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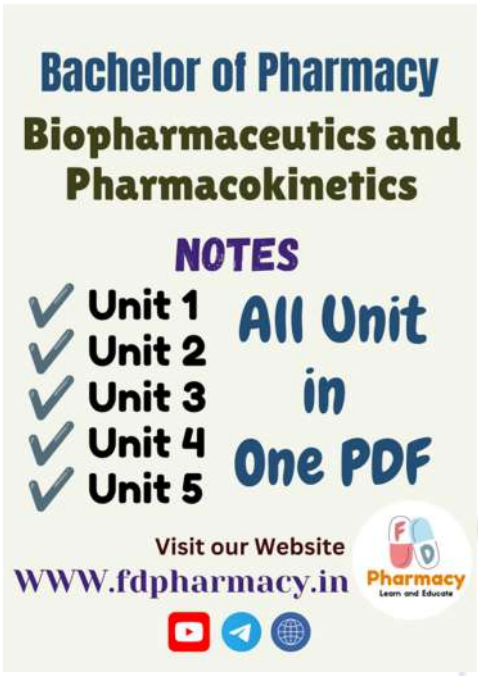
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PHARMACEUTICAL BIOTECHNOLOGY

UNIT 3

TOPIC :

- c) Hypersensitivity reactions, Immune stimulation and Immune suppressions.

Hypersensitivity Reactions

- Hypersensitivity reactions are exaggerated or inappropriate immune responses that cause tissue damage, inflammation, or discomfort rather than protection.
- These reactions occur when the immune system reacts excessively to a substance that is normally harmless, known as an allergen.

Classification of Hypersensitivity Reactions

According to Gell and Coombs Classification, hypersensitivity reactions are divided into four types:

1. Type I – Immediate (Anaphylactic) Hypersensitivity
2. Type II – Cytotoxic Hypersensitivity
3. Type III – Immune Complex-Mediated Hypersensitivity
4. Type IV – Delayed-Type Hypersensitivity

Type I Hypersensitivity

(Immediate or Anaphylactic Hypersensitivity)

Type I hypersensitivity is an immediate allergic reaction mediated by IgE antibodies.

It develops within minutes after exposure to an allergen in previously sensitized individuals.

Common Allergens

- Pollen
- Dust mites
- Animal dander
- Milk
- Eggs
- Peanuts
- Certain drugs
- Insect venom

Mechanism of Type I Hypersensitivity

First Exposure (Sensitization)

1. Allergen enters the body.
2. B-cells produce IgE antibodies.
3. IgE binds to Fc receptors on mast cells and basophils.
4. Individual becomes sensitized.

Re-Exposure

1. Same allergen enters again.
2. Allergen cross-links IgE molecules on mast cells.
3. Mast cells undergo degranulation.
4. Chemical mediators are released.

Mediators Released

Histamine

- Vasodilation
- Increased vascular permeability
- Itching

Leukotrienes

- Bronchoconstriction
- Mucus secretion

Prostaglandins

- Inflammation

Cytokines

- Recruit inflammatory cells

Effects

- Redness
- Swelling
- Itching
- Bronchoconstriction

Examples

- Bronchial asthma
- Allergic rhinitis (hay fever)
- Urticaria (hives)
- Food allergy
- Anaphylaxis

Type II Hypersensitivity

(Cytotoxic Hypersensitivity)

- Type II hypersensitivity occurs when antibodies react against antigens present on the surface of cells or tissues, resulting in cell damage or destruction.

Antibodies Involved

- IgG
- IgM

Mechanism

Step 1

Antigens are present on:

- RBCs
- Platelets
- Tissue cells

Step 2

IgG or IgM antibodies bind to these antigens.

Step 3

Cell destruction occurs by:

A. Complement Activation

- Cell lysis occurs.

B. Opsonization

- Phagocytes engulf and destroy cells.

C. Antibody-Dependent Cellular Cytotoxicity (ADCC)

- Natural Killer (NK) cells destroy target cells.

Examples

Hemolytic Anemia

- Destruction of RBCs by antibodies.

Blood Transfusion Reaction

- Occurs when incompatible blood is transfused.

Rh Incompatibility

- Causes hemolytic disease of the newborn.

Type III Hypersensitivity

(Immune Complex-Mediated Hypersensitivity)

- Type III hypersensitivity occurs when antigen-antibody complexes (immune complexes) form in circulation and become deposited in tissues, causing inflammation and tissue damage.

Antibodies Involved

- IgG
- IgM

Mechanism

Step 1: Formation of Immune Complexes

Soluble antigens combine with antibodies in the blood.

↓

Step 2: Deposition in Tissues

Immune complexes deposit in:

- Blood vessel walls
- Kidneys
- Joints
- Skin

↓

Step 3: Complement Activation

Complement proteins become activated.

↓

Step 4: Recruitment of Neutrophils

Neutrophils migrate to the site.

↓

Step 5: Tissue Damage

Neutrophils release enzymes and reactive oxygen species causing inflammation and tissue injury.

Examples

Systemic Lupus Erythematosus (SLE)

- Immune complexes deposit in multiple organs.

Post-Streptococcal Glomerulonephritis

- Immune complexes deposit in kidney glomeruli.

