

# Vertebrate Immunity

## I. Introduction

- Immunity = ability to recognize and protect against nonself
- Many eukaryotic parasites cause chronic infections
- Cannot be cleared by host immune system; evade immune responses
- Damage associated with parasitic infection often results largely or partly from host's immune response to chronic exposure to parasite antigens
- Resistance may be incomplete:
  - Premunition:** presence of parasite induces immune response that conveys resistance to further infection; parasite remains alive but its reproduction and other activities are restrained.
  - Concomitant Immunity:** presence of parasite induces immune response that conveys resistance to further infection; parasite eliciting response is unaffected

# Vertebrate Immunity

## II. Types of Immunity

### A. Acquired immunity

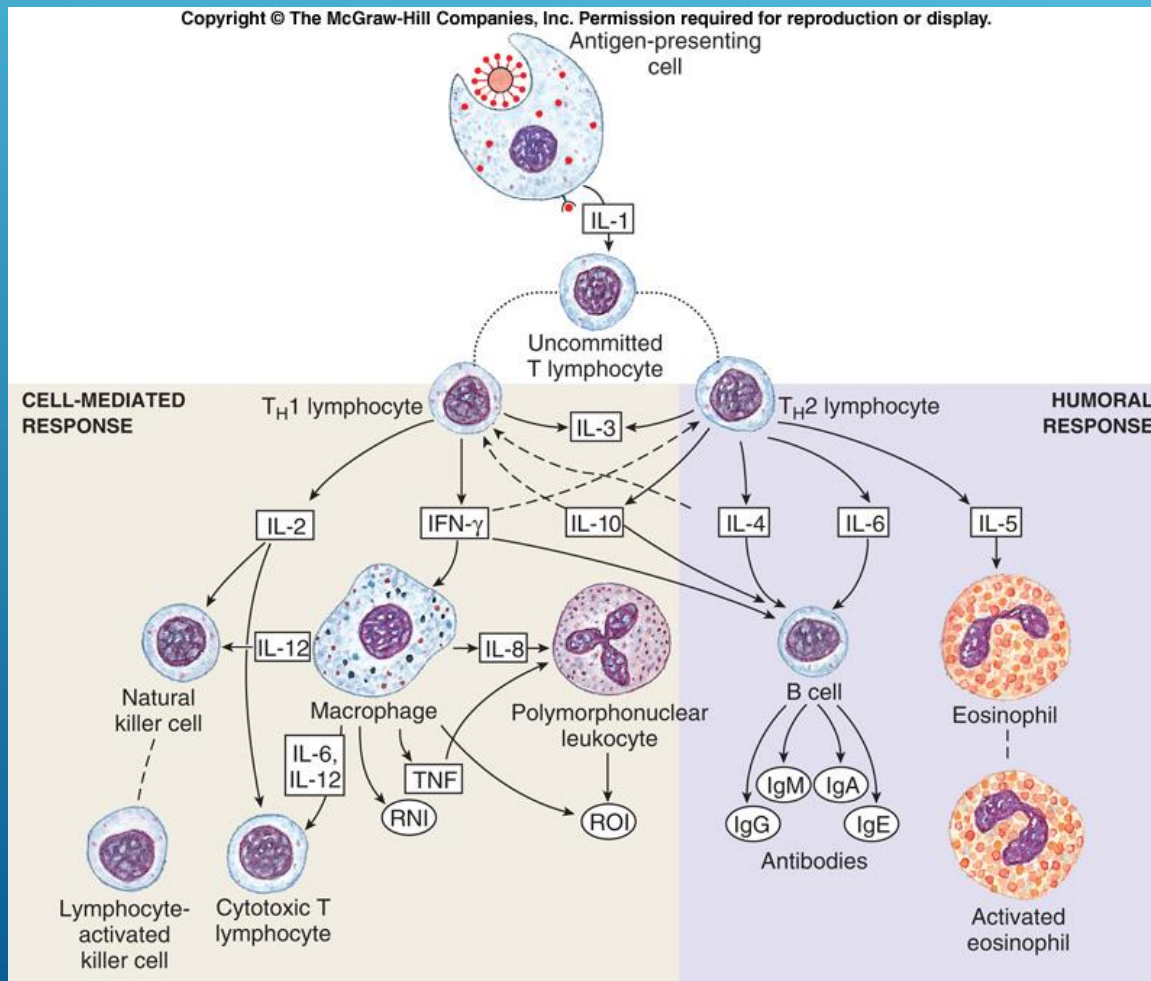
- specific to particular non-self material
- requires prior exposure to invader
- requires time for development during 1<sup>st</sup> exposure
- occurs more rapidly and vigorously on 2<sup>nd</sup> exposure

# Vertebrate Immunity

## II. Types of Immunity

### A. Acquired immunity


1. **Humoral immune response:** involves B-cells & T-cells, and antibodies
2. **Cell mediated immune response:** involves T-cells, no antibodies



# Vertebrate Immunity

## II. Types of Immunity

### B. Innate immunity:

- not specific for one particular pathogen
  - does not require prior exposure
  - occurs rapidly and vigorously with each exposure
  - dramatically influenced and strengthened as a consequence of acquired immune responses.
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# Immunity

## III. Cells of Immune System

### A. Phagocytes

#### 1. function

- can recognize nonself: (recognize microbial molecules)
- carry out phagocytosis

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# Immunity

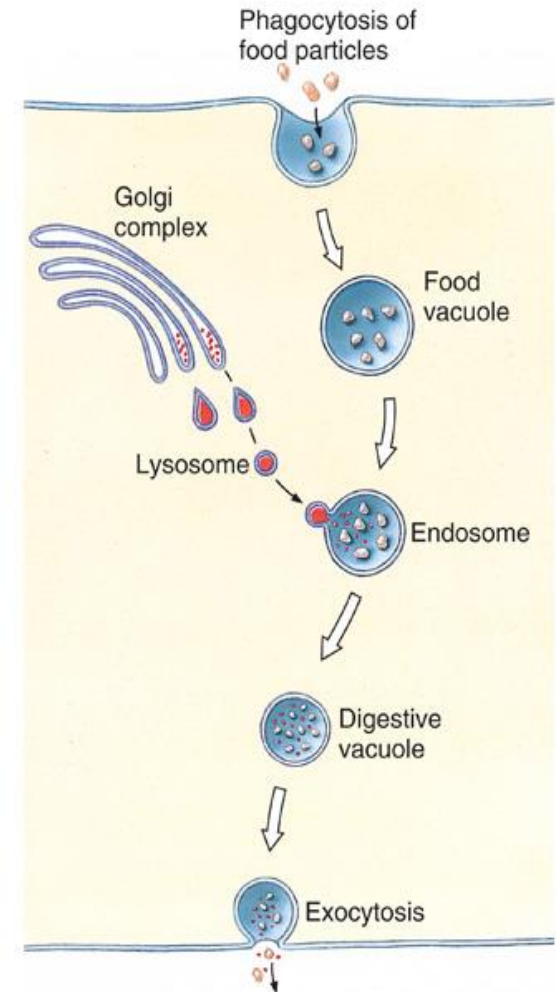
## III. Cells of Immune System

### A. Phagocytes

#### 1. function

- produce lysosomes that release:
  - digestive enzymes
  - enzymes that catalyze production of **cytotoxic compounds**:
    - reactive oxygen intermediates (**ROIs**)  
 $\text{H}_2\text{O}_2$ ,  $\text{O}\cdot$  and  $\text{OH}\cdot$  radicals
    - reactive nitrogen intermediates (**RNIs**)  
nitric oxide (NO), nitrite, nitrate

