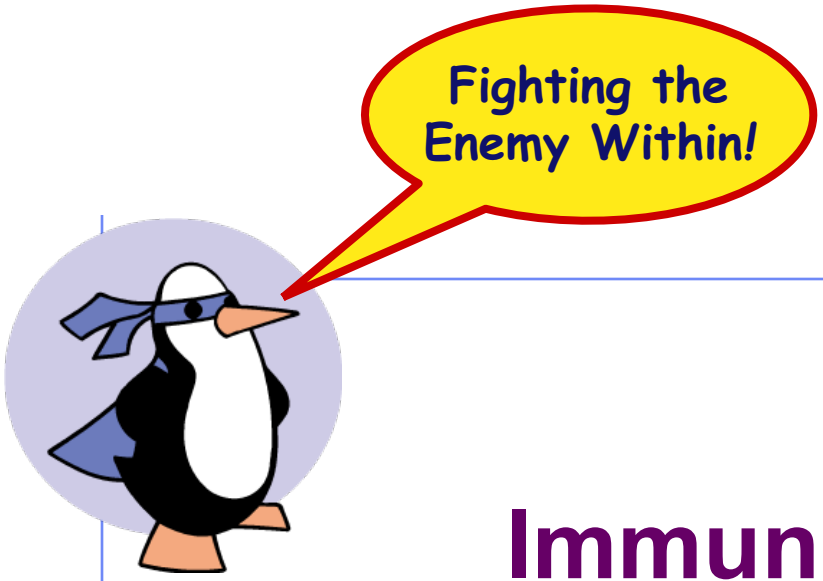
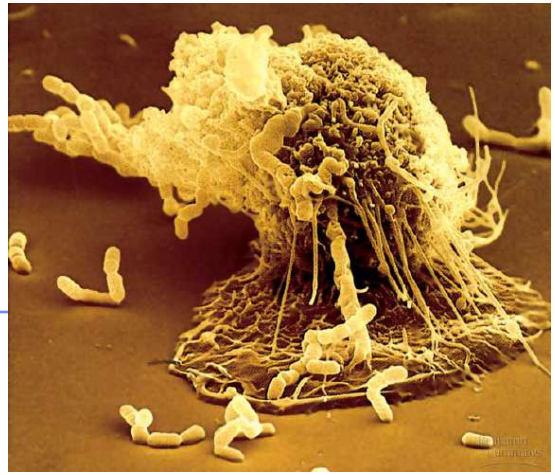
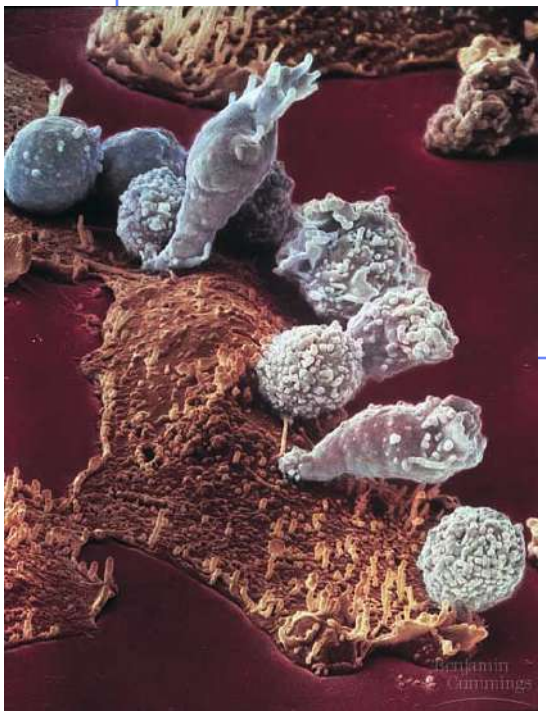




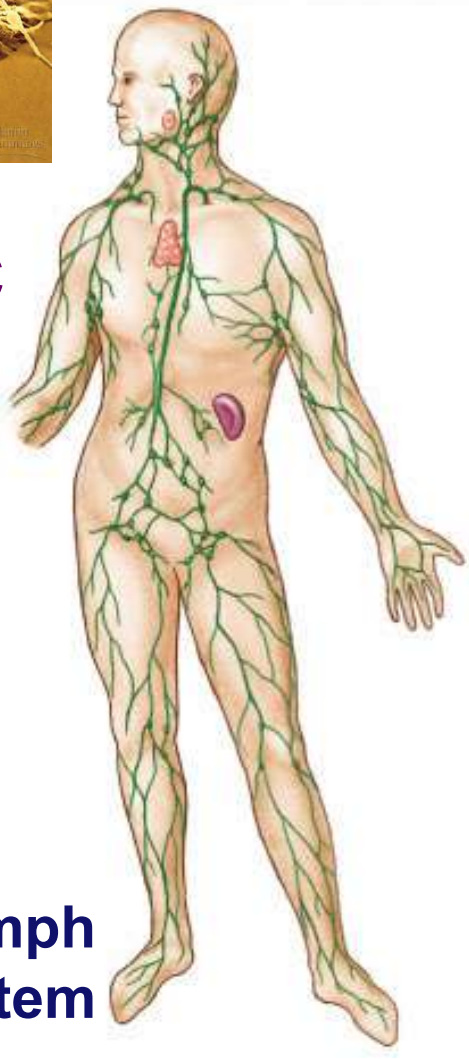
phagocytic leukocyte

Immune / Lymphatic System

NPR
Flu and You



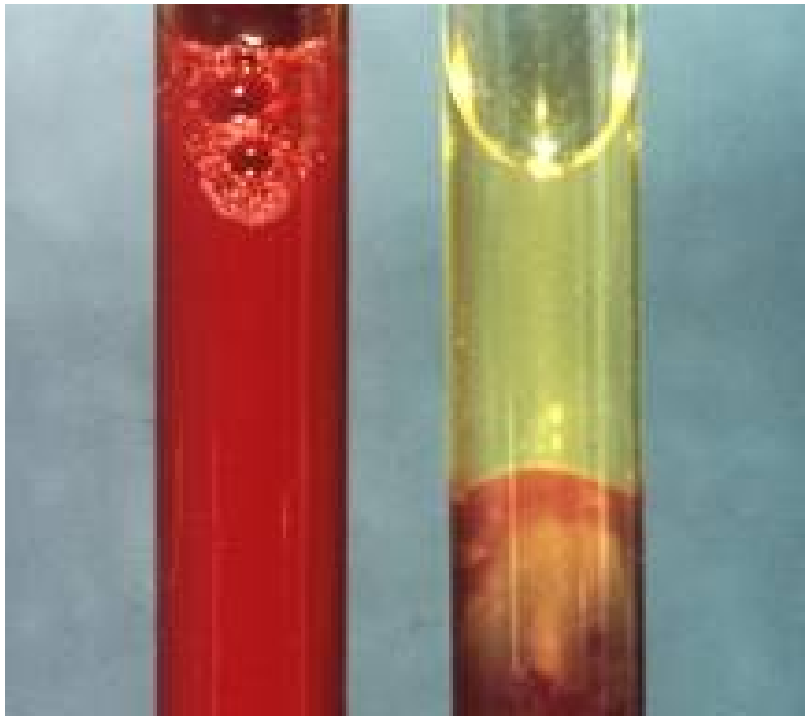
lymphocytes attacking cancer cell



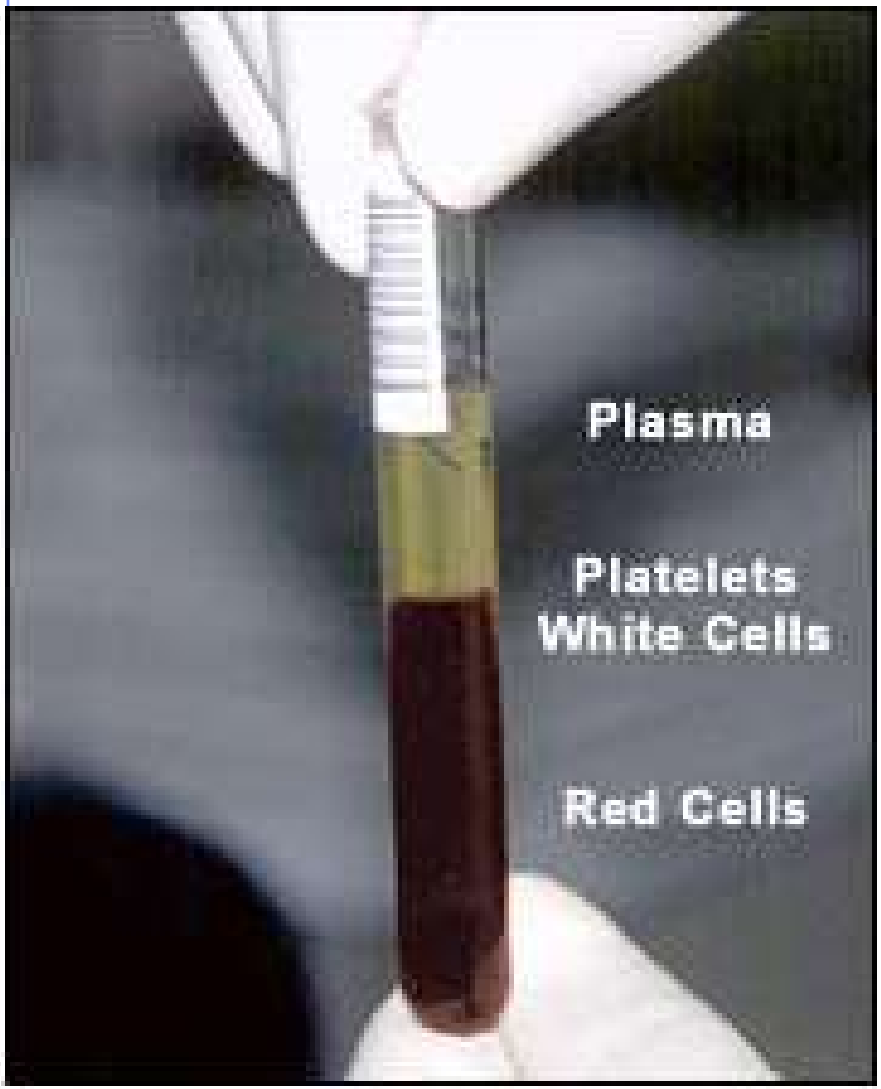
lymph system

Components

- Plasma---55%
- Formed elements---45%
  - platelets
  - erythrocytes
  - leukocytes



Plasma

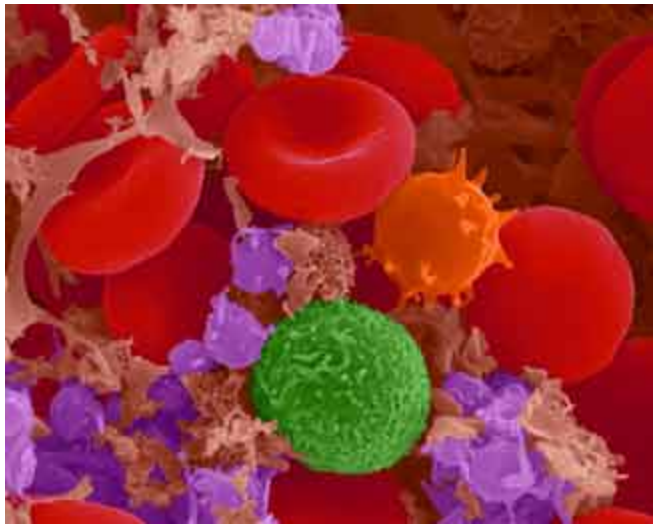


- Straw colored liquid
- 91.5% water; 7% proteins; 1.5% other solutes

Platelets

Platelets Spreading

- 250,000 to 500,000
- Help blood clotting
- Sometimes called thrombocytes
- Work with Fibrin to make clots
- Anucleate

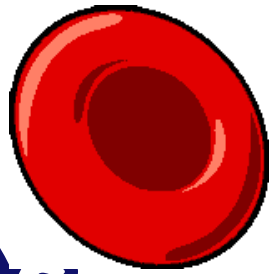


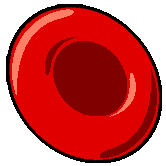
Platelets (stained purple)

Physiological Homeostasis

Erythrocytes: Red Blood Cells

- Biconcave; 8 micrometers in diameter; no nucleus or other organelles
- Contain hemoglobin
- Live only about 120 days
- RBC production takes place in red bone marrow
- 4 to 6 million; Outnumber white blood cells 1000:1





Infection!!! (Immune System)

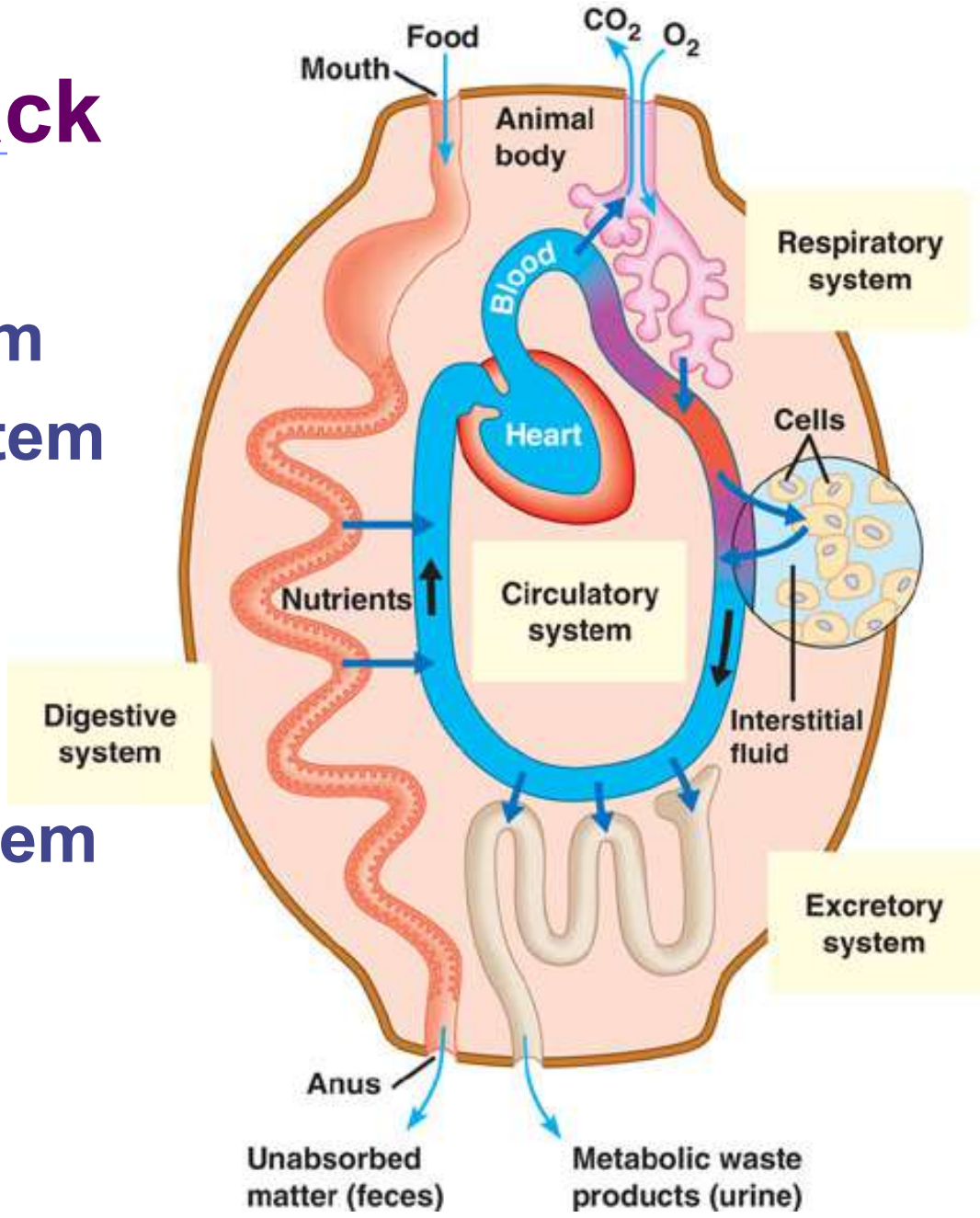
- You have one. How does your body save you?
- First we need to understand what blood is made up of.

