Properties and Overview of Immune Responses

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- What does the immune system do? . . . . . .
- Ever wondered why you don't get the same disease twice?
- Where in your body is the immune system? . . . . . .
- The many cells of the immune system . . . . . .

Definitions

- The term of ***immunity*** *is derived from the Latin word immunitas.*
- The cells and molecules responsible for immunity constitute the **immune system.**
- Their collective and coordinated response to the introduction of foreign substances is called the **immune response.**

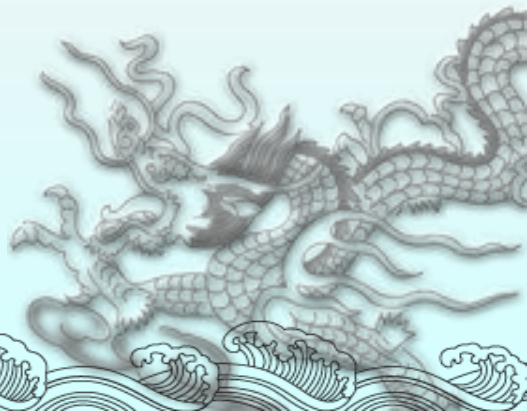
Definitions

- The physiologic function of the immune system is defense against infectious microbes.
- However, even noninfectious foreign substances can elicit immune responses.
- Under some situations, even self molecules can elicit immune responses (so-called autoimmune responses).

BRANCHES OF IMMUNOLOGY

- Basic Immunology:
  - Immunochemistry (Physiochemical Properties)
  - Cellular (Cells) and Molecular (Molecules) Immunology

- Clinical Immunology:
  - Organ transplantation
  - Autoimmune disease
  - Tumor immunology
  - Infectious diseases
  - Immunodeficiency
  - Allergic and Hypersensitivity
  - Reproductive Immunology
  - Immunohaematology

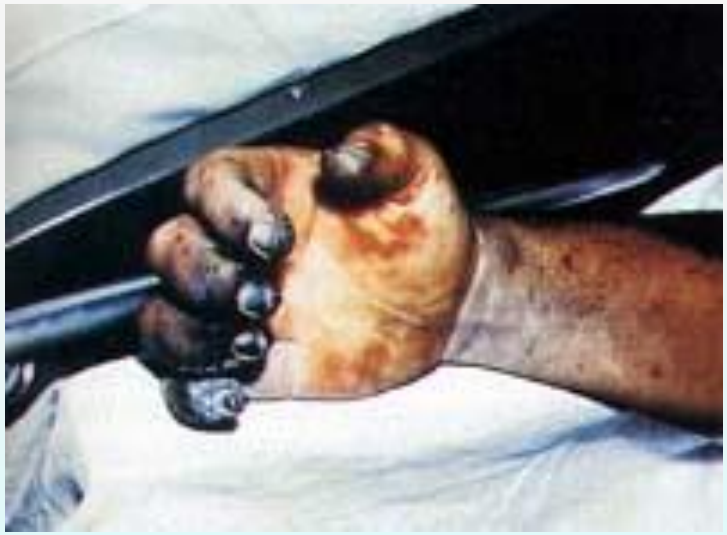


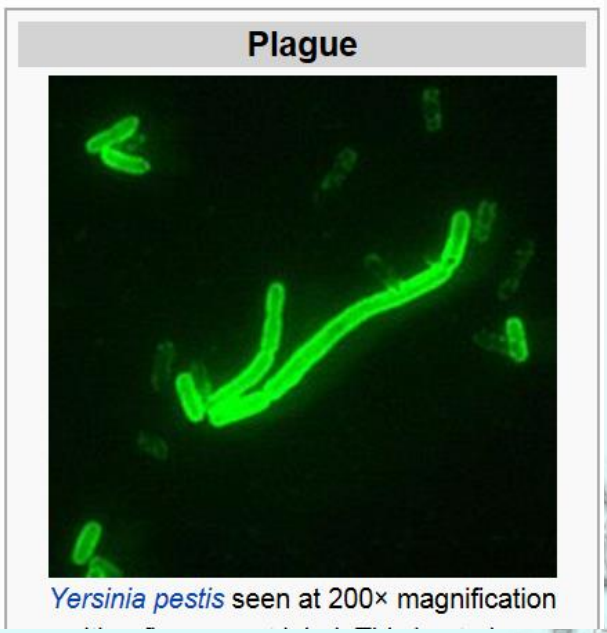
BRANCHES OF IMMUNOLOGY

- Applied immunology:
  - Preparation of monoclonal antibody and genetic engineering antibody
  - Preparation of recombinant cytokines
  - Study on DNA vaccine
  - Study on treatment with immune cells (immunotherapy)

History

- Thucydides, in the fifth century bc in Athens: first mentioned immunity to an infection (plague).
- ***Black Death Disease***

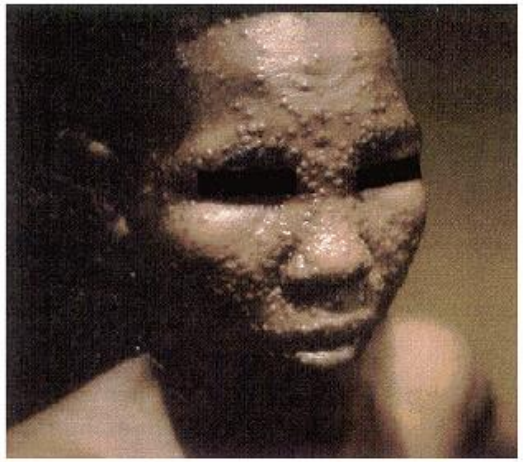




The Triumph of Death. Painting by Brueghel, Pieter the Elder. Museo del Prado, Madrid, Spain. Permission of Art Resource.

History

- The ancient Chinese: the concept of protective immunity to **smallpox**.



Inhalation
1670

History

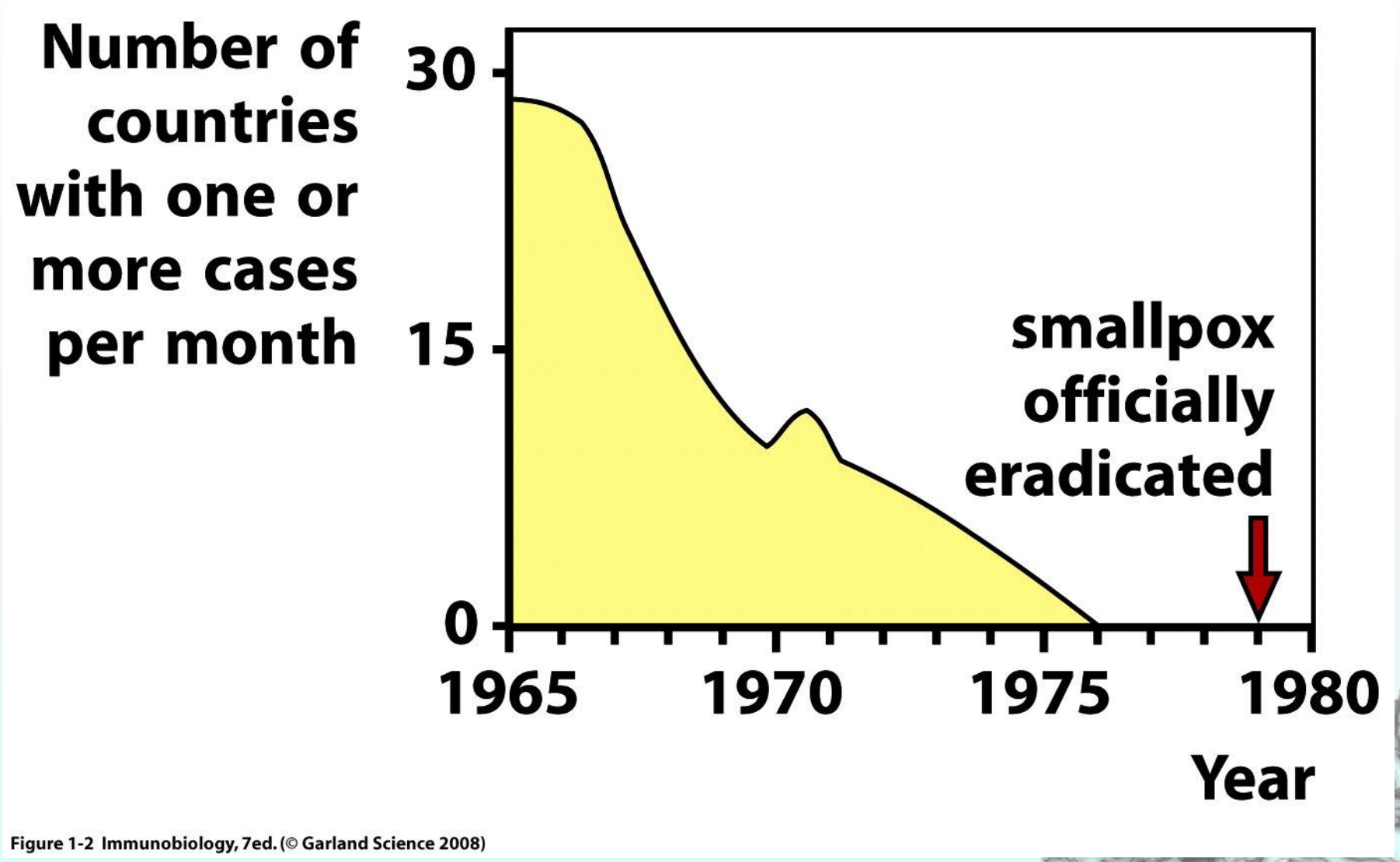
Lady Mary Wortley Montague
(1689-1762)

War on smallpox…

1718- **Lady Montague** became aware of a practice, called variolation or inoculation, and introduced it to Britain after first having her own children treated.

