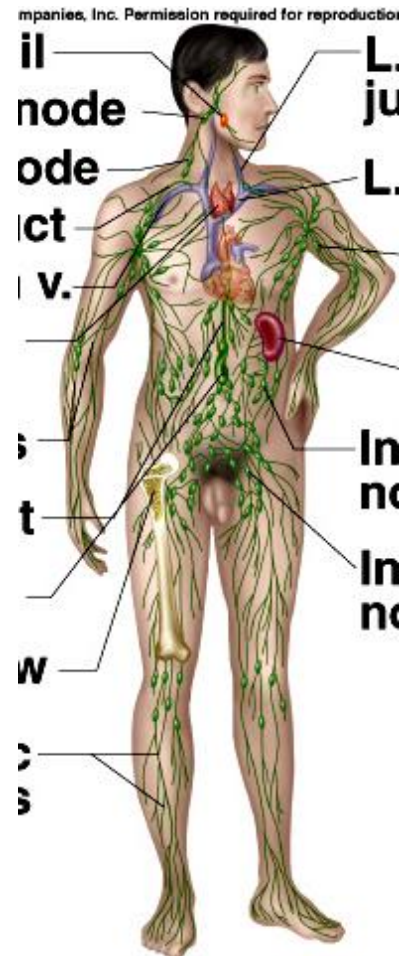


# The Lymphatic System and Our immune response: Did you know?

- Laughing lowers levels of stress hormones and strengthens the immune system. Six-year-olds laugh an average of 300 times a day. Adults only laugh 15 to 100 times a day.
- **3000 BC** The ancient Egyptians recognize the relationship between exposure to disease and immunity.
- **1500 BC** The Turks introduce a form of vaccination called variolation, inducing a mild illness that protects against more serious disease.
- **1720** Lady Mary Wortley Montagu promotes the variolation principle, launching a campaign to inoculate the English against smallpox.
- A macrophage can consume as many as **100** bacteria before undergoing apoptosis.



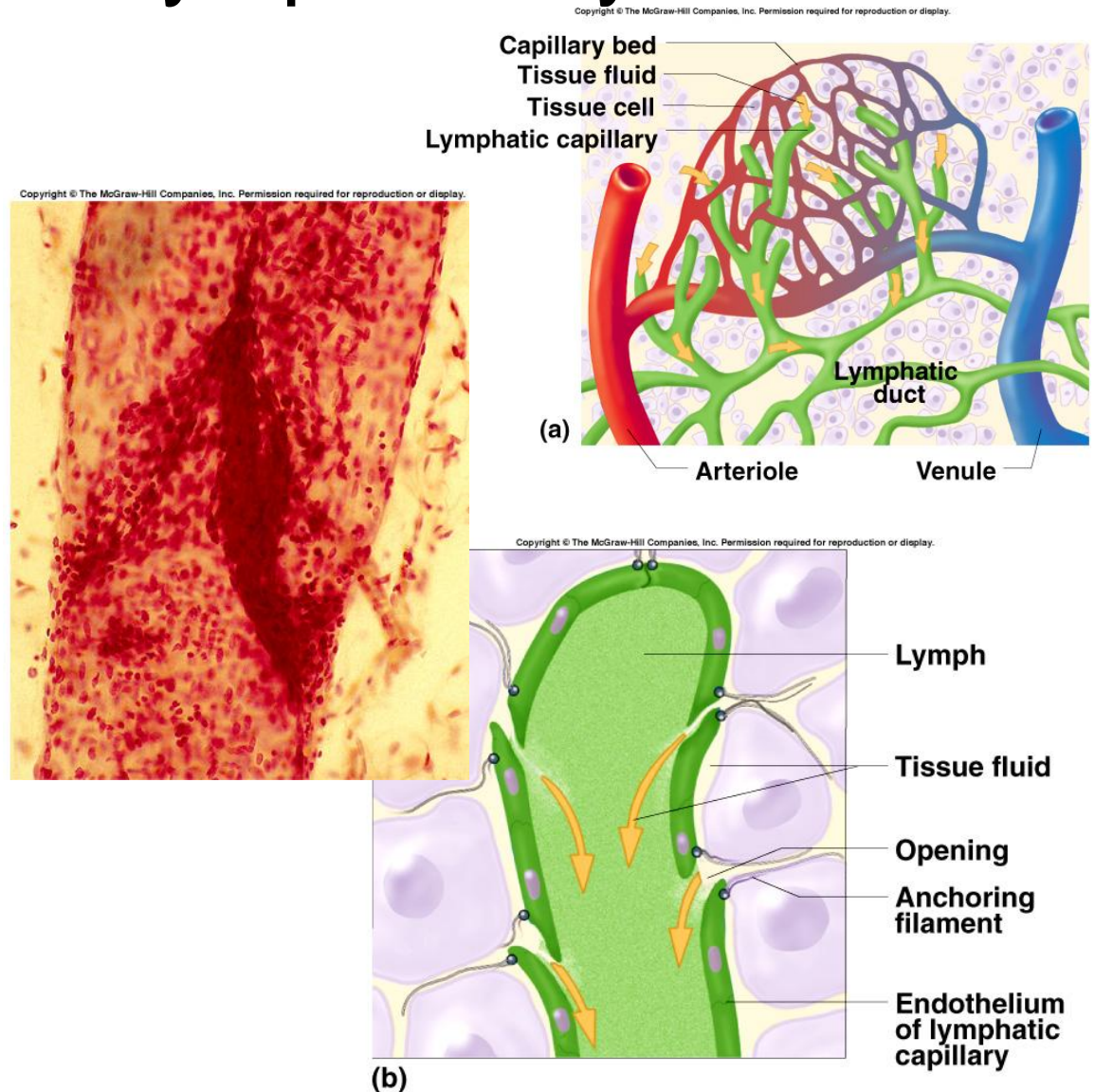
# What does the lymphatic system do?

- Return interstitial fluid
  - Capillaries only reabsorb 15%
  - Funneled into subclavian veins
- Absorb and transport lipids from intestines
- Generate and monitor immune responses



# What is in the lymphatic system?

- Lacteals and lymphatic capillaries
  - Overlapping epithelial cells
- Lymph vessels and ducts
  - What happens if blockage occurs?
    - See next slide!

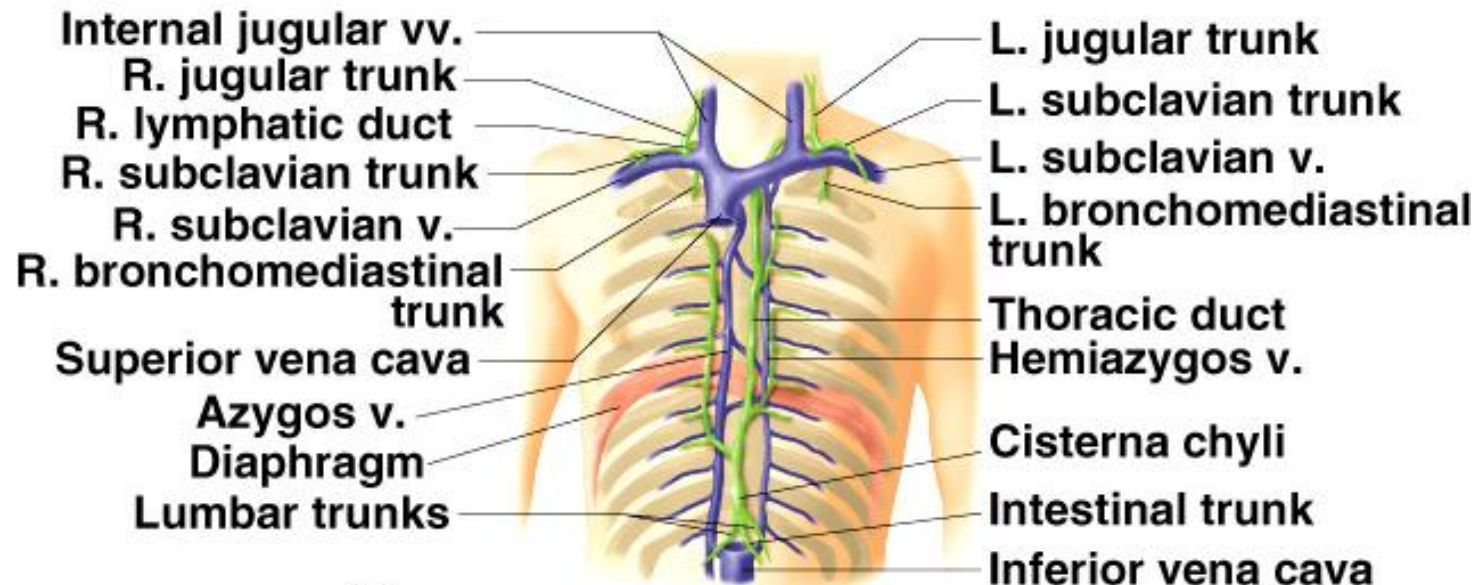


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# What is in the lymphatic system?

