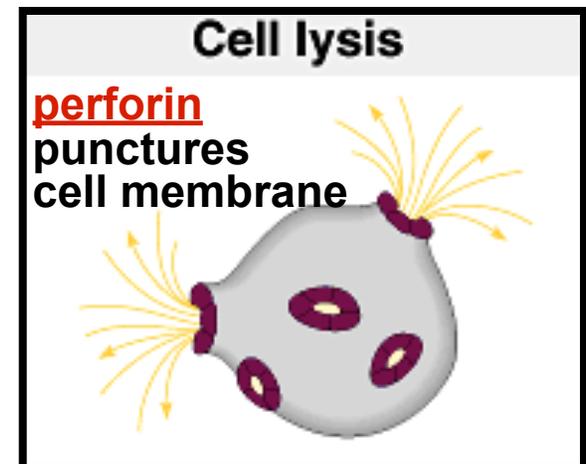
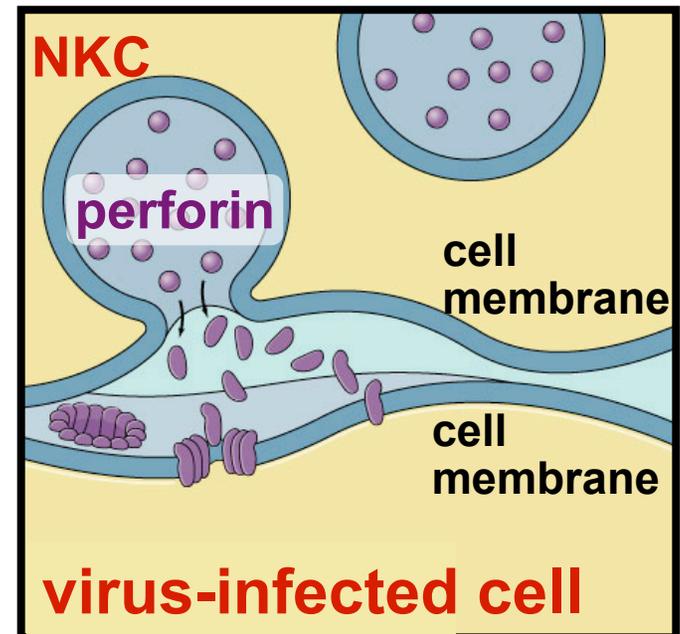
◆ Destroy virus-infected cells & cancer cells

- Body cells have surface proteins called Class I MHC's
 - ◆ After viral infection or cancerous state, cells stop expressing this proteins
- NK recognize this abnormality & destroy these cell

■ NKC's perforate cells!!!

◆ release perforin protein

- Inserts itself into membrane of target cell
- Forms pore allowing fluid to flow in & out of cell
- Cell ruptures = lyses



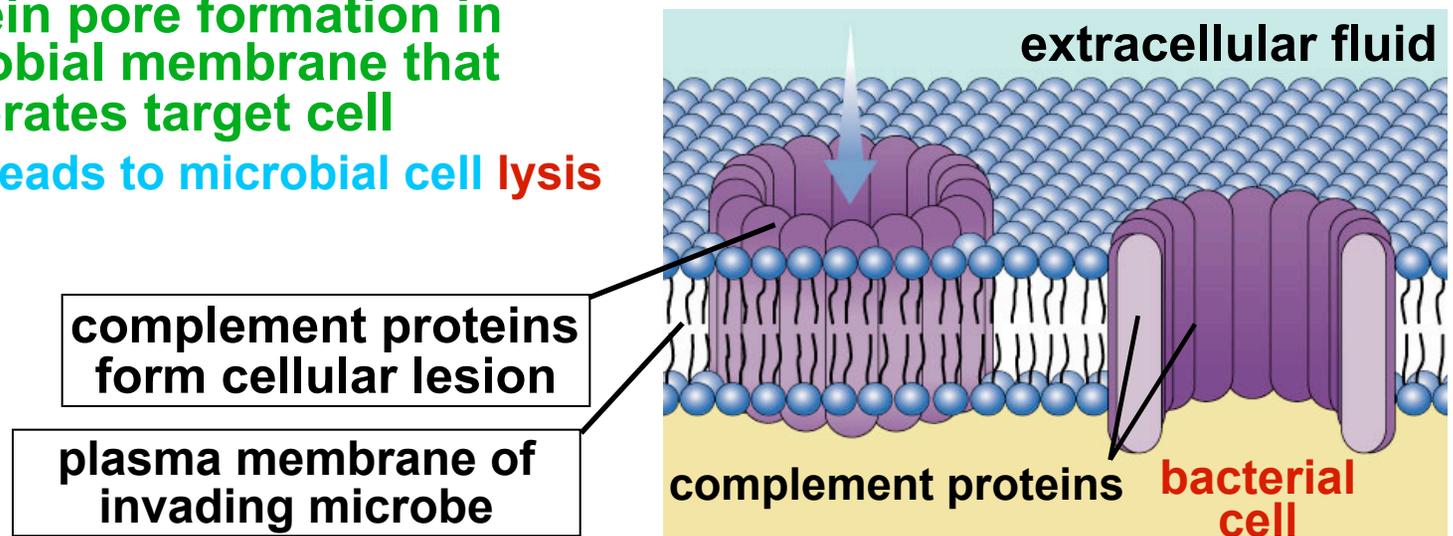
Anti-microbial peptides and proteins

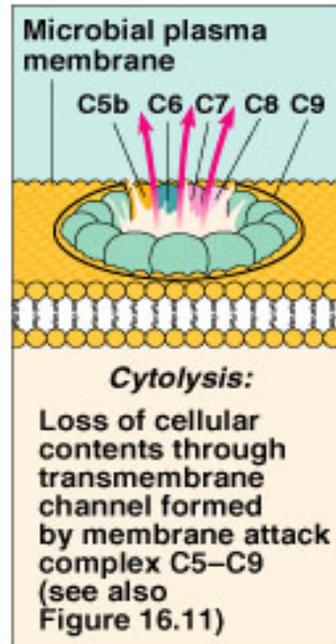
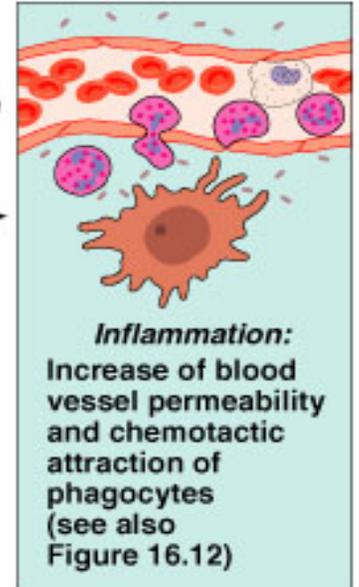
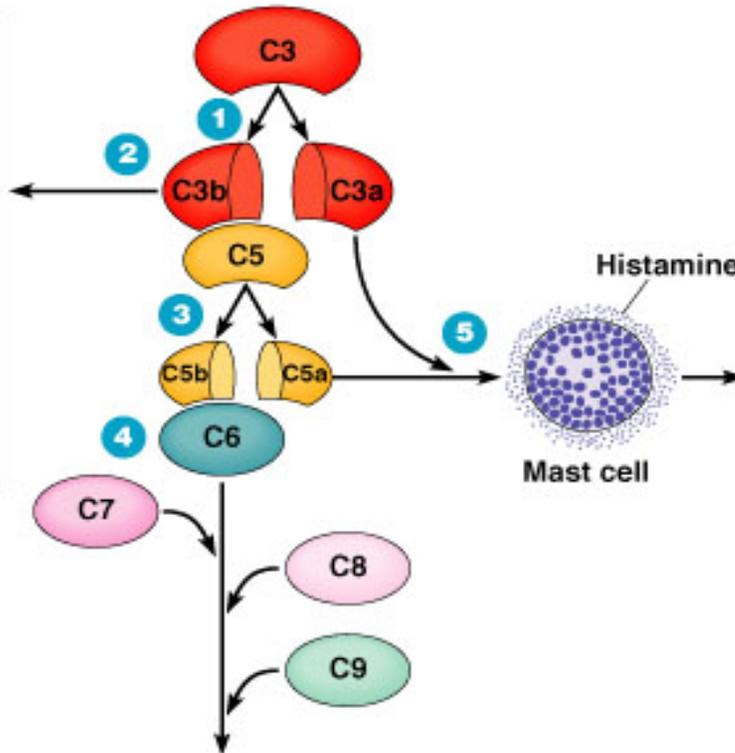
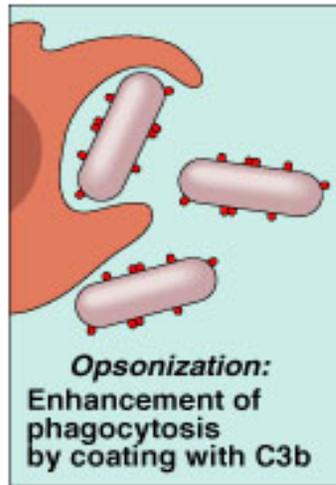
■ Complement system

- ◆ attack bacterial & fungal cells
 - ~30 proteins circulating in blood plasma
 - ◆ Circulate in inactive state
 - ◆ Activated by substances on surfaces of microbes

■ Complement Proteins:

1. Coat microbes and identifying intruder for phagocytotic cells
2. Activate mast cells leading to inflammation reaction
3. Form a membrane attack complex
 - Protein pore formation in microbial membrane that perforates target cell
 - ◆ Leads to microbial cell lysis





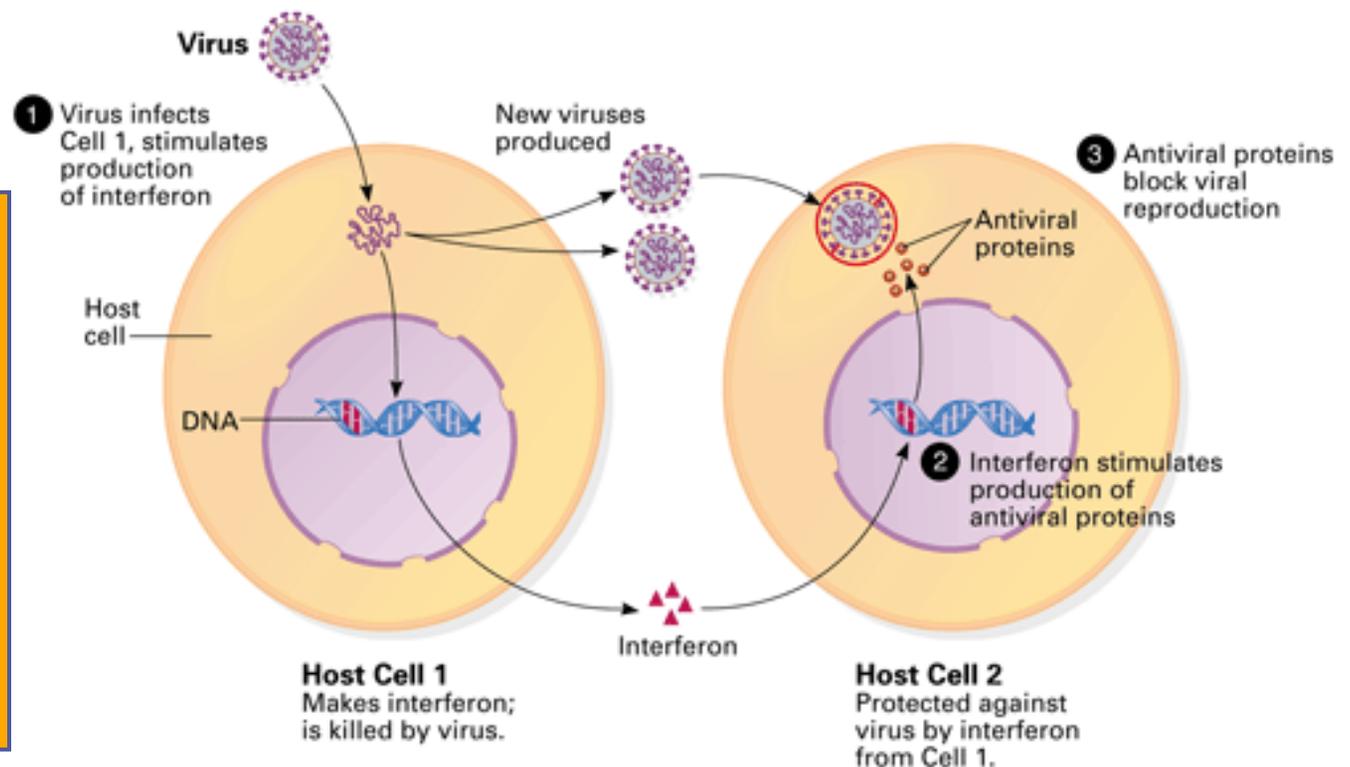
Compliment Activation & Results

Anti-viral proteins - Interferon

- A family of proteins produced by cells in response to becoming infected by a virus.
 - ◆ The infected cell may die. Interferon reaches healthy cells in the area, stimulating them to produce proteins that interfere with virus reproduction

Interferon is effective against many viruses and is therefore **nonspecific**.

Effective against flu and the common cold.

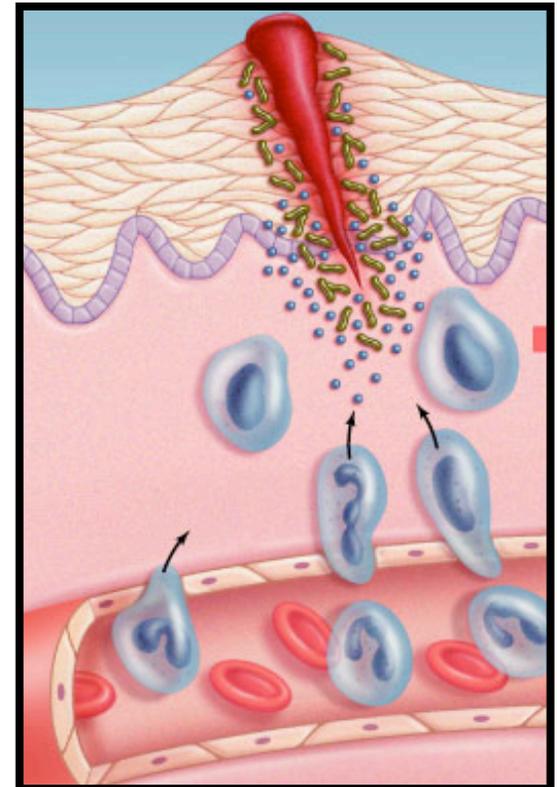


Damage to tissue triggers local non-specific Inflammatory response

- Damaged tissues release chemical signals = histamines & prostaglandins
- Mast cells found in connective tissue
 - ◆ Store histamine in granules for secretion
 - Causes capillaries to dilate, become more permeable (leaky - swelling)
 - ◆ Causes more blood to flow to tissue, delivering macrophages, RBC's, platelets, clotting factors
 - to help fight pathogens
 - aid in clot formation
 - ◆ increases temperature
 - decreases bacterial growth
 - stimulates phagocytosis
 - speeds up repair of tissues

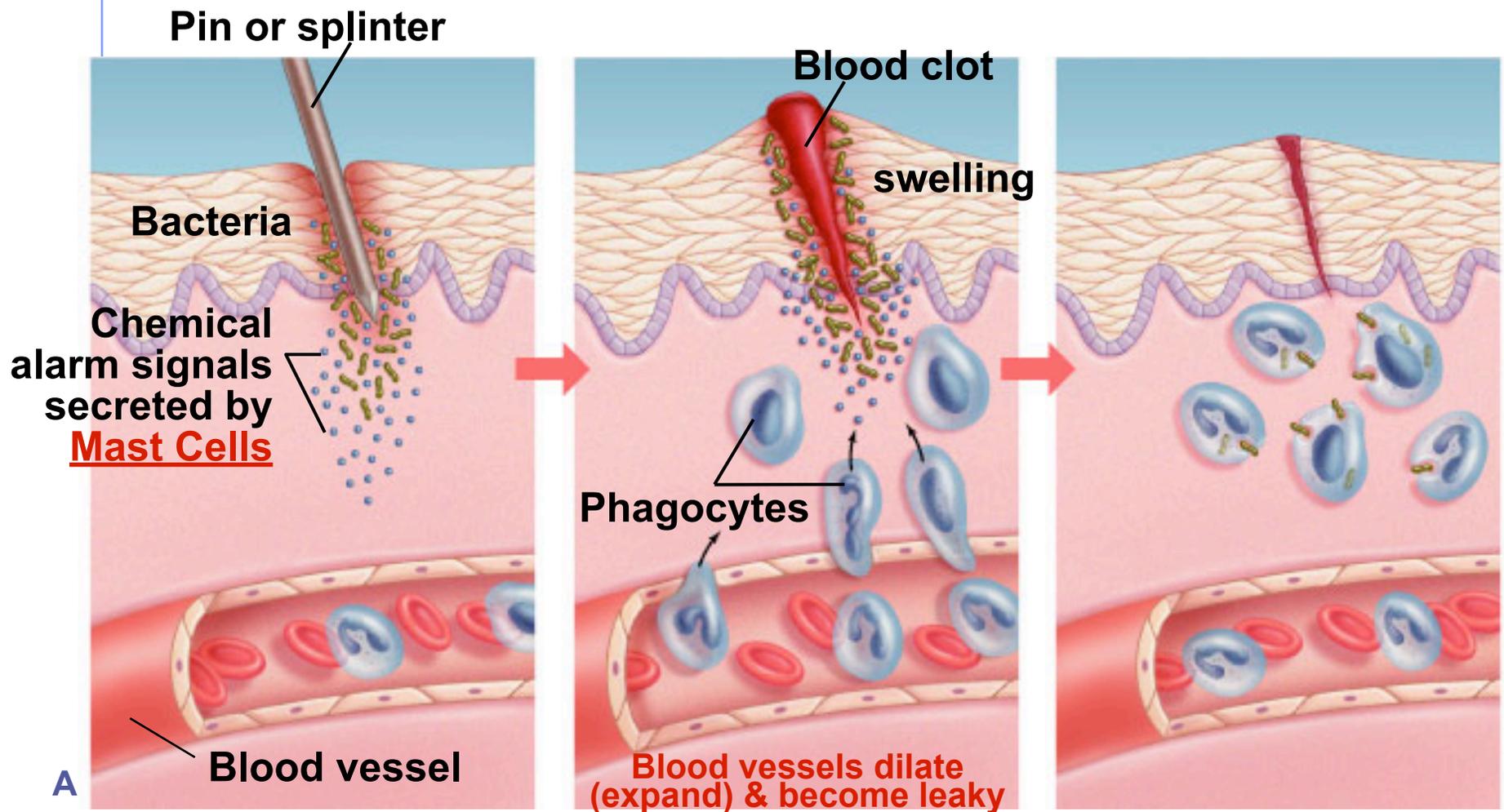


Dermatitis

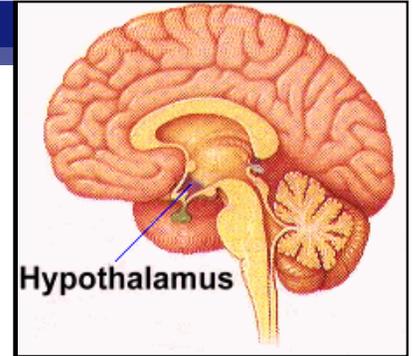


Inflammatory response

- Reaction to tissue damage that causes redness, swelling, pain, heat, and sometimes body-wide fever.



