Disorders of the Immune System

1. Hypersensitivity

2. Autoimmunity

1

1. Hypersensitivity

2

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**

3

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**

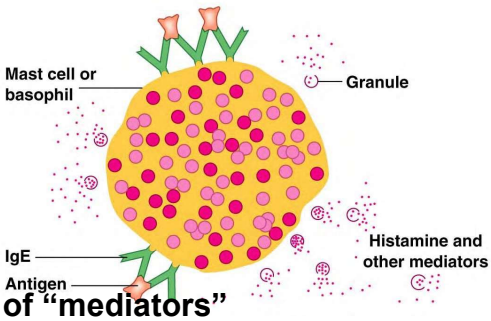
*** Types I-III are all antibody-mediated, Type IV is not!**

4

Type I: Allergic Reactions

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

- **mast cells & basophils have IgE 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**

5

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**

6

Some common Allergens

(a) A micrograph of pollen grains SEM 10 μm

(b) A micrograph of a house dust mite SEM 500 μm

Grains of pollen

Foods

- e.g., corn, eggs, nuts, peanuts, onions

Dust mites

- the allergen is actually dust mite feces

7

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

8

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**

9

The ABO Blood Antigens

TABLE 19.2 The ABO Blood Group System

Blood Group	Erythrocyte or Red Blood Cell Antigens	Illustration	Plasma Antibodies	Blood That Can Be Received	Frequency (% U.S. Population) White	Black	Asian
AB	A and B		Neither anti-A nor anti-B antibodies	A, B, AB, O (Universal recipient)	3	4	5
B	B		Anti-A	B, O	9	20	27
A	A		Anti-B	A, O	41	27	28
O	Neither A nor B		Anti-A and Anti-B	O (Universal donor)	47	49	40

- **A or B type polysaccharide antigens on surface of RBCs**
- **individuals lacking enzymes producing A or B are type O**

10

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)

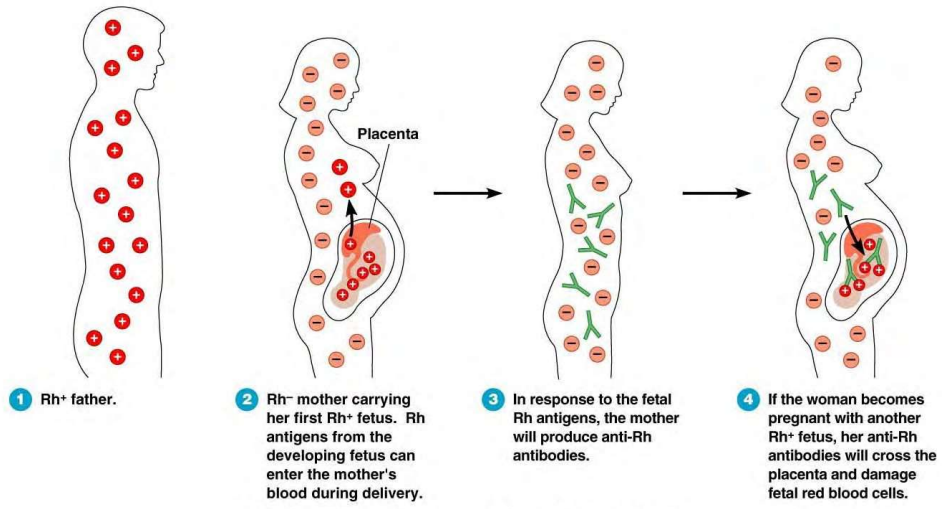
- tolerant to type B antigen, antibodies to A antigen

Blood type "AB" individuals (tolerate all blood types)

