Introduction to Immunology
&
Lymphoid System

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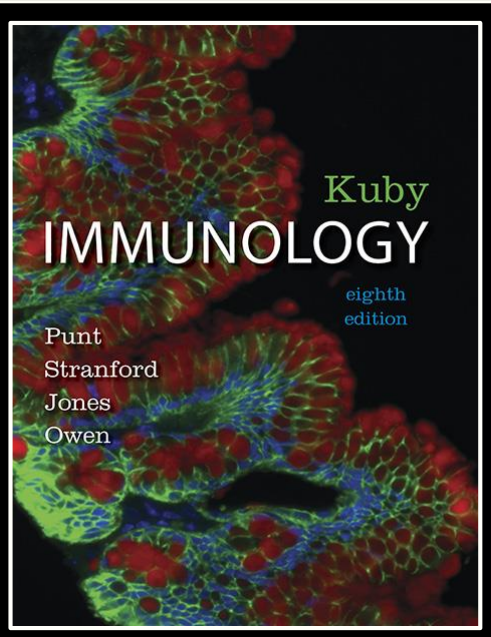


Kuby Immunology

Eighth Edition

CHAPTER 1 & 2

Objectives

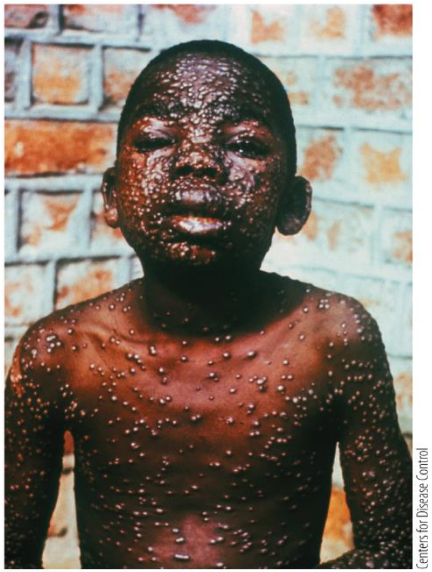
- To know the historical perspective of immunology
- To be familiar with the basic terminology and definitions of immunology
- To recognize immune response cells
- To understand types of immune responses
- To know about the lymphoid system
- To understand T and B cell functions

A historical perspective of immunology

- What is immunity?
  - Immunity is the state of protection against foreign pathogens or substances (antigens)
    - Latin term *immunis*, meaning “exempt,” is the source of the English word **immunity**
  - Observations of immunity go back over 2000 years
    - Thucydides, an ancient historian, wrote in 430 BC of a plague in Athens where those who had recovered could safely nurse the currently ill

A historical perspective of immunology

- Can we generate immunity without inducing disease?
  YES…through vaccination
  - Vaccination prepares the immune system to eradicate an infectious agent before it causes disease
  - Widespread **vaccine** use has saved many lives
  - Classic examples: rabies vaccine and eradication of smallpox



