UNIT 13

IMMUNE SYSTEM IN HEALTH AND DISEASES–I

Structure

13.1 INTRODUCTION

You know by now after studying the earlier Units that antibodies react with antigens which is known as immune response. Such interactions of antibodies with antigens sometimes produce undesirable symptoms in the body. We call such conditions “allergy” or in immunological term as ‘hypersensitivity’. The term allergy and hypersensitivity are sometimes used interchangeably, however we shall learn in detail that they are not quite so. In this Unit, we shall learn various types of hypersensitivity and immunological disorders prevalent in human beings. Often, our immune system starts to attack its own cells, tissues and other constituents which lead to many diseases. Such diseases are known as autoimmune diseases and the phenomenon is referred to as autoimmunity. On the other hand, one’s immune system can be compromised and an individual can be susceptible to any one or all the diseases. Such condition is known as immune deficiency. We shall learn about them in detail in this Unit.

Objectives

After studying this unit you should be able to:

- differentiate between allergy and hypersensitivity,
- discuss different types of hypersensitivity,

- ❖ explain various immunological disorders,
- ❖ describe the mechanism of autoimmunity, and
- ❖ explain various diseases arising from autoimmunity.

13.2 HYPERSENSITIVITY

In general, immune system generates inflammatory response to antigens. Sometimes even under normal condition, our immune system elicits inappropriate reactions in response to antigens. Antigens that are responsible for such inappropriate response are known as allergens. Such reactions are also known as allergy. **Hypersensitivity is a term used to denote excessive immune response to foreign or self antigens.** The term allergy was coined by Clemens von Pirquet and often it is used synonymously with hypersensitivity. **Clemens defined allergy as an altered state of body immune response to foreign substances.** This definition however was applicable for all immunological reactions. But now allergy is known to be a type/class of hypersensitivity. Nonetheless, these immune responses are harmful and cause serious injuries to tissues leading to disease.

13.2.1 Classification of Hypersensitivity

Eukotrienes are a family of inflammatory mediators produced in leucocytes.

Hypersensitivity is composed of two components. It starts with the initial exposure to allergens which is termed as initial dose. Following exposure to the allergens, immune system response may occur within few minutes to days. The second component of hypersensitivity consists of reactions that result in damaging effects. This component is known as *shocking dose*. Based on the nature of reactions and mediator molecules involved Gell and Coombs (1963) classified hypersensitivity into four types as discussed here.

Type-I Hypersensitivity

Allergy comes under type-I hypersensitivity. This type of hypersensitivity is mediated by antibody of certain class, specifically IgE when they react with allergens (antigens) and activate mast cells and basophils. These cells release vasoactive substances such as histamines, leukotriens and prostaglandins (Fig.1). Type-I hypersensitivity is accompanied by clinical symptoms like: anaphylaxis, angioedema, bronchospasm, hypotension etc. Type-I hypersensitivity is further classified into two subtypes depending on the response time:

i) **Immediate reaction type:** Immune reaction occurs within few minutes to the exposure of allergens. It includes release of vasoactive substances.

ii) **Late phase reaction type:** Immune reaction occurs after 2-4 hours to the exposure of allergens. It includes the release of cytokines.

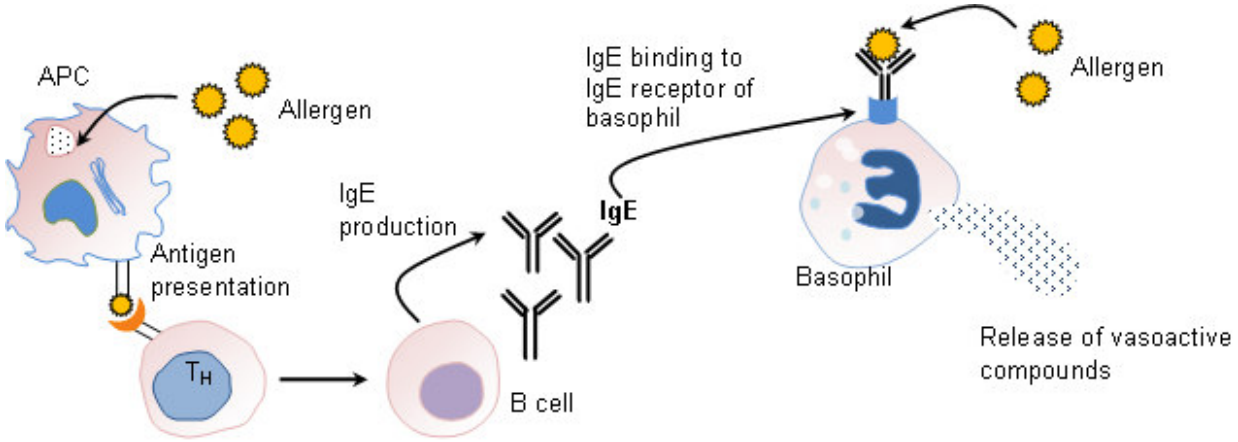

Fig. 13.1: Schematic representation of Type-I hypersensitive reaction through IgE.

