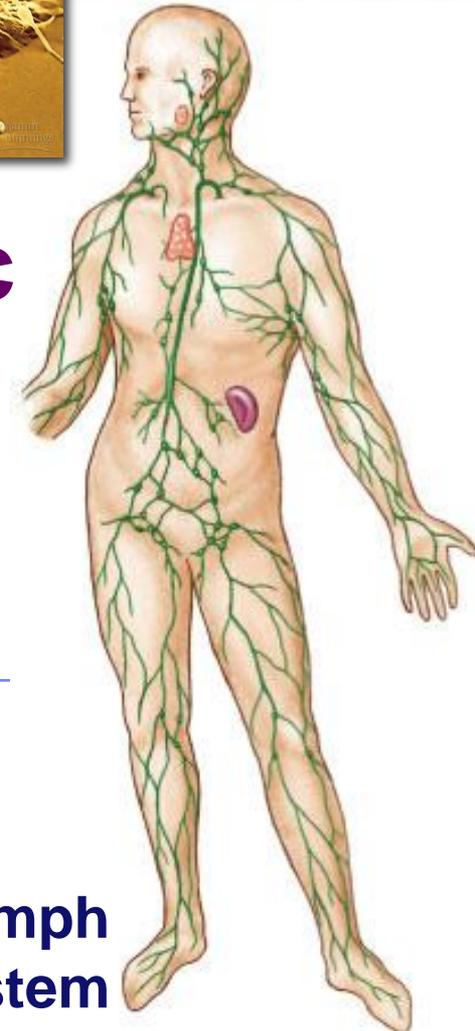


Fighting the
Enemy Within!

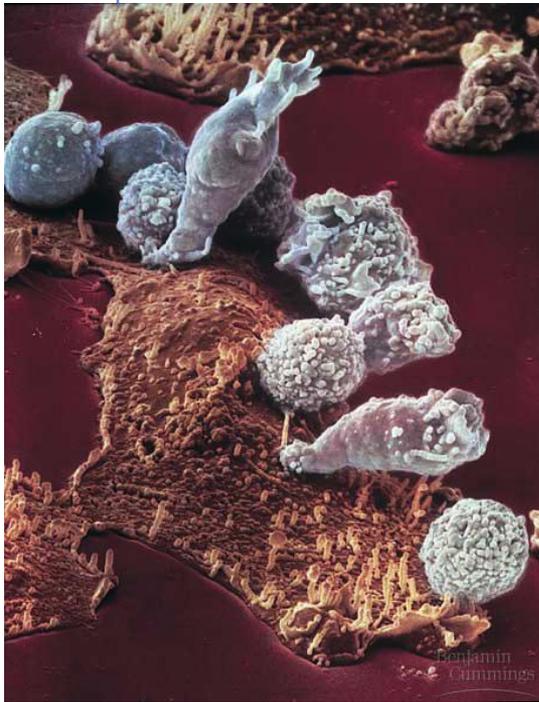


phagocytic
leukocyte

Immune / Lymphatic System



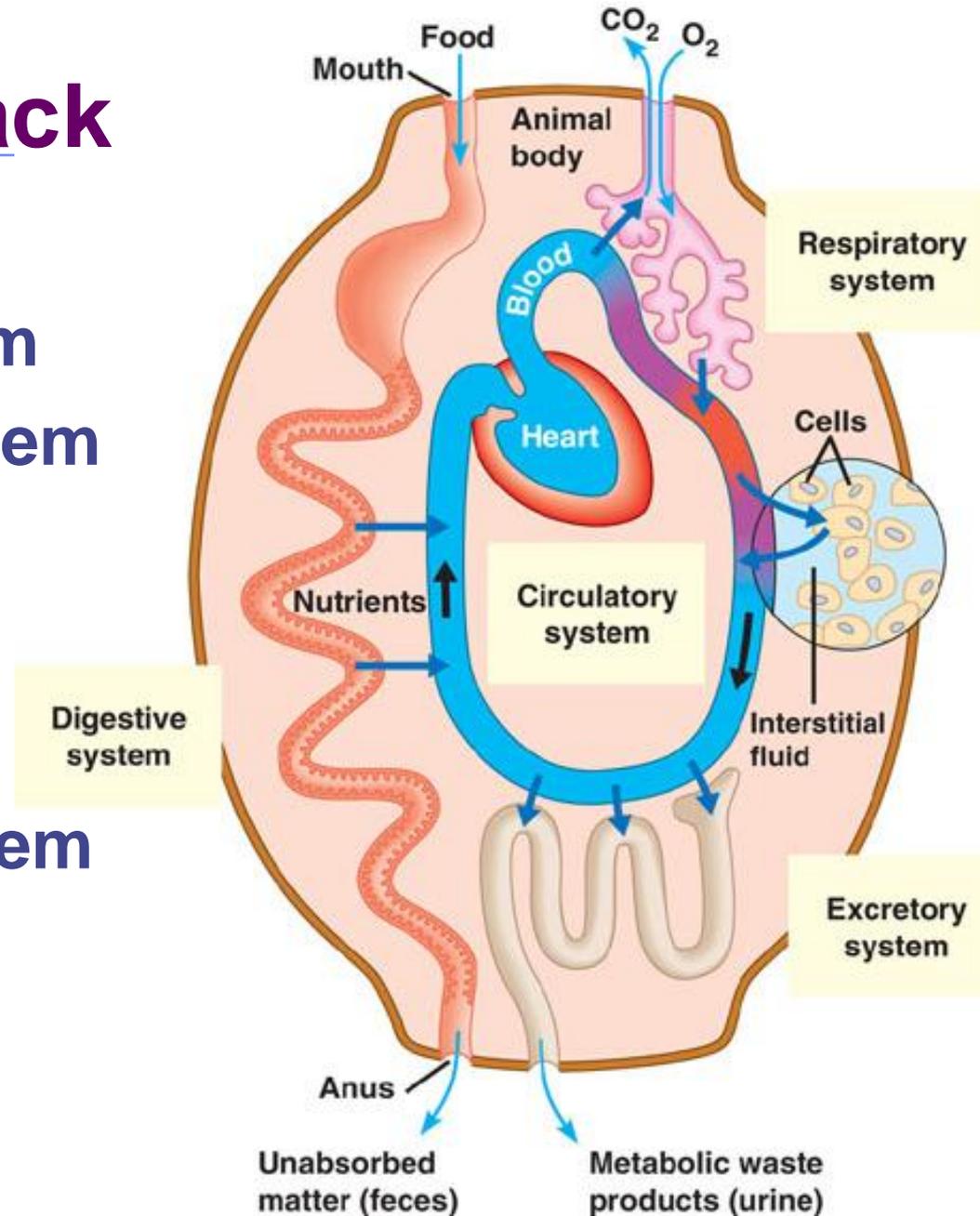
lymph
system



lymphocytes
attacking
cancer cell

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
- ◆ 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