History

- One of the most dramatic ever recorded, was Edward Jenner's successful vaccination against **smallpox.**
  - Jenner's landmark treatise on **vaccination** (Latin *vaccinus,* of or from cows) was published in 1798.



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Attenuated cultured bacteria used for vaccination

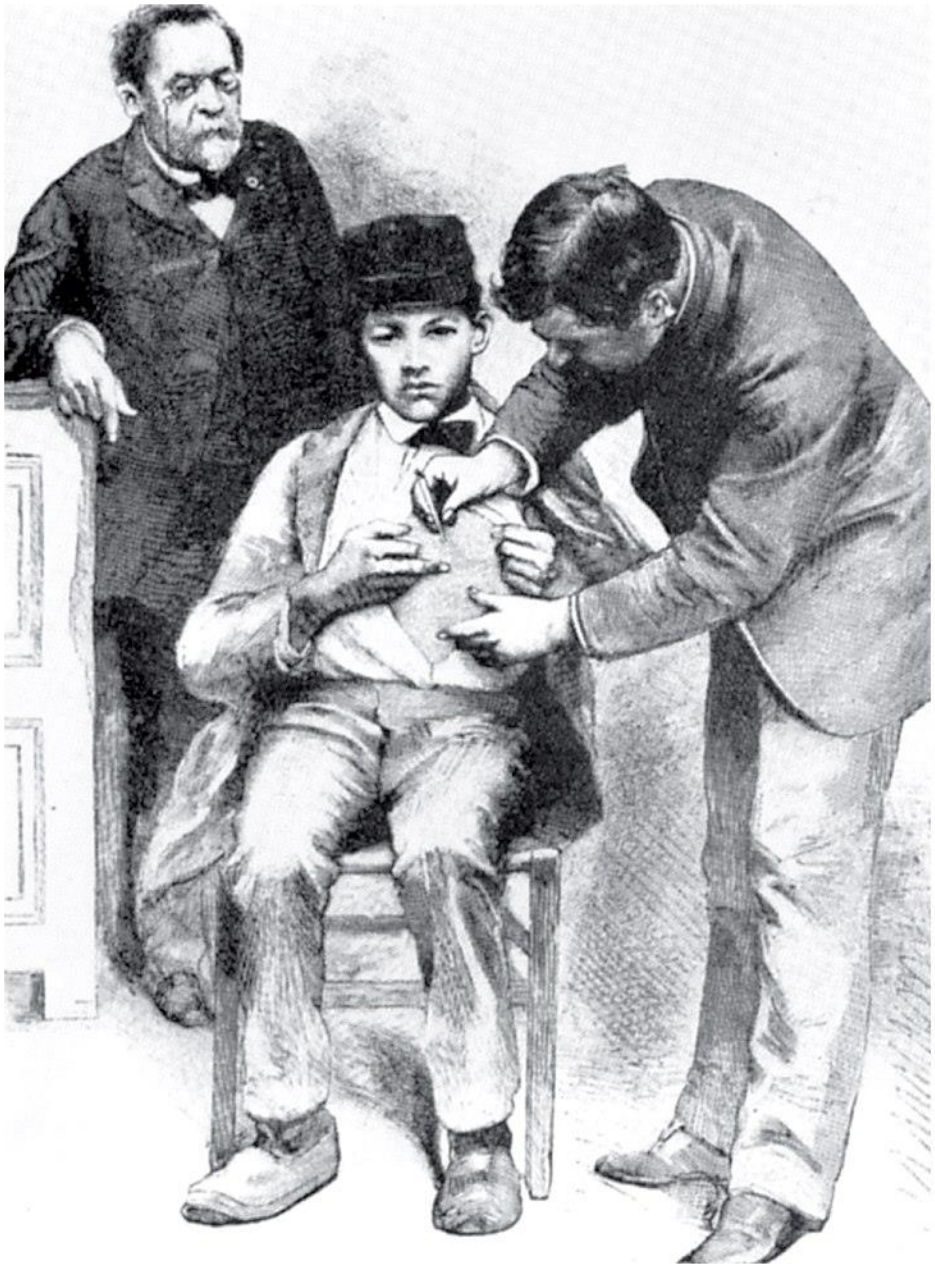
Pasteur inoculating sheep at Msr. Rossignol's farm – May, 1881

Louis Pasteur

1879- discovered that aged bacterial cultures of *Pasteurella* lost virulence. Referred to injection of **weakened culture** a "vaccine" in honor of Jenner

1881- He applied the same technique vs. anthrax

….and then rabies



Louis Pasteur watching as Joseph Meister receives attenuated rabies vaccine (1885)

Figure 1-2
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تاثیر واکسیناسیون در بیماریهای عفونی شایع

Disease	Maximum number of cases (year)	Number of cases in 2004	Percent change
Diphtheria	206,939 (1921)	0	-99.99
Measles	894,134 (1941)	37	-99.99
Mumps	152,209 (1968)	236	-99.90
Pertussis	265,269 (1934)	18,957	-96.84
Polio (paralytic)	21,269 (1952)	0	-100.0
Rubella	57,686 (1969)	12	-99.98
Tetanus	1,560 (1923)	26	-98.33
Haemophilus influenzae type B	~20,000 (1984)	16	-99.92
Hepatitis B	26,611 (1985)	6,632	-75.08

First insights into mechanics of immunity…

Emil von Behring

S. Kitasato

Elie Metchnikoff

1880's- Metchnikoff discovered phagocytic cells that ingest microbes and particles

∴ cells conferred immunity

1890- von Behring and Kitasato discovered blood sera could transfer immunity

∴ liquid of blood conferred immunity

Paul Erlich's side chain hypothesis for antibody formation (1900)

- Pluripotent blood cells with variety of receptor "side chains".
- Contact with foreign molecules (antigen) stimulated increased receptor production
- Specific receptors produced on cells prior to contact with antigen

