Foundations in Microbiology

Fifth Edition

Talaro

Chapter

17

Disorders in Immunity

Chapter 17

Immunopathology

- Allergy, hypersensitivity – an exaggerated, misdirected expression of immune responses
- Involves the same types of immune reactions as those at work in protective immunities.
- Autoimmunity – abnormal responses to self Ag
- Immunodeficiency – deficiency or loss of immunity

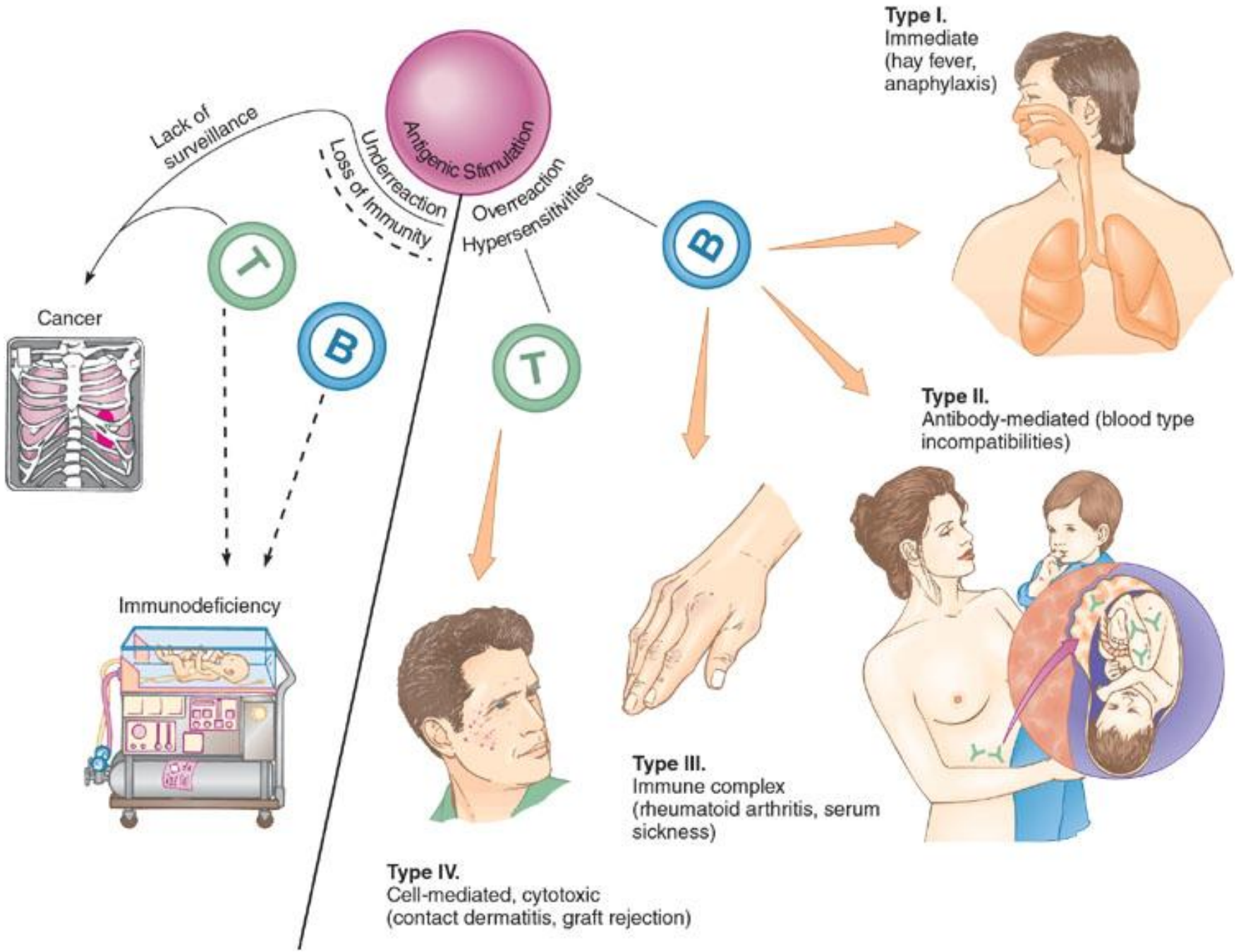


TABLE 17.1

Hypersensitivity States

Type		Systems and Mechanisms Involved	Examples
I.	Immediate hypersensitivity	IgE-mediated; involves mast cells, basophils, and allergic mediators	Anaphylaxis, atopic allergies such as hay fever, asthma
II.	Antibody-mediated	IgG, IgM antibodies act upon cells with complement and cause cell lysis; includes some autoimmune diseases	Blood group incompatibility, pernicious anemia; myasthenia gravis
III.	Immune complex–mediated	Antibody-mediated inflammation; circulating IgG complexes deposited in basement membranes of target organs; includes some autoimmune diseases	Systemic lupus erythematosus; rheumatoid arthritis; serum sickness; rheumatic fever
IV.	T cell–mediated	Delayed hypersensitivity and cytotoxic reactions in tissues	Infection reactions; contact dermatitis; graft rejection; some types of autoimmunity

