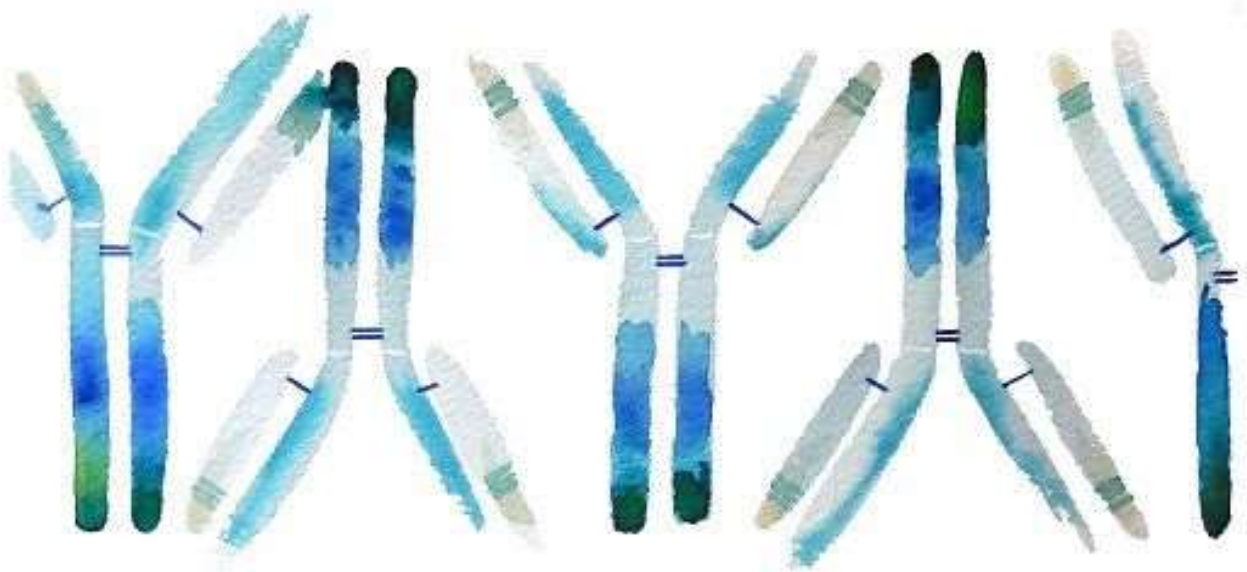
Medical Immunology



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Lecture 1

- **Immunity** is defined as resistance to disease, specifically infectious disease. The collection of cells, tissues, and molecules that mediate resistance to infections is called the **immune system**, and the coordinated reaction of these cells and molecules to infectious microbes comprises an immune response.

- **Immunology** is the study of the immune system, including its responses to microbial pathogens and damaged tissues and its role in disease.

Role of the immune system	Implications
Defense against infections	Deficient immunity results in increased susceptibility to infections; exemplified by AIDS Vaccination boosts immune defenses and protects against infections
Defense against tumors	Potential for immunotherapy of cancer
The immune system can injure cells and induce pathologic inflammation	Immune responses are the cause of allergic, autoimmune, and other inflammatory diseases
The immune system recognizes and responds to tissue grafts and newly introduced proteins	Immune responses are barriers to transplantation and gene therapy

- **Immunology** and its applications helped save millions of lives, and future breakthroughs are expected to save more!

Disease	Maximum number of cases (year)	Number of cases in 2014	Percent change
Diphtheria	206,939 (1921)	0	–100
Measles	894,134 (1941)	669	–99.93
Mumps	152,209 (1968)	737	–99.51
Pertussis	265,269 (1934)	10,631	–95.99
Polio (paralytic)	21,269 (1952)	0	–100
Rubella	57,686 (1969)	2	–99.99
Tetanus	1560 (1923)	8	–99.48
Hemophilus influenza type B	~20,000 (1984)	34	–99.83
Hepatitis B	26,611 (1985)	1,098	–95.87