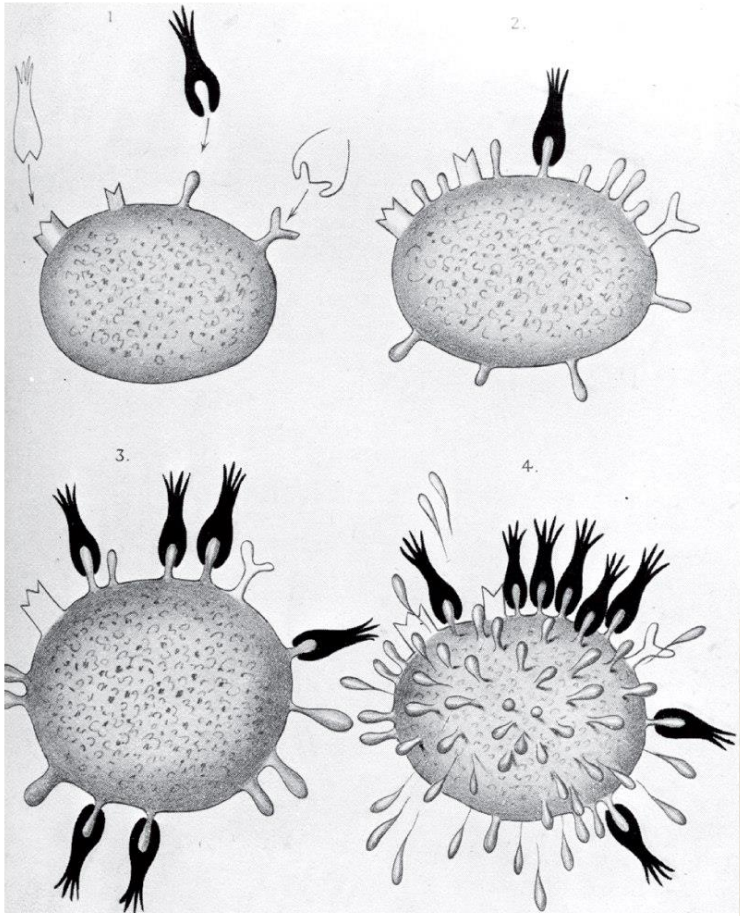

Figure 1-4
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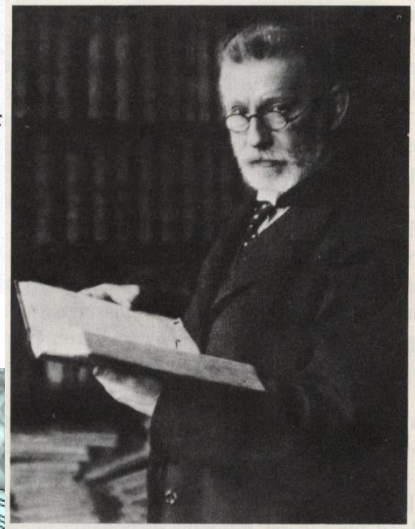
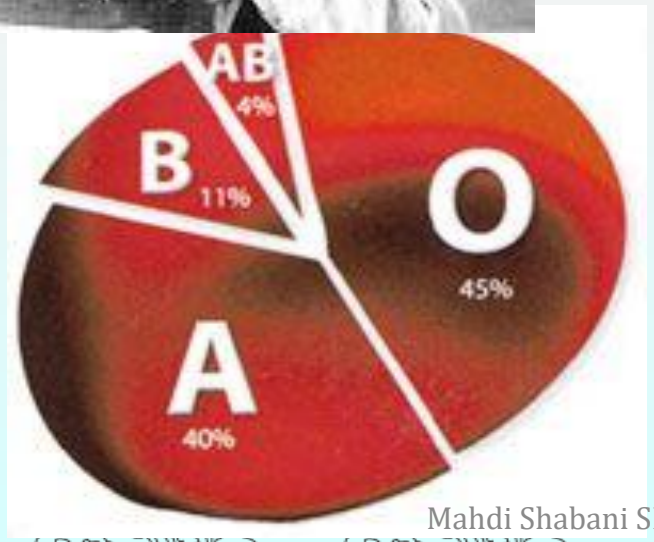


Foundation of selective theory

Understanding specificity of antibody for antigen

Karl Landsteiner



- **Early 1900's**- Landsteiner revealed antibody could be produced vs. most any organic compound
- **Last 20 yrs**- Antibody specificity reveals unlimited range of reactivity – also to newly synthesized chemicals!

Both cells and serum contribute to immunity!

- 1930's – early techniques made it easier to study **humoral** elements [than cellular ones].

  -discovery of active component of blood – gamma globulin "protein"

- 1950's – discovery of T and B cells

  Later discoveries linked lymphocytes to both cellular and humoral immunity

TABLE 1-2 Nobel prizes for immunologic research

Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Bordet	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter Gerald M. Edelman	Great Britain United States	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Dausset Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Cesar Milstein Georges E. Köhler Niels K. Jerne	Great Britain Germany Denmark	Monoclonal antibodies Immune regulatory theories
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by T cells
2002	Sydney Brenner H. Robert Horvitz J. E. Sulston	S. Africa United States Great Britain	Genetic regulation of organ development and cell death (apoptosis)

Table 1-2
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The Immune System

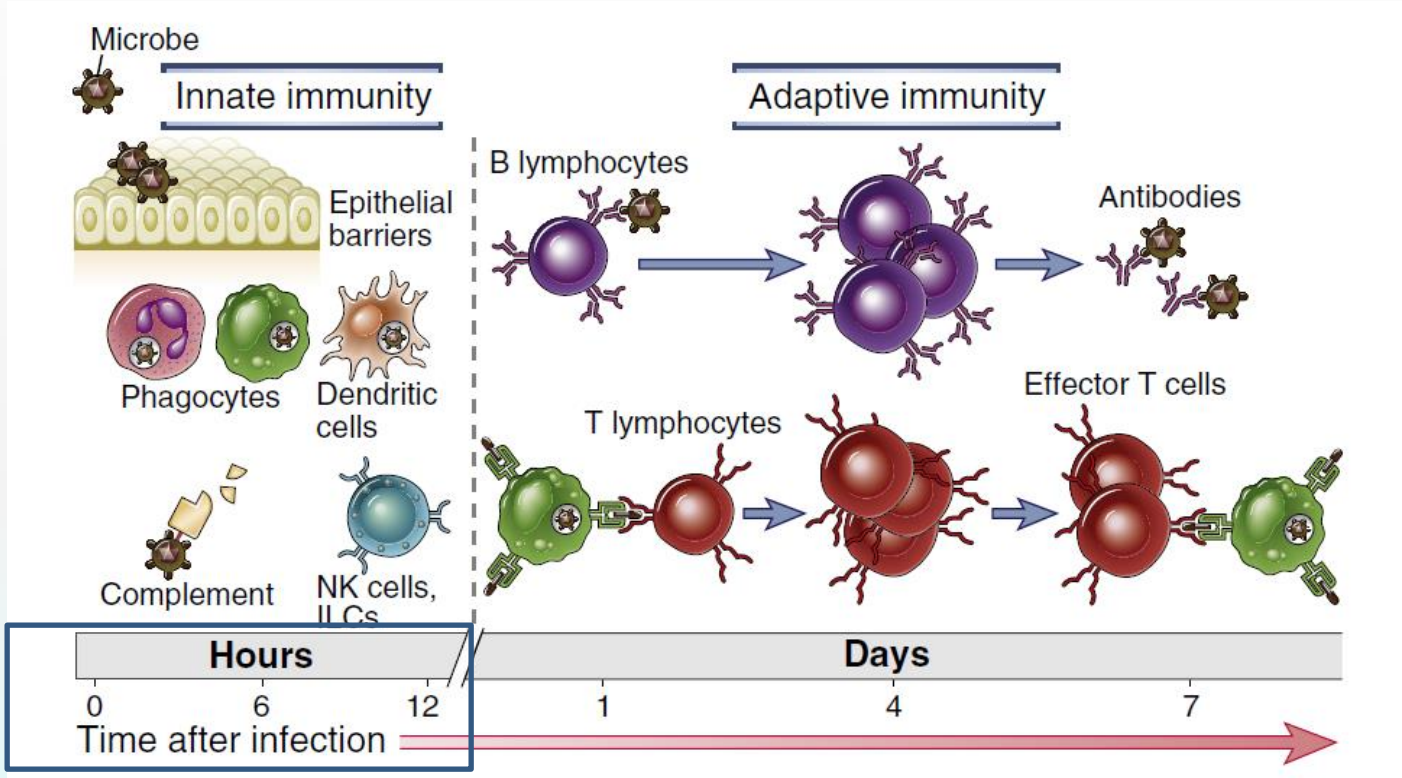
***Defense** against microbes is mediated by the early reactions of **innate immunity** and the later responses of **adaptive immunity**.*

Innate and adaptive responses

- Innate and adaptive immune responses are components of an integrated system of host defense in which numerous **cells** and **molecules** function cooperatively.

- There are numerous connections between the **innate** and **adaptive** immune systems.

Innate and adaptive immunity.

