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Innate Host Resistance

Host Resistance Overview

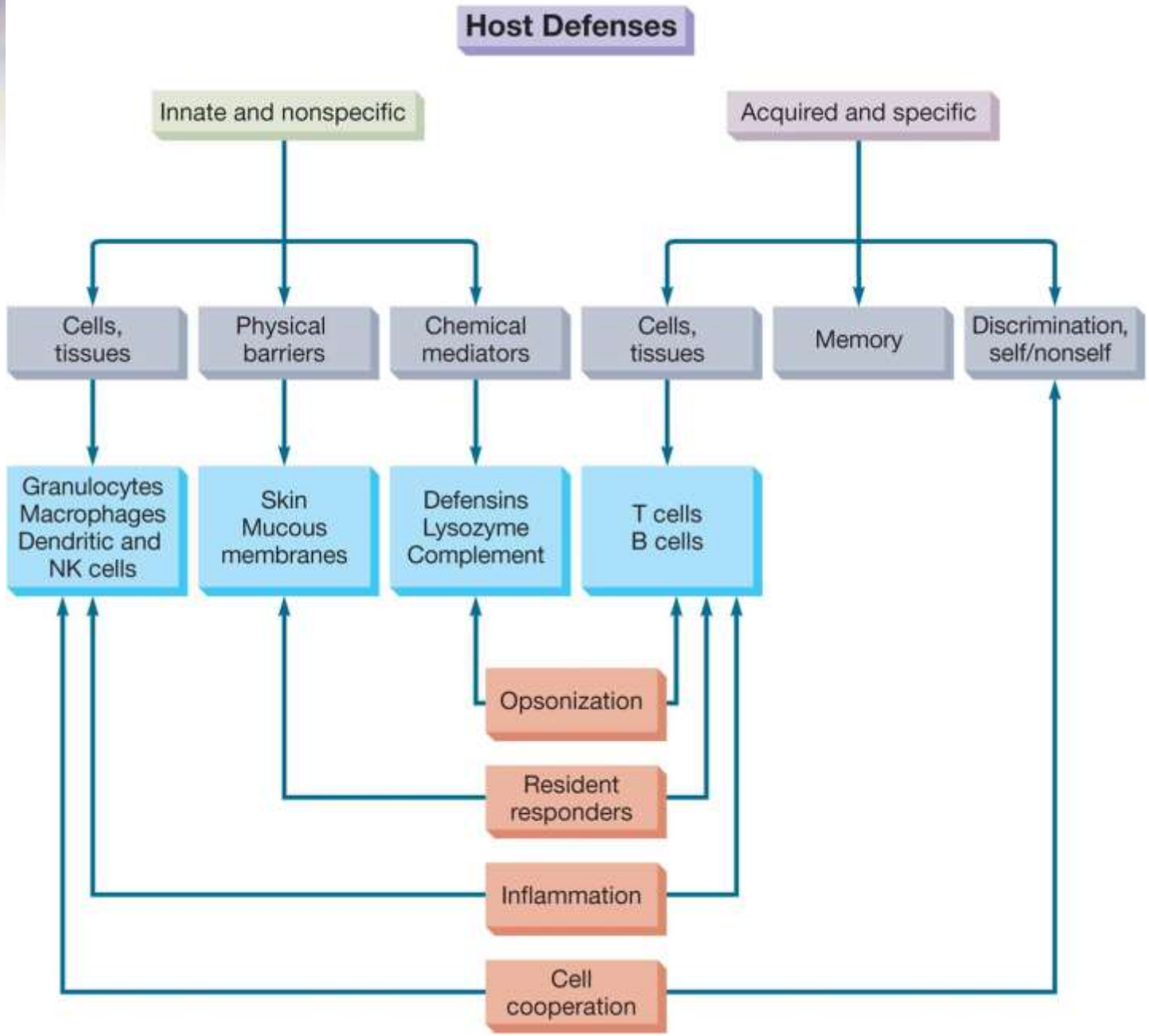
- Most pathogens (disease causing microbes)
  - must overcome surface barriers and reach underlying
  - overcome resistance by host
    - nonspecific resistance
    - specific immune response

Host Resistance Overview…

- Immune system
  - composed of widely distributed cells, tissues, and organs
  - recognizes foreign substances or microbes and acts to neutralize or destroy them
- Immunity
  - ability of host to resist a particular disease or infection
- Immunology
  - science concerned with immune responses

Immunity

- Nonspecific immune response
  - Aka nonspecific resistance, innate, or natural immunity
  - acts as a first line of defense
  - offers resistance to any microbe or foreign material
  - lacks immunological memory
- Specific immune response
  - Aka acquired, adaptive, or specific immunity
  - resistance to a particular foreign agent
  - has “memory”
    - effectiveness increases on repeated exposure to agent