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# Immunity

## III. Cells of Immune System

### A. Phagocytes

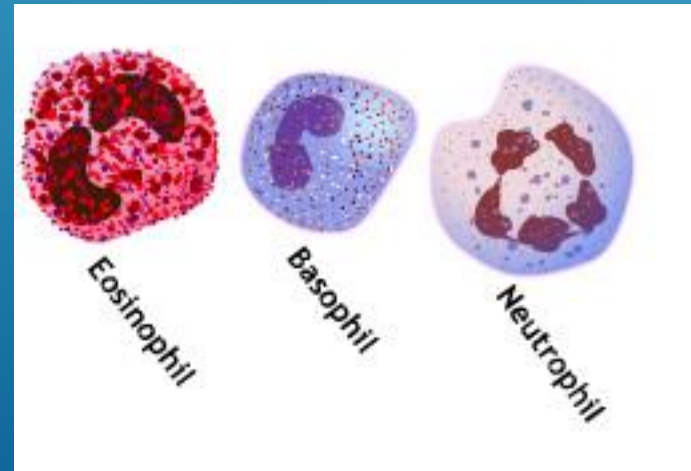
#### 2. categories of phagocytes

##### a. **Mononuclear phagocyte system** (“fixed” phagocytes)

- develop from **monocytes** that arise from stem cells in bone marrow
- can produce **cytokines** (hormones that affect other cells of immune system)
- leave bloodstream and become stationed in different regions throughout body (not circulating)
- in lymph nodes, spleen, lung = **macrophages**
- in liver = **Kupffer cell**
- in CNS = **microglial cells**

##### b. **Polymorphonuclear leukocytes**

- circulating phagocytes in blood; also called **granulocytes**
- **neutrophils**: most abundant; first line of defense
- **eosinophils**:
- **basophils**:



# Immunity

## III. Cells of Immune System

### A. Phagocytes

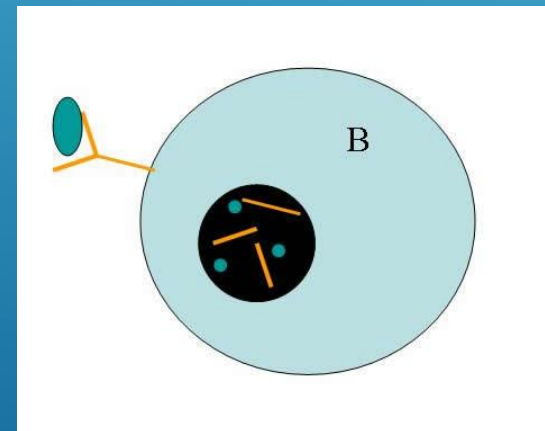
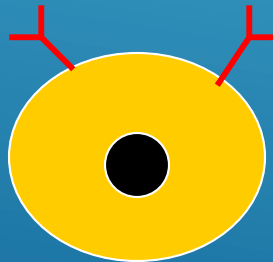
### B. Lymphocytes

#### 1. B cells

- mature in bone marrow
- produce antibodies; have antibody receptors on cell surface
- can recognize nonself

a. **Plasma cells:** produce large amounts of specific antibody, then die

b. **Memory B cells:** long lived; produce specific antibody rapidly upon 2<sup>nd</sup> exposure





# Immunity

## III. Cells of Immune System

### A. Phagocytes

### B. Lymphocytes

#### 1. B cells

#### 2. T cells

-- mature in thymus gland

-- have T-cell receptors; can recognize nonself

-- produce cytokines (as can macrophages); activate transcription factors in target cells

- **Interleukins:** activate macrophages and lymphocytes
- **Tumor necrosis factor (TNF):** mediates inflammation; fever
- **Interferon –  $\gamma$  (INF- $\gamma$ ):** activates endothelial cells to allow lymphocytes and phagocytes to pass through wall of vessel; activates macrophages

# Immunity

## III. Cells of Immune System

### A. Phagocytes

### B. Lymphocytes

#### 1. B cells

#### 2. T cells

##### a. T-helper cells ( $T_H$ )

- have coreceptor protein **CD4** and **CD28**; costimulatory molecules
- **$T_H1$**  active in cell-mediated immunity
- **$T_H2$**  active in humoral immunity

##### b. Cytotoxic T lymphocytes

- have coreceptor protein **CD8**
- bind with target cell and secrete protein that causes pores in membrane  
→ **lysis**

##### c. T-suppressor cells

- inhibit other T- and B-cells and suppress immune responses

##### d. T-memory cells

- long lived; activated during 2<sup>nd</sup> exposure

# Immunity

## III. Cells of Immune System

### A. Phagocytes

### B. Lymphocytes

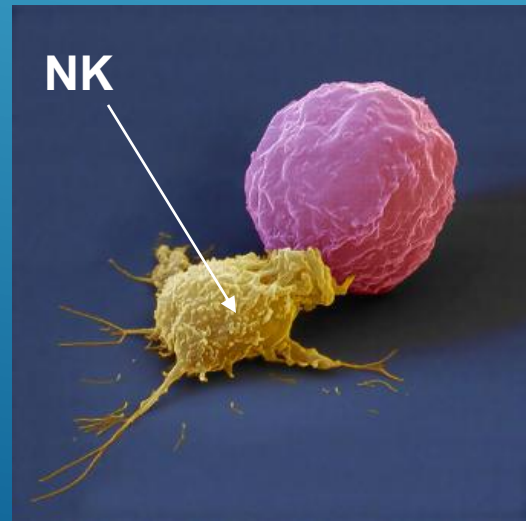
### C. Mast cells

- basophil-like cells; not phagocytic
- when activated release histamines, serotonin, etc.
- involved in inflammation response and allergies

### D. Natural Killer (NK) cells

- lymphocyte-like cells
- kill infected cells (lysis)
- some respond to antibodies; involved in humoral response
- some respond to cytokines = lymphocyte activated killer (**LAK**) cells; involved in cell mediated immune response

Mast cell



# Immunity

## IV. Complement

-- series of proteins activated in a sequence in response to invading pathogen

### A. Classical pathway

- depends upon antibodies bound to surface of pathogen (complement proteins interact with bound Ab)
- causes **lysis** and stimulates phagocytosis

### B. Alternative pathway

- not antibody dependent (complement proteins interact with polysaccharides in outer surface of pathogen)
- causes **lysis** and stimulates phagocytosis

Note: host's own cells are not lysed because regulatory proteins inactivate the first component of complement when it binds to host cells.



# Immunity

## V. Basis of Self/Non-self Recognition

### A. **Major histocompatibility complex (MHC)**

- group of genes that code for proteins embedded in cell surfaces
- MHC proteins among most variable known; each individual is unique

### B. Types of MHC proteins

1. **Class I:** found on surface of virtually all cells
2. **Class II:** found primarily on macrophages and lymphocytes



# Immunity

## VI. Recognition Molecules

### A. **Antibodies = immunoglobulins**

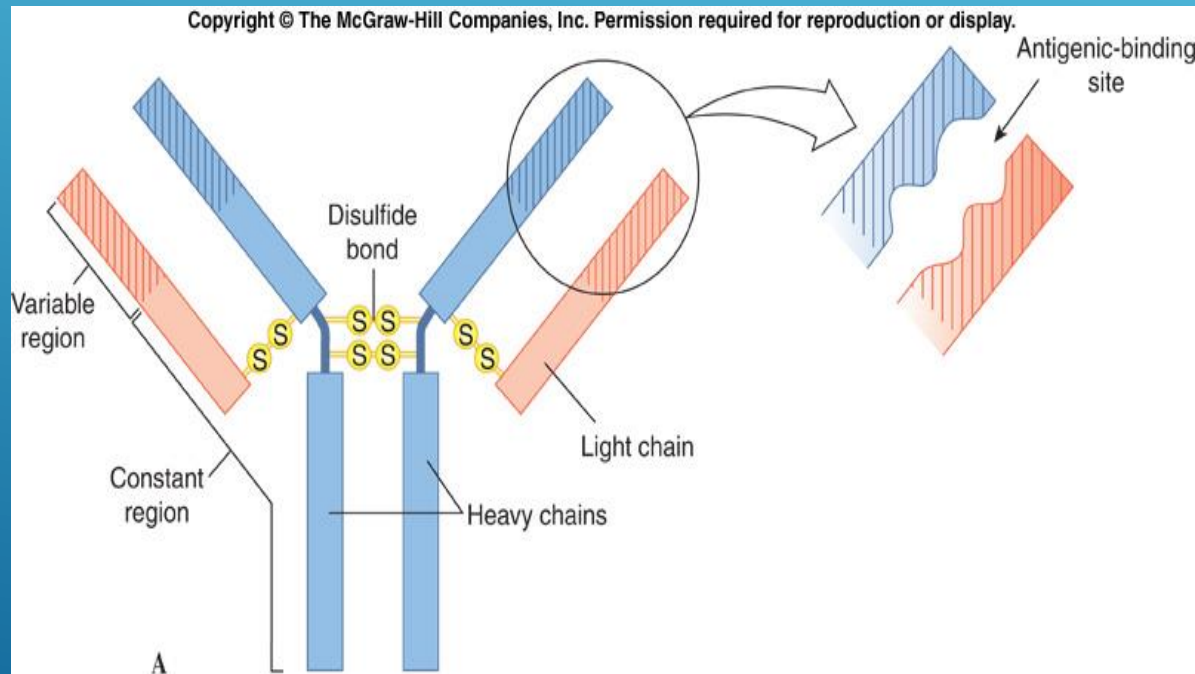
- each individual produces an enormous variety of antibodies
- each antibody binds with only one specific type of **antigen**
- occur on surface of B cells or secreted into blood by plasma cells
- $10^{11}$  types of antibody receptors; results from two **Recombination Activating Genes**, RAG 1 & 2, that rearrange gene segments during development