Hemoglobin

- Iron containing protein
- Binds strongly, but reversibly to oxygen
- Each hemoglobin molecule has four oxygen binding sites
- Each erythrocyte has 250 million hemoglobin molecules

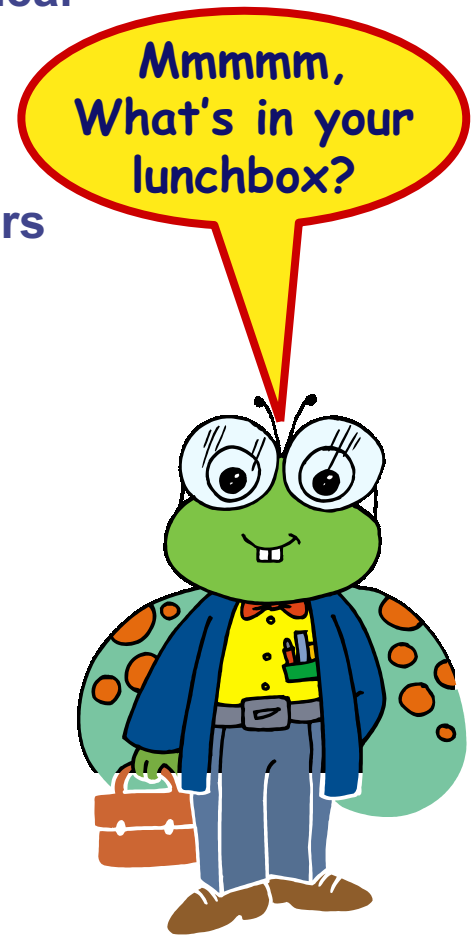
Avenues of attack

- Points of entry
  - digestive system
  - respiratory system
  - urogenital tract
  - break in skin
- Routes of attack
  - circulatory system
  - lymph system



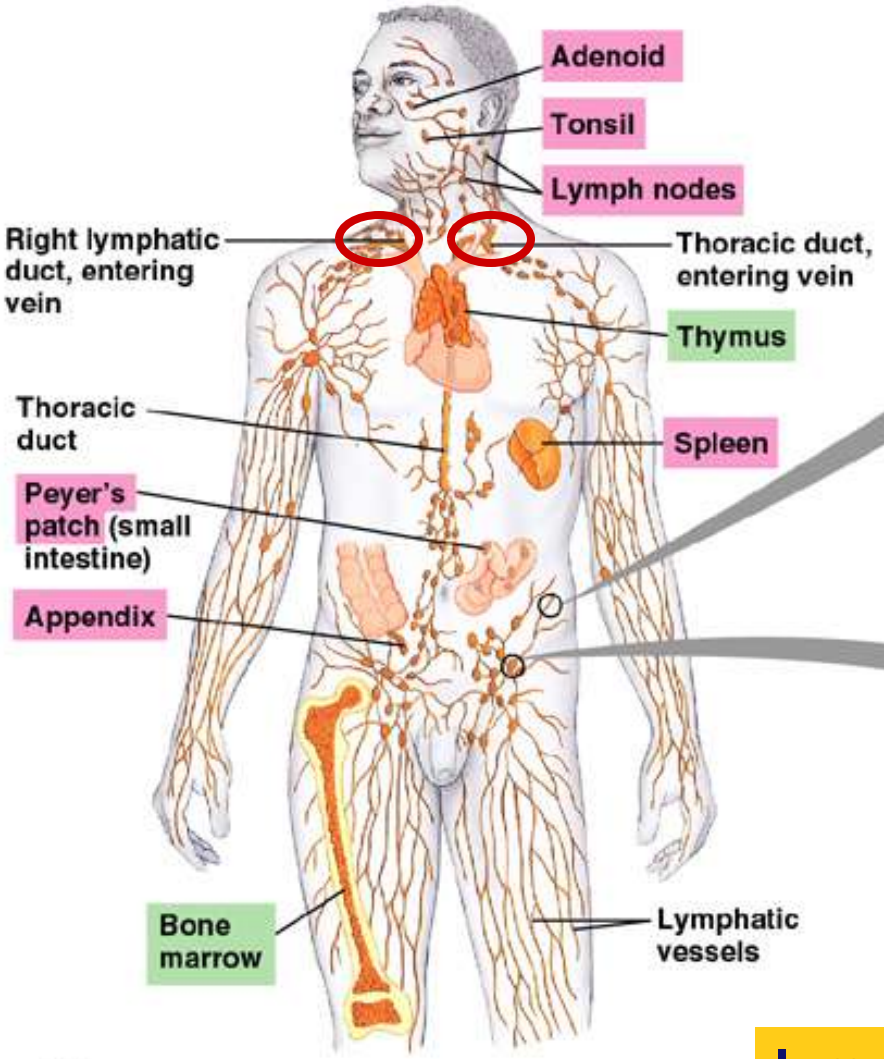
Why an immune system?

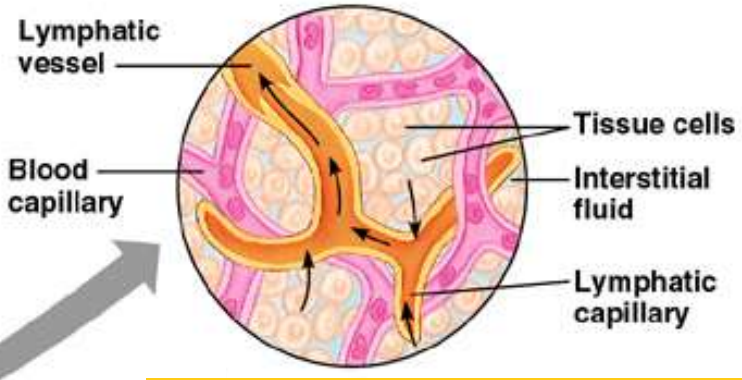
- **Attack from outside**
  - lots of organisms want you for lunch!
  - animals are a tasty nutrient- & vitamin-packed meal
    - cells are packages of macromolecules
    - no cell wall
      - traded mobility for susceptibility
  - animals must defend themselves against invaders
    - viruses
      - HIV, flu, cold, measles, chicken pox, SARS
    - bacteria
      - pneumonia, meningitis, tuberculosis
    - fungi
      - yeast ("Athlete's foot"…)
    - protists
      - amoeba, Lyme disease, malaria
- **Attack from inside**
  - defend against abnormal body cells = cancers



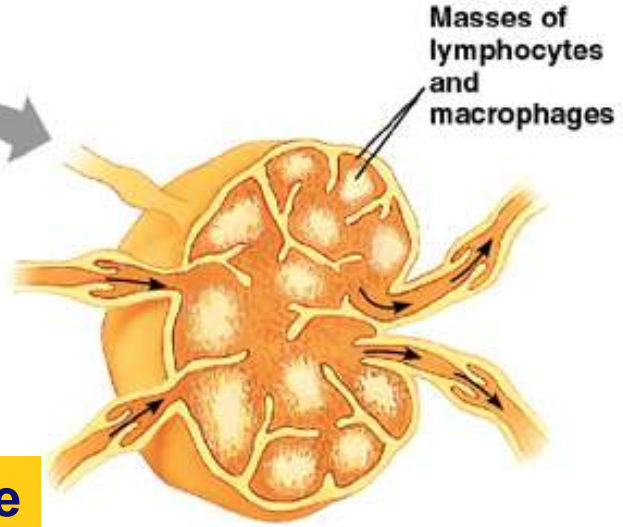
Lymph system

Production & transport of leukocytes
Traps foreign invaders





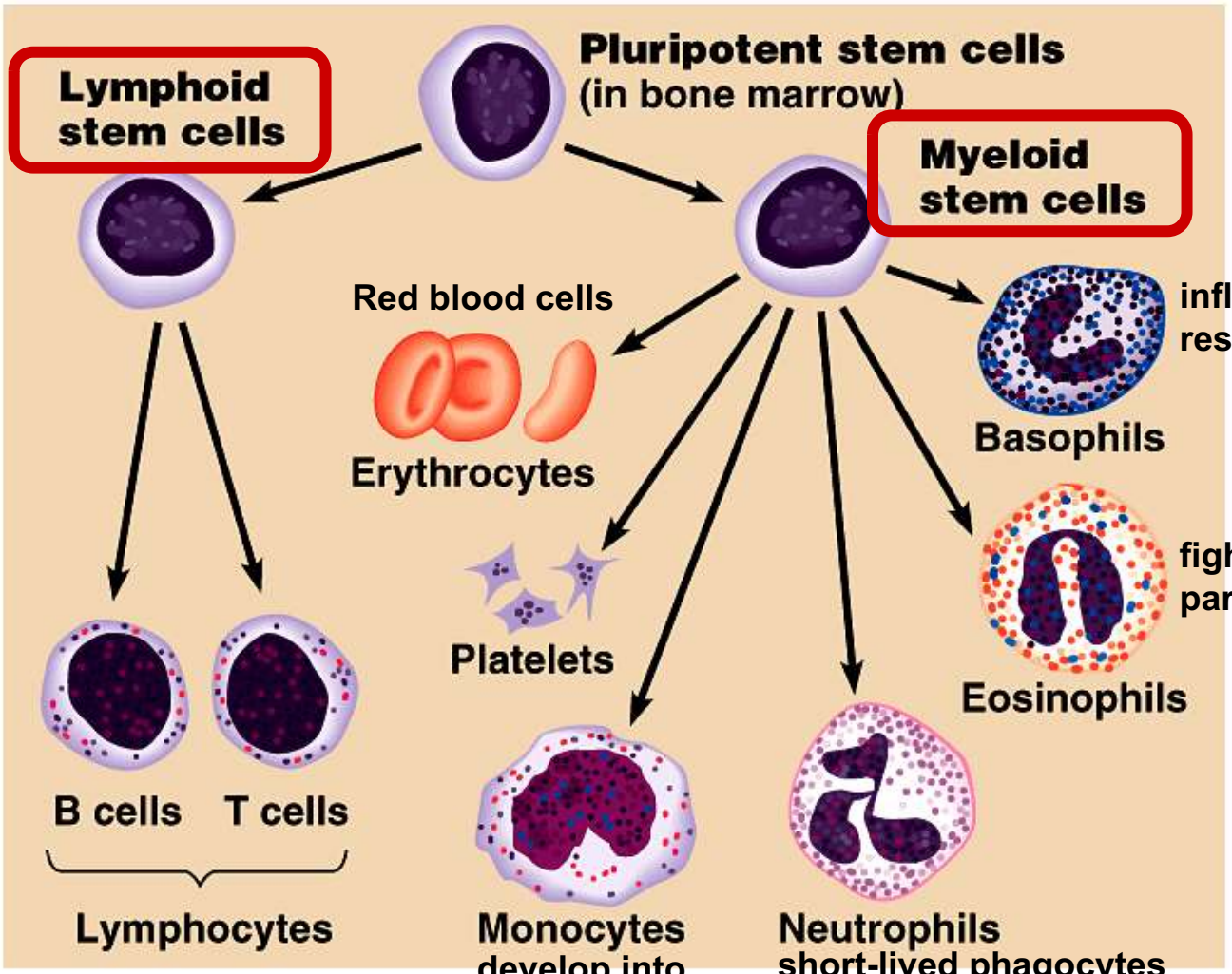
lymph vessels
(intertwined amongst blood vessels)



lymph node

A

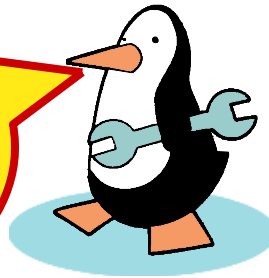
Development of Red & White blood cells



Lines of defense

- 1st line: Barriers
  - broad, external defense
    - "walls & moats"
  - skin & mucus membranes
- 2nd line: Non-specific patrol
  - broad, internal defense
    - "patrolling soldiers"
  - leukocytes = phagocytic WBC
    - macrophages
- 3rd line: Immune system
  - specific, acquired immunity
    - "elite trained units"
  - lymphocytes & antibodies
    - B cells & T cells

Bacteria & insects inherit *resistance*. Vertebrates acquire *immunity*!

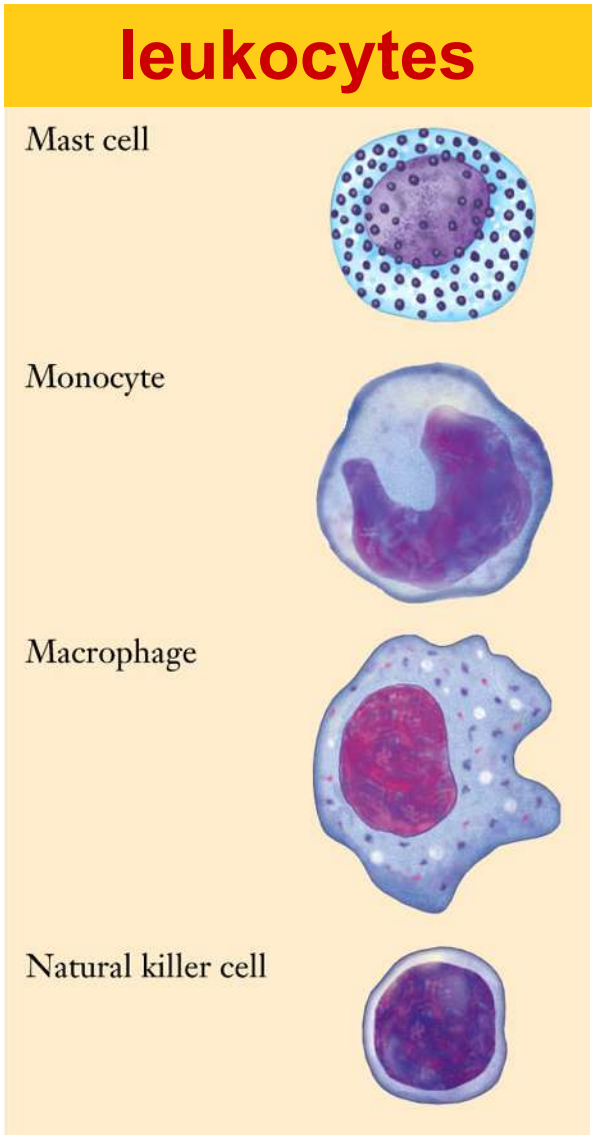


1st line: Chemical barriers on epithelium

- Skin & mucous membrane secretions
  - sweat
    - pH 3-5
  - tears
    - washing action
  - mucus
    - traps microbes
  - saliva
    - anti-bacterial = “lick your wounds”
  - stomach acid
    - pH 2
  - anti-microbial proteins
    - lysozyme enzyme
      - digests bacterial cell walls