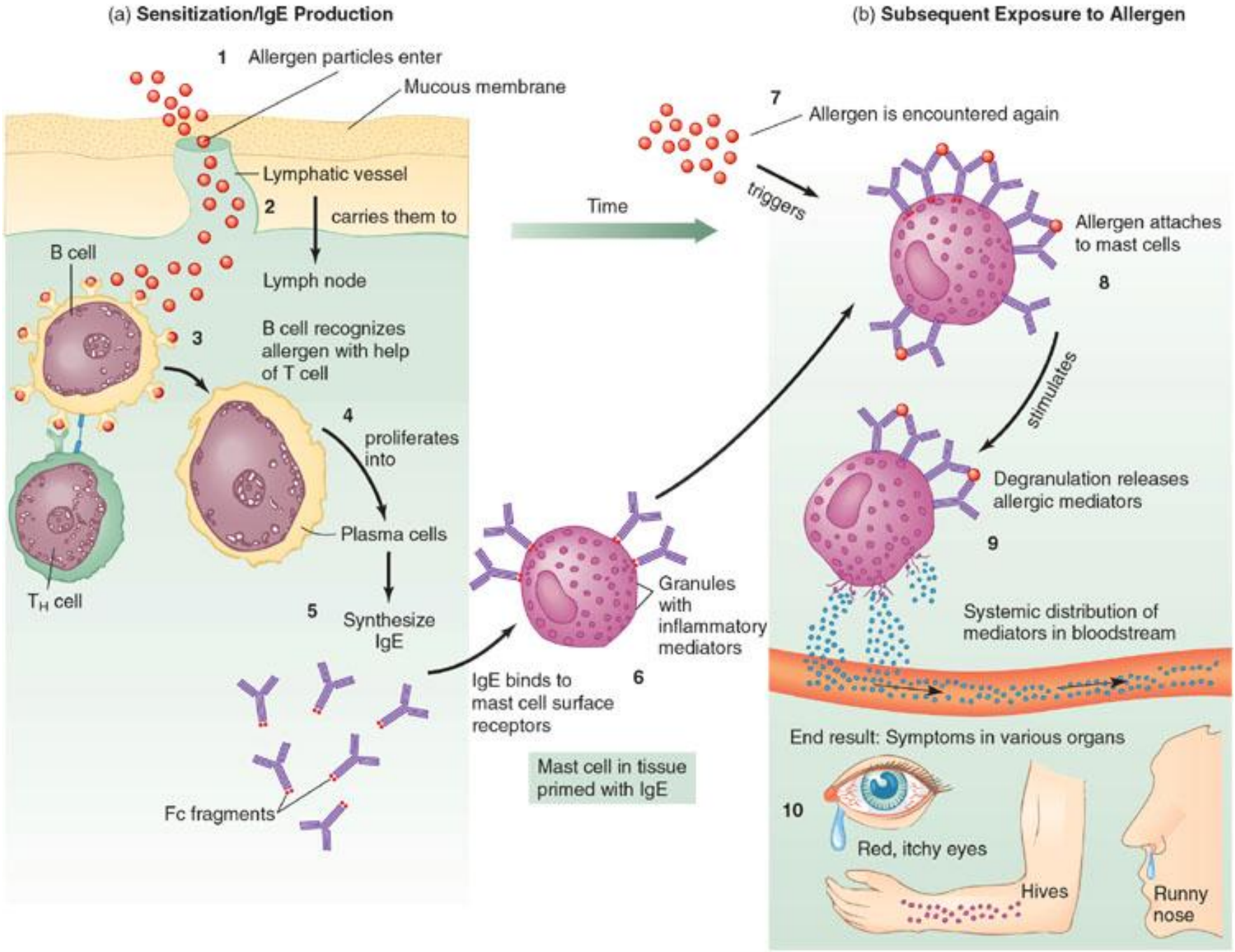
Type I Hypersensitivity

- Atopy – any chronic local allergy such as hay fever or asthma
- Anaphylaxis – a systemic, often explosive reaction that involves airway obstruction and circulatory collapse