Fever



- When a local response is not enough
 - ◆ Produce a system-wide response to infection
 - ◆ Activated macrophages release a special cytokine (hormone) called interleukin-1, aka endogenous pyrogen
 - Triggers blood vessels in the brain to produce prostaglandin E2 (PGE2).
 - ◆ Triggers hypothalamus in brain to readjust body thermostat to raise body temperature
 - ◆ higher temperature helps defense
 - inhibits bacterial growth
 - stimulates phagocytosis
 - speeds up repair of tissues
 - causes liver & spleen to store iron, reducing blood iron levels
 - ◆ bacteria need large amounts of iron to grow



Innate (born with) vs Acquired Immunity (developed over lifetime)

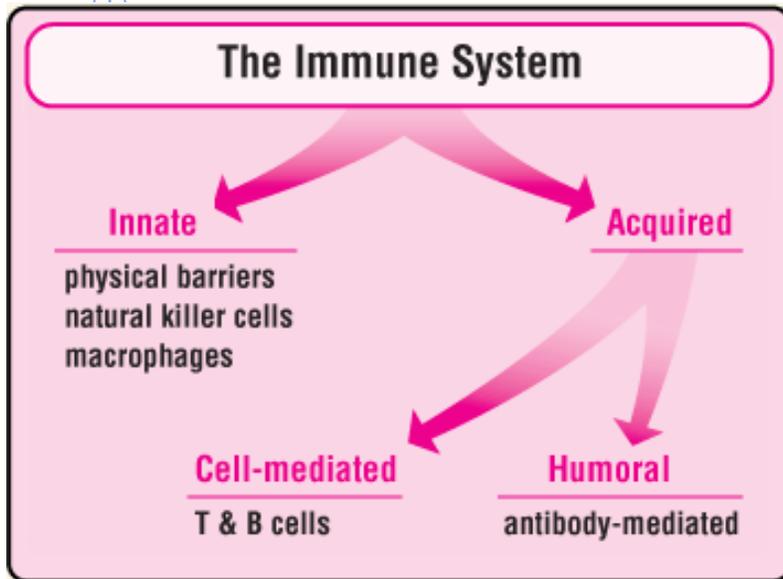
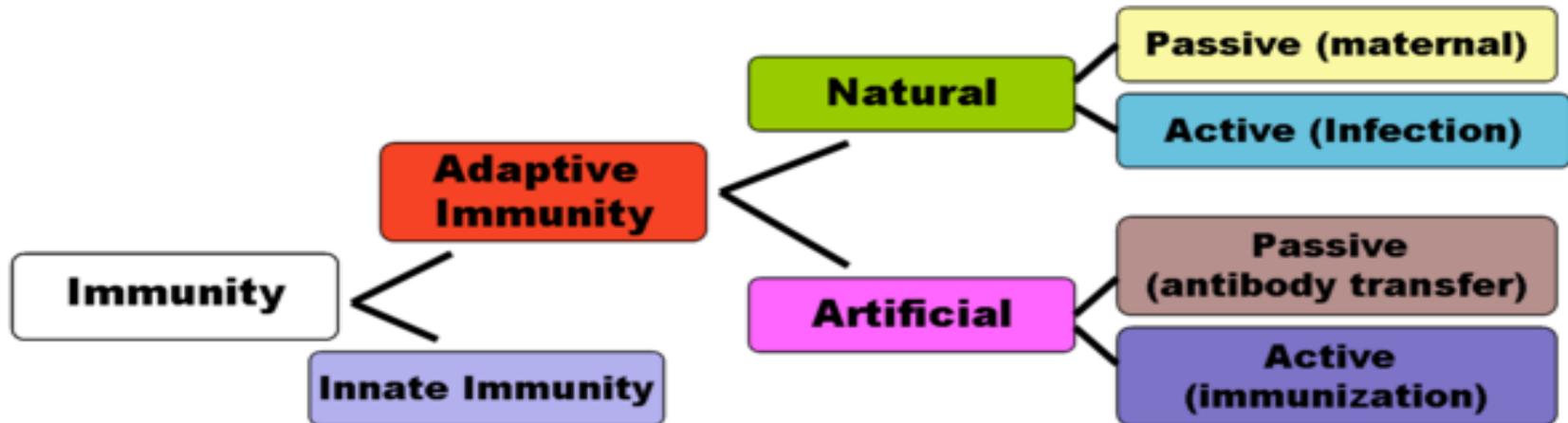
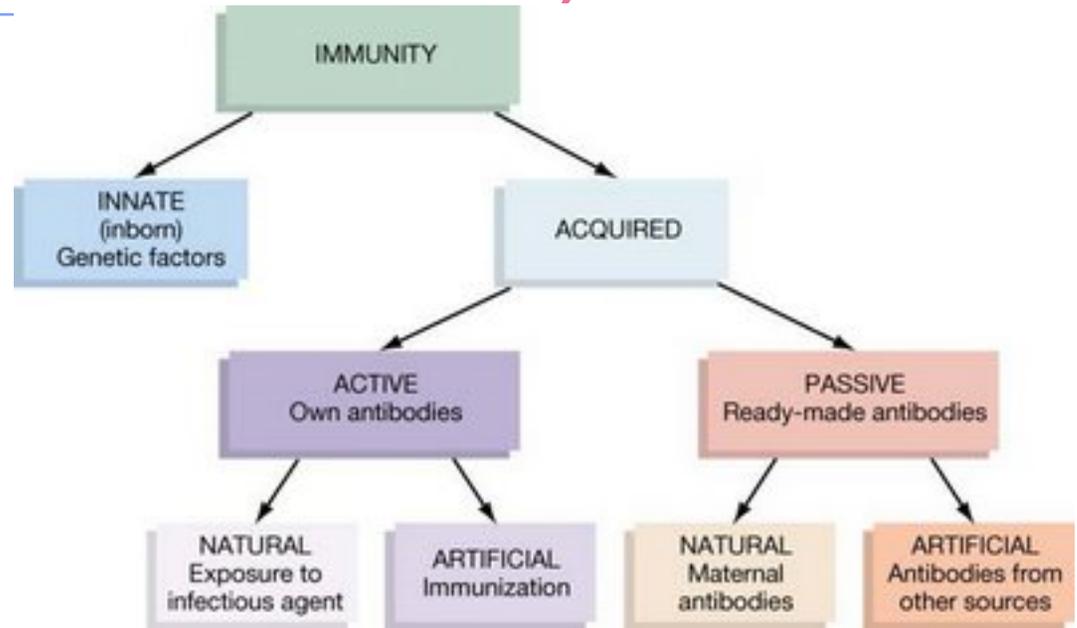


Figure 1. Classifications of immunity.



3rd line: Acquired (active) Immunity

■ Specific defense with memory

◆ Cells: Lymphocytes (WBC)

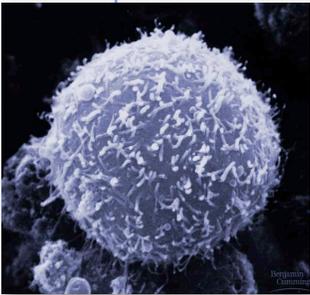
■ B cells

- ◆ Produced from stem cells in bone marrow
- ◆ Mature in Bone marrow

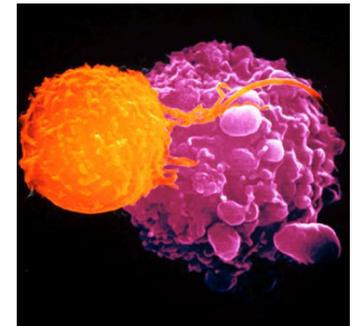
■ T cells

- ◆ Produced from stem cells in bone marrow
- ◆ Mature in thymus (“T”)

B cell



T cell

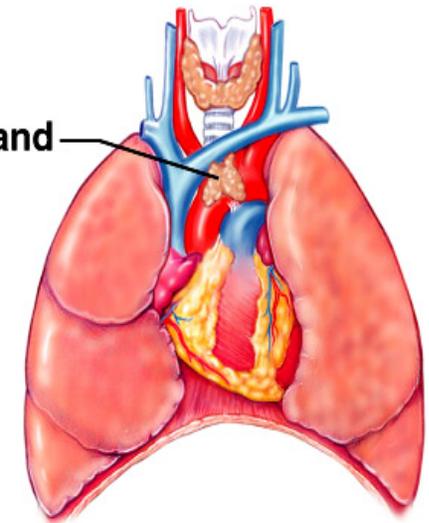


■ Lymphocytes respond to...

◆ antigens

- molecular structures “name tags” (often proteins) on cell surface or part of...
 - ◆ specific pathogens
 - ◆ specific toxins
 - ◆ abnormal body cells (cancer)

Thymus gland
in adult



Lymphocytes of the acquired immune system

■ Undergo “Maturation” & Self-Tolerance

◆ Lymphocytes distinguish “self” from “non-self”

- Body monitors if lymphocytes form with antigen receptors that recognize body’s own cells/antigens as foreign
- These lymphocytes cells are destroyed as they mature...
 - To prevent self-attack & develop self-tolerance
 - Not destroyed in autoimmune disorders

■ B cells

◆ Part of humoral immune response

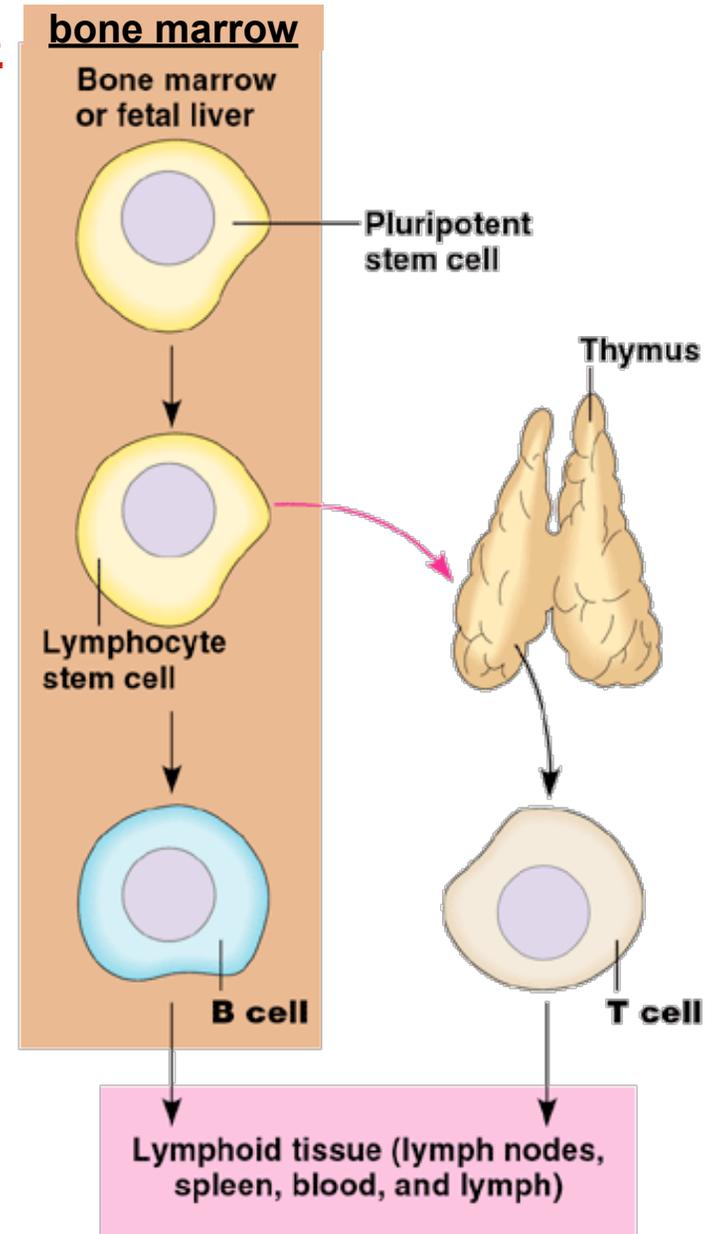
- identify antigens in the “humors” = body fluids
 - ◆ attack pathogens still circulating in blood & lymph

◆ Some produce antibodies

■ T cells

◆ Make up the cell-mediated immune response

- attack invaded and infected body cells



Overview

■ Acquired Immunity:

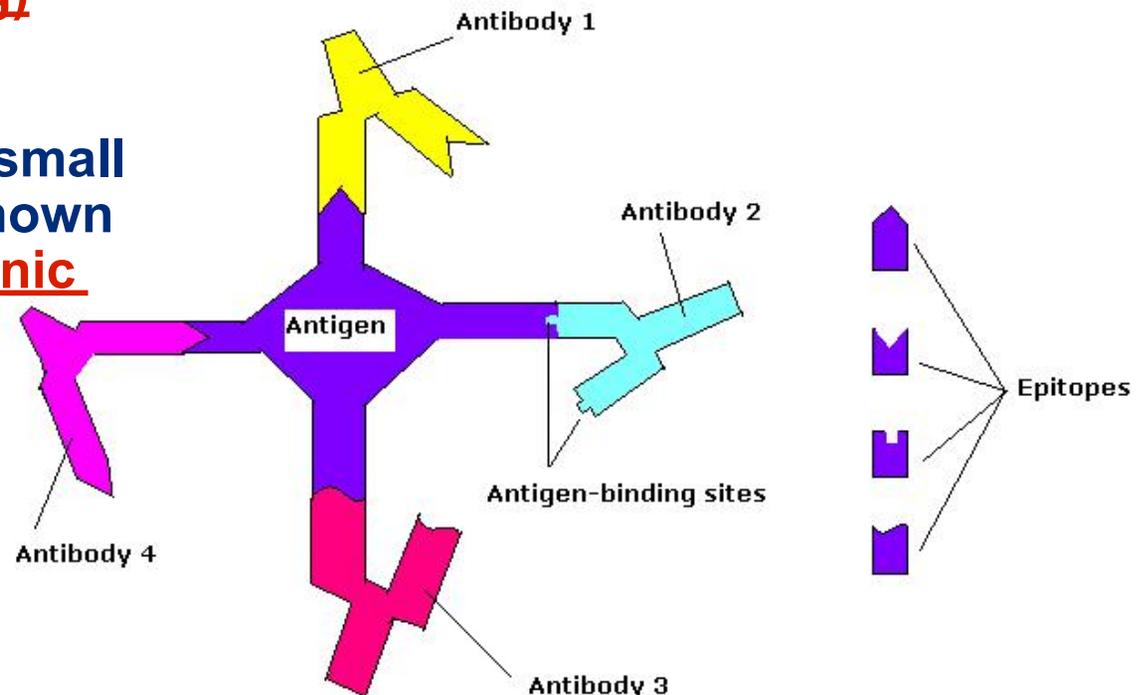
- ◆ **B and T cells have receptor proteins on their surface that bind a particular foreign molecule (antigen)**
 - **All receptors proteins on one lymphocyte are the same version**
 - ◆ Each person makes millions of different lymphocytes that **differ in the version of receptor type** they make and thus the specific antigen or antigen region they recognize
- ◆ **When an invader is detected, B & T cells are activated**
 - **They undergo mitosis and multiply (clone themselves)**
 - ◆ Some T and B cells are set aside to fight any future infection of that same invader (**KEEP MEMORY OF INVADER**)
 - ◆ Some T cells (**T_{Helper} cells**) help activate other lymphocytes
 - ◆ Some T cells (**T_{Killer} cells**) kill infected host cells
 - ◆ Some B cells secrete soluble receptor proteins (**antibodies**) that mark foreign molecules for destruction by other white blood cell (*like phagocytotic macrophages*).

How are invaders recognized: antigens

- B and T cells recognize antigens with their specific **antigen receptors** on their plasma membrane
 - One cell has up to 100,000 copies of one and only one type of antigen receptor on it
 - Lymphocytes thus exhibit **SPECIFICITY**
- ◆ Some B cells develop into **Plasma Cells** that secrete a soluble form of their antigen receptor called an **antibody (immunoglobulin - Ig)**

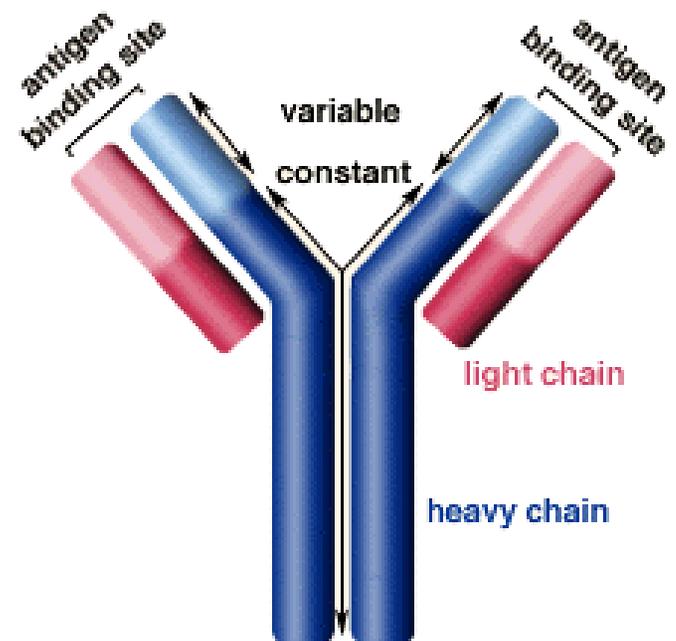
- Antigen receptors and antibodies recognize a small portion of an antigen known as the **epitope or antigenic determinant**

- ◆ One antigen may have many different epitopes

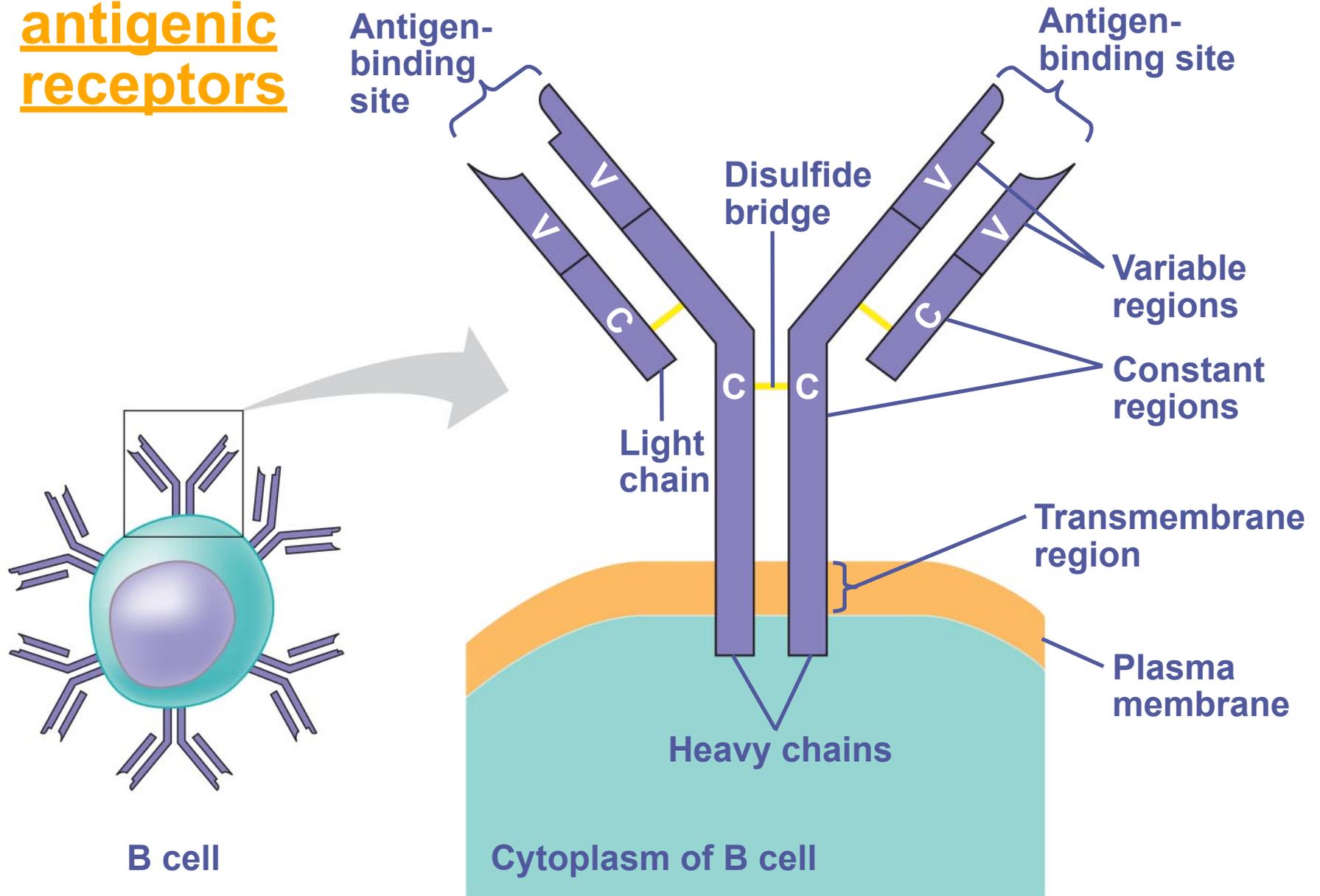


B cell receptors & antibodies

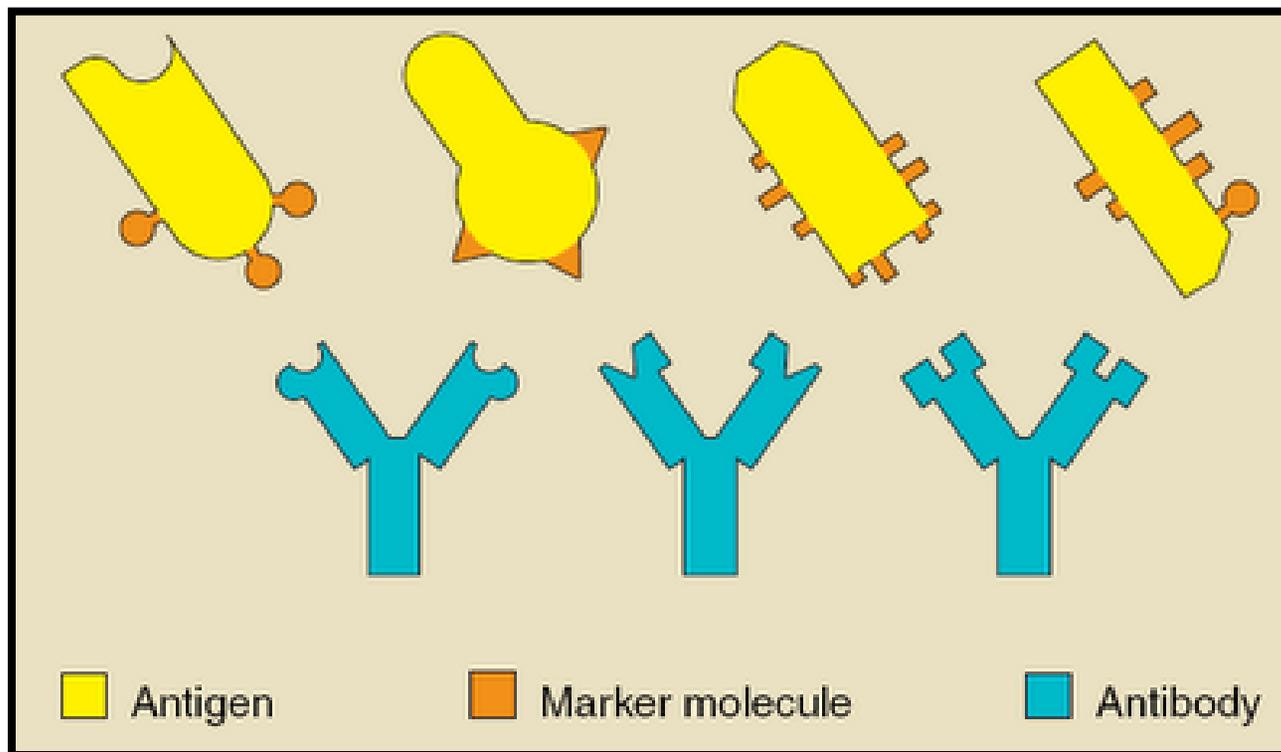
- B cell receptors and antibodies for antigens are Y-shaped molecules
 - ◆ Two identical heavy chains and two identical light chains held by disulfide bridges
 - Constant (C) region
 - ◆ Amino acid sequences vary little among receptors made on different B cells
 - Variable (V) region
 - ◆ Amino acid sequence varies extensively from one B cell to another
 - ◆ Each B cell produces only 1 type of receptor
 - Each receptor has two identical antigen-binding sites