Type IV Hypersensitivity

(Delayed-Type Hypersensitivity)

- Type IV hypersensitivity is a cell-mediated immune reaction involving T-lymphocytes rather than antibodies.
- It is called delayed hypersensitivity because symptoms appear 24–72 hours after antigen exposure.

Cells Involved

- $CD4^+$ Helper T-cells
- $CD8^+$ Cytotoxic T-cells
- Macrophages

Mechanism

Step 1

Antigen enters the body.

Step 2

Sensitized T-cells recognize the antigen.

Step 3

T-cells release cytokines such as:

- Interferon-γ (IFN-γ)
  - Interleukins

Step 4

Macrophages and cytotoxic T-cells become activated.

Step 5

Inflammation and tissue damage occur.

Examples

Contact Dermatitis

Caused by:

- Nickel
- Cosmetics
- Poison ivy

Tuberculin Skin Test (Mantoux Test)

Positive reaction appears after 48–72 hours.

Immunosuppression

- Immunosuppression refers to the reduction or inhibition of the immune response.
- It may occur naturally due to diseases or can be induced therapeutically using drugs.
- Immunosuppression is mainly used when the immune system becomes overactive or starts attacking the body's own tissues.

Objectives of Immunosuppression

- Prevent organ transplant rejection
- Control autoimmune diseases
- Reduce excessive inflammatory reactions
- Manage severe allergic conditions

Mechanism of Immunosuppression

- Immunosuppressive agents act by suppressing the activity, proliferation, and function of immune cells.

Effects on Immune System

- Inhibit T-lymphocyte activation
- Suppress B-lymphocyte function
- Decrease cytokine production
- Reduce antibody formation
- Inhibit antigen presentation
- Reduce inflammatory responses

As a result, the overall immune response is decreased.

Immunosuppressive Drugs

1. Corticosteroids

Examples

- Prednisolone
- Hydrocortisone
- Dexamethasone

Mechanism

- Inhibit inflammatory mediators
- Suppress cytokine production
- Reduce leukocyte migration

Uses

- Autoimmune diseases
- Allergic disorders

2. Cyclosporine

Mechanism

Cyclosporine inhibits calcineurin enzyme.

This prevents:

- Activation of T-cells
- Production of Interleukin-2 (IL-2)

Uses

- Organ transplantation
- Rheumatoid arthritis

3. Methotrexate

Mechanism

- Inhibits folic acid metabolism
- Prevents DNA synthesis
- Suppresses immune cell proliferation

Uses

- Rheumatoid arthritis
- Psoriasis
- Certain cancers

Other Immunosuppressive Drugs

- Tacrolimus
- Azathioprine
- Mycophenolate mofetil

Uses of Immunosuppression

1. Organ Transplantation

Used to prevent rejection of transplanted organs such as:

- Kidney
- Liver
- Heart
- Lung

2. Autoimmune Diseases

Used in diseases where the immune system attacks self-tissues.

Examples

- Rheumatoid arthritis
- Systemic Lupus Erythematosus (SLE)
- Psoriasis
- Multiple sclerosis

3. Allergic and Inflammatory Disorders

Used to control severe:

- Asthma
- Allergic reactions
- Chronic inflammatory conditions

Adverse Effects of Immunosuppression

- Increased risk of infections
- Delayed wound healing
- Increased cancer risk
- Bone marrow suppression
- Liver and kidney toxicity

Immunostimulation

- Immunostimulation refers to the enhancement or activation of the immune response to improve the body's defense mechanisms.
- It is required when the immune system is weak, deficient, or suppressed.

Objectives of Immunostimulation

- Increase resistance to infections
- Improve immune cell activity
- Enhance vaccine effectiveness
- Strengthen host defense mechanisms

Mechanism of Immunostimulation

Immunostimulants enhance the activity and proliferation of immune cells.

Effects on Immune System

- Increase macrophage activity
- Stimulate lymphocyte proliferation
- Activate Natural Killer (NK) cells
- Enhance cytokine production
- Improve antigen presentation
- Promote antibody formation

As a result, immune responses become stronger and more effective.

Immunostimulatory Agents

1. Interferons

Functions

- Enhance antiviral activity
- Activate immune cells
- Increase antigen presentation

Uses

- Viral infections
- Certain cancers

2. Interleukins

Functions

- Stimulate growth of immune cells
- Promote differentiation of lymphocytes
- Enhance immune responses

Example

- Interleukin-2 (IL-2)

Uses

- Cancer immunotherapy

3. Vaccines

Mechanism

Vaccines contain weakened, killed, or antigenic components of pathogens.

They stimulate:

- Antibody production
- Memory B-cell formation
- Memory T-cell formation

Benefits

Provide long-term protection against infectious diseases.

Uses of Immunostimulation

1. Prevention of Infectious Diseases

Through vaccination against diseases such as:

- Polio
- Hepatitis B
- COVID-19
- Measles

2. Immunodeficiency Conditions

Used when immune function is reduced.

Examples

- Primary immunodeficiency disorders
- Immunocompromised patients

3. Cancer Therapy

Used to enhance the body's ability to destroy tumor cells.