Centers for Disease Control

Figure 1-1
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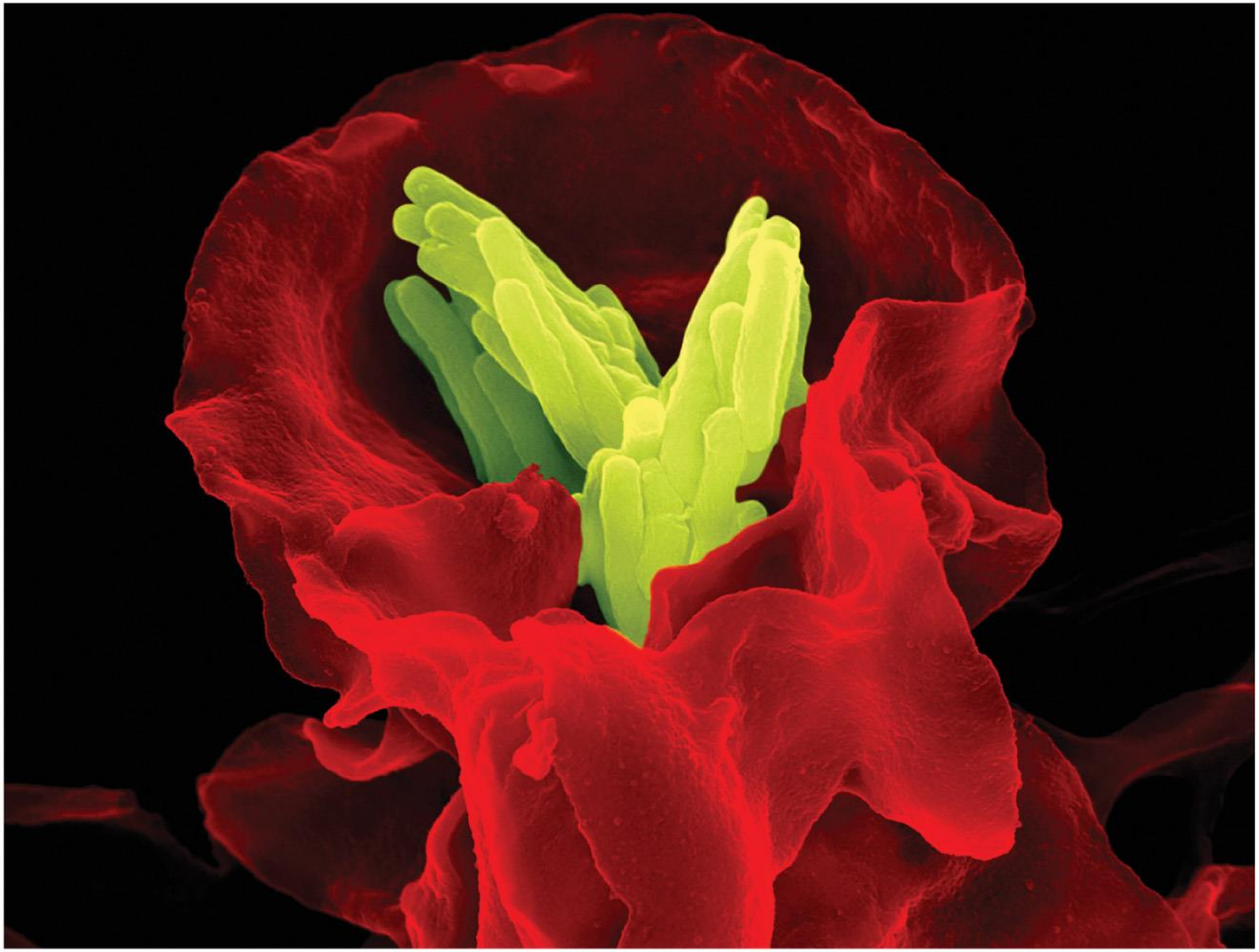
Table 1-1, Cases of selected infectious disease in the United States before and after the introduction of effective vaccines

Disease	ANNUAL CASES/YR: Prevaccine	CASES IN 2016: Postvaccine	Reduction (%)
Smallpox	48,164	0	100
Diphtheria	175,885	0	100
Measles	503,282	79^	99.98
Mumps	152,209	145*	98.90
Pertussis (“whooping cough”)	147,271	964*	99.35
Paralytic polio	16,316	0	100
Rubella (German measles)	47,745	0*	100
Tetanus (“lockjaw”)	1,314 (deaths)	1* (case)	99.92
Invasive *Haemophilus influenzae*	20,000	356*	98.22

Macrophage engulfs a bacteria



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Chapter 1 Opener
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Louis Pasteur's Contributions

- Determined through studies of cholera in chickens that the virulence of a pathogen weakens with age (chickens inoculated with old strains not only survive but become resistant)
  - Attenuated – weakened, non-virulent strain whose exposure can confer resistance to disease

- **Classical experiment**
  - Heat attenuated anthrax bacillus and subsequent challenge with virulent *Bacillus anthracis* in sheep

Louis Pasteur

Louis Pasteur watching the rabies vaccination

From *Harper's Weekly*, 1885, Vol. 29:836; courtesy of the National Library of Medicine