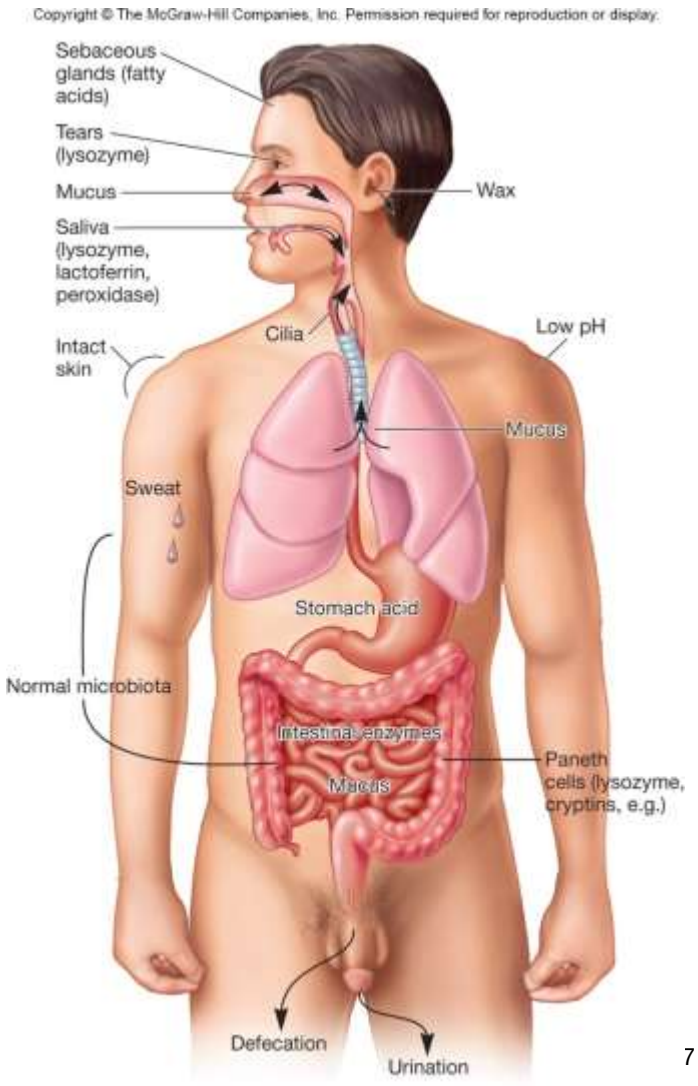


Antigens

- Recognized as foreign
- Invoke immune responses(استدعاء الاستجابات المناعية)
  - presence of antigen in body ultimately(في النهاية) results in B cell activation □ □ production of antibodies
    - antibodies bind to specific antigens, inactivating or eliminating them
    - other immune cells also become activated
- Name comes from antibody generators(مولدات الاجسام المضادة)

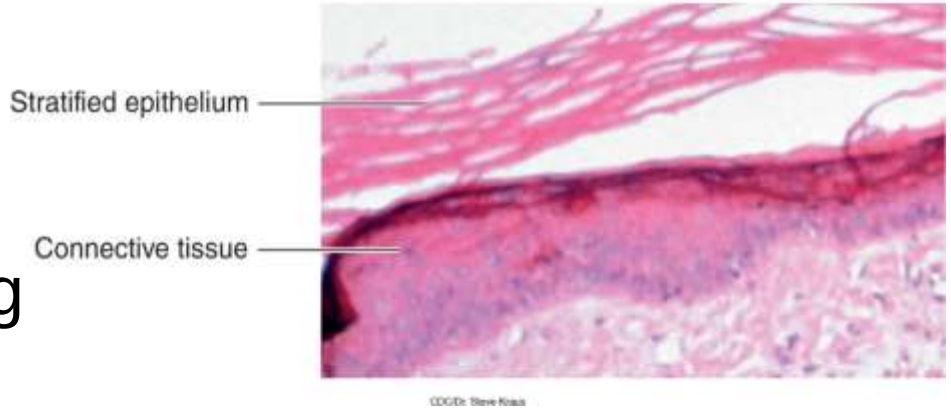
Physical Barriers in Nonspecific (Innate) Resistance

- Effectiveness impacted by:
  - direct factors
    - nutrition, physiology, fever, age, and genetics
  - indirect factors
    - personal hygiene, socioeconomic status, and living conditions
- Along with host's secretions (flushing(صرف/تدفق مائي)), barriers = first line of defense against microbes



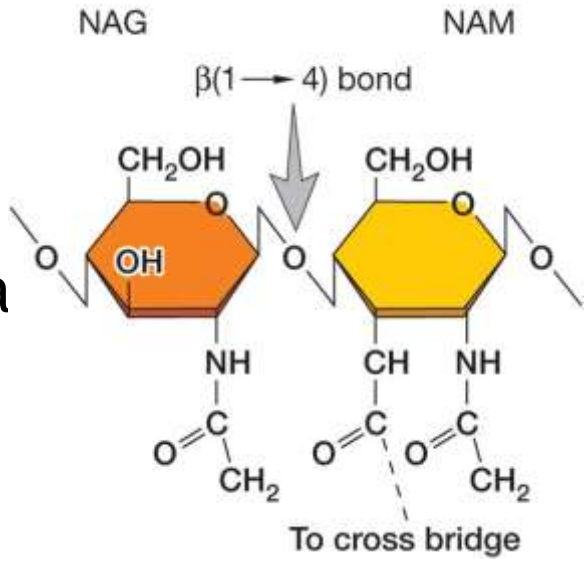
Skin

- Strong mechanical barrier to microbial invasion
  - keratin produced by keratinocytes in outer layer
- Inhospitable environment for microbes
  - attached organisms removed by shedding of outer skin cells
  - pH is slightly acidic
  - high NaCl concentration
  - subject to periodic drying