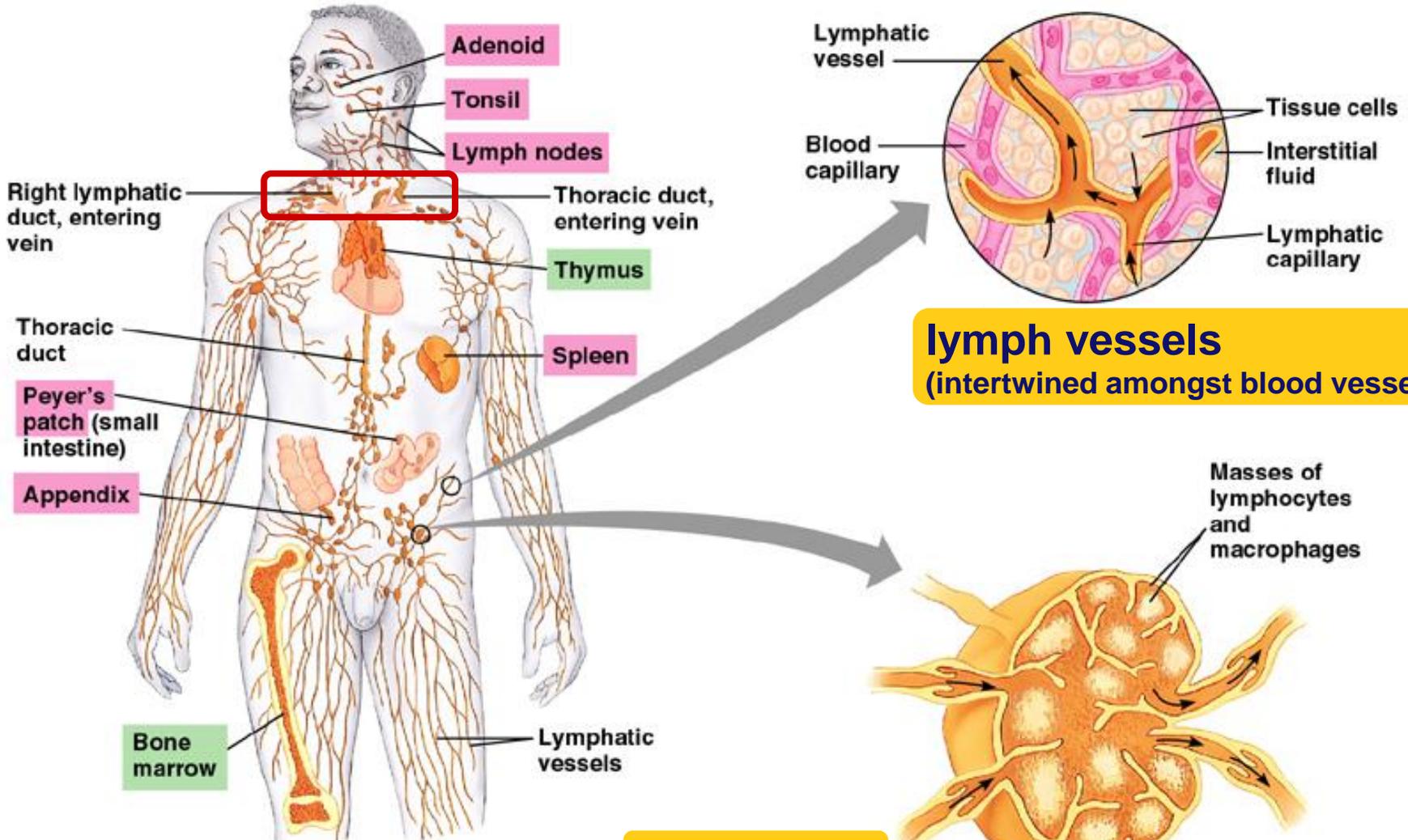
■ Attack from inside

- ◆ cancers = abnormal body cells



Lymph system

Production & transport of leukocytes
Traps foreign invaders

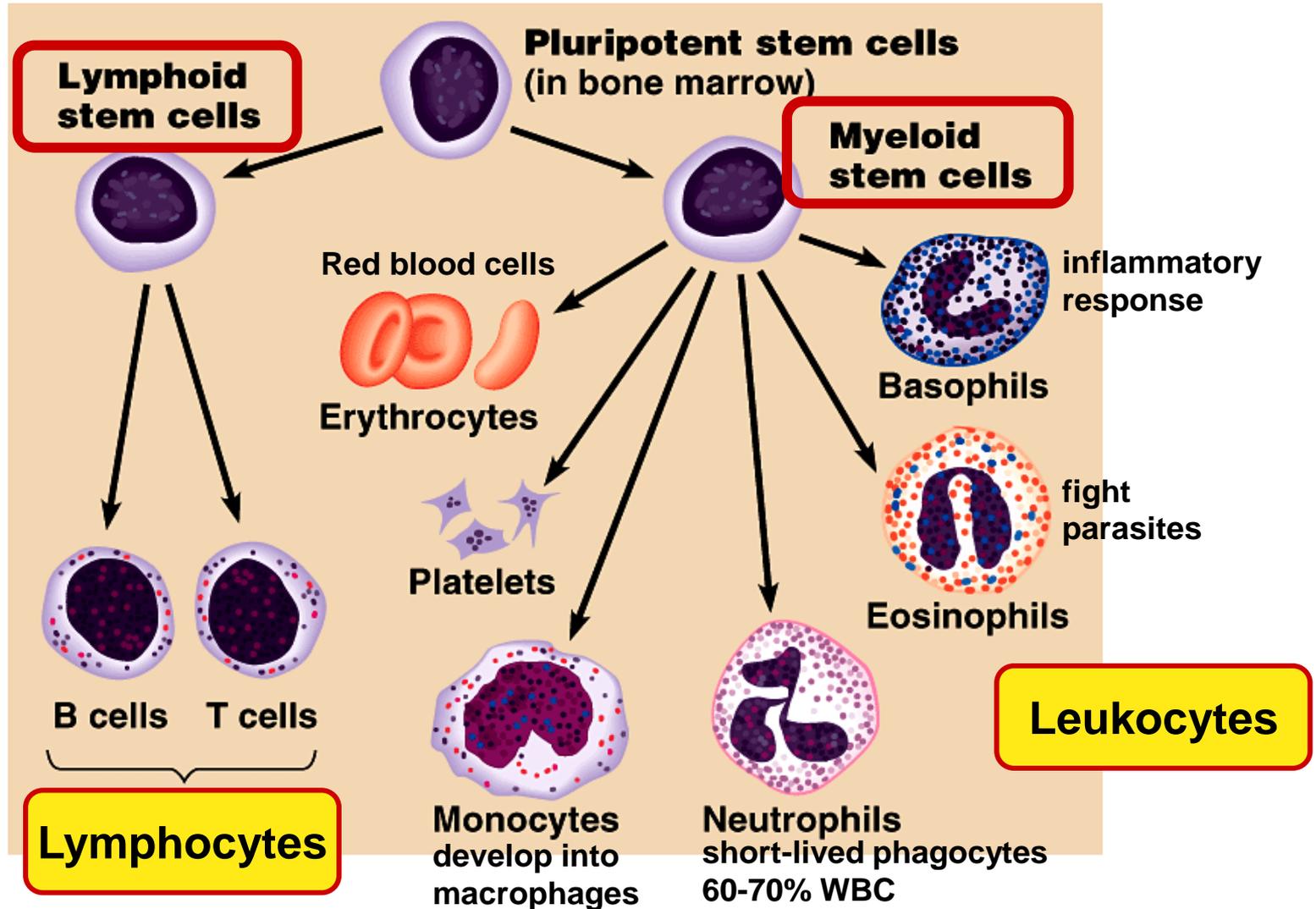


lymph vessels
(intertwined amongst blood vessels)

lymph node

A
(a)

Development of Red & White blood cells



Lines of defense

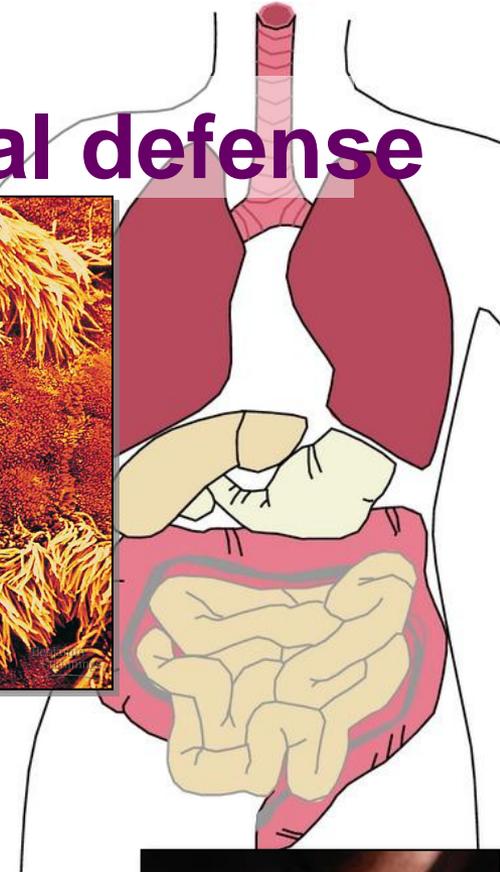
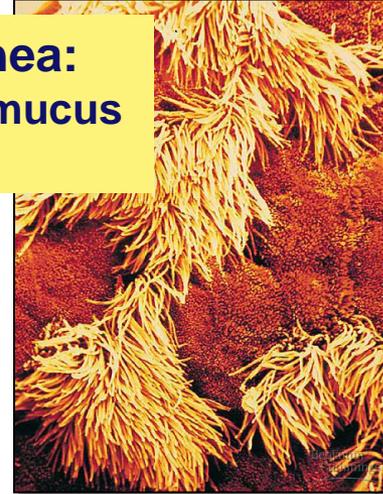
- 1st line: Non-specific barriers
 - ◆ broad, external defense
 - “walls & moats”
 - ◆ skin & mucous membranes
- 2nd line: Non-specific patrols
 - ◆ broad, internal defense
 - “patrolling soldiers”
 - ◆ leukocytes = phagocytic WBC
- 3rd line: True immune system
 - ◆ specific, acquired immunity
 - “elite trained units”
 - ◆ lymphocytes & antibodies
 - B cells & T cells



1st line: Non-specific External defense

- **Barrier**
 - skin
- **Traps**
 - mucous membranes, cilia, hair, earwax
- **Elimination**
 - coughing, sneezing, urination, diarrhea
- **Unfavorable pH**
 - stomach acid, sweat, saliva, urine
- **Lysozyme enzyme**
 - digests bacterial cell walls
 - tears, sweat

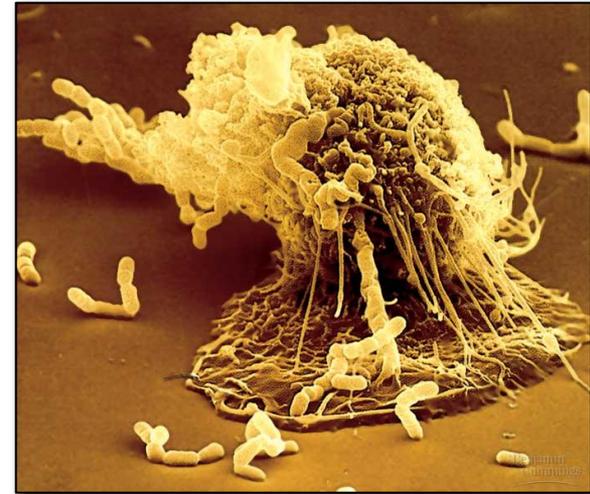
Lining of trachea:
ciliated cells & mucus
secreting cells



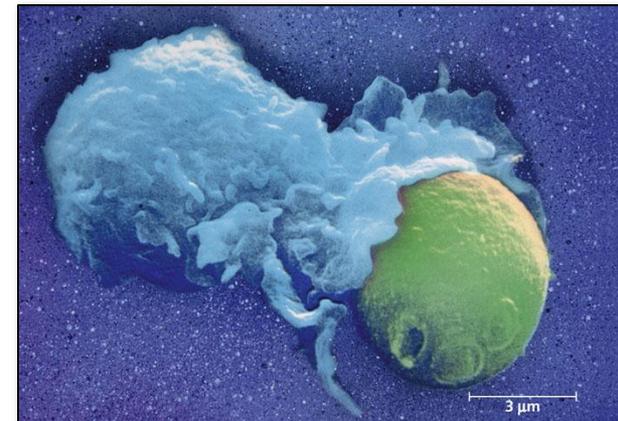
2nd line: Non-specific patrolling cells

- **Patrolling cells & proteins**
 - ◆ attack pathogens, but don't "remember" for next time
 - **leukocytes**
 - ◆ **phagocytic** white blood cells
 - ◆ macrophages, neutrophils, natural killer cells
 - **complement system**
 - ◆ proteins that destroy cells
 - **inflammatory response**
 - ◆ increase in body temp.
 - ◆ increase capillary permeability
 - ◆ attract macrophages

bacteria



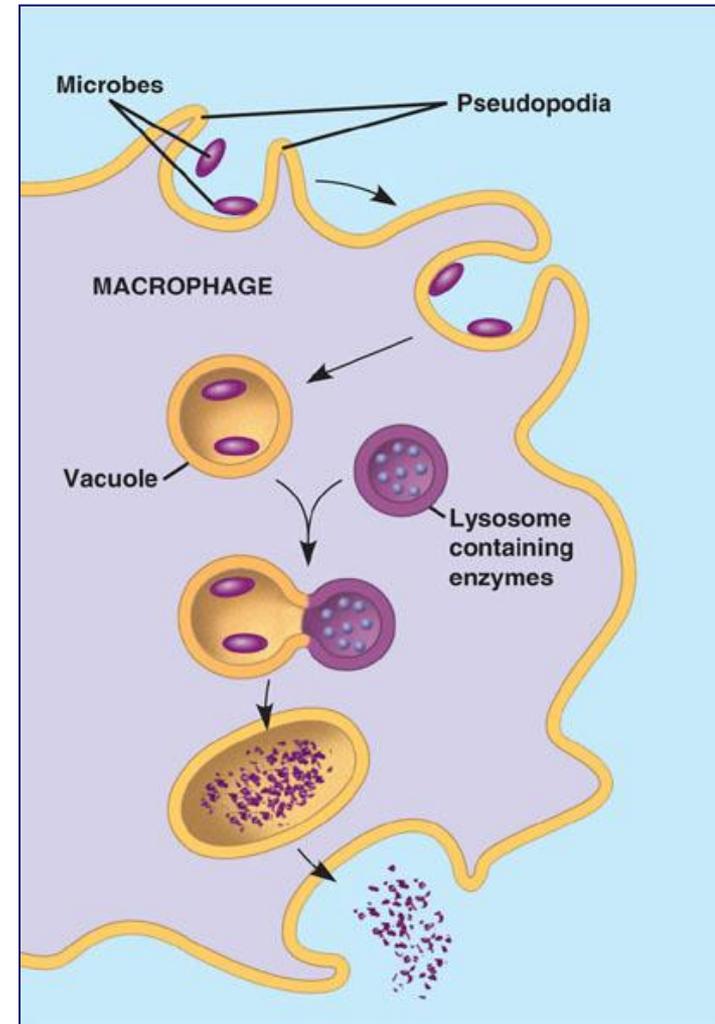
macrophage



yeast

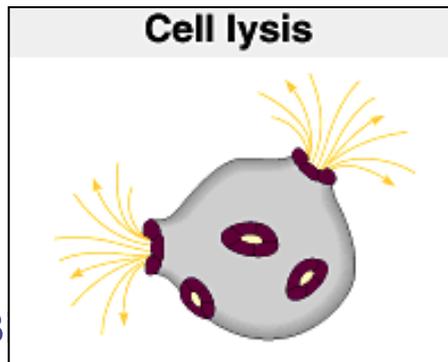
Leukocytes: Phagocytic WBCs

- Attracted by chemical signals released by damaged cells
 - ◆ ingest pathogens
 - ◆ digest in lysosomes
- Neutrophils
 - ◆ most abundant WBC (~70%)
 - ◆ ~ 3 day lifespan
- Macrophages
 - ◆ “big eater”, long-lived
- Natural Killer Cells
 - ◆ destroy virus-infected cells & cancer cells