2nd line: Internal, broad range patrol

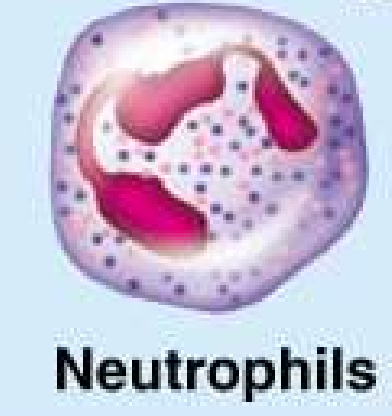
- Innate, general defense
  - rapid response
- Patrolling cells & proteins
  - attack invaders that penetrate body's outer barriers
    - leukocytes
      - phagocytic white blood cells
    - complement system
      - anti-microbial proteins
    - inflammatory response



Computer Lab on White Blood Cells

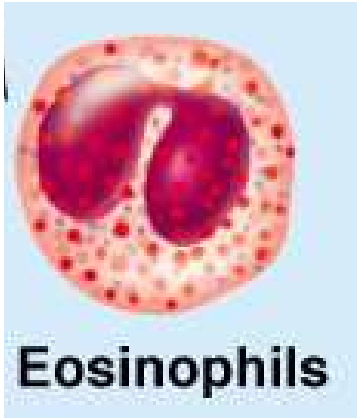
Be Sure to take notes of each type and Draw a Picture of Each

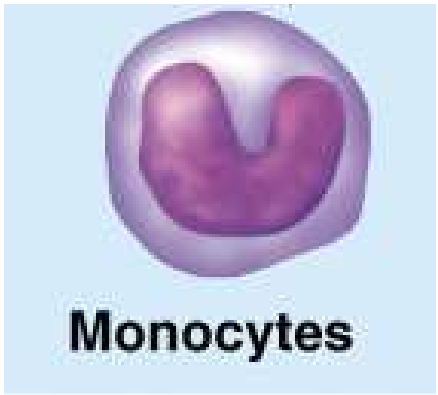
Leukocytes:White Blood Cells The Immune Response


Neutrophils


Basophils


Lymphocytes

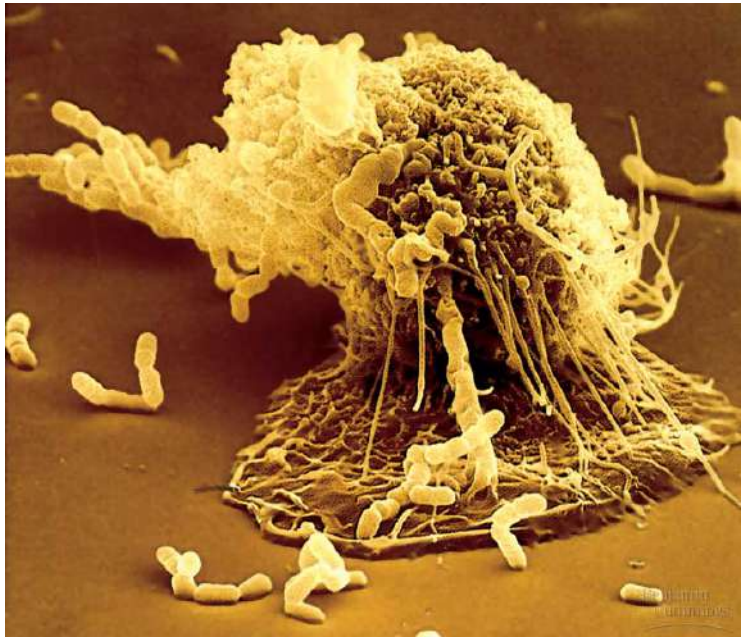

Eosinophils


Monocytes

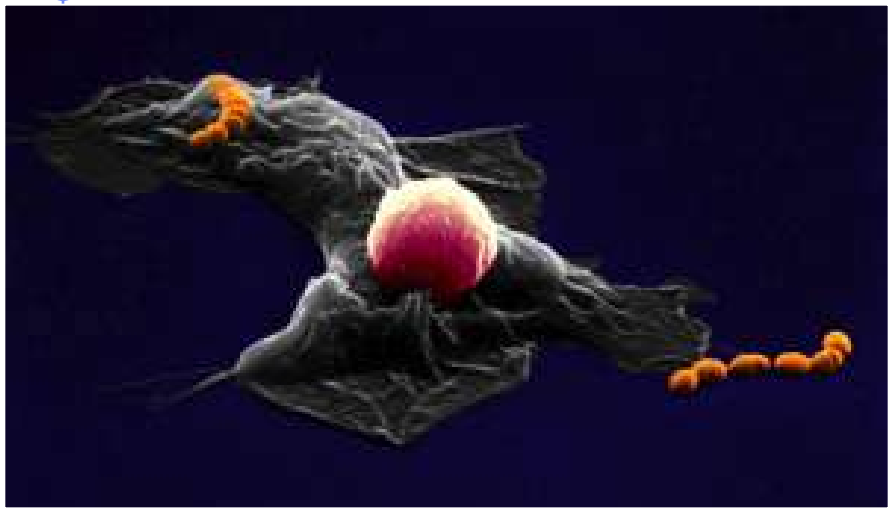
NPR
Flu and You

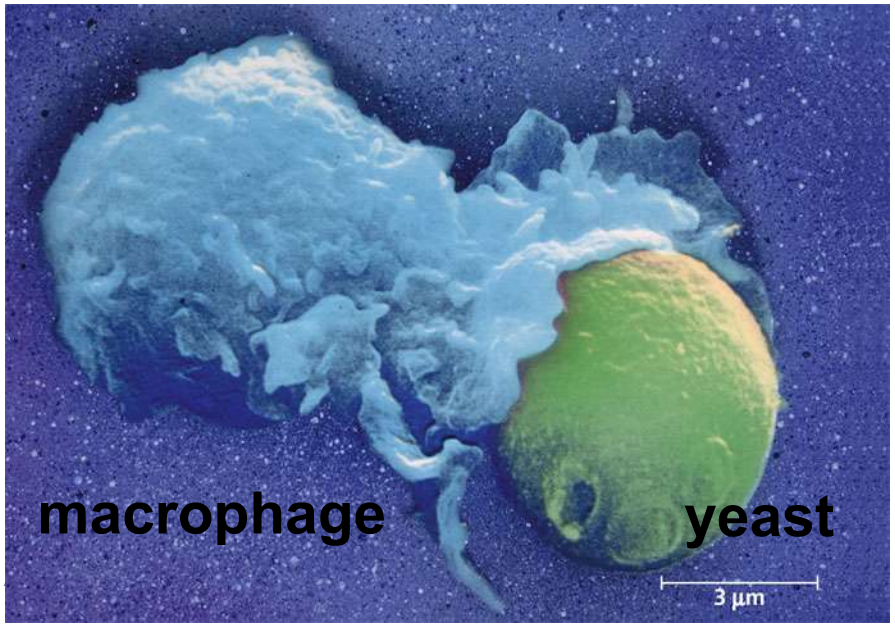
Leukocytes: Phagocytic WBCs

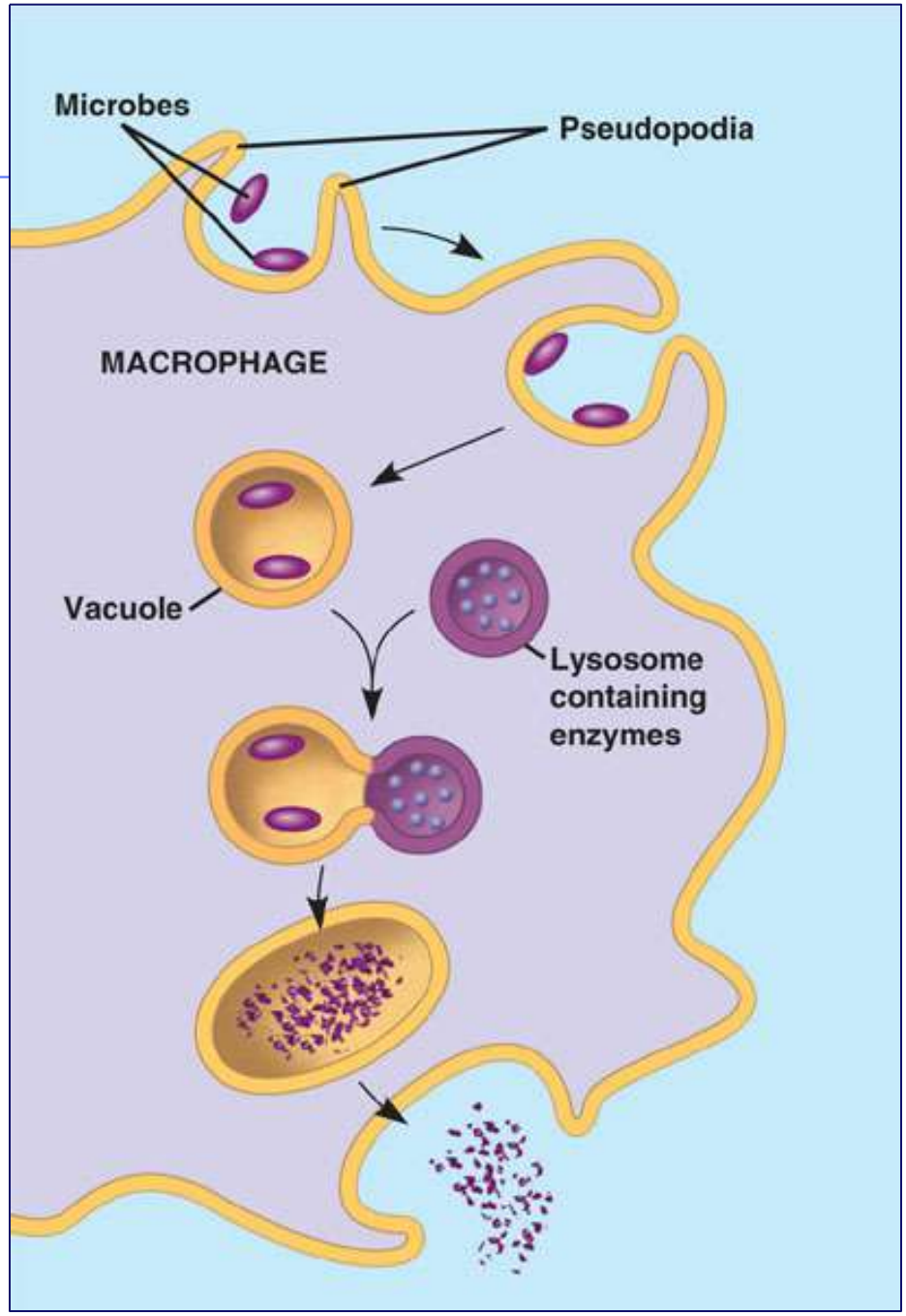
- Attracted by chemical signals released by damaged cells
  - enter infected tissue, engulf & ingest microbes
    - lysosomes
- Neutrophils
  - most abundant WBC (~70%)
  - ~ 3 day lifespan
- Macrophages
  - "big eater", long-lived
- Natural Killer Cells
  - destroy virus-infected cells & cancer cells



Phagocytes

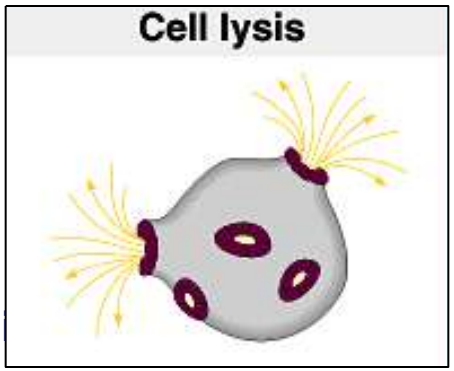



macrophage
yeast
3 µm

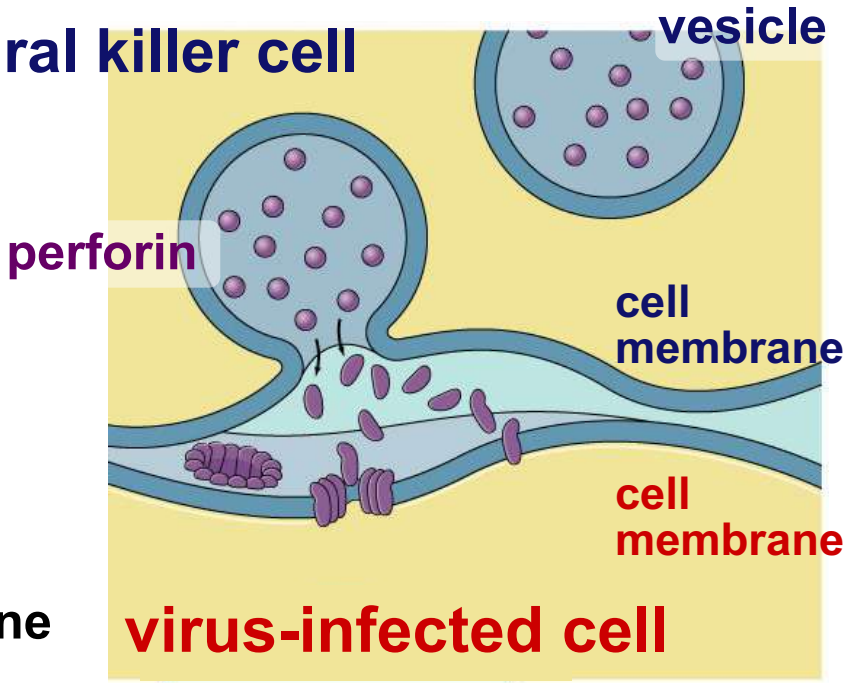

Microbes
Pseudopodia
MACROPHAGE
Vacuole
Lysosome containing enzymes

Destroying cells gone bad!