Video

Mechanism of Type I

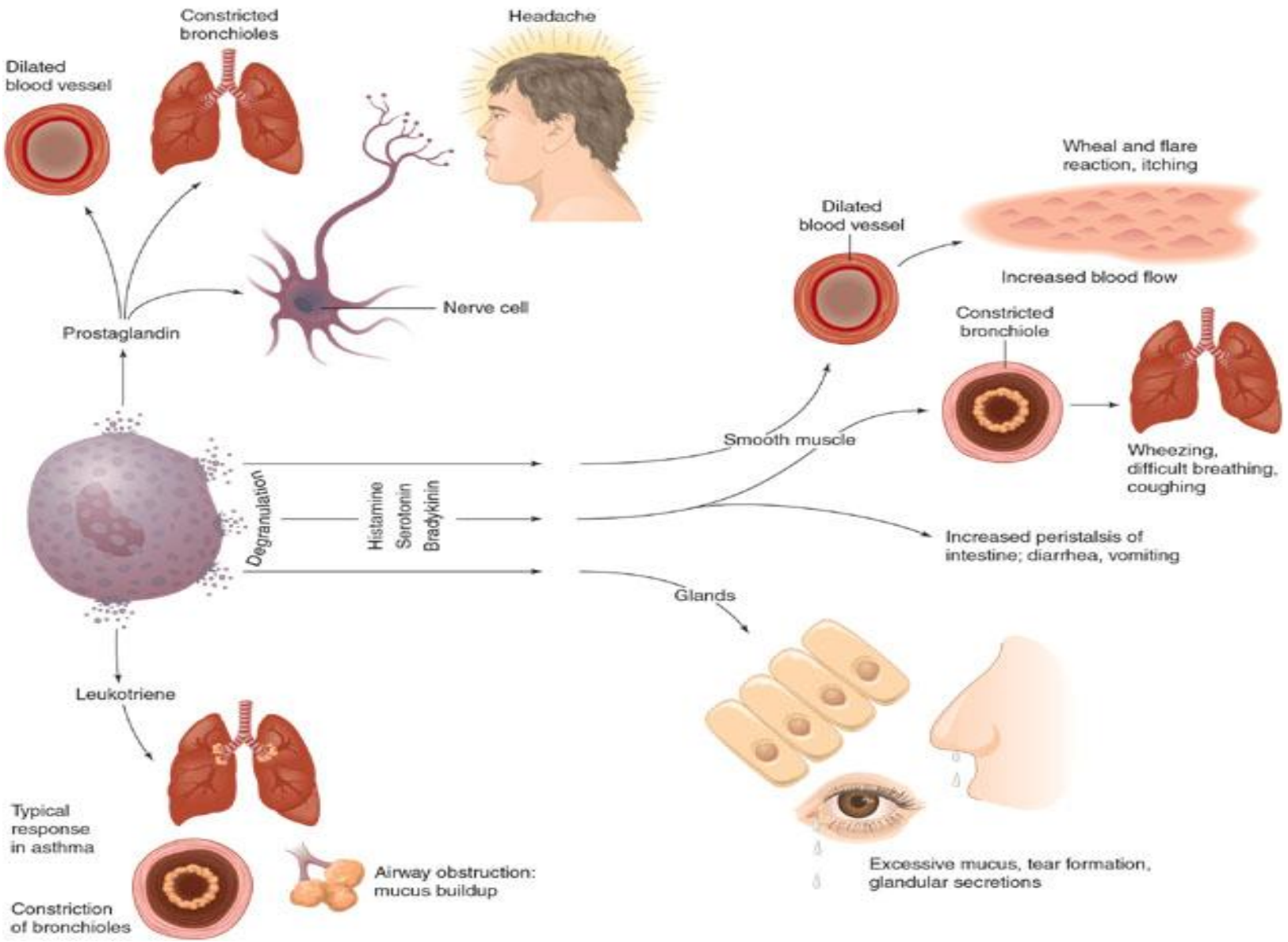
- **sensitizing dose** – on first contact with , specific B cells form IgE which attaches to mast cells and basophils
- **provocative dose** - subsequent exposure with the same allergen binds to the IgE-mast cell complex
- degranulation releases mediators with physiological effects such as vasodilation and bronchoconstriction
- symptoms are rash, itching, redness, increased mucous discharge, pain, swelling, and difficulty breathing



Role of Mast Cells & Basophils

- Mast cells are located in the connective tissue of virtually all organs; high conc. in lungs, skin, GI and genital tract
- Basophils circulate in blood, migrate into tissues
- each cell can bind 10,000-40,000 IgE
- cytoplasmic granules contain physiologically active cytokines, histamine, etc
- cells degranulate when stimulated by

Chemical mediators



(a)

Environmental Allergens

No. 1 Standard Series

	ID 8/85	
	+++	1. Acacia gum
	+++	2. Cat dander
	++++	3. Chicken feathers
	++++	4. Cotton lint
	++	5. Dog dander
	+	6. Duck feathers
	+	7. Glue, animal
	++	8. Horse dander
	><	9. Horse serum
	+++	10. House dust #1
	+	11. Kapok
	+	12. Mohair (goat)
	+	13. Paper
	++++	14. Pyrethrum
	+++	15. Rug pad, ozite
	+	16. Silk dust
	+	17. Tobacco dust
	+	18. Tragacanth gum
	+++++	19. Upholstery dust
	+++	20. Wool

No. 2 Airborne Particles

	ID 8/85	
	+++	1. Ant
	+++++	2. Aphis
	++++	3. Bee
	++++	4. Housefly
	><	5. House mite
	+++	6. Mosquito
	++++	7. Moth
	+++	8. Roach
	++	9. Wasp
	0	10. Yellow jacket
		Airborne mold spores
	++	11. *Alternaria*
	+++	12. *Aspergillus*
	++	13. *Cladosporium*
	+++	14. *Hormodendrum*
	0	15. *Penicillium*
	+	16. *Phoma*
	+++	17. *Rhizopus*
		18. .....