- Lymphatic trunks
  - Lumbar, brachiomediastinal, intestinal, jugular, subclavian, intercostal
- R lymphatic duct: R arm, R thorax, R head
- Thoracic duct: everything else



# What is in the lymphatic system?

- **Red bone marrow**
  - Hemopoiesis: what types of leukocytes are manufactured here?
- **Mucosa-associated lymphatic tissue**
  - Sprinkling of lymphocytes in mucosa membranes
    - **Peyer's patch**: small intestine nodules of lymphatic tissue



# What is in the lymphatic system?

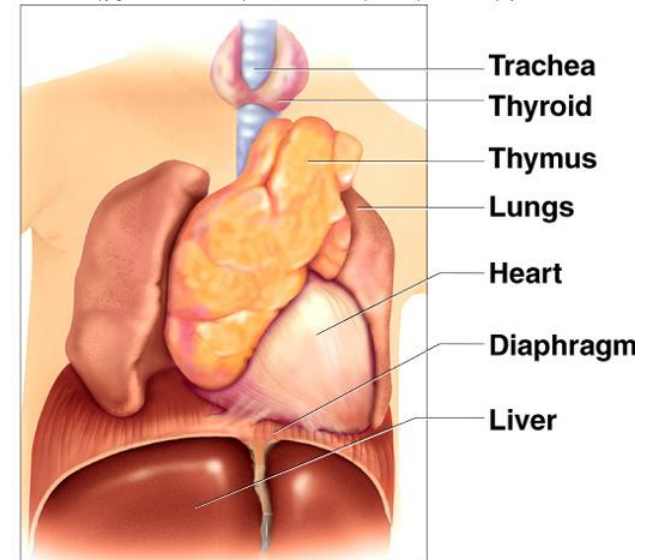
- **Thymus**

- Secretes thymopoietin for T-cell development
- T-cells mature here
- Thymus atrophies with age

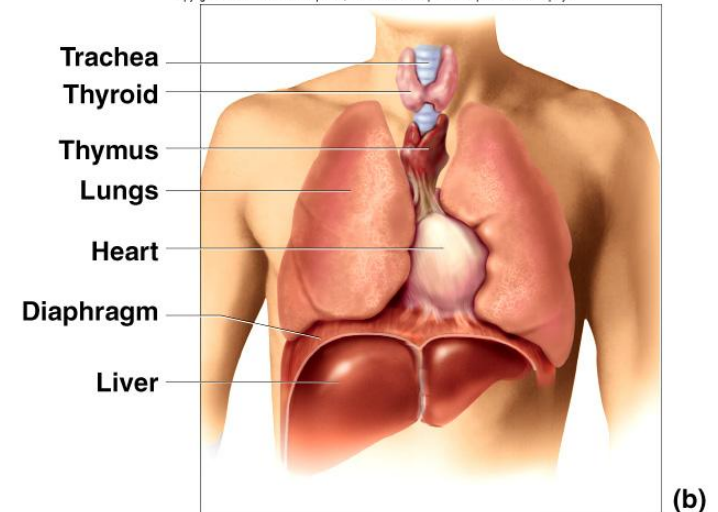
- **Tonsils**

- Palatine (2), lingual (2), pharyngeal (1; adenoid)
  - Tonsillectomy: remove palatines
- Gather, remove and “learn” pathogens from food/air

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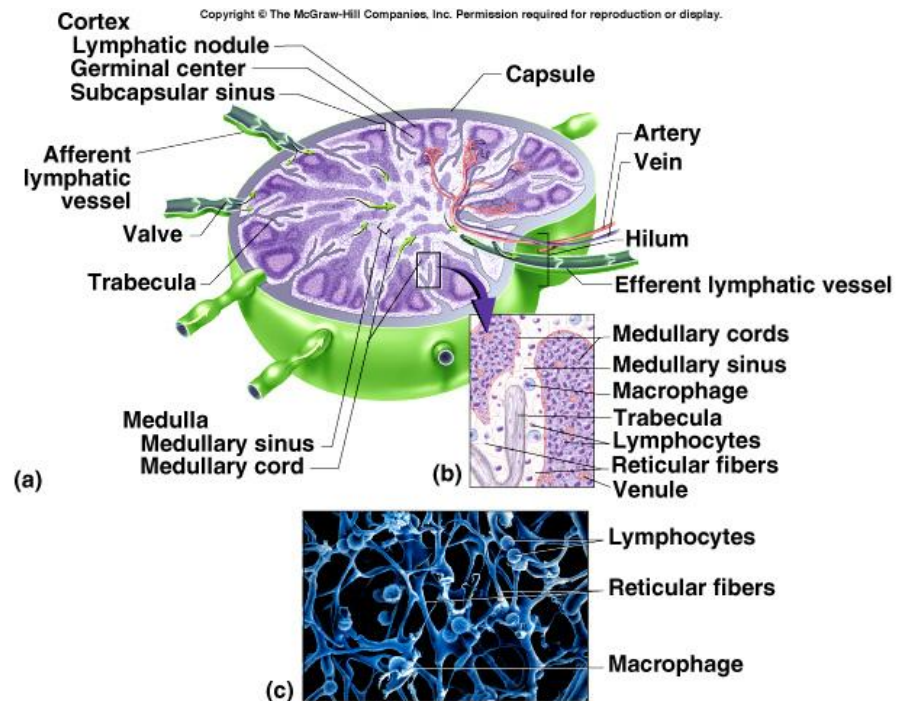


(b)

# What is in the lymphatic system?

- **Lymph nodes**

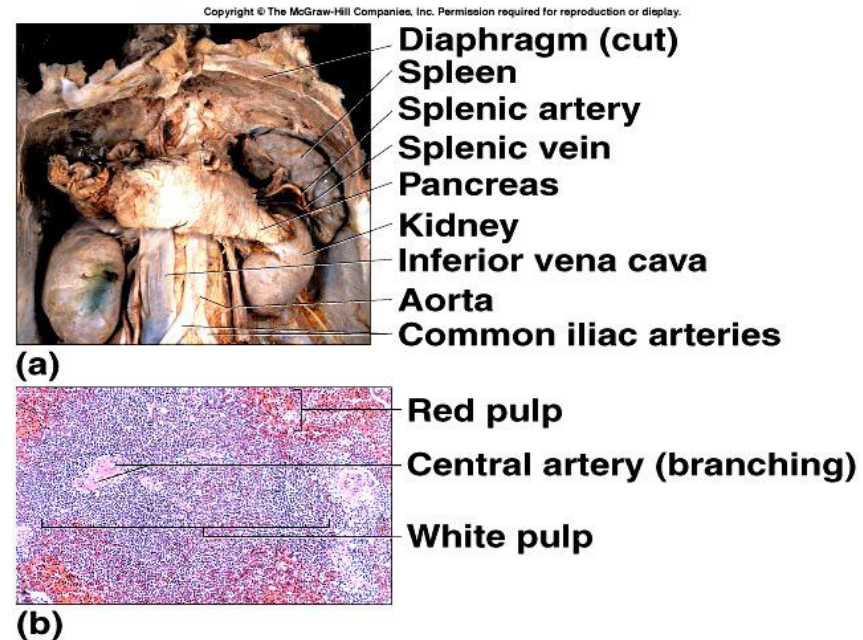
- Filters lymph fluid for antigens, bacteria, etc.
  - B-lymphocytes made here
  - Some T-lymphocytes and macrophages congregate
  - Afferent (more) and efferent (less) vessels
    - lymph fluid exits through hilum
- Common site for cancer—Why?
  - Hodgkin's lymphoma: lymph **node** malignancy
  - Non-Hodgkin's lymphoma: all other cancers of lymphoid tissue
    - Multiplication/metastasis of lymphocytes
    - 5th most common cancer





# What is in the lymphatic system?

- **Spleen**: dense sieve of reticular CT
  - Functions
    - Erythropoiesis in fetus
    - Stores platelets
    - Salvages and stores RBCs parts for recycling (RBC graveyard)
  - Red pulp
    - Dispose of damaged/dead RBCs and pathogens
    - Old RBCs aren't flexible enough to get through sieve
  - White pulp
    - Lymphocytes and macrophages
    - B-cells proliferate here
  - If splenectomy: liver and marrow take over duties



The lymphatic ducts empty directly  
into the

- A. Heart
- B. Subclavian veins
- C. Thoracic veins
- D. Brachiocephalic veins

Which area is not drained by the thoracic duct?

- A. Right leg
- B. Left leg
- C. Right arm
- D. Left arm

**STOP HERE!!!**

# The immune system

# What strategies does the immune system use?

- **Non-specific immunity**
  - Responds without caring about specific type of threat
- **Specific immunity**
  - Tailored to specific pathogens; based on memory
  - Two types
    - **Antibody-mediated immunity** (humoral response)
    - **Cell-mediated immunity**

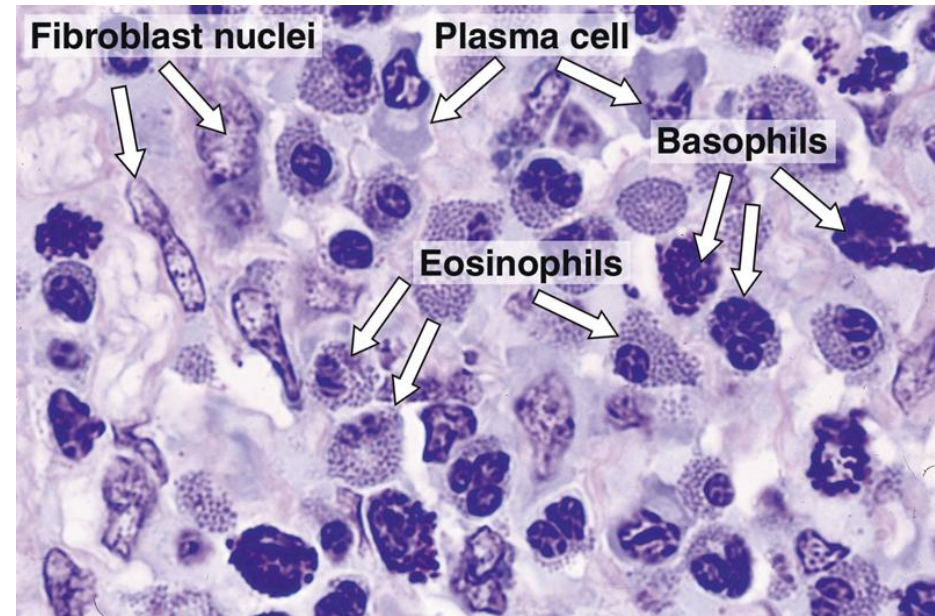
# What's behind non-specific immunity?