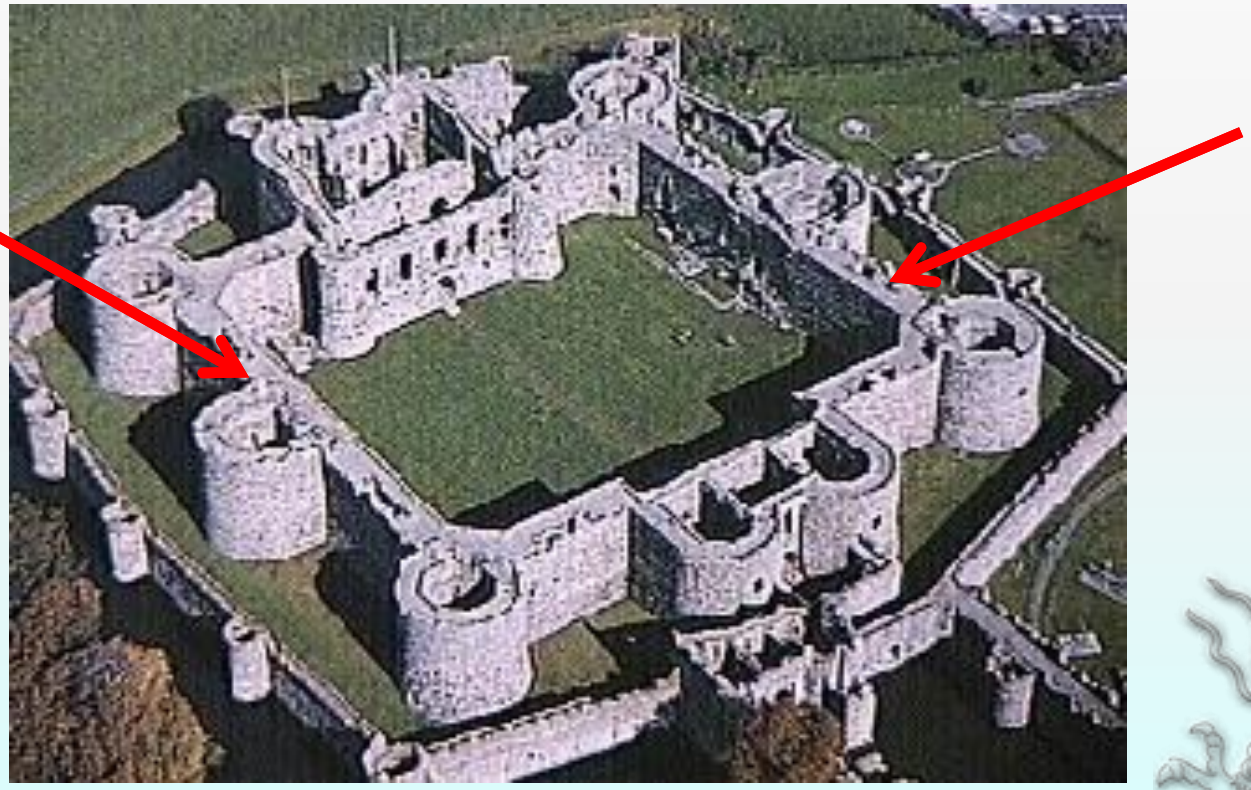


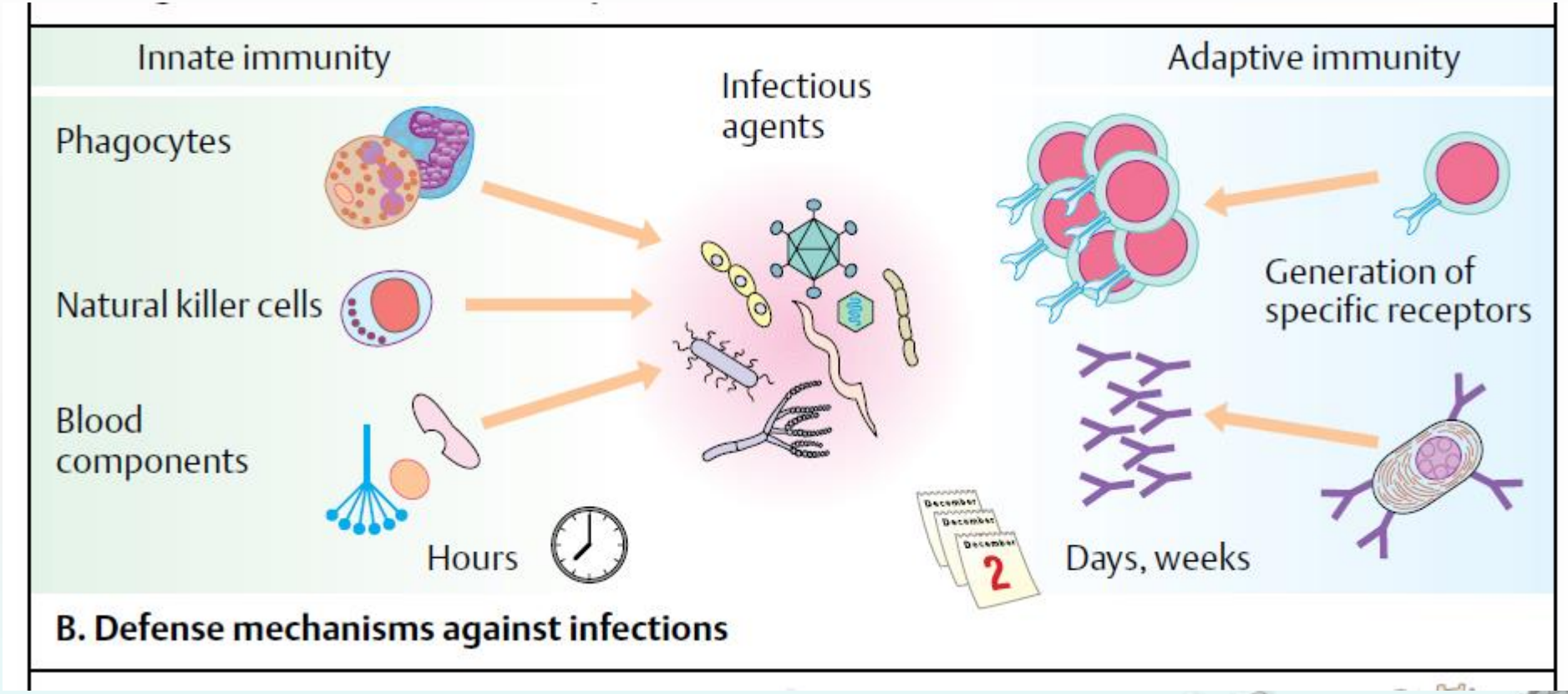
Overview of your immune system

- First line of defense: **Innate immune** system (germline-encoded receptors -- no adaptation to specific pathogens)

Overview of your immune system

- Second line of defense (vertebrates only): Adaptive immune system (adapts to defend against specific pathogens using variable receptors)





B. Defense mechanisms against infections

INNATE IMMUNITY

- **Innate immunity** (also called **natural** or **native immunity**) provides the early line of defense against microbes.
  - They respond in essentially the same way to repeated exposures
  - They may **not** distinguish fine differences between microbes

The principal components of innate immunity are:

- (1) physical and chemical barriers
  - such as epithelia, mucous membrane
  - antimicrobial chemicals produced at epithelial surfaces
- (2) phagocytic cells
  - neutrophils, macrophages,
  - dendritic cells,
  - natural killer (NK) cells
  - other innate lymphoid cells
- (3) blood proteins
  - Including complement system
  - other mediators of inflammation

physical barriers

- **Physical barriers** that viruses, bacteria must cross
  - Skin covers ~2 m^2
  - Mucous membranes that line digestive, respiratory, reproductive tracts cover ~400 m^2

The Early Innate Immune Response to Microbes

- The innate immune system **blocks** the entry of microbes and eliminates or limits the growth of many microbes.

- The cellular innate immune response to microbes consists of two main types of reactions—inflammation and antiviral defense.

The Early Innate Immune Response to Microbes

- **Inflammation** is the process of recruitment of leukocytes and plasma proteins from the blood, their accumulation in tissues, and their activation to destroy the microbes.

- The major leukocytes that are recruited in inflammation are the phagocytes, neutrophils (which have **short life spans** in tissues) and monocytes (which develop into tissue macrophages).