Type-II Hypersensitivity

Type-II hypersensitivity is also known as antibody mediated hypersensitive reaction where IgG and IgM are directed against cells with the allergens or extracellular matrix. This type of hypersensitivity is clinically associated with hemolytic anemia, thrombocytopenia, neutropenia. An allergen that is associated with cells are quickly bound with antibodies IgG or IgM causing cell lysis or tissue damage through one of the following ways:

Prostaglandins are a group of lipids made at sites of tissue damage or infection that are involved in dealing with injury and illness. They control blood flow, inflammation and the formation of blood clots.

i) **Activation of classical complement pathway** that involves marking of the pathogens and final destruction of infected cells through phagocytosis.

ii) **Antibody dependent cell mediated cytotoxic pathway** that involves the binding of antigen coated infected cells through Fc receptors and killing of the target cells by NK cells.

iii) **Anti-receptor activity of the antibody** binding on the cell surface receptor starts to act as opsonin and enhances the phagocytotic activity.

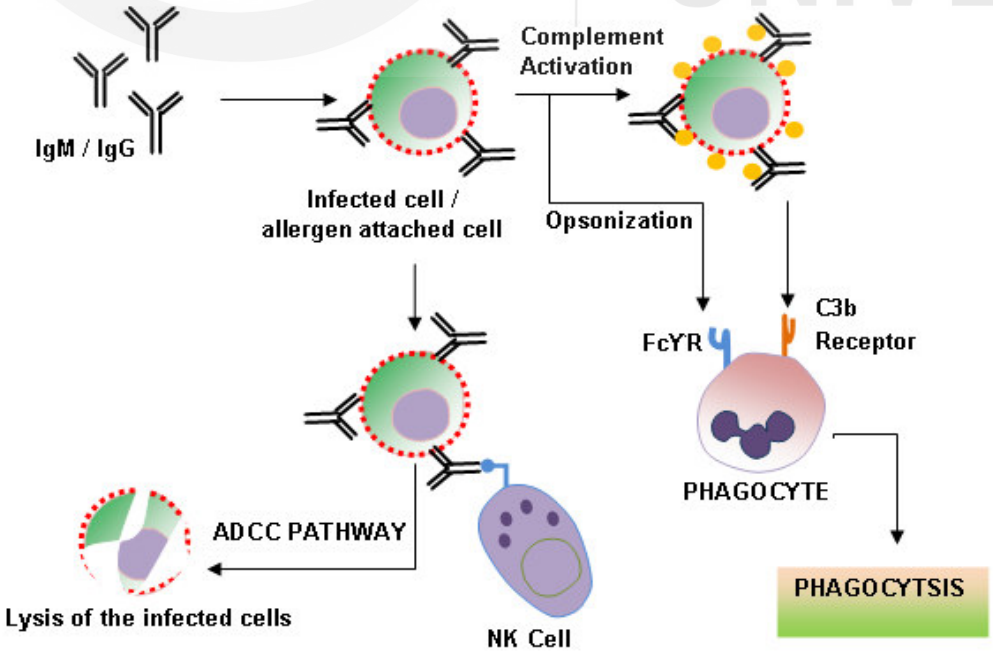

Fig. 13.2: Schematic representation of reaction in Type-II Hypersensitivity through IgM/IgG.

Type-III Hypersensitivity

Serum sickness is a reaction that is similar to an allergy. The immune system can react to antiserum that liquid part of blood that contains antibodies given to person to help protect them against germs.

Type-III hypersensitivity is a condition of immune reactions that arises due to **delayed clearance of antigen-antibody complexes** by the innate immune cells resulting in accumulation of the complex in tissues and blood vessels. This type of hypersensitivity is also known as **immune complex disease.** The deposition of antigen-antibody complexes in tissues or blood vessels causes the activation of complement system along with recruitment of neutrophils to the complex through the Fc region of IgG receptors. Type-III hypersensitivity reactions are clinically associated with serum sickness and Arthus reaction.