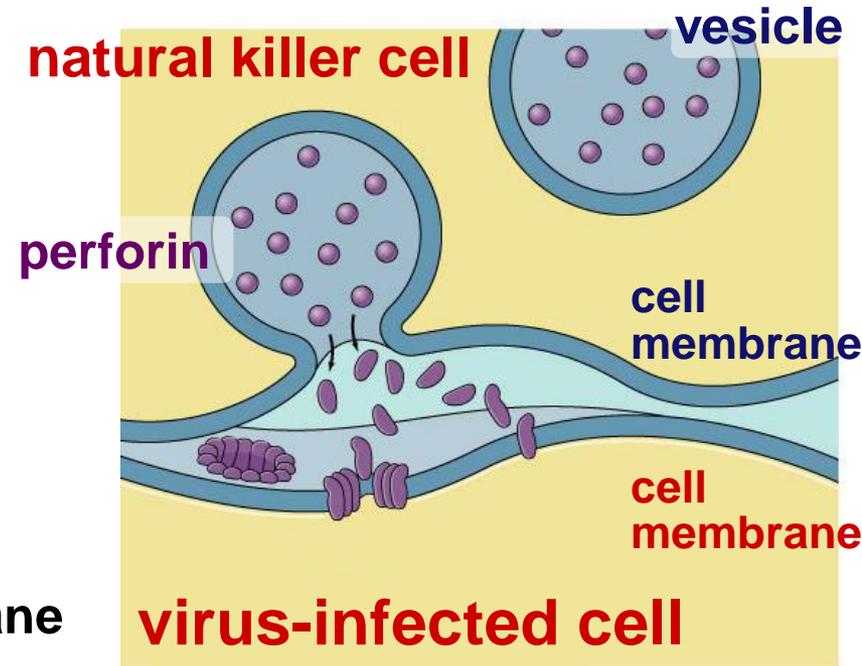


Destroying cells gone bad!

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



perforin
punctures
cell membrane



Anti-microbial proteins

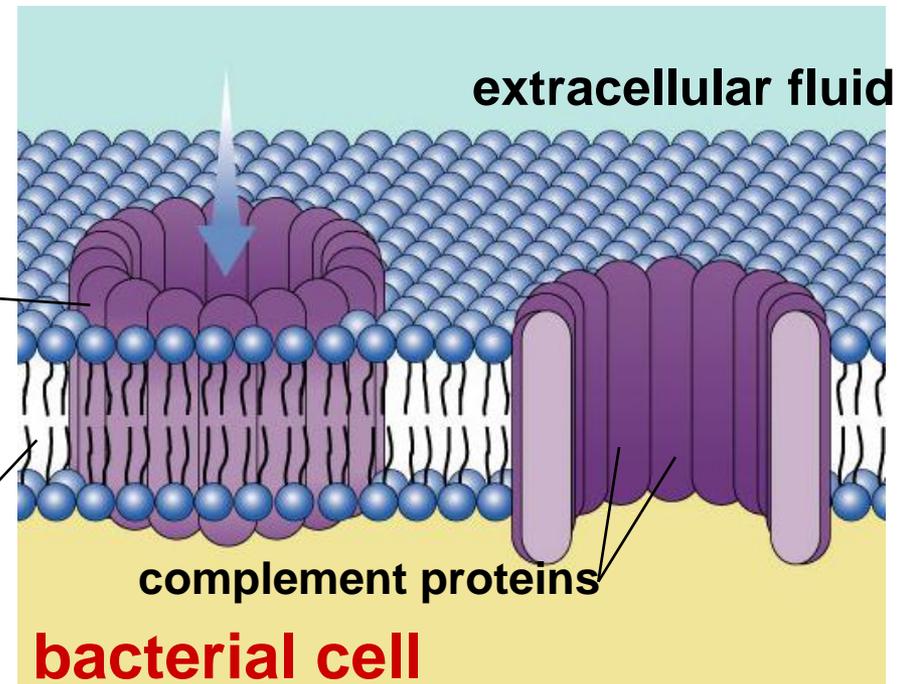
■ Complement system

- ◆ ~20 proteins circulating in blood plasma
- ◆ attack bacterial & fungal cells

- form a membrane attack complex
- perforate target cell
- apoptosis
 - ◆ cell lysis

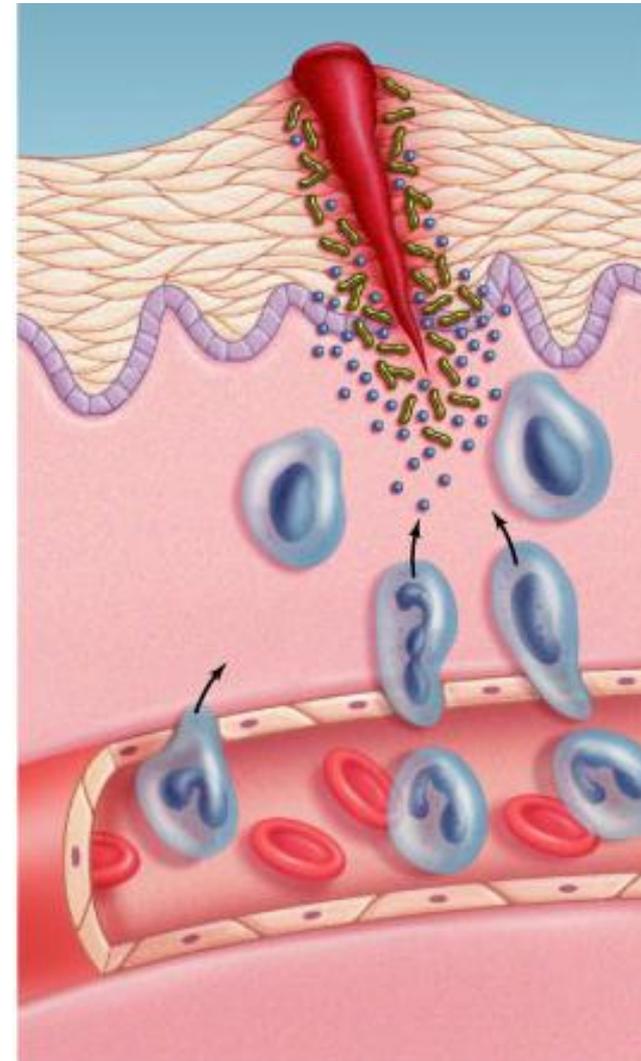
complement proteins
form cellular lesion

plasma membrane of
invading microbe



Inflammatory response

- Damage to tissue triggers local non-specific **inflammatory response**
 - ◆ release chemical signals
 - **histamines** & **prostaglandins**
 - ◆ capillaries dilate, become more permeable (leaky)
 - delivers macrophages, RBCs, platelets, clotting factors
 - ◆ fight pathogens
 - ◆ clot formation
 - ◆ increases temperature
 - decrease bacterial growth
 - stimulates phagocytosis
 - speeds up repair of tissues



Fever

- When a local response is not enough
 - ◆ system-wide 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 with memory

◆ lymphocytes

■ B cells

■ T cells

◆ antibodies

■ immunoglobulins

■ Responds to...

◆ antigens

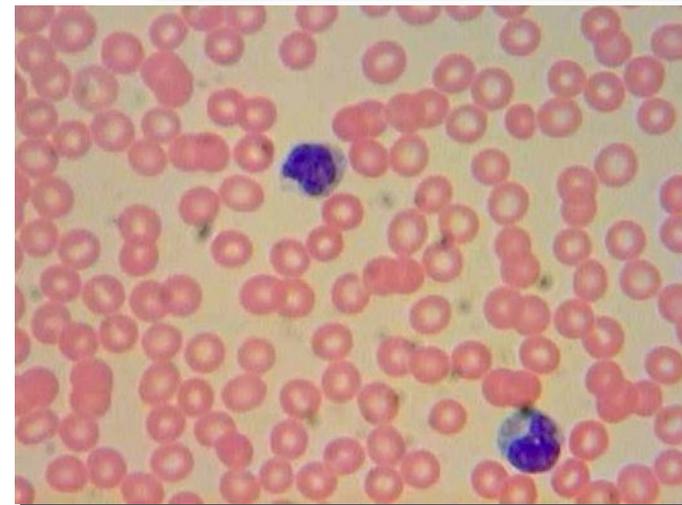
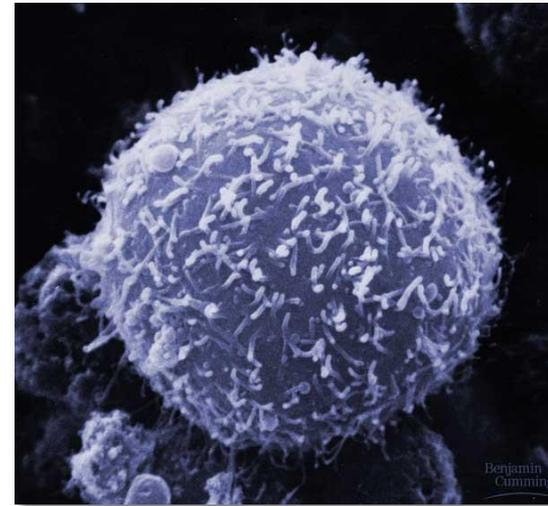
■ cellular name tags

◆ specific pathogens

◆ specific toxins

◆ abnormal body cells (cancer)

B cell



How are invaders recognized?