- External barriers
  - Skin
    - Keratin is tough to penetrate
    - Low pH (lactic acid), very dry, nutrient-poor
    - Anti-microbial proteins: defensins from neutrophils
  - Mucus
    - Urine, saliva, tears and mucus
    - Contain lysozyme (dissolves peptidoglycan wall)
  - Viscous areolar CT matrix

# What's behind non-specific immunity?

- **Phagocytes**

- **Macrophages**: tissue-living monocytes
- **Neutrophils**: digestion and killing zone ( $H_2O_2$ ; superoxide ion and hypochlorite (bleach))
- **Eosinophils**: less avid digesters
- **Basophils and mast cells**: it mobilize other WBCs (via histamine and heparin)
  - some phagocytosis
- **Natural Killer cells** (NK cells): type of T-cell
  - Only attack infected or cancerous host cells





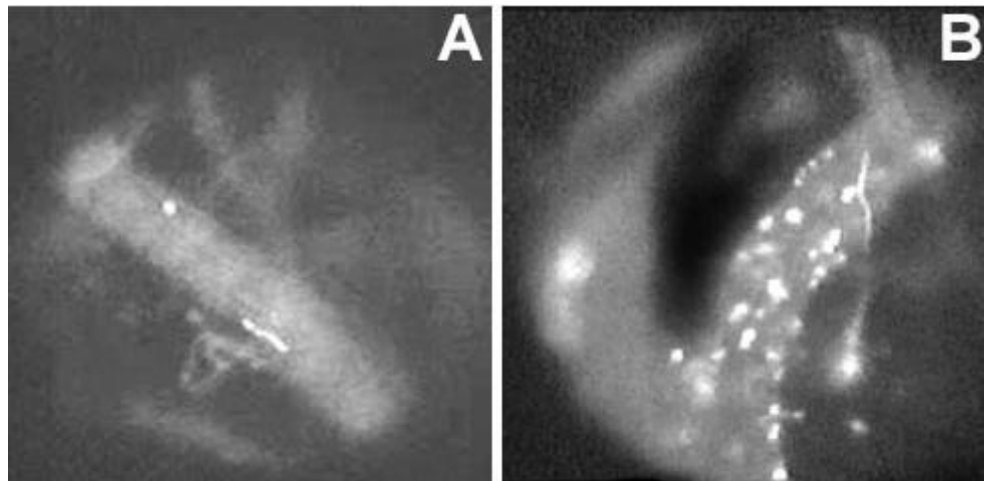
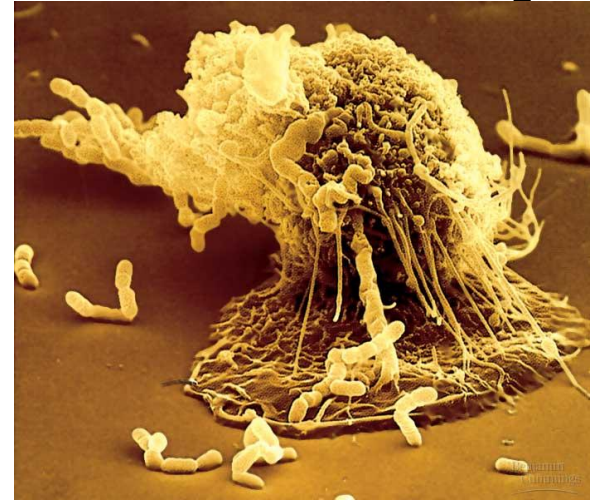
# What's behind non-specific immunity?

- Inflammation

- Redness, swelling, heat, pain

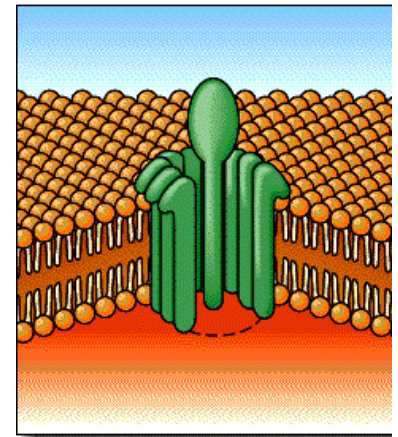
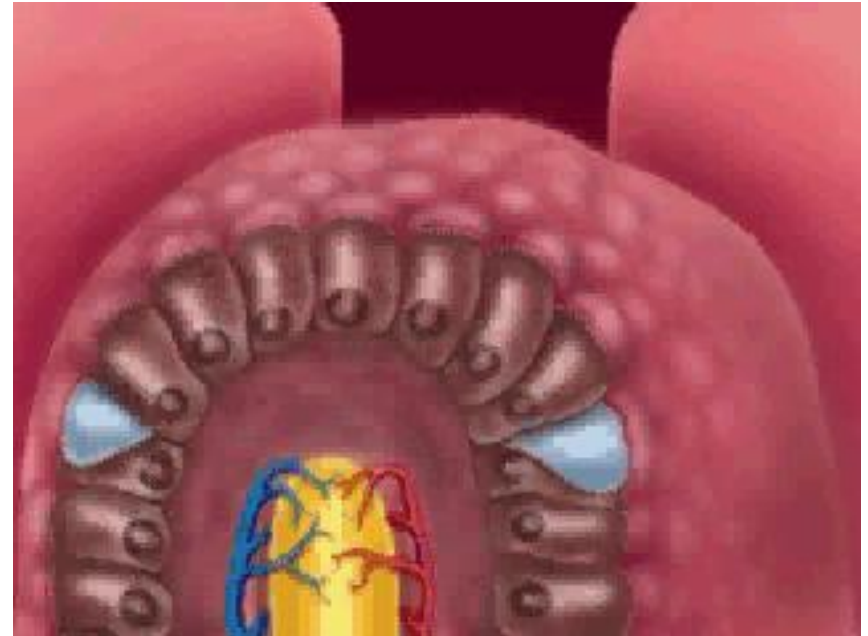
- Bradykinin: pain stimuli from mast cells
- Histamine: what two things does it do?

- Leukocyte migration



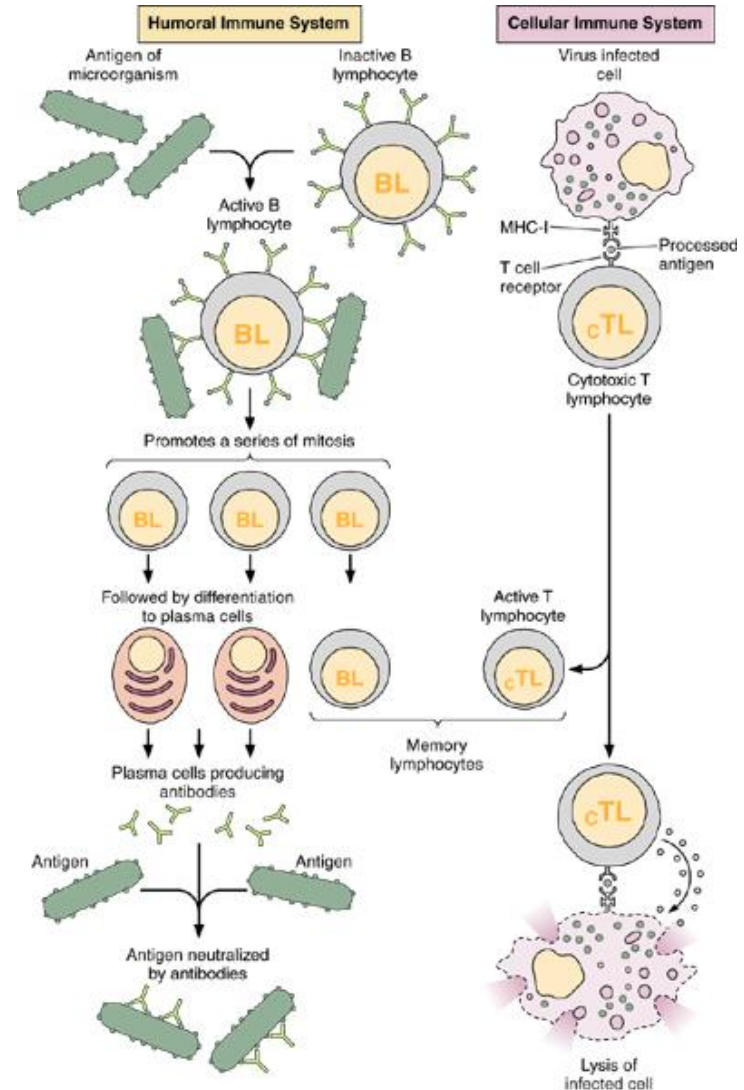
# What's behind non-specific immunity?

