Chapter 7

Immunity

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Immune System

- Responsible for body defenses
  - Nonspecific response (defense)

    First Line: mechanical, skin and mucous membranes and secretions (tears, saliva).

    Second Line: phagocytosis, inflammation, and interferon.
  - Specific response (defense)

    Third Line: humoral and cellular immune systems.

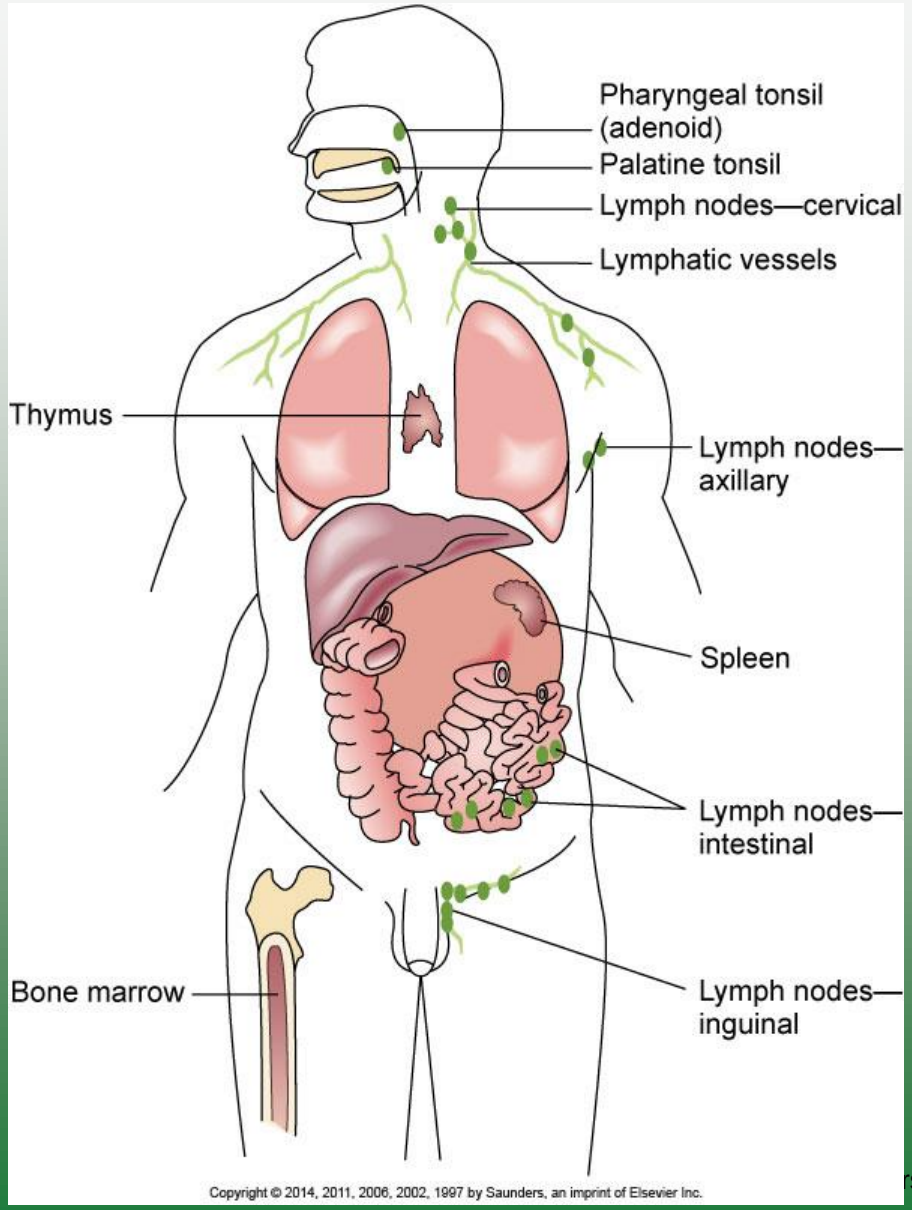
•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Components of the Immune System

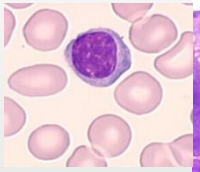
1. Lymphoid structures
   - Lymph nodes
   - Spleen
   - Tonsils
   - Intestinal lymphoid tissue
   - Lymphatic circulation

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

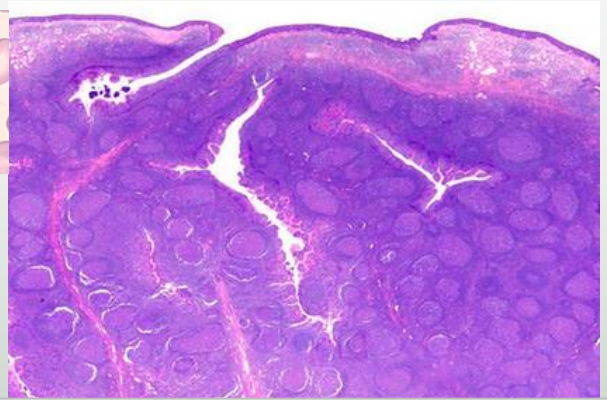
Structures of the Immune System



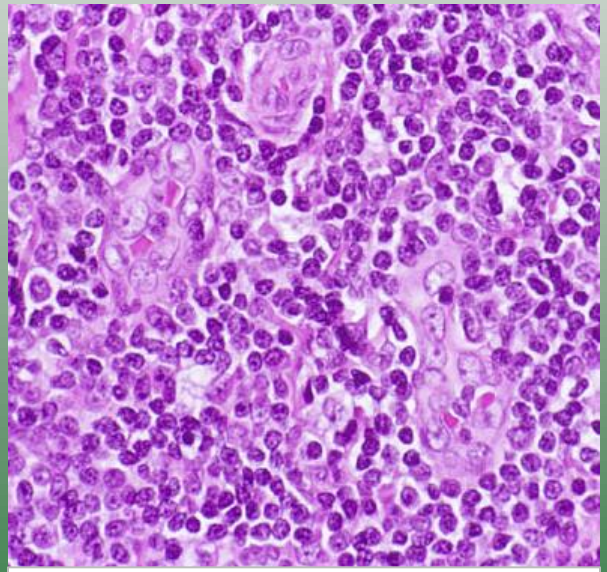
Copyright © 2014, 2011, 2006, 2002, 1997 by Saunders, an imprint of Elsevier Inc.



Lymphocyte



•Lymphoid Tissue (Tonsil) - low magnification



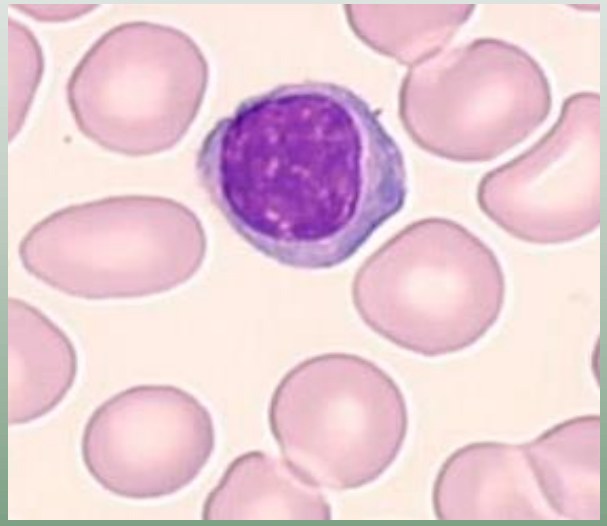
•Lymphoid Tissue - high magnification

rs, an imprint of Elsevier, Inc.

