Lecture: Overview of the Immune system

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12.7.2018

Overview of the Immune system

1. History and general introduction
2. Essential components of the immune system
3. Architecture of the immune system
4. Active and passive immunity

Historical perspectives

Discipline of Immunology grew out observation that individuals recovered from certain infectious diseases were thereafter protected from the disease.

1st recorded crude attempts to induce immunity were performed by Chinese and Turks in the 15th century.

Lady Mary Wortley Montagu -1718

In 1718, Lady M**ary Wortley Montagu** (the wife of British Ambassador to Constantinople)

- observed the positive effects of variolation on the native population and applied the technique to her own children.

Edward Jenner in 1798 exploited the observation that **Milkmaids who contracted cowpox (a mild disease) were immune to small pox**

1798 Edward Jenner Smallpox vaccination

Louis Pasteur's experiments

Studies on fowl cholera led to understand attenuation of pathogens

In 1881, **classical experiment to show that** heat attenuated anthrax bacillus vaccine to protect sheep from virulent *Bacillus anthracis*

In 1885, the **first rabies vaccine to a human**, a young boy 9 years old (Joseph Meister) who had been bitten repeatedly by a rabid dog.

These experiments marked the beginnings of discipline of Immunology.

Discovery of humoral immunity:

Emil von Behring received Nobel prize in Medicine in 1901

1890, **Emil von Behring** and **Shibasaburo Kitasato** made antiserum against diphtheria toxin in Koch's lab (passive immunotherapy)-1st insight into the mechanisms of humoral immunity

Discovery of cellular immunity: Elie Metchnikoff received Nobel prize in Medicine in 1908

Elie Metchnikoff in 1883 in Russia discovered cells also contribute to the immune state of an animal.

He observed that certain **white blood cells** were able to engulf microorganisms. He names these cells **phagocytes**

Received **the Nobel prize in Medicine in 1908**

Nobel prizes in Medicine – (Immunology)

Year:	Recipient & Country	Research
1901:	**Emil von Behring** (Germany)	**serum Abs**
1905:	**Robert Koch** (Germany)	CMI to TB
1908:	**Elie Metchnikoff** (Russia)	phagocytosis
1908:	**Paul Ehrlich** (Germany)	antitoxins
1913:	**Charles Richet** (France)	anaphylaxis
1919:	**Jules Bordet** (Belgium)	complement mediated bacteriolysis

The immune system

Our environment contains a great variety if infectious microbes:

- **Viruses, bacteria, fungi , protozoa, and multi-cellular parasites.**

These pathogens can cause disease,

- **if they multiply unchecked can kill their host.**

Most infections in normal individuals are short-lived & leave little or no permanent damage.

- **This is due the immune system**

Evolution of the immune system

The immune system has evolved to protect us from pathogens

We are engaged in constant warfare with the microbes. Immunity depend on the Processes of **mutation & evolution** that select

- microbes to evade our defense mechanisms.
- hosts to defend against pathogenic microbes

Why study immunology?

1). To understand the immune response against infectious agents

Variety of pathogenic microbes: Bacteria, fungi, viruses & parasites

Virulence Factors

Virulence Factors are specific adaptations that allow pathogen to:

- **Attach selectively to host tissues**
- **Invade or destroy host tissues to gain access to nutrients**
- **avoid host defenses**

Many examples of virulence factors:

1. Specific attachment & entry factors
2. Invasive enzymes
3. Strategies to avoid host defenses
4. Exotoxins
5. Endotoxins
6. Siderophores

(2). Diseases caused by a disturbed immune system

- ALLERGY
- AUTOIMMUNITY
- GRAFT REJECTION
- IMMUNODEFICIENCY: Defects in immune responses e.g. **SCID**

What are the key characteristics of an effective immune system?

1. Self and non-self discrimination
2. Specificity
3. Turning responses off
4. Memory

Need for an organized lymphoid tissue

An organized lymphoid tissue is necessary , in order to carry out following functions.

Primary (central) lymphoid tissue:

1. Bone marrow → Self renewing, multipotential haemotopoietic **stem cells**

Stem cells→ immature B cells→Antigen-in-dependent maturation of B cells → Humoral immunity

Stem cells → immature T cells

2. Thymus →Immature T cells → mature T cells → CMI

<u>Secondary (Peripheral) lymphoid tissue</u>: Mature B and T cells

1. Lymph nodes,
2. Spleen
3. MALT

Components of Human Immune System

T and B cell formation & maturation

Phagocytes:
Produced throughout life by the bone marrow.
Scavengers – remove dead cells and microorganisms.

