Chapter 21
The Immune System: Innate and Adaptive Body Defenses

Human Anatomy & Physiology
Tenth Edition

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The Immune System

• **Immune system** provides resistance to disease

• Made up of two intrinsic systems
  
  – **Innate (nonspecific) defense system**
    
    • Constitutes *first and second lines of defense*
      
      – *First line of defense*: external body membranes (skin and mucosae)
      
      – *Second line of defense*: antimicrobial proteins, phagocytes, and other cells (inhibit spread of invaders; inflammation most important mechanism)

  – **Adaptive (specific) defense system**
    
    • *Third line of defense* attacks *particular* foreign substances (takes longer to react than innate)
Figure 21.1 Simplified overview of innate and adaptive defenses.

**Innate defenses**
- Surface barriers
  - Skin
  - Mucous membranes
- Internal defenses
  - Phagocytes
  - Natural killer cells
  - Inflammation
  - Antimicrobial proteins
  - Fever

**Adaptive defenses**
- Humoral immunity
  - B cells
- Cellular immunity
  - T cells
Antimicrobial Proteins (cont.)

- **Interferons (IFN)**: family of immune modulating proteins
  - Cells infected with viruses can secrete IFNs (type $\alpha$ (alpha) and $\beta$ (beta)) that “warn” healthy neighboring cells
    - IFNs enter neighboring cells, stimulating production of proteins that block viral reproduction and degrade viral RNA
    - IFN-$\alpha$ and IFN-$\beta$ also activate NK cells
  - IFN-$\gamma$ (gamma, also called immune interferon):
    - Is secreted by lymphocytes
    - Has widespread immune mobilizing effects
    - Activates macrophages and NK cells, so indirectly fight cancer
Figure 21.5 The interferon mechanism against viruses.

Innate defenses → Internal defenses

1. Virus enters cell.
2. Interferon genes switch on.
4. Interferon binding stimulates cell to turn on genes for antiviral proteins.
5. Antiviral proteins block viral reproduction.

Host cell 1
- Infected by virus;
- Makes interferon;
- Is killed by virus

Host cell 2
- Binds interferon from cell 1;
- Interferon induces synthesis of protective proteins
Antimicrobial Proteins (cont.)

• Complement
  – **Complement system** consists of ~20 blood proteins that circulate in blood in inactive form
  – Includes proteins C1–C9, factors B, D, and P, and regulatory proteins
  – Provides major mechanism for destroying foreign substances
  – Activation enhances inflammation and also directly destroys bacteria
    • Enhances both innate and adaptive defenses
Activated by antibodies coating target cell

Activated by lectins binding to specific sugars on microorganism’s surface

Activated spontaneously. Lack of inhibitors on microorganism’s surface allows process to proceed

Together with other complement proteins and factors

MACs form from activated complement components (C5b and C6–C9) that insert into the target cell membrane, creating pores that can lyse the target cell.

Opsonization:
Coats pathogen surfaces, which enhances phagocytosis

MAC:
Enhances inflammation:
Stimulates histamine release, increases blood vessel permeability, attracts phagocytes by chemotaxis, etc.

Complement proteins (C5b–C9)
Membrane of target cell
Pore

C3
C3b
C3a
C5b
C6
C7
C8
C9
C5a

Classical pathway
Lectin pathway
Alternative pathway
Part 2 – Adaptive Defenses

• **Adaptive immune system** is a *specific defensive system* that eliminates almost any pathogen or abnormal cell in body

• Activities
  – Amplifies inflammatory response
  – Activates complement

• Shortcoming: must be primed by initial exposure to specific foreign substance
  – Priming takes time
Part 2 – Adaptive Defenses

• Characteristics of adaptive immunity
  – It is **specific**:
  – It is **systemic**:
  – It has **memory**:
  – Two main branches of adaptive system
  1. **Humoral (antibody-mediated) immunity**
  2. **Cellular (cell-mediated) immunity**
21.3 Antigens

- **Antigens**: substances that can mobilize adaptive defenses and provoke an immune response
- Targets of all adaptive immune responses
- Most are large, complex molecules not normally found in body (nonself)
- Characteristics of antigens
  - Can be a **complete** antigen or **hapten** (incomplete)
  - Contain **antigentic determinants**
  - Can be a **self-antigen**
Complete Antigens and Haptens

- Antigens can be *complete* or *incomplete*
- **Complete antigens** have two important functional properties:
  - **Immunogenicity:**
  - **Reactivity:**