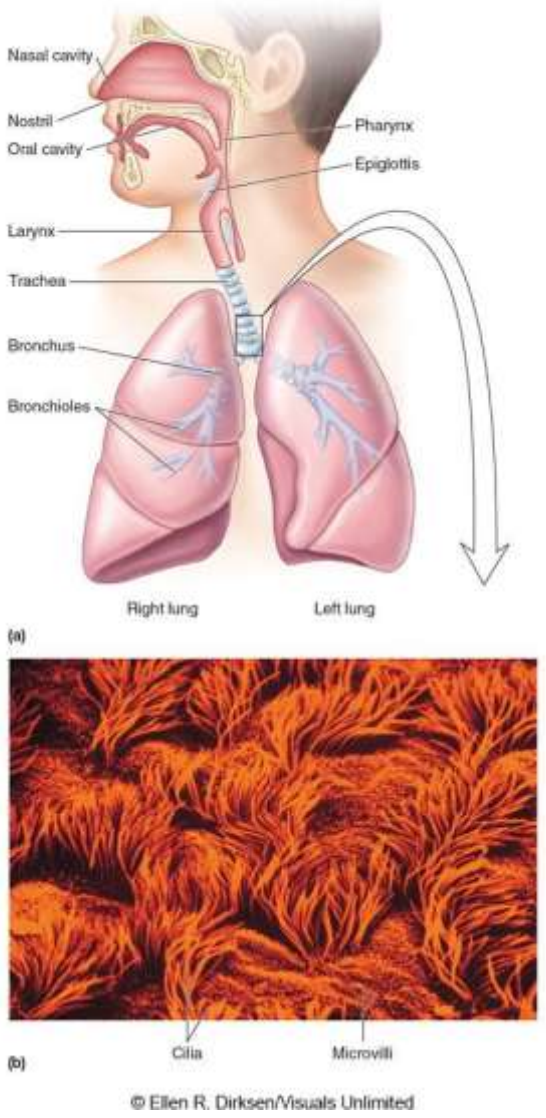
Mucous Membranes

- Form protective covering that resists penetration and traps(حصر) many microbes
- Are often bathed in antimicrobial secretions which contain a variety of antimicrobial substances
  - lysozyme
    - hydrolyzes bond connecting sugars in peptidoglycan
  - lactoferrin
    - secreted by activated macro-phages and PMNs
    - sequesters(تعزل) iron from plasma
  - lactoperoxidase
    - produces superoxide radicals



Respiratory System

- Turbulent air flow deposits microbes onto mucosal surfaces
- Mucociliary blanket
  - mucous secretions trap microbes
  - once trapped, microbes transported away from the lungs (mucociliary escalator)
    - expelled by coughing or sneezing
    - salivation washes microbes to stomach
- Alveolar macrophages
  - phagocytic cells in alveoli(الحويصلات الهوائية) of lungs



Gastrointestinal Tract

- Stomach
  - gastric acid
- Intestines
  - pancreatic enzymes
  - bile
  - intestinal enzymes
  - GALT
  - Peristalsis(انقباضات)
- Intestines
  - shedding of columnar epithelial cells
  - secretory IgA
  - normal microbiota
  - Paneth cells
    - produce lysozyme
    - produce cryptins

Genitourinary Tract

- Unfavorable environment for foreign microbes
  - low pH of urine and vagina
  - vagina has lactobacilli
  - urea and other toxic metabolic end products in urine
  - hypertonic nature of kidney medulla
- Flushing(تدفق/صرف) with urine and mucus
- Distance barrier of male urethra

The Eye

- Mucus secreting epithelial membrane
- Flushing action of tears
- Lysozyme, lactoferrin, and secretory IgA in tears

Cells of the Immune System

- Granulocytes
- Mast cells
- Monocytes and macrophages
- Dendritic cells
- Lymphocytes
- Each has specialized role in defending host
- Leukocytes
  - white blood cells
  - involved in both specific and nonspecific immunity
  - all arise from pluripotent stem cells