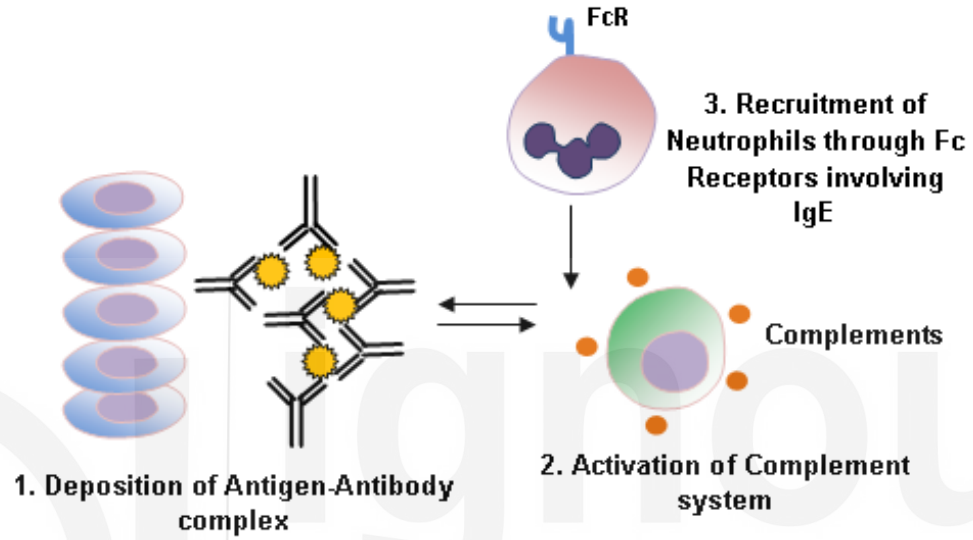

Fig. 13.3: Schematic representation of type-III hyperactivity reaction.

Arthus Reaction is a type of local type III hypersensitivity reaction. This is immune-complex mediated and involves the deposition of antigen/antibody complexes mainly in vascular walls and glomerulus.

Type-IV Hypersensitivity

Type-IV hypersensitivity is also known as delayed hypersensitivity or cell-mediated hypersensitivity. In this type, the immune reaction takes several days to develop and the reaction is mediated by lymphocytes which in other types are mediated by antibody. The exposure of allergens activates T cells which mediates tissue injury through monocytes and macrophages. Type-IV hypersensitivity is clinically associated with **Grave's disease** (You will study it in detail in next section), c**ontact dermatitis** (redness or inflammation of the skin)**, some morbilliform reactions** (generally rash caused by dings) and **severe exfoiliative dermatoses** (extreme shedding of the top layers of the skin). Depending on the type of T cell activated and the type of effector cells recruited, type-IV hypersensitivity can further be divided into four subtypes:

Type IVa: T_H1 and monocytes are activated. Cytokines involved include IL-1, IL-2 and IFNϒ.

Type IVb: T_H2 and eosinophils are activated. Cytokines involved include IL-3, IL-4 and IL-5.

Type IVc: CD8+ T cells are activated. Cytokines like granzyme B, perforin, Fas Ligands are involved.

Type IVd: Cells activated include CD4+, CD8+ T cells and neutrophils. Cytokine IL-8 and GM-CSF (Granulocyte macrophage- colony stimulating factor) are involved.

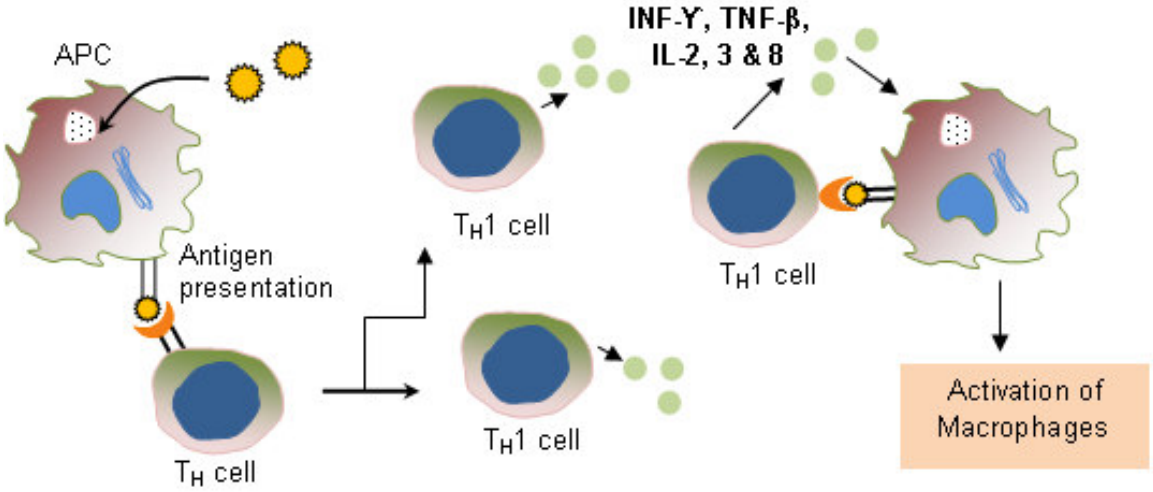

Fig. 13.4: Schematic representation of Type–IV hypersensitivity reaction.