B cell antigenic receptors

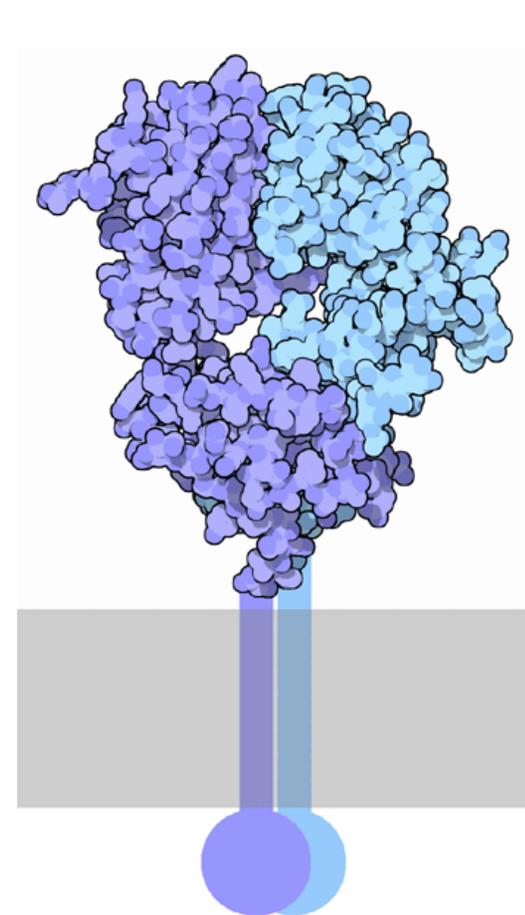


Receptor variation means an ability for the cell to interact with varying epitopes of varying antigens.

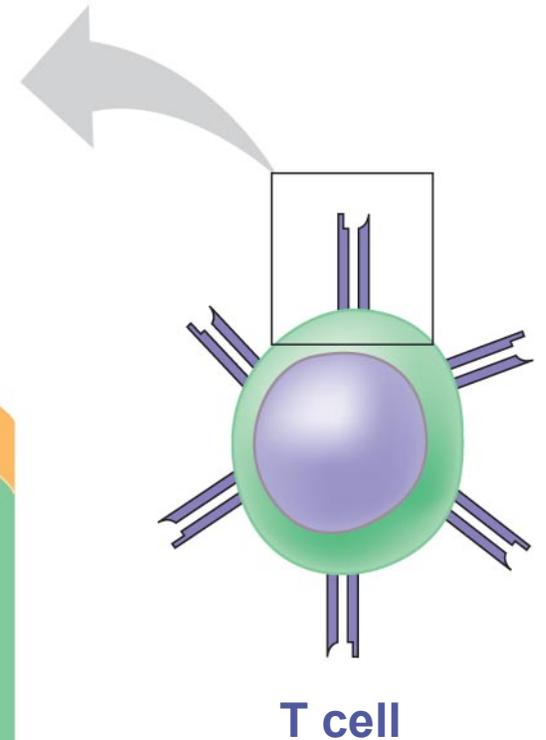
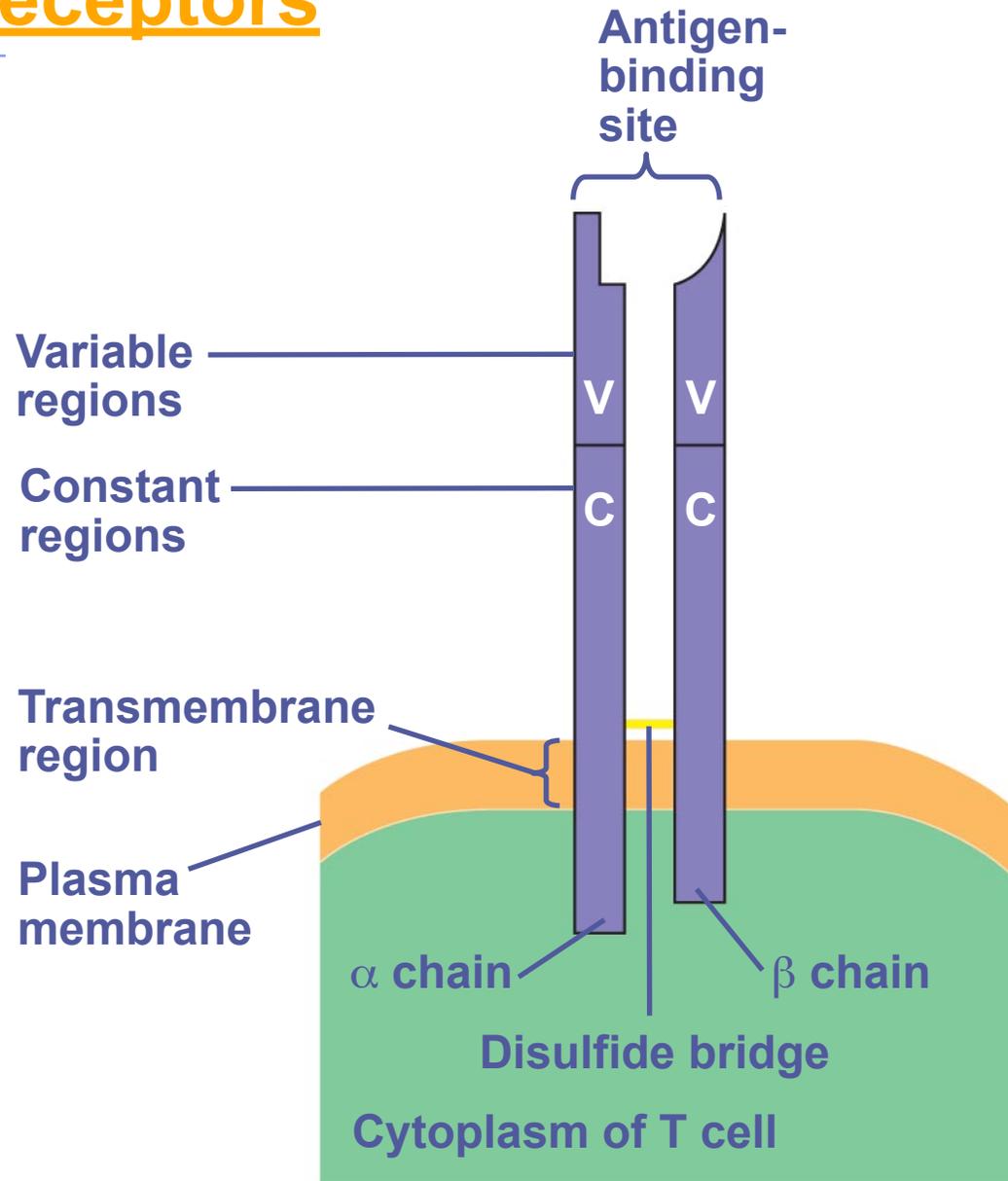


T cell receptors

- T cell receptors consist of one alpha chain and one beta chains held by disulfide bridges
 - Constant (C) region
 - ◆ Amino acid sequences vary little among receptors made on different B cells
 - Variable (V) region
 - ◆ Amino acid sequence varies extensively from one B cell to another
- ◆ Each T cell produces only 1 type of receptor

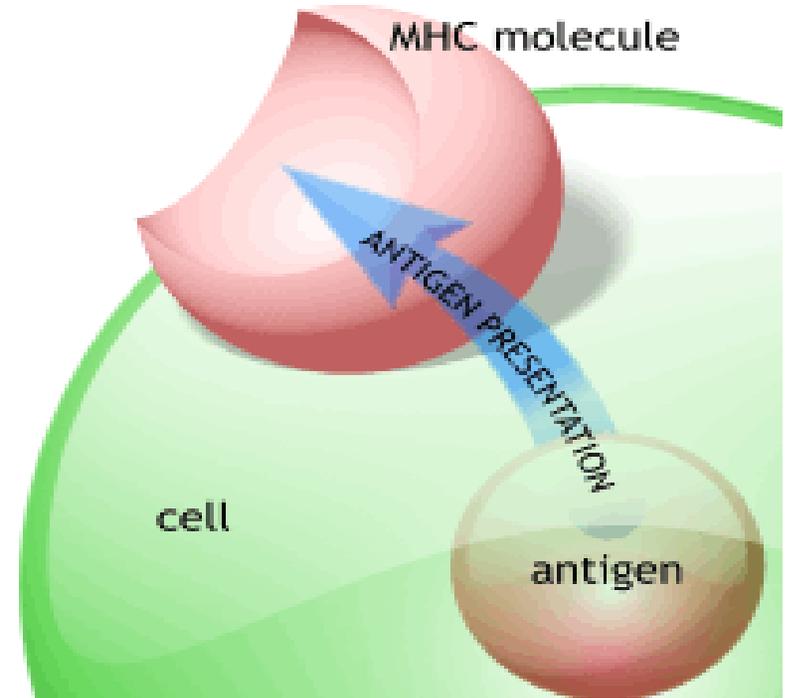


T cell antigenic receptors



How are invaders recognized: antigens

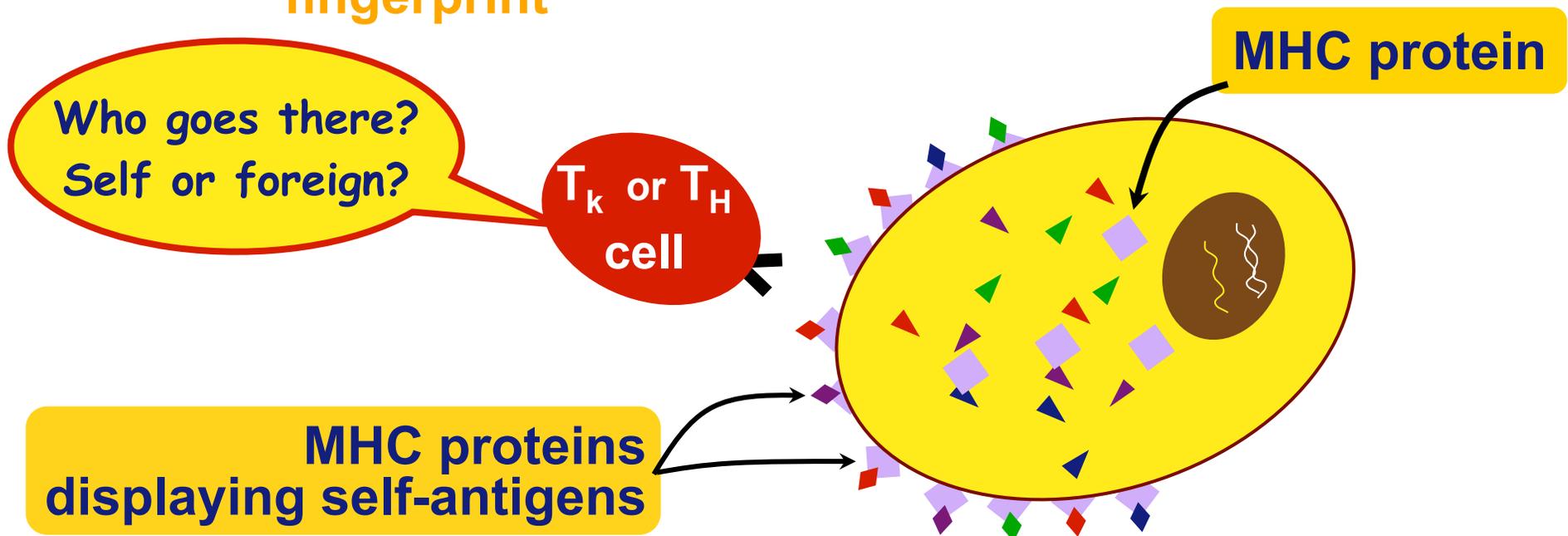
- B cells & T cells respond to different antigens
 - ◆ B cells recognize intact antigens
 - pathogens in blood & lymph
 - ◆ T cells recognize antigen fragments displayed on body cell surfaces
 - pathogens which have already infected cells
 - ◆ Major histocompatibility complex (MHC) genes produces a host cell proteins that can present an antigen fragment to T cell receptors.



How is any cell tagged with antigens?

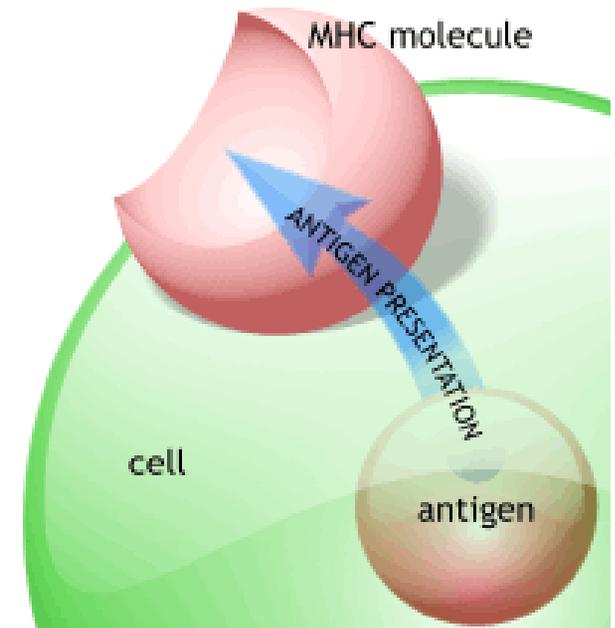
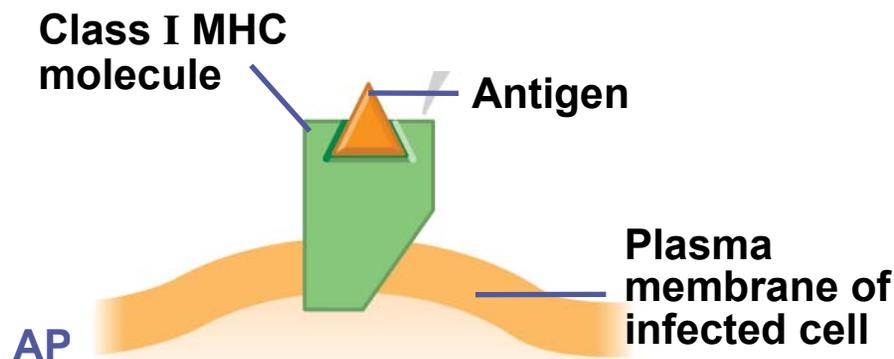
■ Major histocompatibility (MHC) proteins

- ◆ proteins which constantly carry bits of cellular material from the cytosol to the cell surface
- ◆ “snapshot” of what is going on inside cell
- ◆ give the surface of cells a unique label or “fingerprint”

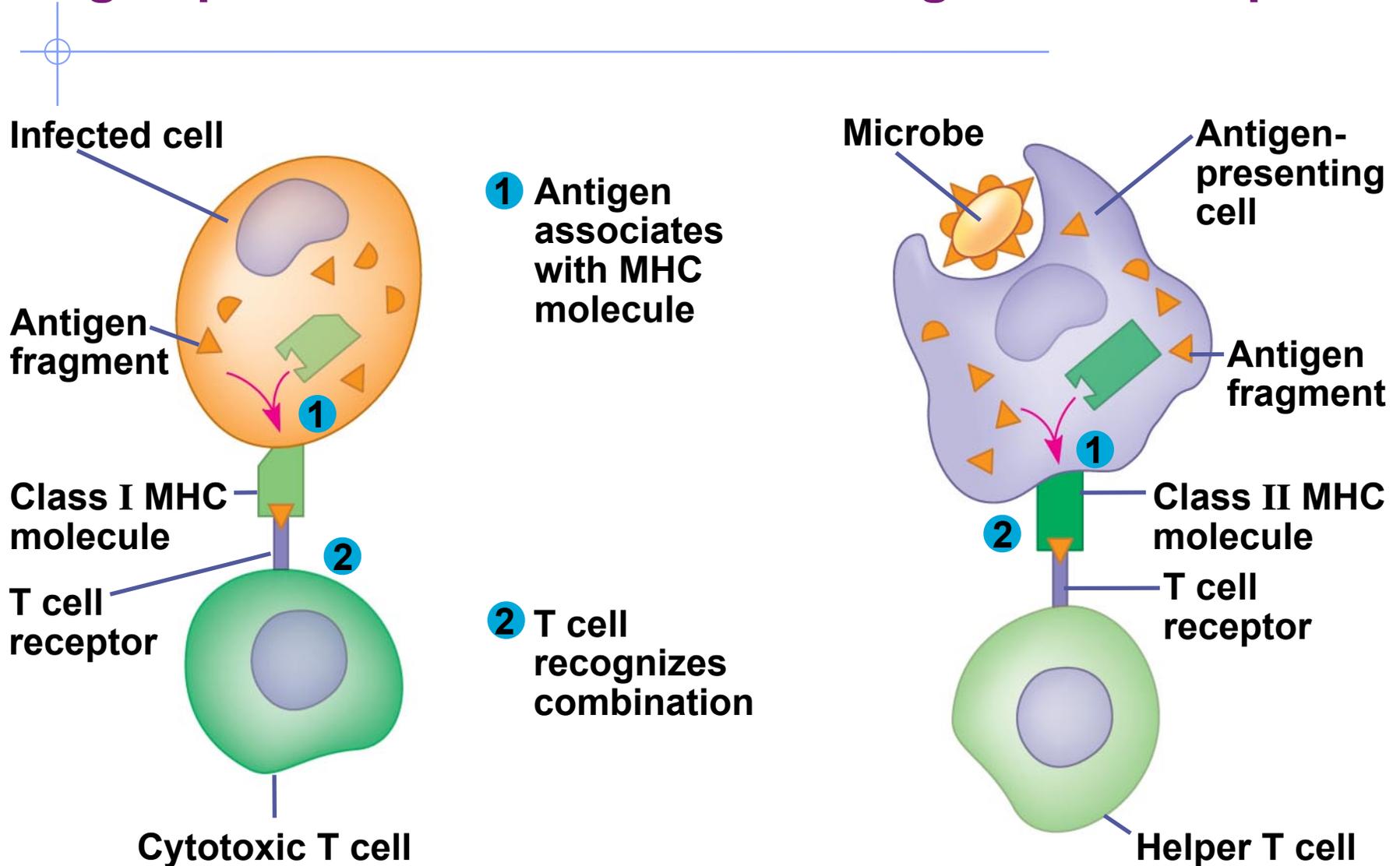


Major Histocompatibility Complexes & T cell recognition

- **Class I MHC molecules can be found on almost all cells**
 - ◆ **If any body cell becomes infected or cancerous, they can display antigen fragments through class I MHC molecules**
 - **Recognized by CYTOTOXIC T CELLS (and their CD8 surface proteins)**
- **Class II MHC molecules can be found on ANTIGEN PRESENTING CELLS**
 1. **Dendritic cells**
 2. **Macrophages**
 3. **B cells**
 - ◆ **Recognized by HELPER T CELLS (and their CD4 surface proteins)**