Immunology introduction / history

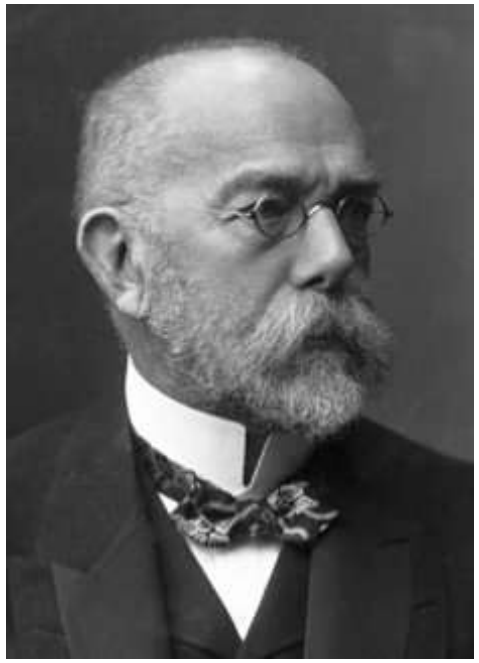
- In Western society, it was not until the late eighteenth century that a rational approach to the origin of disease developed.

- In 1798, Edward Jenner, noticed that milkmaids were protected from smallpox if they had been first infected with cowpox .

A representation by Robert Seymour of the cholera epidemic of the 19th century depicts the spread of the disease in the form of poisonous air.

- **Robert Koch** was one of the main founders of modern bacteriology, he identified the specific causative agents of tuberculosis, cholera, and anthrax and gave experimental support for the **concept of infectious disease (germ theory)**, which included experiments on humans and other animals

- **Pasteur** is renowned for his discoveries of the principles of **vaccination**, microbial fermentation and **pasteurization,** he was responsible for disproving the doctrine of **spontaneous generation.**



Robert Koch 1843 –1910

Louis Pasteur 1822 –1895

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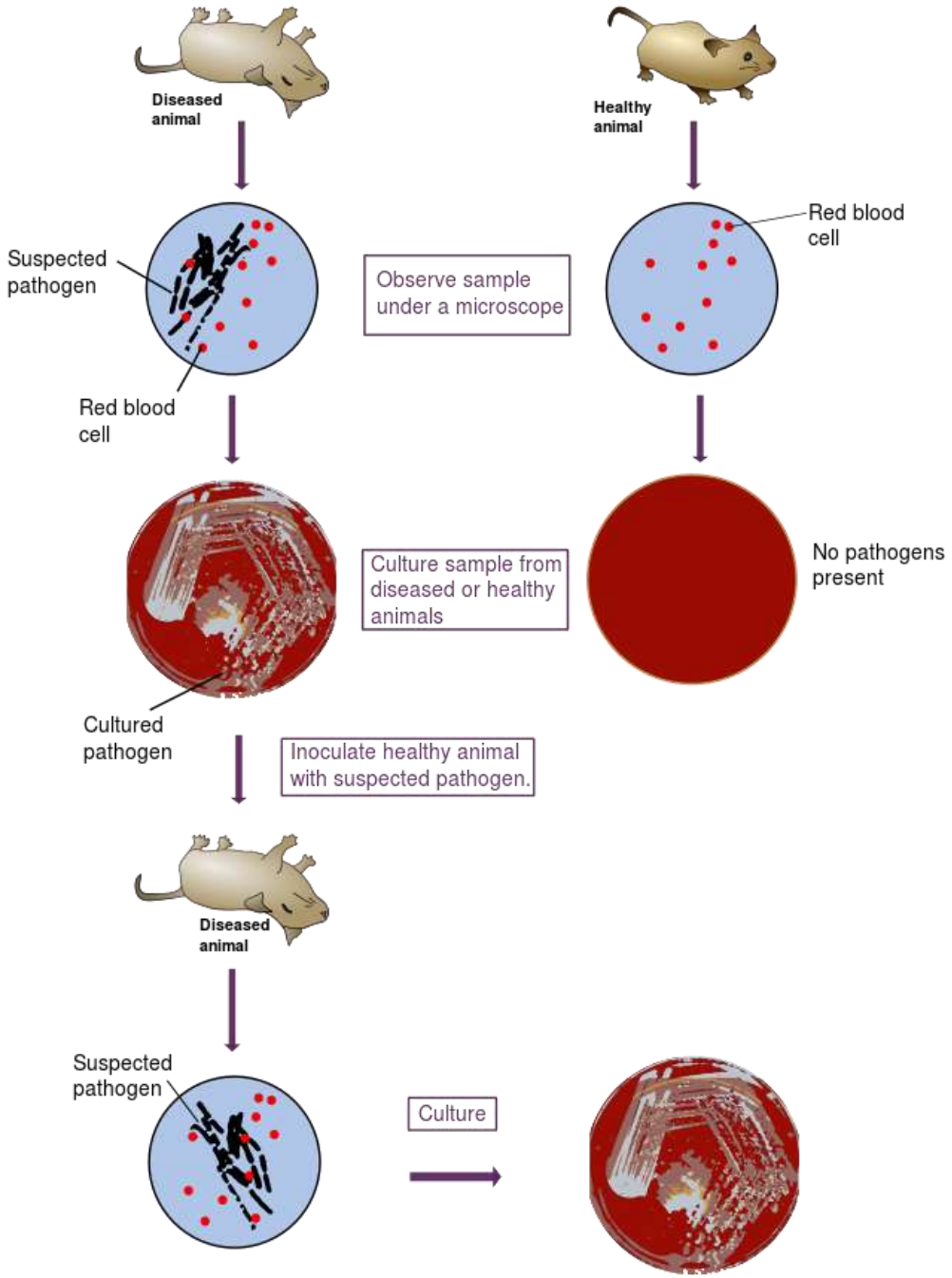
Koch's Postulates:

① The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.

② The microorganism must be isolated from a diseased organism and grown in pure culture.

③ The cultured microorganism should cause disease when introduced into a healthy organism.

④ The microorganism must be reisolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.



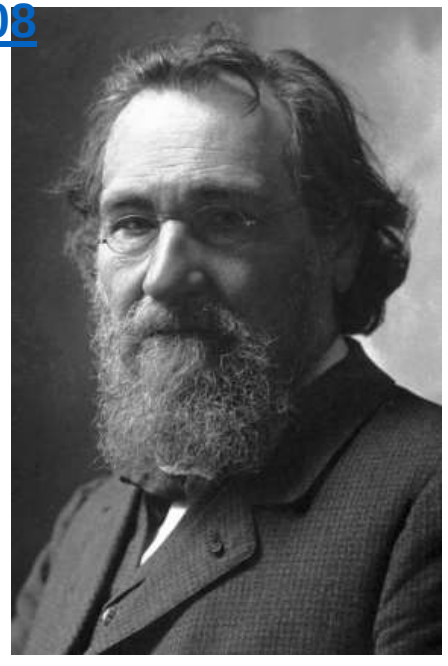
Immunology introduction / history

- **Paul Ehrlich** and others, recognized that a specific **antigen** elicited the production of a specific **antibody** . Ehrlich hypothesized that these antibodies were specialized molecular structures with specific receptor sites that fit each pathogen like a **lock and key**. Thus, the first realization that the body had a **specific defense system** was introduced.

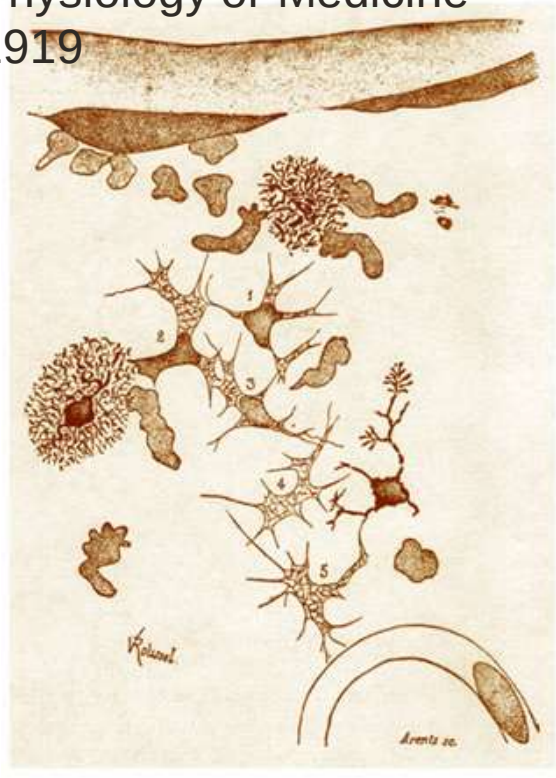
- The idea that specific cells could be directly involved with defending the body was first suggested in 1884 by **Élie Metchnikoff** .