#### 1. Structure

a. 2 heavy chains,  
2 light chains

b. **Variable region**  
(Fab)

- *highly variable*
- forms antigen-binding site
- determines which antigen can bind



# Immunity

## VI. Recognition Molecules

### A. **Antibodies = immunoglobulins**

#### 1. Structure

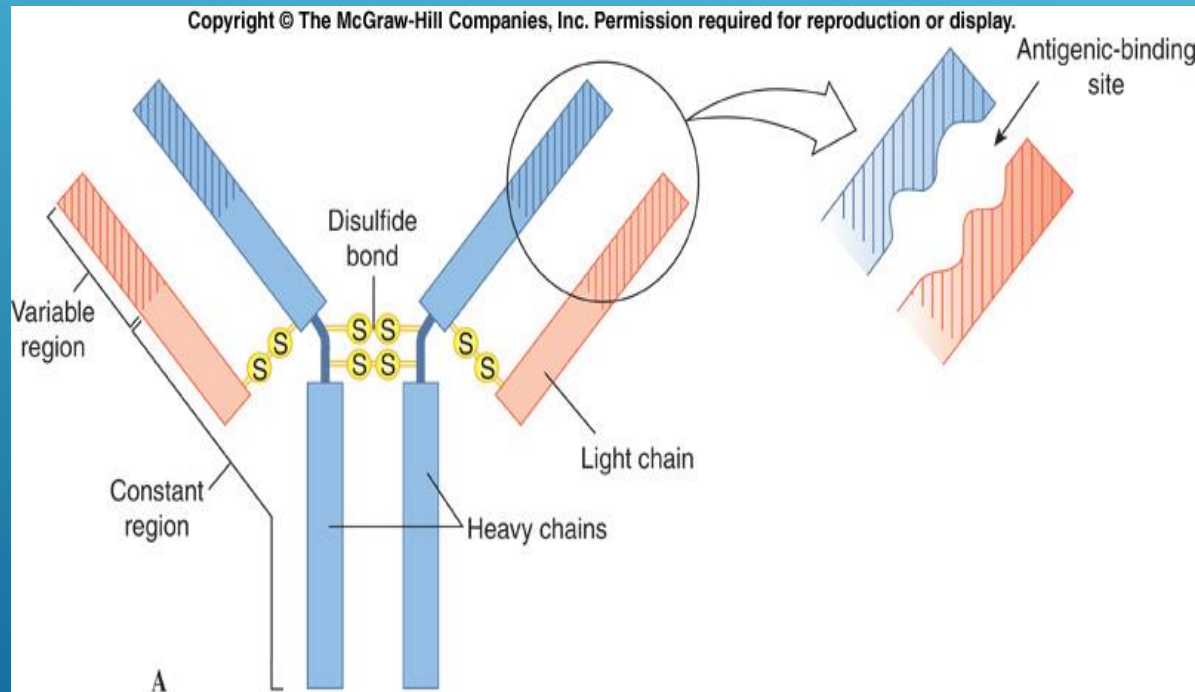
##### c. **Constant region**

(Fc)

-- determines  
class of Ab

- IgM
- IgG
- IgA
- IgE

-- class determines  
what happens once  
Ab binds with  
antigen



# Immunity

## VI. Recognition Molecules

### A. **Antibodies = immunoglobulins**

#### 2. Function

-- Fab regions bind with one particular antigen; label invader for elimination

-- method of elimination depends on projecting Fc region

- Recognized by macrophage → phagocytosis = **opsonization** (IgG)
- Activates classical pathway of complement → lysis
- **Antibody-dependent, cell-mediated cytotoxicity** (ADCC)

-- neutrophils, eosinophils, natural killer cells have receptors for Fc regions of bound Ab

-- phagocytize and/or adhere to pathogen and release cytotoxic compounds

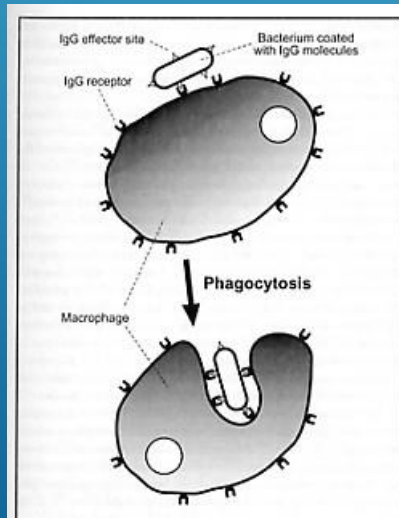
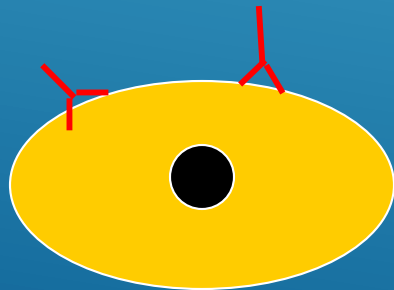
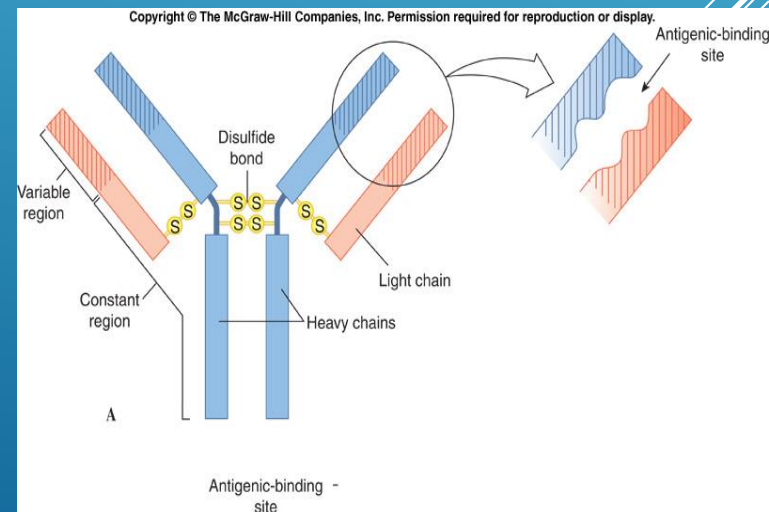


Fig. 15.8. Phagocytosis of a bacterium coated with immunoglobulin IgG molecules (modified and redrawn from Becker and Deamer<sup>35</sup>).