13.3 IMMUNOLOGICAL DISORDERS

13.3.1 Autoimmunity

One of the most important features of our immune system is the ability to differentiate self from foreign entity. The components that are central in differentiating the foreign substances are the antibodies and T cells. When these components fail to recognize self they generate antibodies and T cells in response against itself. Those T cells that are generated against own cells are known as **self-reactive T cells** and the antibodies are **called auto-antibodies**. There are mechanisms within our body to check and ensure the removal of such self-reactive cells. These mechanisms are known as **Tolerance**. During maturation of B cells and T cells in the bone marrow and thymus respectively, the cells carrying self-reactive receptors or antibodies are eliminated. This process of removal is called **Central Tolerance**. However, this elimination is not absolute and some self-reactive cells escape into circulation. These cells are trapped and eliminated in the lymph organs that are located peripherally through a process known as **Peripheral Tolerance**. In addition, the activated lymphocytes have a short life span and they ultimately die by apoptosis or programmed cell death. These mechanisms safeguard the body from self-reactive cells under normal physiological condition. When all the tolerance mechanism breaks down and fails to protect the host from its own immune system, it leads to severe and fatal organ damage. Such condition is known as **Autoimmunity**. The development of autoimmunity in an individual can be caused by several factors like hormones, viruses, genetics, environment and neuro-immunological reasons.

The term autoimmunity was first used by Paul Ehrlich to describe self-toxicity. There are many types of autoimmune disorders related to different tissues like muscle, bone, skin, lungs, nervous system, thyroid, intestinal tract and blood related. Autoimmunity disorder can be specific to an organ or it may affect multiple organs. Accordingly, autoimmunity is classified into two types:

I. Organ Specific Autoimmunity

II. Systemic Autoimmunity

SAQ 1

Match the following with the correct option of Column I with Column II.

Column I		Column II	
a)	Allergy	i	Paul Ehrlich
b)	Autoimmunity	ii	Type-IV hypersensitivity
c)	Cell-mediated hypersensitivity	iii	Type-II hypersensitivity
d)	Antibody-mediated hypersensitivity	iv	Type-III hypersensitivity
e)	Arthus reaction	v	Clemens von Pirquet

I. Organ Specific Autoimmunity

Organ specific autoimmunity is a condition where humoral or cell mediated immune system targets only a particular antigen of a single organ. This phenomenon not only affects the normal functioning of the organ but also causes physical damage. In most cases the damaged tissues of the organs from self-reactive components are replaced by connective tissues leading to fibrosis. Sometimes antibodies could also induce overstimulation or antagonize the normal function of a particular organ. Some important organ specific autoimmunity diseases are discussed below:

- **Grave's Disease**

Grave's disease is a condition of over production of thyroid hormone due to generation of auto-antibodies that bind to the receptors of Thyroid stimulating hormone (TSH) on the thyroid cells. Under normal conditions, TSH binds to the TSH receptor to produce adenyl cyclase that signals the secretion of thyroid hormones (T_3& T_4). Auto-antibodies known as Long-Acting Thyroid stimulating (LATS) antibodies bind with TSH receptors that lead to unregulated stimulation of thyroid cells to produce uncontrolled secretion of thyroid hormones.

- **Hashimoto's Thyroiditis**

Hashimoto's thyroiditis is a condition of inadequate production of thyroid hormone. This condition arises when auto-antibodies and sensitized T_H1 cells start to target thyroglobulin and thyroid peroxidase which are thyroid gland proteins. These two proteins are responsible for the uptake of iodine in the thyroid gland for the synthesis of thyroid hormone. The presence of auto-antibodies and T_H1 lymphocytes in the gland leads to type-IV hypersensitivity recruiting plasma cells and macrophages. This causes the destruction of thyroid cells from the germinal center and lymphatic follicles resulting in hypothyroidism.

- **Goodpasture's Syndrome**

Goodpasture's syndrome is a condition that arises when auto-antibodies are formed against the basement membrane of kidneys or lungs. The auto-antibodies target the basement membrane of glomeruli and alveoli causing damages to the tissue. The condition is further aggravated due to activation of complement system that elicits inflammation response. Such reaction may cause pulmonary hemorrhage and kidney dysfunction, sometimes death within months after its onset.