- tolerant to both A & B antigens

11

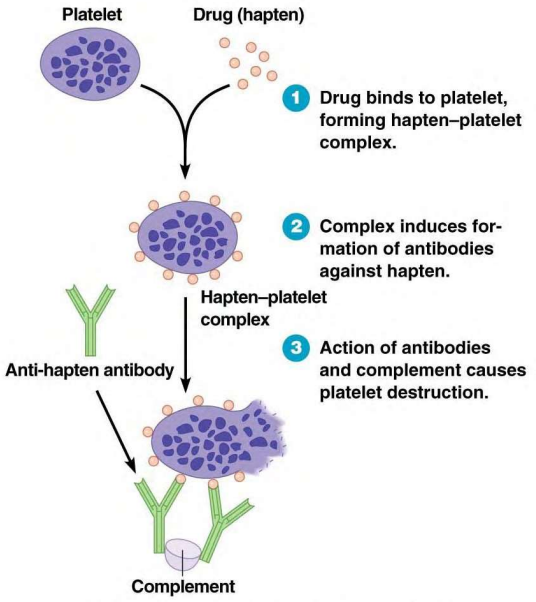
The Rh Blood Cell Antigen



- 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

12

Drug-induced Type II Hypersensitivity



- involves drugs that bind to the surface of cells or platelets
- drug functions as a hapten which in conjunction with cell can stimulate humoral immunity
- antibody binding triggers complement activation, lysis of cells binding the drug

13

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:

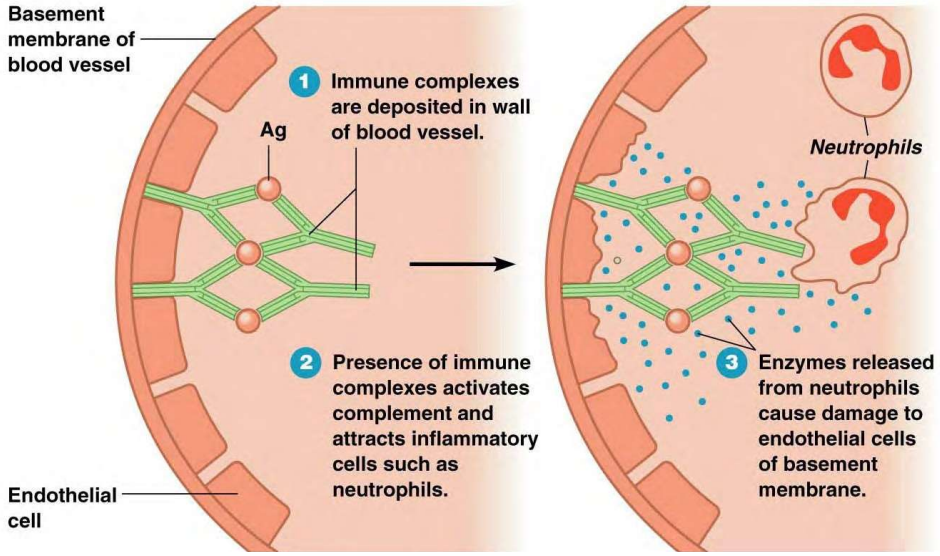
- blood vessel endothelium in kidneys, lungs
- joints

This can result in local cell damage via:

- complement activation
- attraction of phagocytes, other cells involved in inflammation (e.g., neutrophils)

14

Type III: Immune Complex Reactions



- antigen:antibody complexes trapped in endothelium
- inflammatory response damages blood vessel walls

15

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

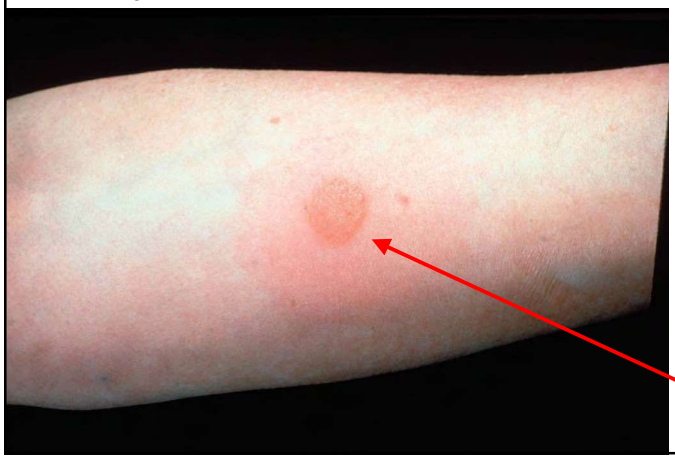
****general response to intracellular bacteria but can also occur with other antigens (latex, poison ivy)****