<u>Phagocytes and relatives</u>

Neutrophils :

60% of WBCs

Large numbers are released during infections

Short lived – die after digesting bacteria

Macrophages

Larger than neutrophils.

Found in the organs, not the blood.

Made in bone marrow as **monocytes,** called macrophages once they reach organs.

Long lived

Initiate immune responses as they display antigens from the pathogens to the lymphocytes.

Lymphocytes

B-cells mature in **bone marrow** then concentrate in lymph nodes and spleen

T-cells mature in **thymus**

Mature B and T cells then circulate in the blood and lymph

Circulation ensures they come into contact with pathogens and each other

Antibodies

Also known as **immunoglobulins**

Globular glycoproteins

The heavy and light chains are polypeptides

How Abs work?

Some act as **labels** to identify antigens for phagocytes

Some work as **antitoxins** i.e. they block toxins for e.g. those causing diphtheria and tetanus

Some attach to bacterial flagella making them less active and easier for phagocytes to engulf

Different Immunoglobulins : IgG,IgM,IgD, IgE, IgA

Defense against infection

Variety of immune responses

Variety of immune responses to deal with different microorganisms.

The site of infection and type of pathogen determine which immune responses will be effective. i.e. which invade host cells and those which do not

Intracellular infections

All viruses, some bacteria (i.e. *Salmonella typhi*) & some protozoan parasites (i.e. *Plasmodiun* spp) replicate inside host cells

to clear an intracellular infection, the immune system must recognize and destroy these infected cells.

Extracellular infections

Many bacteria & larger parasites live in tissues, body fluids or other extracellular spaces.

- These pathogens are destroyed extracellularly.

When intracellular pathogens reach their target cells by moving through blood and tissue fluids.

- Susceptible to elements of the immune system which normally counter extracellular pathogens.

Innate immune system

Innate immunity include nonspecific host defenses

Mechanical/Physical barriers

Chemical barriers

Phagocytes , NK cells

Inflammation

Adaptive immune system.

The Adaptive Immune System is the Third Line of Defense Against Infection

Specificity & memory are two essential features of adaptive immune system

The KEY cell types are the lymphocyte: T & B

T and B cell populations can discriminate between trillions of different Ags

Each mature cell expresses only 1 Ag receptor

Immune system mounts a more effective response on 2nd and subsequent encounters with same Ag

Functions of lymphocytes

Lymphocytes have specialized functions.

- B cells make antibodes
- Cytotoxic T cells kill virally infected cells
- Helper T cells coordinate the immune response by direct cell- cell interactions & Release of cytokines which help B cells to make antibodies
- Antigens and antibodies.

Antigens (Ab generator\Immunogen)

Are ligands (foreign macromolecules or cells*)* that react with the products (Ab/B cell or T cell) of an immune response.

Antibody

Proteins called immunoglobulins which are produced by the immune system when an individual encounters a foreign macromolecule or a cell.

Antigen recognition

Antigen molecules are recognized by receptors on lymphocytes

B lymphocytes recognize intact antigen molecules

T lymphocytes recognize antigen fragments on the surface of other cells.

Clonal selection

Clonal selection involves recognition of antigen by a particular lymphocyte

Each lymphocyte bears a single type of receptor of unique specificity.

Antigen interaction leads to lymphocyte activation.

Clonal selection induces proliferation and increases effector cell frequency

Daughter cells bear identical antigen specificity to the parent cell.

Immune Response

Consists of two phases:

Phase 1: Antigen activates specific lymphocytes that recognize it.

Phase 2: This is the effector phase. Activated lymphocytes coordinate an immune response that

eliminate the source of Ag

Active and Passive Immunity

Active immunity

Lymphocytes are activated by antigens on the surface of pathogens

Natural active immunity - ***acquired due to infection***

Artificial active immunity – ***vaccination***

Takes time for enough B and T cells to be produced to mount an effective response

Natural passive immunity

☼A mother's antibodies pass across the placenta to the foetus and remain for several months.

☼ The first breast milk contains lots of IgA which remain on surface of the baby's gut wall and pass into blood

Artificial passive immunity

☼Used when a very rapid immune response is needed e.g. after infection with tetanus.

☼Human antibodies are injected- antitoxin antibodies.

☼Only provides short term protection as abs destroyed by phagocytes in spleen and liver.

The immune system may break down

Immune system can fail, leading to immuno-pathological reactions. i.e.

- immune deficiency,
- hypersensitivity and
- autoimmunity**.**