- **Myasthenia Gravis**

Myasthenia Gravis is a condition of muscular dysfunction arising from the binding of auto-antibodies to the acetylcholine receptor of muscle motor end plate. The binding of these antibodies not only blocks the acetylcholine binding which is necessary for stimulation of muscle but also induces activation of complement system. The activation of complement system further deteriorates the skeletal muscle from lysis of the membrane and receptors of the cells.

- **Autoimmune Anemia**

When auto-antibodies are generated against RBCs, agglutination of auto-antibodies and RBC occurs. This agglutination results in antibody mediated phagocytosis of RBC or complement mediated lysis of RBC. Such anemia resulting from autoimmunity is known as **autoimmune hemolytic anemia**. Another form of anemia known as **pernicious anemia** which occurs from deficiency of vitamin B12 can be caused due to autoimmunity. Vitamin B12 which is essential for hematopoiesis is absorbed by proteins called intrinsic factor. The generation of auto-antibodies against the intrinsic factor prevents the absorption of vitamin B12 from the intestine leading to anemia.

SAQ 2

State whether the following statement are 'True' or 'False':

i) The removal of self-reactive cells within our body immune system is Tolerance.

ii) The deposition of antigen-antibody complexes in tissues or blood vessels causes the activation of complement system along with recruitment of neutrophils.

iii) Type-I hypersensitivity is accompanied by clinical symptoms like: anaphylaxis, angioedema, bronchospasm, hypotension etc.

iv) Myasthenia Gravis is a condition of muscular dysfunction arising from acetylcholine inadequacy not auto-immunity.

v) Type-IV hypersensitivity is clinically associated with hemolytic anemia, thrombocytopenia, neutropenia.

II. Systemic Autoimmunity

Systemic autoimmunity is a state of autoimmunity where immune response targets vast range of tissues and organs. It not only targets

single antigen but multiple antigens present across many organs. Hence widespread damage across multiple tissues or organs occurs from auto-antibodies and cell mediated immune response. In systemic autoimmunity, there is disregulation of immune system and inappropriate inflammatory responses. Some systemic autoimmune diseases are discussed below:

Systemic Lupus Erythematous (SLE)

Systemic Lupus Erythematousis is a condition that causes inflammation of connective tissues that provides flexibility and strength to the body like cartilage, blood vessels, etc. Individuals with SLE show symptoms of arthritis, pleuritis, skin rashes, kidney dysfunction, fever and weakness. For unknown reasons SLE is more prevalent among women of Hispanic origin and American African who are in the age group of 20 to 40 years than Caucasians. In SLE, auto-antibodies targets wide range of tissues including RBCs, platelets, clotting factor, leucocytes, histone and DNA causing multiple pathological conditions.

The self-reactive antibodies attack the wall of blood vessels to form antigen-antibody complex that accumulates in the tissues. The delayed clearance of the complex induces type-III hypersensitivity reaction to activate complement system. This results in inflammation of the wall of blood vessel. Elevated activity of complement system can induce aggregation of neutrophils through CR3 complement receptors on the neutrophils. The inflammatory damage on the wall of blood vessel and accumulation of neutrophils can cause neutropenia (decreased number of neutrophils in circulation) and blockade of blood vessels (vasculitis). The auto-antibodies targeting RBCs and platelets can also lead to formation of immune complexes that activate complement system. Eventually complement mediated lysis of RBCs and platelets leads to hemolytic anemia and thrombosis respectively.

Multiple Sclerosis (MS)

Multiple sclerosis is an inflammatory disease that exclusively affects white matter of the central nervous system. In MS, auto reactive T-cell mediated attacks the myelin sheath of nerves and cause inflammatory reaction leading to demyelination and neurological disorders. Activated auto reactive T-cells from the blood circulation can also enter the brain and cause lesion. MS is one major neurological disorder especially in the western countries prevalent in men and women from 20-40 years.

Rheumatoid Arthritis

Rheumatoid arthritis is aninflammatory disease affecting mainly the joints including hands and feet. It is a condition in which auto-antibodies are generated against antibody IgG in the Fc region. The auto-antibodies are IgM immunoglobulins and they are referred to as rheumatoid factors. The auto-antibody IgM molecules form complex with IgG and accumulate in the joints. The delayed clearance of the IgM-IgG complexes ensue type-III hypersensitivity reaction, and, activate complement system that leads to chronic inflammation of joints, cardiovascular, respiratory and hematological system.