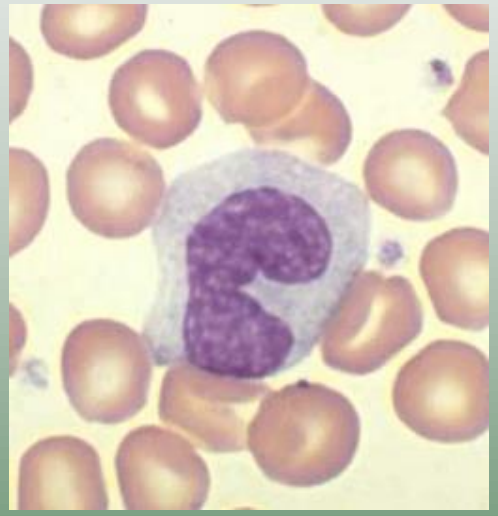
Components of the Immune System

2. Immune cells

- Lymphocytes



Monocytes / Macrophages



•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

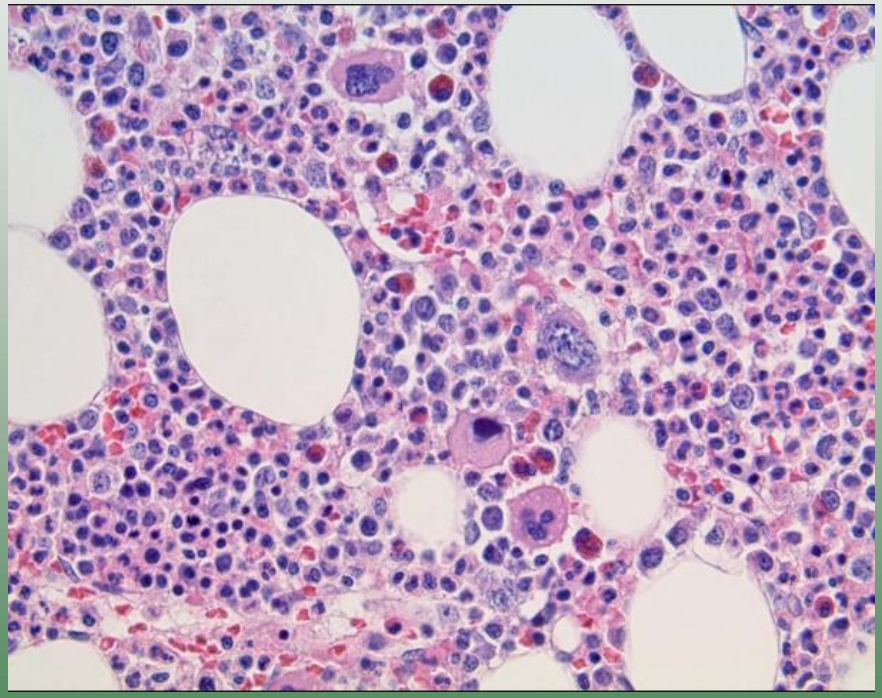
3. Immune Tissues:

Bone marrow

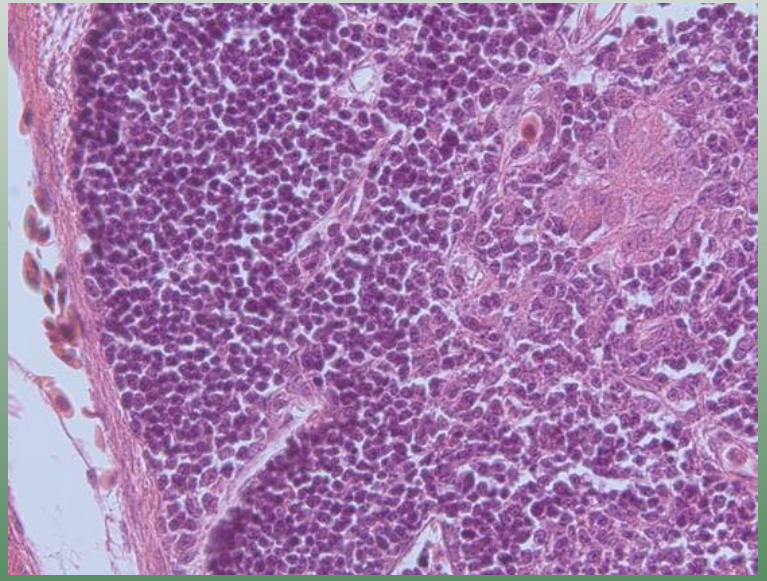
- Origination of all immune cells and B Cell maturation.

Thymus

- Site of T Cell maturation.



Bone Marrow



Thymus

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Components of the Immune System (Cont.)

- Chemical Mediators:
  - Complement, histamine, kinins, prostaglandins, leukotrienes, cytokines, tumor necrosis factor (TNF), and chemotactic factors.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Antigens (Immunogens)

the molecules the immune system reacts to

- Usually exogenous substances
  - Substances from outside the body.
  - Examples: soil (in a wound), a splinter, bee venom.
- Cell surface antigens (on bacteria, fungi, viruses, virus infected cells, cancer cells).
  - Proteins
  - Polysaccharides
  - Glycoproteins

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Elements of the Immune System

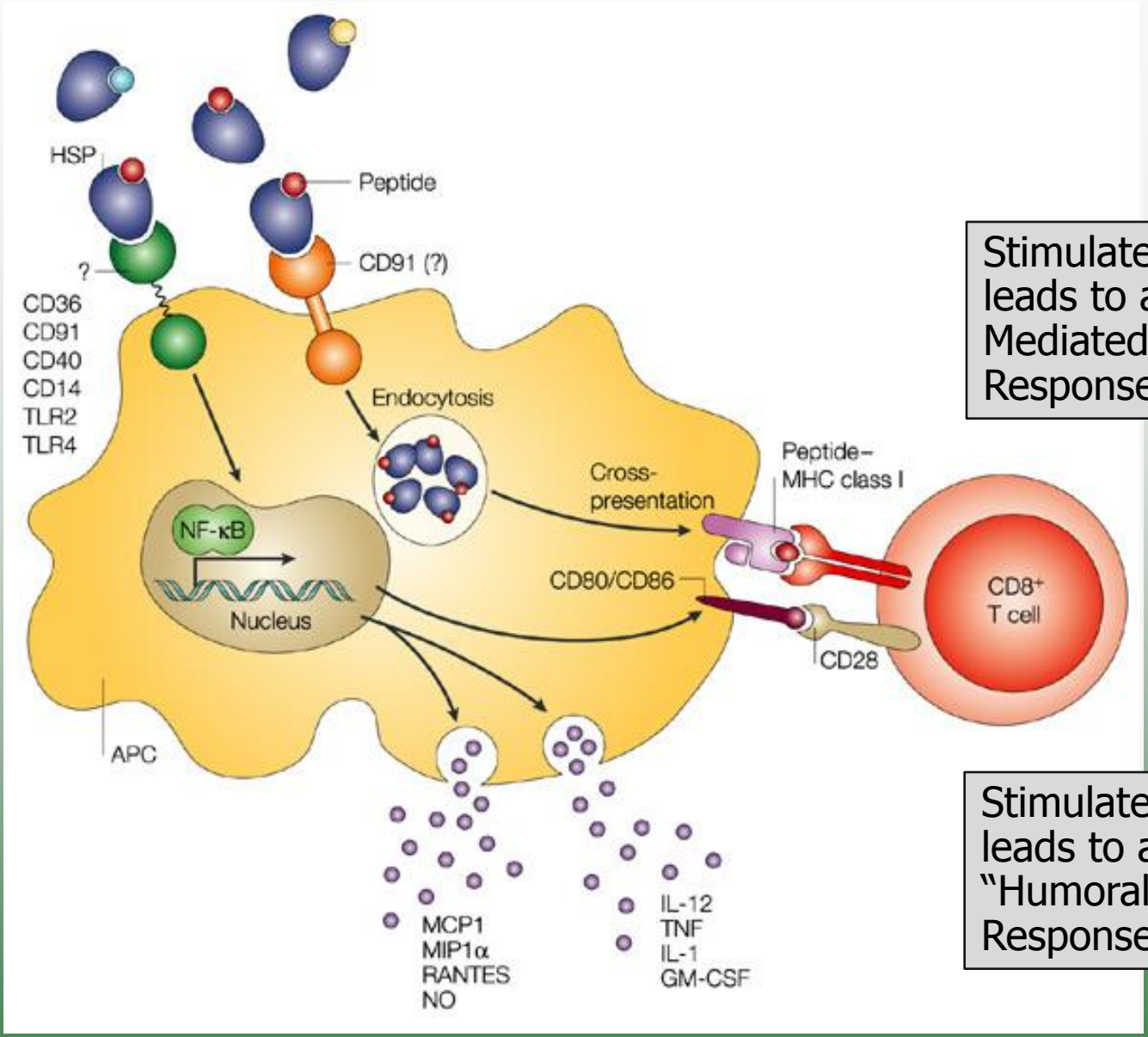
- Antigens
  - Self
    - HLA proteins (part of the “Major Histocompatibility Complex” (MHC) label cells of the individual.
    - Immune system ignores self cells (“**Tolerance**”).
  - Non-self
    - Immune system recognizes specific non-self antigens as foreign.
    - Development of a specific response to that particular antigen
    - Memory cells produced to respond quickly to antigen

