Chapter 18: Disorders of the Immune System

1. Hypersensitivity
2. Autoimmunity
1. Hypersensitivity

Chapter Reading – pp. 527-538
What is Hypersensitivity?

Hypersensitivity is an immunological state in which the immune system “over-reacts” to foreign antigen such that the immune response itself is more harmful than the antigen.

All types of hypersensitivity involve:

- the adaptive immune response
  - i.e., highly specific reactions via T or B cells

- prior exposure to the antigen
  - the initial exposure sensitzes the individual but does NOT cause a hypersensitive reaction

- hypersensitivity is only seen on secondary exposure
Types of Hypersensitivity

Hypersensitivity following secondary exposure to antigen comes in 4 basic forms:

*Type I: allergic reactions (“immediate” hypersensitivity)
  - IgE mediated and very rapid (2-30 minutes)

*Type II: cytotoxic reactions
  - cell damage due to complement activation via IgM or IgG

*Type III: immune complex reactions
  - cell damage due to excess antibody/antigen complexes

Type IV: delayed cell-mediated reactions
  - cell damage involving T cells & macrophages

* Types I-III are all antibody-mediated, Type IV is not!
Type I: Allergic Reactions

Allergic (anaphylactic) reactions involve the activation of mast cells, eosinophils or basophils through binding of antigen to IgE on cell surface:

- Mast cells & basophils have IgE $F_C$ receptors that bind the constant region of any IgE antibody.
- "Cross-linking" of IgE molecules on the cell surface by binding to antigen triggers the release of "mediators."
- Mediators = histamine, prostaglandins & leukotrienes.
Humoral IR leading to Allergy

- primary exposure leads to production of IgE Abs specific for allergen
- subsequent exposure triggers allergic reaction
more on Allergic Reactions

The release of these mediators causes the redness, swelling, itching, mucus, etc, that characterize allergic reactions:

Most allergic reactions are local:

• itching, redness, hives in the skin, mucus, sneezing
• usually due to inhaled or ingested antigens

Systemic allergic reactions can be lethal:

• severe loss of blood pressure, breathing difficulty (anaphylactic shock)
• usu. due to animal venoms or certain foods
• epinephrine can “shut down” the allergic reaction
Some common Allergens

Grains of pollen

Foods
  • e.g., corn, eggs, nuts, peanuts, onions

Dust mites
  • the allergen is actually dust mite feces (yuck!)
Managing Allergic Reactions

Avoidance

• avoiding contact with allergen is by far the safest and most effective way of managing allergies

Medications

• antihistamines
  • drugs that block histamine receptors on target cells
  • histamine is still released but has little effect

• epinephrine (aka – adrenalin)
  • necessary to halt systemic anaphylaxis

Desensitization

• antigen injection protocol to induce tolerance
Type II: Cytotoxic Reactions

Type II cytotoxic reactions involve destruction of cells bound by IgG or IgM antibodies via the activation of complement:

- symptoms take several hours to appear
- most commonly observed with blood transfusions
  - reaction to ABO blood antigens
  - reaction to Rh antigen
- can occur via the Rh antigen in newborns
  - requires Rh⁻ mother and Rh⁺ child
  - Rh⁻ mother produces anti-Rh⁺ IgG following birth
  - subsequent Rh⁺ children are vulnerable
The ABO Blood Antigens

- A or B type polysaccharide antigens on surface of RBCs
- individuals lacking enzymes producing A or B are type O
Hemolysis due to ABO Antigens

1. Transfusion
2. Agglutination and complement binding
3. Hemolysis

Type A antigens on red blood cells
Anti-B antibody
Donated red blood cells with B antigen
Complement
Hemoglobin
ABO mediated Cytotoxicity

Blood type “O” individuals (tolerate type O blood only)
- do not produce type A or type B antigens
- produce antibodies to type A and B antigens and thus will lyse type A, B or AB RBCs via complement