Inflammation causes blood cells to move from blood stream to site of injury

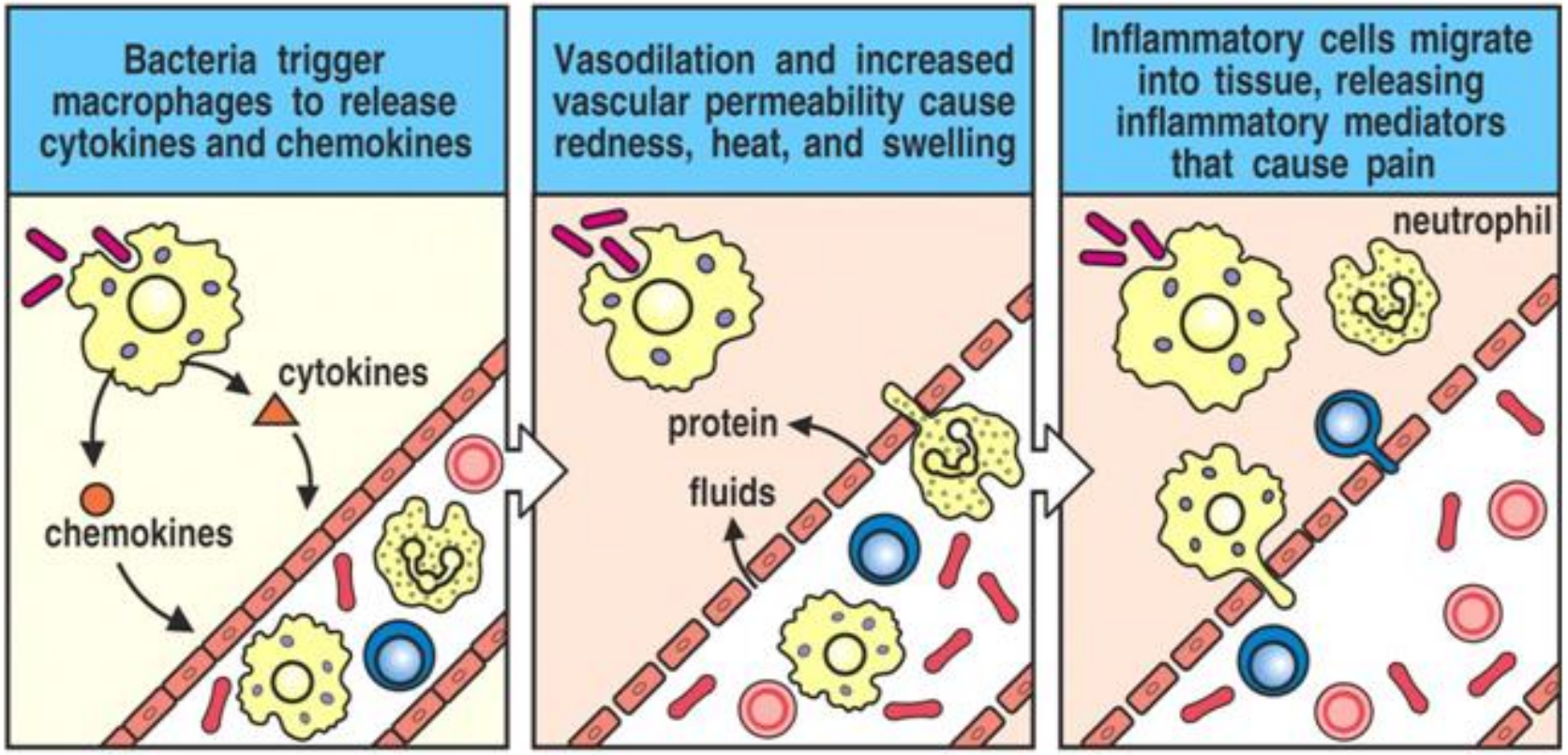


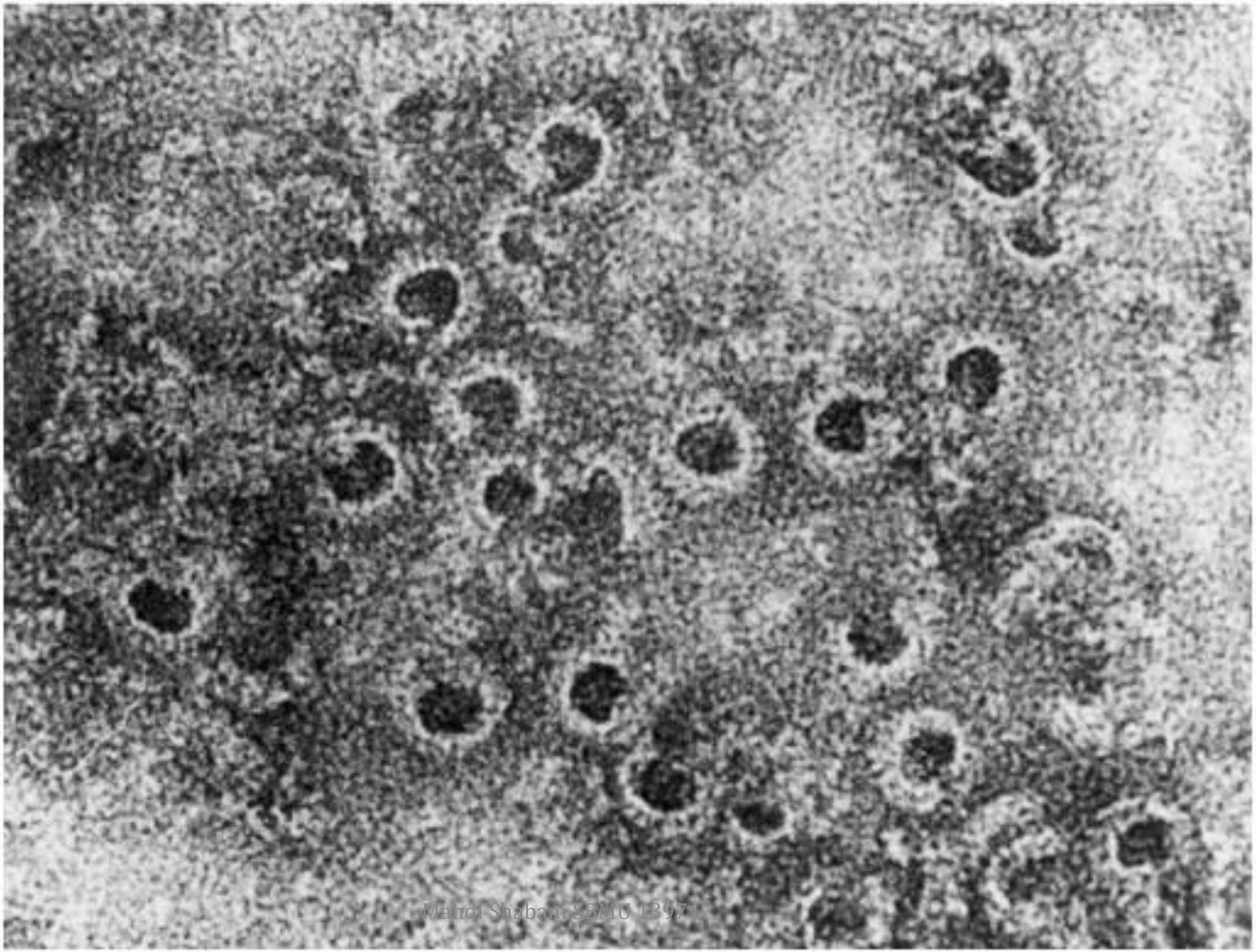
Figure 1-12 Immunobiology, 6/e. (© Garland Science 2005)

The Early Innate Immune Response to Microbes

- **Antiviral defense consists** of a cytokine-mediated reaction in which cells acquire resistance to viral infection and killing of virus infected cells by specialized cells of the innate immune system, natural killer (NK) cells.

- Microbes that are able to withstand these defense reactions in the tissues may enter the blood:
  - the complement system

(b)



- The innate immune response is essential for elimination of a pathogen but not sufficient.

- The adaptive immune response requires certain key players of the innate immune response to become activated.