- **Examples:**
Haptens (incomplete antigens)

- Molecules too small to be seen so are not immunogenic by themselves
  - Examples: small peptides, nucleotides, some hormones
- May become immunogenic if hapten attaches to body’s own proteins
  - Combination of protein and hapten is then seen as foreign
- Causes immune system to mount attack that is harmful to person because it attacks self-proteins as well as hapten
  - Examples: poison ivy, animal dander, detergents, and cosmetics
Antigenic Determinants

• **Antigenic determinants**: parts of antigen that antibodies or lymphocyte receptors bind to

• Most naturally occurring antigens have numerous antigenic determinants that:
  – Mobilize several different lymphocyte populations
  – Form different kinds of antibodies against them

• Large, chemically simple molecules (such as plastics) have little or no immunogenicity
Figure 21.7 Most antigens have several different antigenic determinants.
Self-Antigens: MHC Proteins

- **Self-antigens**: all cells are covered with variety of proteins located on surface that are not antigenic to self, but may be antigenic to others in transfusions or grafts.

- One set of important self-proteins are group of glycoproteins called **MHC proteins**
  - Coded by genes of **major histocompatibility complex (MHC)** and unique to each individual
  - Contain groove that can hold piece of self-antigen or foreign antigen
  - T lymphocytes can recognize only antigens that are presented on MHC proteins
21.4 Lymphocytes and Antigen-Presenting Cells

- Adaptive immune system involves three crucial types of cells
  - Two types of **lymphocytes**
    - B lymphocytes (B cells)—humoral immunity
    - T lymphocytes (T cells)—cellular immunity
  - **Antigen-presenting cells (APCs)**
    - Do not respond to specific antigens
    - Play essential auxiliary roles in immunity
Figure 21.8 Lymphocyte development, maturation, and activation.

Adaptive defenses  
Humoral immunity  
Cellular immunity

Primary lymphoid organs  
(red bone marrow and thymus)

Secondary lymphoid organs  
(lymph nodes, spleen, etc.)

1. **Origin**
   - Both B and T lymphocyte precursors originate in red bone marrow.

2. **Maturation**
   - Lymphocyte precursors destined to become T cells migrate (in blood) to the thymus and mature there.
   - B cells mature in the bone marrow.
   - During maturation lymphocytes develop immunocompetence and self-tolerance.

3. **Seeding secondary lymphoid organs and circulation**
   - Immunocompetent but still naive lymphocytes leave the thymus and bone marrow.
   - They “seed” the secondary lymphoid organs and circulate through blood and lymph.

4. **Antigen encounter and activation**
   - When a lymphocyte’s antigen receptors bind its antigen, that lymphocyte can be activated.

5. **Proliferation and differentiation**
   - Activated lymphocytes proliferate (multiply) and then differentiate into effector cells and memory cells.
   - Memory cells and effector T cells circulate continuously in the blood and lymph and throughout the secondary lymphoid organs.
Figure 21.9 T cell education in the thymus.

1. Positive Selection

T cells **must** recognize self major histocompatibility proteins (self-MHC)

**Antigen-presenting thymic cell**

**Developing T cell**

Failure to recognize self-MHC results in **apoptosis** (death by cell suicide).

Recognizing self-MHC results in survival. Survivors proceed to negative selection.

2. Negative Selection

T cells **must not** recognize self-antigens

Recognizing self-antigen results in **apoptosis**. This eliminates self-reactive T cells that could cause autoimmune diseases.

Failure to recognize (bind tightly to) self-antigen results in survival and continued maturation.
Lymphocytes (cont.)

• **Antigen receptor diversity**
  – Genes, not antigens, determine which foreign substances the immune system will recognize
    • Variety of immune cell receptors are result of acquired genetic knowledge of microbes
  – ~25,000 different genes codes for up to a billion different types of lymphocyte antigen receptors
    • Huge variety of receptors: gene segments are shuffled around, resulting in many combinations
Antigen-Presenting Cells (APCs)

- Engulf antigens and present fragments of antigens to T cells for recognition
- Major types
  - **Dendritic cells** in connective tissues and epidermis
  - **Macrophages** - widely distributed in connective tissues and lymphoid organs
  - **B cells**
21.5 Humoral Immune Response

• When B cell encounters target antigen, it provokes *humoral immune response*
  – Antibodies specific for that particular antigen are then produced
Primary response (initial encounter with antigen)

Antigen binding to a receptor on a specific B lymphocyte (B lymphocytes with noncomplementary receptors remain inactive)

Activated B cells

Proliferation to form a clone

Plasma cells (effector B cells)

Secreted antibody molecules

Antigen

Memory B cell—primed to respond to same antigen
Figure 21.12 Primary and secondary humoral responses.