Figure 1-2
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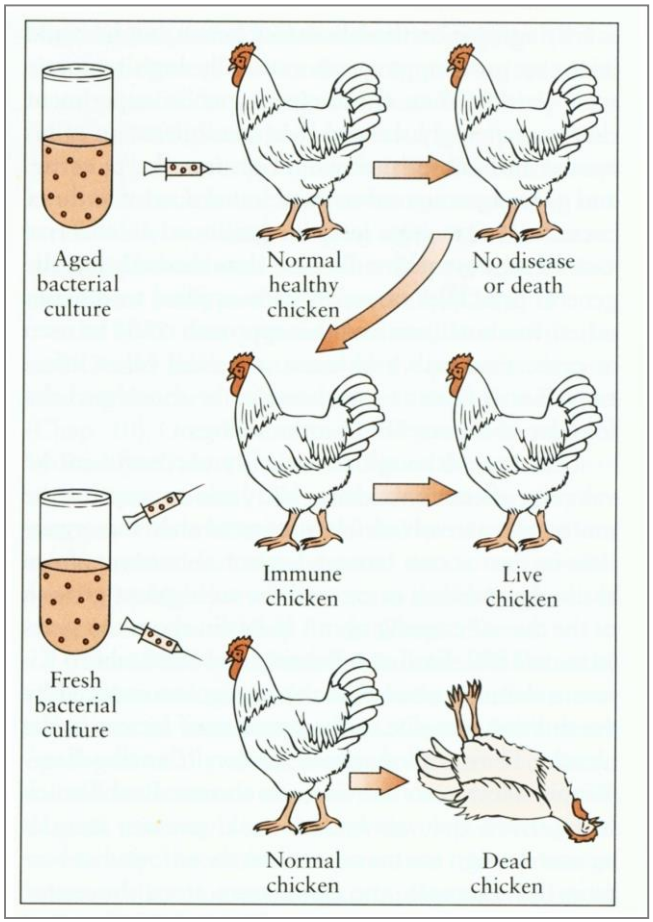
Louis Pasteur Cholera Observation:



Definitions

- **Antigen (Ag):** any substance (usually foreign) that binds specifically to a component of the adaptive immunity.
- **Allergen**: noninfectious antigens that induce Allergy.
- **Innate immunity**: Nonspecific host defenses that exist prior to exposure to Ag.
- **Adaptive Immunity:** Specific host defenses that are mediated by T & B cells following exposure to Ag.

Definitions

- **Pathogen**: a disease causing organism

- **Vaccination:** deliberate induction of protective immunity to a pathogen

- **Immunoglobulin (Ig) or Antibodies:** molecules secreted from plasma cell (B cell) as an adaptive immune response to extracellular Ag.

- **(CD) Cluster of Differentiation:** molecule with a CD designation has a characteristic cell surface protein which are often associated with the cell's function.

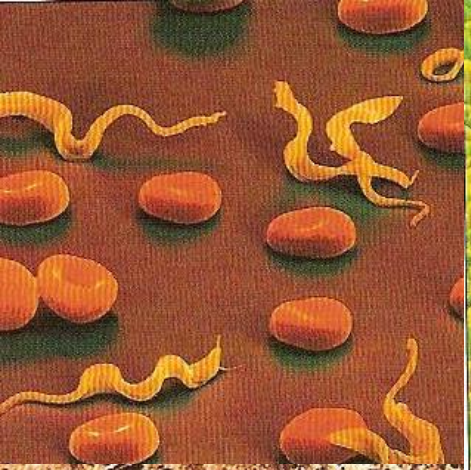
- Three Main lymphocytes populations:

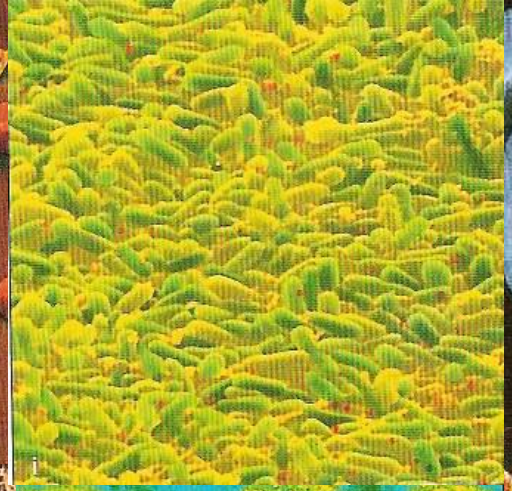
T cell, **B** cell & Natural Killer (**NK**) cell

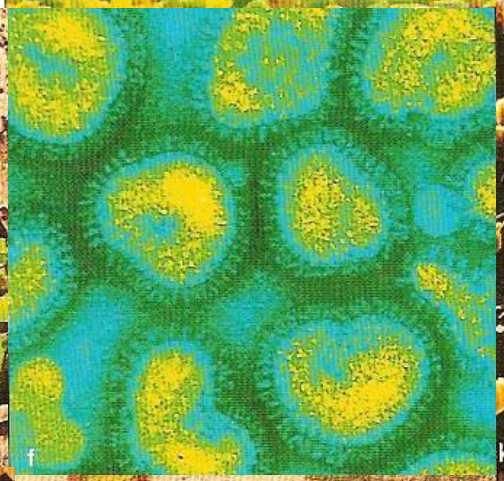
- **CD3** T cell marker
- **CD4** T helper cell marker
- **CD8** T cytotoxic (CTL) marker
- **CD19** B cell marker
- **CD16, CD56** Natural Killer cell markers

