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## OVERVIEW OF IMMUNE SYSTEM

The immune system is a system of tissues, cells and soluble products that recognize, attack and destroy foreign entities that can endanger our health when they enter our bodies.

- Stage of immune response:
  - i. Recognition of invaded pathogens.
  - ii. Immune response.
    - Innate immunity.
    - Adaptive immunity.
  - iii. Return to resting states.
- Three lines of defense
  - i. Physical & chemical barriers
  - ii. Innate immunity → **Rapid but non-specific**.
  - iii. Adaptive immunity  $\rightarrow$  Slower but very specific and long-lasting.

# HISTORY OF IMMUNOLOGY

### SMALLPOX

- 1. Infection
  - a. Caused by Variola major, a human virus with no animal reservoir.
  - b. Causes eruption of small fluid-filled vesicles on the skin (pocks), death, extensive scarring and blindness in survivors.
- 2. Significance
  - a. Smallpox helped European colonist to conquer American.
  - b. Smallpox is the first and the only human infectious disease that has been eradicated.
- 3. Variolation
  - a. Inoculation of someone with material from a smallpox pustule to produce immunity.
  - b. In 1721, Lady Mary Wortley oversaw a trial using prisoners and orphans who contracted a mild illness but survived.
  - c. Variolation was still hazardous, which led to spread of disease and even death.

#### 4. Edward Jenner

- a. Hypothesis: Immunity to cowpox may also be effective against smallpox.
  - i. Milkmaid often did not contract smallpox.
  - ii. They were exposed to cowpox during work.
  - iii. Cowpox is related to smallpox but less virulent.
- b. Experiment in 1796
  - i. He inoculated a young boy James with the pus from the cowpox blisters of the milkmaid.
  - ii. The boy developed a mild fever.

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- iii. The boy was exposed to smallpox variolation and he did not develop symptoms.



#### GERM THEORY OF DISEASE

- 1. Antonie van Leeuwenhoek
  - a. Invention of microscope.
  - b. Discover microbes around 1650.
- 2. Louis Pasteur & Robert Koch
  - a. Proposed germ theory of disease
    - i. Microbes are tiny organisms which cannot be seen by naked eyes, and some can cause disease.
    - ii. A given pathogen can cause a specific disease.
    - iii. Koch's Postulate: Ex. Bacillus anthracis causes anthrax; Mycobacterium tuberculosis causes tuberculosis.
  - b. Pasteur's experiment:



- c. Use attenuated cholera culture to induce immunity to cholera in chickens  $\rightarrow$  Vaccine.
- 3. Rabies
  - a. Rabies is caused by infection of a virus in humans through bites from rabid animals.

- b. Dogs get vaccinated.
- c. Vaccinate people who are bitten by animals to block infection (Vaccine post-exposure).

## MODERN IMMUNOLOGY

- 1. Ilya Metchnikoff (Nobel Prize in 1908)
  - a. Observed phagocytosis (engulf debris or cells) in starfish larva.
  - b. Metchnikoff hypothesized and demonstrated that human white blood cells can phagocytosis and destroy pathogens.
- 2. von Behring & Kitasato
  - a. Discovered humoral immunity.
  - b. Serum from exposed animals contained "anti-toxins", now it is called "antibodies".
  - c. von Behring & Kitasato experiment:



- 3. Paul Ehrlich (Nobel Prize in 1908)
  - a. "Side chain theory" to explain humoral immunity.

- i. "anti-toxins" are receptors whose structure are complimentary to "toxins" (antigens).
- ii. Binding of toxin to a cell-bound receptor leads to production and release of more of the bound receptors.
- iii. Cells can express various anti toxins which will be selected by antigens. (Wrong)



- 4. Frank MacFarlane Burnet
  - a. Proposed clonal selection hypothesis.
    - i. Each cell produces only one kind of antibody.
    - ii. A specific antigen can stimulate a specific cell which then will undergo clonal expansion.



- 5. Karl Landsteiner and Merryl Chase
  - a. a. Proposed about cellular immunity.
  - b. Transfer immunity to tuberculin into non-immunized guinea pigs by transferring white blood cells.

c. James Gowans discovered lymphocytes.

#### 6. Charles Janeway

- a. Vaccination only works when adjuvants are added.
- b. Innate immunity is used to prime the adaptive immune system.



# GENERATION OF IMMUNE CELLS

• All immune cells are derived from hematopoietic stem cell in bone marrow.