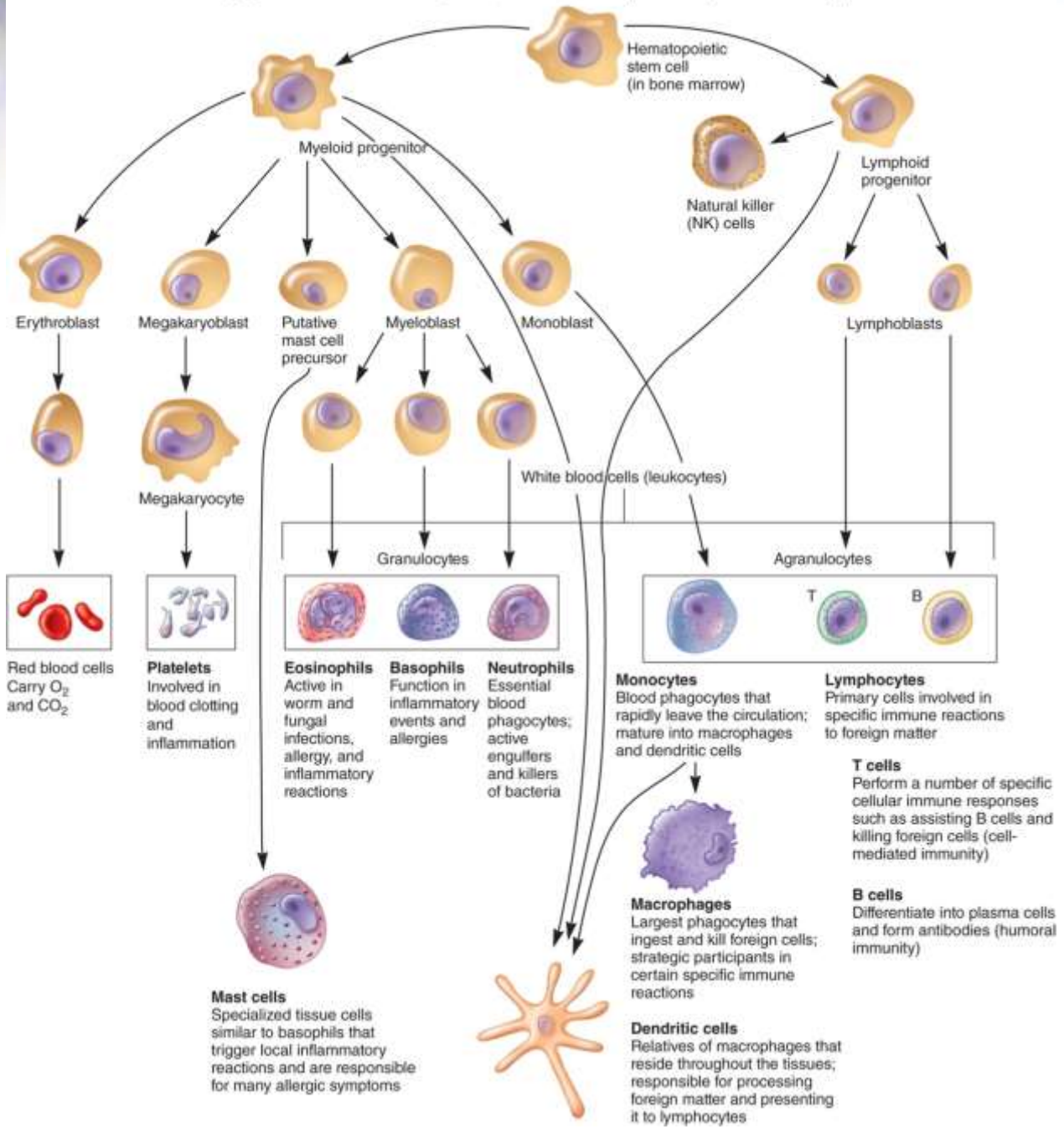


Table 33.4 Normal Adult Blood Count

Cell Type	Cells/mm^3	Percent WBC
Red blood cells	5,000,000	
Platelets	250,000	
White blood cells	7,400	100
Neutrophils	4,320	60
Lymphocytes	2,160	30
Monocytes	430	6
Eosinophils	215	3
Basophils	70	1

Granulocytes

- Irregularly-shaped nuclei with two to five lobes
- Cytoplasm has granules with reactive substances
  - kill microbes, enhance inflammation
- Three types
  - basophils, eosinophils, neutrophils (polymorphonuclear neutrophil (PMN))

Basophils

- Stain bluish-black with basic dyes
- Nonphagocytic
- Release vasoactive mediators
  - e.g., histamine, prostaglandins, serotonin, and leukotrienes from granules
- Play important role in development of allergies and hypersensitivities

Neutrophils

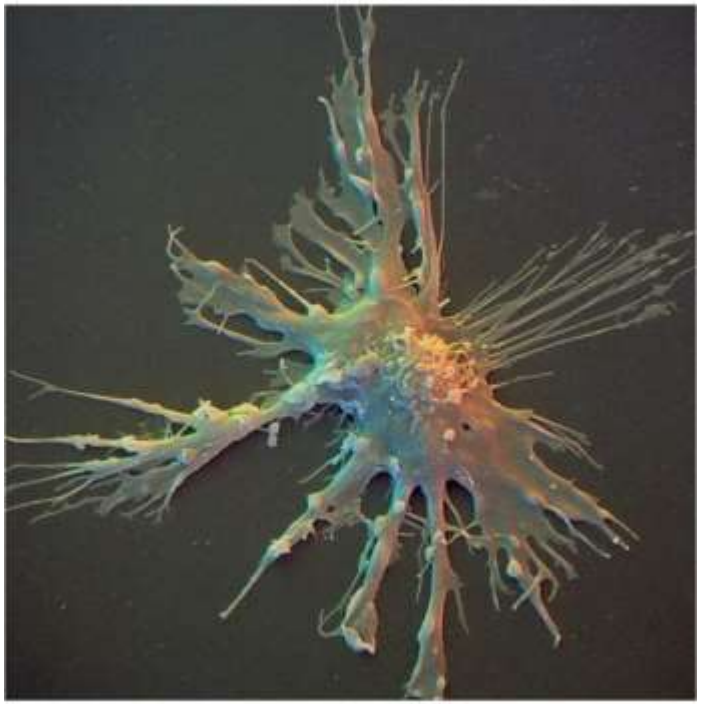
- Stain at neutral pH
- Highly phagocytic
- Circulate in blood then migrate to sites of tissue damage
- Kill ingested microbes with lytic enzymes and reactive oxygen metabolites contained in primary and secondary granules