Antigen presentation to T cells through MHC complexes



Clonal Selection

- Antigen receptor bind to antigen causing a series of actions that lead to activation of B or T cells

- ◆ B and T cells amplify their response by undergoing rapid **mitosis**

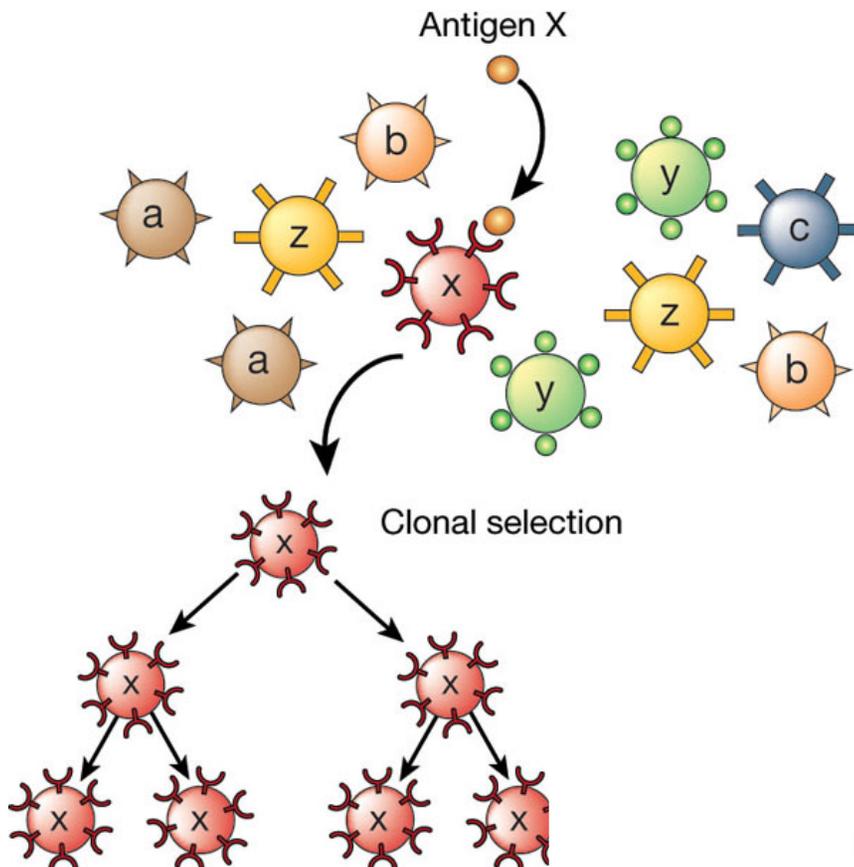
- Two clones of the cells selected for form (**CLONAL SELECTION**)

1. **Effector Cells**

- Short lived
- Attack the antigen and any pathogens producing antigen

2. **Memory Cells**

- Long-lived
- Have specific receptors for that antigen on its surface
- Ready to respond immediately if this antigen ever enter the body in the future again
- Basis for immunological memory - **ACQUIRED IMMUNITY**



Acquired Immunity

■ Two parts

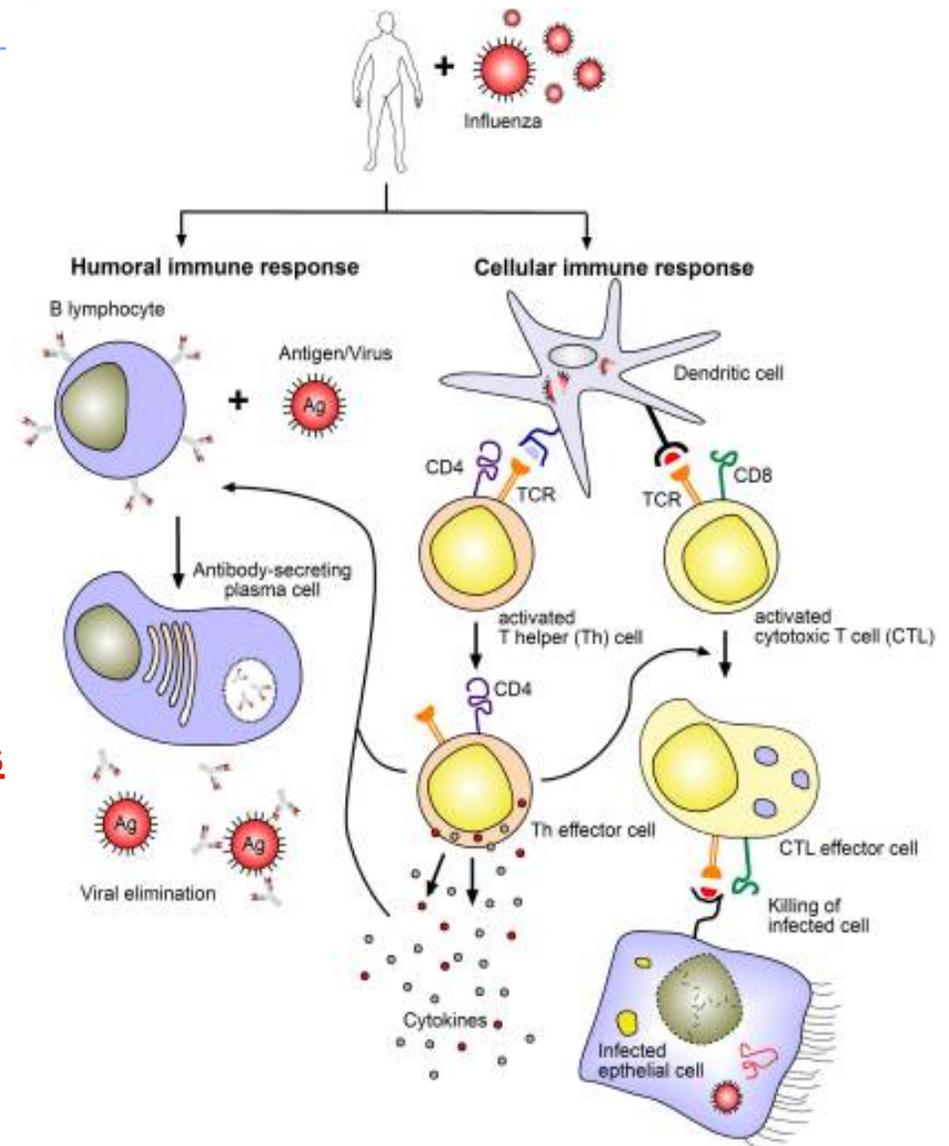
1. Humoral immune (anti-body mediated) response

- Activation and clonal selection of **B cells**
- Some of whom release antibodies

2. Cell-mediated immune response

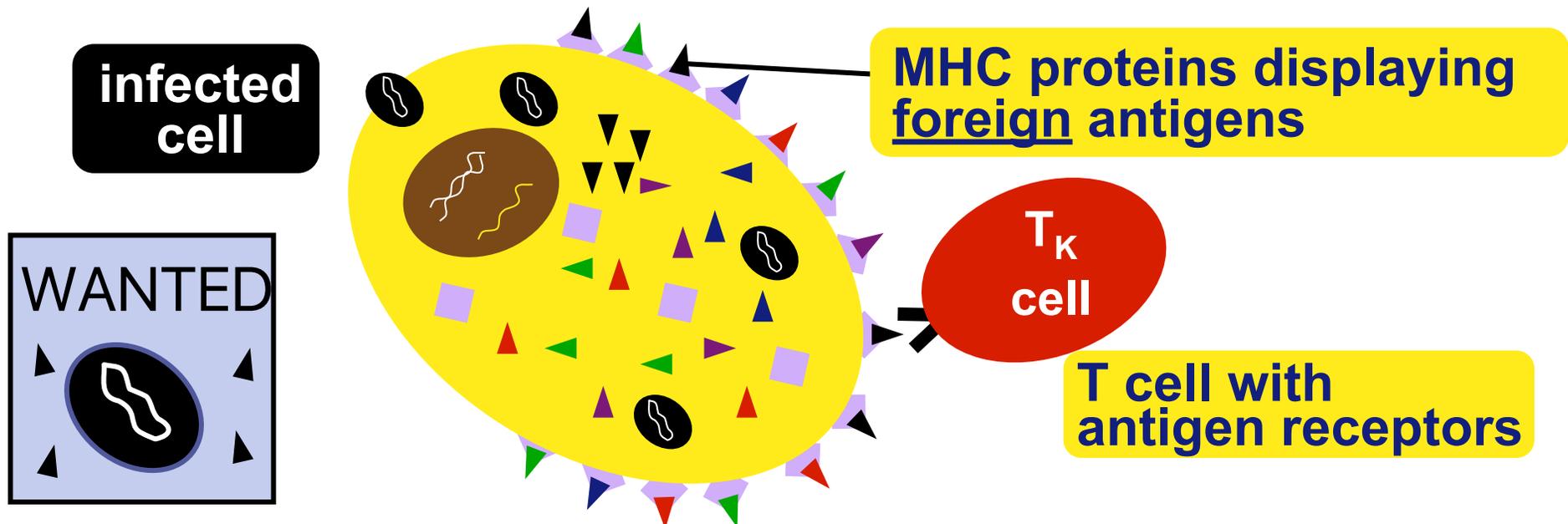
- Activation and clonal selection of **cytotoxic T cells**
- Some of whom identify and destroy target cells with their secretions

- Both are aided by helper T cells!

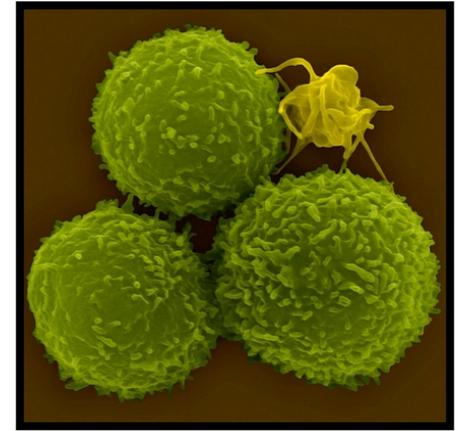


How do T cells know a cell is infected?

- Infected cells or cells that digest some pathogens have MHC proteins on their surface
 - ◆ MHC proteins carry pieces of pathogens to cell surface
 - foreign antigens now on cell membrane
 - ◆ Phagocytotic cells are called Antigen Presenting Cell (APC)
Ex: macrophages can also serve as APC
- tested by Helper T cells or Cytotoxic T cells



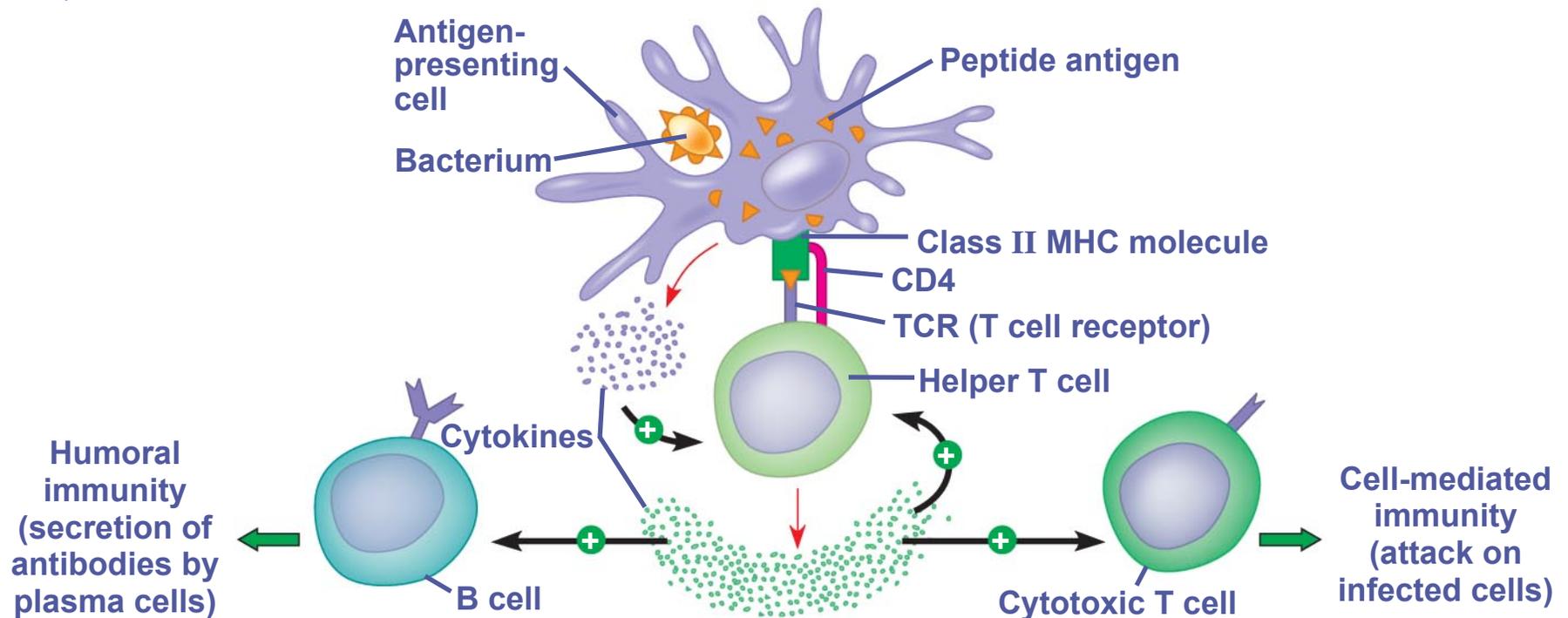
Helper T cells



- Respond to nearly all antigens
- Activate B and cytotoxic T cells
 - ◆ **How?**
 1. T_H cells have antigen receptors on surface
 2. T_H cell encounters an antigen-presenting cell displaying an antigen fragment on their surface class II MHC complex
 3. T_H cell's receptor variable region matches antigen fragment
 4. Additional T_H cell membrane protein CD4 helps join antigen-presenting cells and T_H cell
 5. Cytokines are released by both antigen-presenting cells and bound T_H cell
 - **Cytokines = proteins that help recruit and activate lymphocytes**
 6. T_H cell activated
 7. T_H cell proliferates by mitosis
 8. Clones differentiate into active T_H cells and memory T_H cells
 9. Activated T_H cells secrete cytokines
 10. Stimulate activation of B cells and cytotoxic T cells

Helper T Cell Activation & Effects

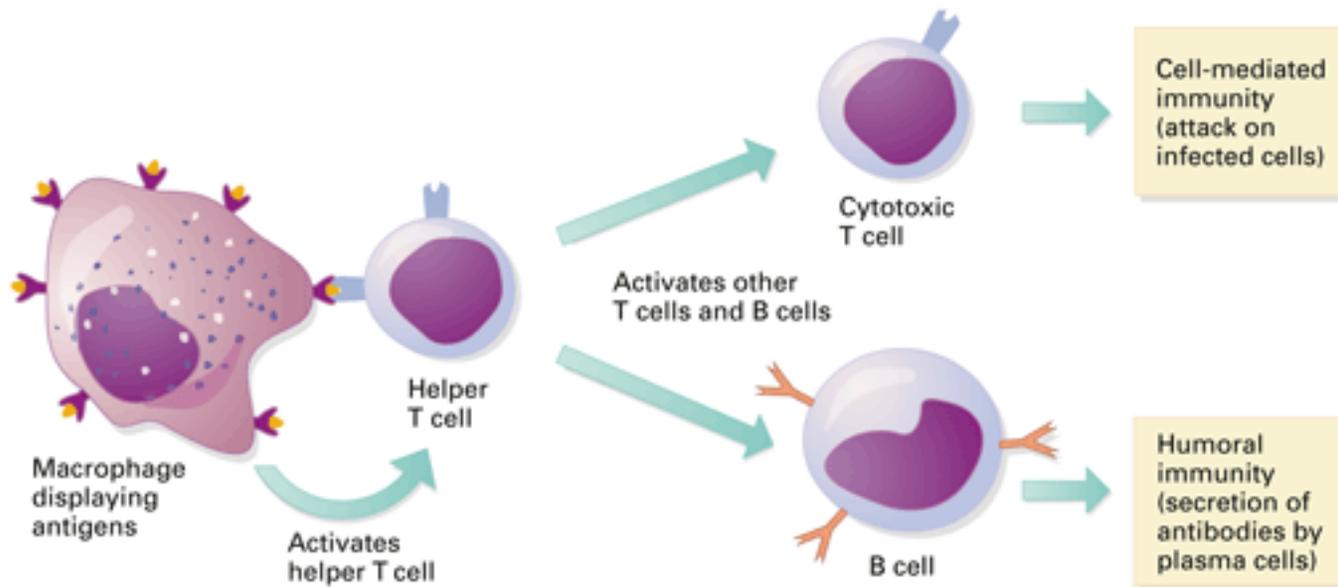
- **Helper T cells enhance humoral and cell-mediated responses**



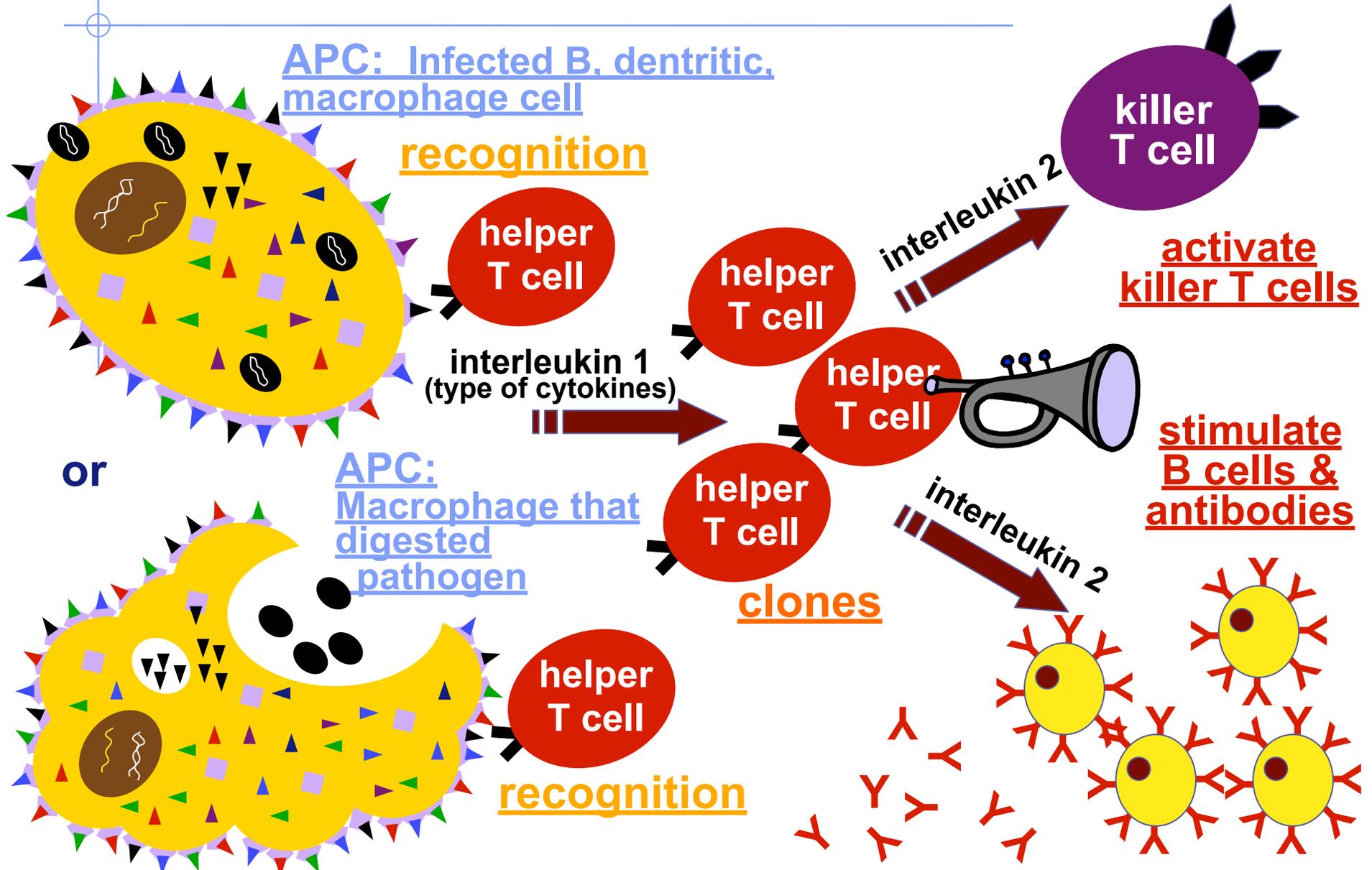
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Helper T Cells are critical:

Without them Cytotoxic T cells and B cells cannot clone themselves and fight infection!