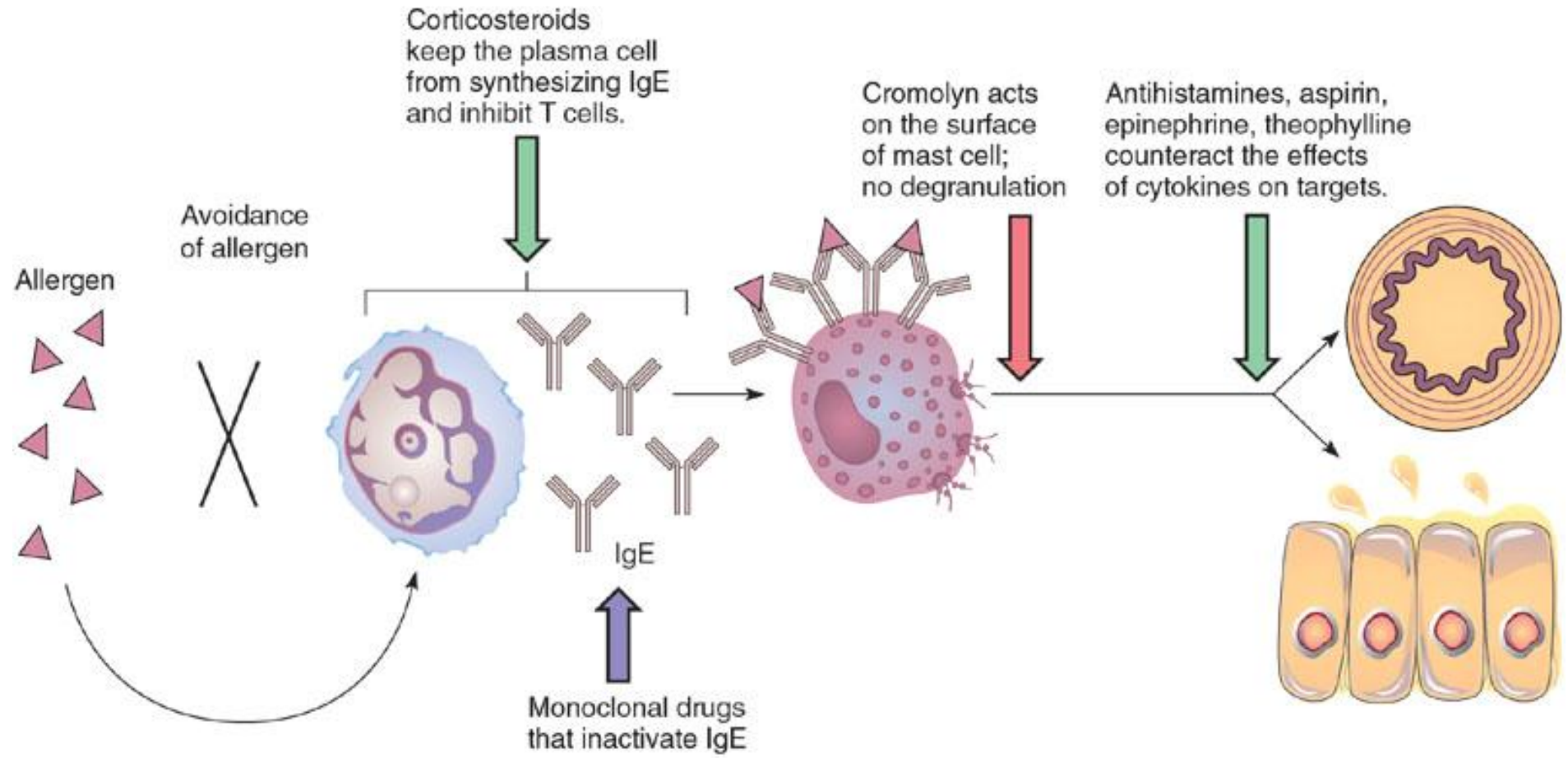
>< - not done
0 - no reaction
\+ - slight reaction
++ - mild reaction
+++ - moderate reaction
++++ - severe reaction

(b)