Monocytes and Macrophages

- Highly phagocytic cells
- Monocytes
  - are mononuclear phagocytic leukocytes
  - after circulating for ~8 hours, mature into macrophages
- Macrophages
  - larger than monocytes, reside(يقيم) in specific tissues, highly phagocytic
  - have a variety of surface receptors (including pattern recognition receptors)
    - bind pathogen associated molecular patterns (PAMPs)
  - named according to tissue in which they reside

Dendritic Cells

- Heterogeneous group of cells with neuron-like appendages(زوائد)
  - from lymphoid and myeloid lines
- Present in small numbers in blood, skin, and mucous membranes of nose, lungs, and intestines
  - also express pattern recognition receptors
  - contact, phagocytose, and process antigens display foreign antigens on their surfaces (antigen presentation)



Lymphocytes

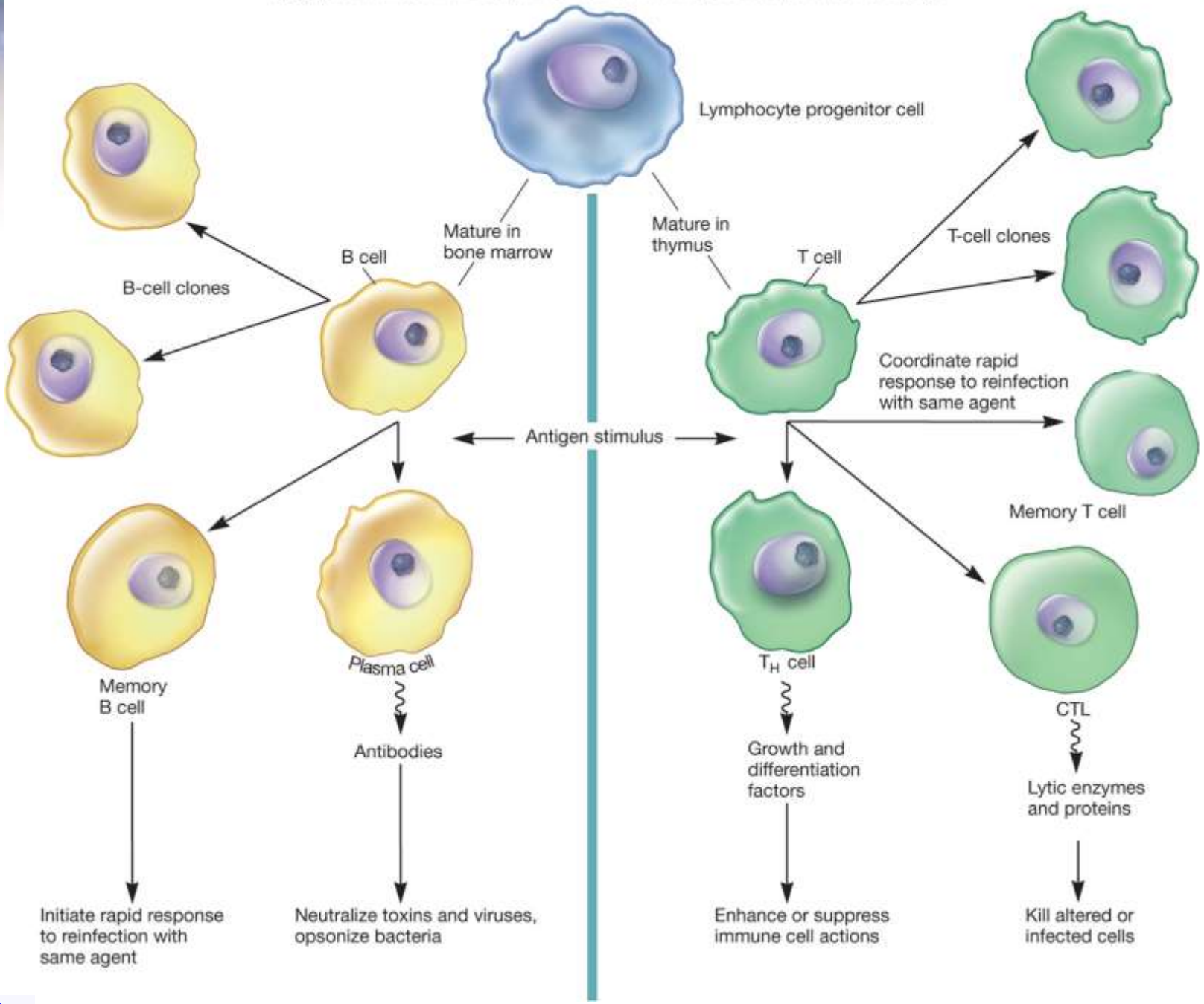
- Major cells of the immune system
- Major populations include T cells, B cells, and natural killer (NK) cells
- B and T lymphocytes differentiate in bone marrow from stem cells
  - are only activated by binding of specific antigen onto lymphocyte surface receptors
  - after activation replication continues as lymphocytes circulate and enter lymphoid tissue
  - memory cells are activated lymphocytes that do not immediately replicate, but will do so later in host's life when antigen is again present