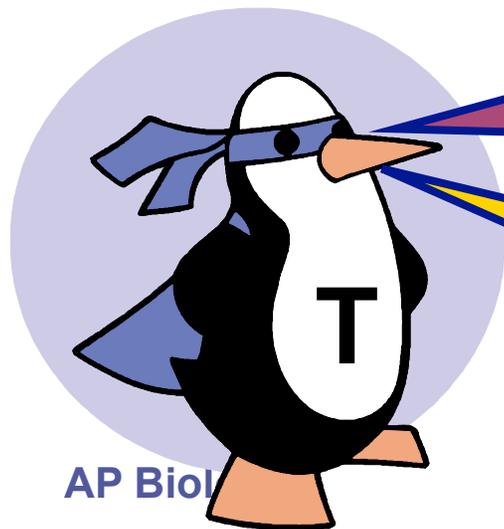


T_H cell response



Fungi & bacterial live outside our cells, but what if the attacker (virus) gets past the B cells & innate blockades in the blood & actually infects (hides in) some of your cells?

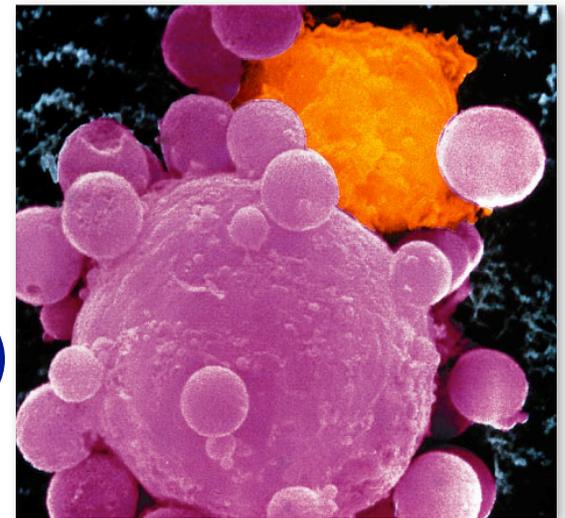
You need trained assassins to recognize & kill off these infected cells!



AP Biol

**Attack
of the
Killer T cells!**

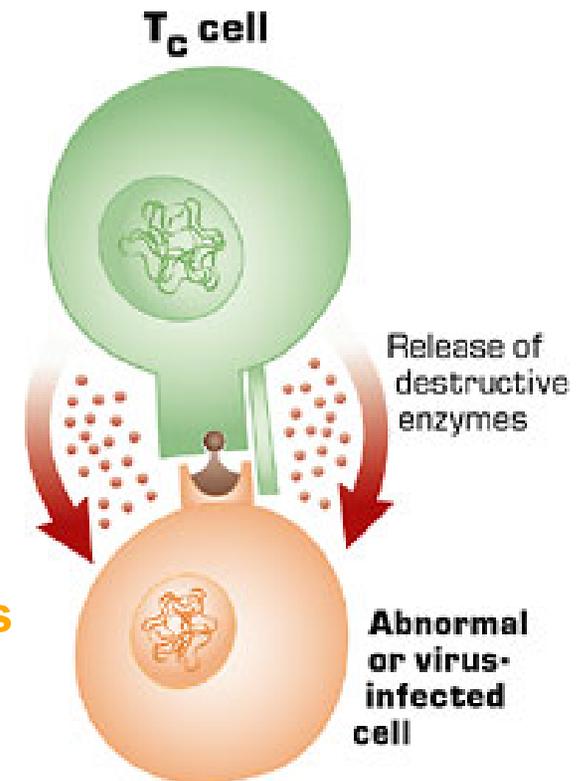
**But how do T cells
know someone is
hiding in there?**



Cytotoxic T cells - Destroy infected cells

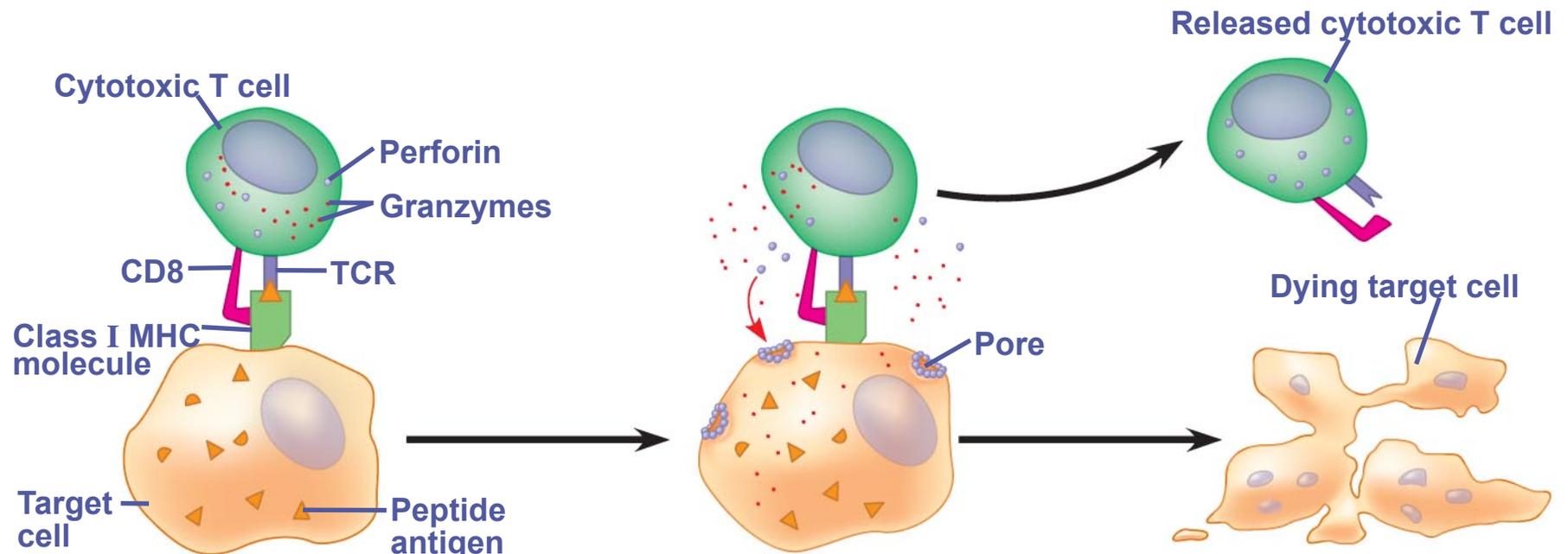
Cell-Mediated Immunity:

1. T_C cells recognize antigen fragments held in class I MHC molecules on the surface of antigen-presenting cells
2. T_C cell's receptor variable region matches antigen fragment
3. T_C cell's surface protein CD8 helps keep antigen presenting cell and T_C cell in contact
4. T_C cell is activated
5. T_C cell undergoes rapid mitosis to produce memory T_C cells and active T_C cells
6. Activated T_C cells destroys infected cell displaying antigen fragment
 - T_C cells releases perforin = forms pore in membrane allowing water and ions to enter and causing cell lysis
 - T_C cells release granzymes = enter infected cell by endocytosis and initiate apoptosis
7. Activated T_C cells go on to destroy other cells found with same antigen fragment on class I MHC complex



Cytotoxic T cells - Destroy infected cells

- **By killing infected body cell....**
 - ◆ Intracellular pathogen deprived of place to reproduce
 - ◆ Pathogen inside cell released and exposed to antibodies in fluids who can neutralize the antigen or tag it for future destruction



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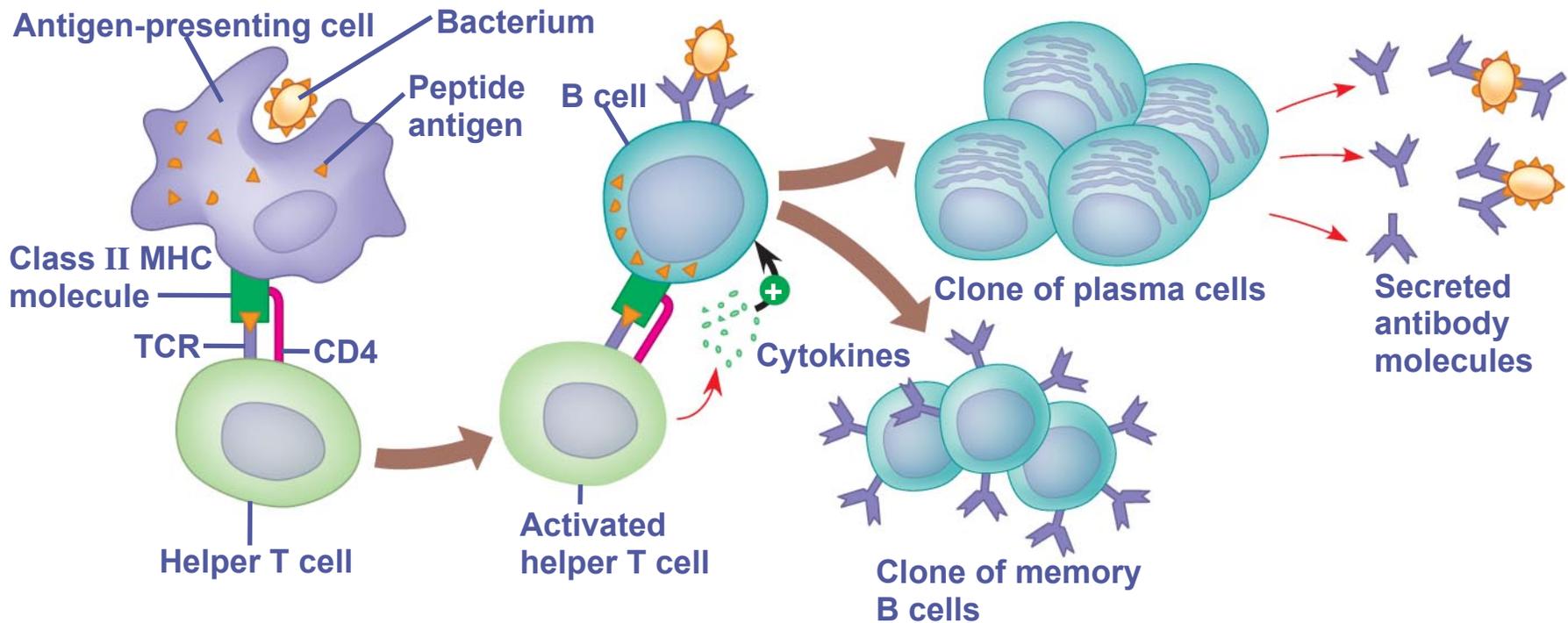
B Cells- Respond to extracellular pathogens

Humoral immune response:

- Produce antibodies that disable and mark antigens for destruction
- How?
 - ◆ A B cell with coated in receptors binds an antigen
 - ◆ B cells internalize antigens and display fragments with class II MHC proteins on their surface
 - ◆ Cloned activated Helper T cells bind to B cells with antigen fragment on surface specific for this T_H cells receptor
 - ◆ T_H cell released cytokines
 - ◆ B cell is activated
 - ◆ Activated B cell proliferates through mitosis
 - One group of clones becomes memory B cells
 - One group of clones becomes plasma cells
 - ◆ Secrete antibodies specific for antigen fragment that initiated response

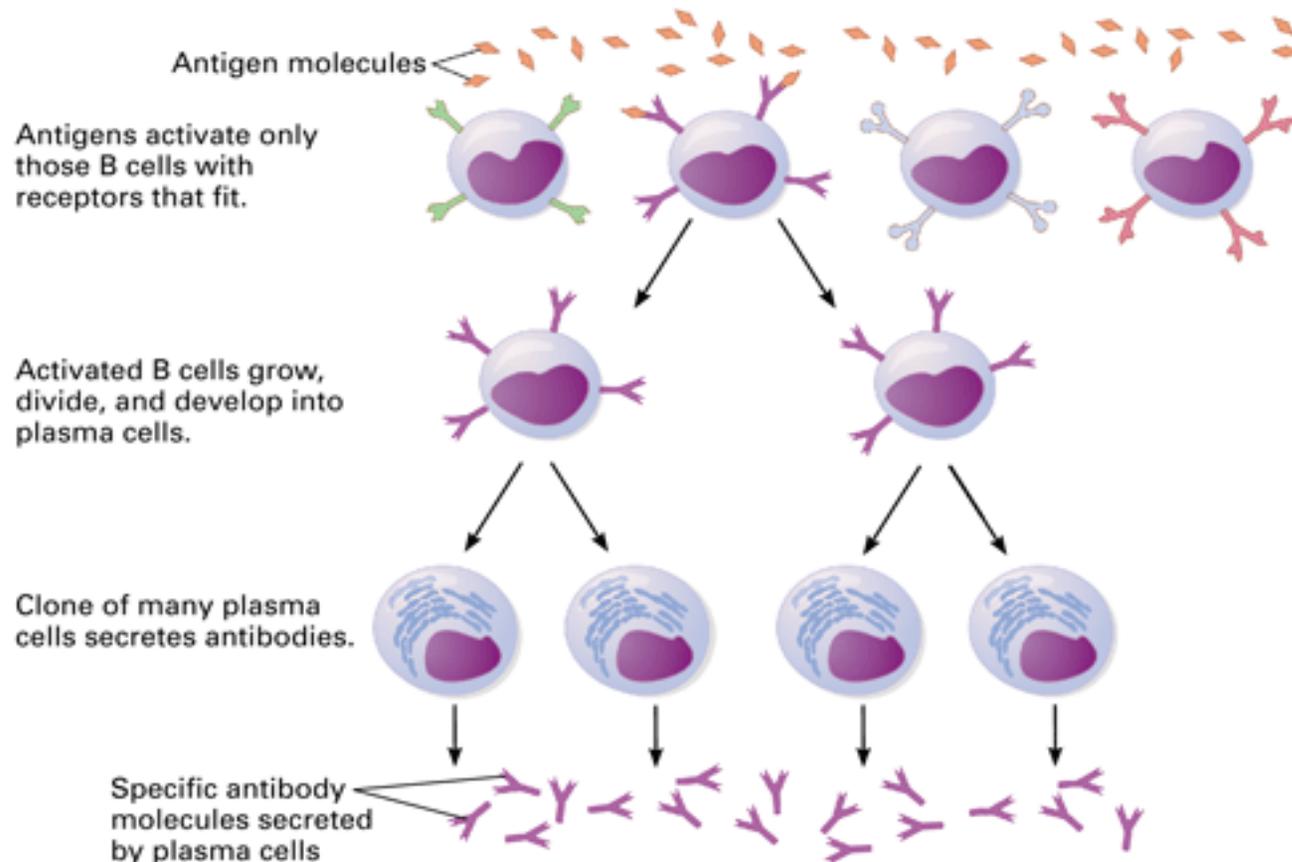
B Cells- Respond to extracellular pathogens

- Each plasma B cell produced secreted 2000 antibodies for a specific antigen per second!



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When the B cell with the right membrane receptor recognize a foreign antigen.... It undergoes mitosis



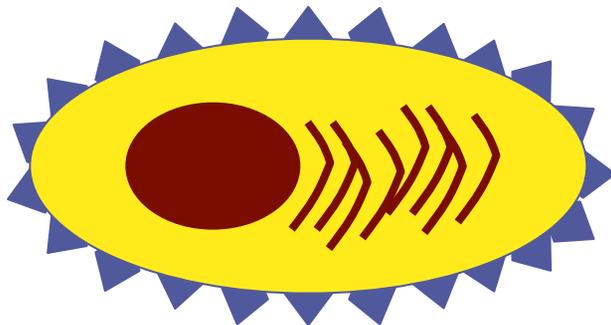
- All the clones of that one B cell now can recognize the same antigen found on all the pathogens of the same type.
 - ◆ Now there are many cells that can help **SPECIFICALLY** destroy just **THAT** pathogen!

How are invaders recognized?

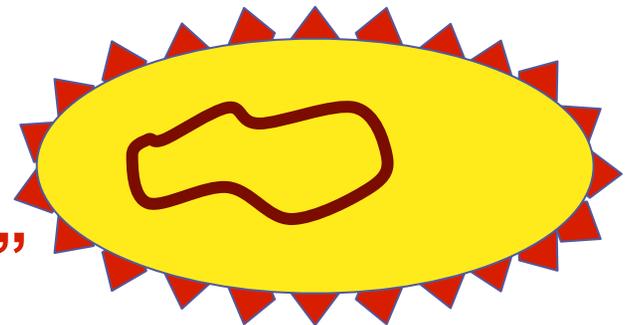
■ Antigens

- ◆ Foreign molecules are specifically recognized by lymphocytes and produce a response in them
 - “self” recognition involves the immune system **NOT** responding to any surface molecules on your own cells
 - ◆ no response from WBCs
 - “foreign” antigens come in many forms
 - ◆ Toxins secreted by bacteria
 - ◆ Large molecules on surface of pathogens: **viruses, bacteria, protozoa, parasitic worms, fungi, toxins**
 - ◆ Large molecules on surface of non-pathogens: **cancer cells, transplanted tissue, pollen**
 - Often antigens are proteins or polysaccharides