**Primary immune response** to antigen A occurs after a delay.

**Secondary immune response** to antigen A is faster and larger; **primary immune response** to antigen B is similar to that for antigen A.

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Antibody titer (antibody concentration in plasma (arbitrary units))</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>$10^4$</td>
</tr>
<tr>
<td>14</td>
<td>$10^3$</td>
</tr>
<tr>
<td>21</td>
<td>$10^2$</td>
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<td>35</td>
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<td>42</td>
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<tr>
<td>49</td>
<td>$10^{-2}$</td>
</tr>
<tr>
<td>56</td>
<td>$10^{-3}$</td>
</tr>
</tbody>
</table>

First exposure to antigen A  
Second exposure to antigen A; first exposure to antigen B
Figure 21.11-2 Clonal selection of a B cell.

Memory B cell—primed to respond to same antigen

Secondary response (can be years later)

Clone of cells identical to ancestral cells

Subsequent challenge by same antigen results in more rapid response

Plasma cells

Secreted antibody molecules

Memory B cells
Figure 21.13 Active and passive humoral immunity.

**Humoral immunity**

**Active**
- Naturally acquired
  - Infection; contact with pathogen
- Artificially acquired
  - Vaccine; dead or attenuated pathogens

**Passive**
- Naturally acquired
  - Antibodies passed from mother to fetus via placenta; or to infant in her milk
- Artificially acquired
  - Injection of exogenous antibodies (gamma globulin)
Antibodies

• **Antibodies**—also called **Immunoglobulins (Igs)**—are proteins secreted by plasma cells
  – Make up **gamma globulin** portion of blood
• Capable of binding specifically with antigen detected by B cells
• Grouped into one of five Ig classes
Figure 21.14a Antibody structure.

Adaptive defenses → Humoral immunity

Antigen-binding site

Heavy chain

Light chain

Hinge region

Stem region

(a)

Heavy chain variable region

Light chain variable region

Heavy chain constant region

Light chain constant region

Disulfide bond
Antibodies (cont.)

• Antibody targets and functions
  – Antibodies do not destroy antigens; they inactivate and tag them
    • Form antigen-antibody (immune) complexes
  – Defensive mechanisms used by antibodies
    • Neutralization
    • Agglutination
    • Precipitation
    • Complement fixation
  – OYO – Learn Table 21.5 p. 789
Adaptive defenses ➔ Humoral immunity

Antigen-antibody complex

Inactivates by

Neutralization (masks dangerous parts of bacterial exotoxins; viruses)

Agglutination (cell-bound antigens)

Precipitation (soluble antigens)

Fixes and activates

Complement

Enhances

Phagocytosis

Inflammation

Cell lysis

Enhances

Enzymes

Chemotaxis

Histamine release

Leads to

Phagocytosis

Inflammation

Cell lysis

Chemotaxis

Histamine release

1/25/2016

MDufilho
Parasitic infections by worms such as *Ascaris* and *Schistosoma* require different immune attack strategies

- Worms are too big for regular PLAN attack (Precipitation, Lysis (by complement), Agglutination, or Neutralization)

**IgE** antibodies still play a critical role in worm’s destruction by binding to surface of worm, marking it for destruction by eosinophils

Eosinophils bind to exposed stems of **IgE**, which triggers eosinophils to release their toxic contents onto prey, lysing it from the outside
Clinical – Homeostatic Imbalance 21.2

- Monoclonal antibodies as clinical and research tools
  - Monoclonal antibodies: commercially prepared pure antibodies that are specific for a single antigenic determinant
  - Produced by hybridomas, cell hybrids formed from fusion of tumor cell and B cell
    - Tumor cell portion allows cells to proliferate indefinitely, while B cell portion allows production of single type of antibody
  - Used in research, clinical testing, and cancer treatment
• Summary of antibody actions
  – Antigen-antibody complexes do not destroy antigens; they prepare them for destruction by innate defenses
  – Antibodies go after extracellular pathogens; they do not invade solid tissue unless lesion is present
    • Recent exception found: antibodies can act intracellularly if attached to virus before it enters cell
      – Activate mechanisms that destroy virus
• T cells provide defense against intracellular antigens
• Some T cells directly kill cells; others release chemicals that regulate immune response
• T cells are more complex than B cells both in classification and function
• Two populations of T cells are based on which cell differentiation glycoprotein receptors are displayed on their surface
21.6 Cellular Immune Response

