PHARMACEUTICAL MICROBIOLOGY and IMMUNOLOGY

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Immunology

OBJECTIVES

- Definition Hypersensitivity Reactions
- Hypersensitivity Types
- Type I (Immediate-Anaphylactic) Hypersensitivity
- Type II (Cytotoxic) Hypersensitivity
- Type III (Immune-Complex Mediated) Hypersensitivity
- Type IV (Cell Mediated-Delayed) Hypersensitivity

Hypersensitivity Reactions

- Hypersensitivity refers to undesirable (damaging, sometimes fatal) reactions produced by the normal immune system.
- Hypersensitivity reactions require a pre-sensitized (immune) state of the host.

Hypersensitivity Types

On the basis of mechanisms involved and time taken for the reaction, hypersensitivity reactions can be classified into four types:

- **Type I (Immediate-Anaphylactic) Hypersensitivity**
- **Type II (Cytotoxic) Hypersensitivity**
- **Type III (Immune-Complex Mediated) Hypersensitivity**
- **Type IV (Cell Mediated-Delayed) Hypersensitivity**

Type I (Immediate-Anaphylactic) Hypersensitivity

In type 1 hypersensitivity, an antigen is presented to cells specific to the antigen that stimulate B-cell production of Ig E antibodies also specific to the antigen.

During sensitization, the Ig E antibodies bind to Fc receptors on the surface of tissue mast cells and blood basophils. Mast cells and basophils coated by Ig E antibodies are "sensitised."

Type I (Immediate-Anaphylactic) Hypersensitivity

Later exposure to the same allergen cross-links the bound Ig E on sensitized cells, resulting in degranulation and the secretion of pharmacologically active mediators such as histamine, leukotriene and prostaglandin that act on the surrounding tissues.

The principal effects of these products are vasodilation and smooth-muscle contraction.

Exposure may be by ingestion, inhalation, injection, or direct contact

Type I (Immediate-Anaphylactic) Hypersensitivity

Atopy: the genetic predisposition to synthesize inappropriate levels of Ig E specific for external allergens

Anaphylaxis is an acute, life-threatening hypersensitivity reaction, involving the whole body, which is usually brought on by something eaten or injected.

It may occur within seconds of exposure to something a person is allergic to.

Anaphylaxis is a medical emergency that develops rapidly and can be fatal.

Type II (Cytotoxic) Hypersensitivity

In type II (cytotoxic) hypersensitivity the antibodies produced by the immune response bind to antigens on the patient's own cell surfaces.

The antigens recognized in this way may either be intrinsic ("self" antigen, innately part of the patient's cells) or extrinsic (adsorbed onto the cells during exposure to some foreign antigen, possibly as part of infection with a pathogen).

These cells are recognized by macrophages or dendritic cells, which act as antigen-presenting cells. This causes a B cell response, wherein antibodies are produced against the foreign antigen.

Type II (Cytotoxic) Hypersensitivity

Ig G and Ig M antibodies bind to these antigens to form complexes that activate the classical pathway of complement activation to eliminate cells presenting foreign antigens (lyse the cell and destroy it).

Type II Allergic Reactions:

- Transfusion reactions
  - ABO Blood Group System
  - Rh Blood Group System

Type II Allergic Reactions:

- Erythroblastosis fetalis

Type II (Cytotoxic) Hypersensitivity

Type II Allergic Reactions:

- Erythroblastosis fetalis
  - ✓ Rh– mother become sensitized when Rh+ blood (from a previous pregnancy of an Rh+ baby or a Rh+ transfusion) causes her body to synthesis Rh antibodies
  - ✓ Rh antibodies of a sensitized Rh– mother cross the placenta and attack and destroy the Red Blood Cells of an Rh+ baby

Type II (Cytotoxic) Hypersensitivity

Type II Allergic Reactions:

- Autoimmune Diseases

- **Myastenia Gravis**: Myasthenia gravis is an autoimmune neuromuscular disease characterized by weakness and fatigue of the skeletal muscles of the face and extremities.

- **Rheumatic Fever:** Acute rheumatic fever is a systemic disease of childhood ,often recurrent that follows group A beta hemolytic streptococcal infection. It is a diffuse inflammatory disease of connective tissue primarily involving heart, blood vessels and joints.

Type II (Cytotoxic) Hypersensitivity

Type II Allergic Reactions:

- Autoimmune Diseases

- **Hashimoto's Thyroiditis:** A type of autoimmune thyroid disease in which the immune system attacks and destroys the thyroid gland.

- **Hyperacute Graft Rejection:** The antibodies are not seen in routine histological staining. Hyperacute rejection can occur immediately after transplantation.

Type III (Immune-Complex Mediated) Hypersensitivity

Type III hypersensitivity is also known as immune complex hypersensitivity. It occurs when there is accumulation of immune complexes (antigen-antibody complexes) that have not been adequately cleared by innate immune cells

Antigens combines with antibody within circulation and form immune complex. Wherever in the body they deposited. They activate compliment system. Polymorphonuclear cells are attracted to the site. Result in inflammation and tissue injury.

The reaction may take 3 - 10 hours after exposure to the antigen (as in Arthus reaction). The reaction may be general (e.g., serum sickness) or may involve individual organs including or other organs.

Type III (Immune-Complex Mediated) Hypersensitivity

Type III Allergic Reactions:

Arthus Reaction: a hypersensitivity reaction that occurs several hours to days following the intradermal injection of a vaccine into an animal and is marked by the formation of antigen-antibody complexes accompanied by localized inflammation, pain, redness and sometimes tissue destruction

Serum Sickness: a hypersensitivity reaction in humans against to proteins in antiserum derived from a non-human animal source, occurring 4–10 days after exposure.

Rheumatoid Arthritis: is a long-lasting autoimmune disorder that primarily affects joints

Type III (Immune-Complex Mediated) Hypersensitivity

Type III Allergic Reactions:

Systemic lupus erythematosus (SLE): SLE is a multi-system auto-immune disease that is caused by tissue damage resulting from antibody and complement fixing immune complex deposition

Post-streptococcal glomerulonephritis (PSG): PSG is caused by prior infection with specific nephritogenic strains of group A beta-hemolytic streptococcus.

Type IV (Cell Mediated-Delayed) Hypersensitivity

- Delayed hypersensitivity is a function of T Lymphocytes (not antibody). The response is delayed. The reaction takes two to three days (48-72 hours) to develop.
- Caused by inflammation resulting from cytokines produced by CD4+ T cells and cell killing by CD8+ T cells.

Type IV (Cell Mediated-Delayed) Hypersensitivity

Type IV Allergic Reactions:

Contact Dermatitis: Allergic contact dermatitis can result from exposure to accelerators and other chemicals used in the manufacture of rubber gloves as well as from exposure to other chemicals found in the dental practice setting. Allergic contact dermatitis often manifests as a rash beginning hours after contact and, like irritant dermatitis, is usually confined to the areas of contact.

Type IV (Cell Mediated-Delayed) Hypersensitivity

Type IV Allergic Reactions:

Tuberculin Skin Test: An injection of tuberculin (PPD) beneath the skin causes reaction in individual exposed to tuberculosis or tuberculosis vaccine. Used to diagnose contact with antigens of Mycobacterium tuberculosis. Red, hard swelling develops in individuals previously infected or immunized.