- Natural Killer Cells perforate cells
  - release perforin protein
  - insert into membrane of target cell
  - forms pore allowing fluid to flow into cell
  - cell ruptures (lysis)
    - apoptosis

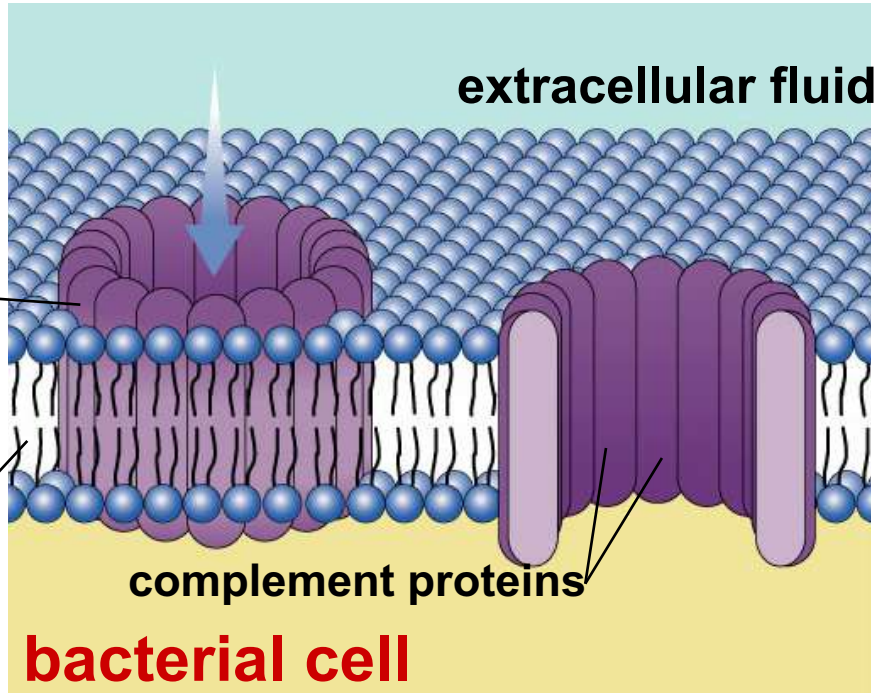


perforin
punctures
cell membrane



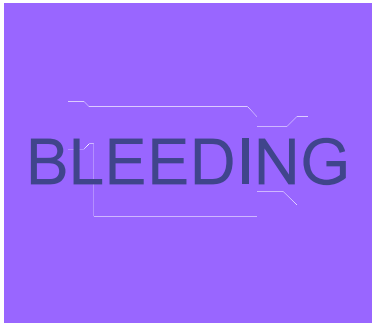
Anti-microbial proteins

- Complement system
  - ~20 proteins circulating in blood plasma
  - attack bacterial & fungal cells
    - form a membrane attack complex
    - perforate target cell
    - apoptosis
      - cell lysis



Hemostasis

- Stoppage of blood flow
- Result of a break in a blood vessel
- Hemostasis involves three phases
  - Platelet plug formation
  - Vascular spasms
  - Coagulation



Blood Clotting

- Blood usually clots within 3 to 6 minutes
- The clot remains as endothelium regenerates
- The clot is broken down after tissue repair

Details of Blood Clotting

Video Clip Of Blood Clot

Undesirable Clotting

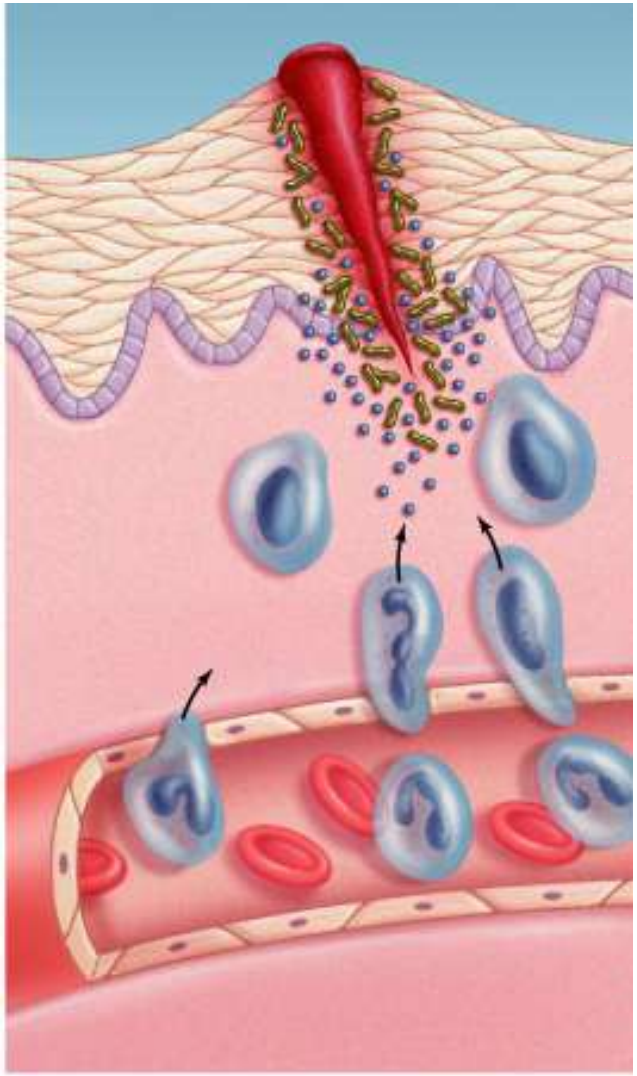
- Thrombus
  - A clot in an unbroken blood vessel
  - Can be deadly in areas like the heart
- Embolus
  - A thrombus that breaks away and floats freely in the bloodstream
  - Can later clog vessels in critical areas such as the brain

Bleeding Disorders

- Thrombocytopenia
  - Platelet deficiency
  - Even normal movements can cause bleeding from small blood vessels that require platelets for clotting
- Hemophilia
  - Hereditary bleeding disorder
  - Normal clotting factors are missing

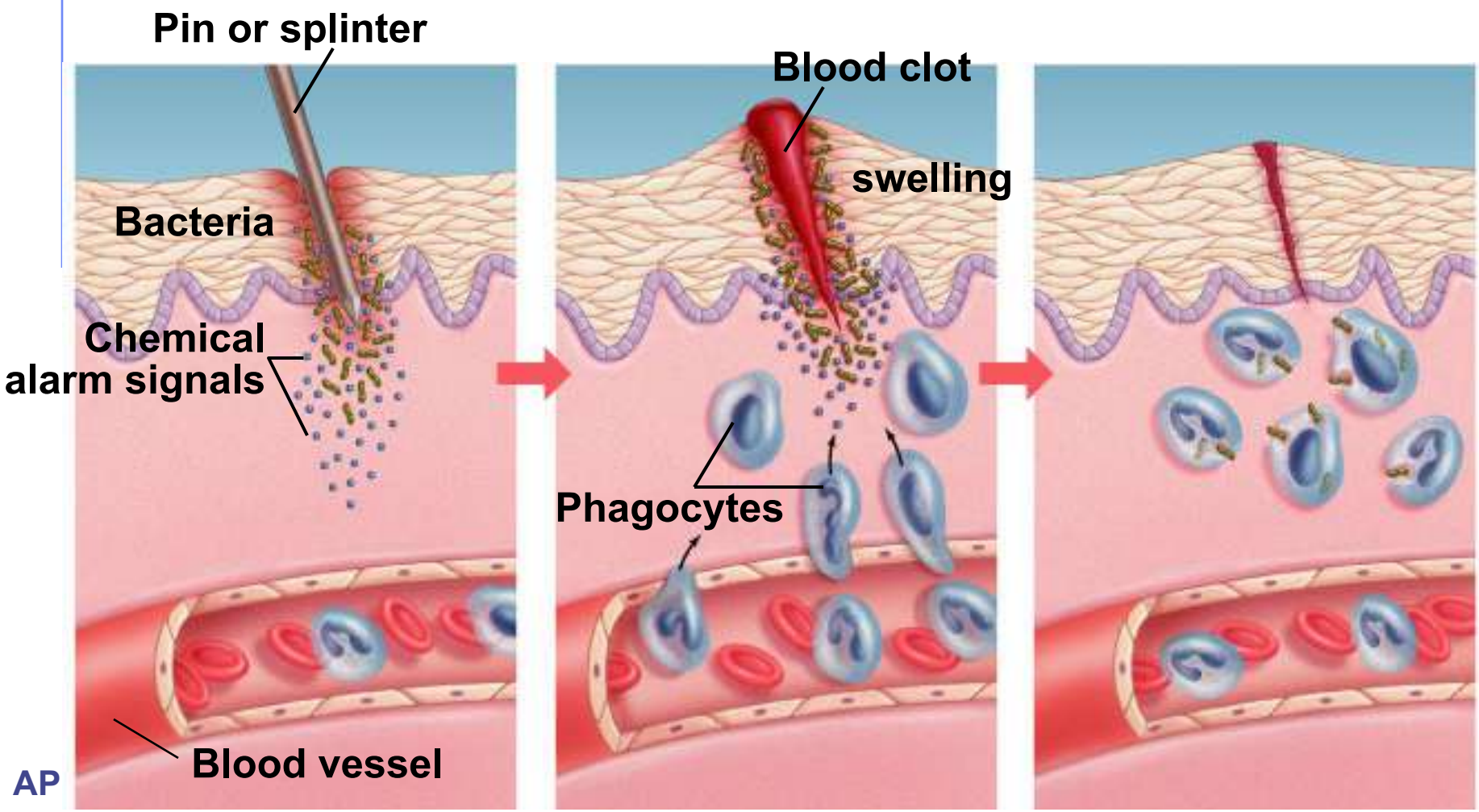
Inflammatory response

- Damage to tissue triggers local non-specific inflammatory response
  - release histamines & prostaglandins
  - capillaries dilate, more permeable (leaky)
    - increase blood supply
    - delivers WBC, RBC, platelets, clotting factors
    - fight pathogens
    - clot formation
    - accounts for swelling, redness & heat of inflammation & infection



Inflammatory response

- Reaction to tissue damage



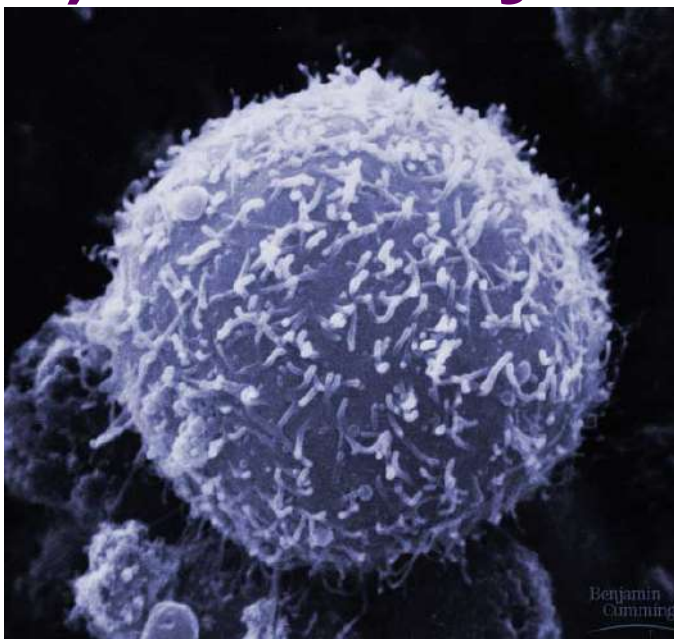
AP

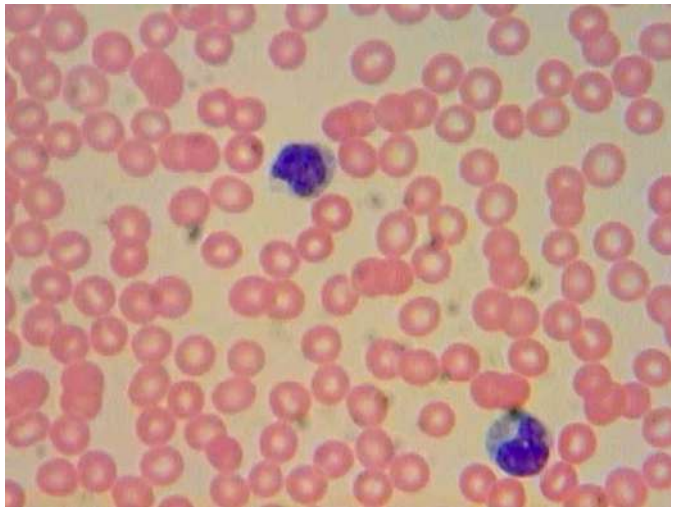
Fever

- When a local response is not enough
  - systemic response to infection
  - activated macrophages release interleukin-1
    - 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

3rd line: Acquired (active) Immunity

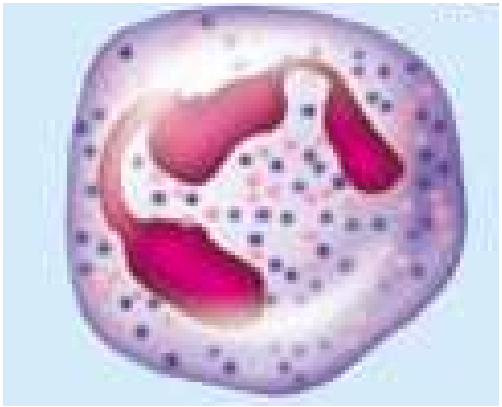
- Specific defense
  - lymphocytes
    - B lymphocytes (B cells)
    - T lymphocytes (T cells)
  - antibodies
    - immunoglobulins
- Responds to…
  - antigens
    - specific pathogens
    - specific toxins
    - abnormal body cells (cancer)



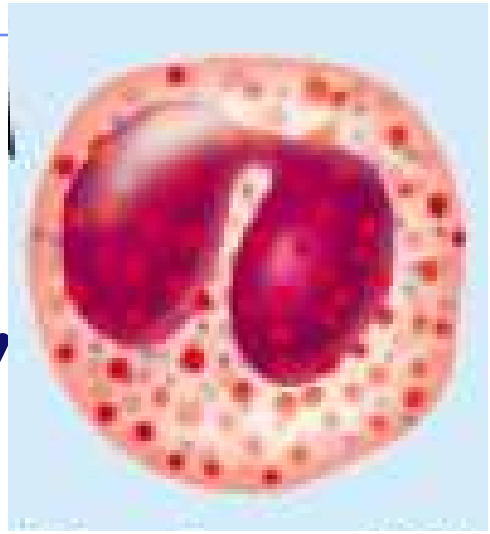


Neutrophils

- 60 to70 % of all WBCs
- Active phagocytes
- Number increases rapidly during short term or acute infections



Eosinophils



- ✓2 to 4 % of all WBCs
- ✓Increase during allergy attacks
- ✓React to parasitic worms
- ✓Inactivate some inflammatory chemicals

The Parasite

Lymphocytes

Cytotoxic T-Cell

T-Cell Killing Target

- ✓20 to 25 % of all WBCs
- ✓Provides Immunity (eg. Killer T-Cell)
- ✓Produces antibodies
- ✓Nucleus fills most of the cell

Humoral Immunity
B-Cells

- Long Term Memory
- B-Cells make antibodies which trigger a T-Cell reaction to kill the invader
- Vaccines, Chicken Pox, Viral Infections

Humoral Immunity (Go animation)

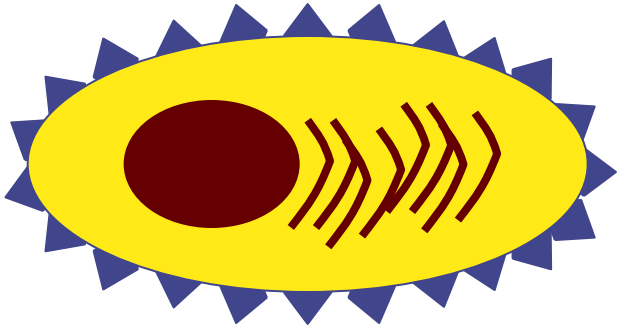
Leukemia

- Type of cancer than can be found in the Bone marrow or lymphocytes
- Produces too many white blood cells
- Symptoms: Cold, Fever, Easy Bruising, Bone Pain, Blood does not clot
- Treatment: Chemotherapy, Blood transfusion, Bone Marrow Transplant, and Stem Cell Transport

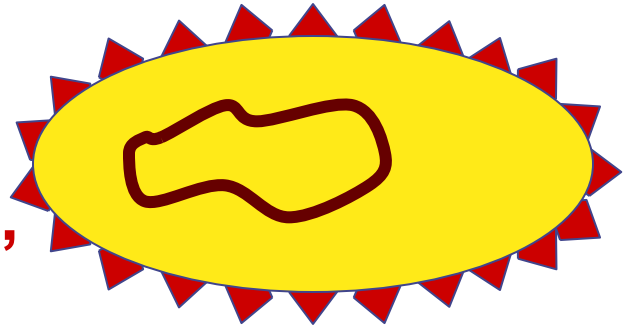
How are invaders recognized: antigens

- **Antigens**
  - proteins that serve as cellular name tags
    - **foreign antigens** cause response from WBCs
      - viruses, bacteria, protozoa, parasitic worms, fungi, toxins
      - non-pathogens: pollen & transplanted tissue
- **B cells & T cells respond to different antigens**
  - B cells recognize intact antigens
    - pathogens in blood & lymph
  - T cells recognize antigen fragments
    - pathogens which have already infected cells