■ Antigens

◆ cellular name tag proteins

■ “self” antigens

◆ no response from WBCs

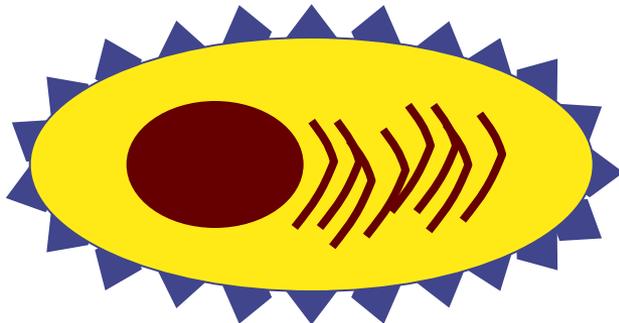
■ “foreign” antigens

◆ response from WBCs

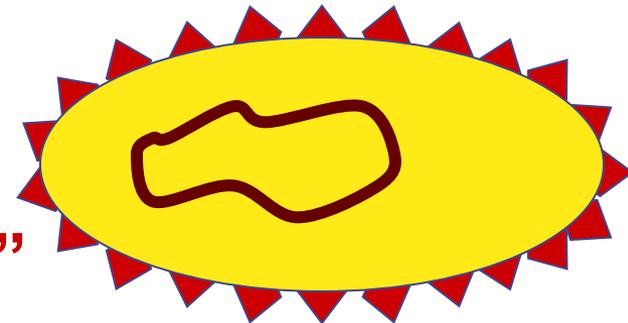
◆ pathogens: viruses, bacteria, protozoa, parasitic worms, fungi, toxins

◆ non-pathogens: cancer cells, transplanted tissue, pollen

“self”



“foreign”



Lymphocytes

■ B cells

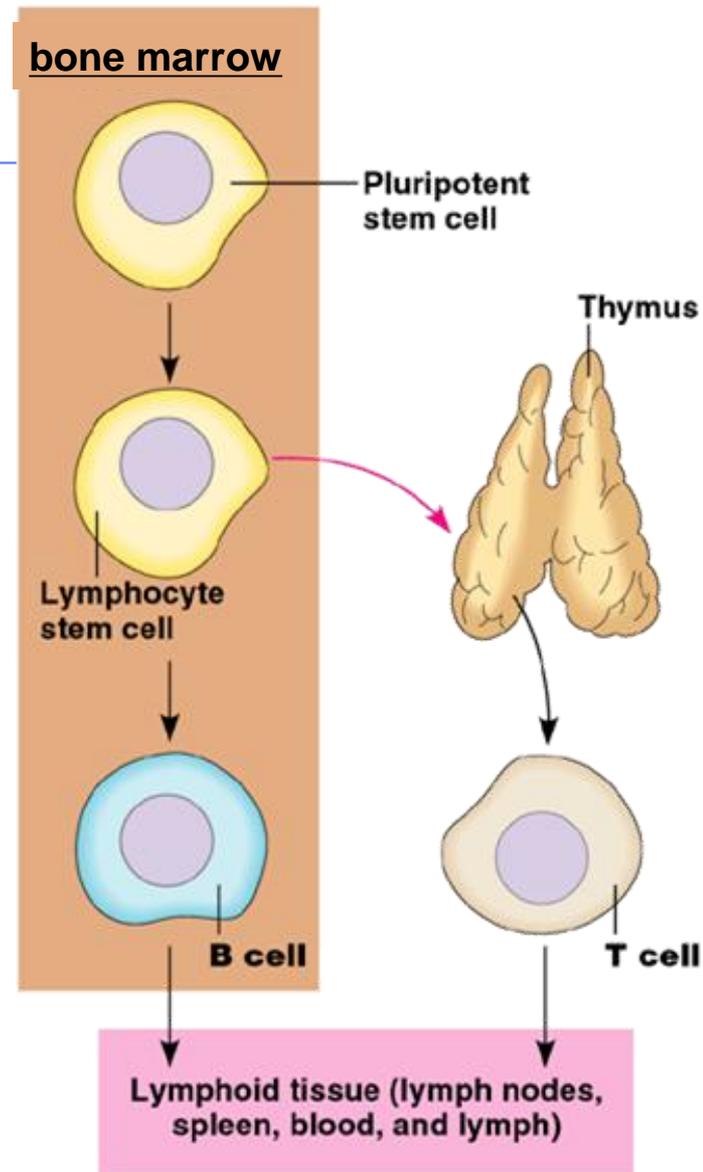
- ◆ mature in bone marrow
- ◆ humoral response system
 - “humors” = body fluids
 - attack pathogens still circulating in blood & lymph
- ◆ produce antibodies

■ T cells

- ◆ mature in thymus
- ◆ cellular response system
 - attack invaded cells

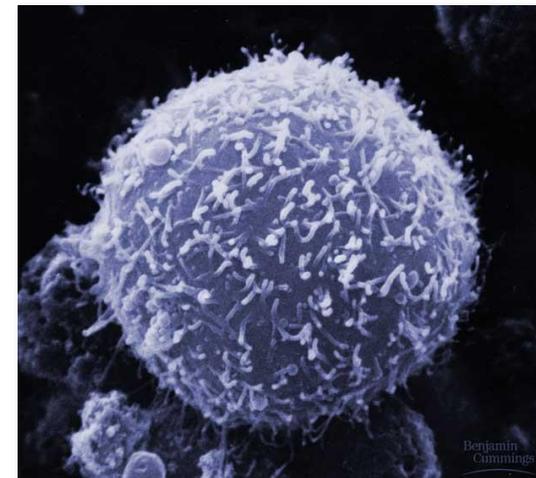
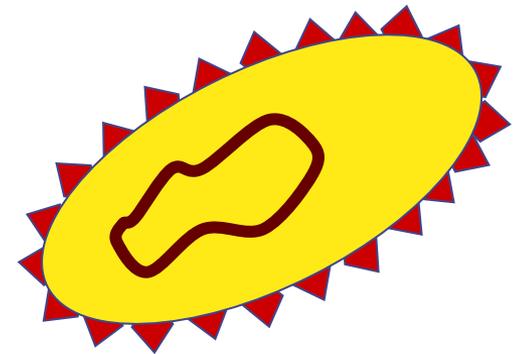
■ “Maturation”

- ◆ learn to distinguish “self” from “non-self” antigens
 - if react to “self” antigens, cells are destroyed during maturation

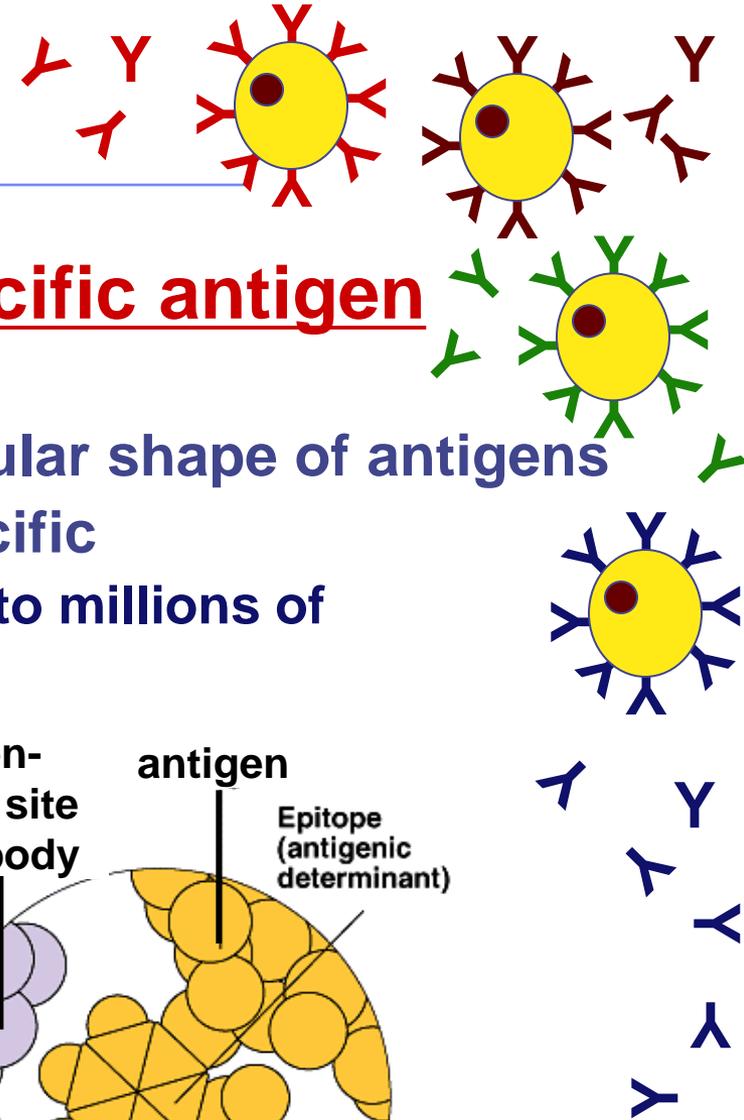


B cells

- Attack, learn & remember pathogens circulating in blood & lymph
- Produce specific antibodies against specific antigen
- Types of B cells
 - ◆ plasma cells
 - immediate production of antibodies
 - rapid response, short term release
 - ◆ memory cells
 - continued circulation in body
 - long term immunity

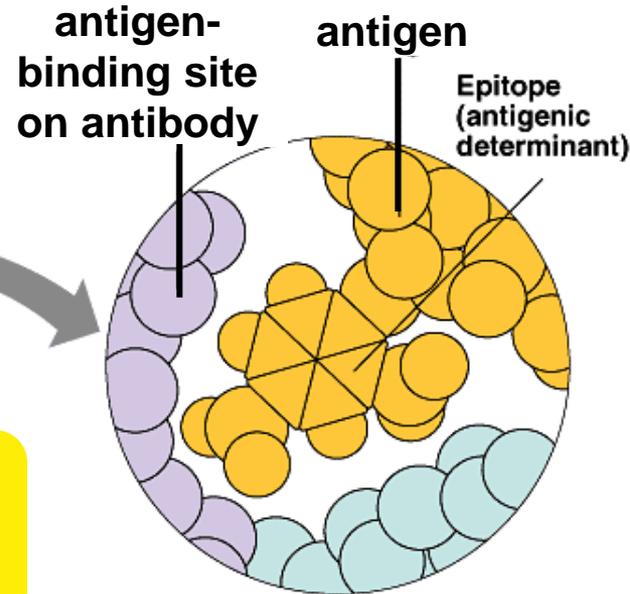
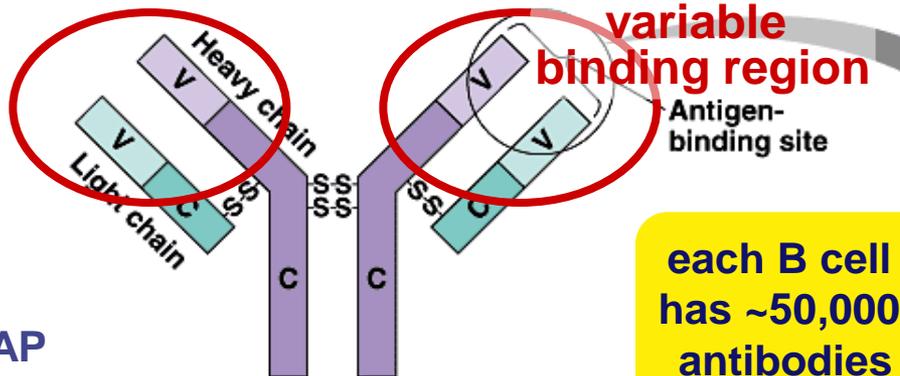