B Lymphocytes

- B cells (B lymphocytes)
  - mature in bone marrow
  - circulate in blood
  - can settle in lymphoid organs
  - after maturation and activation are called plasma cells and produce antibodies

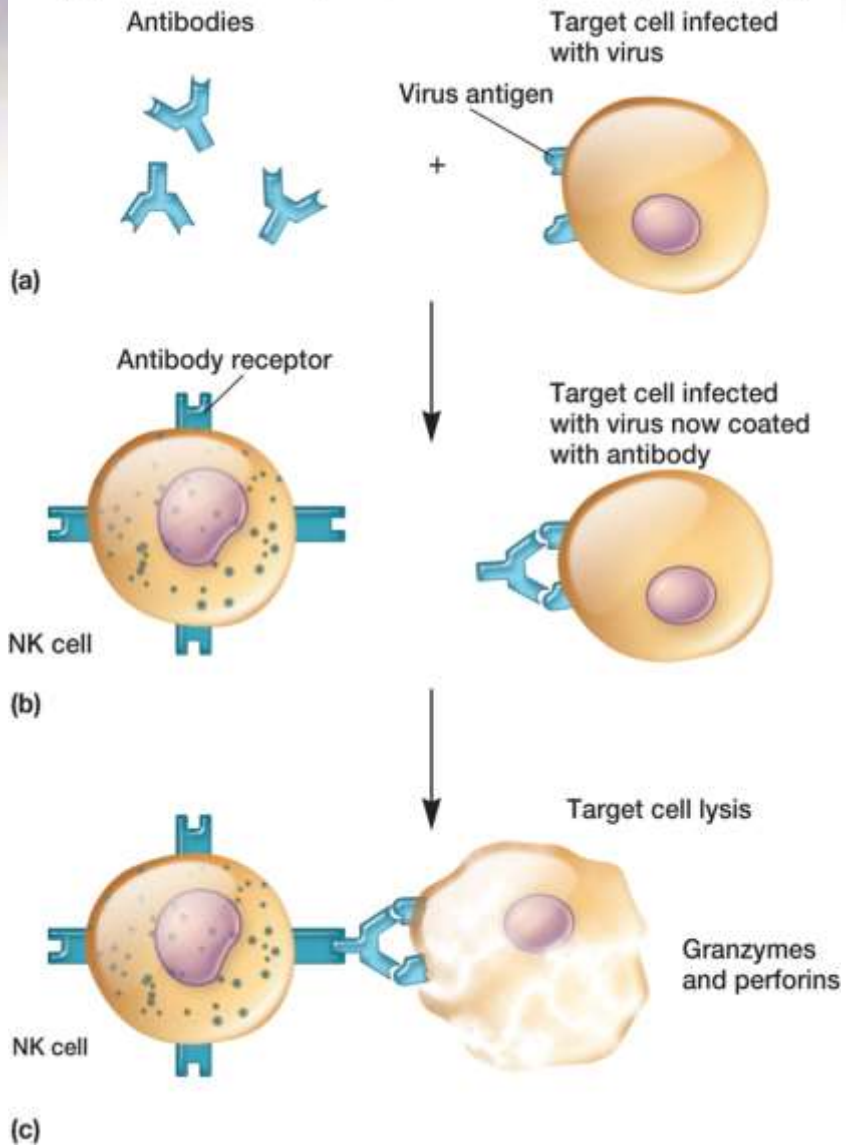
T Lymphocytes (T cells)

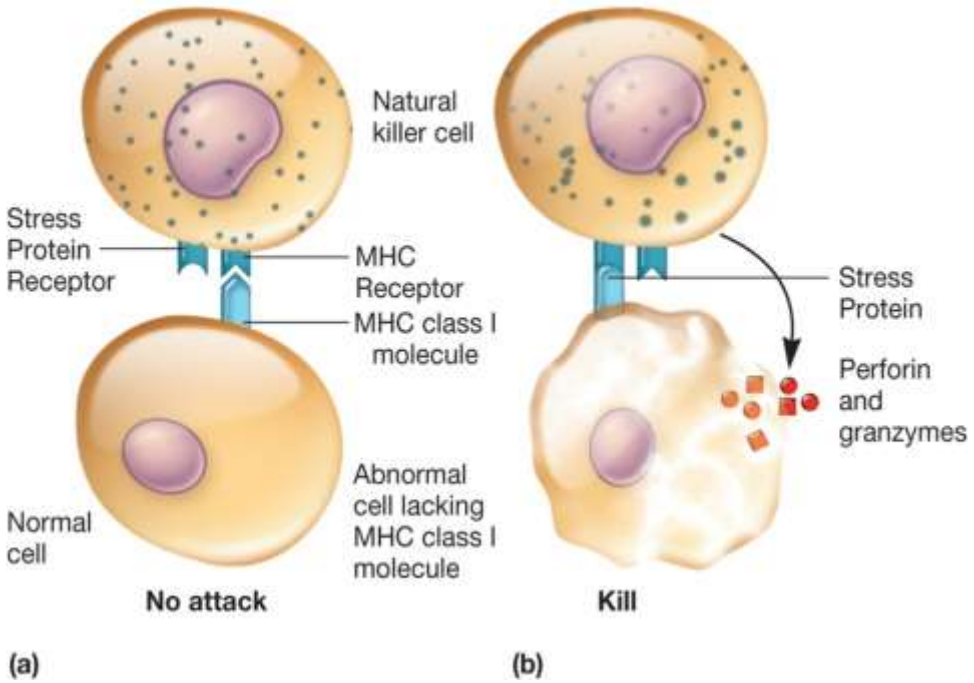
- Mature in thymus
- Can remain in thymus, circulate in blood, or reside in lymphoid tissue
- Like B cells, require antigen binding to surface receptors for activation and continuation of replication
- Activated T cells differentiate into helper T cells (TH) and cytotoxic lymphocytes (CTLs)
- Secrete cytokines, chemicals that have effects on other cells, are produced and secreted by activated T cells