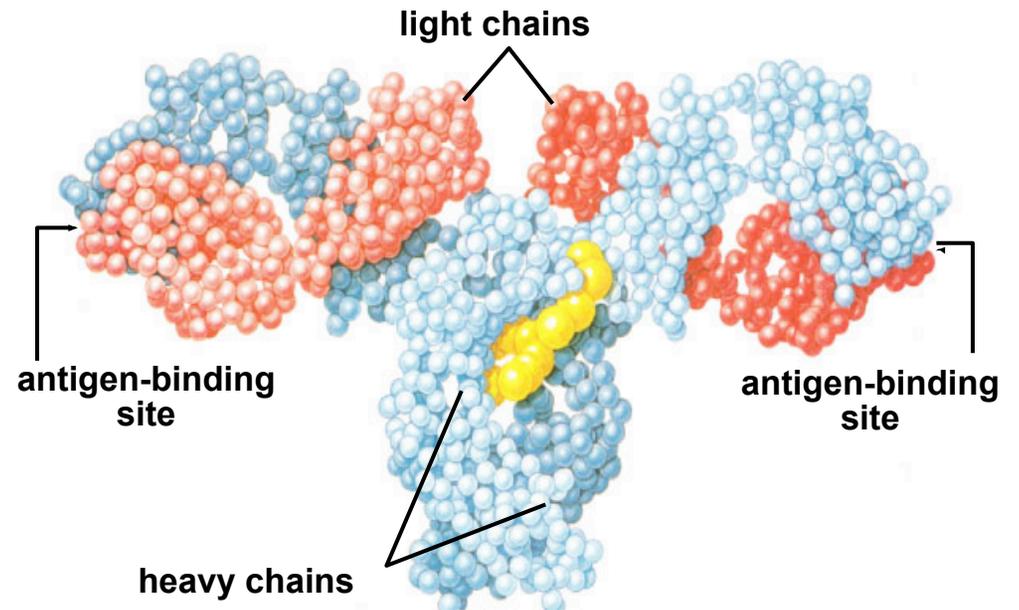
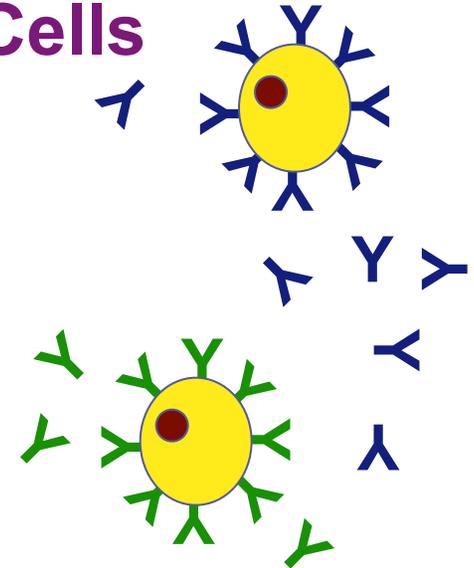
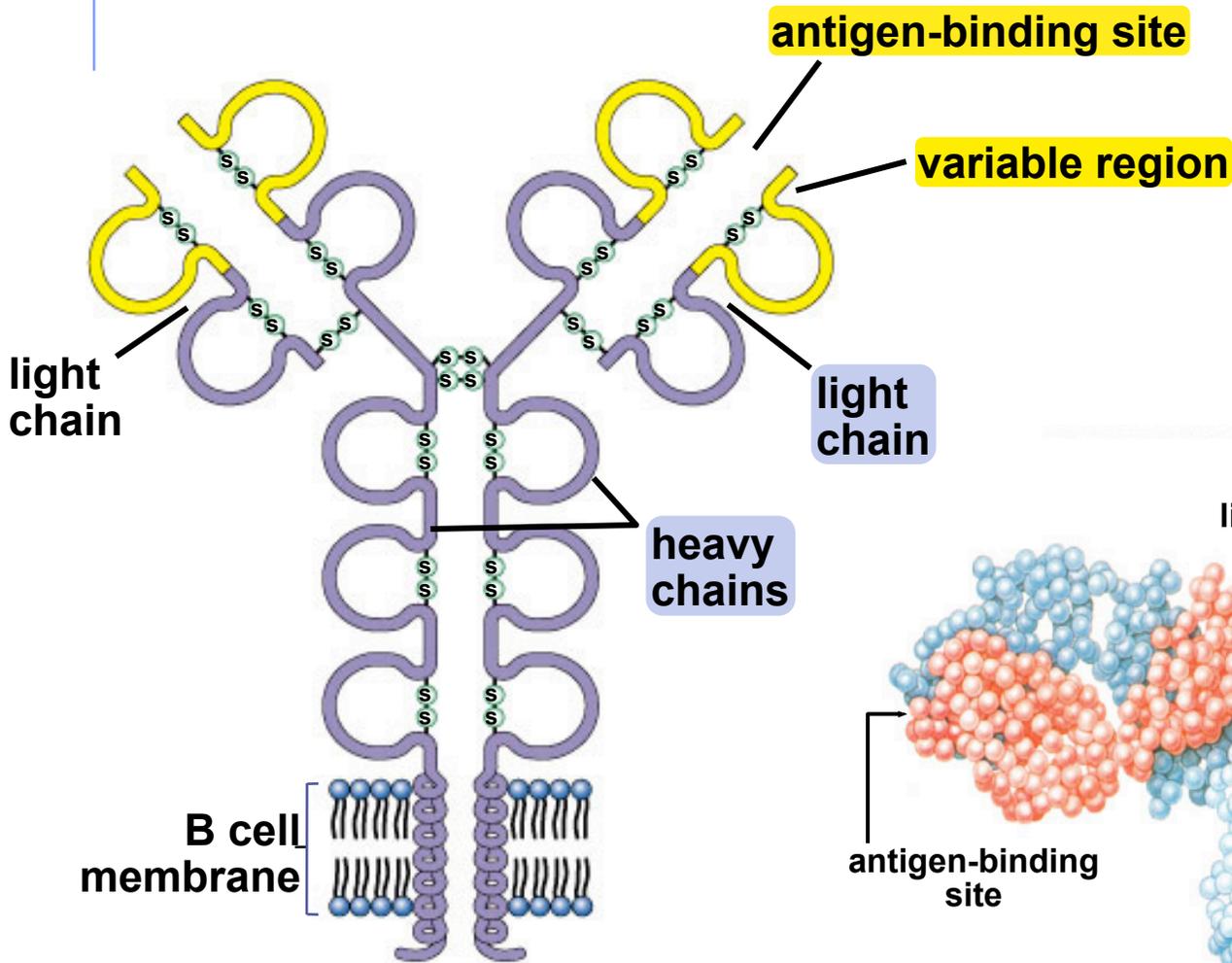
“self”



“foreign”



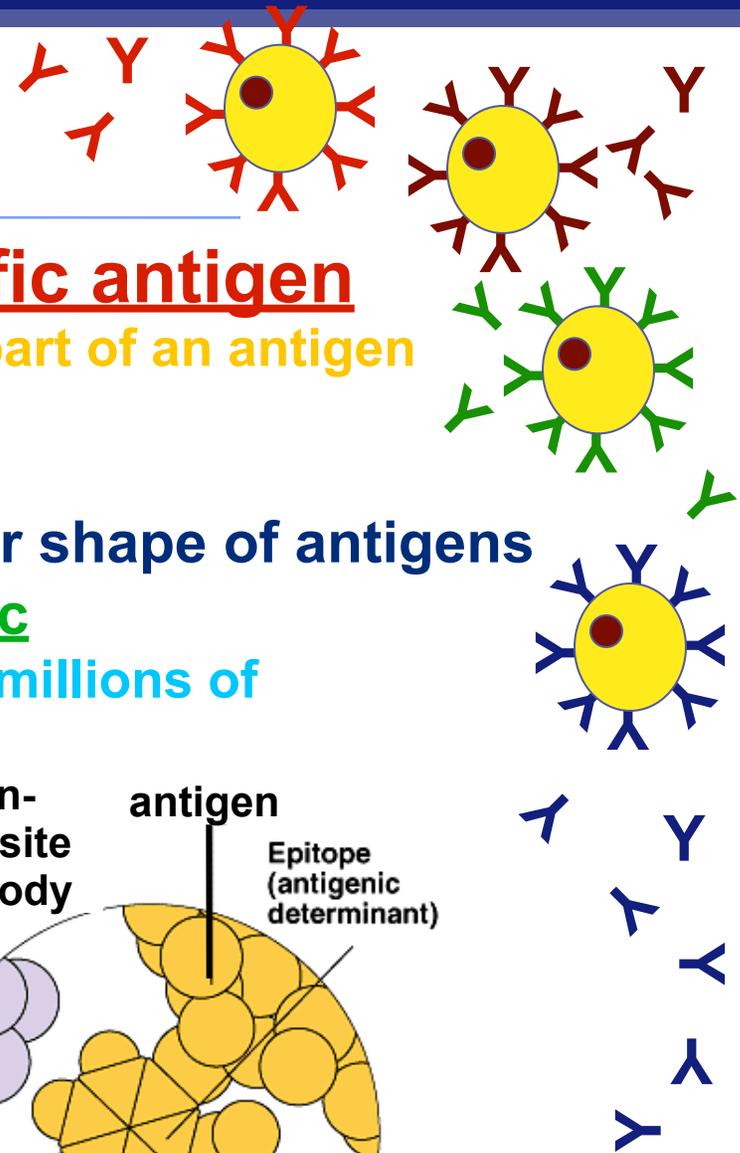
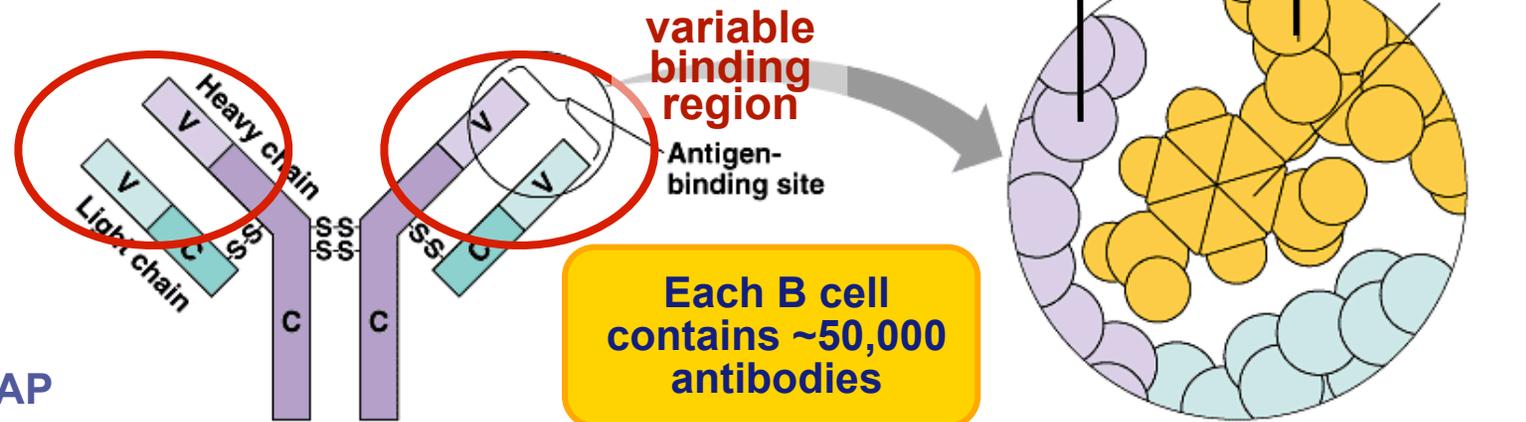
Structure of antibodies Secreted by B Cells



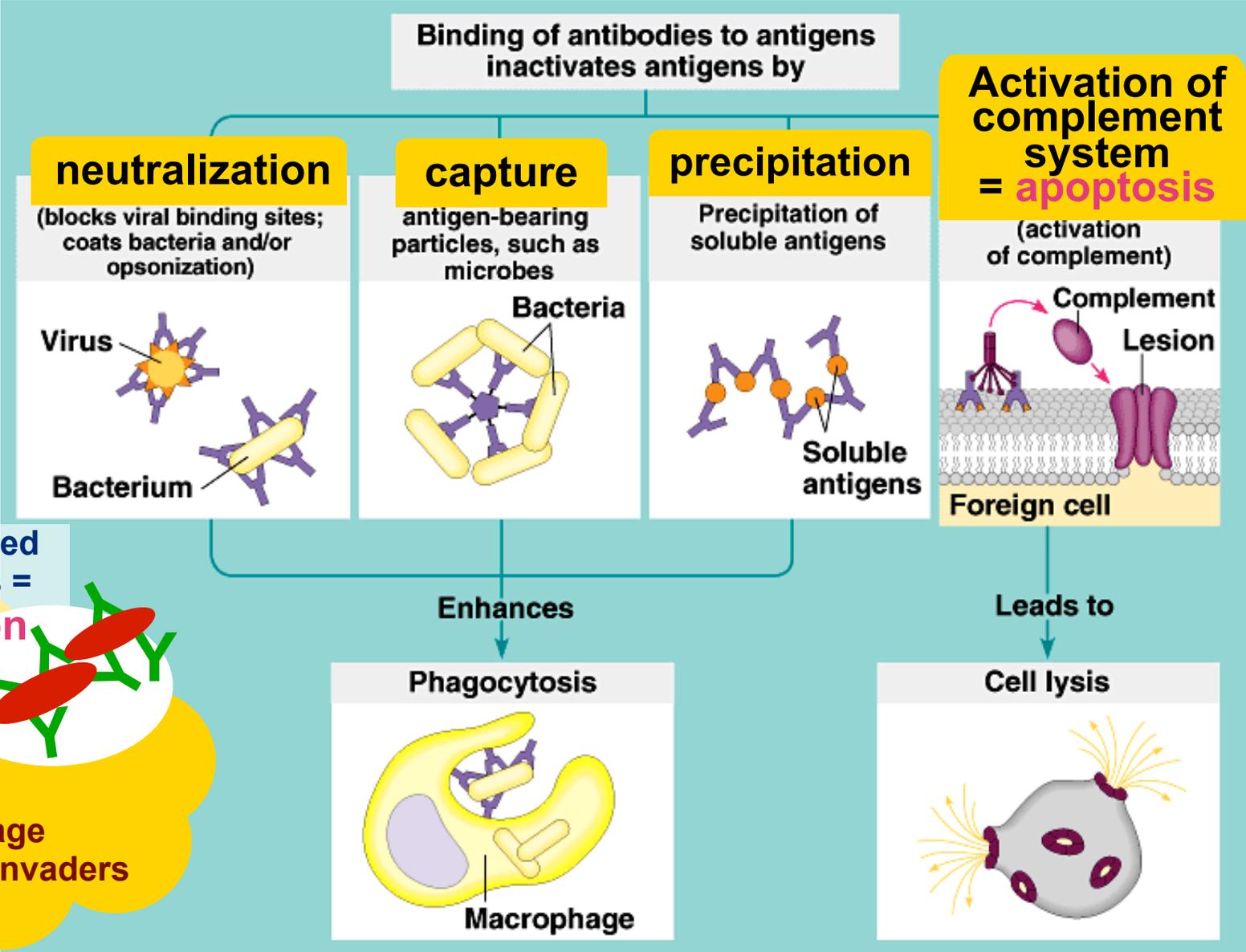
Antibodies

■ Proteins that bind to a specific antigen

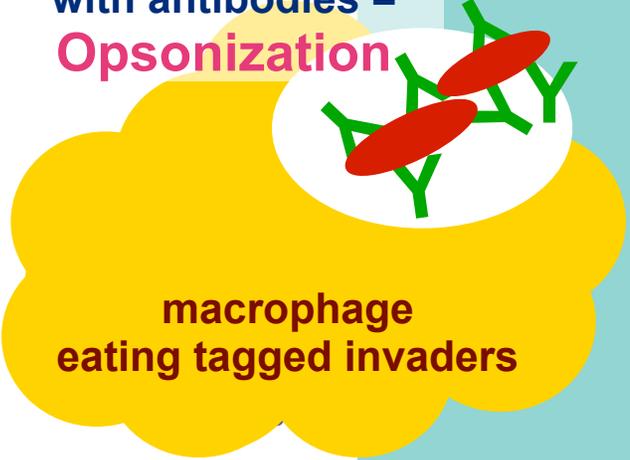
- Specifically, they bind to a small part of an antigen called the **epitope**
- ◆ multi-chain proteins
- ◆ binding region matches molecular shape of antigens
- ◆ each antibody is **unique & specific**
 - millions of antibodies respond to millions of foreign antigens
- ◆ tagging = “handcuffs”
 - antibodies ID which particle needs destroying



What do antibodies do to invaders?

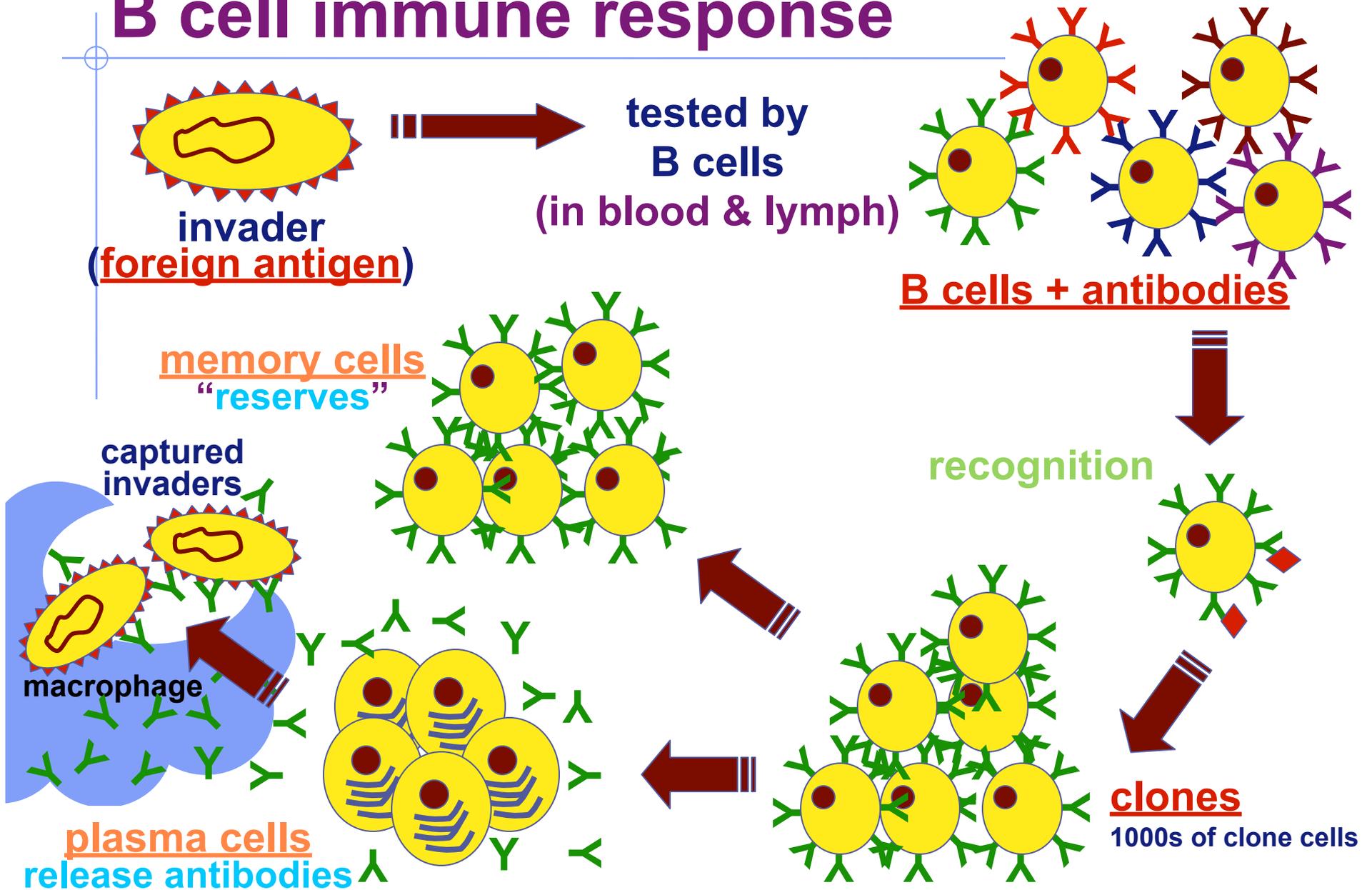


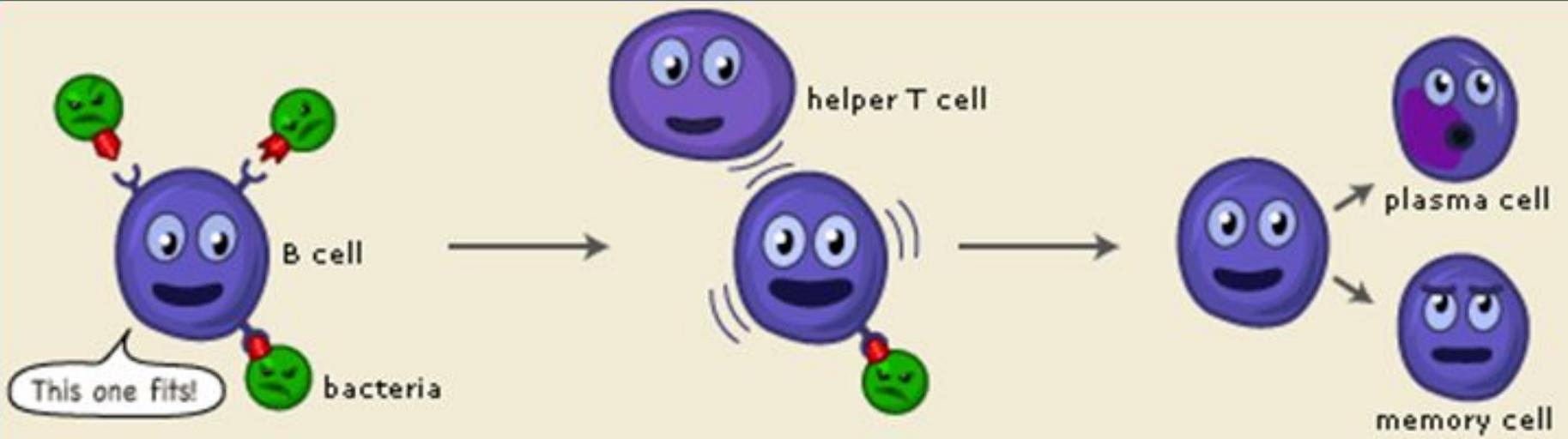
pathogens tagged with antibodies = **Opsonization**