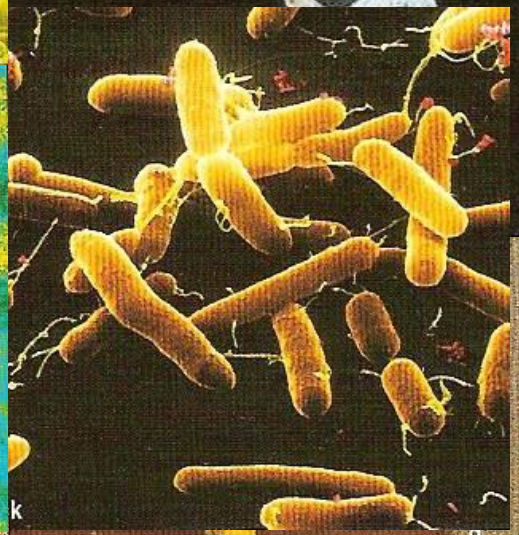
Where & what are antigens?

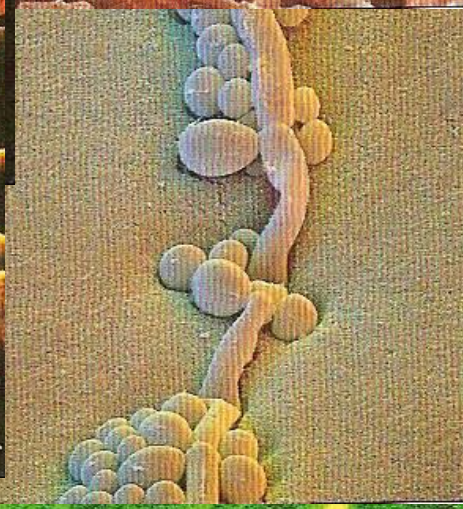
- Microorganisms & their related products (proteins, polysaccharides, lipids)
- Environmental substances
- Drugs
- Organs, tissues, cells