Antibodies



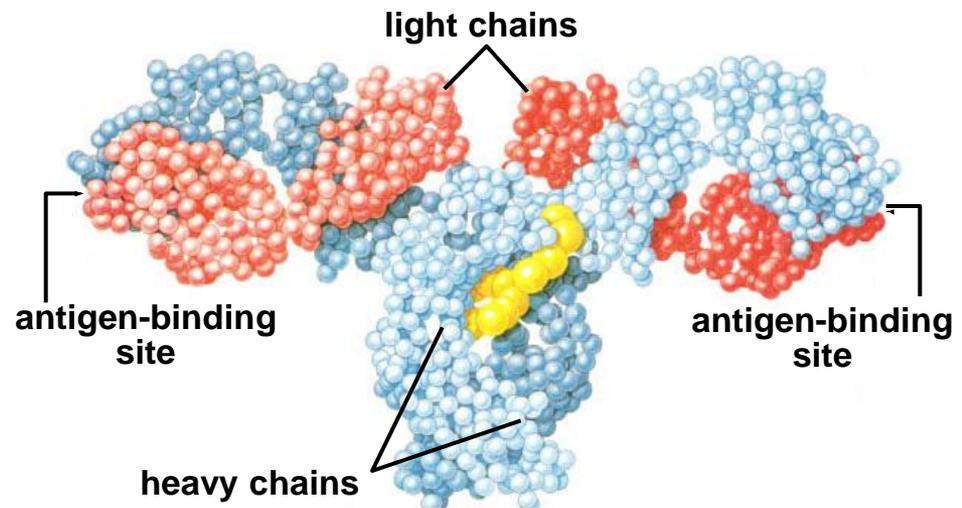
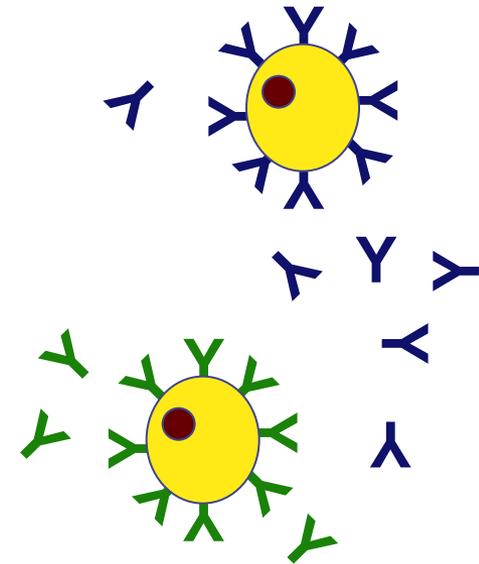
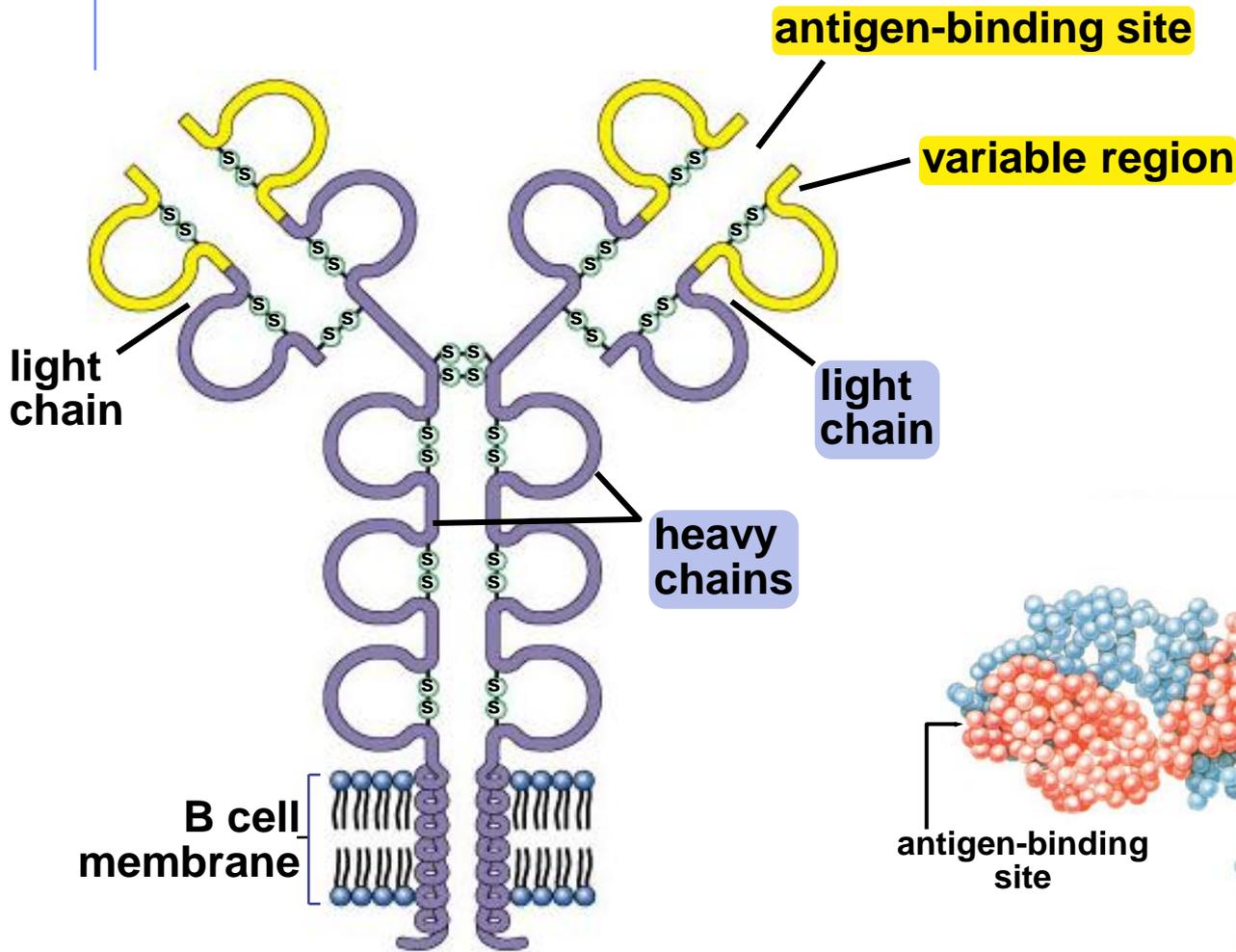
■ Proteins that bind to a specific antigen

- ◆ 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”
 - “this is foreign...gotcha!”

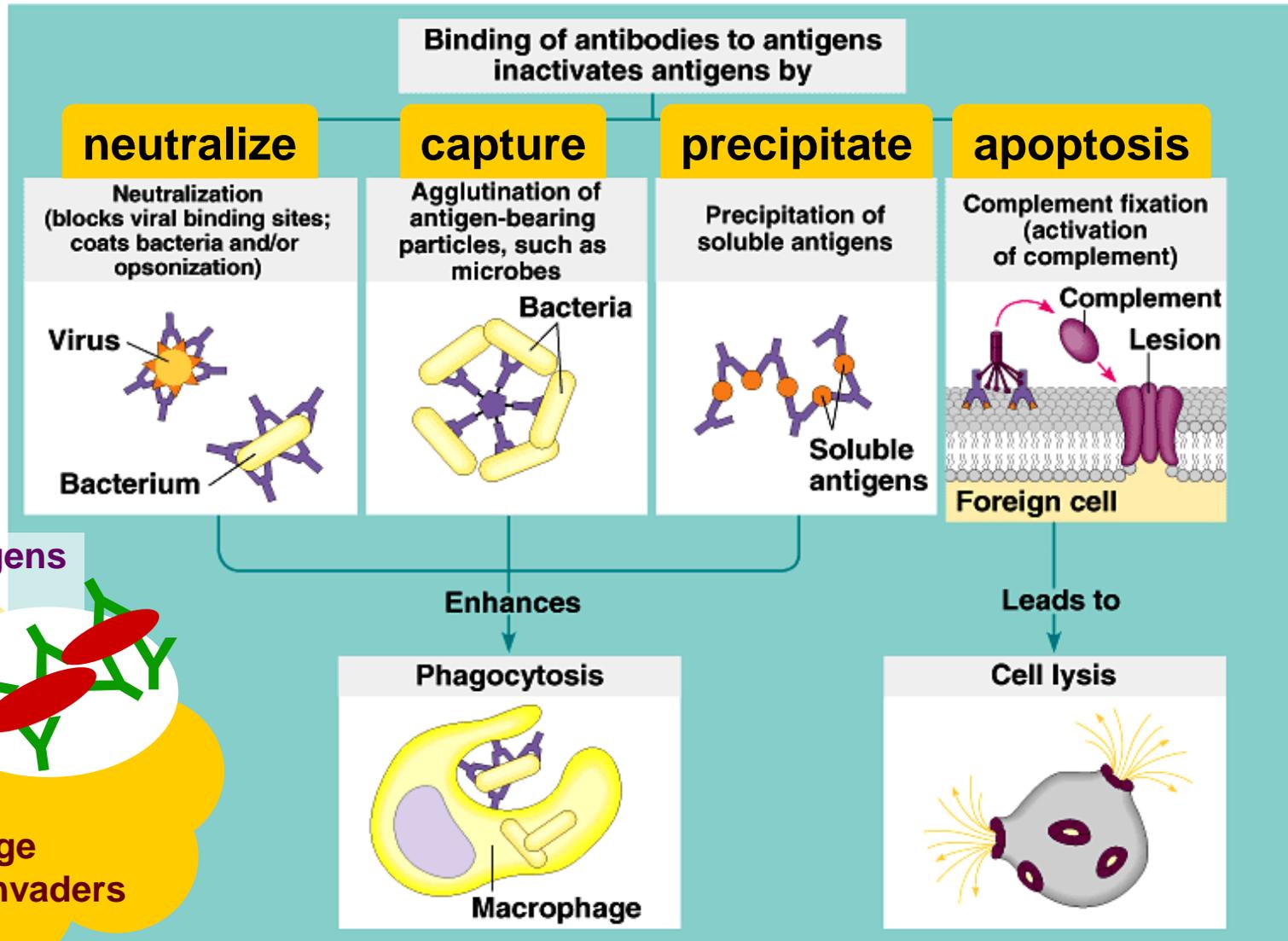


each B cell has ~50,000 antibodies

Structure of antibodies



What do antibodies do to invaders?



invading pathogens
tagged with
antibodies

macrophage
eating tagged invaders

Classes of antibodies

■ Immunoglobulins

◆ IgM

- 1st immune response
- activate complement proteins

◆ IgG

- 2nd response, major antibody circulating in plasma
- promote phagocytosis by macrophages

◆ IgA

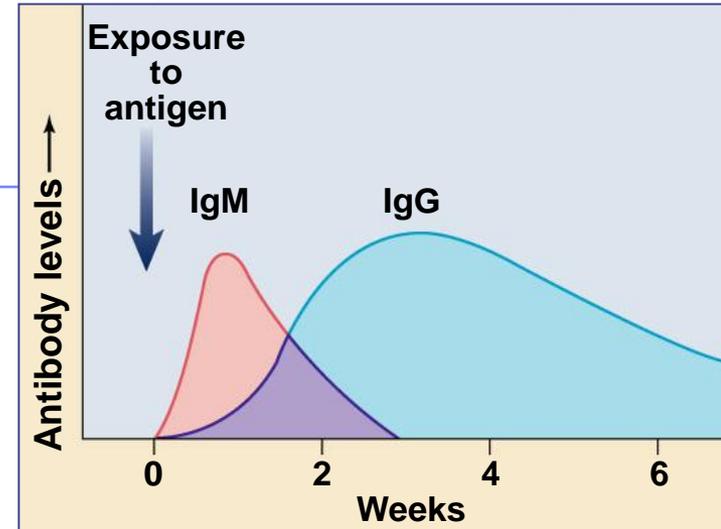
- in external secretions, sweat & mother's milk

◆ IgE

- promote release of histamine & lots of bodily fluids
- evolved as reaction to parasites
- triggers allergic reaction