10 to 17 days for full response

B cell immune response

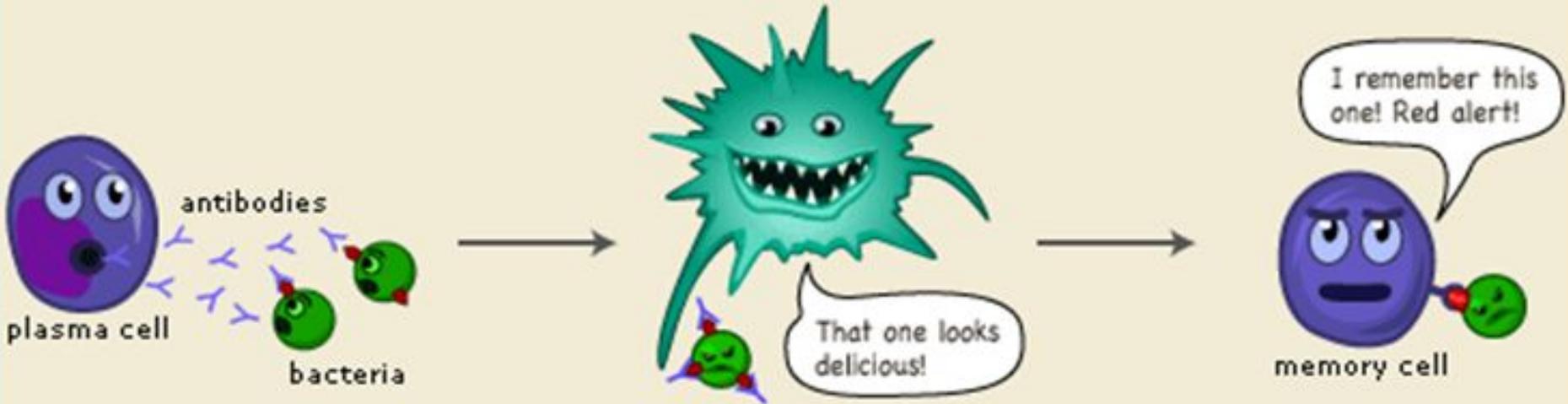




1. The B cell finds an antigen which matches its receptors.

2. It waits until it is activated by a helper T cell.

3. Then the B cell divides to produce plasma and memory cells.

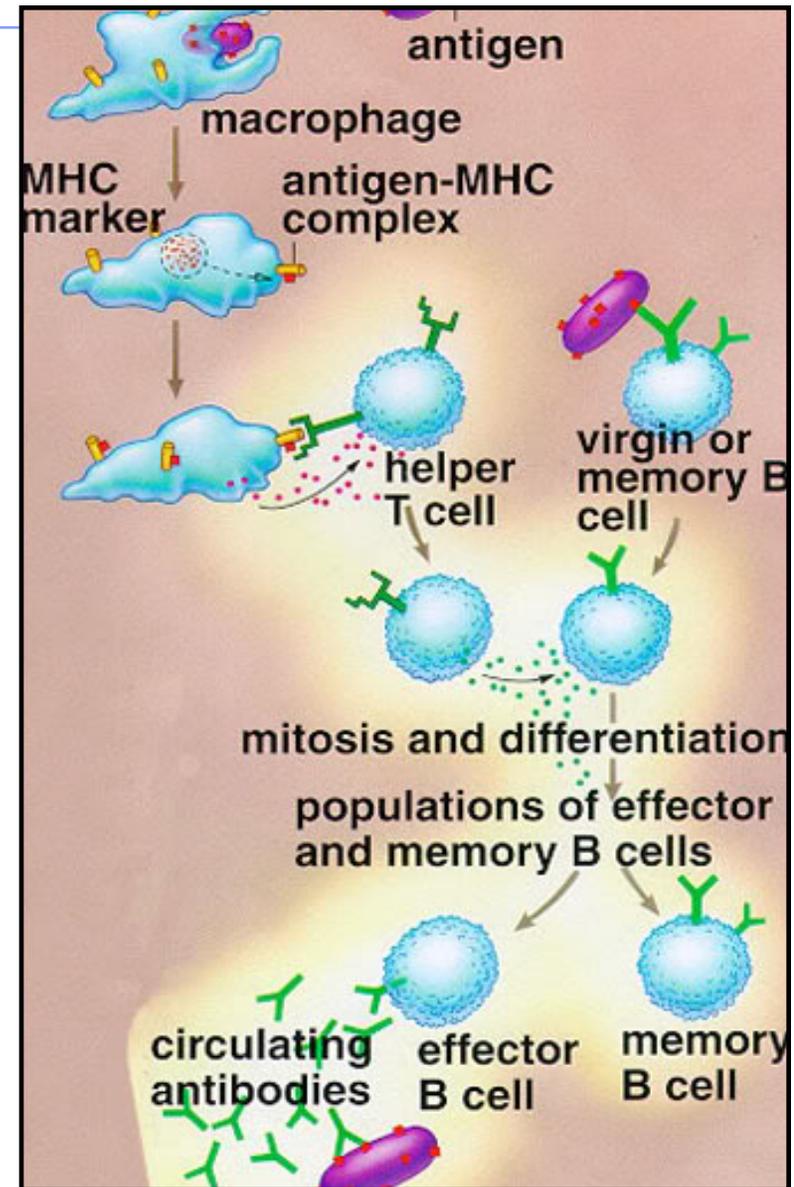
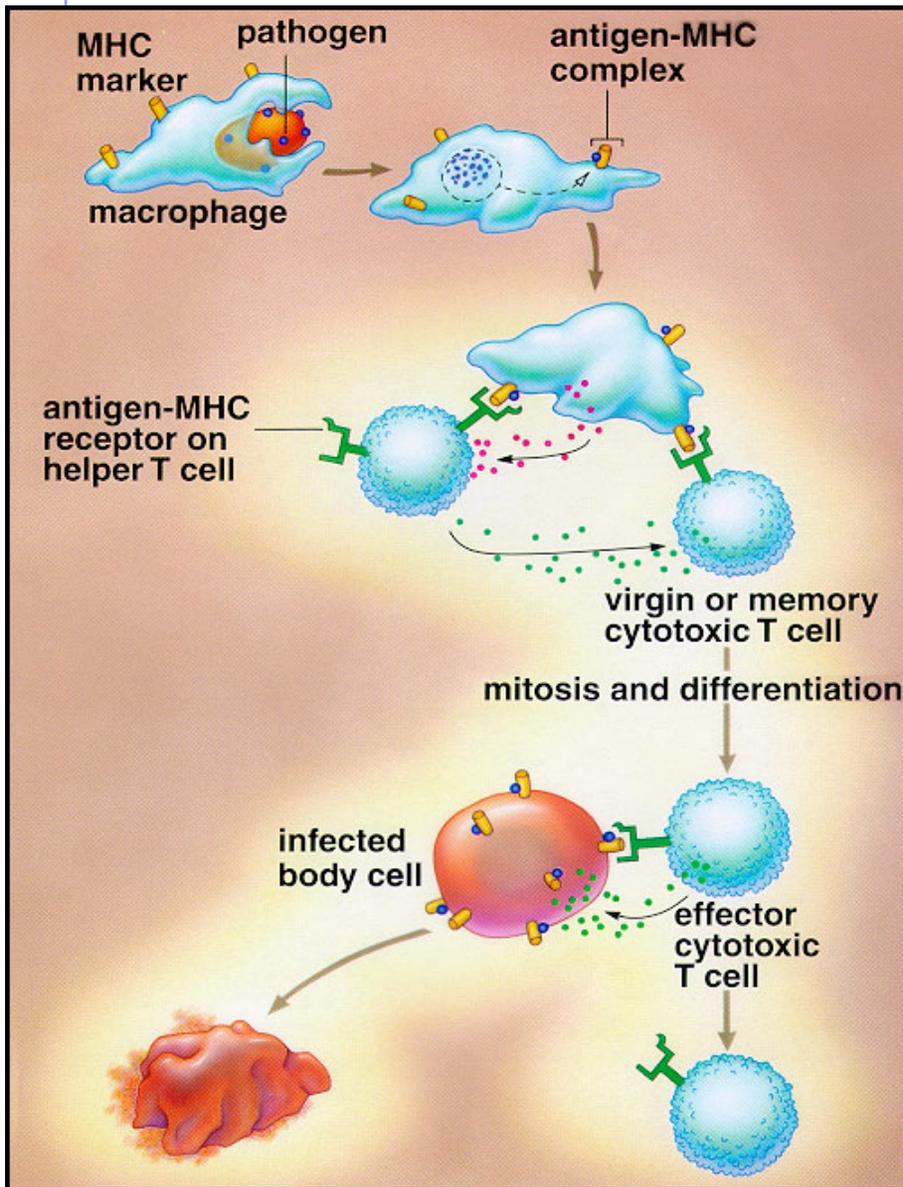


4. Plasma cells produce antibodies that attach to the current type of invader.

5. "Eater cells," prefer intruders marked with antibodies, and "eat" loads of them.

6. If the same intruder invades again, memory cells help the immune system to activate much faster.

Though B and T_C Cells can recognize antigens, T_H are needed for them to form clones



Passive immunity



- **Active immunity**

- ◆ When you make your own antibodies and memory cells

- **Passive immunity**

- ◆ when antibodies are provided from an outside source
 - **No memory cells form though!**

- **Ex: injecting antibodies**

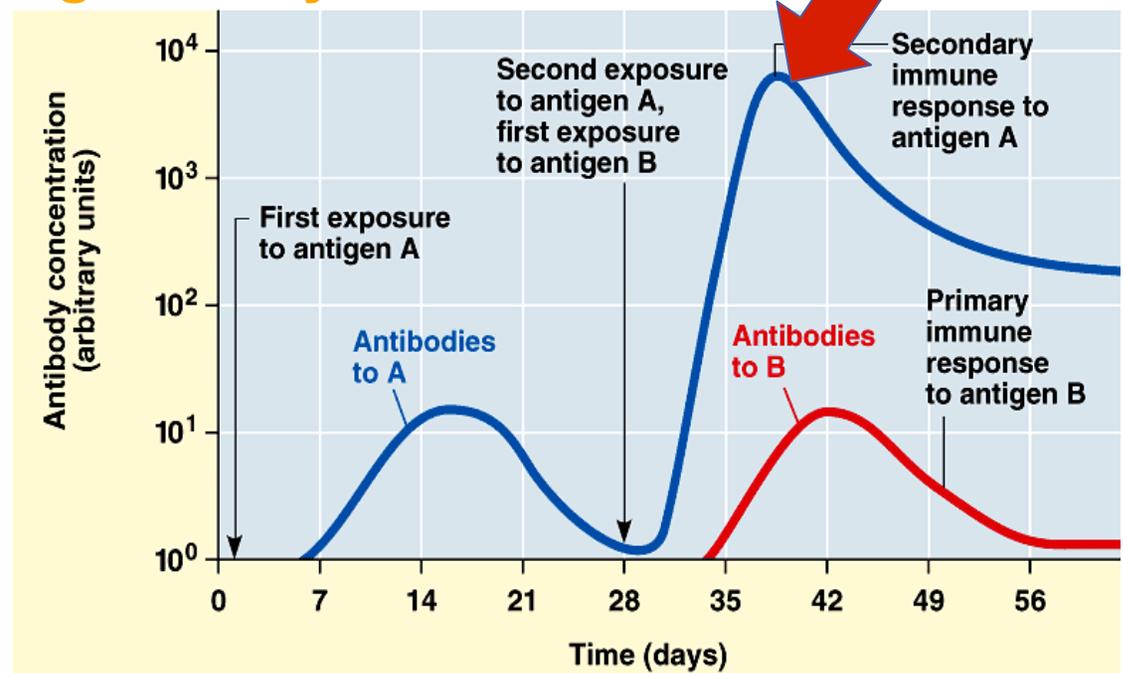
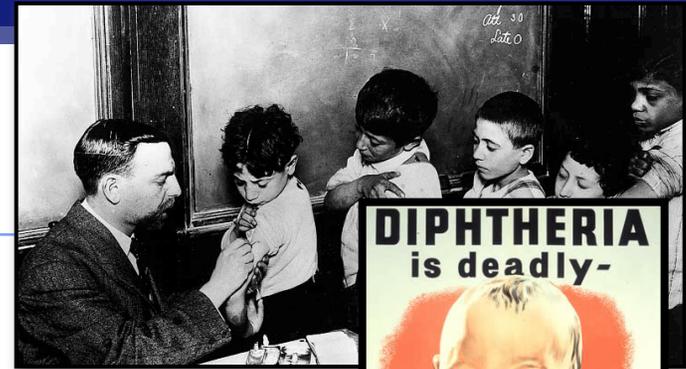
- **Ex: antibodies passed to newborn in breast milk**

EXCUSE YOU!!!



Vaccinations

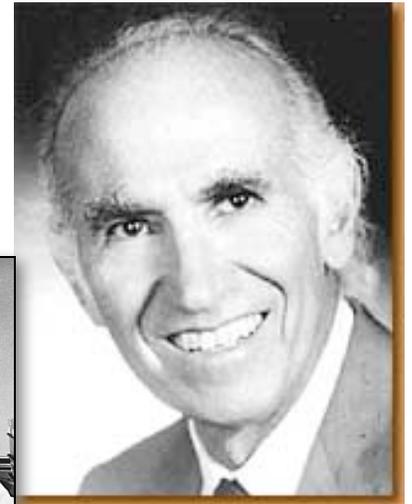
- Immune system exposed to harmless version of pathogen or some of a pathogen's surface molecules
 - ◆ stimulates B cell system to produce antibodies to pathogen
 - Artificially induces “active immunity”
 - ◆ Creates long-lasting memory B and T cells
 - ◆ Now you will have a rapid response on future exposure
 - Creates immunity without getting disease!
- Most successful against viruses



1914 – 1995

Jonas Salk

- Developed first vaccine **April 12, 1955**
 - ◆ against **polio**
 - attacks motor neurons



Albert Sabin
1962

oral polio vaccine



Polio epidemics



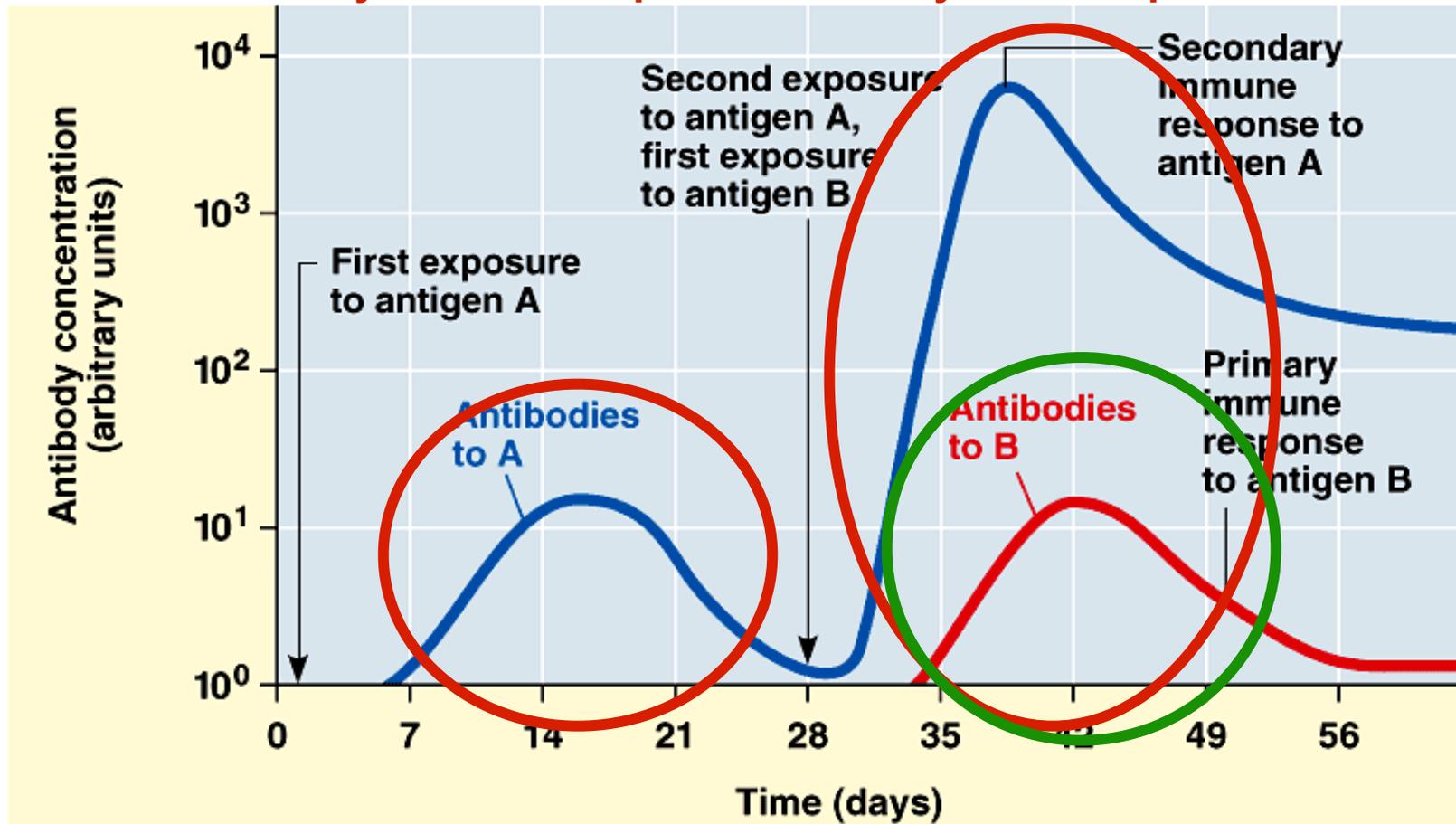
1994:
Americas polio free
2002:
Europe polio free



Iron lungs create negative pressure to help breathing

1° vs. 2° response to disease

- Memory B cells allow a rapid, amplified response with future exposure to pathogen
 - ◆ Primary immune response = 10 - 17 days after exposure
 - ◆ Secondary immune response = 2-7 days after exposure



Vaccines or Inoculations

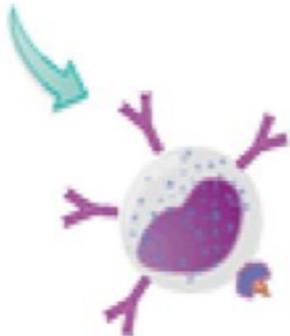


- Some vaccines are made from just the antigens (parts of external molecules) of the pathogen.
 - ◆ The antigens in the vaccine stimulate the immune response
- Other vaccines are created by grinding up or heating the dangerous pathogen so that it is no longer functional. We call this an attenuated pathogen.
- Some vaccines consist of a slightly different version of the pathogen that "fools" the body into reacting as if exposed to the real antigen.
 - ◆ For example, the vaccine for the virus that causes smallpox (a deadly disease) is actually made from a closely related virus that causes cowpox (a mild disease).

Stages in Vaccine-Induced Immunity

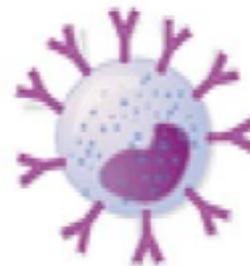
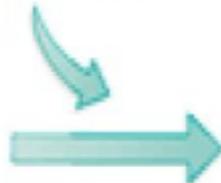


Stage 1
Deactivated virus (vaccine)
is injected into body.

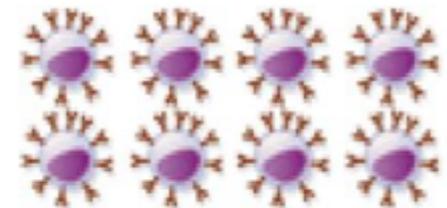


Stage 2
Antigens in vaccine
stimulate primary
immune response.