Adaptive immunity

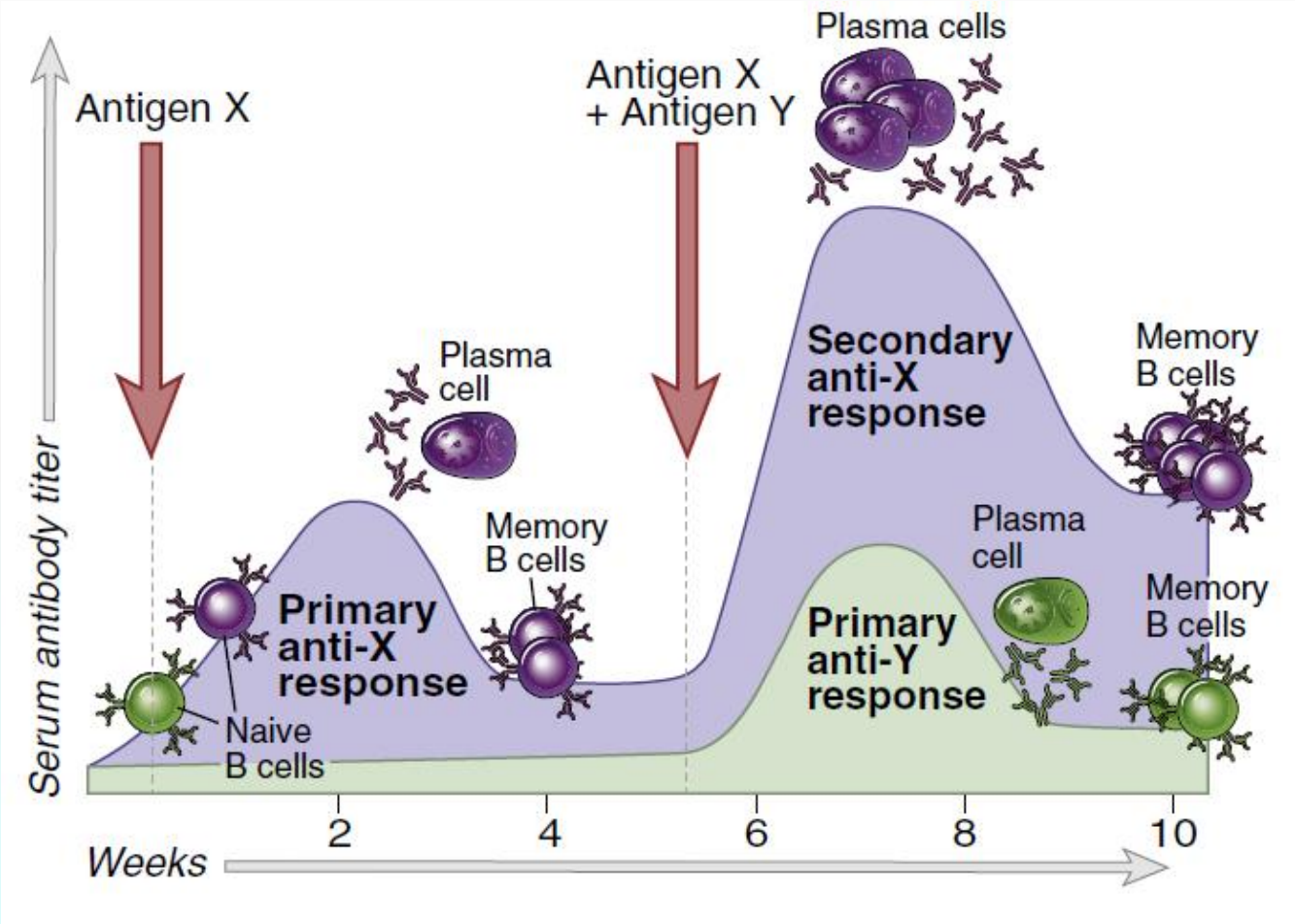
- Adaptive immunity is stimulated by exposure to infectious agents and **increase** in magnitude and defensive capabilities with each **successive exposure** to a particular microbe.

- Because this form of immunity develops as a response to infection and adapts to the infection, it is called **adaptive immunity** (also called **specific** or **acquired immunity**).

Adaptive immunity

- The defining characteristics of adaptive immunity are:
  - the ability to distinguish different substances, called **specificity**,
  - the ability to respond more vigorously to repeated exposures to the same microbe, known as **memory**.

Specificity, memory, and contraction of adaptive immune responses



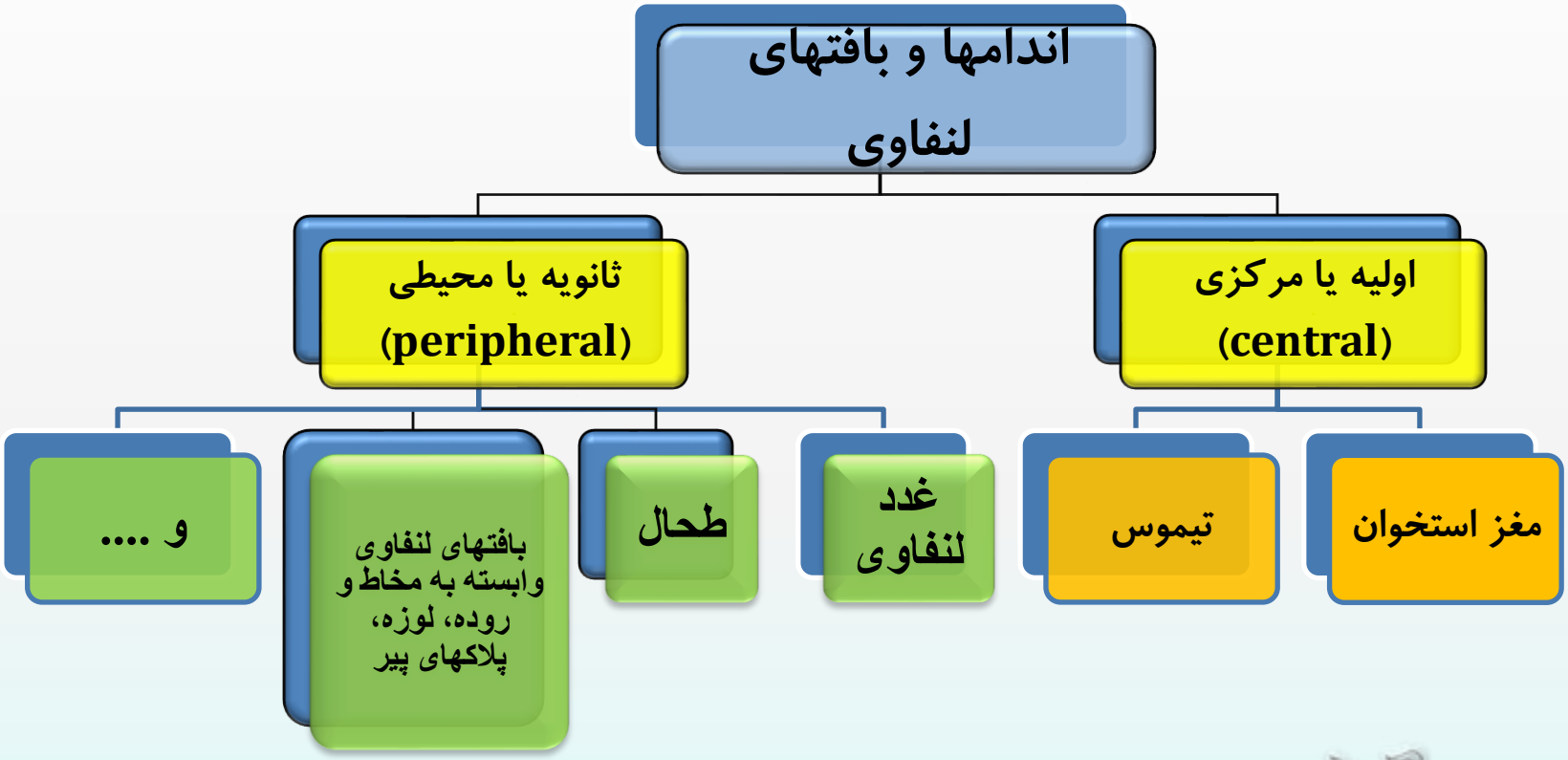
Cardinal Features of Adaptive Immune Responses

- ***Specificity and diversity*.**
  - ***Antigen* determinants** or **epitopes**
  - **clonal selection**
  - **Diversity**
- ***Memory***
- ***Nonreactivity to self (self tolerance)***