# Immunity

## VI. Recognition Molecules

### B. T-cell receptors

-- each individual produces an enormous variety of T-cell receptors

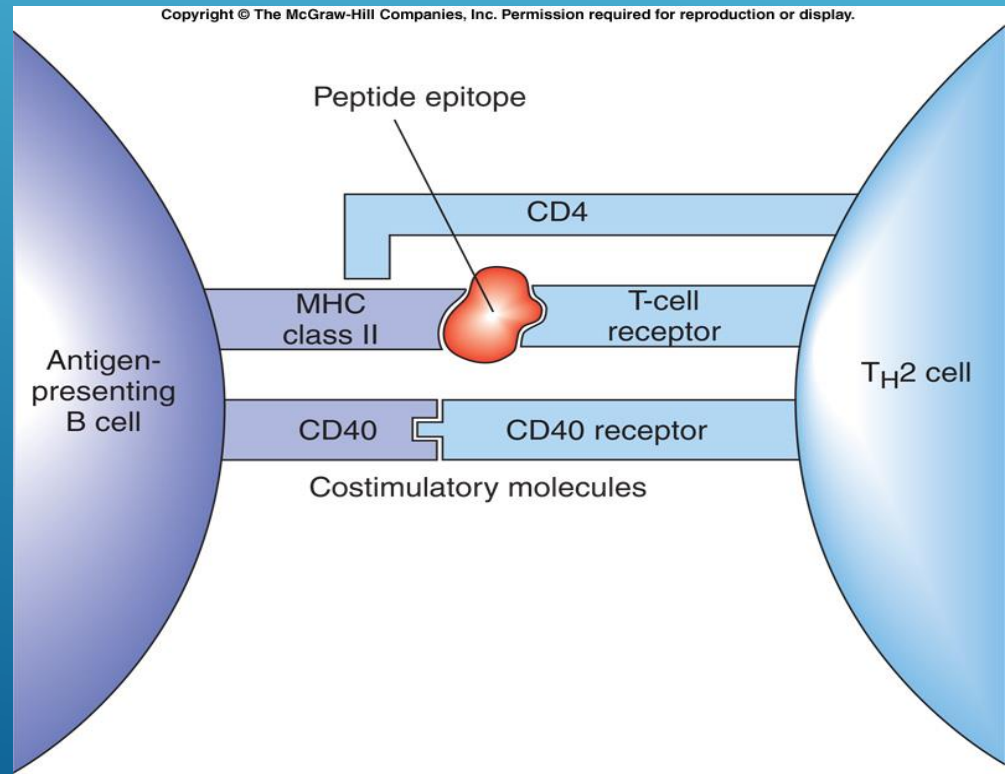
#### 1. structure

-- each receptor has variable region and constant region

-- variable region binds with only one specific type of **antigen**

-- occur on surface of T cells (constant region is transmembrane)

-- have associated **coreceptors** (also transmembrane) & costimulatory molecules



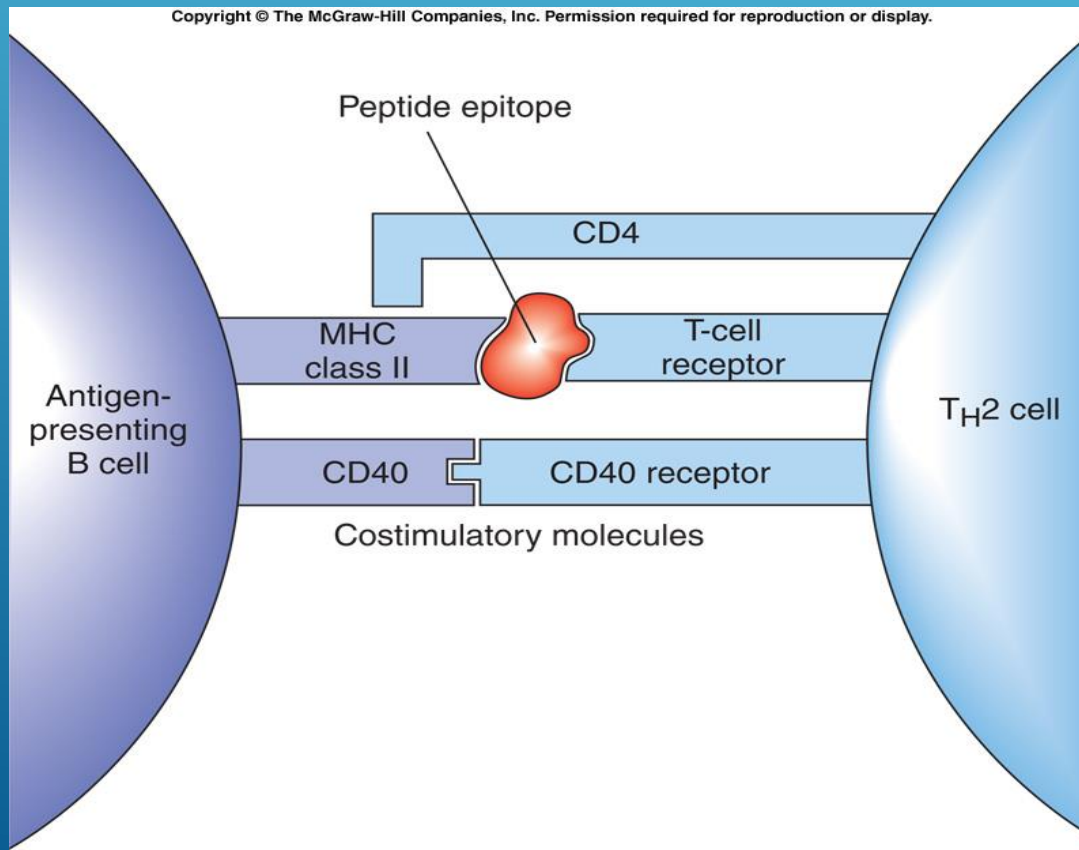
# Immunity

## VI. Recognition Molecules

### B. T-cell receptors

#### 2. function

- T-cell receptor binds to antigen (**epitope**); coreceptor binds with MHC class II
- transmit signals into T cell; cytokines produced



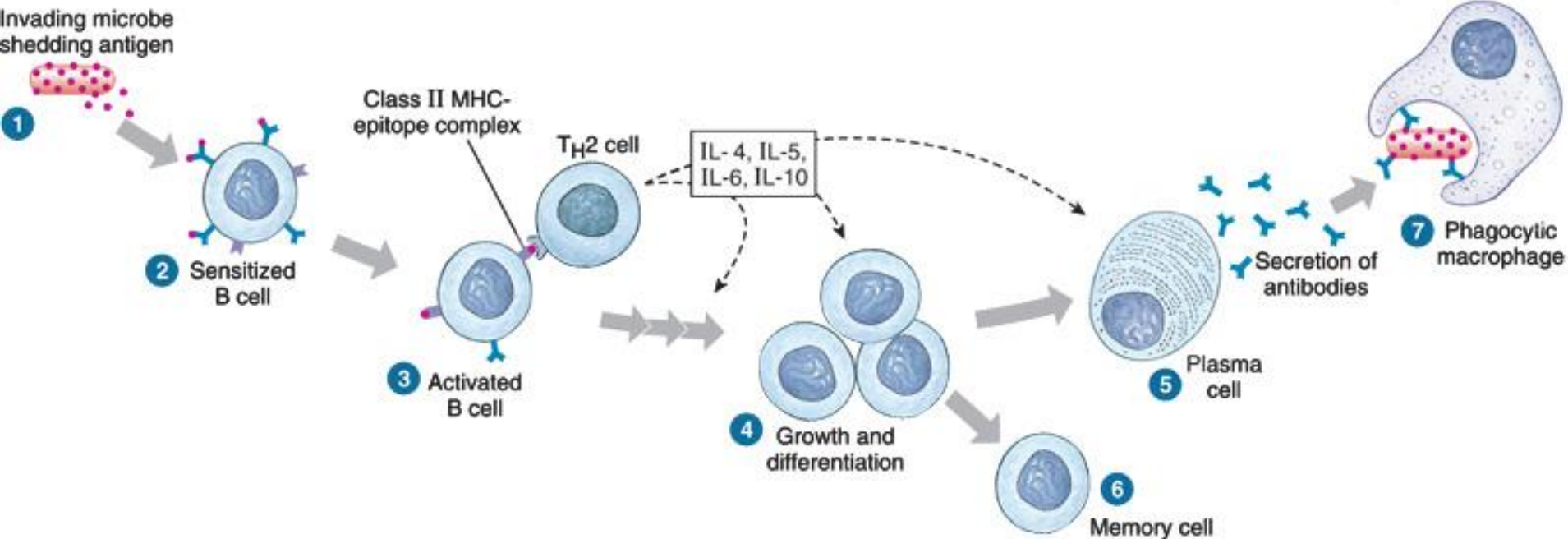
# Immunity

## VII. Acquired Immune Response

### A. Humoral immune response

1. B cell with appropriate Ab on surface binds with antigen
  - internalizes Ab-antigen complex
  - moves portion of antigen (**epitope**) to cleft in MHCII protein on its own surface (= **antigen presenting cell** or APC)
  - is now a sensitized B cell