16

Infection Allergy

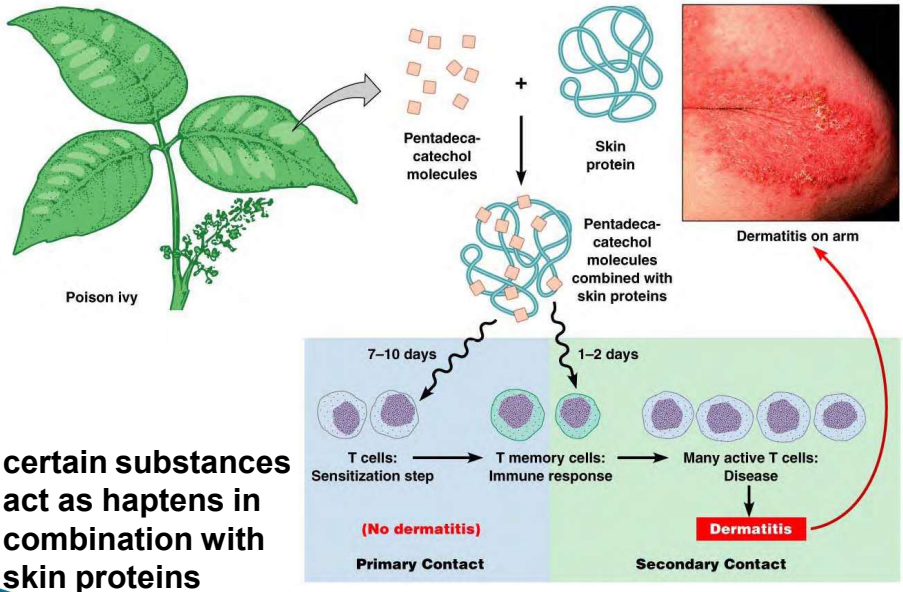
A type of delayed cell-mediated hypersensitivity resulting from infection with an intracellular bacterial pathogen:

- **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**

17



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

18

Summary of Hypersensitivity Reactions

TABLE 19.1 Types of Hypersensitivity

Type of Reaction	Time Before Clinical Signs	Characteristics	Examples
Type I (anaphylactic)	<30 min	IgE binds to mast cells or basophils; causes degranulation of mast cell or basophil and release of reactive substances such as histamine	Anaphylactic shock from drug injections and insect venom; common allergic conditions, such as hay fever, asthma
Type II (cytotoxic)	5–12 hours	Antigen causes formation of IgM and IgG antibodies that bind to target cell; when combined with action of complement, destroys target cell	Transfusion reactions, Rh incompatibility
Type III (immune complex)	3–8 hours	Antibodies and antigens form complexes that cause damaging inflammation	Arthus reactions, serum sickness
Type IV (delayed cell-mediated, or delayed hypersensitivity)	24–48 hours	Antigens activate T_C that kill target cells.	Rejection of transplanted tissues; contact dermatitis, such as poison ivy; certain chronic diseases, such as tuberculosis

19

2. Autoimmunity

20

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**

21

How is Autoimmunity Generated?

It's not entirely clear, however some factors thought to trigger autoimmunity are:

- **genetic factors**
  - **e.g., certain HLA (human MHC class I) alleles are associated with particular autoimmune diseases**
- **foreign antigens that mimic self antigens**
  - **peptide antigens from certain viral and bacterial pathogens are very similar to specific self peptides**
  - **once an immune response is generated to pathogen, these T and B cells continue to respond to tissues expressing the similar self peptide**

22

Common Autoimmune Diseases

Lupus

- **antibodies to self including DNA and histone proteins**

Rheumatoid Arthritis

- **immune response to self antigens in synovial membranes of joints**

Type I Diabetes

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

Multiple Sclerosis

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

23

SUPPORT

- BIO C PLUS 2 X 2 F
- IAG 1-2 tbsp
- BALANCED B8 1tsp
- SELENOMETHIONINE 1-2 F
- ZN ZYME FORTE 1-2 F
- BIO Ashwagandha 2 x 2 E
- INTENZYME FORTE 10 X 3 E
- ADHS 2 x 2 E
- HISTOPLEX, HISTOPLEX AB 2 X 2 E
- TOLERAID 1-3 F

24