- Interferons
  - Virus-infected cells secrete warning
  - Can promote cancer cell destruction
- Complement proteins
  - 20+ beta-globulins which perforate bacterial cells (cytolysis)
- Fever (pyrexia)
  - Promotes interferon activity
  - Elevates BMR
  - Discourages bacteria/viral reproduction



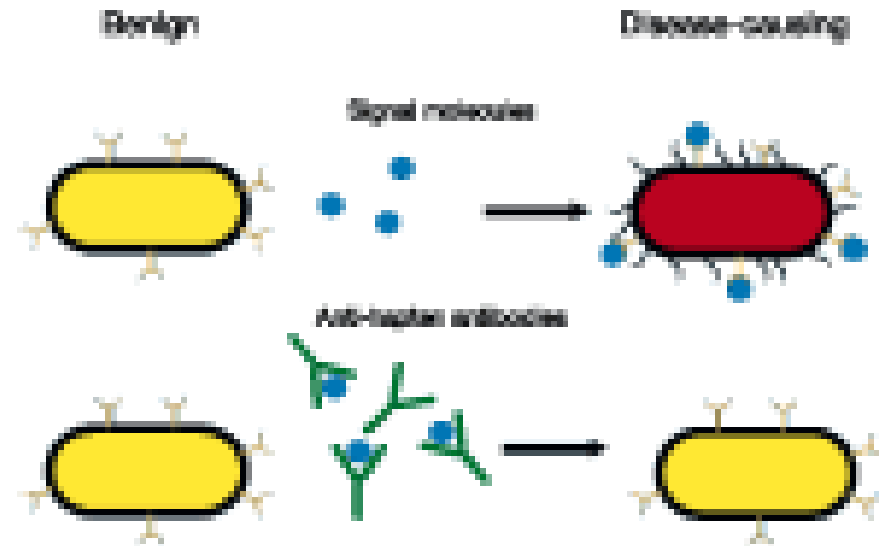
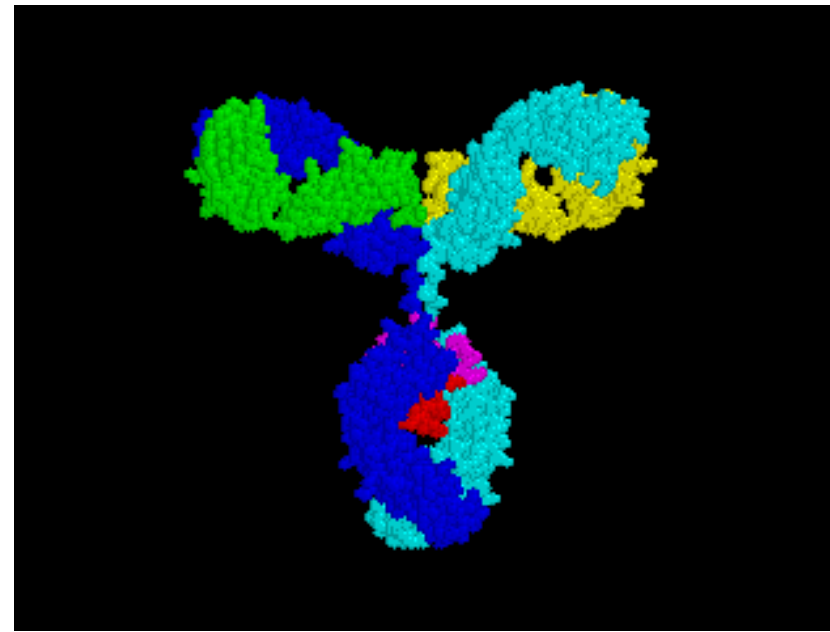
# What is specific immunity?

- Specific response
- Memory for future reinvasion
- Antibody-based
  - B cells primary (but not only) actors
- Cell-mediated
  - T cells only



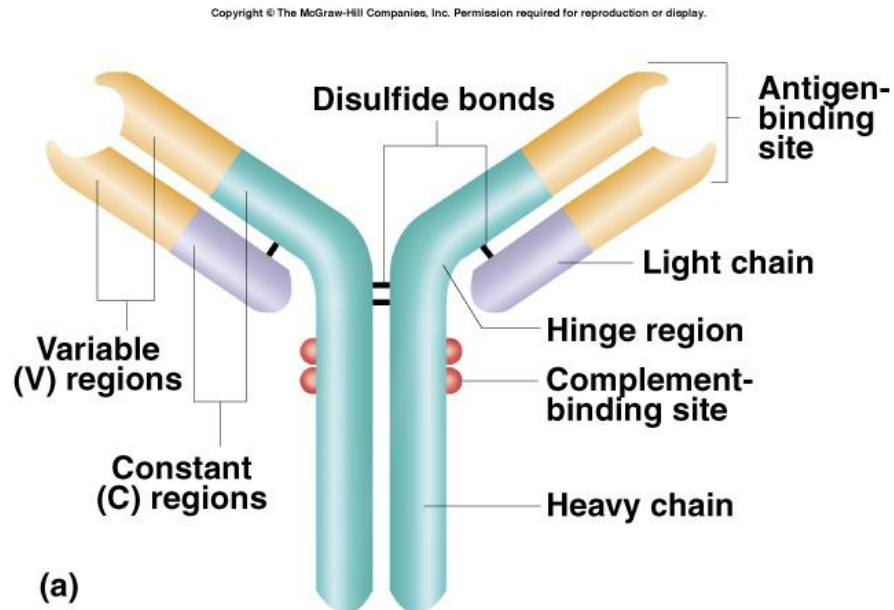
# What are antibodies?

- Antibody: gamma globulin (protein) which complexes with a specific antigen
  - AKA **Immunoglobulin** (Ig)
- Antigen (Ag): any molecule which causes an immune response
  - Not necessarily always dangerous antigen



# What do antibodies look like?

- Protein with quaternary structure
  - Two light chains, two heavy chains
  - Each chain has **variable region**
    - Combine to form antigen-binding site
  - Remainder of chains = **constant region**




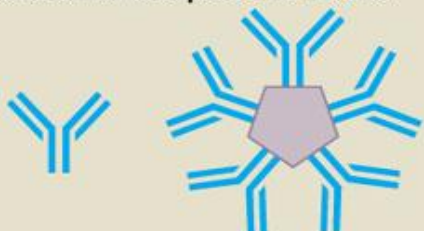


# What are the five antibody classes?

- **IgA**: prevents pathogens from sticking to epithelia
  - Can form dimers
- **IgD**: antigen receptor in B-cell PM
- **IgE**: stimulates basophils/mast cells
  - Secrete histamines, also causes allergic response
- **IgG**: most common antibody (75-85%)
  - Primary Ig of secondary immune response
- **IgM**: antigen receptor in B-cell PM
  - Can form pentamers
  - Predominant Ig of primary immune response
  - Includes anti-A and Anti-B of ABO blood groups

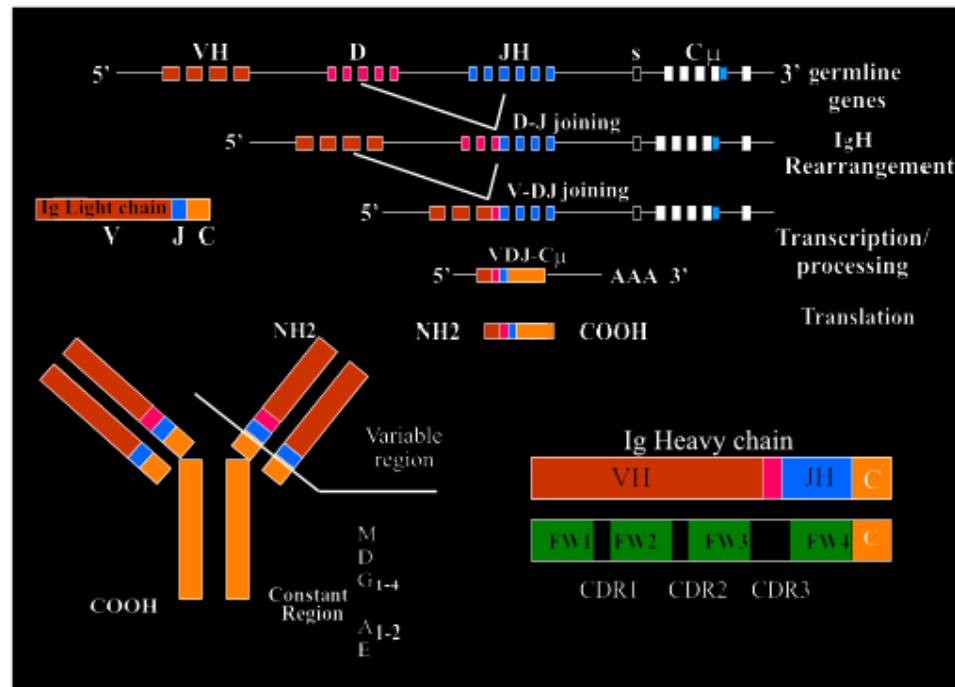
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Table 21.4 The Five Classes of

Class	Structure
IgA	Monomer and dimer forms 
IgD	Monomer
IgE	Monomer 
IgG	Monomer 
IgM	Monomer and pentamer forms 

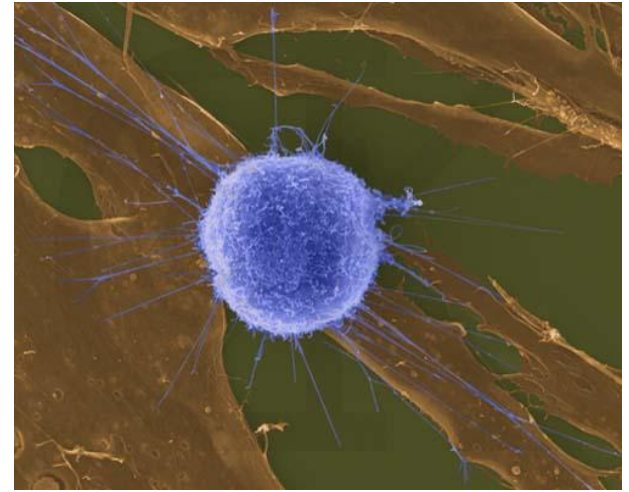
# How many different antibodies are there?

