Introduction to Immunology &
Lymphoid System

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

<table>
<thead>
<tr>
<th>Disease</th>
<th>ANNUAL CASES/YR: Prevaccine</th>
<th>CASES IN 2016: Postvaccine</th>
<th>Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>48,164</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>175,885</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Measles</td>
<td>503,282</td>
<td>79^</td>
<td>99.98</td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209</td>
<td>145*</td>
<td>98.90</td>
</tr>
<tr>
<td>Pertussis (&quot;whooping cough&quot;)</td>
<td>147,271</td>
<td>964*</td>
<td>99.35</td>
</tr>
<tr>
<td>Paralytic polio</td>
<td>16,316</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Rubella (German measles)</td>
<td>47,745</td>
<td>0*</td>
<td>100</td>
</tr>
<tr>
<td>Tetanus (&quot;lockjaw&quot;)</td>
<td>1,314 (deaths)</td>
<td>1* (case)</td>
<td>99.92</td>
</tr>
<tr>
<td>Invasive Haemophilus influenzae</td>
<td>20,000</td>
<td>356*</td>
<td>98.22</td>
</tr>
</tbody>
</table>
Macrophage engulfs a bacteria
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

Observation:

Louis Pasteur watching the rabies vaccination

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

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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)
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

(\textit{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) is an 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+)**
- **T cytotoxic lymphocyte (CD8+)**
Subtypes of T Helper (CD4+) & their functions

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

- **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.
- **T_{fh}**: 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