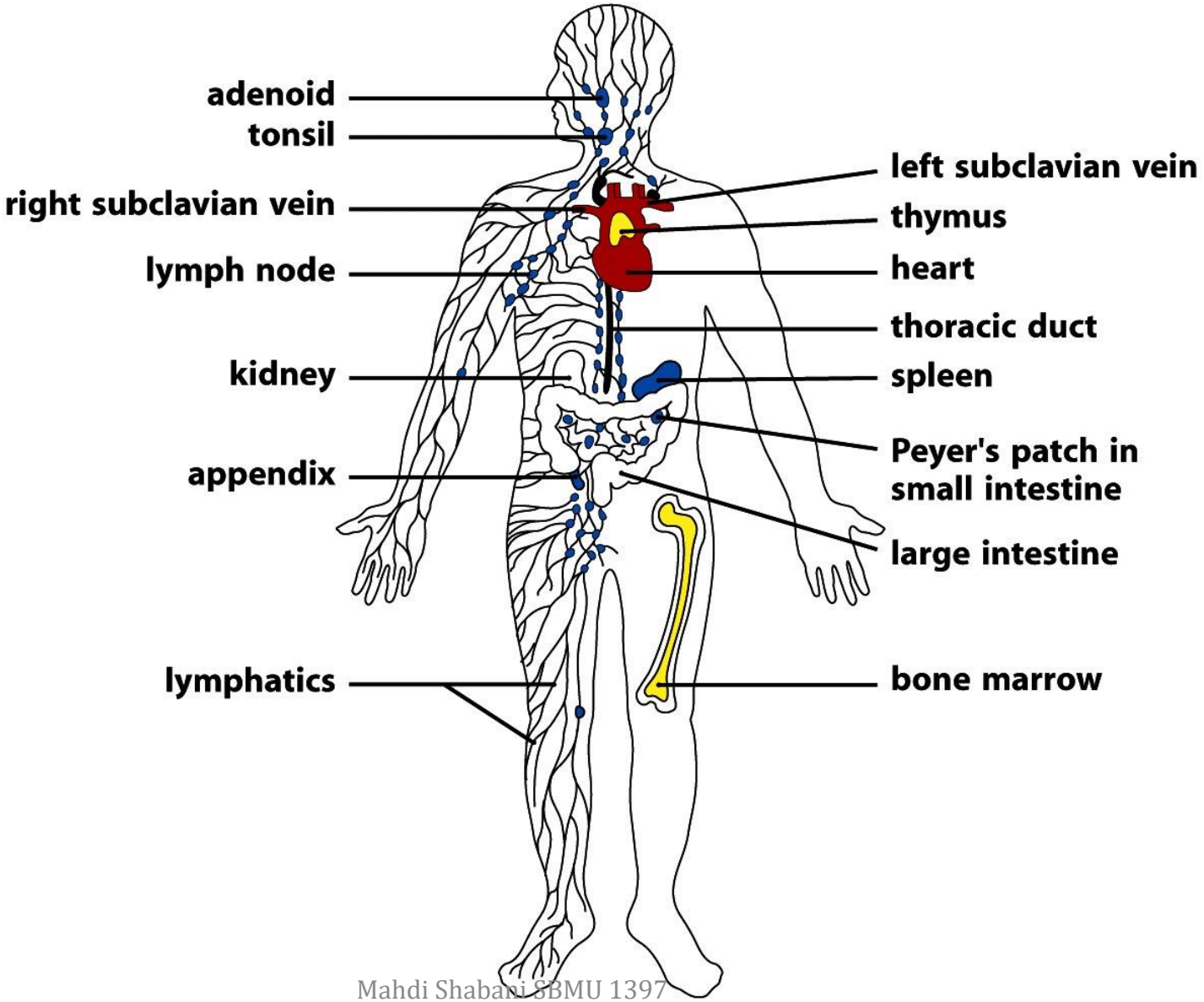
Adaptive immunity

- The unique components of adaptive immunity are
  - cells called **lymphocytes**
  - their secreted products, such as **antibodies.**

- Foreign substances that induce specific immune responses **(Immunogens)** or are recognized by lymphocytes or antibodies are called **antigens.**


اندامها و بافتهای لنفاوی
اولیه یا مرکزی (central)
ثانویه یا محیطی (peripheral)
مغز استخوان
تیموس
غدد لنفاوی
طحال
بافتهای لنفاوی وابسته به مخاط و روده، لوزه، پلاکهای پیر
و ....

اندامها و بافتهای لنفاوی



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TYPES OF ADAPTIVE IMMUNE RESPONSES

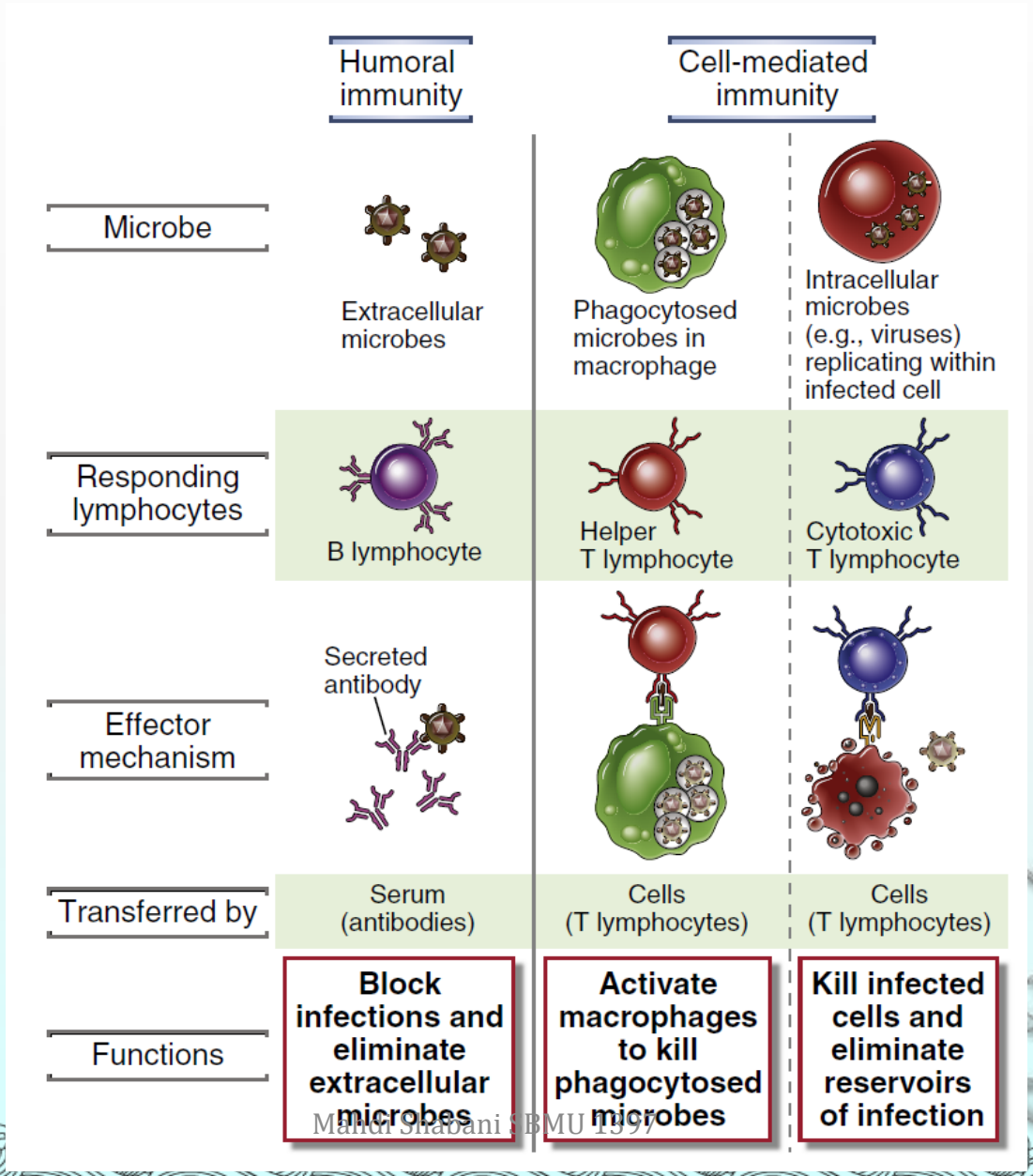
- There are two types of adaptive immune responses, called
  - humoral immunity
  - cell-mediated immunity

- that are mediated by different components of the immune system and function to eliminate **different types of microbes**.

The Adaptive Immune Response

- The adaptive immune system uses three main strategies to combat microbes:
  - ***Antibodies.*** ***Secreted antibodies bind to extracellular*** microbes, block their ability to infect host cells, and promote their ingestion and subsequent destruction by phagocytes.
  - ***Phagocytosis. Phagocytes ingest microbes and kill*** them, and antibodies (opsonization) and helper T cells (INFγ) enhance the microbicidal abilities of the phagocytes.
  - ***Cell killing. Cytotoxic T lymphocytes (CTLs) destroy*** cells infected by microbes that are inaccessible to antibodies and phagocytic destruction.

Types of adaptive immunity



Humoral immunity

- **Humoral immunity** is mediated by molecules in the blood and mucosal secretions, called **antibodies**, which are produced by cells called **B lymphocytes** (also called **B cells**).

- Antibodies recognize microbial antigens, neutralize the infectivity of the microbes, and target microbes for elimination by various effector mechanisms.

Humoral immunity

- Humoral immunity is the principal defense mechanism against extracellular microbes and their toxins.