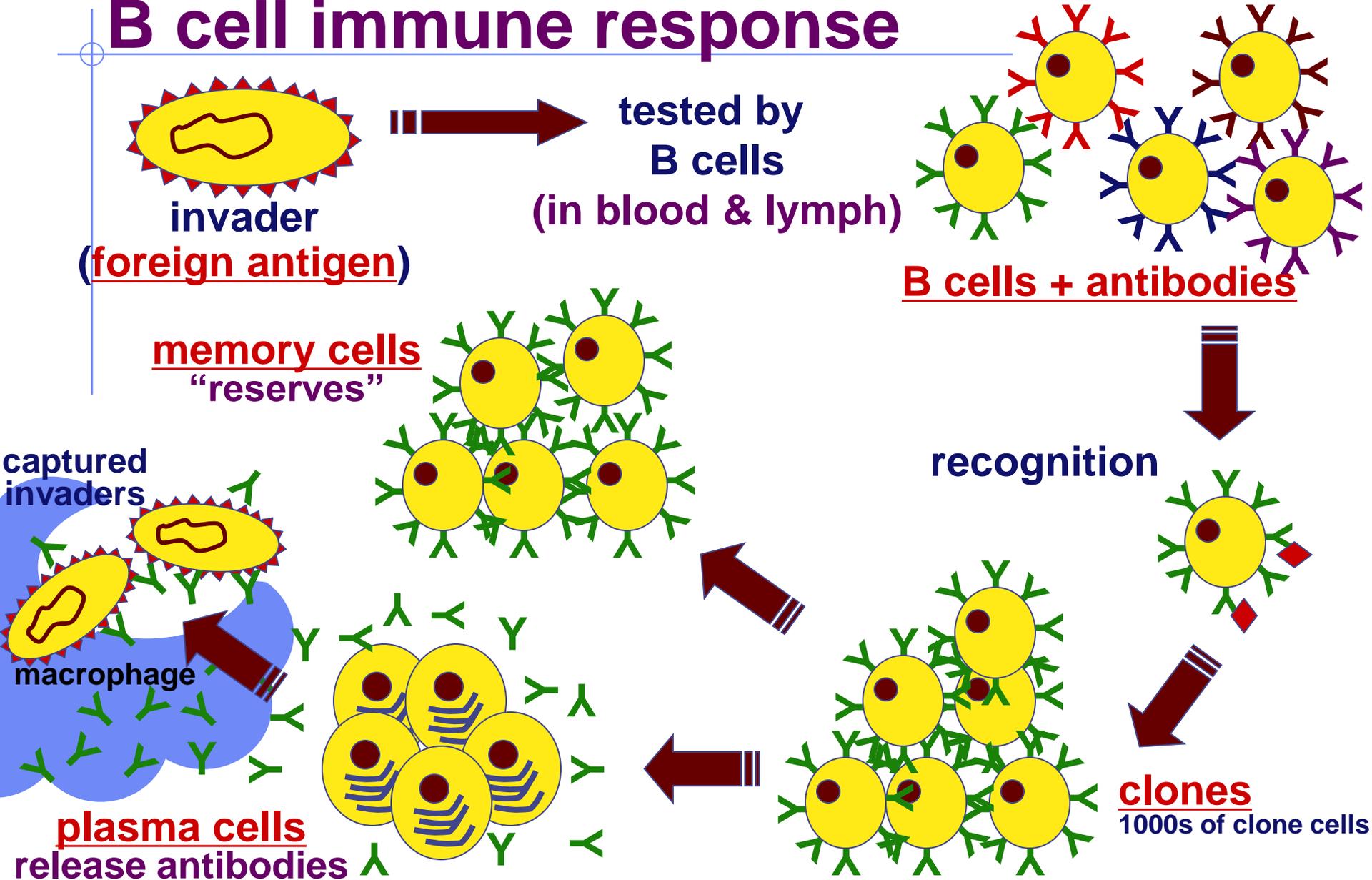
◆ IgD

- receptors of B cells???



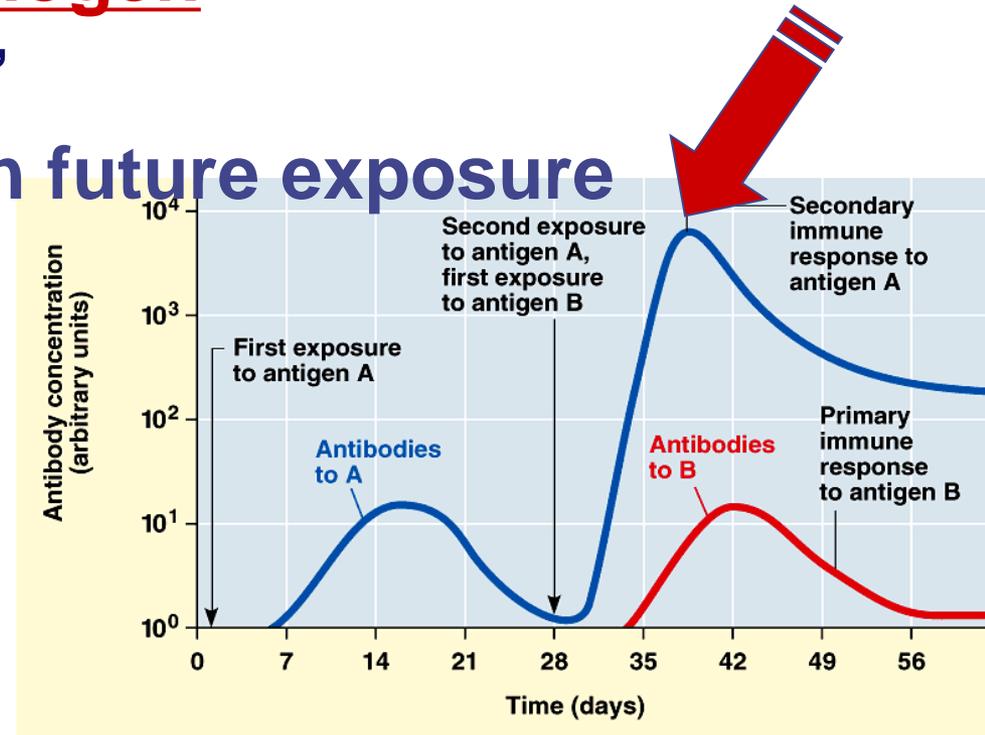
10 to 17 days for full response

B cell immune response



Vaccinations

- Immune system exposed to harmless version of pathogen
 - ◆ stimulates B cell system to produce antibodies to pathogen
 - “active immunity”
 - ◆ rapid response on future exposure
 - ◆ creates immunity without getting disease!
- Most successful against viruses

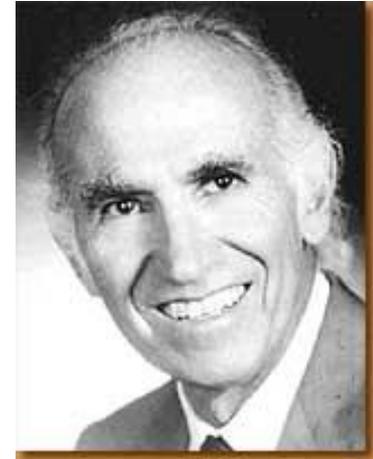


1914 – 1995

Jonas Salk

April 12, 1955

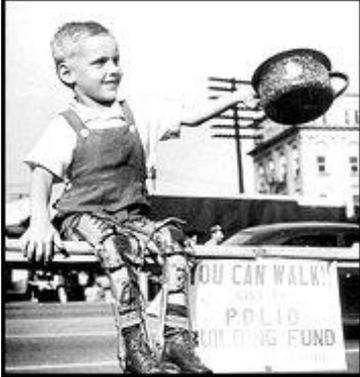
- Developed first vaccine
 - ◆ against polio
 - attacks motor neurons



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**



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

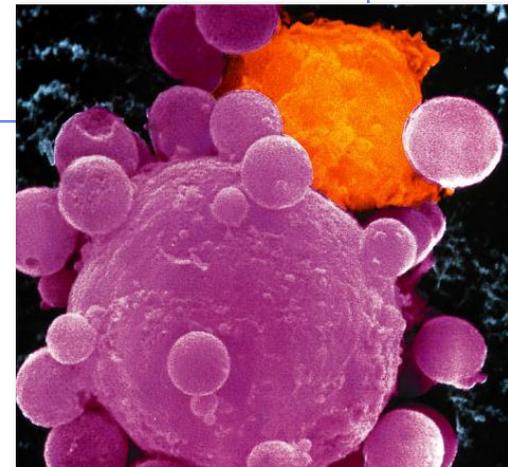
You need trained assassins to recognize & kill off these infected cells!

Attack
of the
Killer T cells!

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



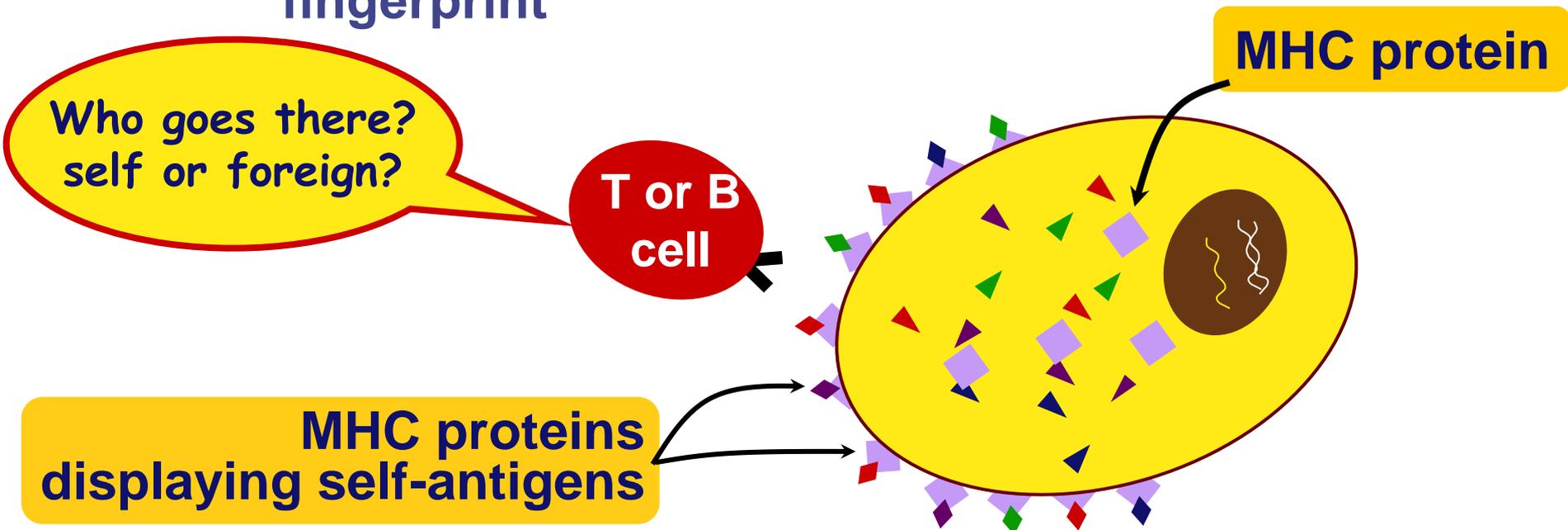
AP Biol



How is any cell tagged with antigens?

