Immunity is crucial in protecting the human body from pathogenic microorganisms. Skin physically prevents foreign microorganisms from invading the body. The human body coexists with microorganisms on the surface of the skin, in the intestines and in mucous membranes. It thereby maintains a balance; however, if the balance collapses for whatever reason, the microorganisms begin to harm the body, and the immune system is activated.

The immune system performs the following functions:

- Distinguishing between “self” and “non-self.”
- Excluding “non-self.”
- Remembering what has invaded (immunologic memory).

These functions are performed by the immunocompetent cells, such as lymphocytes and antigen-presenting cells, both of which are derived from bone marrow (Fig. 3.1). How these cells act against various pathogens is briefly described below.

**b. Reaction pattern**

Foreign substances (antigens) including bacteria, viruses, transplanted organs and certain proteins are distinguished as “non-self” by the immune system. The receptor, also called the major histocompatibility complex (MHC), plays a critical role in identifying whether a substance is self or non-self. In humans, it is called HLA (human leukocyte antigen), because it was discovered in leukocytes. HLA is classified as class I (HLA-A,B,C) or class II (HLA-DP,DQ,DR)(Fig. 3.2). Every human has a different HLA pattern that identifies what is non-self. Some diseases that are thought to occur in individuals with specific HLA have been revealed (Table 3.1).

A cell or a protein recognized as non-self is phagocytosed by a histiocyte (macrophage) or a dendritic cell, such as a cutaneous Langerhans cell. The phagocytosed substance is processed, and
part of it is recognized by lymphocytes as antigenic information associated with MHC class II molecules. The cells that actively engulf the foreign substance and transmit the information to T cells by MHC class II molecules are called antigen-presenting cells (APC). Cells infected by latent viruses degrade the virus-derived proteins and transmit the information to T cells by the function of MHC class I molecules. The information of the antigen is conveyed by the combination of a T-cell receptor (TCR) and MHC, resulting in immune activation and reaction (Fig. 3.3).

c. Humoral immune reaction

1. Antibodies

The antibodies, proteins produced by B cells, react against infectious agents or pathogenic proteins (antigens) to inhibit infections and neutralize protein toxicity. Numerous specific B cells and antibodies corresponding to the antigens exist in the body. There are five immunoglobulins in descending order of concentration from IgG, IgM, IgA, IgD, to IgE (Table 3.2). IgG, produced at the time of infection or in the late stage of infection, accounts for 75% of immunoglobulins and plays a central role in the humoral immune reaction (Fig. 3.4). IgM appears preceding IgG at the early stages of infection and strongly activates protein complements. IgA is seen abundantly in exocrine secretions, such as mucus, where it prevents invasion of causative factors. IgE reacts to basophils and mast cells to evoke type I allergy.
The complements, proteins contained in serum, are classified into nine types from C1 to C9, and can be subclassified. In the classical pathway, C1 reacts to IgG or IgM antibodies, followed by continuous reaction of complements, and finally the pathogens and infectious cells are penetrated. In the alternative pathway, the reaction is evoked mostly by bacterial components, which directly activate C3, factor B and factor D.

**Table 3.2 Basic characteristics of immunoglobulins.**

<table>
<thead>
<tr>
<th></th>
<th>IgG</th>
<th>IgM</th>
<th>IgA (secretory)</th>
<th>IgD</th>
<th>IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>150,000</td>
<td>970,000</td>
<td>160,000 (390,000)</td>
<td>184,000</td>
<td>188,000</td>
</tr>
<tr>
<td>Serum concentration (mg/ml)</td>
<td>12.0</td>
<td>1.5</td>
<td>3.0</td>
<td>0.03</td>
<td>0.00005</td>
</tr>
<tr>
<td>Half-life in blood (days)</td>
<td>21</td>
<td>5</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Antigen type of heavy chain</td>
<td>(\gamma)</td>
<td>(\mu)</td>
<td>(\alpha)</td>
<td>(\delta)</td>
<td>(\epsilon)</td>
</tr>
<tr>
<td>Transport across the placenta</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Activity of complement fixation</td>
<td>(+)</td>
<td>(+)</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Basic structure</td>
<td>(monomer)</td>
<td>(dimer)</td>
<td>secretory piece</td>
<td>J chain</td>
<td>J chain</td>
</tr>
</tbody>
</table>

**Fig. 3.3 Immune reactions classified by MHC class.**

Each class of MHC presents antigen information to different types of T cells.

**Fig. 3.4 Basic structure of human immunoglobulin (IgG).**

B. Immunocompetent cells

a. Immunocompetent cells in general

1. T cells

T cells express T-cell receptors that recognize the antigen information associated with MHC molecules (Fig. 3.3). T cells are produced in the bone marrow and develop in the thymus. T cells are classified by function into CD4 positive helper T cells (helper T lymphocyte; Th) and CD8 positive cytotoxic T lymphocytes (Tc).

Th contains CD4 on the cell surface, by which Th adheres to MHC class II. Therefore, Th reacts against antigen-presenting cells and B cells, which contain MHC class II. Th differentiates into subtype Th1 or Th2, depending on the surrounding cytokine environment (Fig. 3.3). Th1 secretes cytokines such as IL-2 and IFN-γ, activating histiocytes (macrophages) primarily, and it induces cellular immunity by evoking various inflammatory reactions. Th2 secretes IL-4 and IL-5, activates antibody production in B cells, and inactivates foreign substances (humoral immunity). It is known that Th1 is involved mostly in type IV allergy while Th2 is involved in type I allergy (atopic diseases).

Tc contains CD8, by which Tc is associated with MHC class I to initiate cytotoxic immunity (Fig. 3.3); in this way, non-self cells and virus-infected cells are destroyed. Tc is important in transplantation immunity, tumor immunity and viral infections.

Recently, the presence of another subtype – regulatory T cell (Treg) – has been identified. Treg is considered to be involved in immune control, including suppression of autoimmune disease onset. It is also known that some Th and Tc circulate in the blood after an immune reaction to guard against re-infection.

2. B cells

B cells derive from hematopoietic stem cells in the bone marrow, after which they differentiate. They react against foreign antigens in lymph nodes, the spleen, and peripheral tissues to differentiate into antibody-forming cells (plasma cells); B cells produce antibodies in this process. B cells contain MHC class II and