- > 2M
- But we only have ~30,000 genes (not 100,000)
  - Central dogma (one gene = one protein) doesn't appear to apply
- Somatic recombination creates variety

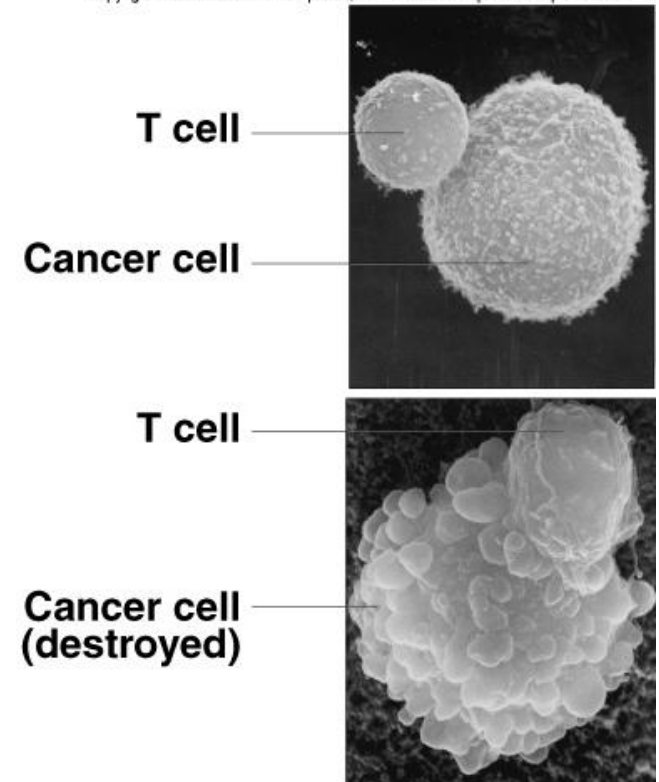


# What are T cells?

- Migrate from marrow and develop in thymus
  - Have antigen receptors on PM = immunocompetent
    - Mitosis produces clones
  - Clonal deletion destroys self-reactive clones
- Good at destroying cells and stimulating B cells
  - They do NOT secrete antibodies as B cells do



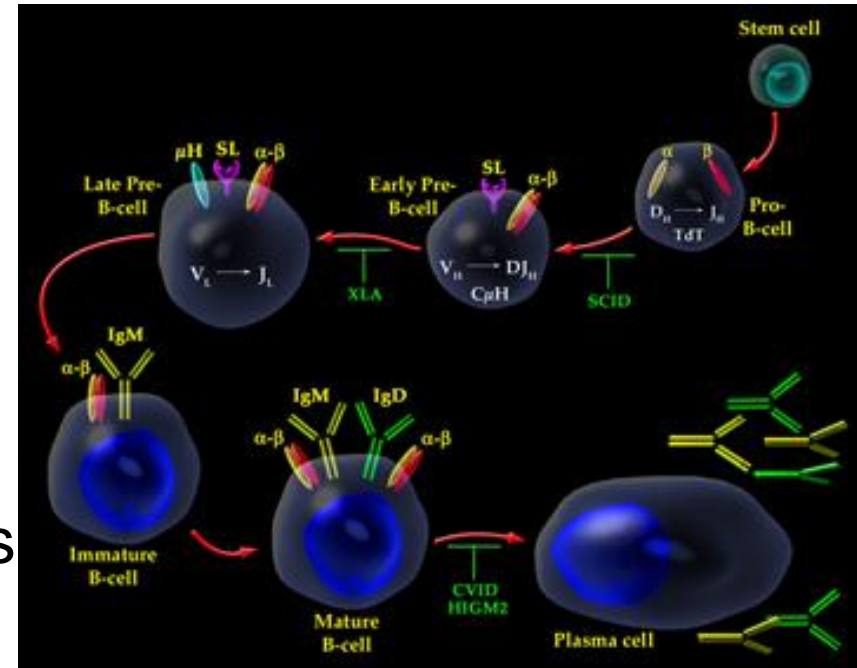
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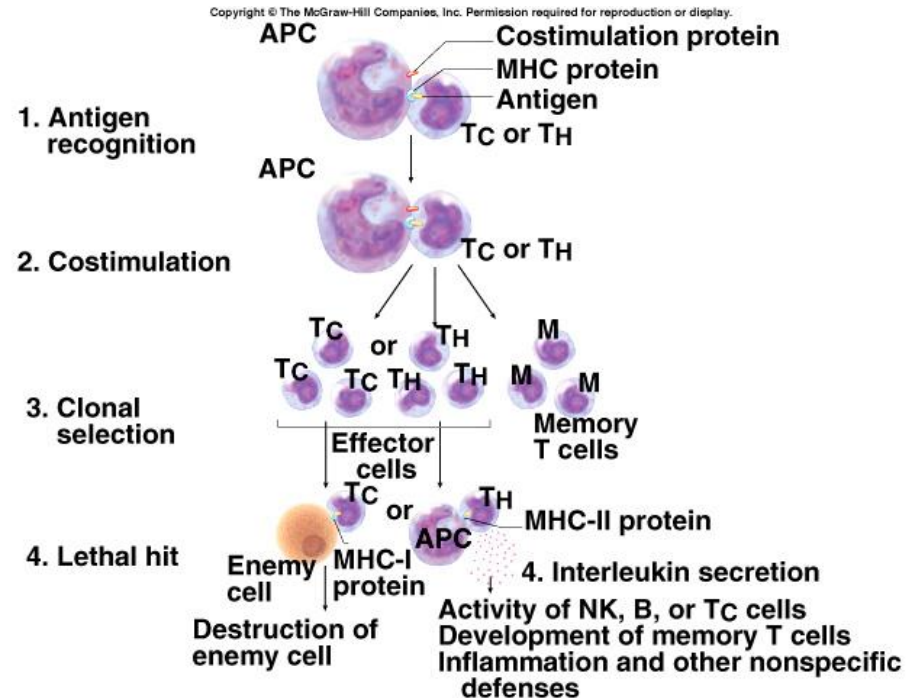
# What are B cells?

- From marrow: colonize lymph tissues, organs when mature
  - Developing B cells synthesize PM antibody
    - Each cell has a different antibody covering it
  - Mitosis: immunocompetent clones
  - One B cell responds to only one antigen
- Serve as antigen-presenting cells (APC)
  - So do macrophages
  - Lets T cells “see” the antigen
- Secrete antibodies into blood, but do NOT kill cells as T cells do



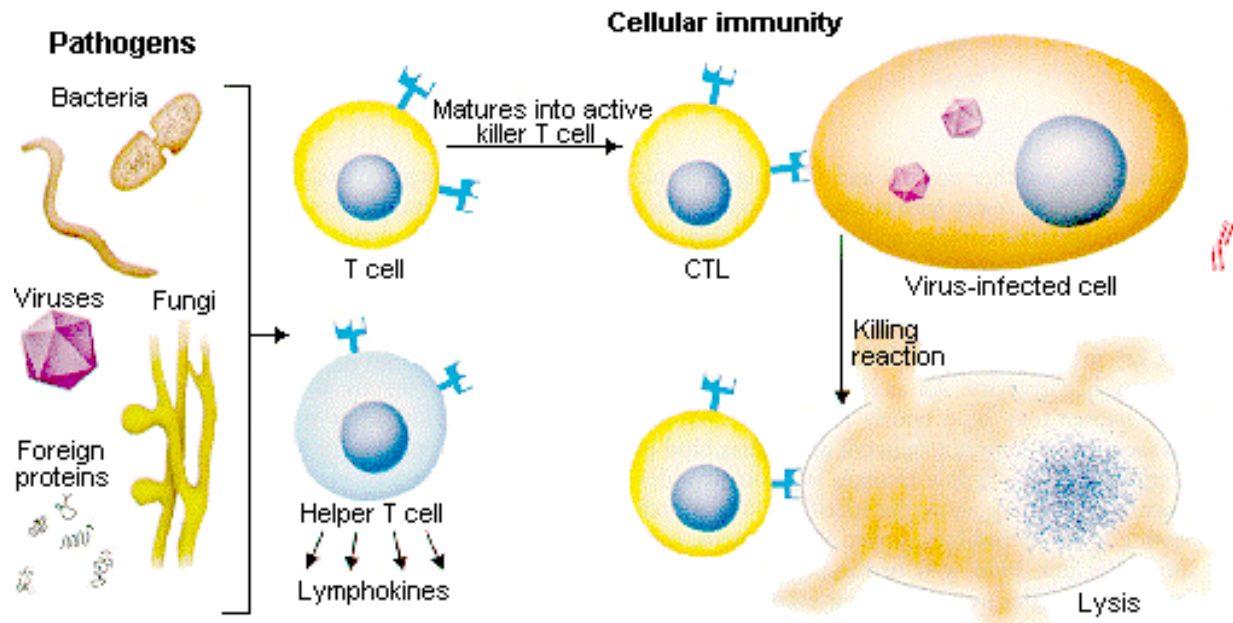
# What happens in a cell-mediated response?