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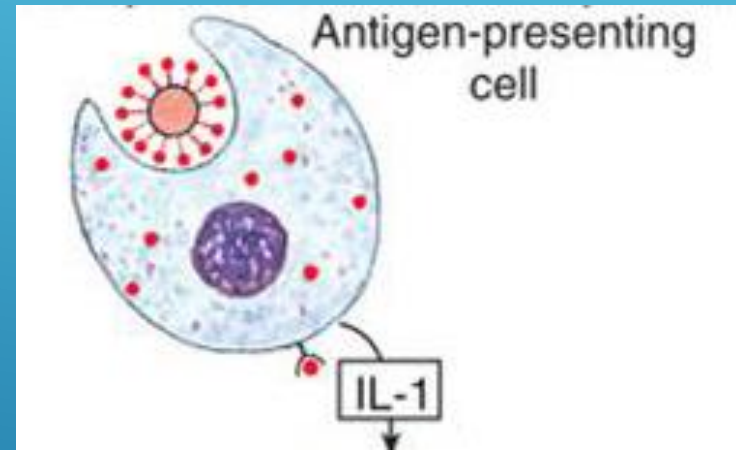
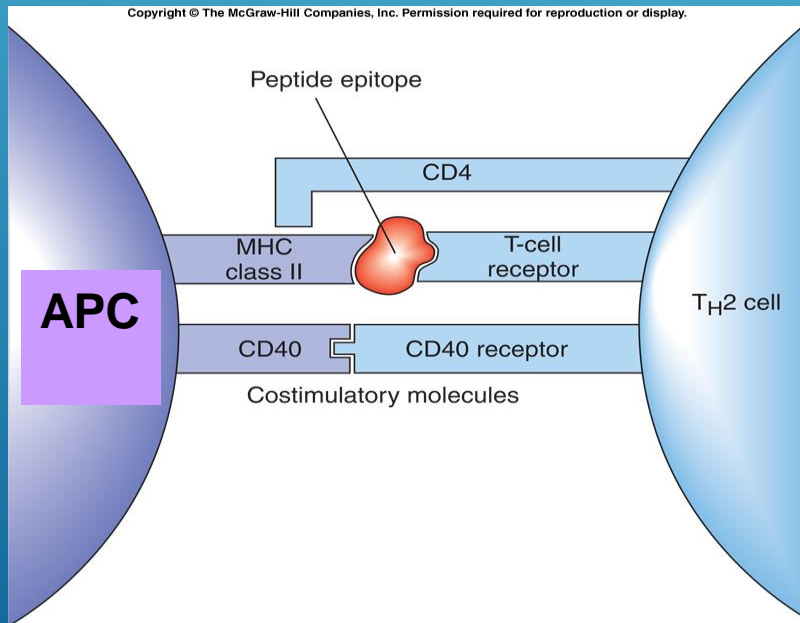
# Immunity

## VII. Acquired Immune Response

### A. Humoral immune response

1. Simultaneously, a macrophage engulfs antigen and presents epitope in cleft of MHC-II protein

- recognized by TH cell with T-cell receptor for specific antigen
- secretes IL-1; contributes to activation of T<sub>H</sub>2 cells



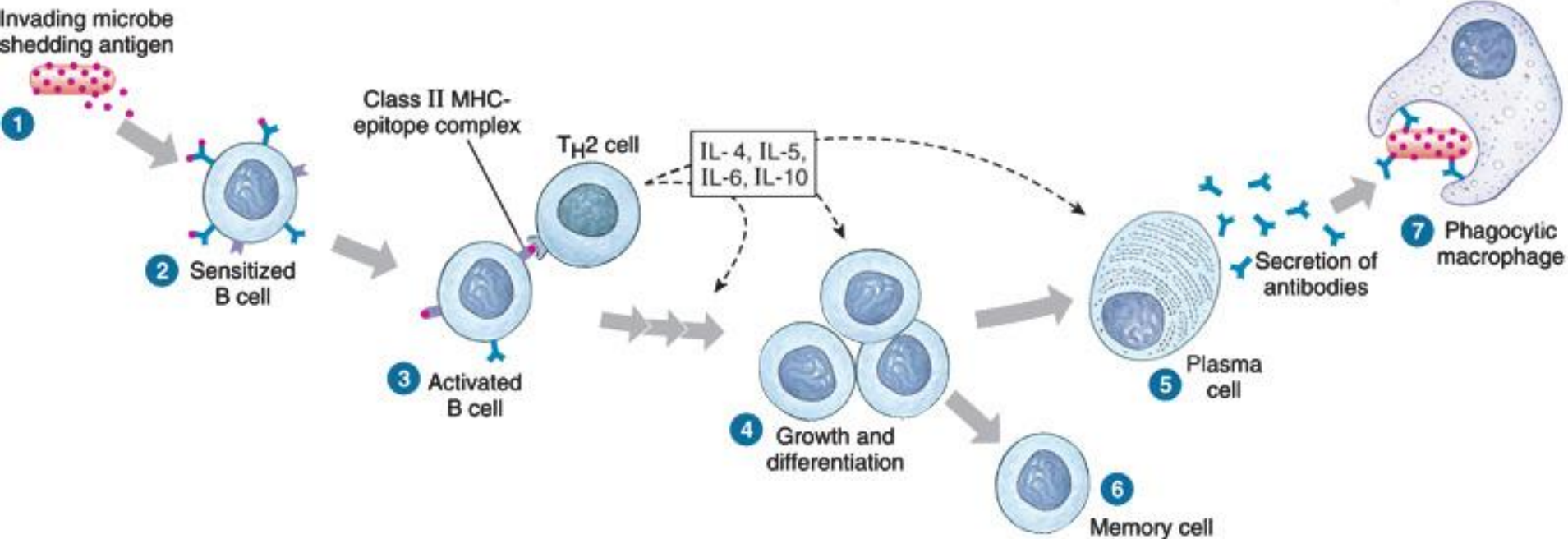
# Immunity

## VII. Acquired Immune Response

### A. Humoral immune response

2. activated TH2 with receptor for the specific epitope recognizes epitope bound to MHCII on sensitized B cell  
-- T-cell receptor binds with epitope-MHCII complex; CD4 coreceptor binds with MHCII