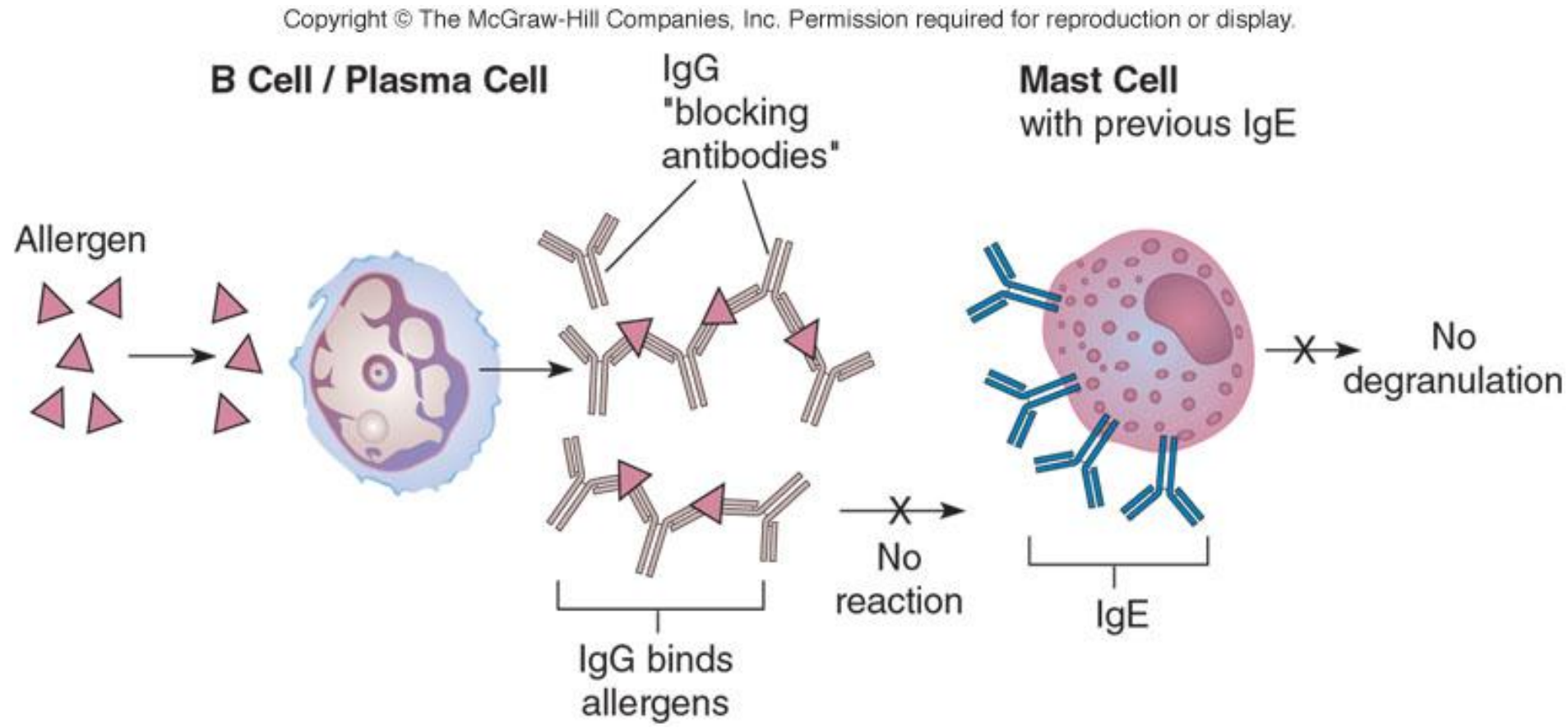
Systemic Anaphylaxis

- Sudden respiratory and circulatory disruption that can be fatal in a few minutes
- Allergen and route are variable
- Bee stings, antibiotics or serum injection