Blood type “A” individuals (tolerate blood types A & O)
- produce only type A antigens
- i.e., tolerant to type A antigen, antibodies to B antigen

Blood type “B” individuals (tolerate blood types B & O)
- tolerant to type B antigen, antibodies to A antigen

Blood type “AB” individuals (tolerate all blood types)
- tolerant to both A & B antigens
The Rh Blood Cell Antigen

- Rh antigen is also a polysaccharide on red blood cells
- Rh⁻ mother produces antibodies during birth of 1ˢᵗ Rh⁺ child, which can harm later Rh⁺ children
Type III: **Immune Complex Reactions**

Caused by high levels of antigen-antibody complexes (due to foreign or self Ag) that are not cleared efficiently by phagocytes and tend to deposit in certain tissues:

- blood vessel endothelium in kidneys, lungs
- joints

This can result in local cell damage via:

- complement activation
- attraction of phagocytes, other cells involved in inflammation (e.g., neutrophils)
1. Antigens combine with antibodies to form antigen-antibody complexes.

2. Phagocytes remove most of the complexes, but some lodge in the walls of blood vessels.

3. There the complexes activate complement.

4. Antigen-antibody complexes and activated complement attract and activate neutrophils, which release inflammatory chemicals.

5. Inflammatory chemicals damage underlying blood vessel wall.

- Antigen:antibody complexes get trapped in endothelium
- Inflammatory responses damage blood vessel walls (especially kidneys & lungs)
Type IV: *Delayed Hypersensitivity*

Delayed cell-mediated hypersensitivity takes 1 or 2 days to appear and involves the action of T cells & macrophages, NOT antibodies:

- Proteins from foreign antigen induce $T_{H1}$ response
- Secondary exposure results in the activation of memory $T_{H1}$ cells which attract monocytes to area
- Monocytes activated to become macrophages
- Macrophages release toxic factors to destroy ALL cells in the immediate area

**General response to intracellular bacteria but can also occur with other antigens (latex, poison ivy)**
Infection Allergy

A type of delayed cell-mediated hypersensitivity resulting from infection with an intracellular bacterial pathogen:

- a $T_c$ cell-mediated reaction, NOT IgE based allergy

- basis of the tuberculin test

- previous exposure to *Mycobacterium tuberculosis* gives a positive test result
Contact Dermatitis

- certain substances act as hapten in combination with skin proteins
- activates a potent T cell mediated response upon secondary exposure (e.g., poison ivy)
2. Autoimmunity

Chapter Reading – pp. 540-542
What is Autoimmunity?

Autoimmunity refers to the generation of an immune response to self antigens:

• normally the body prevents such reactions
  • T cells with receptors that bind self antigens are eliminated (or rendered anergic*) in the thymus
  • B cells with antibodies that bind self antigens are eliminated or rendered anergic in the bone marrow or even in the periphery (i.e., outside the bone marrow)
• however in rare cases T and/or B cells that recognize self antigens survive & are activated

*anergic = non-reactive or non-responsive
Common Autoimmune Diseases

Multiple Sclerosis

• immune response to myelin basic protein in Schwann cells (form myelin sheath of neurons)

Lupus

• antibodies to self including DNA and histone proteins

• leads to a systemic type III hypersensitivity
Type I Diabetes

• immune response to self antigens in pancreatic β cells (insulin-producing cells)

• lack of insulin production leads to this form of type I diabetes

Rheumatoid Arthritis

• immune response to self antigens in synovial membranes of joints (type III hypersensitivity)
Key Terms for Chapter 18

- sensitization, types I, II, III & IV hypersensitivity
- anaphylaxis, anaphylactic shock
- histamine, prostaglandins, leukotrienes
- ABO & Rh blood antigens
- autoimmunity, anergic
- infection allergy, contact dermatitis

Relevant Chapter Questions
MC: 1-3, 5-6, 10   TF: 1-4   SA: 2, 3