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Cells

- Macrophages
  - Develop from monocytes
  - Initiation of immune response
  - Part of the mononuclear phagocytic system
  - Engulf foreign material
  - Display fragments of foreign material on their cell surface to interact with T Cells.
  - Secrete chemicals
    - Examples: monokines, interleukins

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.



Stimulated T Cell leads to a "Cell Mediated" Immune Response.

Stimulated B Cell leads to a "Humoral" Immune Response.

Antigen Presentation

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

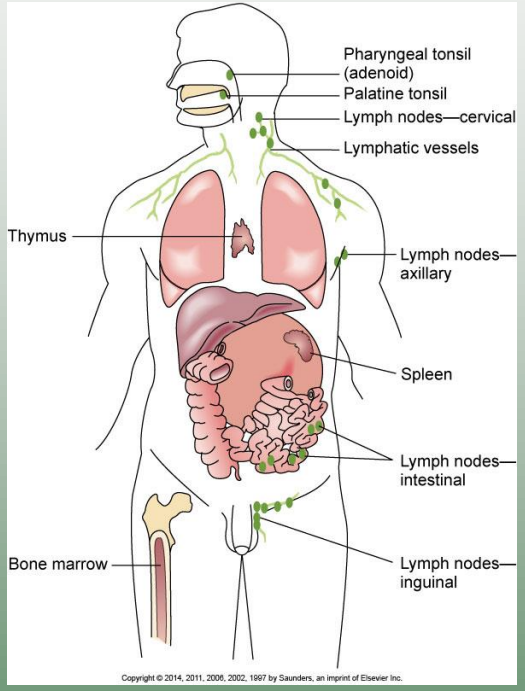
Types of Immunity

- Cell-mediated immunity (CMI): Lymphocytes are programmed to attack non-self cells to protect the body.
- Humoral immunity: Antibodies are produced to protect the body.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Cells

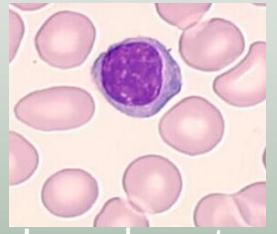
- Lymphocytes
  - T lymphocytes
    - From bone marrow stem cells
    - Further differentiation in thymus
    - Cell-mediated immunity
    - Cytotoxic T killer cells
    - Helper T cells
    - Memory T cells



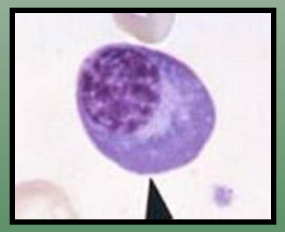
•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Cells (Cont.)

- Lymphocytes
  - B lymphocytes
    - Responsible for production of antibodies
    - Humoral immunity
    - Mature in bone marrow
      - Proceed to spleen and lymphoid tissue to be available for stimulation and transformation to plasma cells.
    - Plasma cells
      - Produce antibodies
    - B memory cells
      - Can quickly form clone of plasma cells when there is a re-exposure to an antigen.

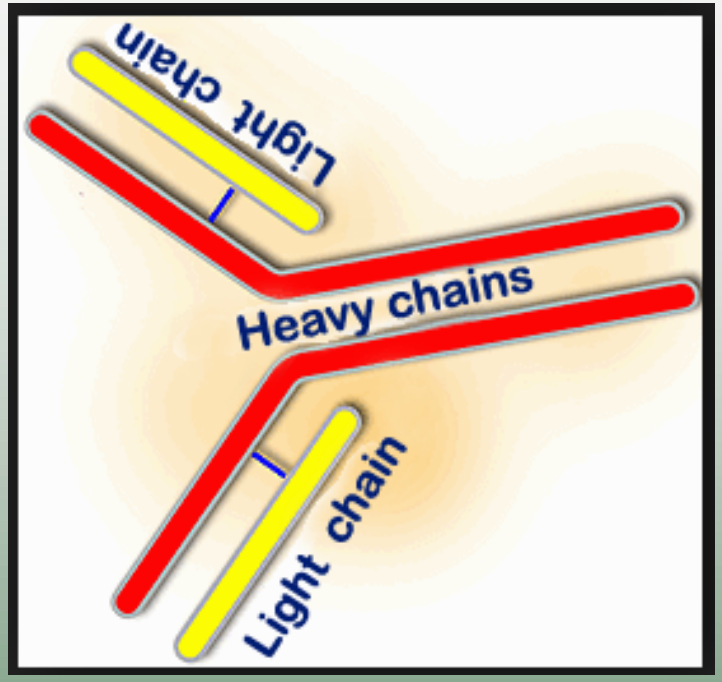


Lymphocyte



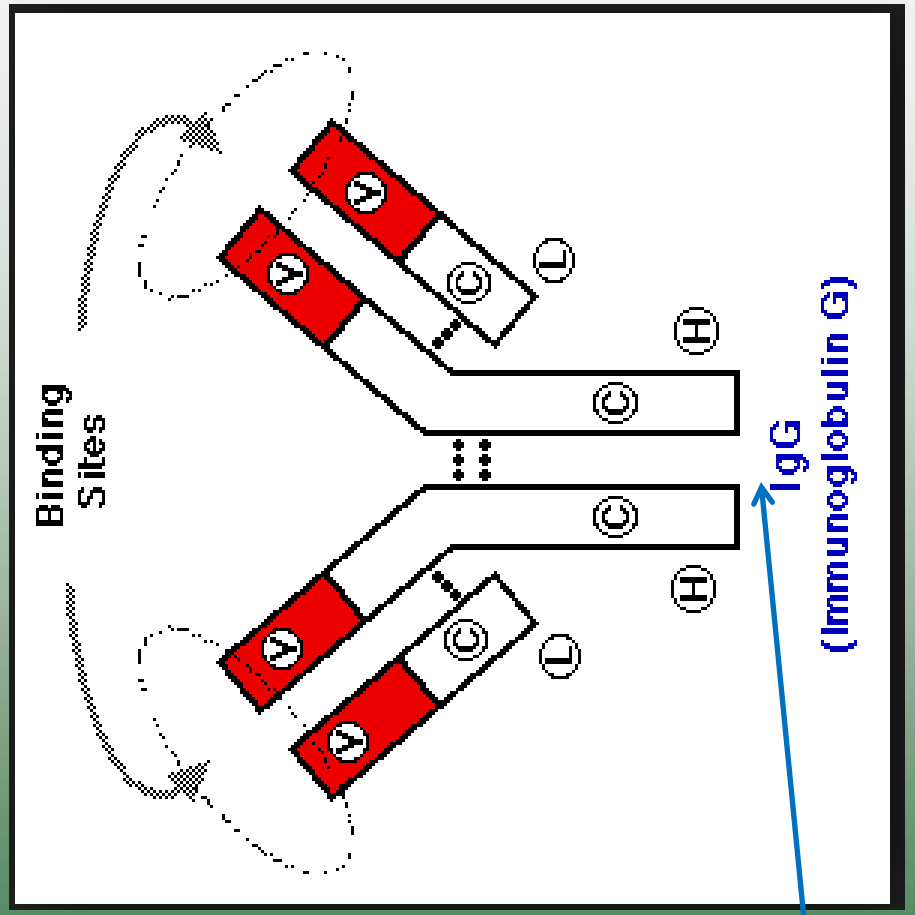
Plasma Cell

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.