Strategies for circumventing allergic attacks

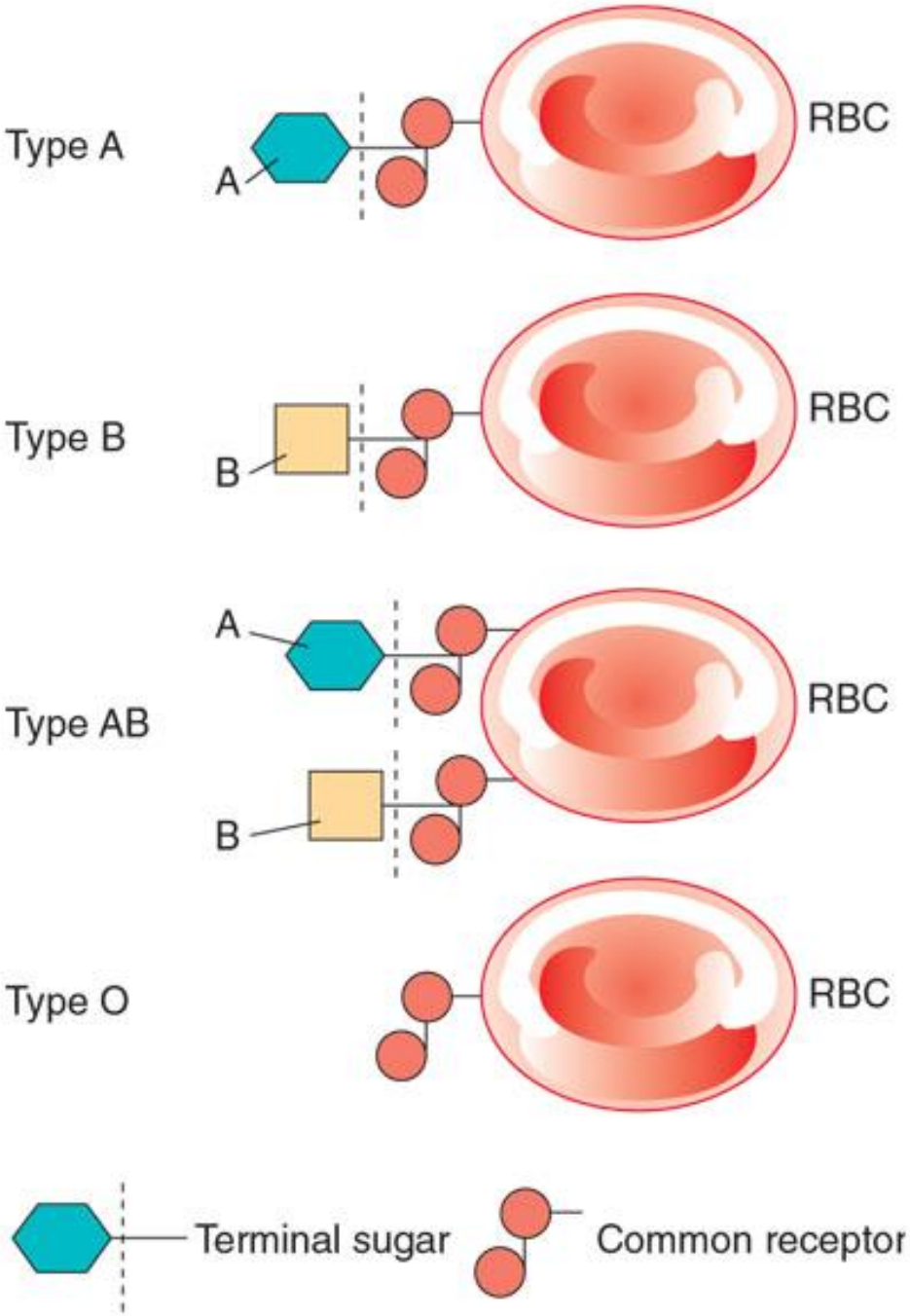


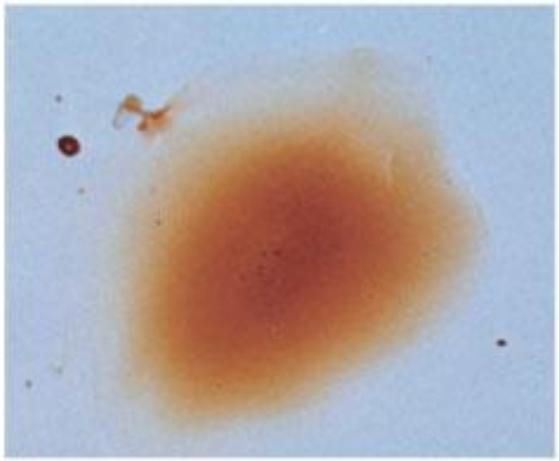
Blocking Ab


Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.
B Cell / Plasma Cell
IgG
"blocking
antibodies"
Mast Cell
with previous IgE
Allergen
No
degranulation
No
reaction
IgE
IgG binds
allergens

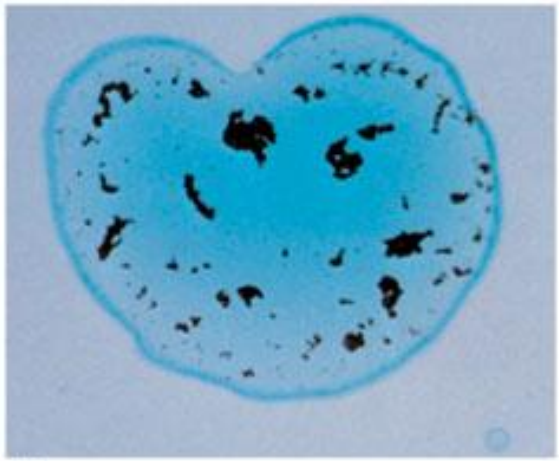
Type II Hypersensitivity

- Reactions that lyse foreign cells
- Involve antibodies, complement, leading to lysis of foreign cells **Video**
- Transfusion reactions
  - ABO blood groups
  - Rh factor – hemolytic disease of the newborn