- The key players:
  - Antigen-presenting cell
  - Cytotoxic (killer) T cells (CD8 cells)
  - Helper T cells (CD4 cells)
    - The ones attacked in HIV infection
  - Suppressor T cells
  - Memory T cells
- T cells are “blind” to free-floating antigens



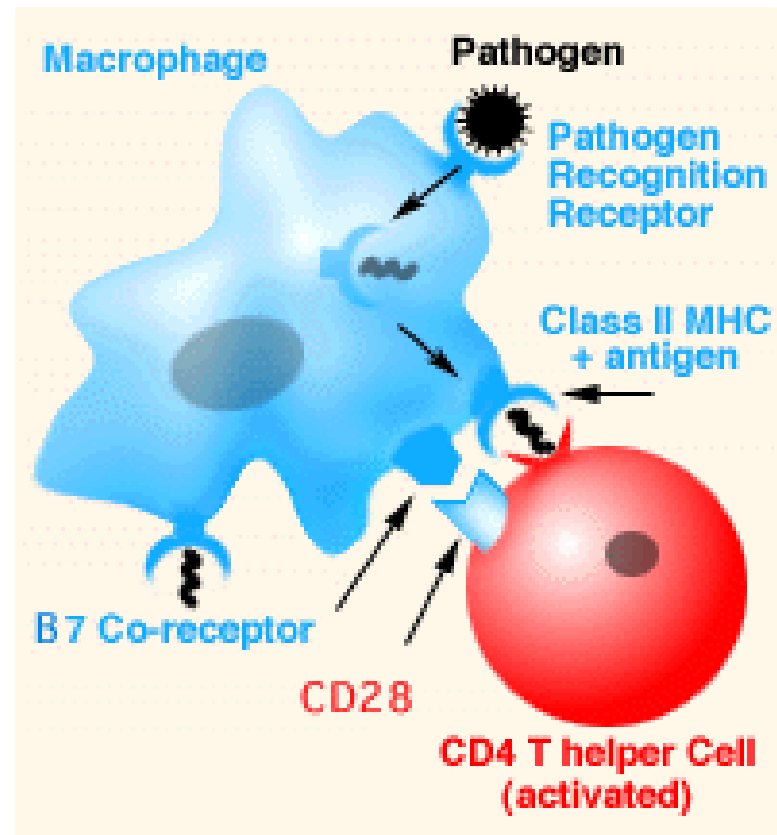
# What happens in a cell-mediated response?

- The key events:
  - Surveillance and recognition
  - Attack
  - Memory



# What happens during surveillance?

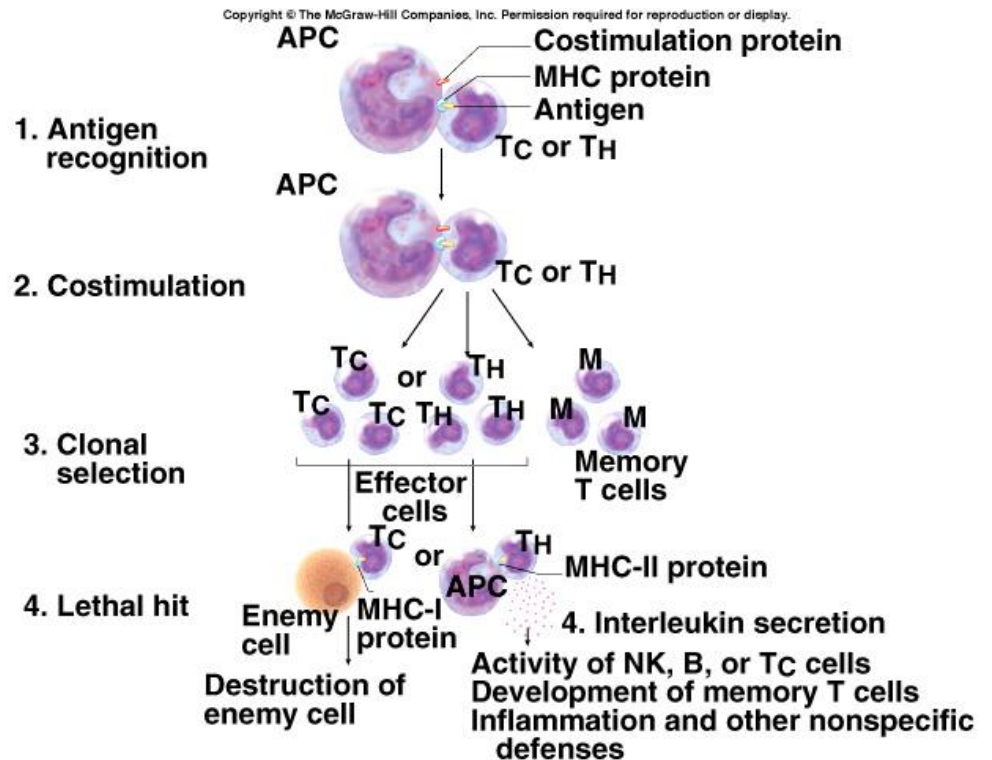
- T cells (helper and cytotoxic) “feel” cells
  - Check for MHC (hotdog bun)
    - MHC = major histocompatibility complex
    - MHC-I on all cells
    - MHC-II only on APCs
    - HLA (human leukocyte antigen) group = MHC





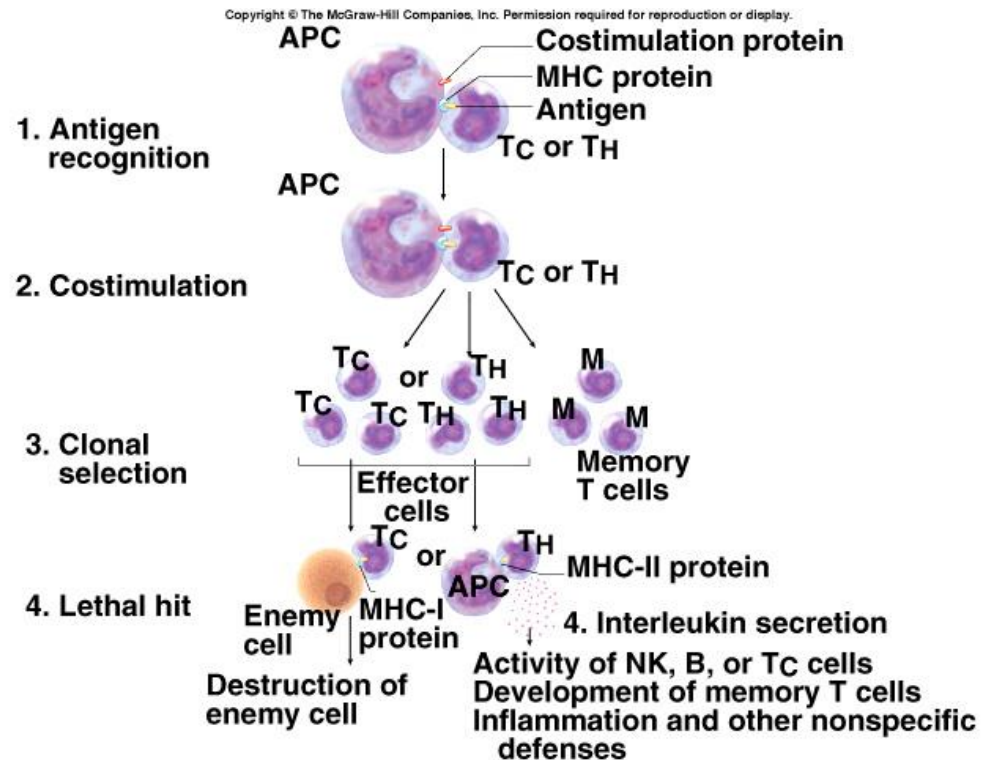
# What happens during attack?

- Interleukins stimulate T cells, Helper T cells and (we'll get to this later) B cells
- The “right” T cells and helper T cells produce clones
  - Cytotoxic clones use perforin to kill infected or cancerous cells (“touch kill”):
    - <http://www.cellsalive.com/ctl.htm>
    - <http://www.cat.cc.md.us/courses/bio141/lecguide/unit3/cellular/cmdefine/ctls/ctlapop.html>
  - Helper T cell clones stimulate more cytotoxic T cells (and B cells)



# What happens during the memory phase?

- During cloning, some T cells are put in reserve
  - Thousands of these “hang out” in the body
  - Launch immediate attack if same antigen appears again
  - Attack is so quick, no symptoms develop



Which of the following activates the cytotoxic T cells?

- A. Interferon
- B. Interleukin-I
- C. Interleukin-II
- D. Interleukin-IV



T cells may produce \_\_\_\_\_ which is lethal to the target cells invaded by a pathogen

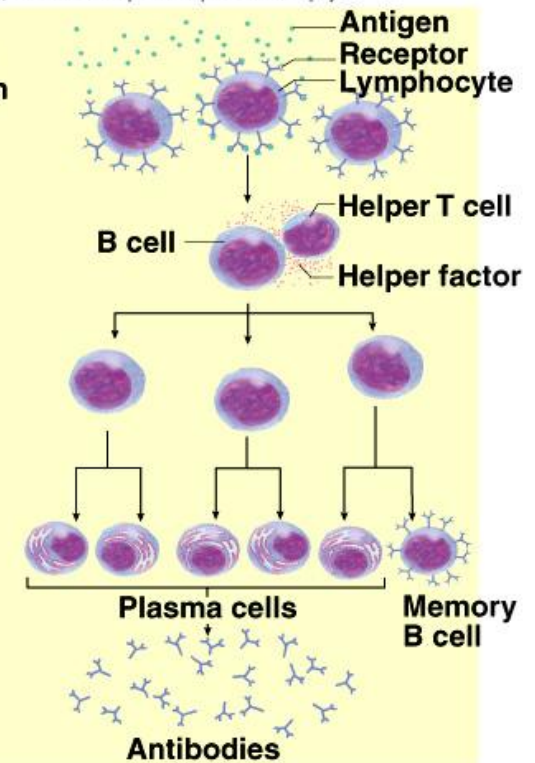
- A. Interleukin-II
- B. Perforin
- C. Interferon
- D. Interleukin-IV

# What happens in an antibody-mediated response?

- The key events:
  - Recognition
  - Attack
  - Memory
- The key players:
  - B cells (plasma and memory cells)
  - Helper T cells
  - Free-floating antigens