"self"

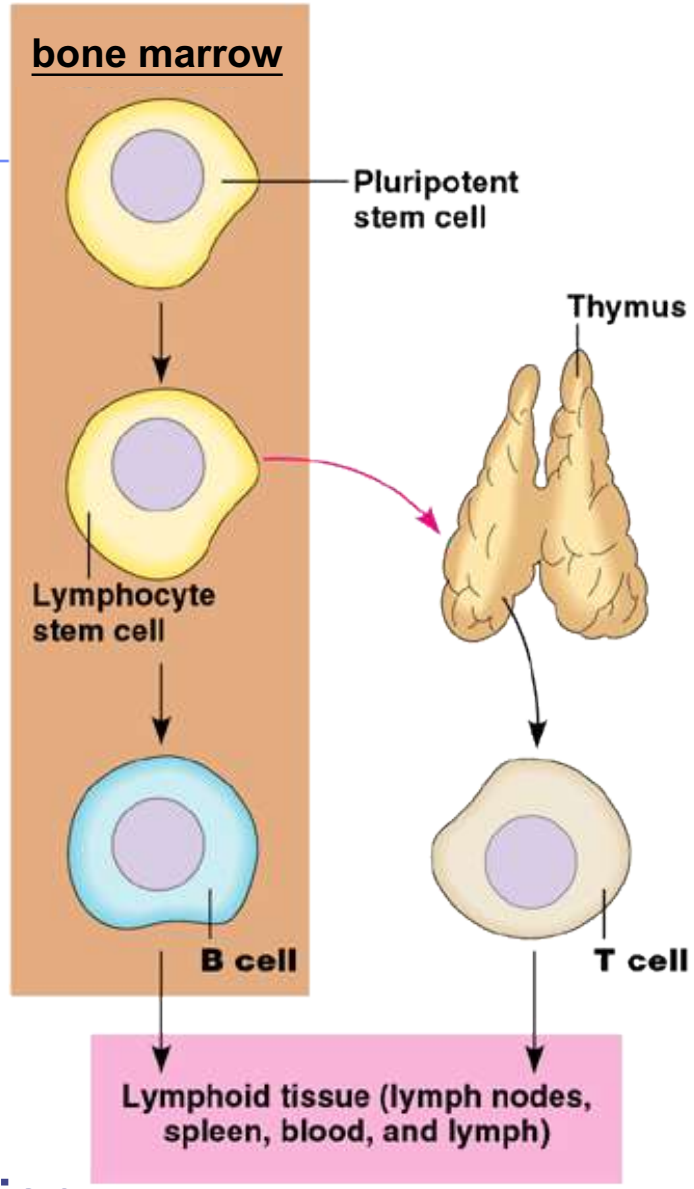


"foreign"



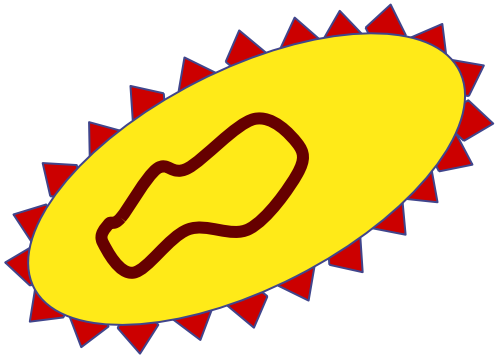
Lymphocytes

- **B cells**
  - mature in **bone marrow**
  - **humoral** response system
    - "humors" = body fluids
    - produce antibodies
- **T cells**
  - mature in **thymus**
  - **cellular** response system
- **Learn to distinguish "self" from "non-self" antigens during maturation**
  - if they react to "self" antigens, they are destroyed during maturation

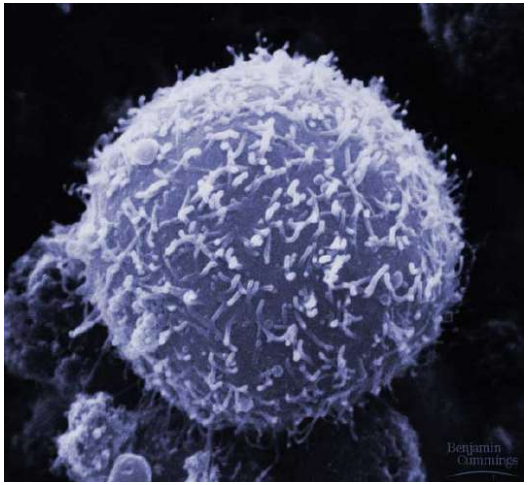


B cells

- **Humoral response** = "in fluid"
  - defense against attackers circulating freely in blood & lymph
- Specific response
  - produce specific **antibodies** against specific **antigen**

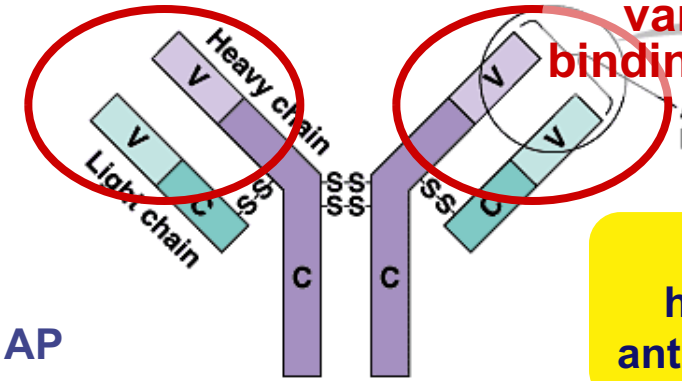


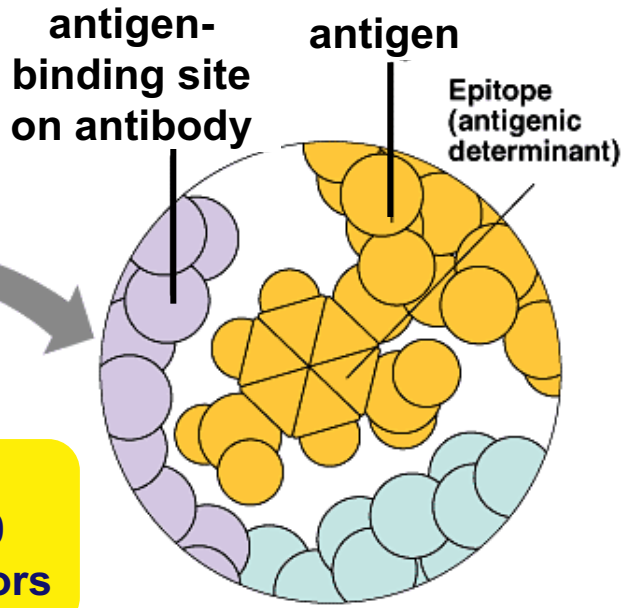
- Types of B cells
  - **plasma cells**
    - immediate production of antibodies
    - rapid response, short term release
  - **memory cells**
    - long term immunity



Antibodies

- **Proteins that bind to a specific antigen**
  - multi-chain proteins produced by B cells
  - binding region matches molecular shape of antigens
  - each antibody is unique & specific
    - millions of antibodies respond to millions of foreign antigens
  - tagging "handcuffs"
    - "this is foreign…gotcha!"

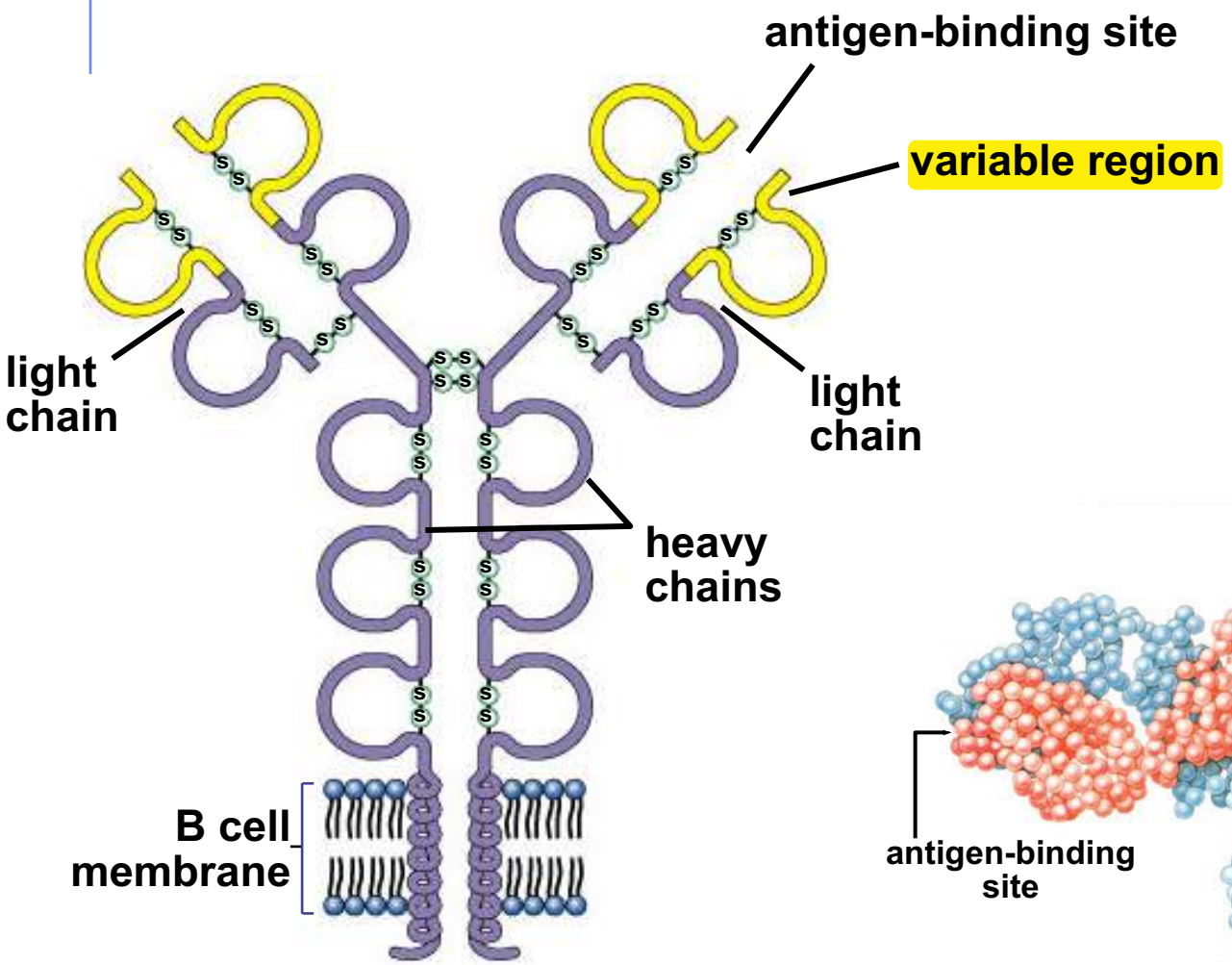


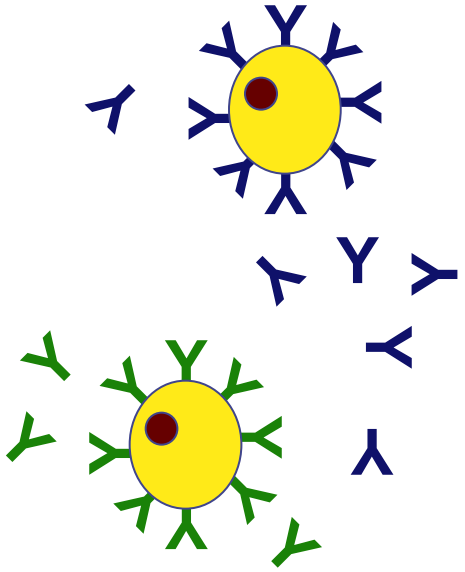


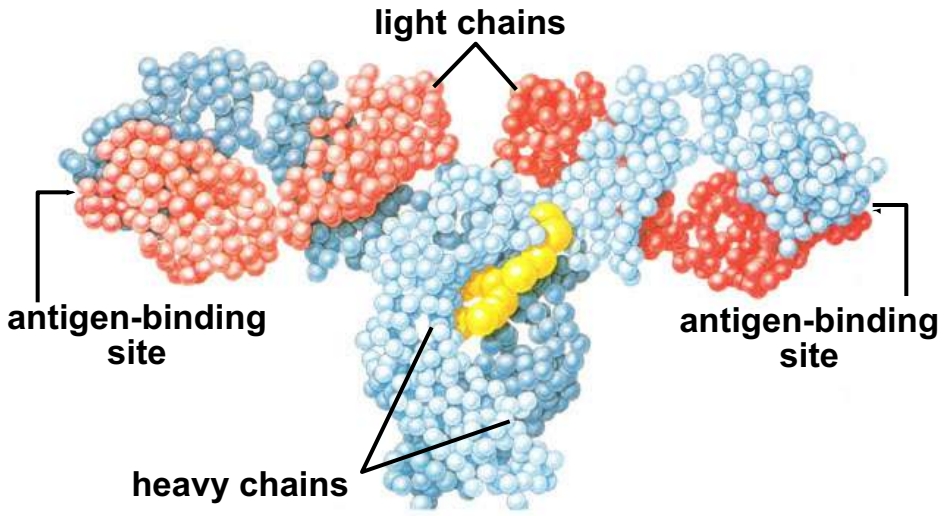
each B cell has ~100,000 antigen receptors