Light Chains (2 types): κ, λ

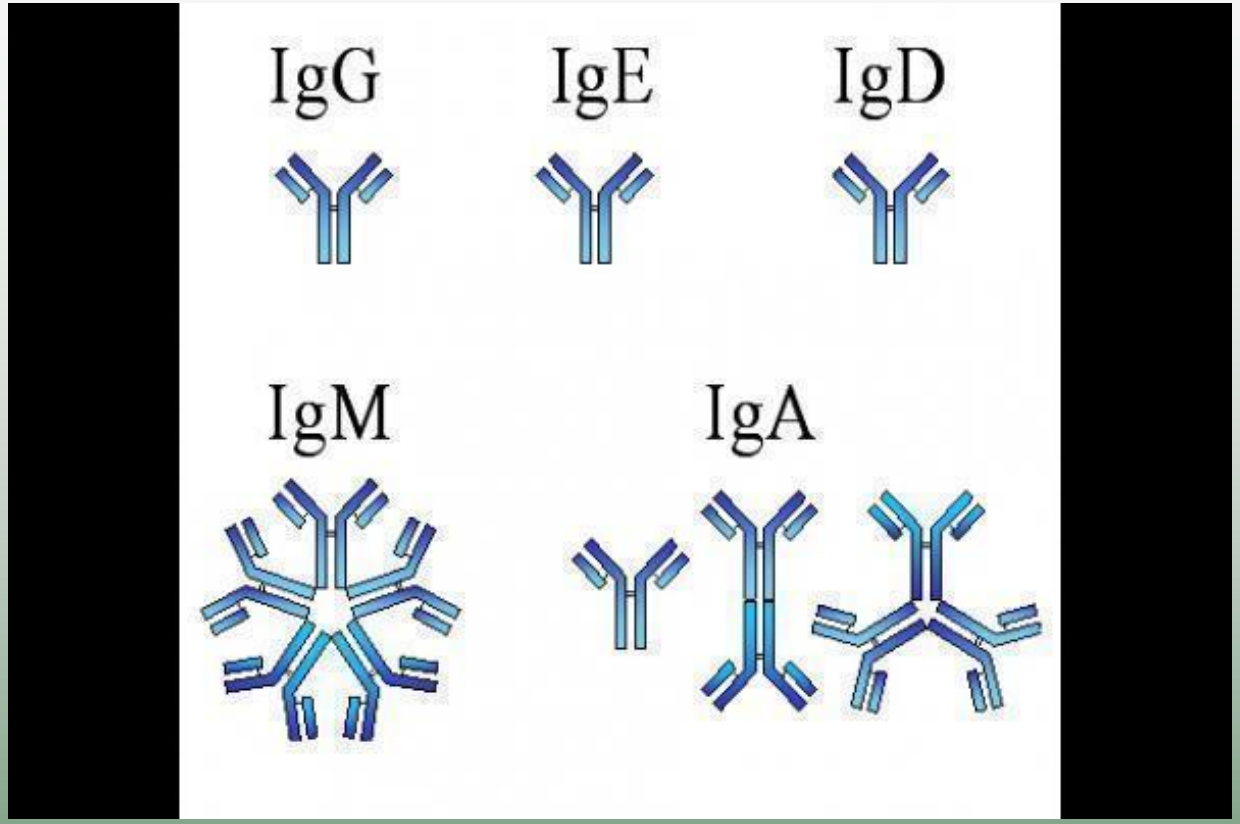
Heavy Chains (5 types): γ,α,μ,ε,δ



•Fc portion binds Fc receptors on phagocytes

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

5 Types of Immunoglobulin (GAMED)



IgG – gamma (γ) heavy chains and kappa or lambda light chains.

IgA – alpha (α) heavy chains and kappa or lambda light chains

IgM – mu (μ) heavy chains and kappa or lambda light chains

IgE – epsilon (ε) heavy chains and kappa or lambda light chains

IgD - delta (δ) heavy chains and kappa or lambda light chains

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Antibodies and Immunoglobulins

- IgG
  - Most common in blood
- IgM
  - First to increase in immune response
- IgA
  - In secretions
    - Tears
    - Saliva and mucous membranes
    - Colostrum

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Antibodies and Immunoglobulins (Cont.)

- IgE
  - Allergic response
  - Causes release of histamine and other chemicals
  - Results in inflammation
- IgD
  - Attached to B cells
  - Activates B cells

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

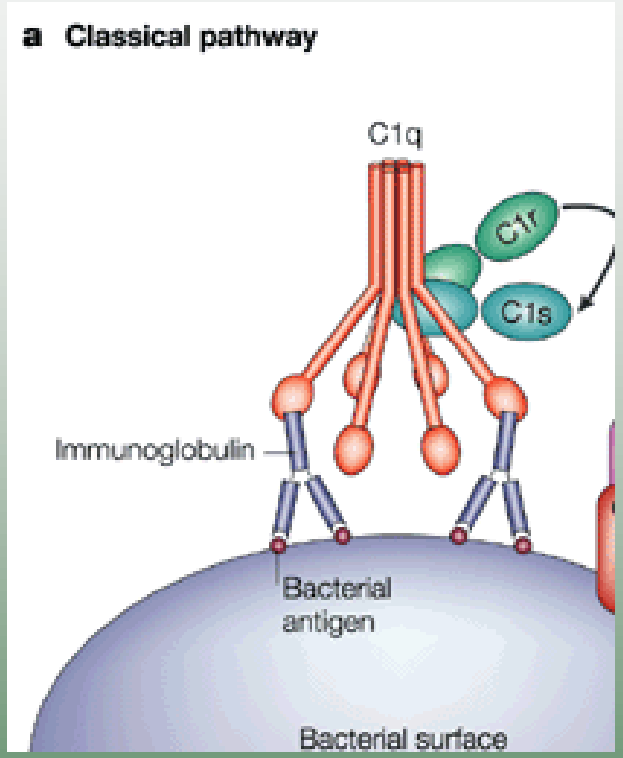
Complement System

A family of nine proteins (C1-C9) that are activated in a cascade starting with an antigen-antibody complex with C1 and ending in a polymer of C9 that forms a pore (effectively a hole) in the target cell.