- **CD4 cells** usually become **helper T cells** ($T_H$) that can activate B cells, other T cells, and macrophages; direct adaptive immune response
  - Some become **regulatory T cells**, which moderate immune response
  - Can also become memory T cells

- **CD8 cells** become **cytotoxic T cells** ($T_C$) that are capable of destroying cells harboring foreign antigens
  - Also become memory T cells
Figure 21.16 Major types of T cells.

Adaptive defenses → Cellular immunity

Imature lymphocyte

Red bone marrow

Thymus

Class II MHC protein displaying antigen

CD4 cell

T cell receptor

Maturation

T cell receptor

Class I MHC protein displaying antigen

CD8 cell

APC (dendritic cell)

Activation

Memory cells

CD4

Lymphoid tissues and organs

Effector cells

CD4 cells become either helper T cells or regulatory T cells

CD8 cells become cytotoxic T cells

Blood plasma

APC (dendritic cell)

1/25/2016
MHC Proteins and Antigen Presentation (cont.)

- Two classes of MHC proteins:
  - **Class I MHC proteins**: displayed by all cells except RBCs
  - **Class II MHC proteins**: displayed by APCs (dendritic cells, macrophages, and B cells)

- Both types are synthesized in ER and bind to peptide fragments
### Table 21.6 Role of MHC Proteins in Cellular Immunity

<table>
<thead>
<tr>
<th>Class I MHC Proteins</th>
<th>Class II MHC Proteins</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Displayed by</strong></td>
<td>All nucleated cells</td>
</tr>
<tr>
<td><strong>Recognized by</strong></td>
<td>Naive CD8 cells and cytotoxic T cells</td>
</tr>
<tr>
<td></td>
<td>Naive CD4 cells and helper T cells</td>
</tr>
<tr>
<td><strong>Foreign antigens on MHC are</strong></td>
<td>Endogenous (intracellular pathogens or proteins made by cancerous cells)*</td>
</tr>
<tr>
<td></td>
<td>Exogenous (phagocytized extracellular pathogens)</td>
</tr>
<tr>
<td><strong>Cells displaying foreign antigens on MHC send this message</strong></td>
<td>If the cell is an APC: “I belong to self, but have captured a foreign invader. This is what it looks like. Kill any cell that displays it.”</td>
</tr>
<tr>
<td></td>
<td>“I belong to self, but have captured a foreign invader. This is what it looks like. Help me mount a defense against it.”</td>
</tr>
<tr>
<td></td>
<td>If the cell is not an APC: “I belong to self, but have been invaded or become cancerous. Kill me!”</td>
</tr>
</tbody>
</table>

*Dendritic cells are an exception because they can present another cell’s endogenous antigens on their class I MHC proteins to activate CD8 cells.*
Activation and Differentiation of T cells

• T cells can be activated only when antigen is presented to them
• Activation is a two-step process
  1. Antigen binding
  2. Co-stimulation
• Both occur on surface of same APC
• Both are required for clonal selection of T cell
Figure 21.17 Clonal selection of T cells involves simultaneous recognition of self and nonself.

Adaptive defenses ➔ Cellular immunity

1. **Antigen presentation**
   - Dendritic cell engulfs an exogenous antigen, processes it, and displays its fragments on class II MHC protein.

2. **Double recognition**
   2a. CD4 T cell recognizes antigen-MHC complex. Both TCR and CD4 proteins bind to antigen-MHC complex.
   2b. Co-stimulatory molecules bind their receptors.

3. **Clone formation**
   - Activated CD4 T cells proliferate (clone), and become memory and effector cells.