- However, it was not until the 1940s that his theories were accepted and the **cell mediated**, as opposed to the **humoral**, immune response was recognized

[The Nobel Prize in Physiology or Medicine 1908]



Jules Bordet
The Nobel Prize in Physiology or Medicine 1919



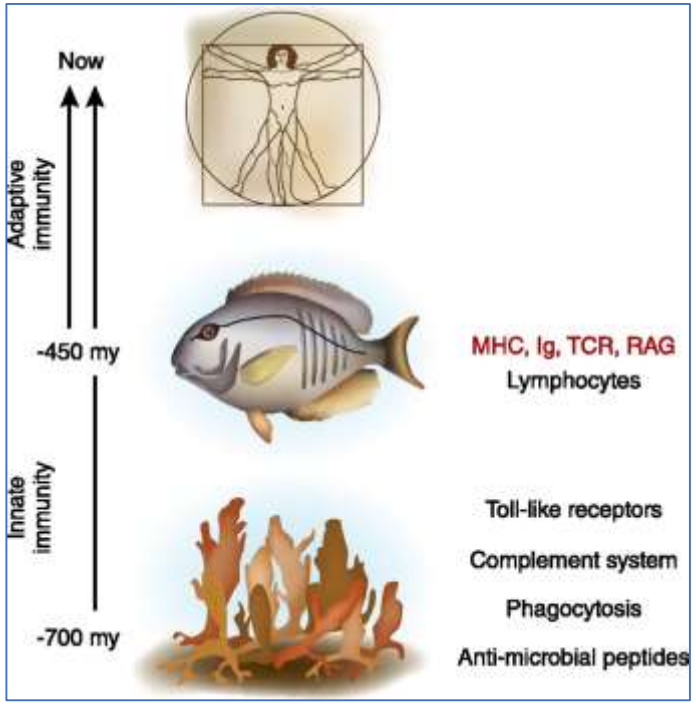
Nature Reviews | Molecular Cell Biology

Immunology introduction

- The immune system includes the role of **physical**, **cellular**, and **chemical systems** that are in place and that respond to all aspects of **foreignness**.
- The immune system targets any “foreign” object, so the first step is to **recognize** what is self and non- self.
- The second step is to **restore** homeostasis by eliminating the foreign object.
- The third step is to **remember** the invading pathogen to respond better the next time it is encountered .
- The immune system is not **only** active when danger arises, but is constantly sensing danger and is **important for normal physiology and homeostasis** similar to the cardiovascular and renal systems.

- Mechanisms for discriminating "**self" from "non-self"** evolved to accomplish the task of fighting pathogens, launching a long history of **host-pathogen co-evolution.**
- Virtually all organisms have at least one form of defence that helps repel disease-causing organisms.
- Pathogens evolve new strategies to over come immune mechanisms, and so the host defence becomes more complex to defend against invading pathogens.
- **Jawed vertebrates** have developed higher complexity of defence reflected in the **adaptive immune response**.