AP

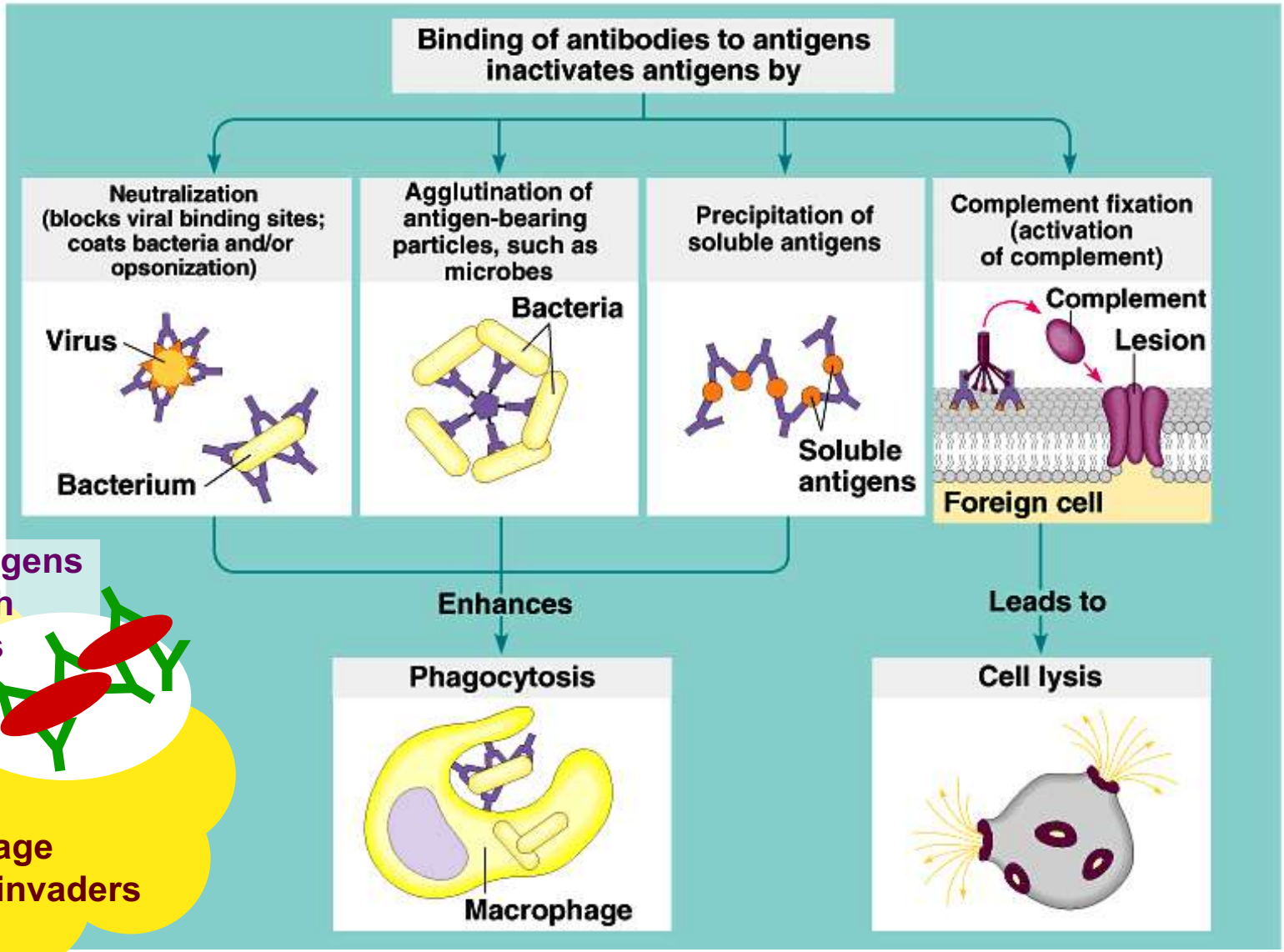
Structure of antibodies







How antibodies work

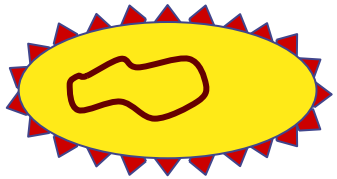


invading pathogens tagged with antibodies

macrophage eating tagged invaders

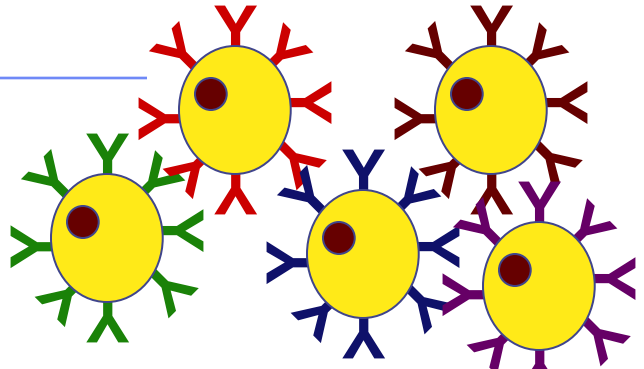
10 to 17 days for full response

B cell immune response



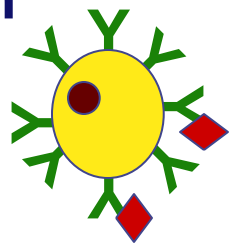
invader
(foreign antigen)

tested by
B cells
(in blood & lymph)

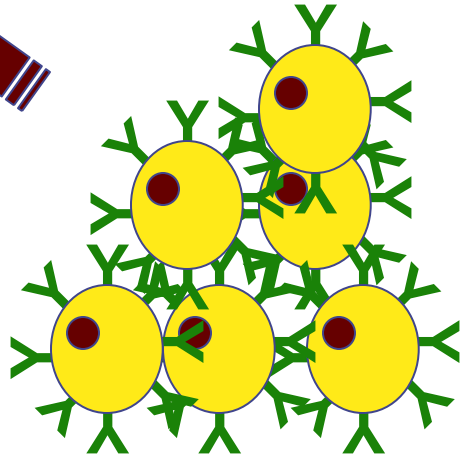


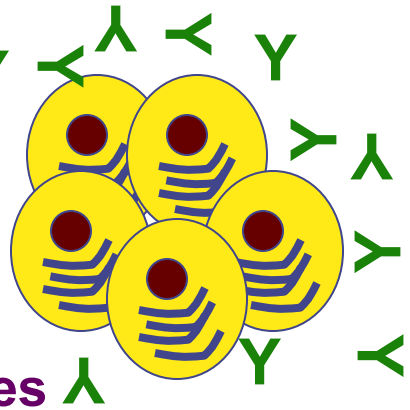
B cells + antibodies

recognition



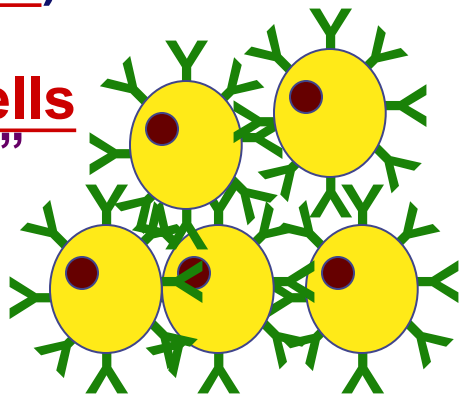
clone
1000s of clone cells





plasma cells
release antibodies

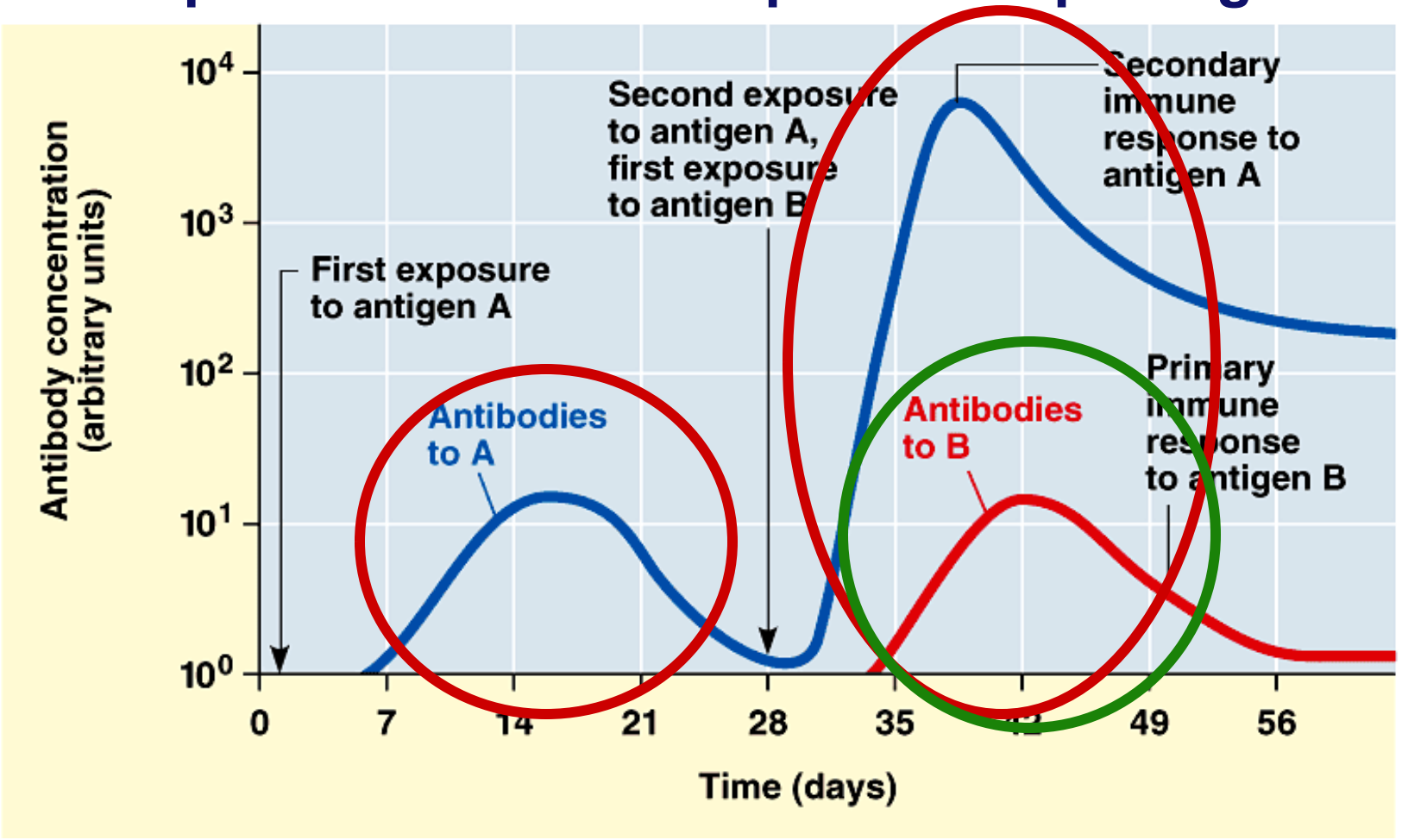
captured
invaders



memory cells
"reserves"

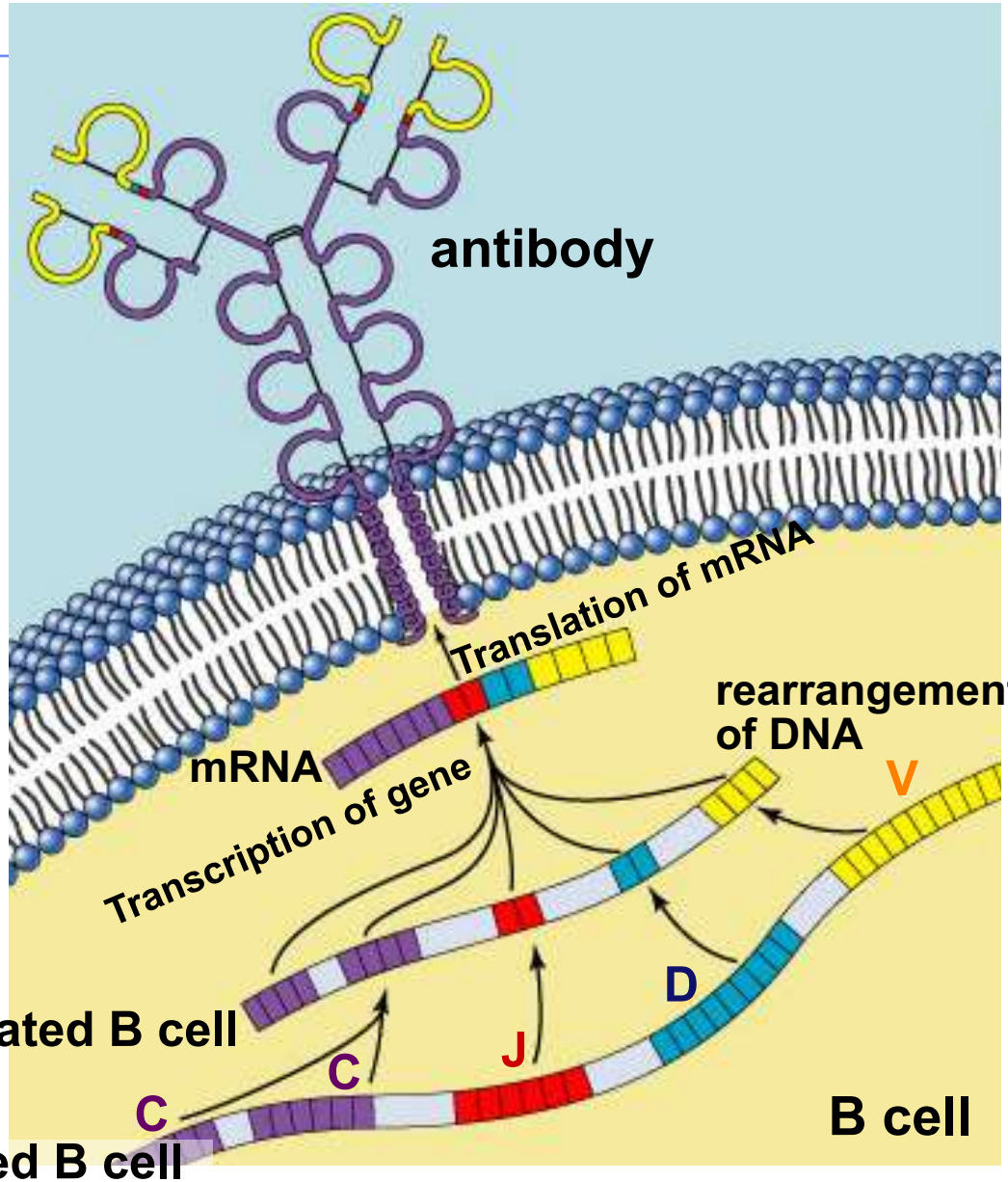
1° vs 2° response to disease

- Memory B cells allow a rapid, amplified response with future exposure to pathogen



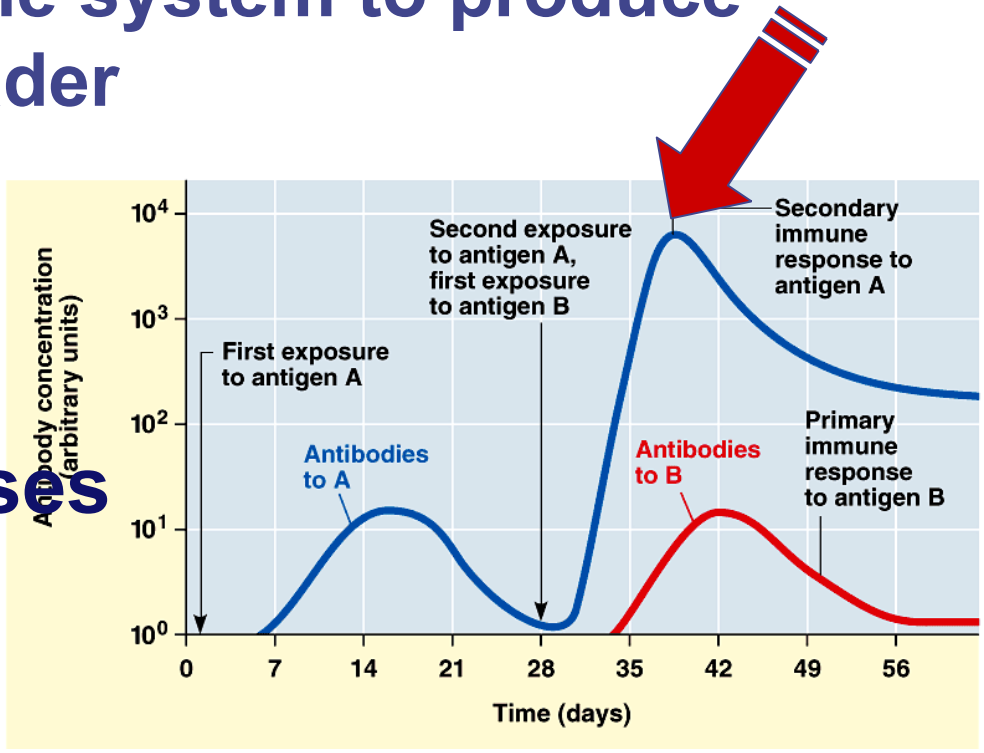
How do vertebrates produce millions of antibody proteins, if they only have a few hundred genes coding for those proteins?