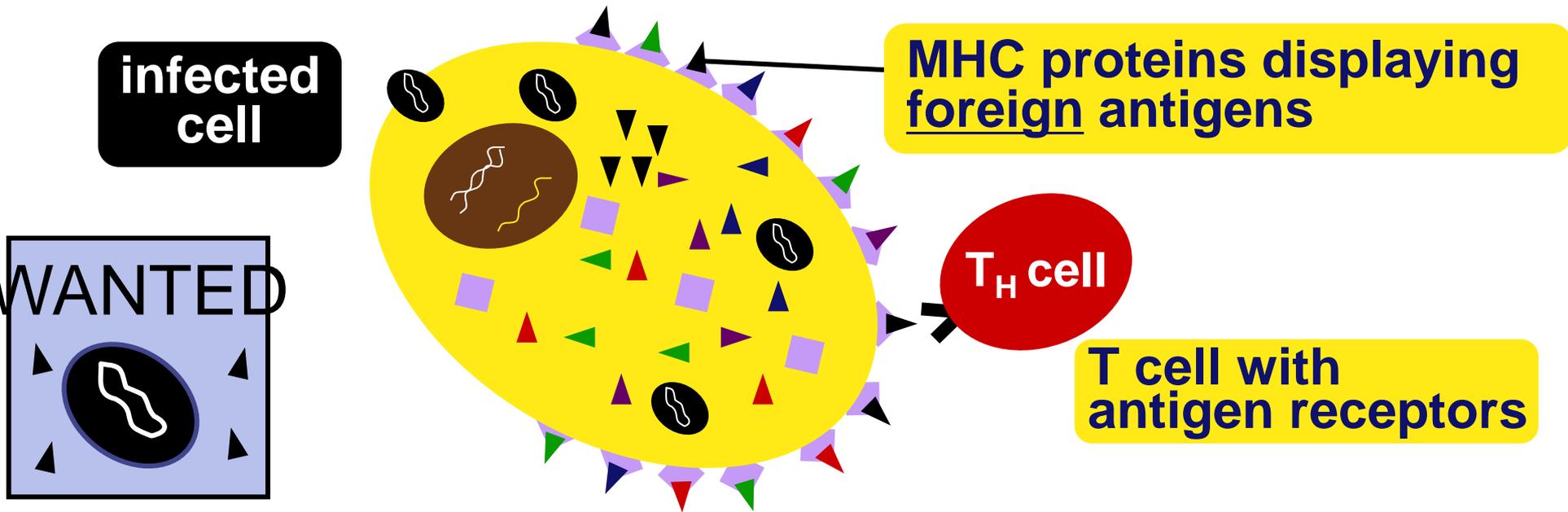
■ Major histocompatibility (MHC) proteins

- ◆ 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”



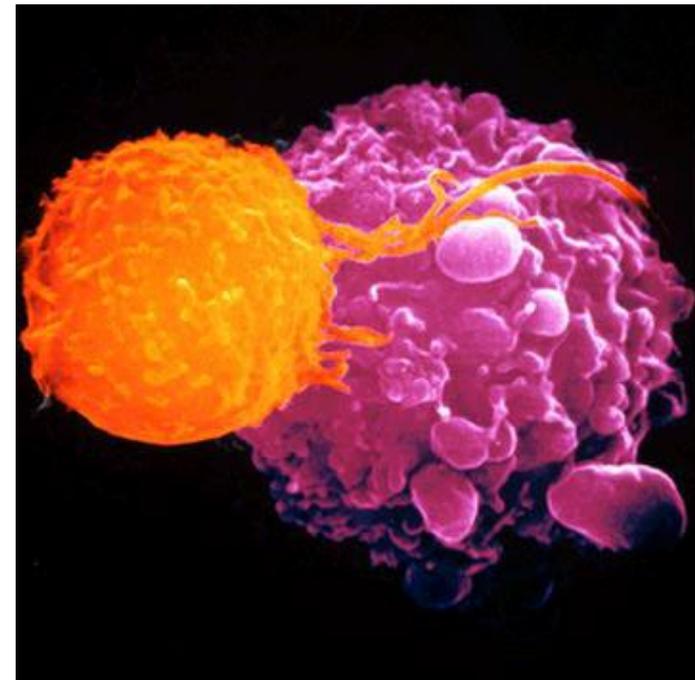
How do T cells know a cell is infected?

- Infected cells digest some pathogens
 - ◆ MHC proteins carry pieces to cell surface
 - foreign antigens now on cell membrane
 - called **Antigen Presenting Cell (APC)**
 - ◆ macrophages can also serve as APC
 - tested by Helper T cells



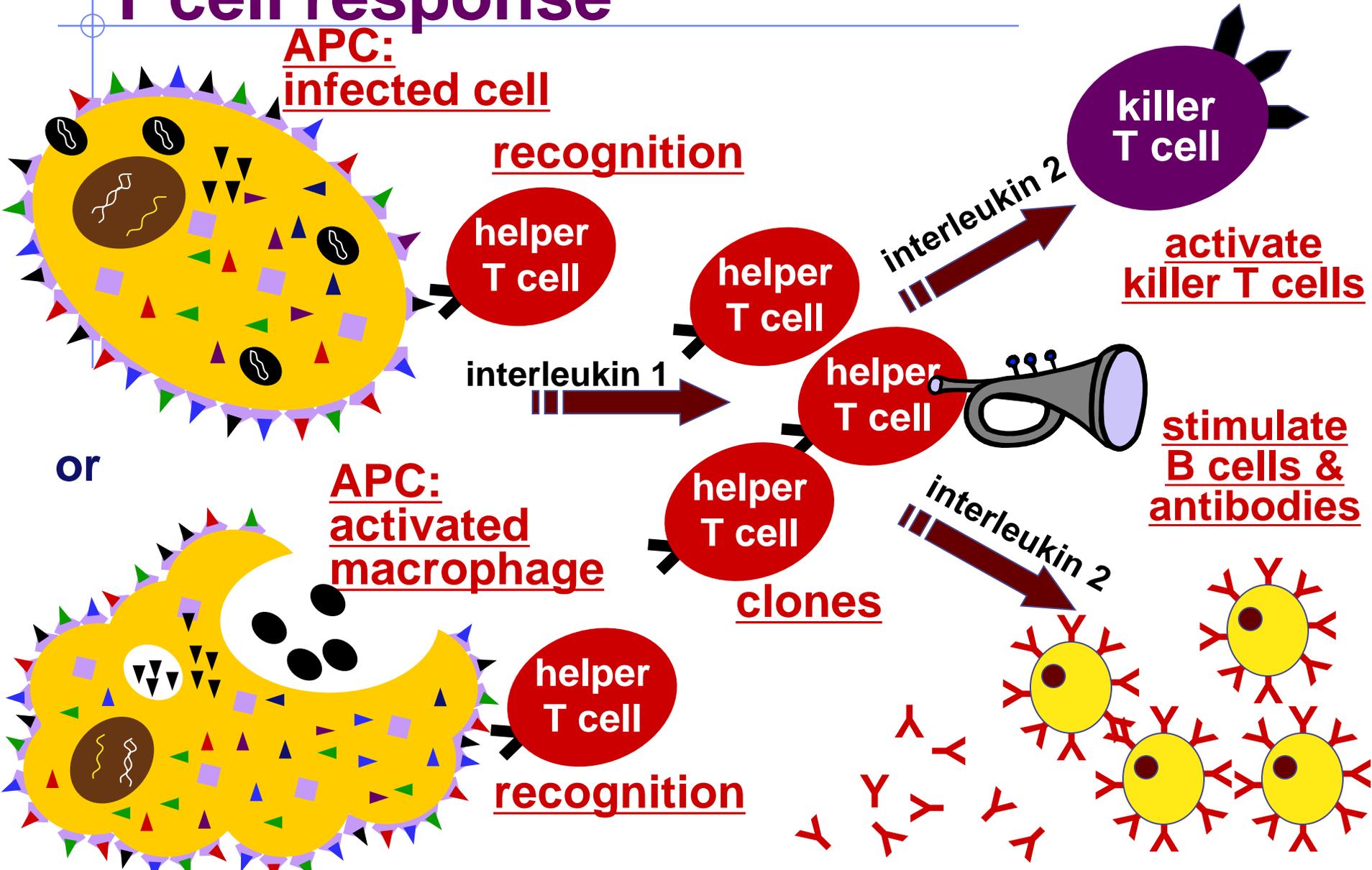
T cells

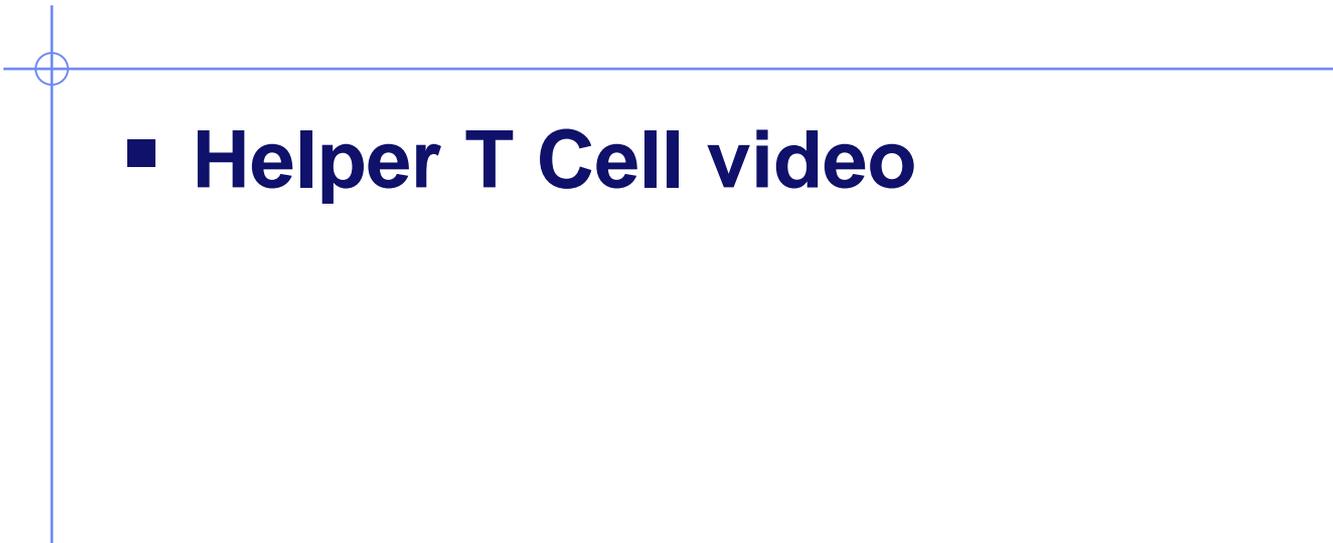
- Attack, learn & remember pathogens hiding in infected cells
 - ◆ recognize antigen fragments
 - ◆ also defend against “non-self” body cells
 - cancer & transplant cells
- Types of T cells
 - ◆ helper T cells
 - alerts rest of immune system
 - ◆ killer (cytotoxic) T cells
 - attack infected body cells
 - ◆ memory T cells
 - long term immunity