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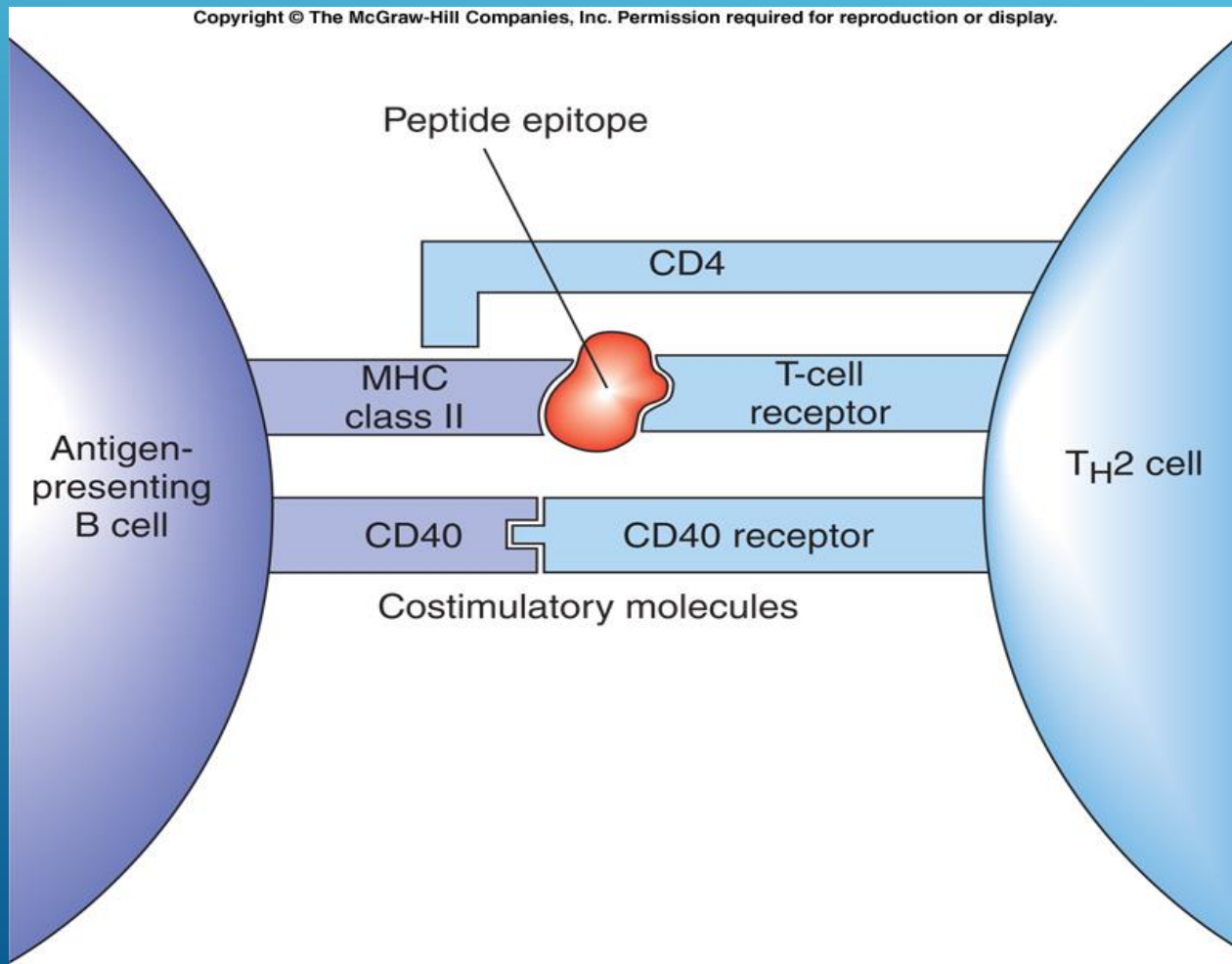
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## VII. Acquired Immune Response

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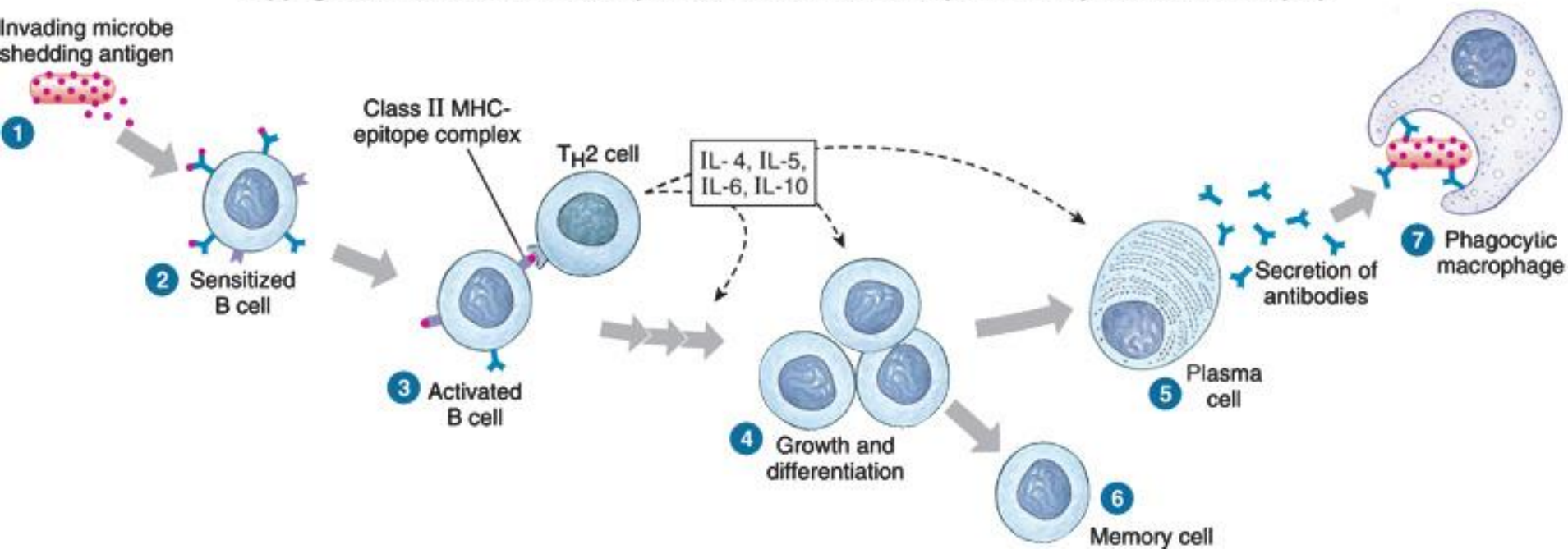
# Immunity

## VII. Acquired Immune Response

### A. Humoral immune response

2. activated TH2 with receptor for the specific epitope recognizes epitope bound to MHCII on B cell
  - T-cell receptor binds with epitope-MHCII complex; CD4 coreceptor binds with MHCII
  - TH2 secretes IL-4, IL-5, IL-6, IL-10
3. Interleukins activate B cells with same epitope and MHCII protein on surface (B cell moves from recognition phase to proliferation phase)

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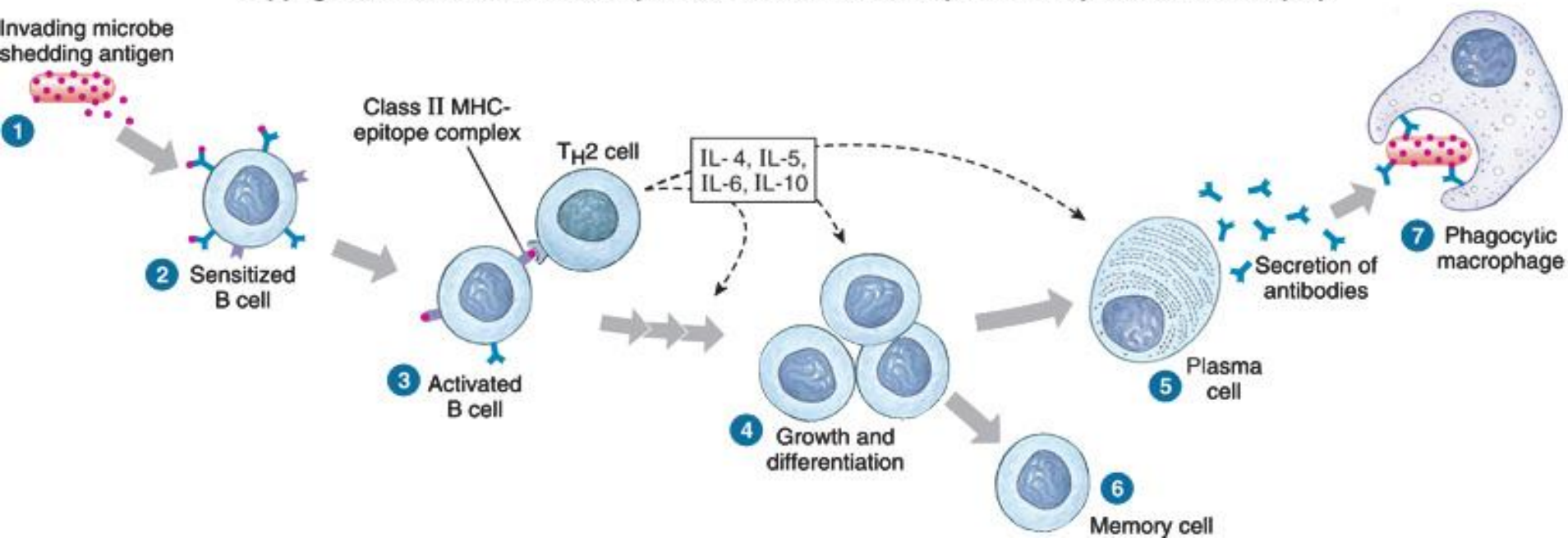
# Immunity