SAQ 3

Fill in the blanks:

a) Hypersensitivity is composed of two components …….. and …….. dose.

b) Autoimmunity is under the regulatory mechanism of …….. and …….. tolerance.

c) In systemic autoimmunity there is …….. of immune system and inappropriate …….. responses.

d) Goodpasture's syndrome is a condition where auto-antibodies are formed against the basement membrane of …….. or …….. .

e) …….. is a disease condition that causes inflammation of connective tissues that provides flexibility and strength to the body.

13.3.2 Immune Deficiency

Immune deficiency is a state where the ability of immune system to fight against infection is compromised partially or totally. It is also known as immune-compromisation. In such conditions, an individual becomes more vulnerable to opportunistic infections than others. Such an individual is said to be immune-compromised. Immune deficiency can be of two types:

Primary Immunodeficiency

Primary immunodeficiency (PID) is also known as congenital immunodeficiency where the immune system of an individual is weak or does not function normally from birth. Most PIDs are diagnosed in children under the age of one. Those suffering from PID show persistent infections, auto-inflammatory disorders, disorders of various organs and tumors. PID disorders are genetic in nature.PID disorders are classified into following types:

i) **B Lymphocytes deficiency:** Primary immunodeficiency disorders caused from B cell deficiency include X-linked Agammaglobulinemia also known as Bruton disease and Selective Immunoglobulin IgA deficiencies (For details see Table 13.1).

ii) **T Lymphocytes deficiency:** PID disorders caused from T lymphocyte deficiency include congenital thymic aplasia also known as DiGeorge syndrome, Chronic Mucocutaneous candidasis and Hyper-IgM syndrome (Table 13.1).

iii) **B and T cell deficiency:** Primary immunodeficiency due to combined B and T-cell deficiency includes Severe combined immunodeficiency disease (SCID), Wiskott-Aldrich Syndrome and MHC deficiency or Bare leukocyte syndrome (Table 13.1).

iv) **Phagocyte deficiency:** PID disorders caused by deficiency of phagocytes include chronic granulomatous disease and Leukocyte adhesion deficiency syndrome (Table 13.1).

v) **Complement deficiency:** Primary immunodeficiency disorder caused from complement deficiency includes hereditary angioedema, recurrent infections and autoimmune diseases (Table 13.1).

Table 13.1: Characteristics of primary immunodeficiency disorders.

Type of Primary Immunodeficiency disorders		Characteristics
B Lymphocytes deficiency:	X-linked Agammaglobulinemia or Bruton disease	• X-chromosome linked disorder • Pre-B cells do not differentiate into mature B cells • Mutation in tyrosine kinase encoding gene • All the Igs present in lox level
	Selective Immunoglobulin IgA deficiencies	• Deficiency in IgA • Malfunction in heavy chain switching • Prone to lung infection and recurrent sinus
T Lymphocytes deficiency:	Congenital Thymic Aplasia or DiGeorge syndrome,	• Tetanic seizure prominent • Prone to viral and fungal infection • Treatment through fetal thymus transplantation
	Chronic Mucocutaneous candidasis	• Selective T-cell function defect • T-cell response to other microbes normal not candida • B cell response normal • Suffers parathyroid deficiency
	Hyper-IgM syndrome	• Very high level of IgM • Normal Lymphocytes count • IgA, IgG, IgE, IgD defective • Compromised B-cell and T-cell immune-cooperation • Failure to interact with CD40
B and T cell	Severe combined immunodeficiency	• Early stem cell fails to differentiate into B and T-cells

deficiency	disease (SCID),	• Prevalent deficiency of IL-2 receptors • Defective Janus Kinase 3, ZAP-70 genes • Defective immune cell receptors RAG1 and RAG2 • Characterized by variety of infections
	Wiskott-Aldrich Syndrome	• Reduced IgM concentration • Elevated IgA and IgE level • Normal T-cell population but reduced function • Reduced F-actin polymerization
	MHC deficiency or Bare leukocyte syndrome	• Lower CD4+ count than normal • Low CD8+ T lymphocytes • Impaired antibody production • Susceptible to bacteremia (bacteria in blood)
Phagocyte deficiency	Chronic Granulomatous Disease	• X-linked disorder • Defective NADPH • Formation of granuloma • Blockade of oesophagus, stomach or bladder due to granuloma
	Leukocyte adhesion deficiency syndrome	• Autosomal recessive disease • Defective phagocytosis of bacteria • Impaired cell adhesion • Pyogenic infection like otitis and pneumonia
Complement deficiency	Hereditary Angioedema	• Autosomal dominant disorder • Causative factor due to deficiency in Complement protein C1 • Formation of edema

	Recurrent infections	• Deficiency in Complement protein C3 • Deficiency in complement protein C5 • Susceptible to bacteremia
	Autoimmune diseases	• Deficiency of complement protein C2 • Deficiency of complement protein C4 • Similar to systemic lupus erymatous