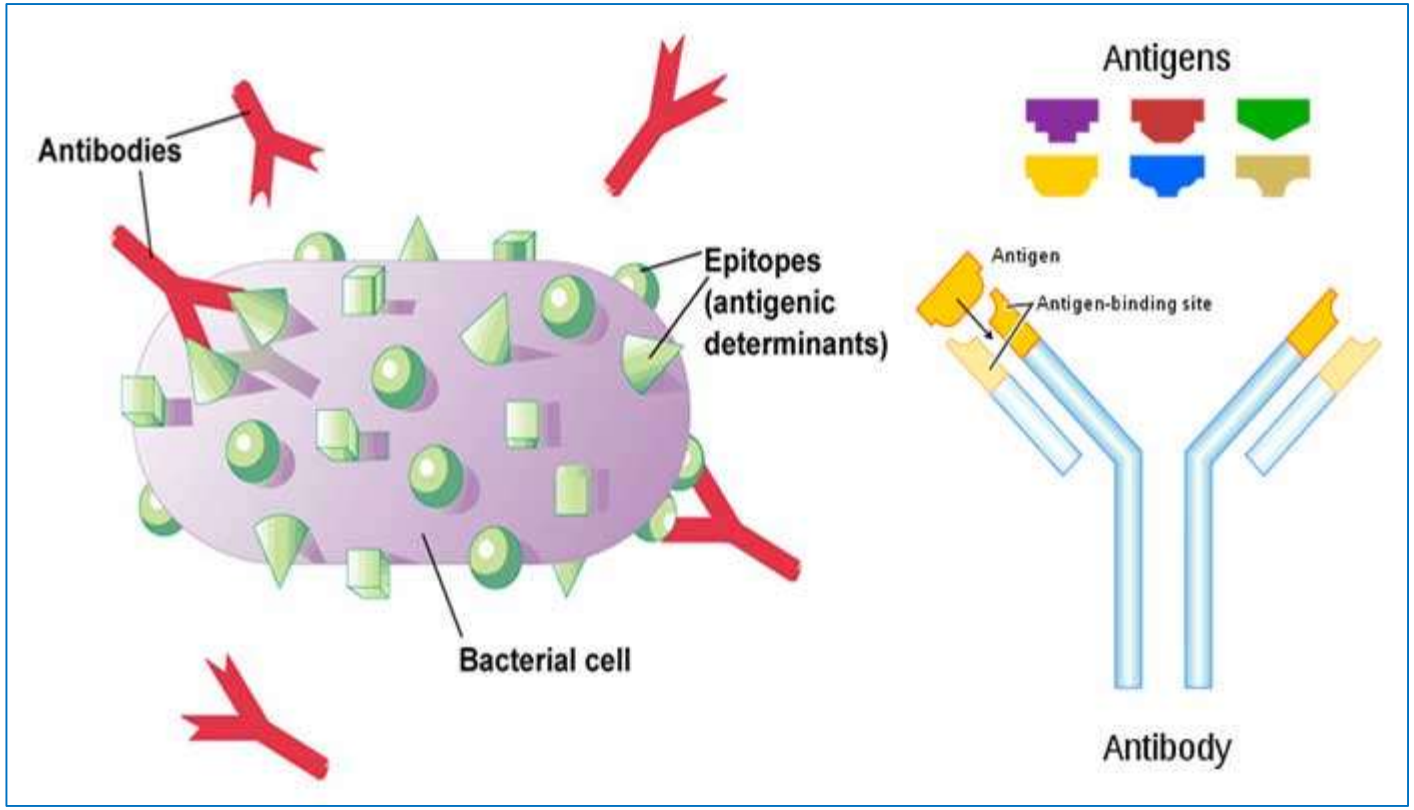
Transplantation of parts of sponge to other sponges is met by an immune response