Natural Killer (NK) Cells

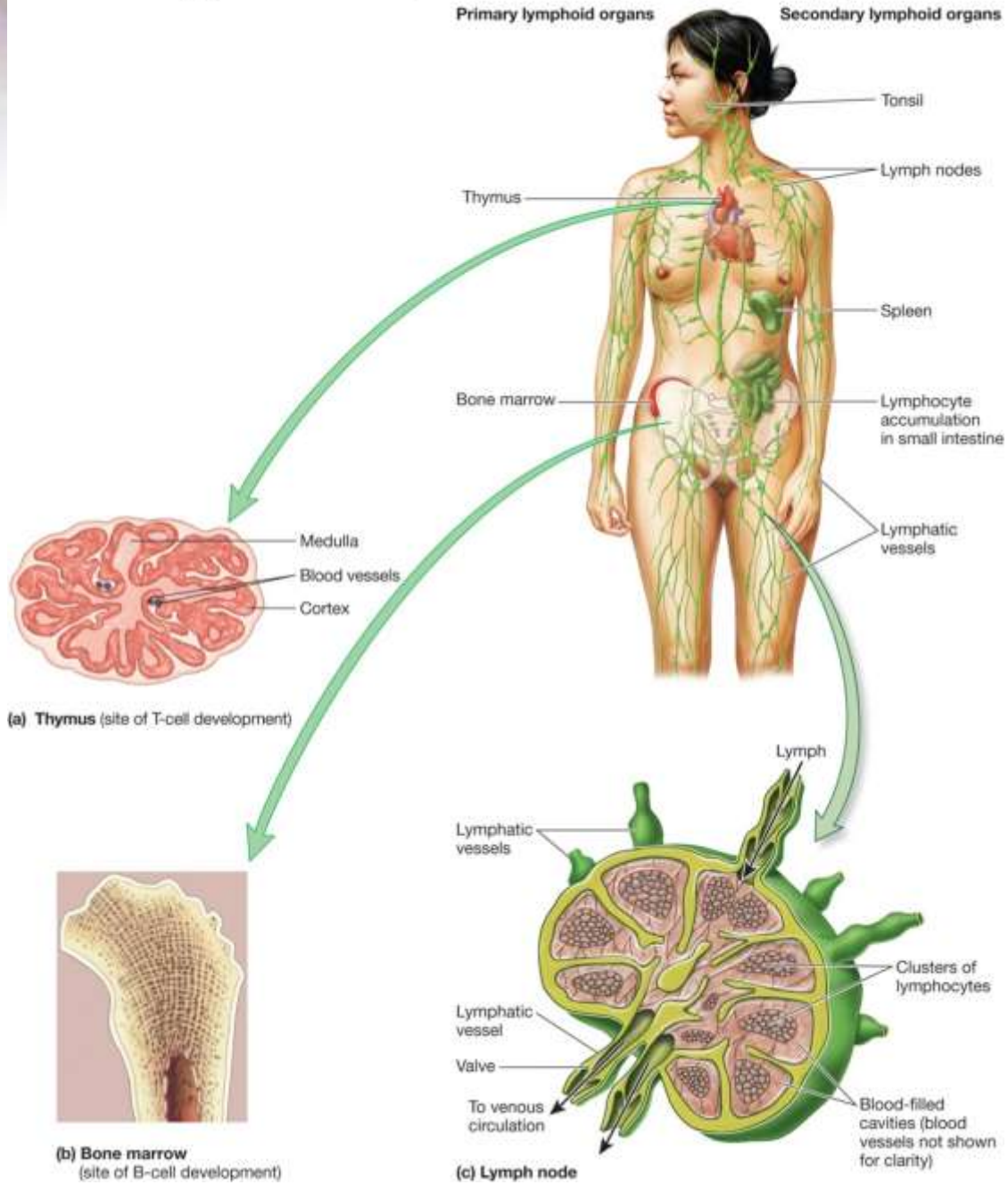
- Small population of large non-phagocytic granular lymphocytes
  - important role in innate immunity
  - kill malignant cells(خلايا خبيثة) and cells infected with pathogens by releasing granzymes (cytotoxic enzymes)
- Two ways of recognizing target cells
  - bind to antibodies which coat infected or malignant cells (antibody-dependent cell-mediated cytotoxicity (ADCC)
  - recognizes cells that have lost their class I major histocompatibility antigen due to presence of virus or cancer