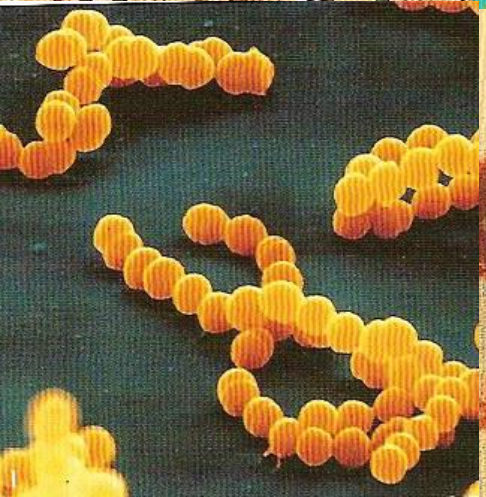


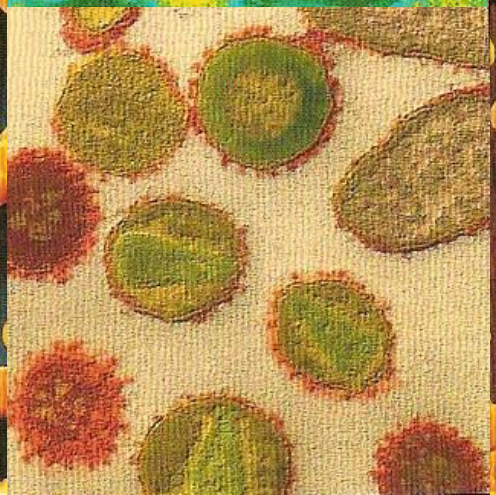


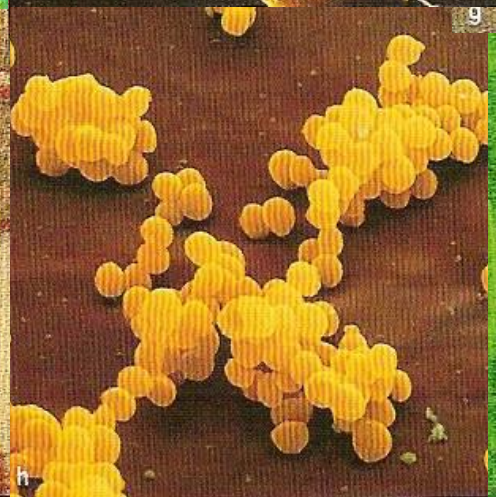












Cells of the immune system

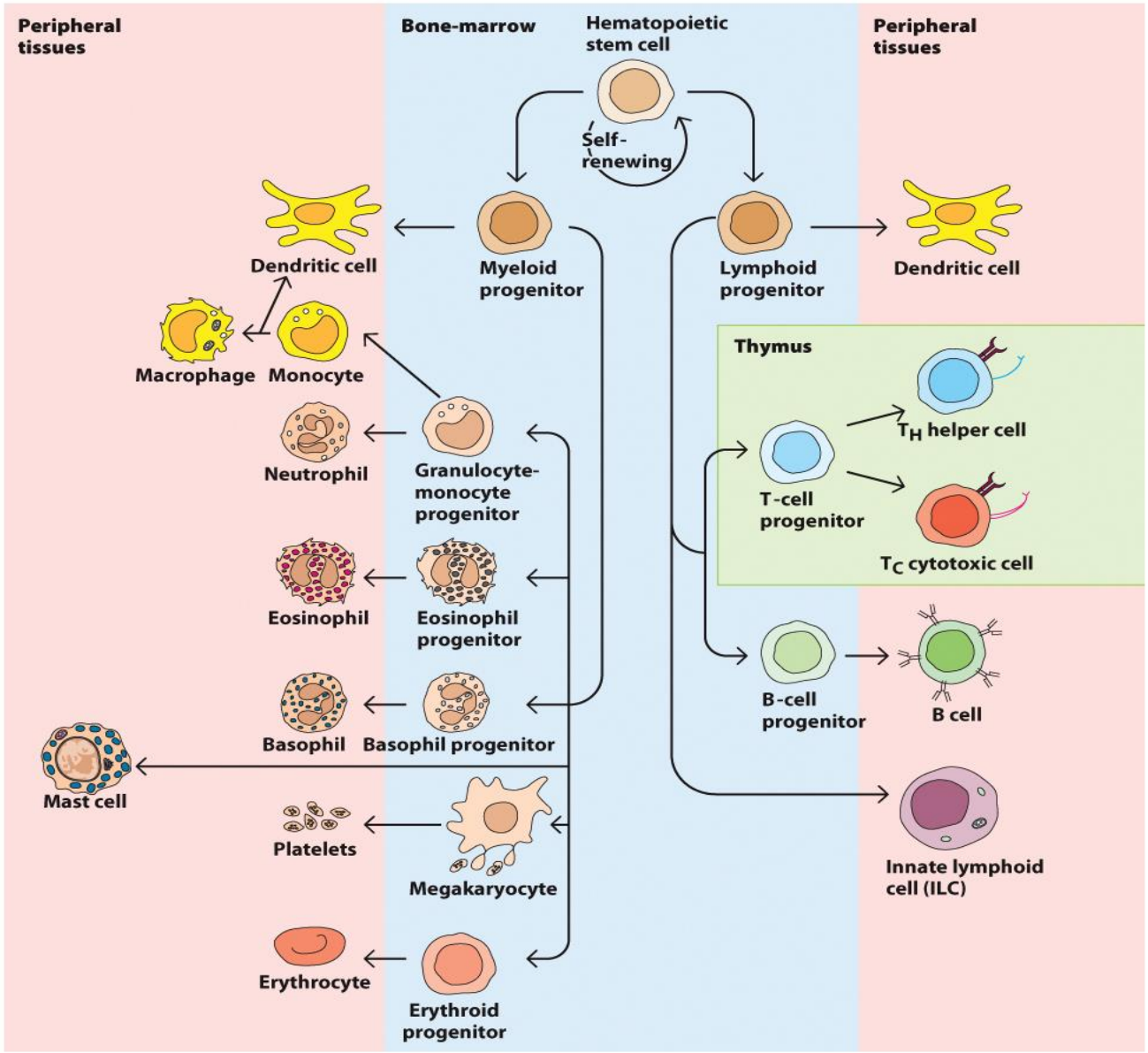


Figure 2-1
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Cells of the immune system

- **B cells** also express the **B cell receptor** (BCR)
- **T cells** also express the **T cell receptor** (TCR)