By DNA rearrangement & somatic mutation vertebrates can produce millions of B & T cells



Vaccinations

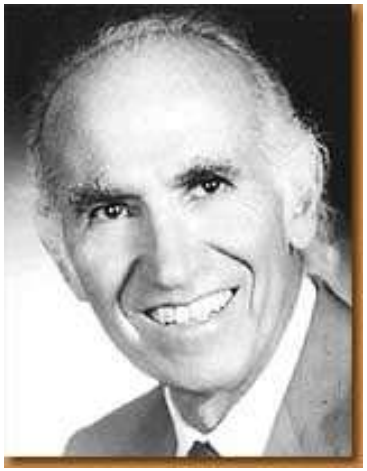
- Immune system exposed to harmless version of pathogen
  - triggers **active immunity**
  - stimulates immune system to produce antibodies to invader
  - rapid response if future exposure
- Most successful against viral diseases



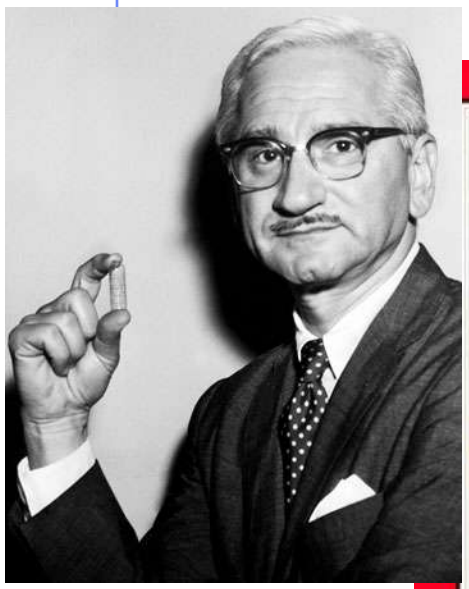
Jonas Salk

1914 – 1995

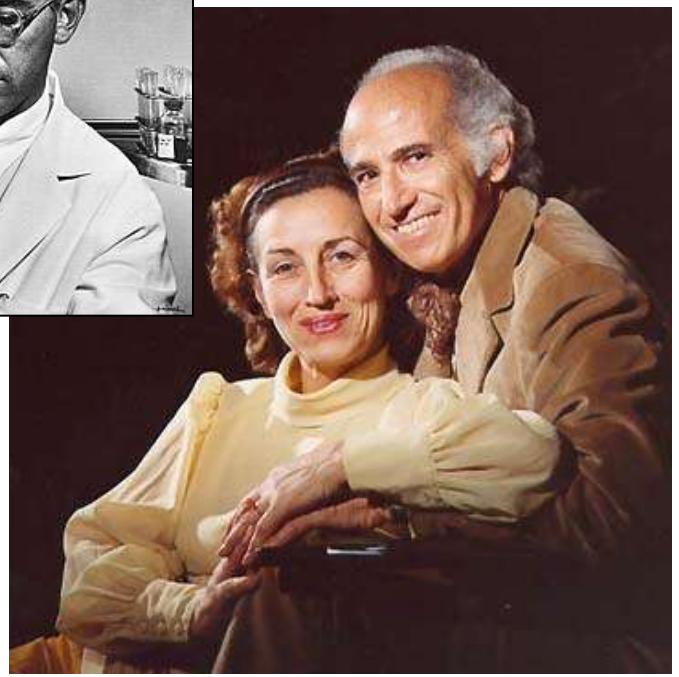
April 12, 1955



- Developed first vaccine
  - against polio
    - attacks motor neurons

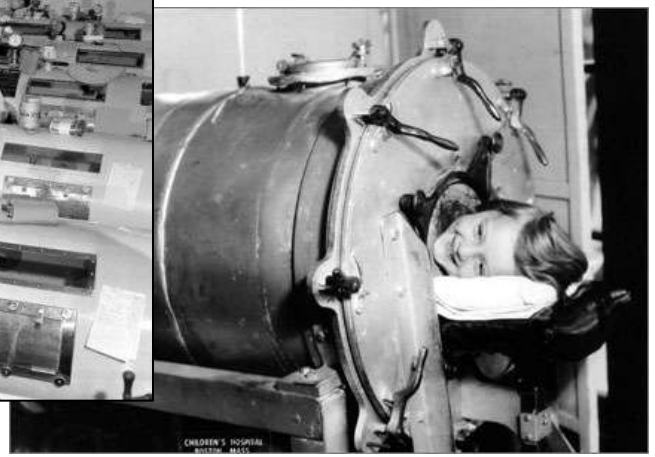


Albert Sabin
1962
oral vaccine



Polio epidemics

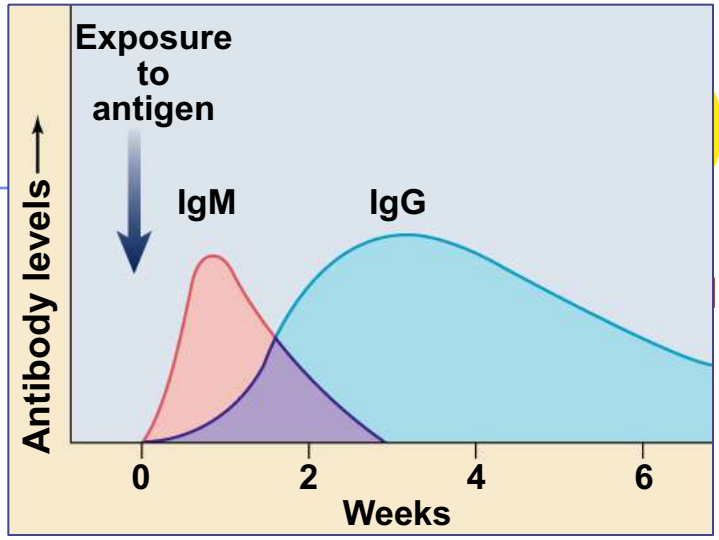
1994:
Americas polio free



Passive immunity

- Obtaining antibodies from another individual
- Maternal immunity
  - antibodies pass from mother to baby across placenta or in mother's milk
  - critical role of breastfeeding in infant health
    - mother is creating antibodies against pathogens baby is being exposed to
- Injection
  - injection of antibodies
  - short-term immunity

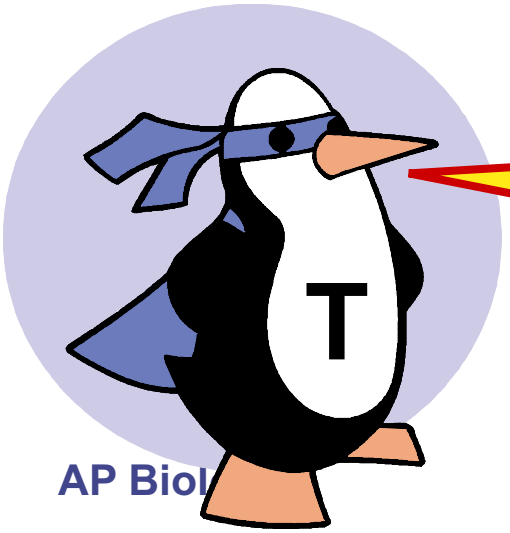
Classes of antibodies



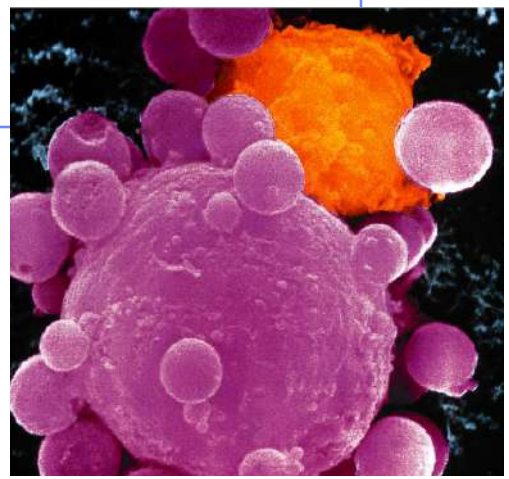
- Immunoglobulins
  - IgM
    - 1st immune response
    - activate complement proteins
  - IgG
    - 2nd response, major antibody circulating in plasma
    - promote phagocytosis by macrophages
  - IgA
    - in external secretions, sweat & mother's milk
  - IgE
    - promote release of histamine & lots of bodily fluids
    - evolved as reaction to parasites
    - triggers allergic reaction
  - IgD
    - receptors of B cells???

What if the attacker gets past the B cells in the blood & actually infects some of your cells?

You need trained assassins to kill off these infected cells!

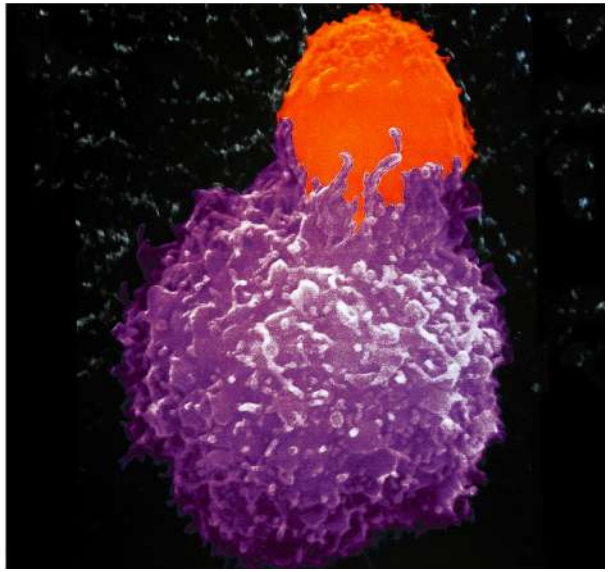


Attack of the Killer T cells!



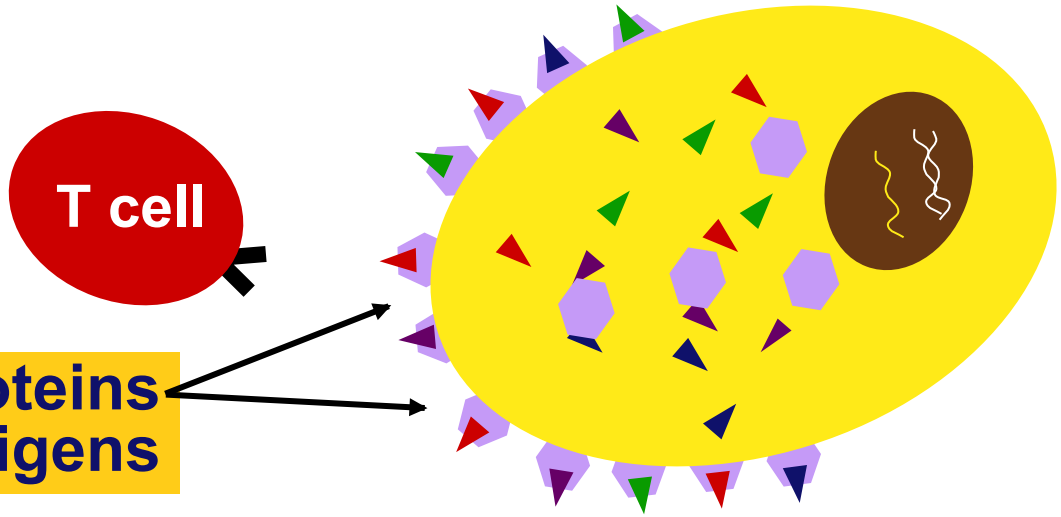
T cells

- **Cell-mediated response**
  - immune response to infected cells
    - viruses, bacteria & parasites (pathogens) within cells
  - defense against "non-self" cells
    - cancer & transplant cells
- **Types of T cells**
  - **helper T cells**
    - alerts immune system
  - **killer (cytotoxic) T cells**
    - attack infected body cells



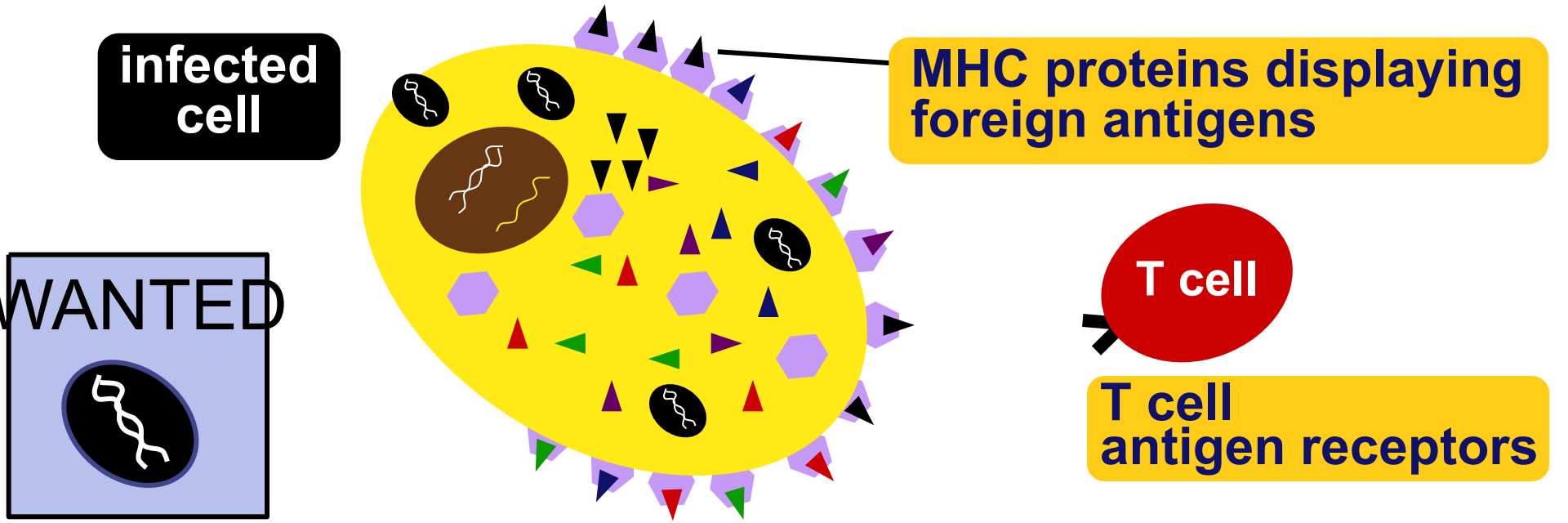
How are cells tagged with antigens

- **Major histocompatibility (MHC) proteins**
  - antigen **glycoproteins**
- **MHC proteins 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"

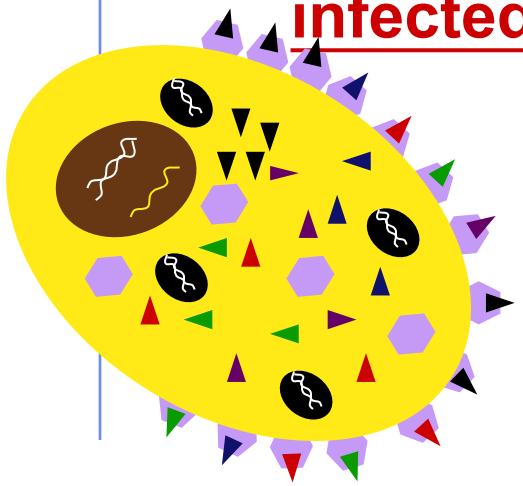


How do T cells know a cell is infected

- Infected cells digest pathogens & MHC proteins bind & carry pieces to cell surface
  - antigen presenting cells (APC)
  - alerts Helper T cells