## VII. Acquired Immune Response

### A. Humoral immune response

4. activated B cell multiplies rapidly producing many plasma cells & memory B cells
5. Plasma cells secrete large quantities of antibody specific for the particular antigen
6. antibodies bind to antigen; trigger opsonization, classical complement, ADCC
7. memory B cells give rapid, vigorous Ab response to subsequent exposure to antigen

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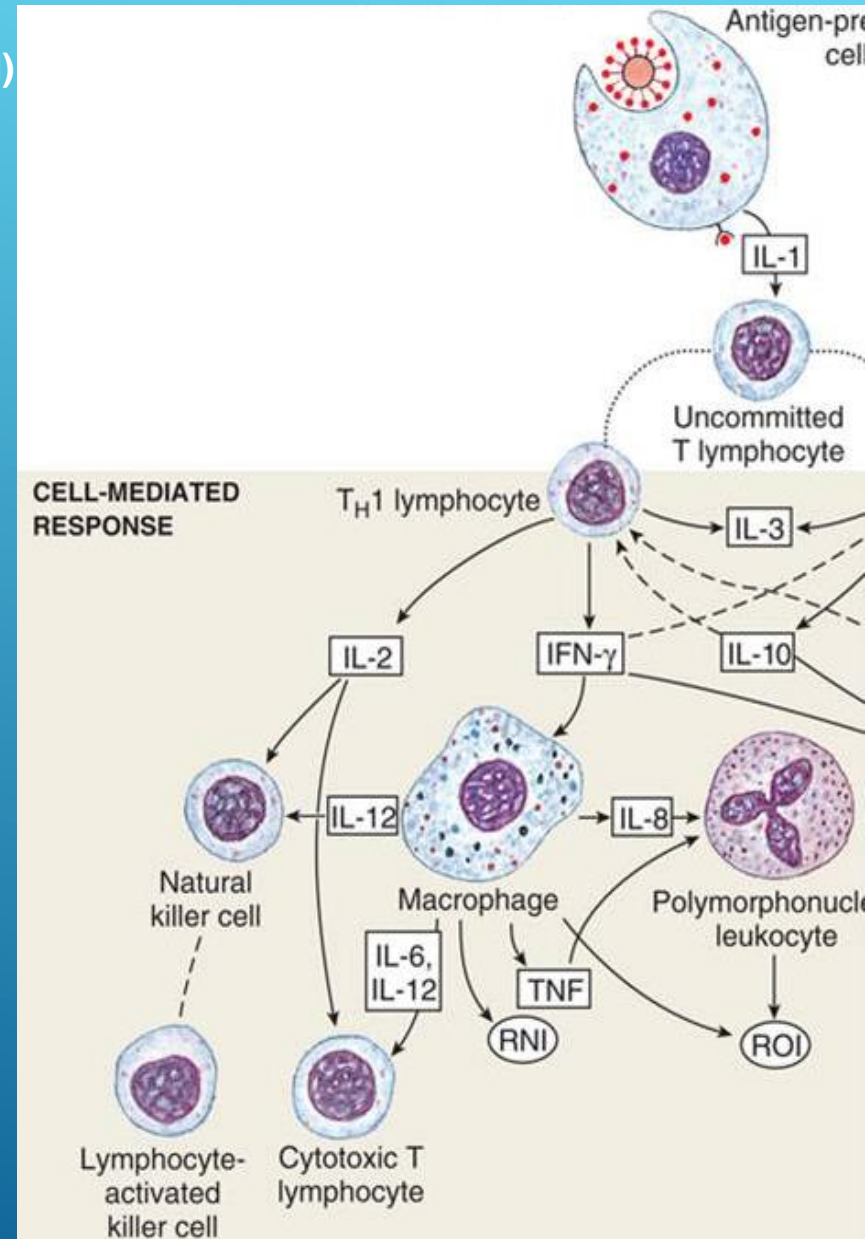


# Immunity

## VII. Acquired Immune Response

### B. Cell-mediated immune response

1. Epitope presented by APC (macrophage; infected cell)
2. Secrete IL-1, activate TH1; recognize epitope-MHCII complex
3. Activated TH1 secretes IL-2, TNF, INF- $\gamma$
4. IL-2 :
  - promotes activity of activated B and T cells
  - activates NK cells  $\rightarrow$  **lymphocyte-activated killer cells (LAK)**
  - also activates cytotoxic T cells (CD8+ cells)
5. INF- $\gamma$ :
  - activates macrophages
  - promotes B-cell proliferation
  - affects endothelial cells so lymphocytes can pass through into surrounding tissue (TNF also does this)
  - causes inflammation
6. Activated macrophages secrete ROIs, RNIs; secrete TNF  $\rightarrow$  activates polymorphonuclear leukocytes (inflammation); cytokines
7. Memory T cells



# Immunity

## VII. Acquired Immune Response

### C. Inflammation:

-- mobilization of body's defenses against invader or tissue damage, and for repair

#### 1. **Delayed type hypersensitivity** (DTH)

-- type of cell mediated immunity; depends on activated macrophages

-- requires at least 24 hrs from antigen introduction to response

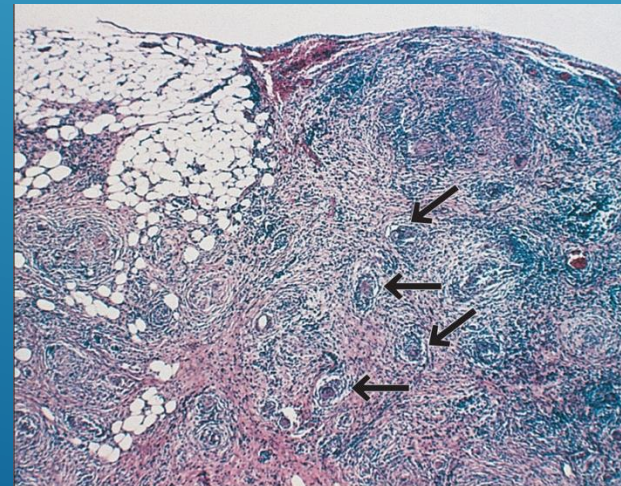
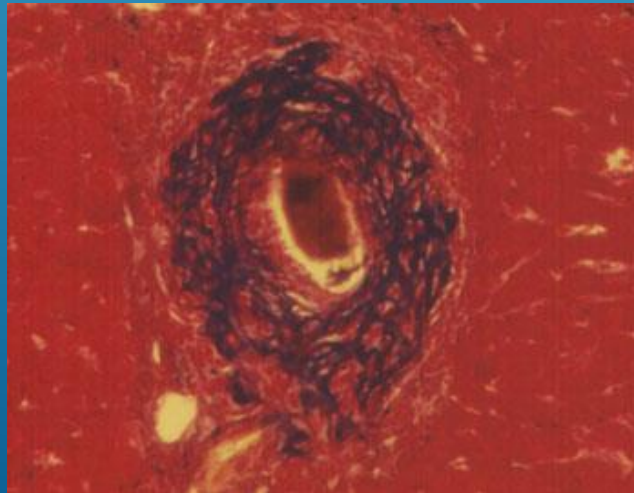
-- TH1 recognize specific antigen, secrete IL-2, TNF, INF- $\gamma$

-- TNF and INF- $\gamma$  activate endothelial cells; macromolecules & leucocytes move into surrounding tissue

-- fibrinogen  $\rightarrow$  fibrin; area becomes swollen & firm

-- activated macrophages phagocytize antigen, secrete cytokines, promote healing

-- if antigen cannot be removed  $\rightarrow$  deposition of fibrous tissue = **fibrosis**;  
nodules of inflammatory tissue (**granulomas**) accumulate