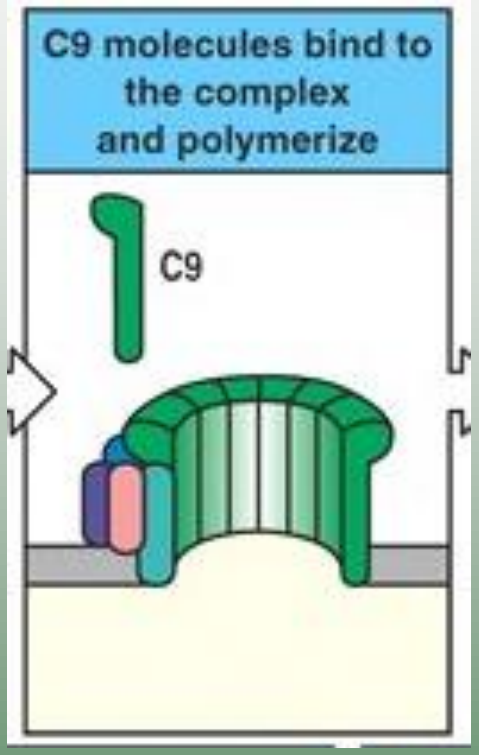
In the cascade, some products act as inflammatory mediators, stimulating inflammation.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

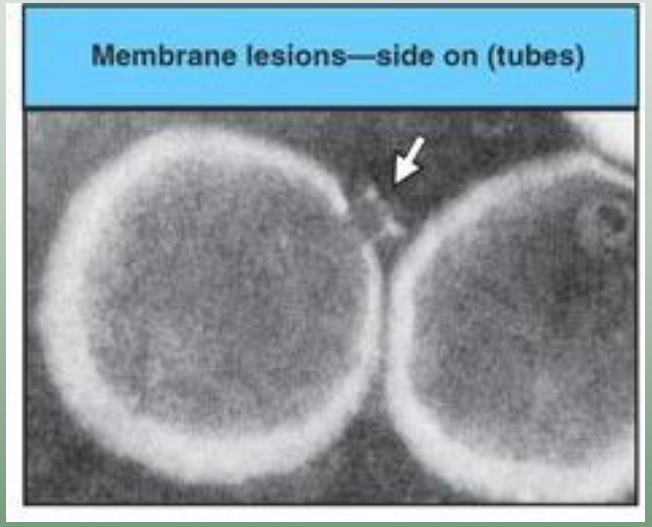
Complement System, C1 >>> C9



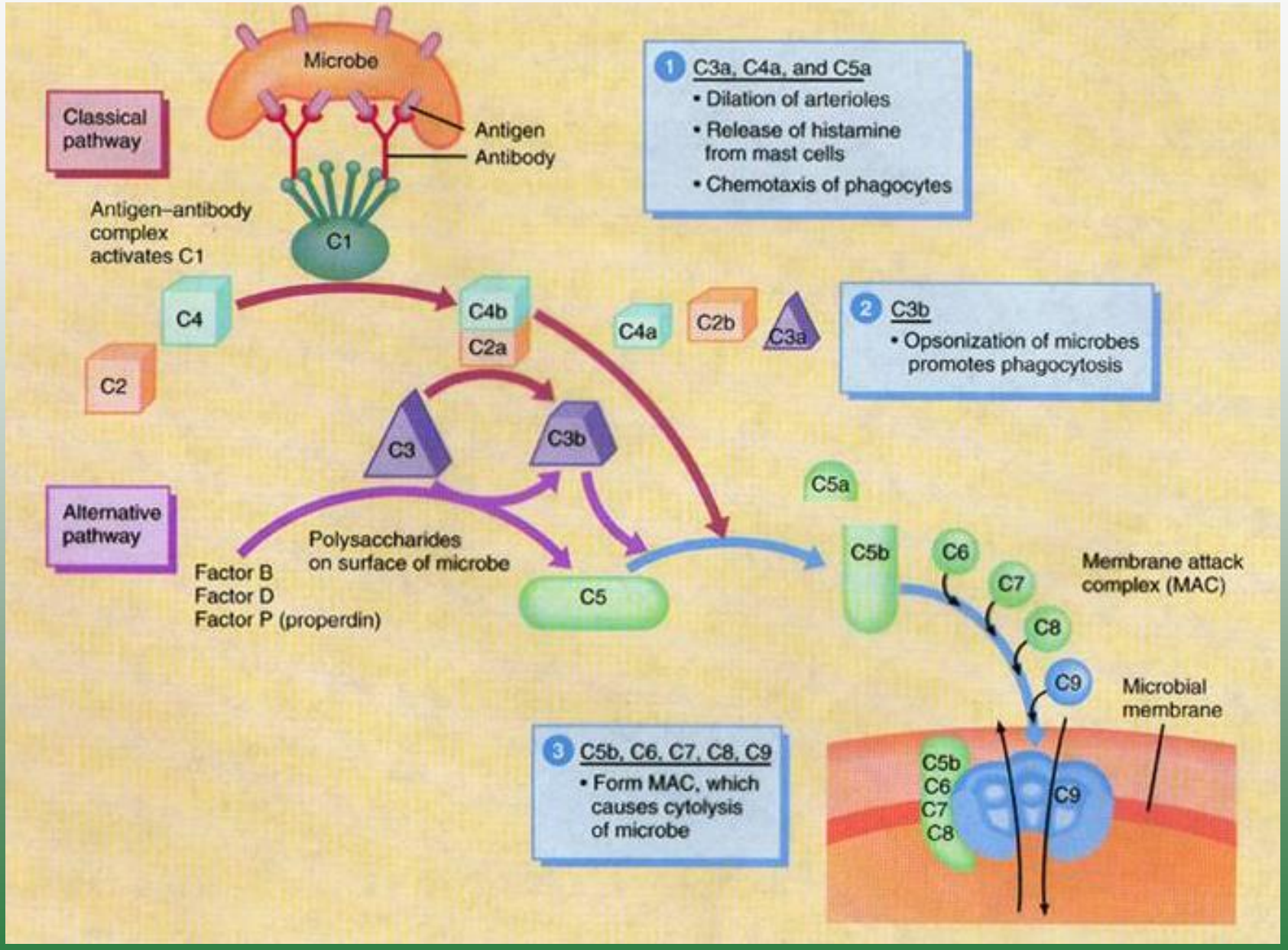
Cascade starts with C1 binding to antibodies ("complement fixation")



Cascade ends with C9 polymer forming a pore in target cell.



•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.



•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Immunity

- Natural immunity
  - Species-specific
- Innate immunity
  - Gene-specific
  - Related to ethnicity

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

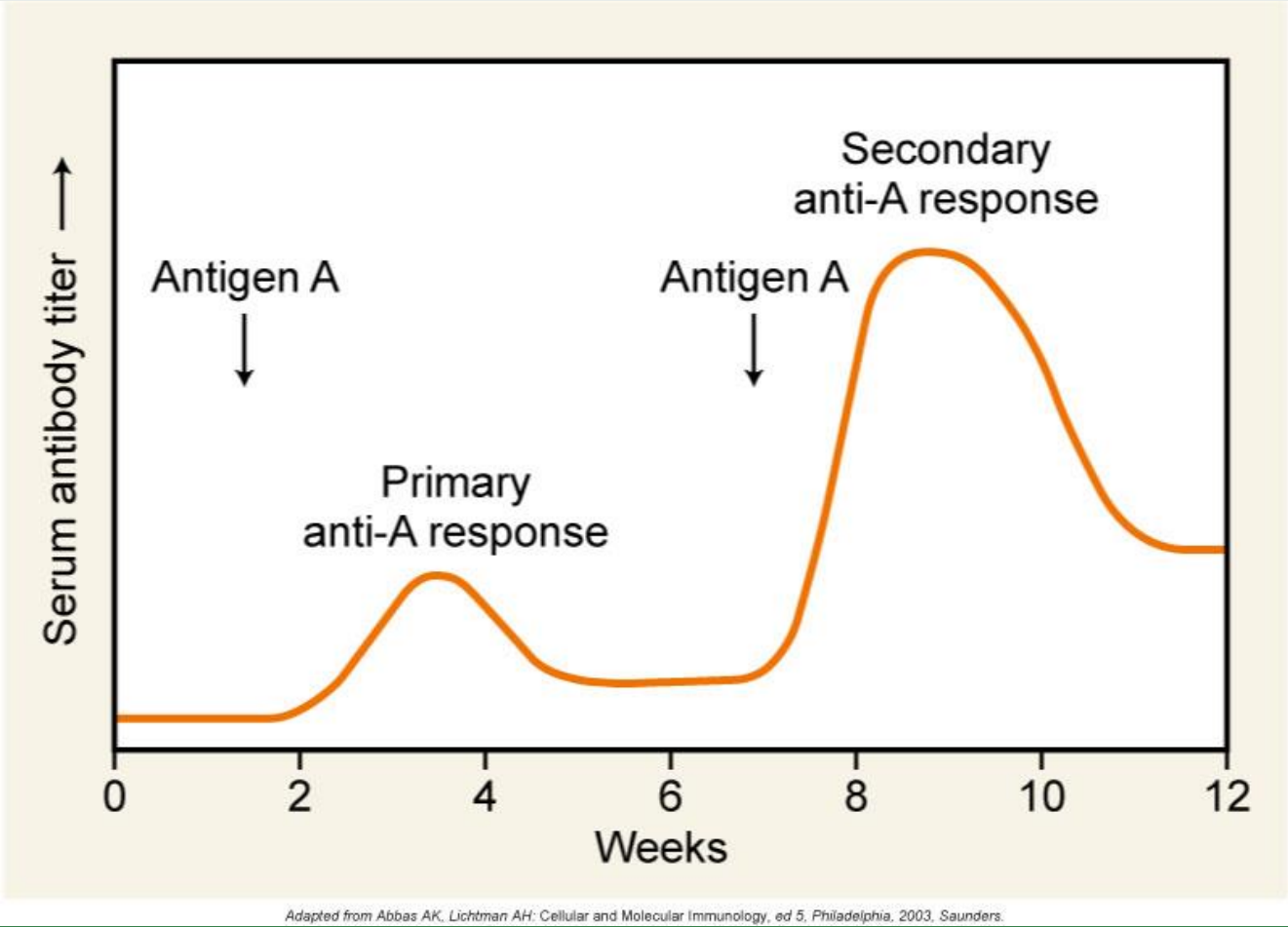
- **Titer:** is a term that reflects the concentration of an antibody in the plasma. If you have a test for the antibody, an antibody at high concentration can be diluted until the test is no longer positive. The highest dilution that still reads positive for the antibody is the titer. If your test was positive at a dilution of 1:1000 and negative at 1:10,000, then the titer is 1:1000.