T cell response



helper T cell

interleukin 1

helper T cell

helper T cell

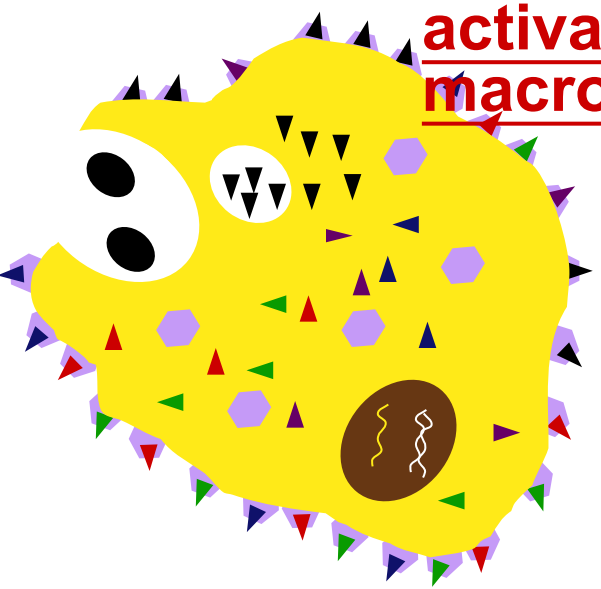
helper T cell

interleukin 2

killer T cell

activate killer T cells

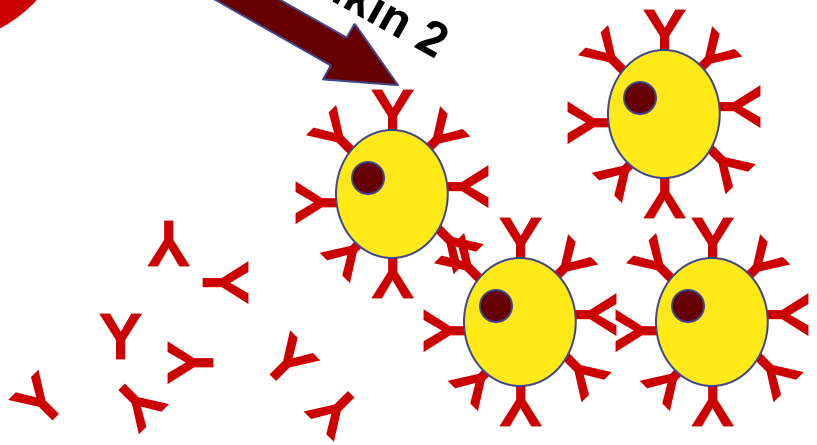
or



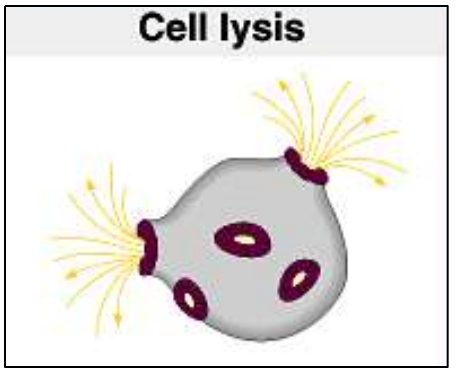
helper T cell

interleukin 2

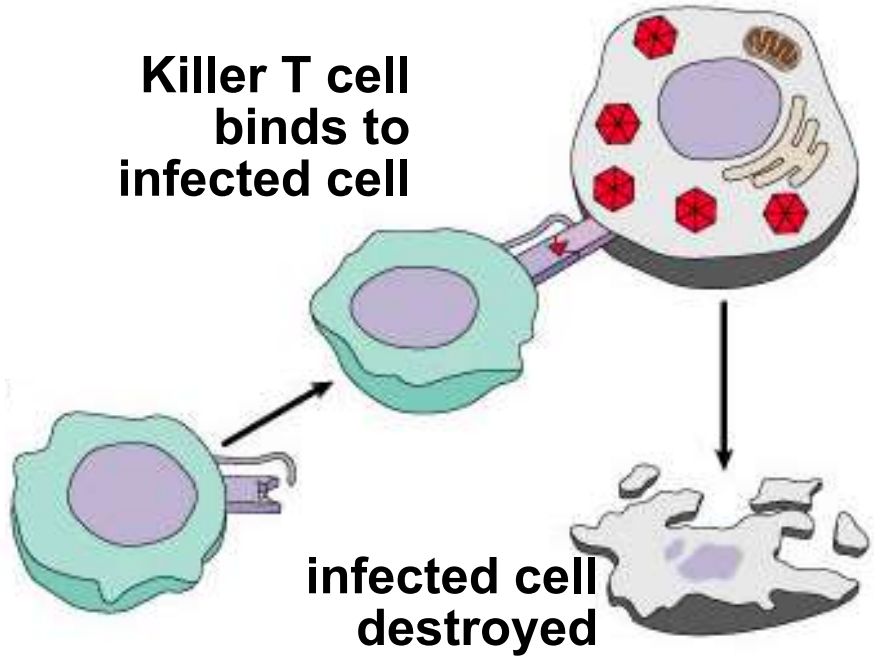
stimulate B cells & antibodies

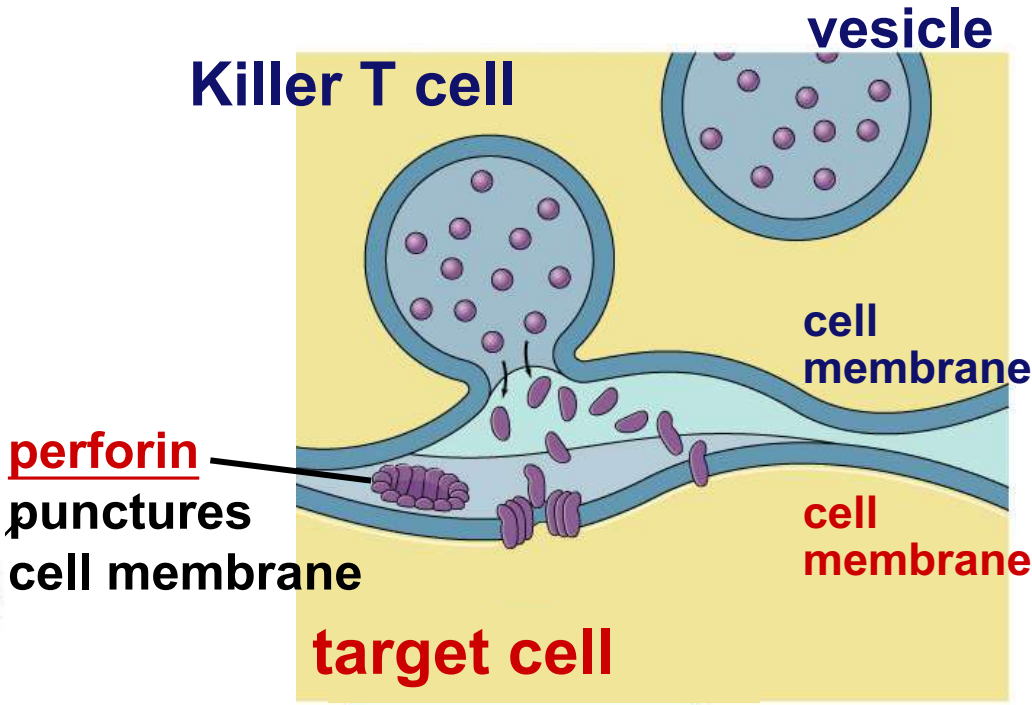


Attack of the Killer T cells



- Destroys infected body cells
  - binds to target cell
  - secretes perforin protein
    - punctures cell membrane of infected cell





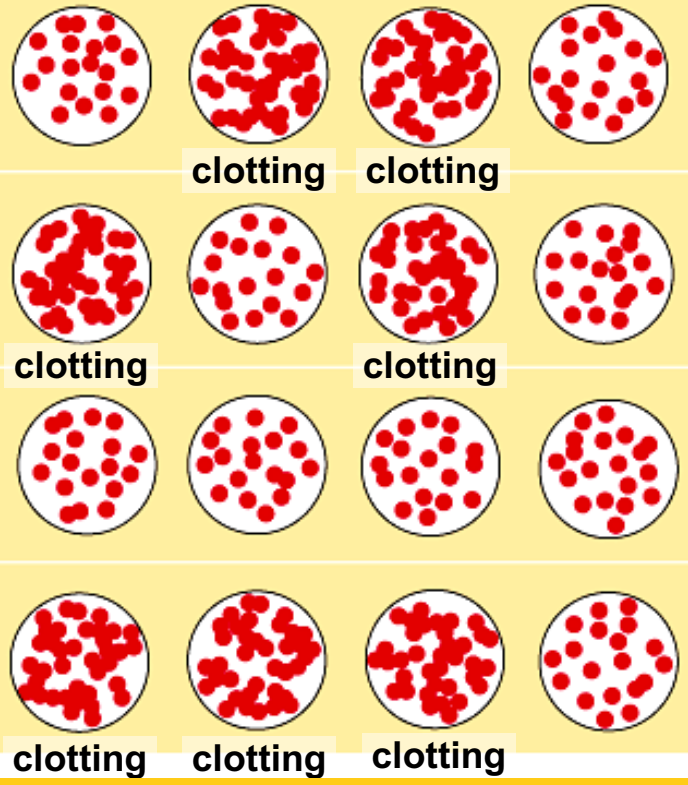
Incidence of Blood Types in the United States

Blood Type (percentage)

Population Group	O	A	B	AB	Rh+
White	45	40	11	4	85
Black	49	27	20	4	95
Korean	32	28	30	10	100
Japanese	31	38	21	10	100
Chinese	42	27	25	6	100
Native American	79	16	4	1	100

Blood donation

(a) Phenotype (blood group)	(b) Genotypes (see p.258)	(c) Antibodies present in blood serum	(d) Results from adding red blood cells from groups below to serum from groups at left			
			A	B	AB	O
A	$I^A I^A$ or $I^A i$	Anti-B		clotting	clotting	
B	$I^B I^B$ or $I^B i$	Anti-A	clotting		clotting	
AB	$I^A I^B$	—				
O	ii	Anti-A Anti-B	clotting	clotting	clotting	

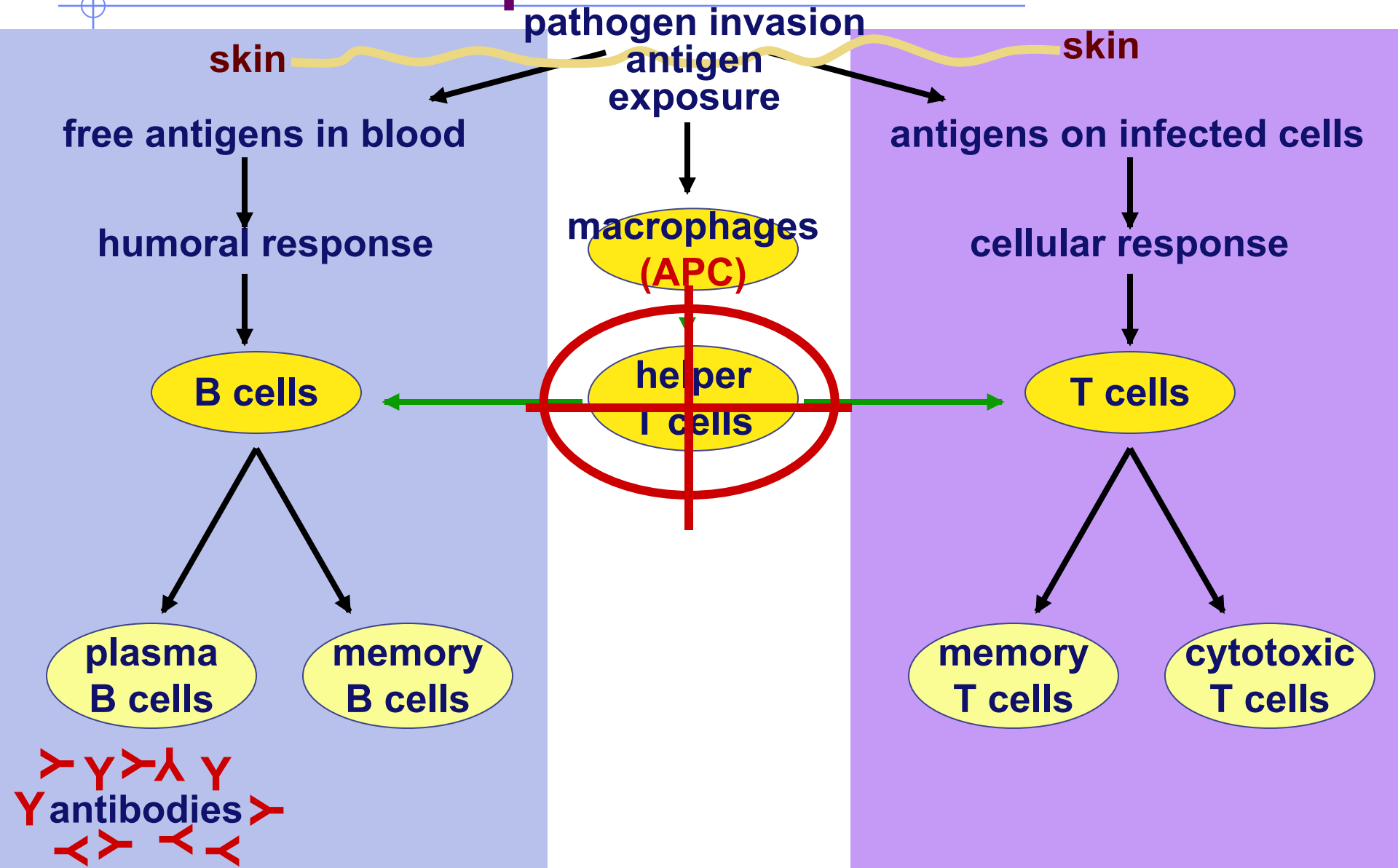


Matching compatible blood groups is critical for blood transfusions

A person produces antibodies against foreign blood antigens

- The mismatch of an Rh^- mother carrying an Rh^+ baby can cause problems for the unborn child
  - The first pregnancy usually proceeds without problems
  - In a second pregnancy, the mother's immune system produces antibodies to attack the Rh^+ blood (hemolytic disease of the newborn)

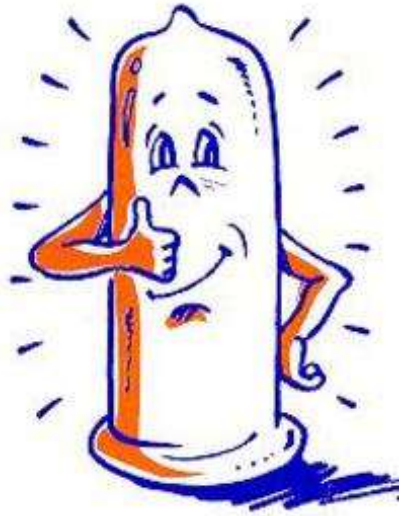
Immune response



HIV & AIDS

- Human Immunodeficiency Virus
  - virus infects helper T cells
  - helper T cells don't activate rest of immune system: T cells & B cells
    - also destroy T cells
- Acquired ImmunoDeficiency Syndrome
  - infections by opportunistic diseases
  - death usually from other infections
    - pneumonia, cancer

How to protect yourself…



Immune system malfunctions

- **Auto-immune diseases**
  - immune system attacks own molecules & cells
    - 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

Key attributes of 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 to reduce auto-immune disease

It's safe to Ask Questions!

2007-2008