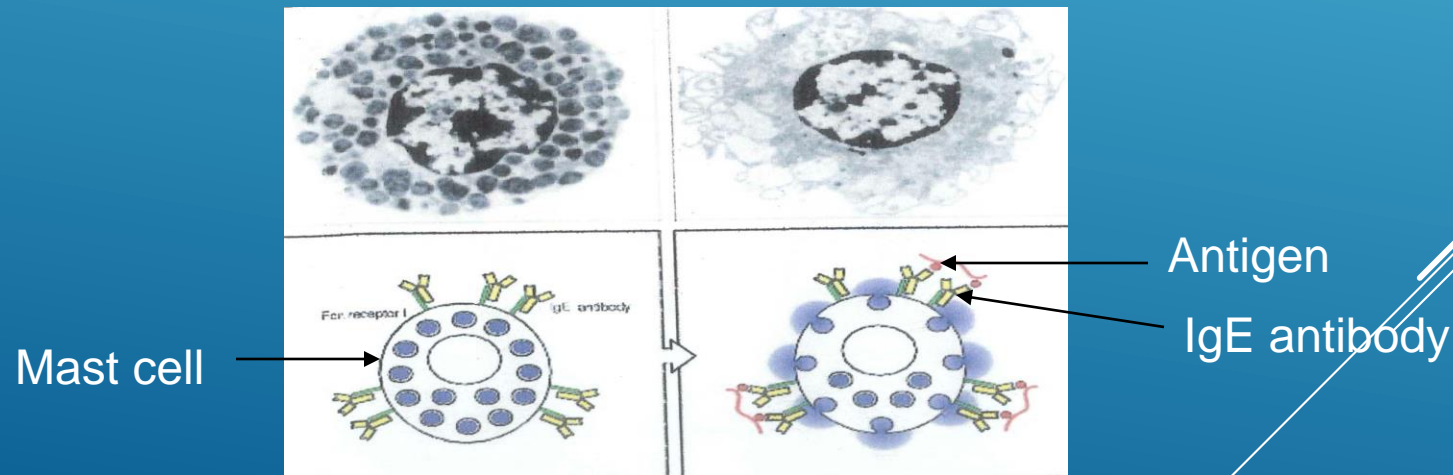
# Immunity

## VII. Acquired Immune Response

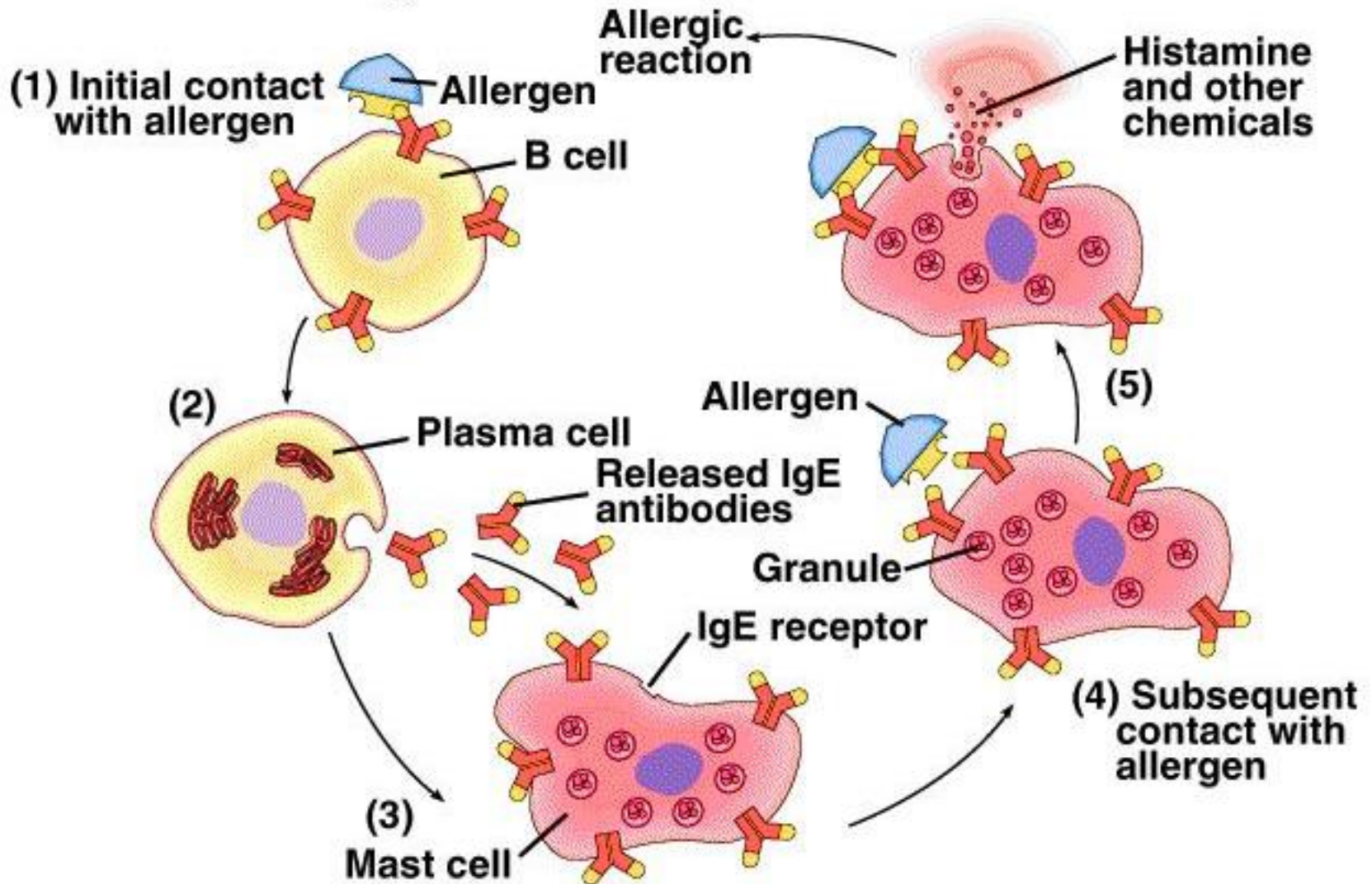
### C. Inflammation

#### 2. immediate hypersensitivity

- involves mast cells with receptors for Fc region of IgE antibodies
- when antigen binds to bound IgE antibody, causes mast cell to release histamine, etc.
- histamine causes dilation of local blood vessels & increased permeability
- blood plasma escapes causing swelling; redness
- neutrophils move out and attack first; then macrophages; pus forms
- if systemic = **anaphylaxis**
- basis of allergic reactions and asthma: ex. Bee sting
  - first exposure to venom causes overproduction of IgE
  - second exposure causes massive mast cell response; anaphylaxis



# An Allergic Reaction — Overview



# Immunity

## VIII. Innate Immune Response:

- non-acquired; not dependent upon prior exposure
- interacts with and strengthened by acquired immune responses

### A. Physical barriers


1. skin (may be **cornified** or **sclerotized**)
2. mucus layers

### B. Chemical and cellular barriers antimicrobial substances

- low pH of stomach and vagina
- digestive enzymes
- breast milk: **IgA, IgG, lysosyme**
- mucus with **IgA** and **lysozyme** (attacks cell walls of bacteria)
- **interferons**: inflammation
- **TNF**: inflammation, fever
- complement: esp. alternative pathway
- **defensins**: each type effective against a different category of microbes

# Immunity

## IX. Pathogenesis of Parasite Infections

- A. **Physical trauma:** destruction of cells and tissues
  - B. **Nutrition robbing:** often associated with gut parasites
  - C. **Toxin production:** IgG and IgM can bind and neutralize
  - D. **Host immune response and inflammation:** (immunopathology)
- 

# Immunity

## X. Parasite evasion of host immune responses

A. intracellular; occupy gut lumen; secrete protective cysts

B. Infect cells of immune system

C. Circumvent (to manage to get around) antibodies

- Shift surface antigens
- Shed surface antigens
- Adsorb host antigens
- Inhibit binding of Fc region
- Cleave off Fc region of bound antibodies
- Migrate around body of host

D. Circumvent cytokines

- Inhibit IL-1, IL2
- cause nonspecific proliferation of B cells (polyclonal B cell activation) and exhaustion of immune system
- Produce antioxidants