- Primary response
  - First exposure to antigen
  - 1 to 2 weeks before antibody titer reaches efficacy

- Secondary response
  - Repeat exposure to the same antigen
  - More rapid response, with efficacy in 1 to 3 days

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Primary and Secondary Immune Responses



Adapted from Abbas AK, Lichtman AH: Cellular and Molecular Immunology, *ed 5, Philadelphia, 2003, Saunders.*

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Immunity

active or passive ; natural or artificial

- Active natural immunity
  - Natural exposure to antigen
  - Development of antibodies
- Active artificial immunity
  - Antigen purposefully introduced to body
  - Stimulation of antibody production
  - Immunization
  - Booster immunization

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Immunity (Cont.)

- Passive natural immunity
  - IgG transferred from mother to fetus:
    - Across placenta
    - Through breast milk
  - Protection of infant for the first few months of life or until weaned
- Passive artificial immunity
  - Injection of antibodies
  - Short-term protection

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Tissue and Organ Transplant Rejection

- Hyperacute rejection
  - Immediately after transplantation.
  - Humoral response with pre-existing antibodies.
- Acute rejection
  - Develops after several weeks.
  - Lymphocytes attack organ cells.
- Chronic, late rejection
  - Occurs after months or years.
  - Chronic blood vessel damage.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Immunosuppression

- Reduction of immune response to prevent rejection
- Commonly used drugs
  - Cyclosporine, azathioprine, prednisone
- High risk of infection
  - Caused by immunosuppression
  - Opportunistic organisms
- Increased Risk of Cancer (lymphoma)

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Hypersensitivity Reactions

- Type I hypersensitivity—allergic reactions
  - Common
    - Caused by allergen
    - Skin rashes
    - Hay fever
  - Causative mechanism
    - Exposure to allergen
    - Development of IgEs
    - Mast cells release histamine (treated with antihistamines).
  - Complications
    - Anaphylaxis

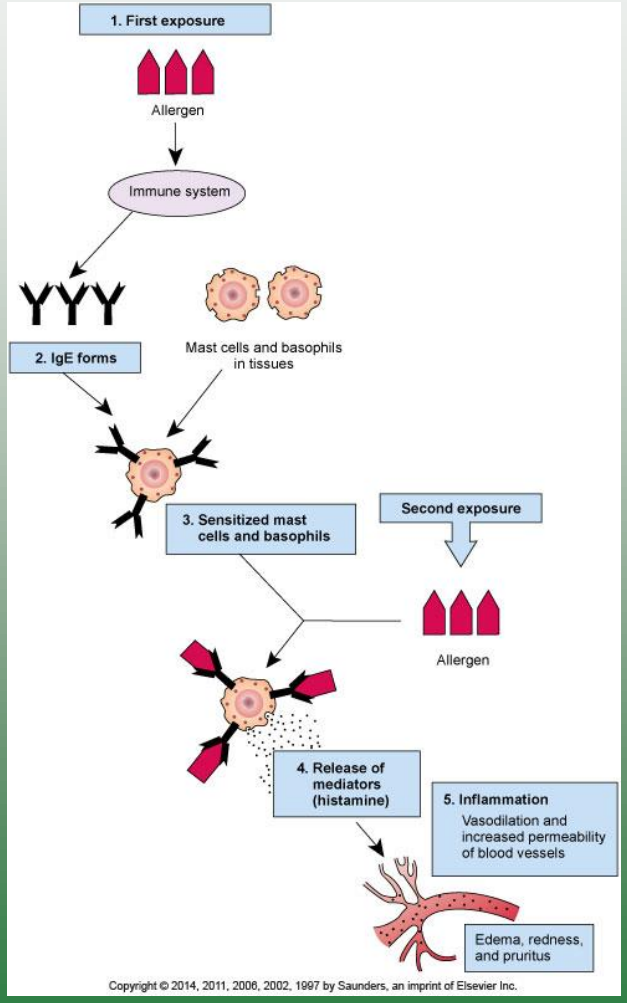
Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Hypersensitivity Reactions (Cont.)

- Type I hypersensitivity–allergic reactions (Cont.)
  - Hay fever: allergic rhinitis
    - Nasal mucosa
  - Food allergies
    - Digestive tract mucosa
  - Atopic dermatitis/eczema
    - Skin
  - Asthma
    - Bronchial mucosa

Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Type I Hypersensitivity



•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Anaphylaxis: Anaphylactic Shock

- Severe, life-threatening
- Systemic hypersensitivity reaction
- Decreased blood pressure caused by release of histamine
- Airway obstruction
- Severe hypoxia
- Can be caused by:
  - Latex materials
  - Insect stings
  - Nuts or shellfish; various drugs
  - **Treat with Epinephrine - Patient carries Epi Pen**

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

The Epi Pen has a spring loaded needle that is intended to penetrate clothing and deliver the dose of epinephrine.

After use of the Epi Pen you still call 911 as the effects of the epinephrine can wear off in a short period (as little as 15 minutes).