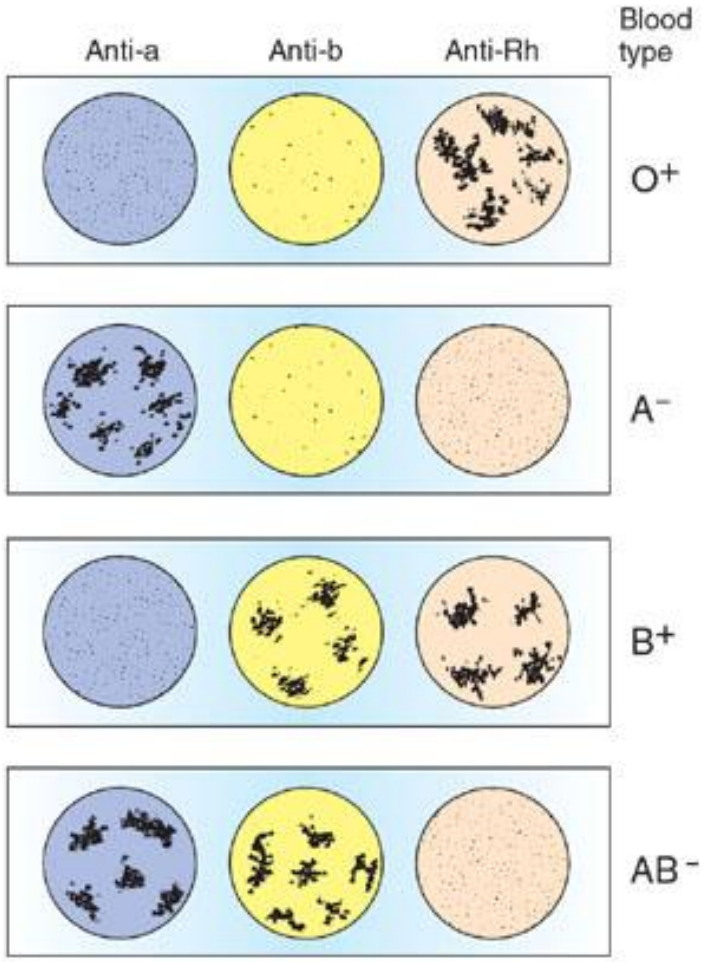




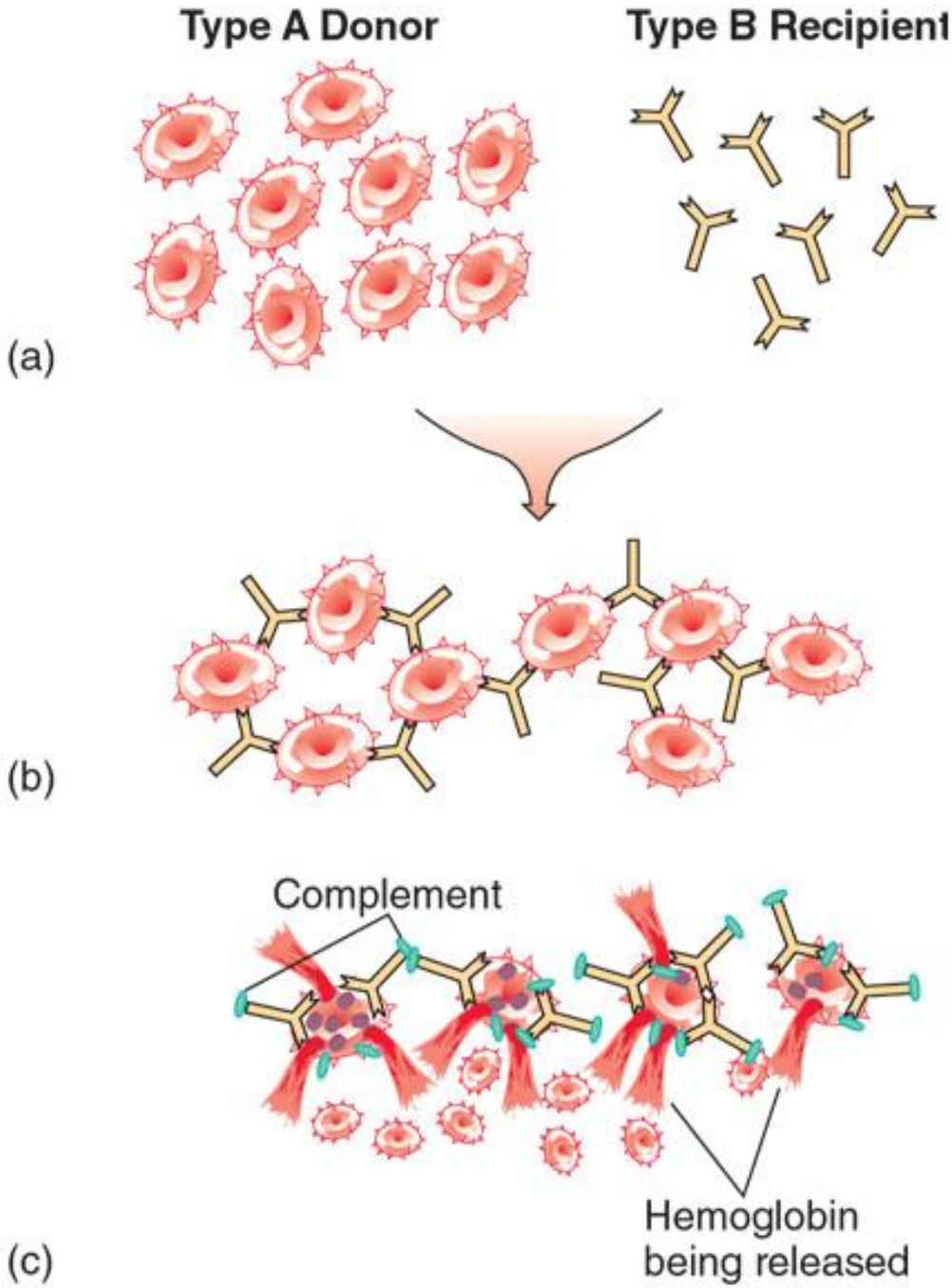
(a)

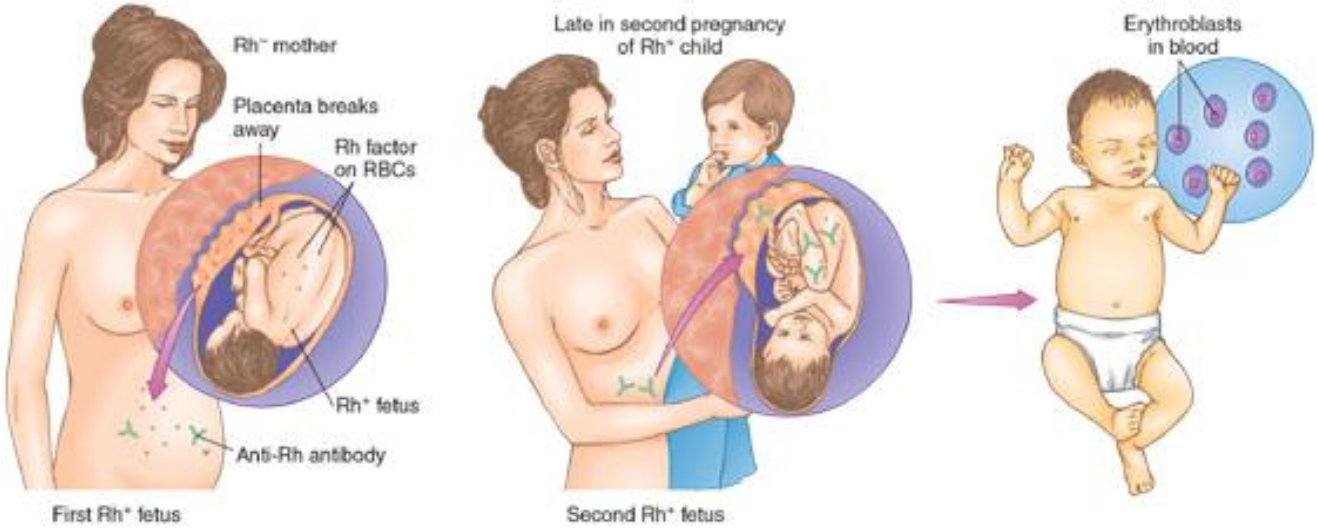


(b)