Secondary Immunodeficiency

Secondary immunodeficiency (SID) is also known as acquired immunodeficiency. Secondary immunodeficiency disorders are more common than PID disorders. SID disorder is an impairment of immune system resulting from infectious agents, malnutrition, metabolic disorders, medications or environmental factors. The impaired immune system can be reversed if the underlying illness and the causing agent is taken care of. Based on the causative agent or factor SID can be categorized as:

i) Malnutrition related SID

Malnutrition is considered as the most common cause of SID especially in the developing countries. Malnutrition in early age causes kwashiorkor and marasmus which are protein energy (calorie) malnutrition disease. Such individuals are underlined by underweight and muscle wasting. The thymus glands where maturation of T cells occurs are often atrophic in severe malnutrition case with reduced production of thymic hormones. Consequently, CD4+ differentiation of T-cells, lymphocyte proliferation and T-cell mediated hypersensitivity reactions are significantly reduced. Though, production of antibodies is not affected but the ability of the B-cells in antigen processing is compromised. Their neutrophils, polymorph nuclear leucocytes and natural killer cells do not function normally.

ii) Infection related SID

Certain infections from microbes like bacteria, fungi and virus cause impairment of the immune system. Bacterium *Mycobacterium leprae* that causes leprosy, is observed to be closely associated with abnormal T-cell immune response. Impairment in delayed-type hypersensitivity reaction to fungi infection (histoplasmosis and candidiasis) coupled with inability to process antigens.

SID disorders are closely associated with viral infections. Viruses like measles virus cause impairment of functions of B-cells, T-cells and natural killer cells. Cytomegalo virus attacks macrophages rendering inability to process and present antigens. Infection from Epstein-Barr virus causes immune-suppression. Severe infection leads to mononucleosis and reduced natural killer function.

Classical example of SID from infection is Auto-immune Deficiency Syndrome (AIDS). Infection from Human Immunodeficiency Virus (HIV) is marked by progressive reduction in T-cells and B-cells types. Acute depletion in CD4+ T-cell count with low CD4+/CD8+ ratio is observed. In addition, HIV causes impaired natural killer and antibody specific response along with loss of antigen presentation ability of macrophages.

iii) Drug related SID

Use of drugs to improve or cure any immune response related disease is a conventional clinical practice. Most of the drugs with immune-suppression property can be categorized into, corticosteroids, calcineurin inhibitors and cytotoxic drugs. The side effect of all these drugs amount to weakening of immune response. Corticosteroids which include glucocorticoids and mineralocorticoids are good anti-inflammatory drugs for reducing tissue damage against infection. The use of this steroid beyond the saturation of receptor level, results in reduced production of cytokines (TNF-α, IL-1, IL-6), impaired chemotaxis, cell adhesion and phagocytic property of leukocytes. At high dose, impairment of delayed-hypersensitivity response and antibody response can render susceptibility to viral, bacterial and fungal infection.

Calcineurin inhibitor drugs are mostly used for preventing organ graft rejection. They inhibit activation of IL-2 transcription, T-cell response and rapamycin protein which is important for cell activation and proliferation. Cytotoxic drugs are also used in anti-graft rejection medication to control cell growth and removal of bone marrow for transplantation. Cytotoxic drugs prevent DNA synthesis in the S-phase of cell cycle and induce apoptosis. They induce immunodeficiency by inhibiting B-cell and T-cell proliferation, T-cell response activity and macrophage functions.

iv) Aging related SID

Immunity of an individual is affected by aging. This is from the fact that size of thymus glands decreases annually by 3% after reaching puberty till middle age. After which, the size of the gland reduces by 1% annually. Therefore in adult life thymus produces fewer T cells. The T-cell pool is maintained by peripheral proliferation of cell. In addition, impaired neutrophils, macrophages and NK-cell activity leading to immune deficiency has been observed in old age individuals.

v) Environmental factors related SID

Environmental factors that can cause SID disorder include exposure to ionizing radiations, heavy metals and pesticides. Continuous exposure to ionizing radiation weakens immune system as it depletes bone marrow and affects all blood cell lineages. However, immune responses such as phagocytosis and humoral response are observed to be resistant to radiation. Exposure to heavy metals such as lead, cadmium and mercury, through food and water, over a period of time shows decreased polymorphonuclear phagocytic activity, reduced immunoglobulin and complement responses.Immune disorders such as rheumatoid arthritis and systemic lupus erythematosus have been strongly linked with pesticides. But the evidence of immune-suppression is still scarce.