Bacterial antigen

Class II MHC protein displaying processed bacterial antigen

Co-stimulatory molecule

Dendritic cell

CD4 protein

T cell receptor (TCR)

Co-stimulatory molecule receptor

Clone formation

Memory CD4 T cell

Helper T cells
Activation and Differentiation of T cells

- **Cytokines** - Chemical messengers of immune system
  - Mediate cell development, differentiation, and responses in immune system
  - Include interferons and interleukins
    - **Interleukin 1 (IL-1)** is released by macrophages and stimulates T cells to release interleukin 2 (IL-2)
    - IL-2 is a key growth factor, acting on same cells that release it and other T cells to divide rapidly
  - Other cytokines amplify and regulate innate and adaptive responses
    - Example: gamma interferon—enhances killing power of macrophages
Roles of Specific Effector T Cells

• **Helper T (T_H) cells**
  – Play central role in adaptive immune response
  – Activate both humoral and cellular arms
  – Once primed by APC presentation of antigen, helper T cells:
    • Help activate B cells and other T cells
    • Induce T and B cell proliferation
    • Secrete cytokines that recruit other immune cells

• **Without T_H, there is no immune response**
Figure 21.18 The central role of helper T cells in mobilizing both humoral and cellular immunity.

(a) Helper T cells help in humoral immunity

1. $T_H$ cell binds with the self-nonself complexes of a B cell that has encountered its antigen and is displaying it on MHC II on its surface.
2. $T_H$ cell releases interleukins as co-stimulatory signals to complete B cell activation.

(b) Helper T cells help in cellular immunity

1. $T_H$ cell binds dendritic cell.
2. $T_H$ cell stimulates dendritic cell to express co-stimulatory molecules.
3. Dendritic cell can now activate CD8 cell with the help of interleukin 2 secreted by $T_H$ cell.
Cytotoxic T cells attack infected and cancerous cells.

**Adaptive defenses → Cellular immunity**

1. $T_C$ identifies foreign antigens on MHC I proteins and binds tightly to target cell.
2. $T_C$ releases **perforin** and **granzyme** molecules from its granules by exocytosis.
3. Perforin molecules insert into the target cell membrane, polymerize, and form transmembrane pores (cylindrical holes) similar to those produced by complement activation.
4. Granzymes enter the target cell via the pores. Once inside, granzymes activate enzymes that trigger apoptosis.
5. The $T_C$ detaches and searches for another prey.

**(a) A mechanism of target cell killing by $T_C$ cells.**
Roles of Specific Effector T Cells (cont.)

– Subsets of $T_H$ cells

• $T_H1$—mediates most aspects of cellular immunity

• $T_H2$—defends against parasitic worms, mobilizes eosinophils; activates responses dependent on humoral immunity; promotes allergies

• $T_H17$—links adaptive and innate immunity by releasing IL-17
  – May play role in autoimmune disease
Roles of Specific Effector T Cells (cont.)

• Cytotoxic T (T_C) cells (cont.)
  – Natural killer cells recognize other signs of abnormality that cytotoxic T cells do not look for, such as:
    • Cells that lack class I MHC proteins
    • Antibodies coating target cell
    • Different surface markers seen on stressed cells
  – NK cells use same key mechanisms as T_C cells for killing their target cells
  – **Immune surveillance:** NK and T_C cells prowl body looking for markers they each recognize
Roles of Specific Effector T Cells (cont.)

- Regulatory T (TReg) cells
  - Dampen immune response by direct contact or by secreting inhibitory cytokines such as IL-10 and transforming growth factor beta (TGF-β)
  - Important in preventing autoimmune reactions
    - Suppress self-reactive lymphocytes in periphery (outside lymphoid organs)
    - Research into using them to induce tolerance to transplanted tissue
Figure 21.20 Simplified summary of the primary immune response.
Organ Transplants and Prevention of Rejection

- Most common type of organ transplant is an *allograft*: transplant from same species
- Success depends on similarity of tissues
  - ABO, other blood antigens, and MHC antigens are matched as closely as possible
- After surgery
  - Patient treated with immunosuppressive therapy
  - Many of these therapies have severe side effects
12.7 Immune Problems

Immunodeficiencies

- Congenital or acquired conditions that impair function or production of immune cells or molecules
  - Severe combined immunodeficiency (SCID) syndrome: genetic defect with marked deficit in B and T cells
    - Defective adenosine deaminase (ADA) enzyme allows accumulation of metabolites lethal to T cells; fatal if untreated
  - Hodgkin’s disease is an acquired immunodeficiency that causes cancer of B cells, which depresses lymph node cells and thus leads to immunodeficiency
Immunodeficiencies (cont.)