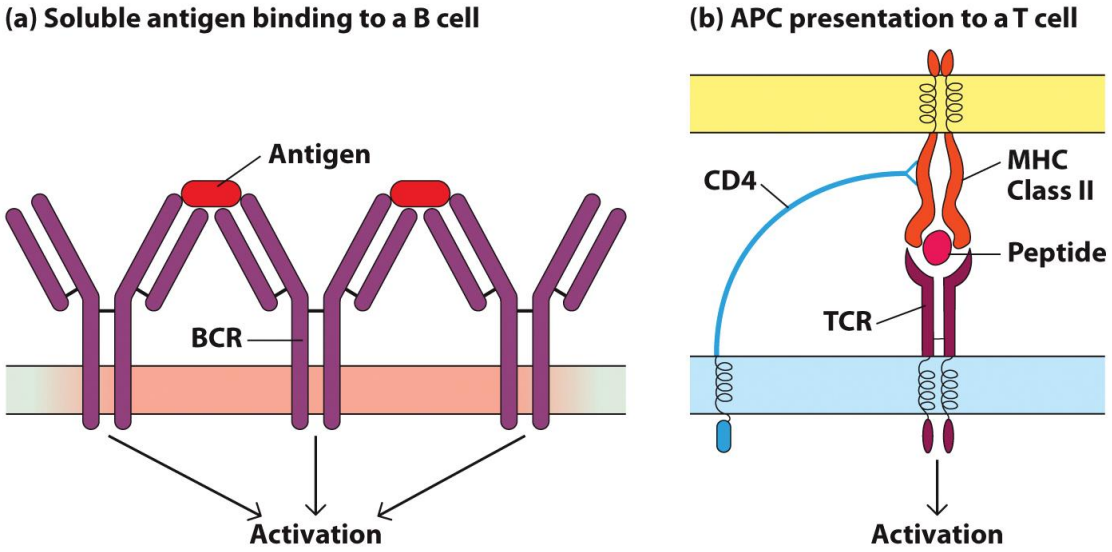

Figure 2-7
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Types of Immunity

1. **Innate (Natural) Immunity**
   - First line of defense
   - **Fast**, But **Nonspecific**
   - Also uses **phagocytic cells**
   - Shorter duration
   - No memory

2. Adaptive (Acquired) Immunity

- Adaptive specific Immunity **Specificity**
- Response of a specific **B and T lymphocytes** to an antigen
- Exhibit **Immunological Memory**
- **Self / non-self recognition**
- **Slower to develop 5–6 days (or more)**

Two Major Branches:

Humoral immunity (AbMI)

Immunity that is mediated by antibodies (B cells)

Cell Mediated Immunity (CMI)

Immune response in which antigen specific T cells dominate

Important concepts for understanding the immune response

Innate and Adaptive immunity work **cooperatively**

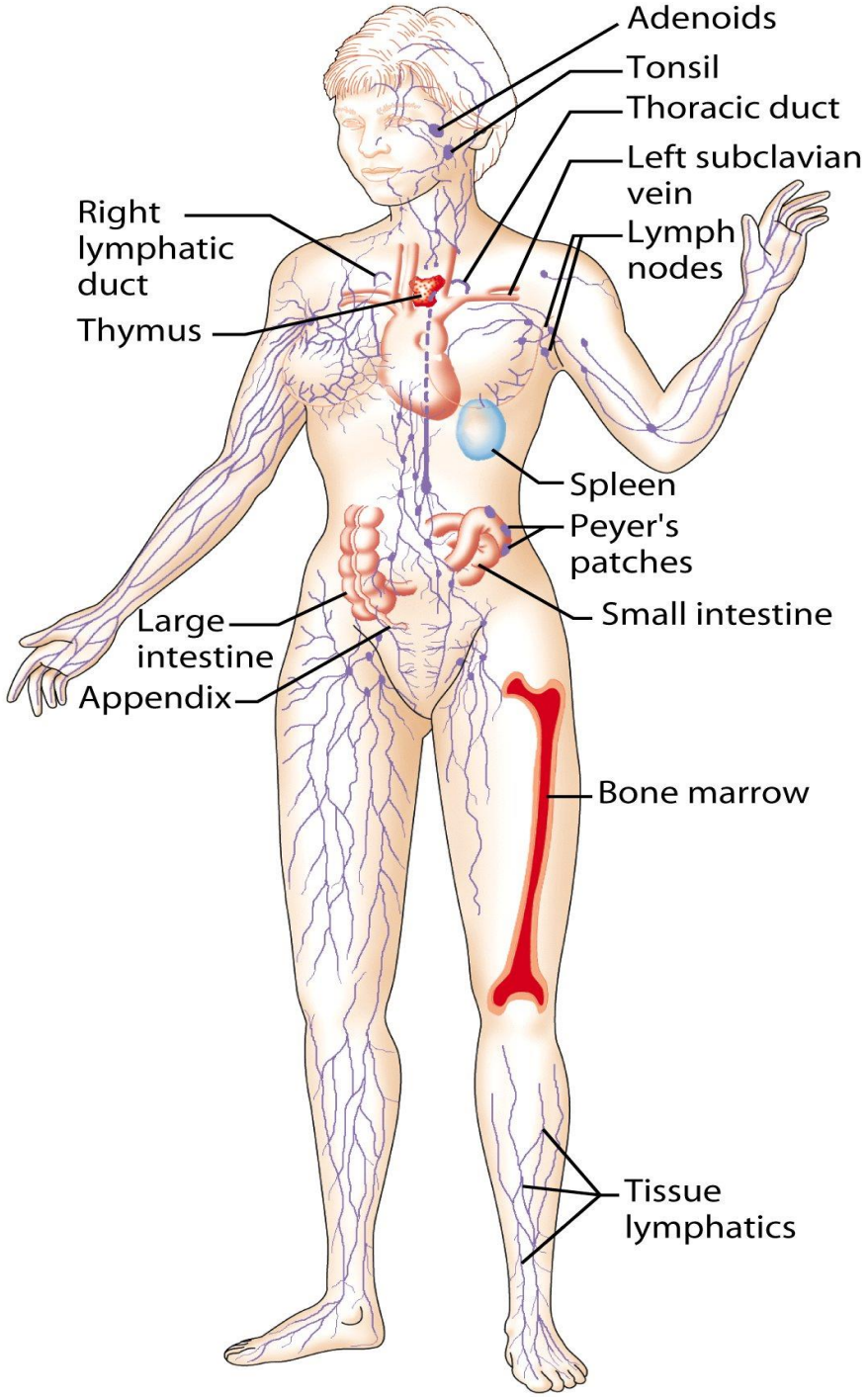
Activation of innate immune responses produces signal molecules (cytokines)