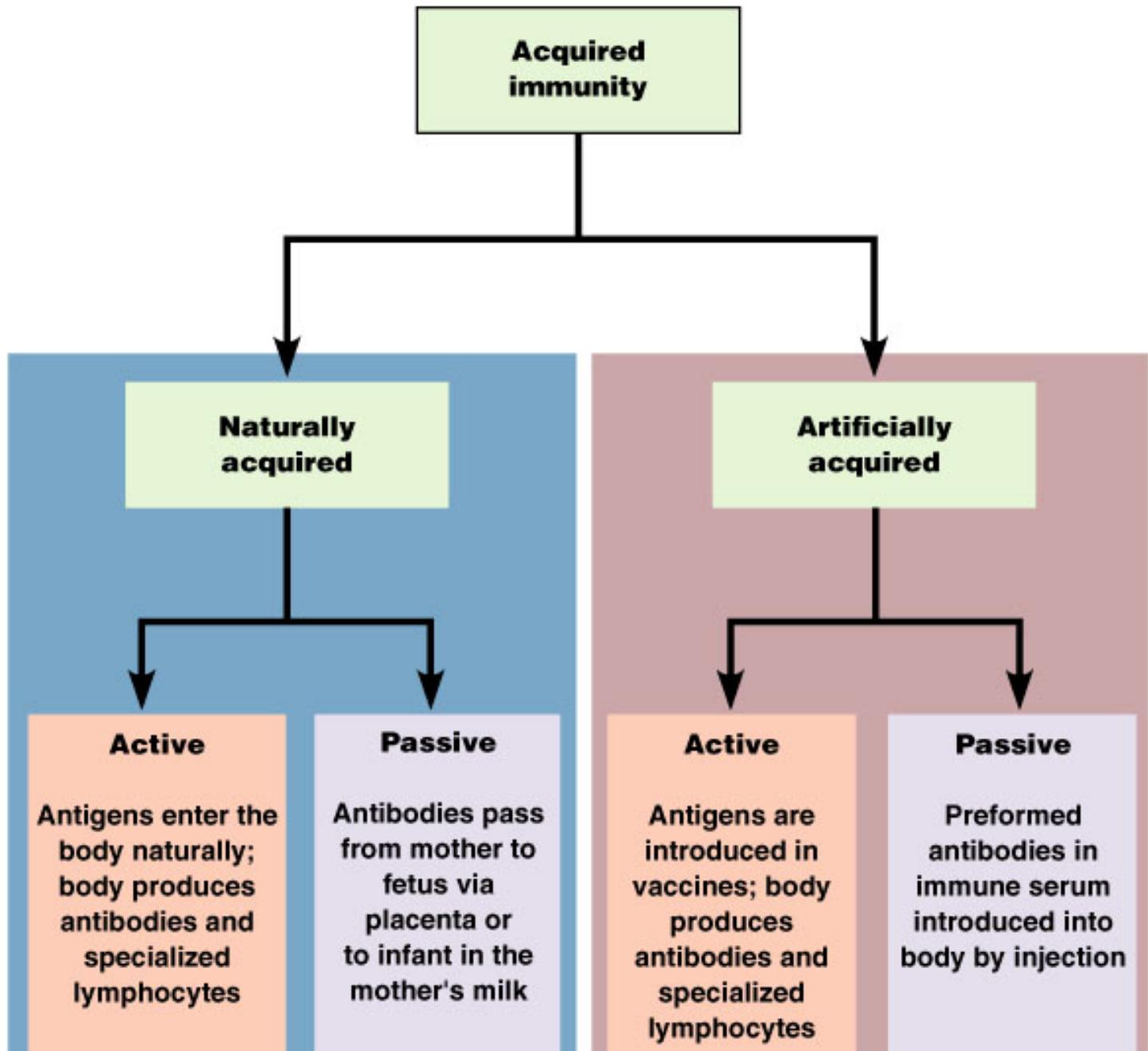
Booster Stage
Some vaccines
require a
booster shot.



Stage 3
Memory cells are
formed that match
the antigens in the
vaccine.



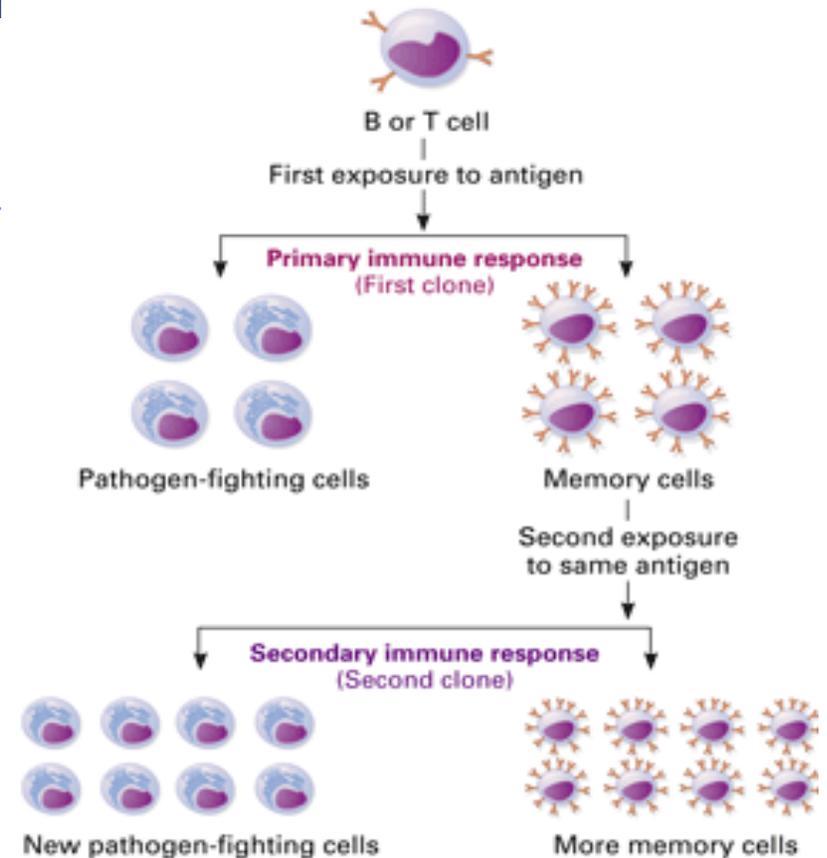
Stage 4
Later exposure to same
virus stimulates rapid
secondary immune
response.



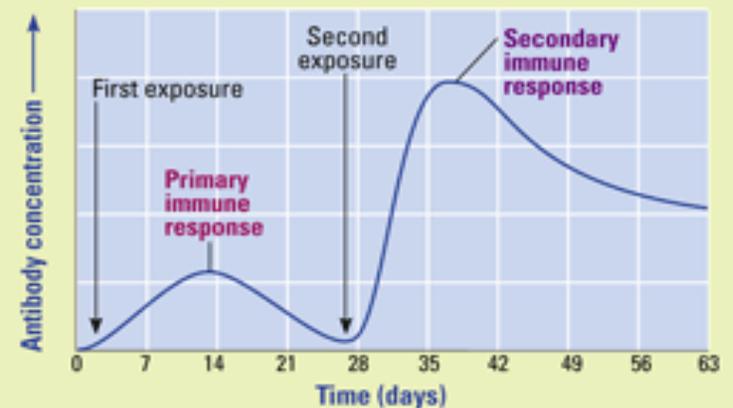
The “Acquired Immune System” can **REMEMBER** a pathogen!

- If you ever get the same pathogens in you in the future, the many memory cells left behind since your last infection can now undergo mitosis and produce more quickly a new even bigger army of fighting cells helping prevent the pathogen from successfully surviving in your body for long.
 - ◆ This means you do not get as sick or do not get sick at all the second time you see that same antigen

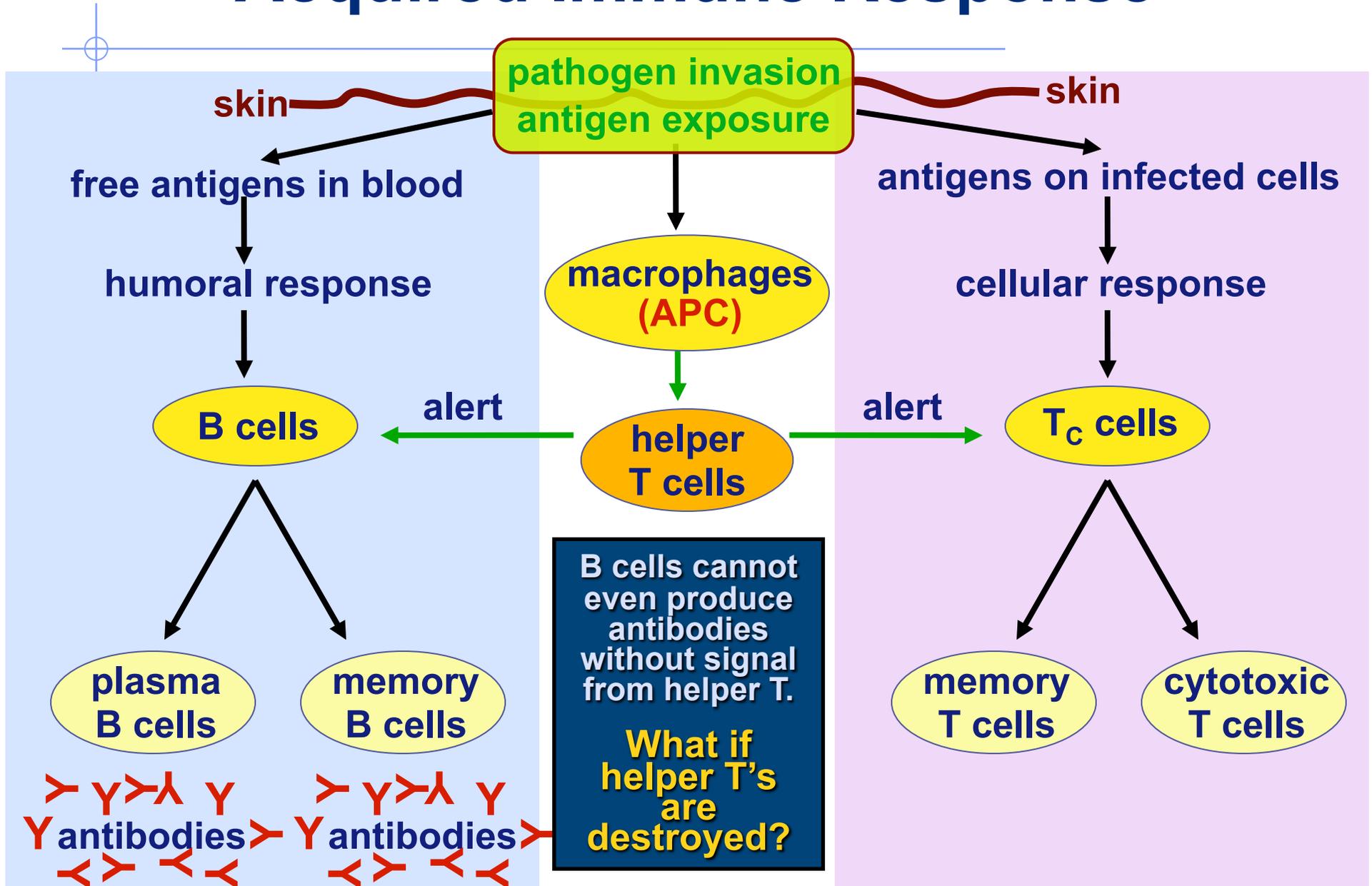
How the Immune System “Remembers” Pathogens



Primary and Secondary Immune Responses



Acquired Immune Response



HIV & AIDS

■ Human Immunodeficiency Virus

◆ virus infects helper T cells

(and macrophages)

- helper T cells don't activate rest of immune system:
killer T cells & B cells

◆ Eventually destroys all helper T cells

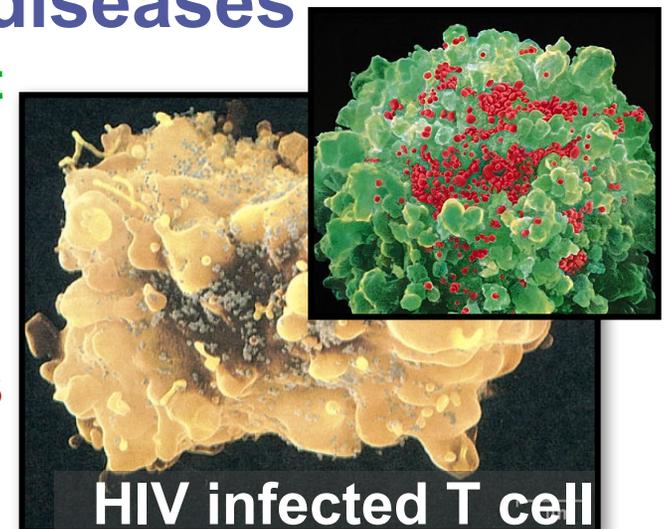
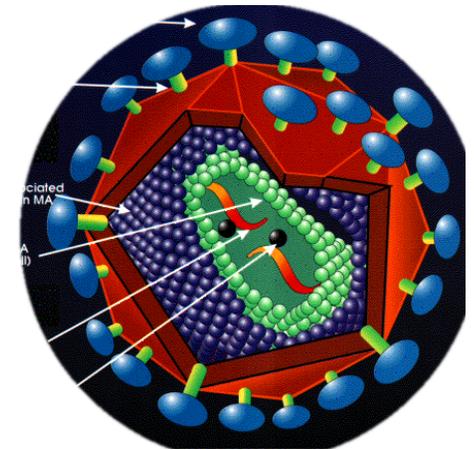
■ AIDS: Acquired ImmunoDeficiency Syndrome

◆ infections by opportunistic diseases

- normally body would be able to fight these microbes or cancer cells

◆ death occurs usually from “opportunistic” infections

- **Pneumonia (bacteria), cancers**



T_H Cells help stimulate B and T_C (killer T) Cells do clone themselves

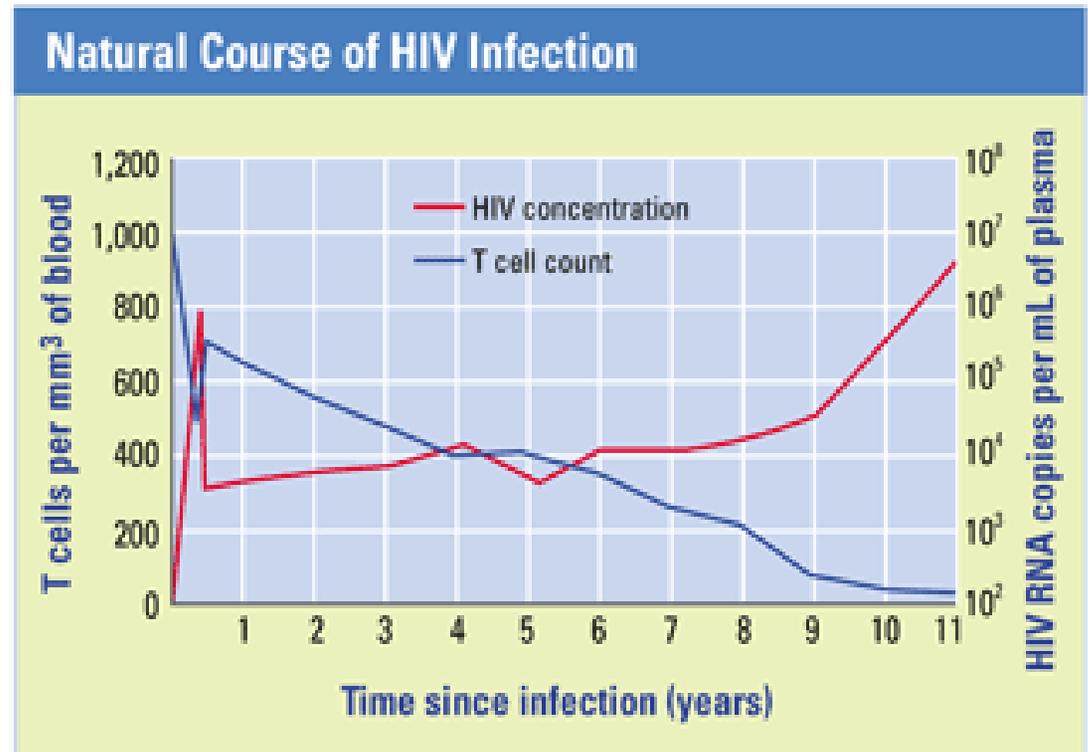
HIV is deadly because it destroys the immune system, leaving the body unable to defend itself against pathogens and certain cancers.

HIV infects especially **helper T cells** so the immune system cannot activate other T cells or B cells.

- ◆ **Both the humoral and cell-mediated immune responses are impaired**

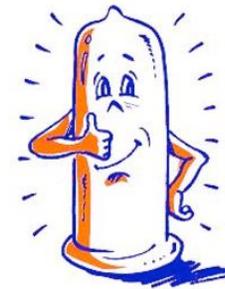
- **Death usually occurs from another infection, such as pneumonia, or from certain types of cancer.**

- ◆ **When we cannot fight infections, we say AIDS has developed.**



How to protect yourself...

Don't share
body fluids:
Blood,
semen,
vaginal
secretions



what's the point of trying to look cool...
IF YOU'RE DEAD!



Immune system malfunctions

■ Auto-immune diseases

◆ immune system attacks own molecules & cells because it cannot distinguish self from nonself

■ lupus

◆ antibodies against many molecules released by normal breakdown of cells

■ rheumatoid arthritis

◆ antibodies causing damage to cartilage & bone

■ diabetes

◆ beta-islet cells of pancreas attacked & destroyed

■ multiple sclerosis

◆ T cells attack myelin sheath of brain & spinal cord nerves

■ Allergies

◆ over-reaction to environmental antigens

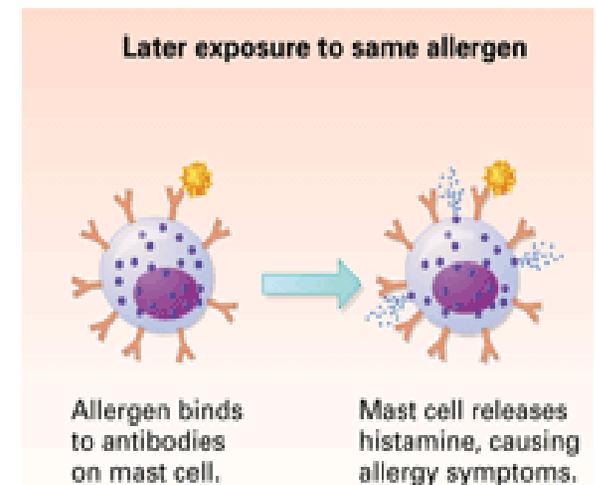
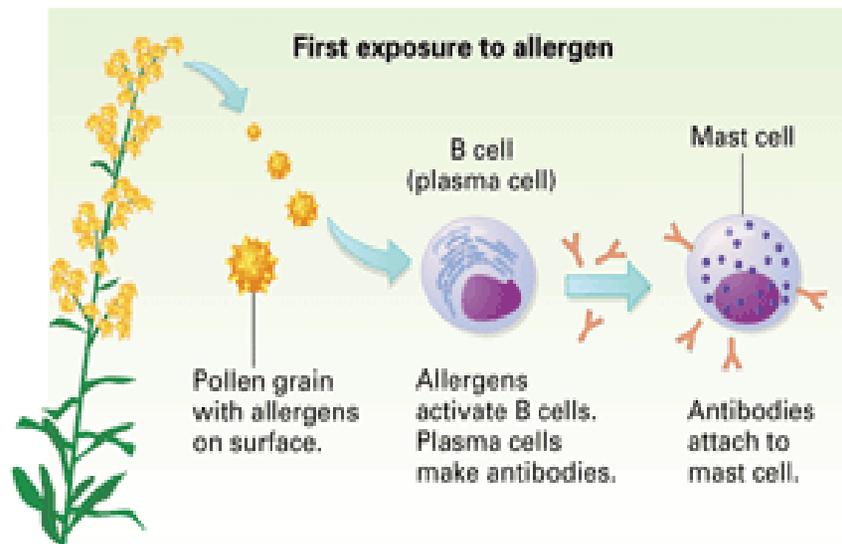
■ allergens = proteins on pollen, dust mites, in animal saliva

◆ stimulates release of histamine

Allergies

- The pollen grains have allergens on their surface that trigger B cells to produce a class of antibodies different from those that protect against pathogens.
 - ◆ These "allergic antibodies" attach to receptor proteins on the surface of cells called mast cells
 - Mast cells produce histamine.
 - ◆ Histamine triggers the inflammatory response which causes watery eyes & a runny nose due to dilating local blood vessels.

- **Antihistamine drugs block action of histamine**



Key attributes of vertebrate immune system

■ 4 attributes that characterize the immune system as a whole

◆ specificity

- antigen-antibody specificity

◆ diversity

- react to millions of antigens

◆ memory

- rapid 2° response

◆ ability to distinguish self vs. non-self

- maturation & training process reduces chances of auto-immune disease or self-recognition and

destruction



**It's safe
to Ask Questions!**

