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 sensitizes 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 Fc 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**

<table>
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<tr>
<th>Blood Group</th>
<th>Red Blood Cells</th>
<th>Plasma Antigens</th>
<th>Blood That Can Be Received</th>
<th>Frequency (%)</th>
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<td>AB</td>
<td>A and B</td>
<td>Neither anti-A</td>
<td>A, B, AB, O (Universal)</td>
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<tr>
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<td>B</td>
<td>Anti-A</td>
<td>B, O</td>
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<tr>
<td>A</td>
<td>A</td>
<td>Anti-B</td>
<td>A, O</td>
<td>41</td>
</tr>
<tr>
<td>O</td>
<td>Neither A or B</td>
<td>Anti-A and Anti-B</td>
<td>O (Universal donor)</td>
<td>47</td>
</tr>
</tbody>
</table>

- 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. Complement
3. Agglutination and complement binding
4. Hemolysis
5. Donated red blood cells with B antigen
6. Type A antibodies on red blood cells
**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

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**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

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**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)
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 TH1 response
- secondary exposure results in the activation of memory TH1 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 Tc 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 haptens 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