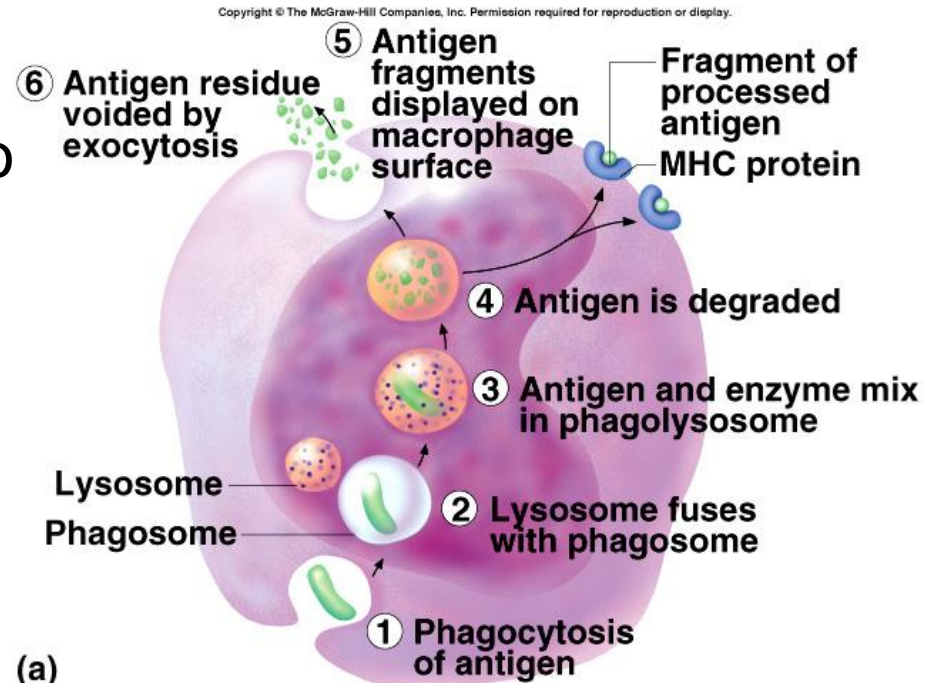
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1. Immunocompetent B cells exposed to antigen. Antigen binds only to B cells with complementary receptors.
2. B cell displays processed antigen fragments. Helper T cell binds to B cell and secretes helper factor.
3. Helper factor stimulates B cell to divide repeatedly and form a clone.
4. Some cells of the clone become memory B cells. Most differentiate into plasma cells.
5. Plasma cells synthesize and secrete antibody.



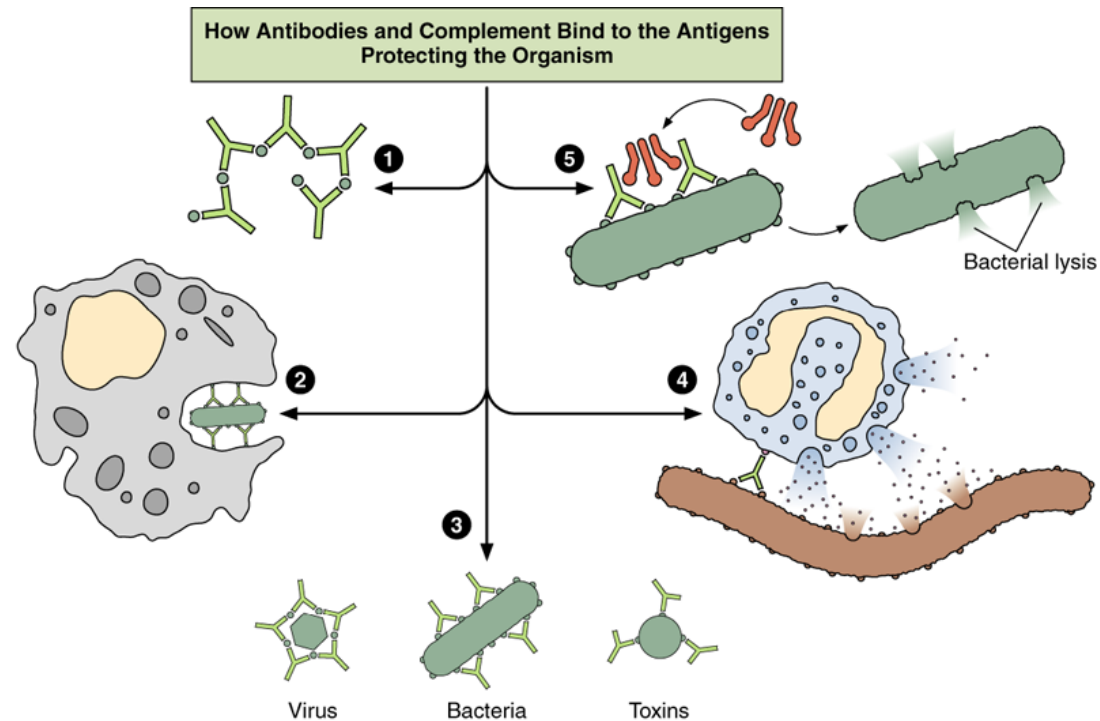
# What happens during recognition?

- **Capping**: free-floating antigen binds to B cell with correct antibody on its PM
- **Endocytosis** of antigen-antibody complex
- **Display** of hotdog + bun
  - Helper T cell binds, secretes interleukin-2
  - Gives B cell the “go” signal
- **Clonal selection**: only B cells with correct antibody clone (a)
- **Plasma cell differentiation**: large B cells with lots of rough ER
- [antigen presentation animation](#)



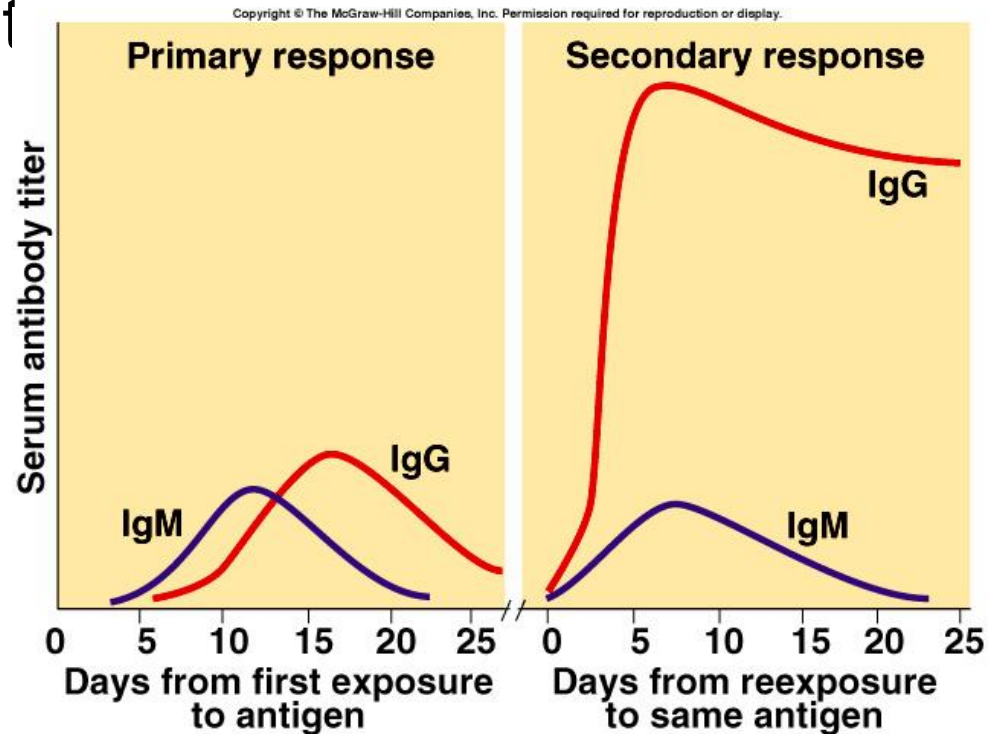
# What happens during attack?

- Plasma cells make millions of antibodies (IgM) and distribute in blood plasma
- Antibodies incapacitate antigens:
  1. Agglutination
  2. Neutralization
  3. Precipitation
  4. Complement fixation
- Eosinophils or T cells then destroy antigens



# What happens during memory?

- Primary response (first exposure)
  - takes 3 to 6 days to produce plasma cells
- Secondary response
  - Memory B cells in reserve form plasma cells in mere hours
  - IgG produced to combat antigen



If a patient has a high level of IgM in the blood, you can assume

- A. He has leukocytosis
- B. He has just been infected with chicken pox for the first time
- C. He has just been re-exposed to chicken pox
- D. He is having a severe allergy attack

Only \_\_\_\_\_ can recognize  
MHC-II.