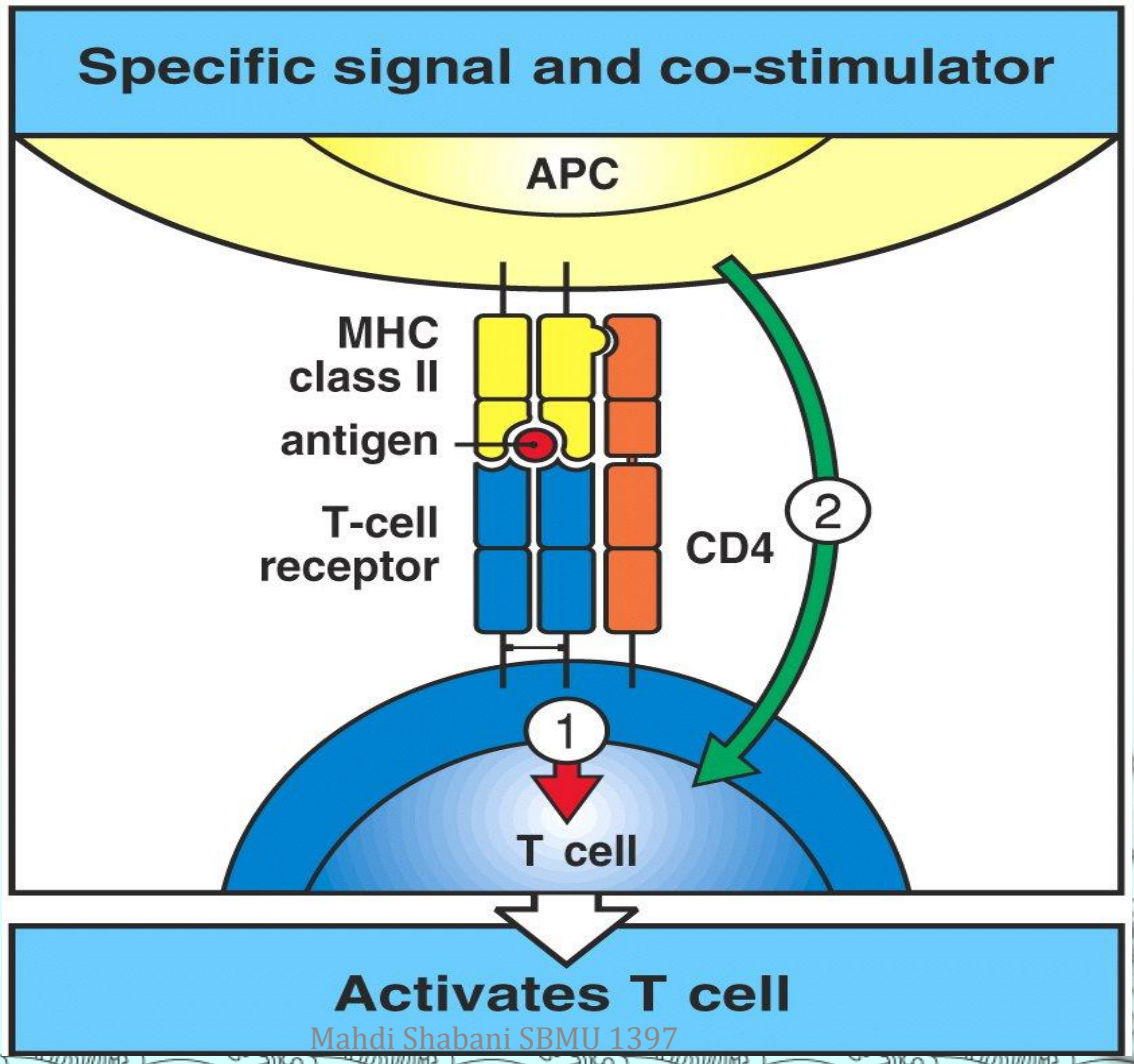
- Antibodies themselves are specialized and may activate different mechanisms to combat microbes (**effector mechanisms**).

Cell-mediated immunity

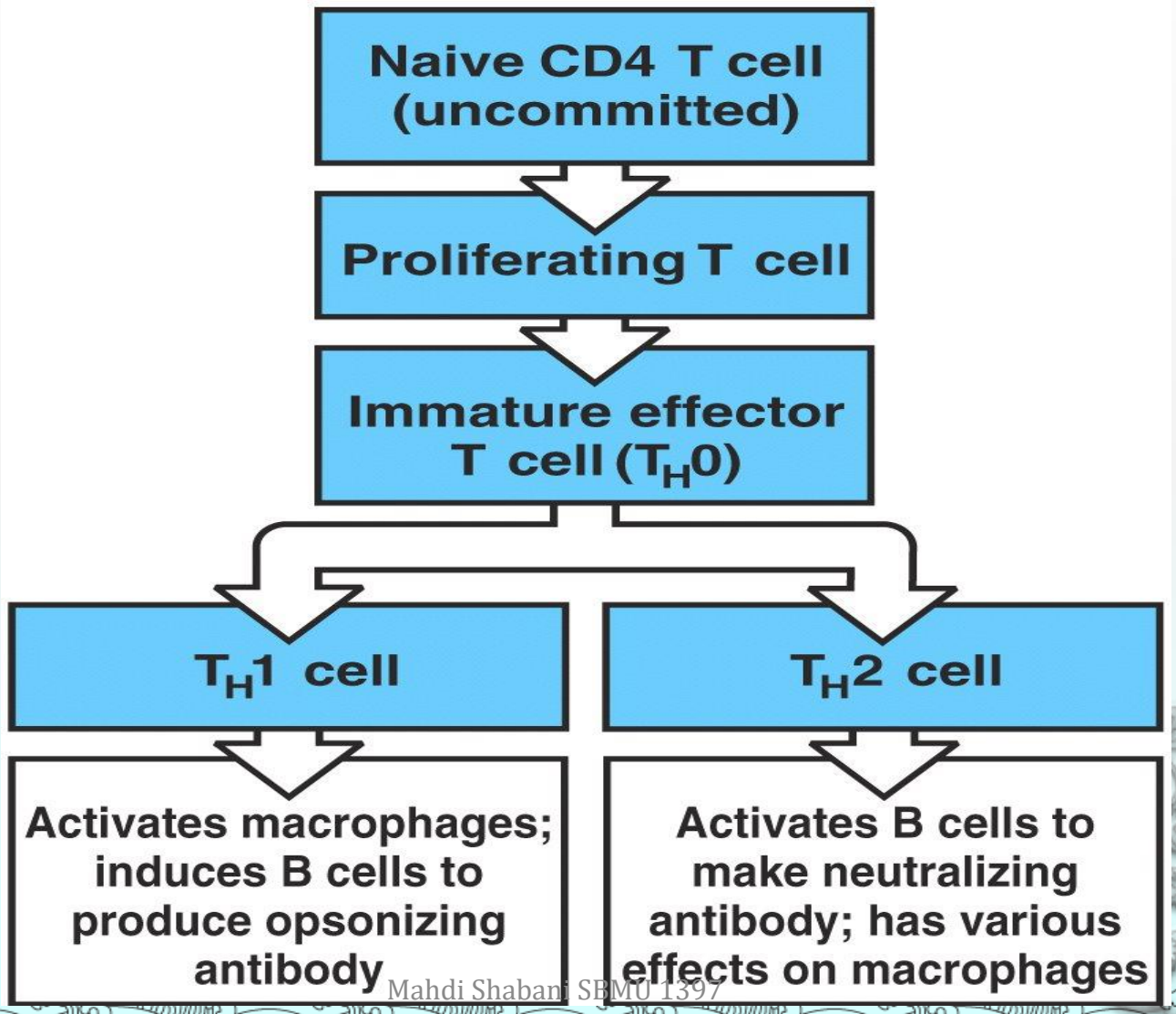
- **Cell-mediated immunity**, also called **cellular immunity**, is mediated by **T lymphocytes** (also called **T cells**).

- Defense against intracellular microbes is a function of cell-mediated immunity, which promotes the destruction of microbes residing in phagocytes or the killing of infected cells to eliminate reservoirs of infection.

Activation of naïve T cells requires two independent signals delivered by the same APC



The stages of activation of CD4 T cells



Summery

TABLE 1.2 Features of Innate and Adaptive Immunity

	Innate	Adaptive
Characteristics		
Specificity	For molecules shared by groups of related microbes and molecules produced by damaged host cells	For microbial and nonmicrobial antigens
Diversity	Limited; recognition molecules encoded by inherited (germline) genes	Very large; receptor genes are formed by somatic recombination of gene segments in lymphocytes
Memory	None or limited	Yes
Nonreactivity to self	Yes	Yes
Components		
Cellular and chemical barriers	Skin, mucosal epithelia; antimicrobial molecules	Lymphocytes in epithelia; antibodies secreted at epithelial surfaces
Blood proteins	Complement, various lectins and agglutinins	Antibodies
Cells	Phagocytes (macrophages, neutrophils), dendritic cells, natural killer cells, mast cells, innate lymphoid cells	Lymphocytes

مرجع

ایمونولوژی سلولی و مولکولی

Cellular and Molecular Immunology, Abbul K. Abbas, Andrew H. Lichtman, Shiv Pillai,

موفق باشید