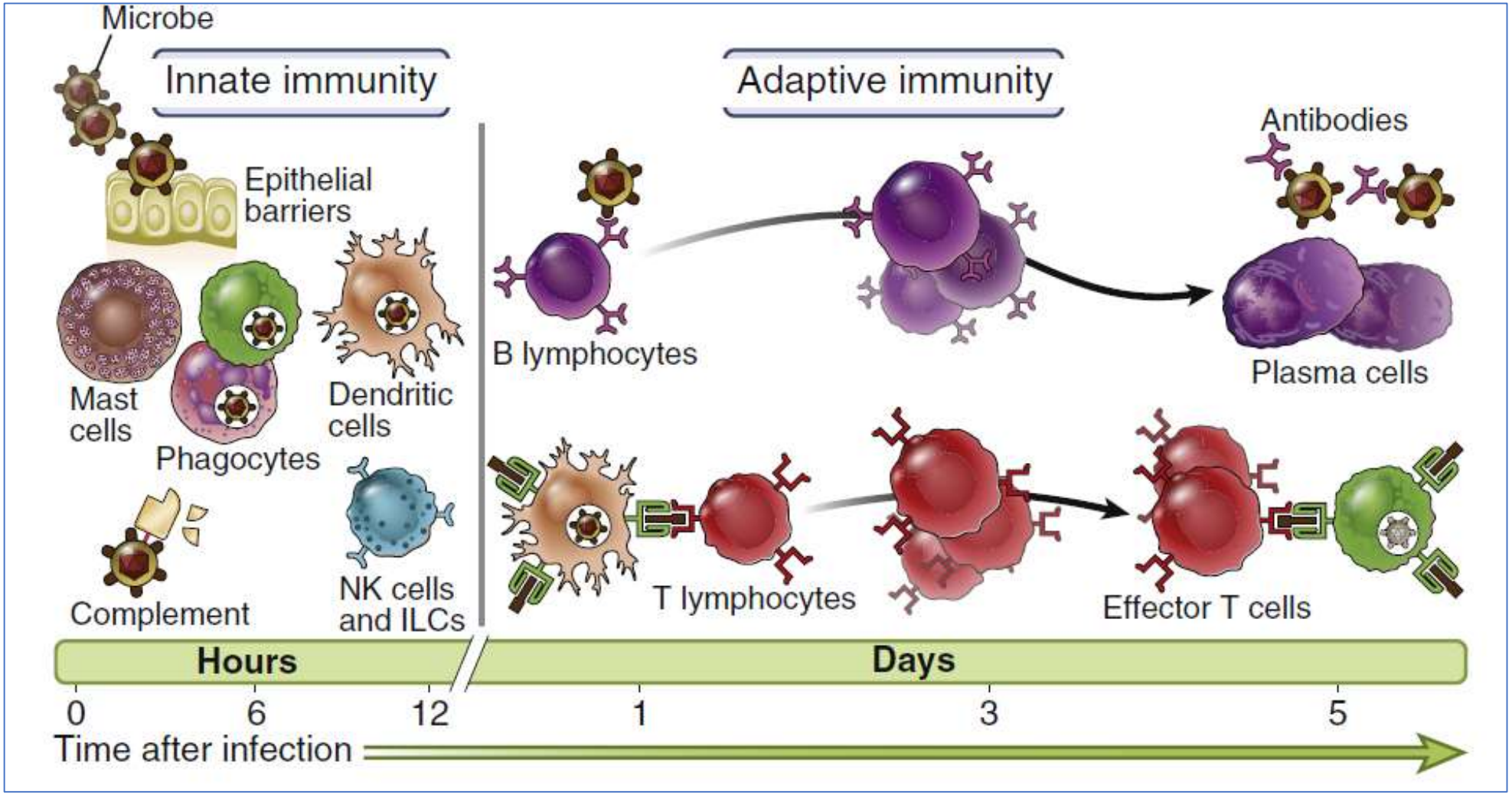


- **Antibodies**, also called immunoglobulins, Y-shaped molecules are proteins manufactured by the body that help fight against foreign substances called **antigens**.

- **Antigens** are any substance that stimulates the immune system to produce **antibodies**. **Antigens** can be bacteria, viruses, or fungi that cause infection and disease.

- **Antigens** may also originate from within the body ("self-antigen"), but should not be attacked by the immune system in normal situations.





- Host defenses are grouped under **innate** immunity, which provides **immediate** protection against microbial invasion, and **adaptive** immunity, which develops **more slowly** and provides more specialized defense against infections