13.4 SUMMARY

Let us summarise whatever you have learnt so far:

- Immune system generates inflammatory response against antigens. Sometimes our immune system elicits inappropriate reactions also in response to antigens.
- Antigens that are responsible for such inappropriate response are known as allergens and the reactions are known as allergy.
- Hypersensitivity starts with initial exposure to allergens which is termed as initial dose. After the exposure to allergens, immune system response results in damaging effects. This component is known as shocking dose.
- Gell and Coombs (1963) classified hypersensitivity into four types i.e. Type I, II, III and IV.
- Type I hypersensitivity is mediated by antibody of certain class, specifically IgE, when they react with allergens (antigens) and activate mast cells and basophils. Allergy comes under type-I hypersensitivity.
- Type-II hypersensitivity reaction involves IgG and IgM and are directed against cells with the allergens or extracellular matrix. They are also known as antibody mediated hypersensitivity.
- Type-III hypersensitivity is a condition that arises due to delayed clearance of antigen-antibody complexes that result in accumulation of the complex in tissues and blood vessels. This type of hypersensitivity is also known as immune complex disease.
- Type-IV hypersensitivity is also known as delayed hypersensitivity or cell-mediated hypersensitivity where the immune reaction takes several days to develop and they are mediated by lymphocytes.
- When all the tolerance mechanism breaks down and fails to protect the host from its own immune system, it leads to severe and fatal organ damage. Such condition is known as autoimmunity.
- Autoimmunity disorder can be specific to an organ or it may affect multiple organs.
- Organ specific autoimmunity is humoral or cell mediated and targets only a particular organ. This phenomenon not only affects the normal functioning of the organ but also causes physical damage.
- Systemic autoimmunity is a type of immune response that targets vast range of tissues and organs.Hence widespread damage across multiple tissues or organs occurs from auto-antibodies and cell mediated immune response.
- Immune deficiency is a state of condition where the ability of immune system to fight infection is compromised partially or totally. It is also known as immunocompromisation. Immune deficiency is of two types- primary and secondary immune deficiency.

- Primary immune deficiency is also known as congenital where the individual has inherent weak immune system.
- Secondary immune deficiency is also known as acquired immune deficiency as an individual may acquire it from environmental factors like infection or chemotherapy or malnutrition.

13.5 TERMINAL QUESTIONS

1. Define allergy.
2. What are the different types of hypersensitivity according to Gell and Coombs?
3. Explain how our immune system prevents autoimmunity?
4. What is immune deficiency?

13.6 ANSWERS

Self Assessments Questions

1. a) v, ii) i, c) ii, d) iii, e) iv.
2. i) T, ii) T, iii) T, iv) F, v) F.
3. i) Initial dose, Shocking
   ii) Central, Peripheral
   iii) Disregulation, Inflammatory
   iv) Kidney, Lungs
   v) Systemic Lupus Erythematous

Terminal Questions

1. Allergy can be defined as inappropriate reactions of immune system in response to antigens.
2. Gell and Coombs (1963) classified hypersensitivity into four types:
   i) **Type I hypersensitivity:** It is mediated by antibody of certain class, specifically IgE.They react with allergens (antigens) and activate mast cells and basophils. Allergy comes under type-I hypersensitivity.
   ii) **Type-II hypersensitivity:** It is also known as antibody mediated hypersensitivity. Since it involves IgG and IgM that are directed against cells with the allergens or extracellular matrix.
   iii) **Type-III hypersensitivity:** It is a condition that arises due to delayed clearance of antigen-antibody complexes that result in accumulation of the complex in tissues and blood vessels. This type of hypersensitivity is also known as immune complex disease.

iv) **Type-IV hypersensitivity:** It is also known as delayed hypersensitivity or cell-mediated hypersensitivity where the immune reaction takes several days to develop and they are mediated by lymphocytes which in other types are mediated by antibodies.

3. There are mechanisms within our body immune system to check and ensure the removal of self-reactive cells. These mechanisms are known as Tolerance. During maturation of B cells and T cells in the bone marrow and thymus respectively, those cells carrying self-reactive receptors or antibodies are eliminated. This process of removal is called Central Tolerance. Those self-reactive cells that escaped into circulation are trapped and eliminated in the lymph organs that are located peripherally through a process known as Peripheral Tolerance. Also the activated lymphocytes have a short life span and they ultimately die by apoptosis or programmed cell death. These mechanisms safeguard the body from self-reactive cells under normal physiological condition.

4. Immune deficiency is a state of condition where the ability of immune system to fight against infection is compromised partially or totally. An individual can have inherent weak immune system i.e, since birth or an individual may acquire it from environmental factors like infection or chemotherapy or malnutrition.