- A. B cells
- B. Macrophages
- C. Cytotoxic-T cells
- D. Helper-T cells

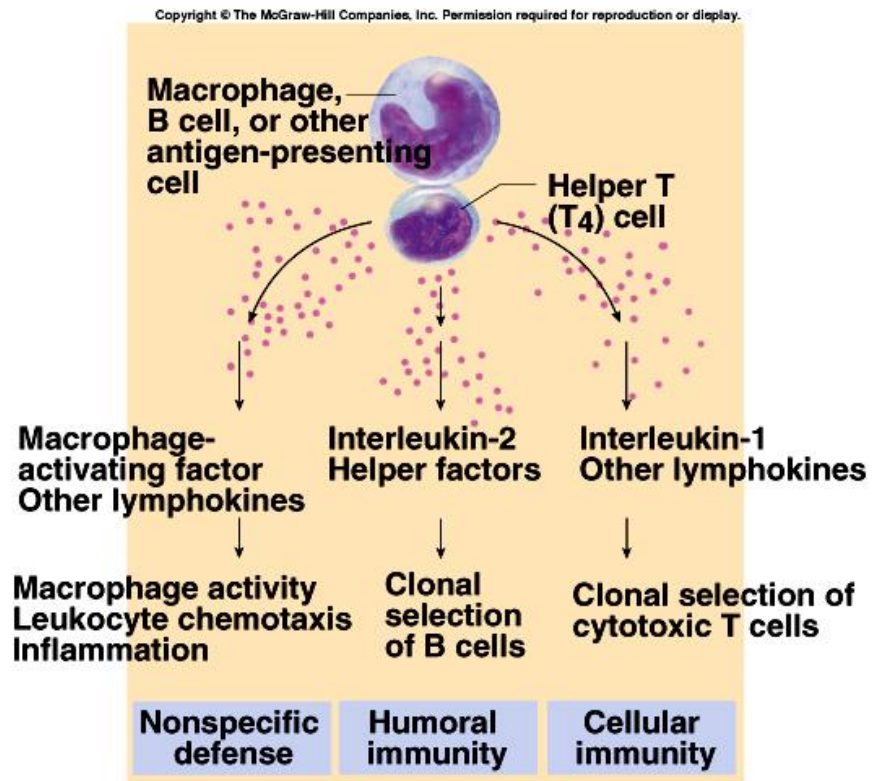
Which is not a part of the recognition process?

- A. Display
- B. Capping
- C. Exocytosis
- D. Clonal selection



# Who can't you do without in specific immunity?

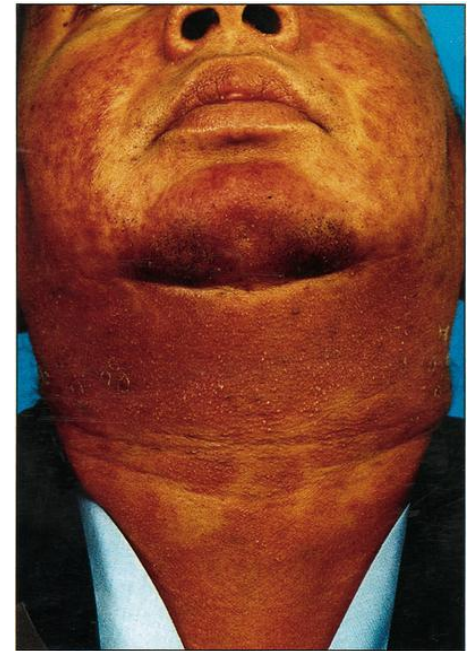
- \_\_\_\_\_ cells are the lynch pins for both antibody- and cell-mediated immunity
- Why?



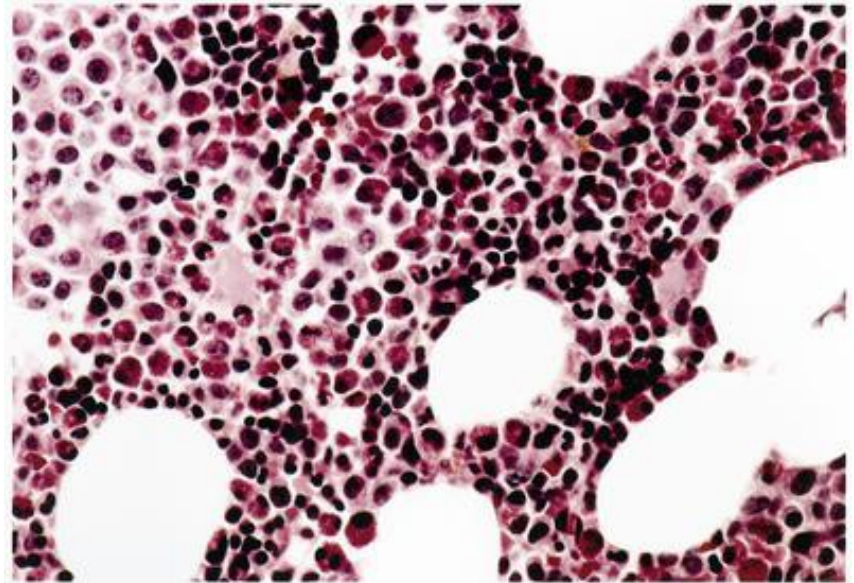
# Immunization and immune disorders

# What is hypersensitivity?

- Excessive reaction to an antigen (allergen) to which most people do not react
  - Includes
    - Allergies
    - Alloimmunity (transplants)
    - Autoimmunity
  - Four types



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# What are the four types?

- Type I--Acute hypersensitivity
  - IgE-mediated, often non-dosage dependent
  - Degranulation of basophils and mast cells
  - Food allergies, asthma, anaphylaxis (severe type I)
- Type II--antibody-dependent cytotoxic hypersensitivity
  - IgG or IgM attacks antigens bound on a cell surface
    - **Blood transfusion** reactions, penicillin allergy, some drugs, toxic goiter, myasthenia gravis



# What are the four types?

- Type III: immune complex hypersensitivity
  - IgG or IgM bind directly to free-floating antigens causing precipitation in blood or tissues
    - This activates complement and inflammation
    - Necrosis follows
  - Some autoimmune diseases (e.g. lupus, glomerular nephritis)
- Type IV: delayed hypersensitivity
  - Cell-mediated, after 1/2 to 3 days
  - APCs display antigen to CD4 cells, which activate CD8 cells: specific and non-specific responses
  - Allergies to haptens (poison oak, make-up), graft rejection, TB skin test, type I diabetes



# What is immunization?

- Active immunization
  - Vaccine prompts antibody manufacture
    - Also creates B memory cells
    - Lasts for years
- Passive immunization
  - Injection of antibodies (gamma globulin serum)
    - Also breastfeeding
  - Can prevent infection after exposure
  - Antibodies eventually degrade
  - No memory B cells formed



[vaccination movie](#)

# Naturally acquired passive immunity results from

- A. A bee sting
- B. Immunization
- C. A flu shot
- D. Placental transfer

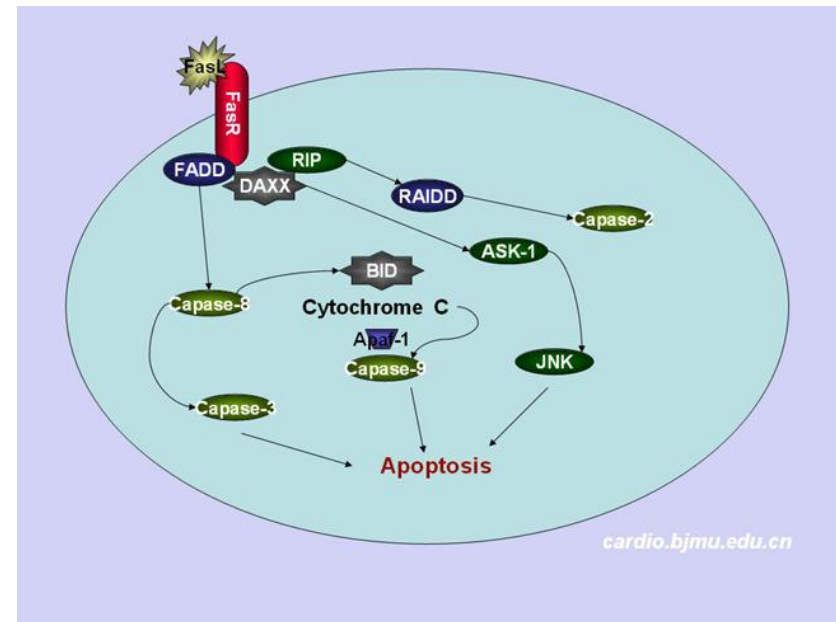
# During type II hypersensitivity

- A. Immunoglobins attack antigens bound to a cell
- B. A cell-mediated response happens days after exposure
- C. Anaphylaxis is common
- D. Immunoglobins bind to free-floating antigens causing inflammation



# Why are organ transplants often rejected?

- T-cells attack foreign cell, kill them
  - Immunosuppressive drugs counteract this
  - Problem: may have to take these drugs for rest of life
- Future therapy: add FasL markers to transplanted cells
  - When T-cells w/Fas markers contact FasL, they commit cell suicide (apoptosis)
  - <http://www.cat.cc.md.us/courses/bio141/lecguide/unit3/cellular/cmidefense/ctls/fasan.html>
  - This is what naturally occurs in the testes, anterior chamber of eye, brain (immunologically privileged areas)



# What are autoimmune diseases?

- Self-attack by immune system
  - Produce autoantibodies
- Lupus erythematosus: inflammation of CTs
  - Fever, fatigue, joint pain, light sensitivity
- Rheumatic fever: antibodies attack mitral and aortic valves
- Others: rheumatoid arthritis, Type I diabetes, multiple sclerosis, Grave's disease



# What are immunodeficiency diseases?

- Immune system weakened or fails to respond
- Severe combines immunodeficiency disease (SCID)
  - Rare/absent T and B cells (hereditary)
- Acquired immunodeficiency syndrome (AIDS)
  - Develops from HIV infection

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# How does HIV cause AIDS?

- HIV: a retrovirus
  - What does this mean?
  - Extremely high mutation rate
- Infects helper T cells, neutrophils, macrophages
  - Recall: helper Ts needed to stimulate both T and B cells
    - Infects only a small number of helper Ts though
      - Possibly infected cells have FasL which destroys healthy helper Ts
- Incubation: several months to years
  - Final stages: AIDS
    - No immune response capability
    - Kaposi's sarcoma common