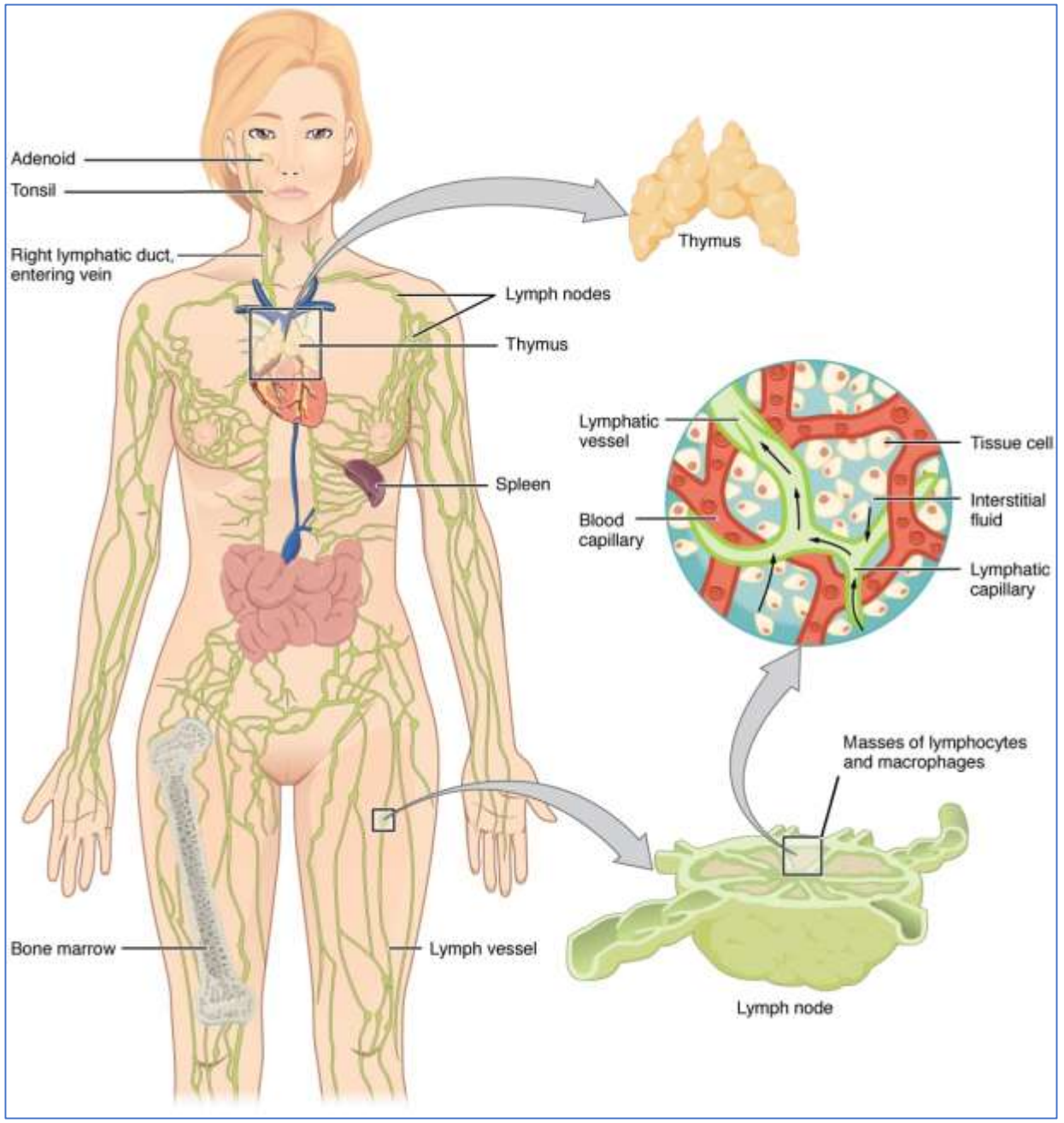
Immunology introduction / INNATE AND ADAPTIVE IMMUNITY

	Innate immunity	Adaptive Immunity
Components	 1. Physical and chemical barriers 2. Phagocytic leukocytes 3. Dendritic cells 4. Natural Killer cells 5. Plasma proteins (complement)	 1. Humoral immunity (B cells, which mature into antibody secreting plasma cells) 2. Cell-mediated immunity (T cells, which mature into effector helper and cytotoxic T cells)
Activity	Always present	Normally silent
Response and potency	Immediate response, but has a limited and lower potency	Slower response (over 1-2 weeks, but is much more potent
Specificity	General: can recognize general classes of pathogens (i.e. bacteria, viruses, fungi, parasites) but cannot make fine distinctions	Recognizes highly specific antigens
Course	Attempts to immediately destroy the pathogen, and if it can't, it contains the infection until the more powerful adaptive immune system acts.	Slower to respond; effector cells are generally produced in 1 week and the entire response occurs over 1-2 weeks. However, this course can vary somewhat during different responses in an individual.

- The immune system duty is to survey the whole body so it should be present **everywhere**. But there are sites where immune cells collect to fulfil their function (e.g. lymph nodes).

- For example, in the small intestine there is lymphatic tissue that surveys intestinal pathogens called Peyer's patches.

- The bone marrow is an important place for generation of immune and non-immune blood cells.



- Immunology is a relatively **recent science** with **applications** that extend to other medical sciences, thus it is important for medical students.

- The immune system in an **ancient** defence mechanism composed of tissues, cells and molecules that interact with each other with **great complexity**.

- Parts of the immune system are continuously active, and help in maintaining **homeostasis**.

- Specialized immune cells are mainly in the **bone marrow** and then circulate the blood or aggregate in lymph nodes.

- The **immune system arms** can be divided in general into **innate** and **adaptive**.

Further reading:

- BASIC IMMUNOLOGY Functions and Disorders of the Immune System FIFTH EDITION.

Chapter 1. Introduction to the Immune System: Nomenclature, General Properties, and Components