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Treatment for Anaphylaxis

- Requires first aid response:
  - Administer EpiPen if available
  - Call 911 (many paramedics can start drug treatment and oxygen)
- Treatment in emergency department:
  - Epinephrine
  - Glucocorticoids
  - Antihistamines
  - Oxygen
  - Stabilize BP

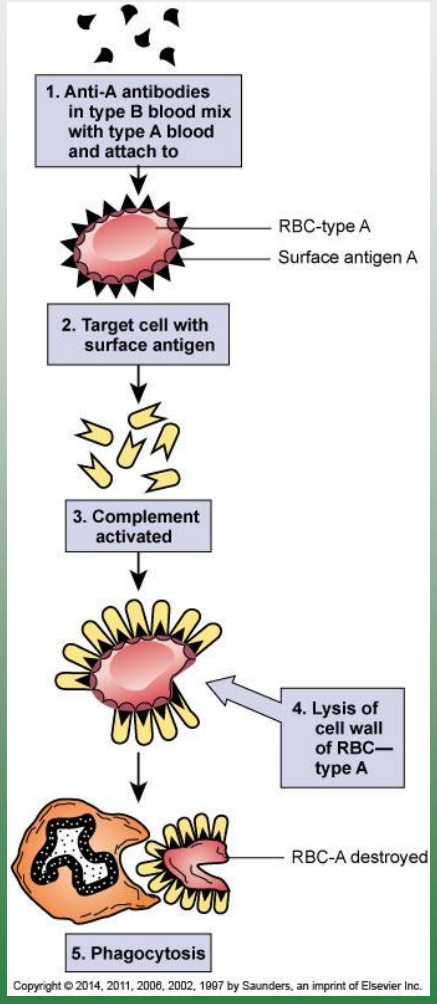
•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Type II: Cytotoxic Hypersensitivity

- Antigen is present on cell membrane
  - May be normal body component or exogenous
- Circulating IgGs react with antigen
  - Destruction by phagocytosis or cytolytic enzymes
- Example
  - Response to incompatible blood transfusion

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Type II Hypersensitivity



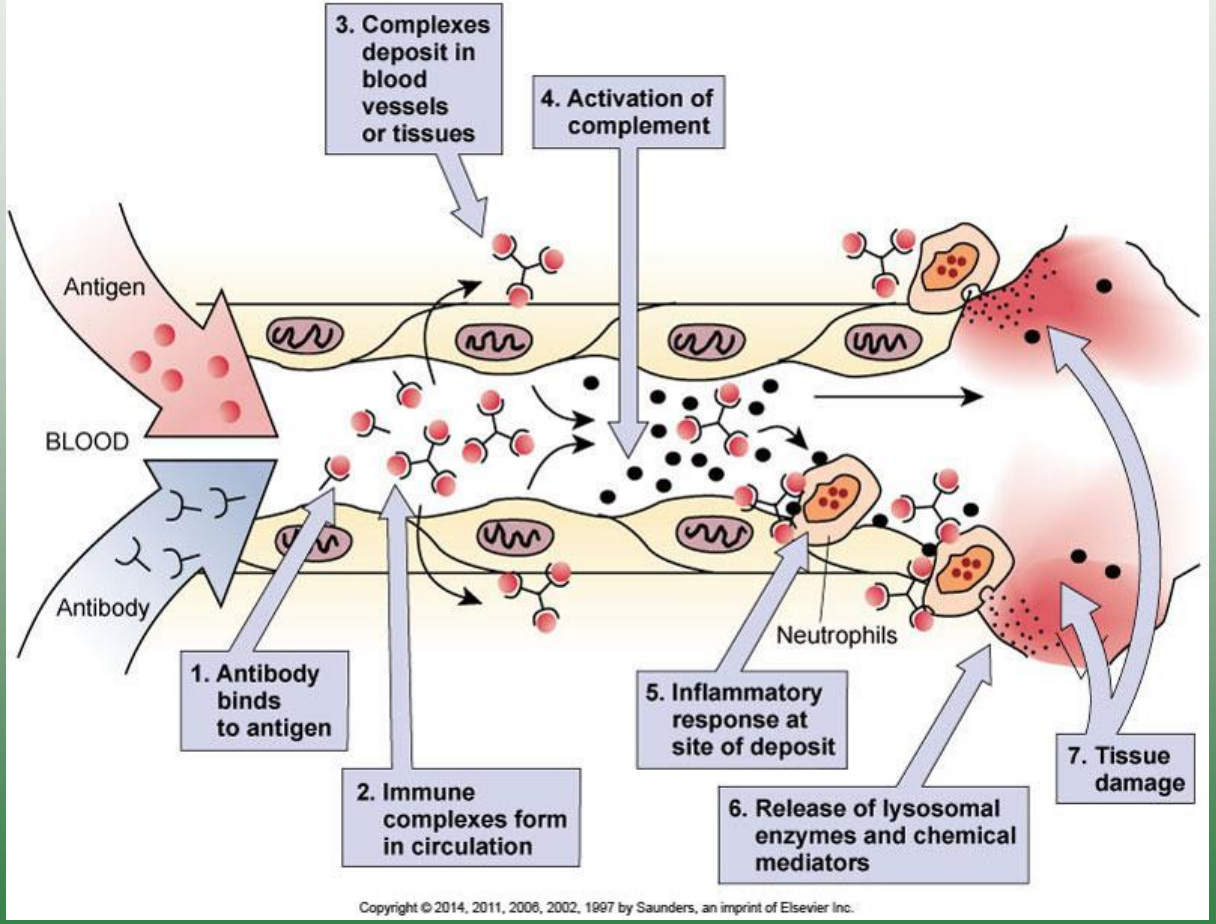
•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Type III: Immune Complex Hypersensitivity

- Antigen combines with antibody
  - Forms immune complexes, deposited in tissue
  - Activation of complement system
- Process causes inflammation and tissue destruction
- Examples:
  - Glomerulonephritis
  - Rheumatoid arthritis

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Type III: Immune Complex Reaction



•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Type IV: Cell-Mediated or Delayed Hypersensitivity

- Delayed response by sensitized T lymphocytes
- Release of lymphokines
- Inflammatory response
- Destruction of the antigen
- Examples:
  - Tuberculin test
  - Contact dermatitis
  - Allergic skin rash
  - Poison Ivy
  - Transplant rejection

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Autoimmune Disorders

- Development of antibodies against own cells or tissues
- Autoantibodies are antibodies formed against self-antigens—loss of self-tolerance.
- Disorder can affect single organs or tissues or can be generalized.
- Examples:
  - Hashimoto thyroiditis, systemic lupus erythematosus, rheumatic fever, myasthenia gravis, scleroderma, pernicious anemia

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Immunodeficiency

- Partial or total loss of one or more immune system components
- Increased risk of infection and cancer
- Primary deficiencies
  - Genetic disorder, infants and children
- Secondary or acquired immunodeficiencies
  - Loss of the immune response from specific causes
  - Can occur at any time during the life span
    - Infections, splenectomy, malnutrition, liver disease, immunosuppressant drugs, radiation, chemotherapy (cancer)

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

Acquired Immunodeficiency Syndrome (AIDS)

- AIDS—chronic infectious disease caused by the human immunodeficiency virus (HIV)
- HIV destroys helper T cells—CD4 lymphocytes (needed for both Cell Mediated and Humoral Immunity)
- Loss of immune response
- Increased susceptibility to secondary infections and cancer
- Prolonged latent period
- Development may be suppressed by antivirals

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

- **HIV-positive** when the virus is known to be present in the body, but few if any clinical signs have developed.

- **Acquired immunodeficiency syndrome** is the stage of active infection, with marked clinical manifestations and multiple complications. An individual may be HIV positive for many years before he or she develops AIDS.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

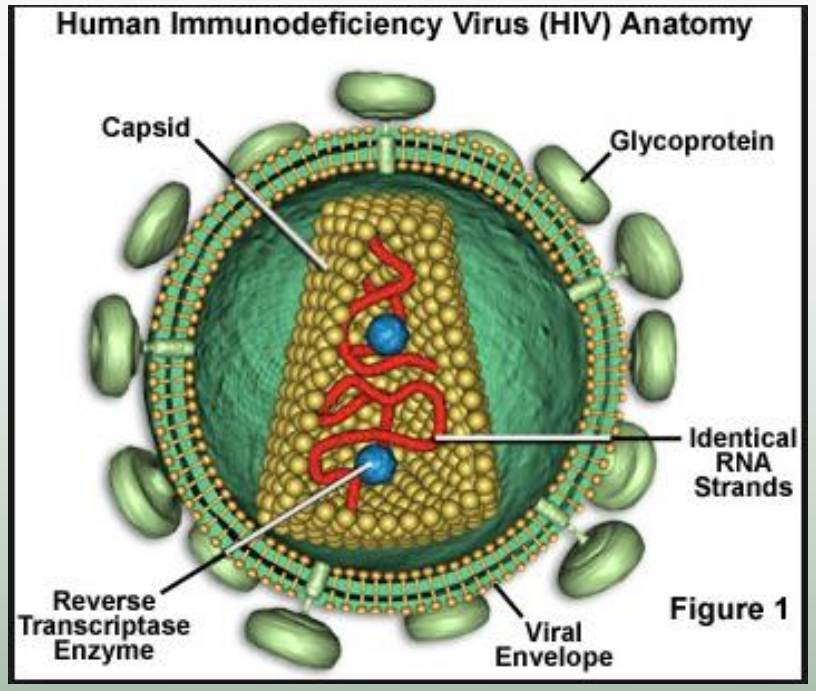
- The first sporadic cases of AIDS in the US appear to have occurred as early as the 1950s, but a significant presence of the disease began in the early 1980's.