• Acquired immune deficiency syndrome (AIDS) caused by Human immunodeficiency virus (HIV)
  – cripples immune system by interfering with activity of helper T cells

• HIV is transmitted via body fluids: blood, semen, and vaginal secretions

• HIV can enter the body via:
  – Blood transfusions; blood-contaminated needles; sexual intercourse and oral sex; mother to fetus

• HIV destroys $T_H$ cells, thereby depressing cellular immunity
Autoimmune Diseases

- **Autoimmune disease** results when immune system loses ability to distinguish self from foreign

- **Autoimmunity**: production of autoantibodies and sensitized \( T_C \) cells that destroys body tissues

- Examples
  - Rheumatoid arthritis: destroys joints
  - Myasthenia gravis: impairs nerve-muscle connections
  - Multiple sclerosis: destroys white matter myelin
  - Graves’ disease: causes hyperthyroidism
  - Type 1 diabetes mellitus: destroys pancreatic cells
  - Systemic lupus erythematosus (SLE): affects multiple organs
  - Glomerulonephritis: damages kidney
Hypersensitivities

- **Hypersensitivities**: immune responses to perceived (otherwise harmless) threat that cause tissue damage
- Different types are distinguished by:
  1. Their time course
  2. Whether antibodies or T cells are involved
- Antibodies cause **immediate** and **subacute hypersensitivities**
- T cells cause **delayed hypersensitivity**
Hypersensitivities (cont.)

- **Immediate hypersensitivity**
  - Also called *acute (type I) hypersensitivities* (*allergies*); begin in seconds after contact with *allergen*, antigen that causes allergic reaction
  - Initial contact with allergen is asymptomatic but sensitizes person
  - Activated IgE against antigen binds to mast cells and basophils
  - Later encounter with same allergen causes flood of histamine release from IgE, resulting in induced inflammatory response
Figure 21.21 Mechanism of an acute allergic (immediate hypersensitivity) response.

**Sensitization stage**

1. Antigen (allergen) invades body.
2. Plasma cells produce large amounts of class IgE antibodies against allergen.
3. IgE antibodies attach to mast cells in body tissues (and to circulating basophils).

**Subsequent (secondary) responses**

4. More of same antigen invades body.
5. Antigen combines with IgE attached to mast cells (and basophils), which triggers degranulation and release of histamine (and other chemicals).
6. Histamine causes blood vessels to dilate and become leaky, which promotes edema; stimulates secretion of large amounts of mucus; and causes smooth muscles to contract. (If respiratory system is site of antigen entry, asthma may ensue.)

- Outpouring of fluid from capillaries
- Release of mucus
- Constriction of small respiratory passages (bronchioles)
Hypersensitivities (cont.)

• Subacute hypersensitivities
  – Caused by IgM and IgG transferred via blood plasma or serum
  – Slow onset (1–3 hours) and long duration (10–15 hours)
  – Cytotoxic (type II) reactions
    • Antibodies bind to antigens on specific body cells, stimulate phagocytosis and complement-mediated lysis of cellular antigens
    • Example: mismatched blood transfusion reaction
Hypersensitivities (cont.)

- Subacute hypersensitivities (cont.)
  - Immune complex (type III) hypersensitivity
    - Antigens widely distributed in body or blood
    - Insoluble antigen-antibody complexes form
    - Complexes cannot be cleared from particular area of body
    - Intense inflammation, local cell lysis, and cell killing by neutrophils
    - Example: systemic lupus erythematosus (SLE)
• **Delayed hypersensitivities (type IV)**
  – Slow onset (1–3 days)
  – Mechanism depends on helper T cells
  – Cytokine-activated macrophages and cytotoxic T cells cause damage
  – Example: allergic contact dermatitis (e.g., poison ivy)
  – Agents act as haptens
  – TB skin test depends on this reaction
Developmental Aspects of Immune System

- Immune system stem cells develop in liver and spleen in weeks 1–9
- Bone marrow becomes primary source of stem cells later and through adult life
- Lymphocyte development continues in bone marrow and thymus
- $T_H2$ lymphocytes predominate in newborn; $T_H1$ system educated as person encounters antigens
• Influences on immune system function
  – Nervous system: depression, emotional stress, and grief impair immune response
  – Diet: vitamin D is required for activation of CD8 cells → TC cells
Developmental Aspects of Immune System

• With age, immune system begins to wane
  – Greater susceptibility to immunodeficiency and autoimmune diseases
  – Greater incidence of cancer
  – Why immune system fails is unknown, but may be due to atrophy of thymus and decreased production of naive T and B cells