▼ ▼ ▼

These signal molecules stimulate and direct adaptive immune responses

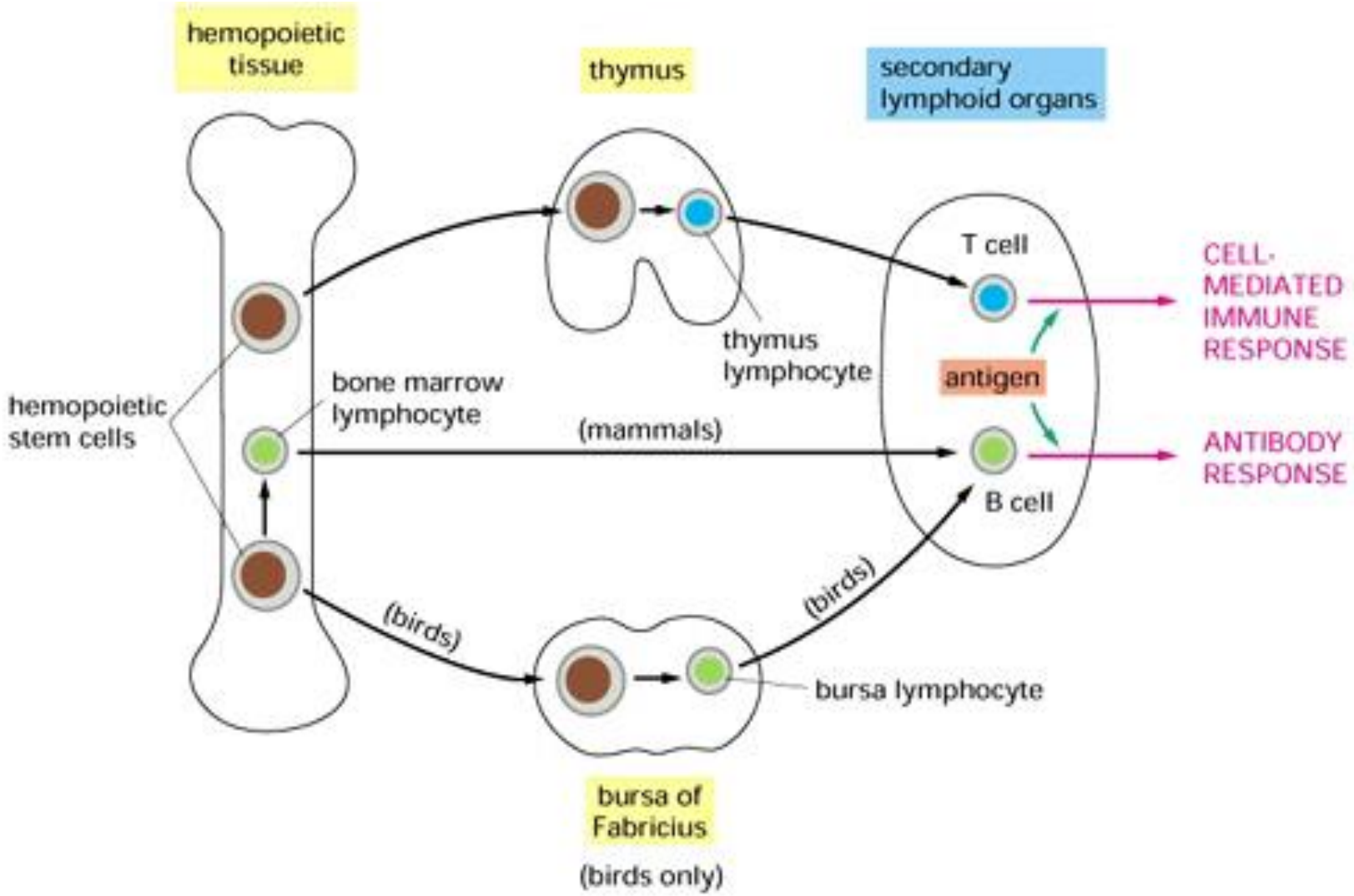
Lymphoid System

Lymphatic vessels and lymphoid organs



Primary Lymphoid Organs

(Development & Differentiation of immune cells)



Secondary Lymphoid Organs
(where the immune response occurs):

- Spleen
- Lymph nodes
- Tonsils
- MALT (Mucosa Associated Lymphoid Tissue)
- Peyer's patches
- Appendix

Secondary Lymphoid Organs

- **Lymph nodes and spleen are the most highly organized secondary lymphoid organs**
- **Differentiation into effector cells takes place in follicles of secondary lymphoid organs**
- **Both B and T lymphocytes will develop into long-lived memory cells in these areas, as well**
- **The spleen is the first line of defense against blood-borne pathogens**
- **Mucosa-associated lymphoid tissue (MALT) Important layer of defense against infection at mucosal and epithelial layers.**

Lymphoid series comprise of main lymphocyte populations

T cells / B cells / Natural Killer

T-Lymphocyte Differentiation

- T cells originate in Bone Marrow then migrate to Thymus for development.
- T cell precursors differentiate into mature T cells in Thymus. All of them have CD3 proteins on their cell surface
- During their passage through thymus they differentiate into T cells expressing either markers (**CD4 T helper cell** or **CD8 T cytotoxic cell**)

Two Major populations:

T helper lymphocytes (CD4+)

OR

T cytotoxic lymphocyte (CD8+)

Subtypes of T Helper (CD4+) & their functions

Th1/ Th2/ Th17/ T_{reg} / Tfh

- **Th1**: (Inflammatory T helper cell) mediates inflammation via helping macrophages in CMI during inflammatory response. Also helps CD8+ cells to become activated cytotoxic T cells.