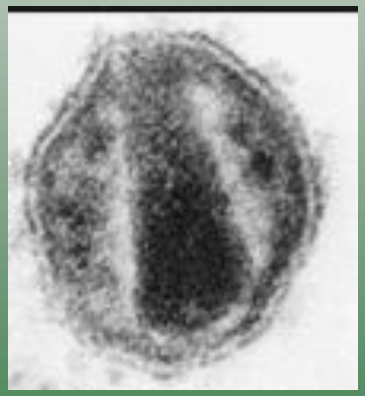
- Acquired immunodeficiency syndrome is now considered a worldwide pandemic, and cases still are multiplying.

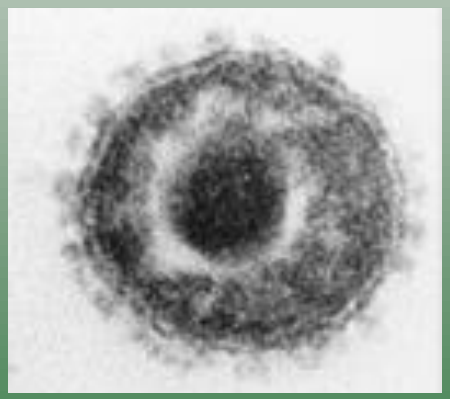
•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

- Contracted in anal or vaginal sex. Fetus can get infected, but antibodies in the newborn are mother's antibodies that cross placenta.
- High risk groups include gay males, prostitutes, prisoners, and IV drug abusers.
- Anti-Retrovirals slow the disease, but worldwide 90% of affected individuals are not treated.
- In 2011, 34 million people world wide living with HIV. 70% are in Sub-Saharan Africa.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.







Steps in infection:

1. HIV attaches to CD4+ Lymphocyte and enters cell

2. Reverse transcriptase converts the viral RNA to DNA. [blocked by AZT].

3. Viral DNA integrates into human DNA.

4. Host cell makes more virus parts.

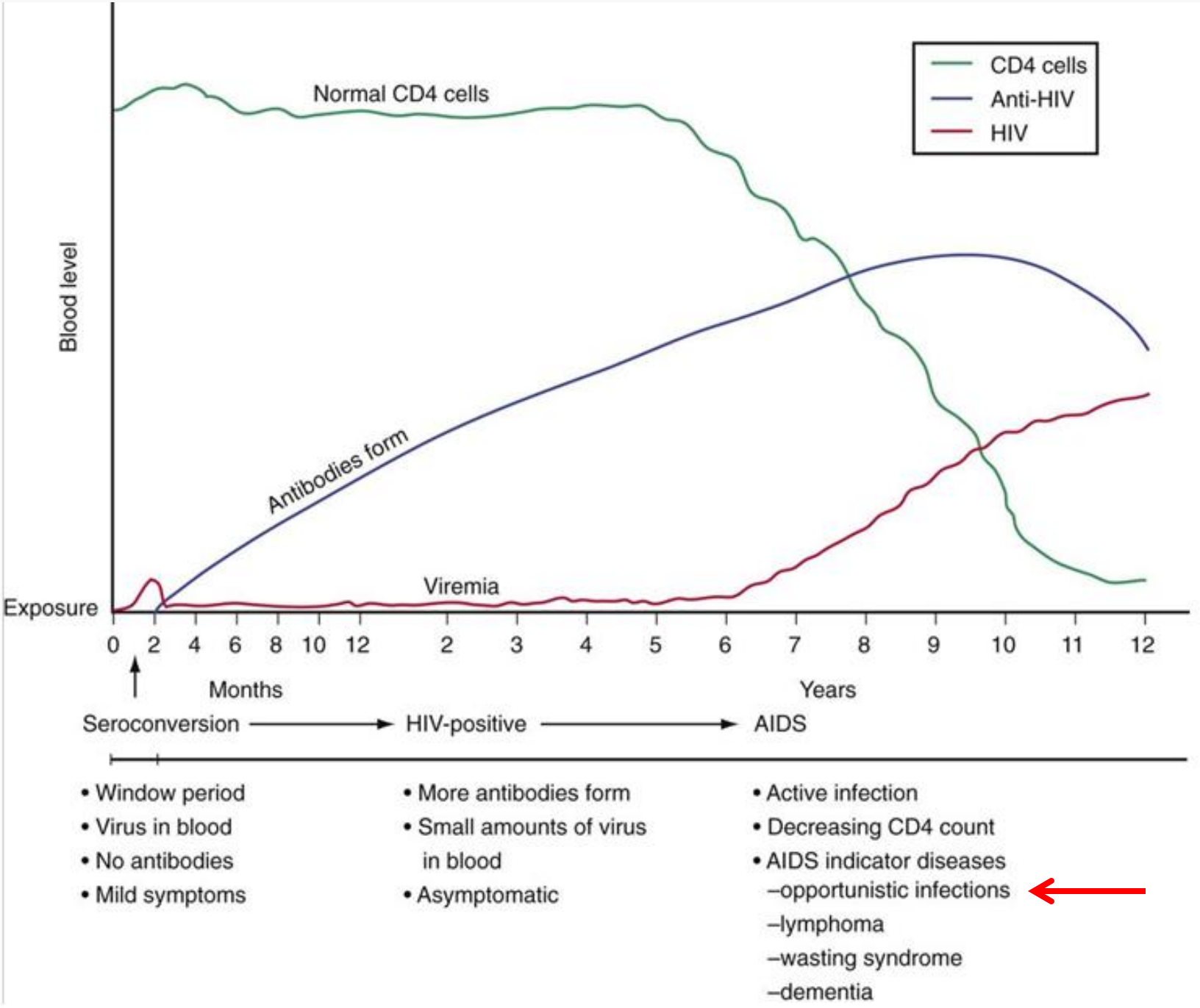
5. Virus parts are assembled [blocked by Anti-HIV protease inhibitor drugs]

6. Virus is shed and cell dies.

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.

- Phases of HIV Infection:
  - Phase 1 of Infection (3-6 weeks) flu like symptoms. HIV positive in 2-10 weeks.
  - Phase 2 of Infection. Latent phase, may last years.
  - Phase 3 of Infection. AIDS with low CD4+ lymphocytes, severe opportunistic infections, cancer, wasting, and CNS deficits. **Pneumocystis carinii** is an opportunistic pulmonary infection that is the **most common cause of death in AIDS patients.**

•Copyright © 2014, 2011, 2006 by Saunders, an imprint of Elsevier, Inc.


CD4 cells
Anti-HIV
HIV
Normal CD4 cells
Blood level
Antibodies form
Viremia
Exposure
0 2 4 6 8 10 12 2 3 4 5 6 7 8 9 10 11 12
Months
Years
Seroconversion
HIV-positive
AIDS
• Window period
• Virus in blood
• No antibodies
• Mild symptoms
• More antibodies form
• Small amounts of virus in blood
• Asymptomatic
• Active infection
• Decreasing CD4 count
• AIDS indicator diseases
–opportunistic infections
–lymphoma
–wasting syndrome
–dementia