T cell attacking cancer cell

T cell response

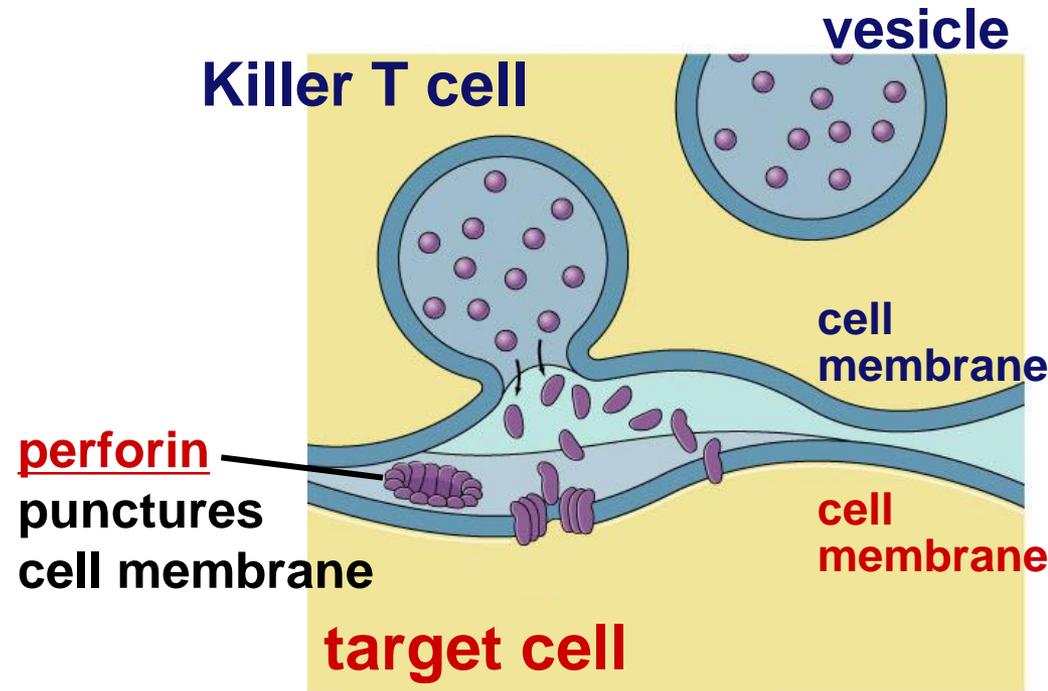
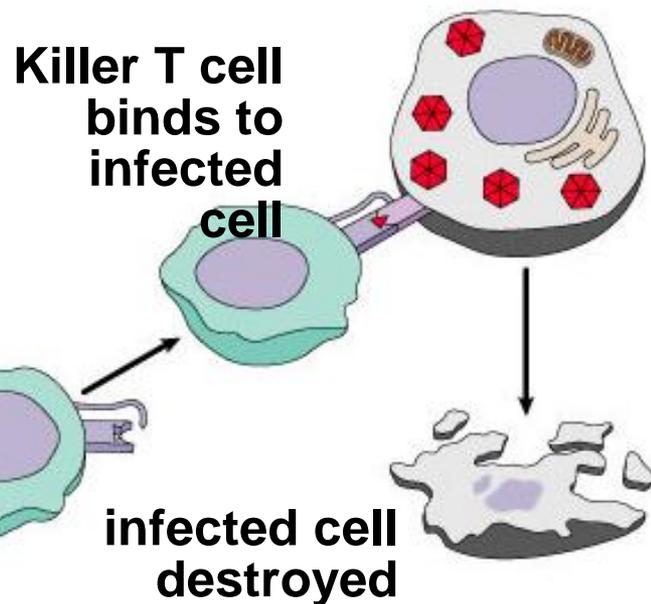
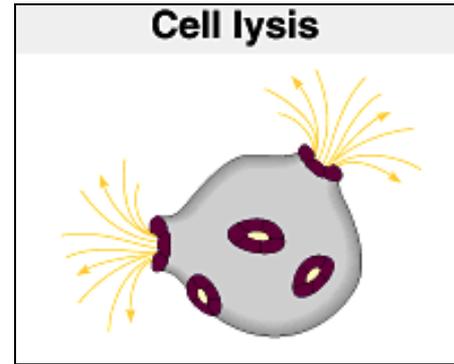




- **Helper T Cell video**

Attack of the Killer T cells

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

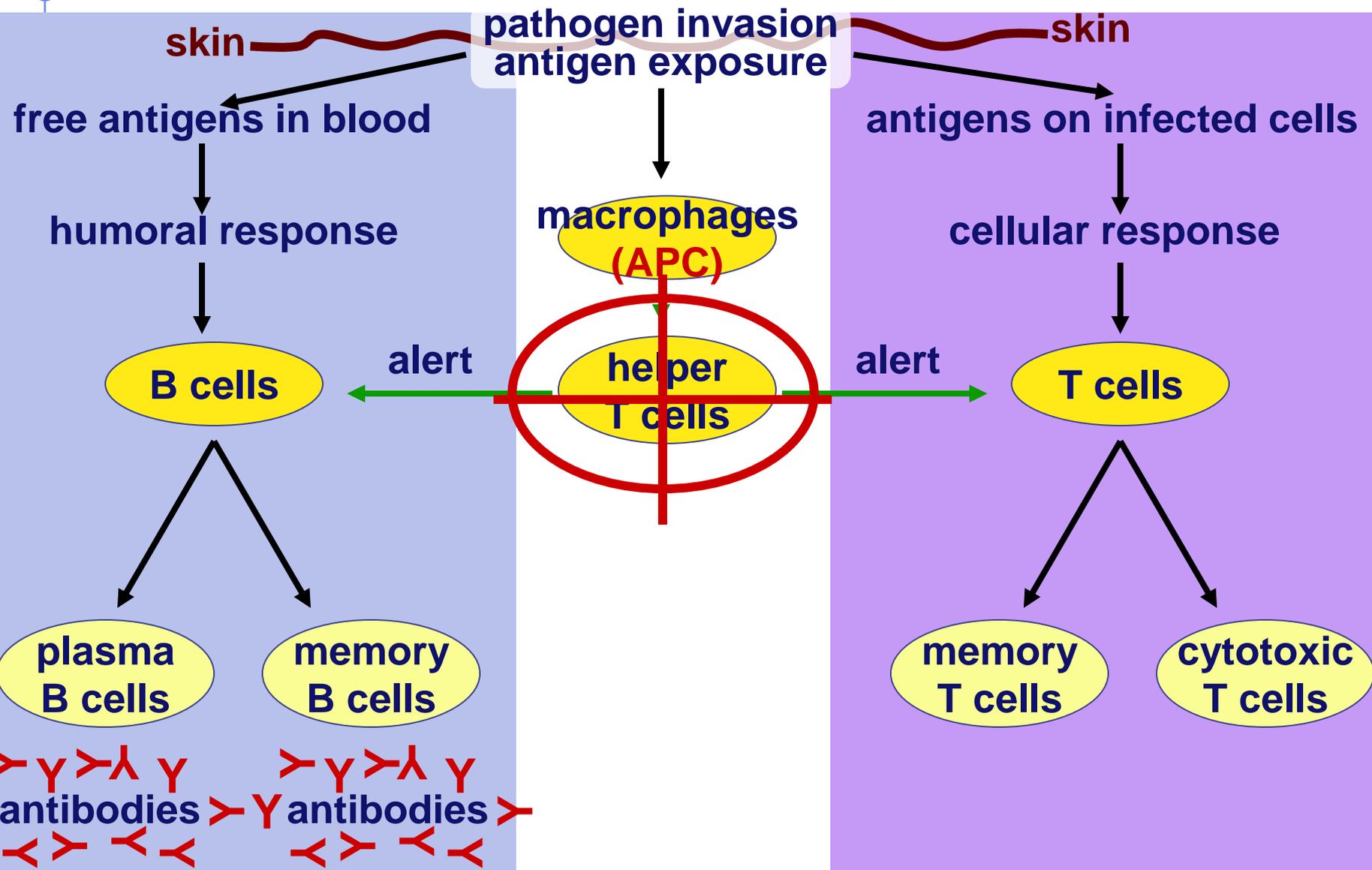


Immune system & Blood type

blood type	antigen on RBC	antibodies in blood	donation status
A			—
B			—
AB			
O			

Matching compatible blood groups is critical for blood transfusions
A person produces antibodies against foreign blood antigens

Immune response



HIV & AIDS

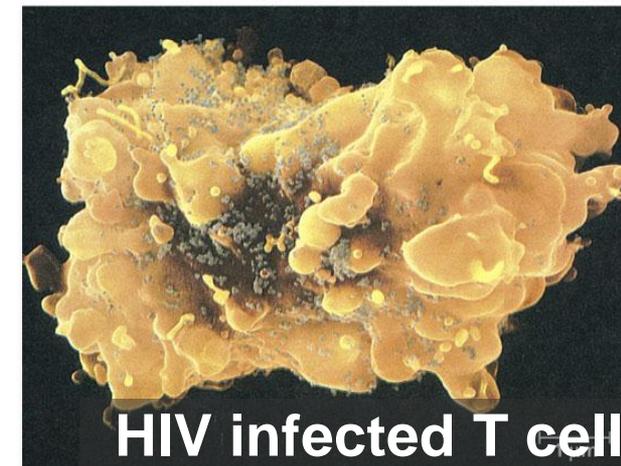
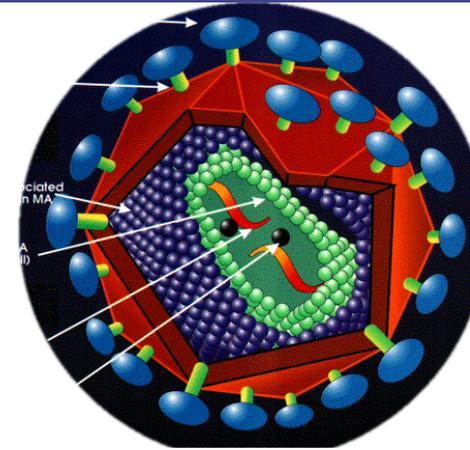
■ Human Immunodeficiency Virus

◆ virus infects helper T cells

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

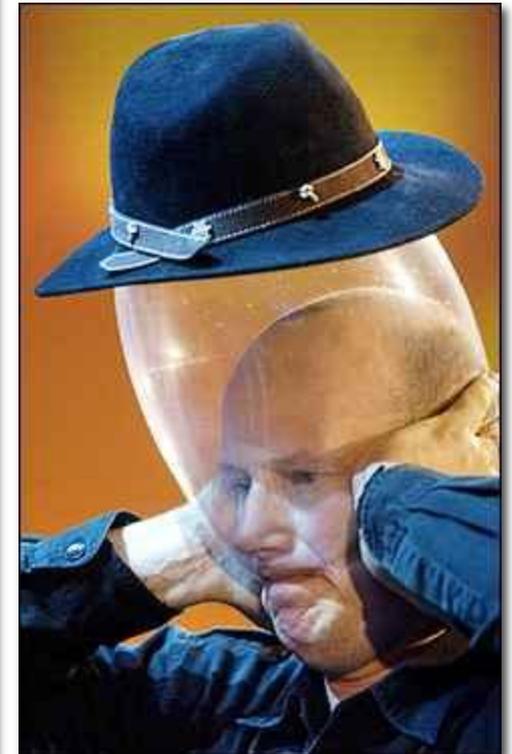
■ AIDS: Acquired ImmunoDeficiency Syndrome

- ◆ infections by opportunistic diseases
- ◆ death usually from
- ◆ “opportunistic” infections
 - pneumonia, cancers



HIV infected T cell

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

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