- **Th2**: provides help to B cell to produce antibody
- **Th17**: has a role in innate Immunity & the pathogenesis of autoimmune diseases.
- **T_{reg}.:** repress the growth and function of T cell helper and cytotoxic subsets.
- **Tfh**: T follicular helper are critical to prevent autoimmunity.

T Cytotoxic (CD8+) Cells

- About 35% of peripheral blood T cells
- Perform cytotoxic functions
- They mediate the killing of:
  - Virus-infected cells
  - Tumors
  - Allograft cells (transplant)

B cells

- **Origin**
  - During embryogenesis – fetal liver
  - Migrate to bone marrow – final destination
- They do not require thymus for maturation

B cells

- **B cell progenitors: Pro-B cells, Pre-B cells and immature B cells are normally found in bone marrow**
- **Mature B cells are found circulating in body fluids and lymphoid organs**
- **Mature B cells display surface IgM and IgD which serves as antigen receptor (Maturation Markers)**

The good, bad, and ugly of the immune system

The Role of Immune system is to **PROTECT**
Dysfunction of this role when it is **Abnormal**:

- Overly active: Hypersensitivity / Autoimmunity
- Defects in the immune response: Immunodeficiency
- Rejection of transplanted tissue or organ
- Cancer

Take home message

- Normal healthy state is maintained by intact immune response either innate (natural immunity) and/or adaptive (acquired immunity after exposure to antigens)
- Cell mediated immunity and humoral immunity is mediated by T and B lymphocytes respectively
- Lymphoid system provides suitable environment for development, maturation and proper functioning of cells of immune system