Organs and Tissues of the Immune System

- Primary organs and tissues
  - sites where lymphocytes mature and differentiate into antigen-sensitive mature B and T cells
- Secondary organs and tissues
  - areas where lymphocytes may encounter and bind antigen
    - followed by proliferation and differentiation into fully mature effector cells



Primary Lymphoid Organs and Tissues

- Thymus
  - precursor cells move enter from bone marrow and proliferate(تكاثر)
  - thymic deletion removes T cells recognizing self antigens
  - remaining cells become mature T cells
  - enter bloodstream and recognize nonself antigens
- Bone marrow
  - site of B cell maturation in mammals
  - maturation involves removal of nonfunctioning and self-reactive cells

Secondary Lymphoid Organs and Tissues

- Spleen
  - most highly organized lymphoid organ
  - filters blood
  - macrophages and dendritic cells trap(تحاصر) microbes and antigens
    - present antigens to B and T cells
      - most common way that lymphocytes become activated to carry out their immune functions

Secondary Lymphoid Organs and Tissues

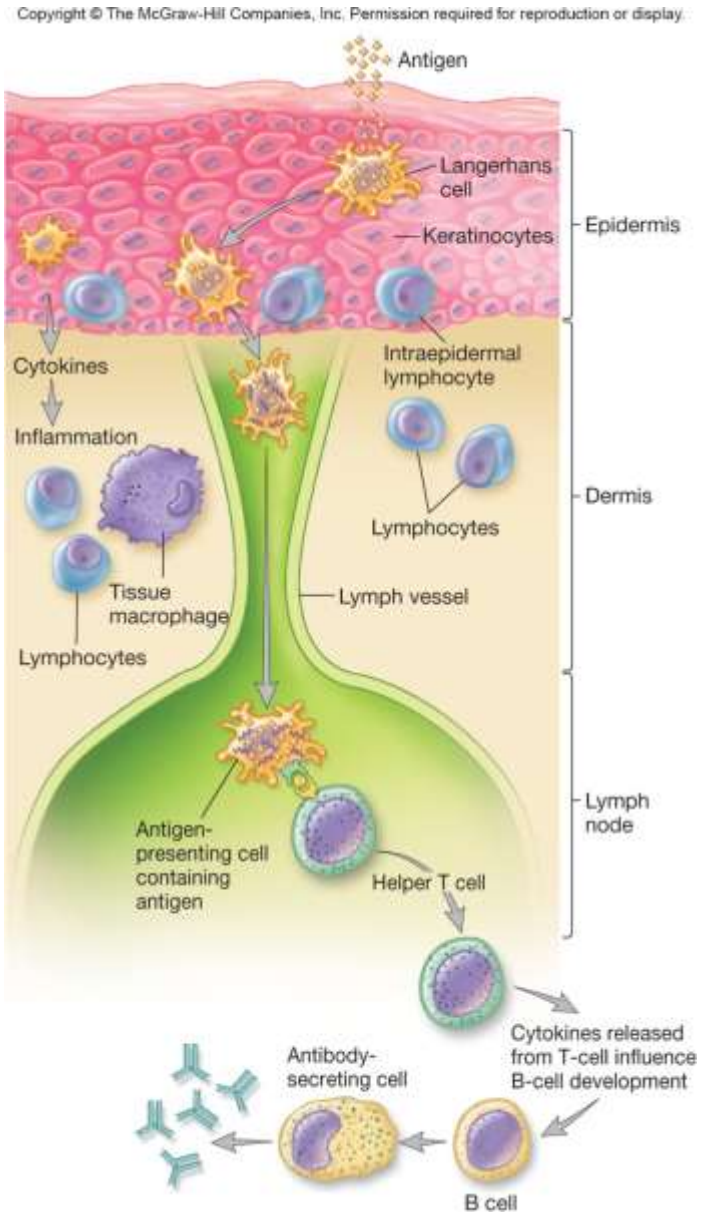
- Lymph nodes
  - most highly organized lymphoid tissue
  - filter lymph
  - microbes and antigens trapped and phagocytosed by macrophages and dendritic cells
  - B cells differentiate into memory and plasma cells within lymph nodes

Secondary Lymphoid Organs and Tissues

- Lymphoid tissue
  - located throughout the body
  - serve as interface between innate and acquired host immunity
  - act as areas of antigen sampling and processing
  - some lymphoid cells are found closely associated with specific tissues
    - e.g., skin-associated lymphoid tissue (SALT)
    - e.g., mucous-associated lymphoid tissue (MALT)

Skin Associated Lymphoid Tissue (SALT)

- Contains specialized cells
  - Langerhans cell
    - dendritic cell that can phagocytose antigens
    - differentiates into interdigitating dendritic cell – presents antigen to and activates T cells
  - intraepidermal lymphocyte
    - function as T cells



Mucosal-Associated Lymphoid Tissue (MALT)

- Specialized immune barrier
  - gut-associated lymphoid tissue (GALT)
  - bronchial-associated lymphoid tissue (BALT)
  - urogenital system(النظام البولي التناسلي) MALT