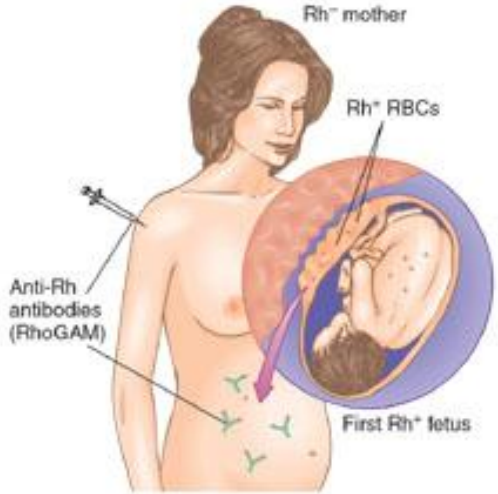


(c)





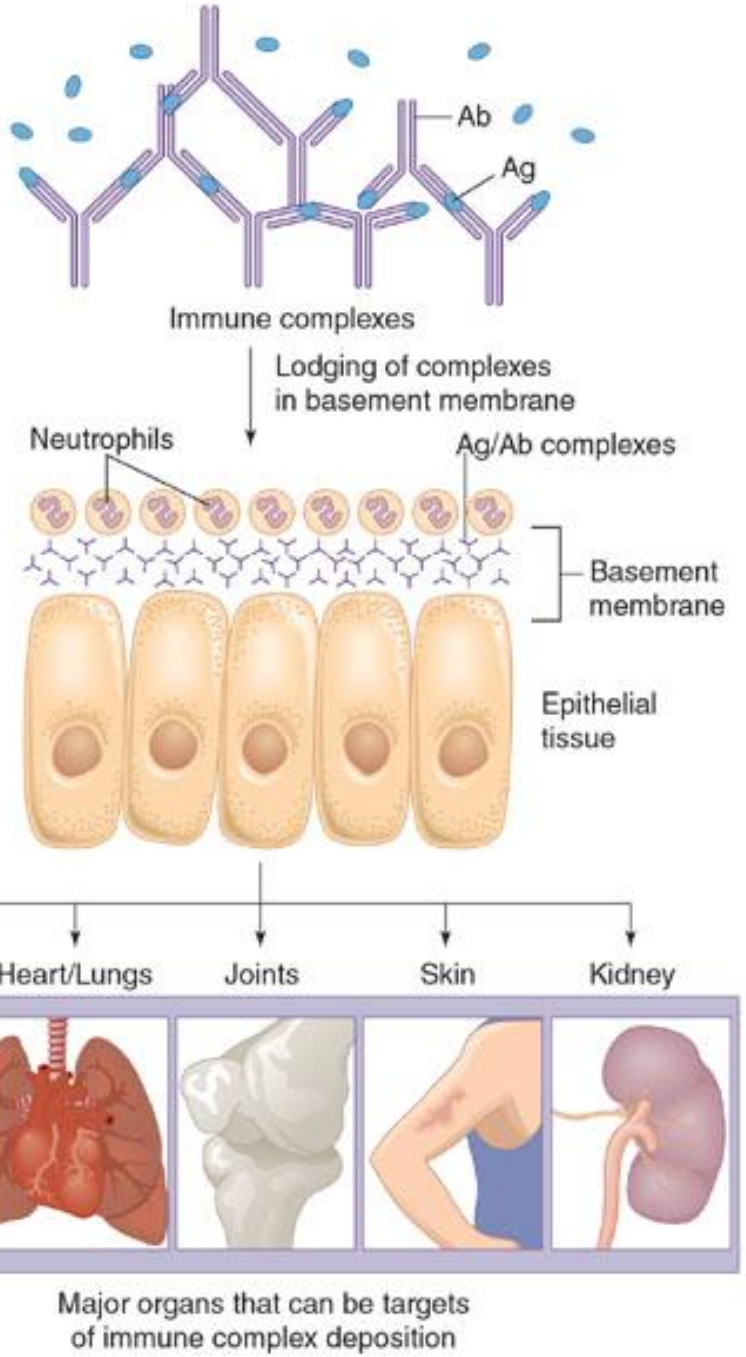
(a) **The development and aftermath of Rh sensitization**
Initial sensitization of the maternal immune system to fetal Rh⁺ factor occurs when fetal cells leak into the Rh⁻ mother's circulation late in pregnancy, or during delivery, when the placenta tears away. The child will escape hemolytic disease in most instances, but the mother, now sensitized, will be capable of an immediate reaction to a second Rh⁺ fetus and its Rh-factor antigen. At that time, the mother's anti-Rh antibodies pass into the fetal circulation and elicit severe hemolysis in the fetus and neonate.



(b) **Prevention of erythroblastosis fetalis with anti-Rh immune globulin (RhoGAM)**
Injecting a mother who is at risk with RhoGAM during her first Rh⁺ pregnancy helps to inactivate and remove the fetal Rh-positive cells before her immune system can react and develop sensitivity.

Type III Hypersensitivity

- A large quantity of soluble foreign Ag stimulates Ab that produce small, soluble Ag-Ab complexes
- Immune complexes become trapped in tissues & incite a damaging inflammatory response **Video**
  - Arthus reaction – local reaction to series of injected Ag to same body site **Video**
  - Serum sickness – systemic disease resulting from repeated injections of foreign proteins



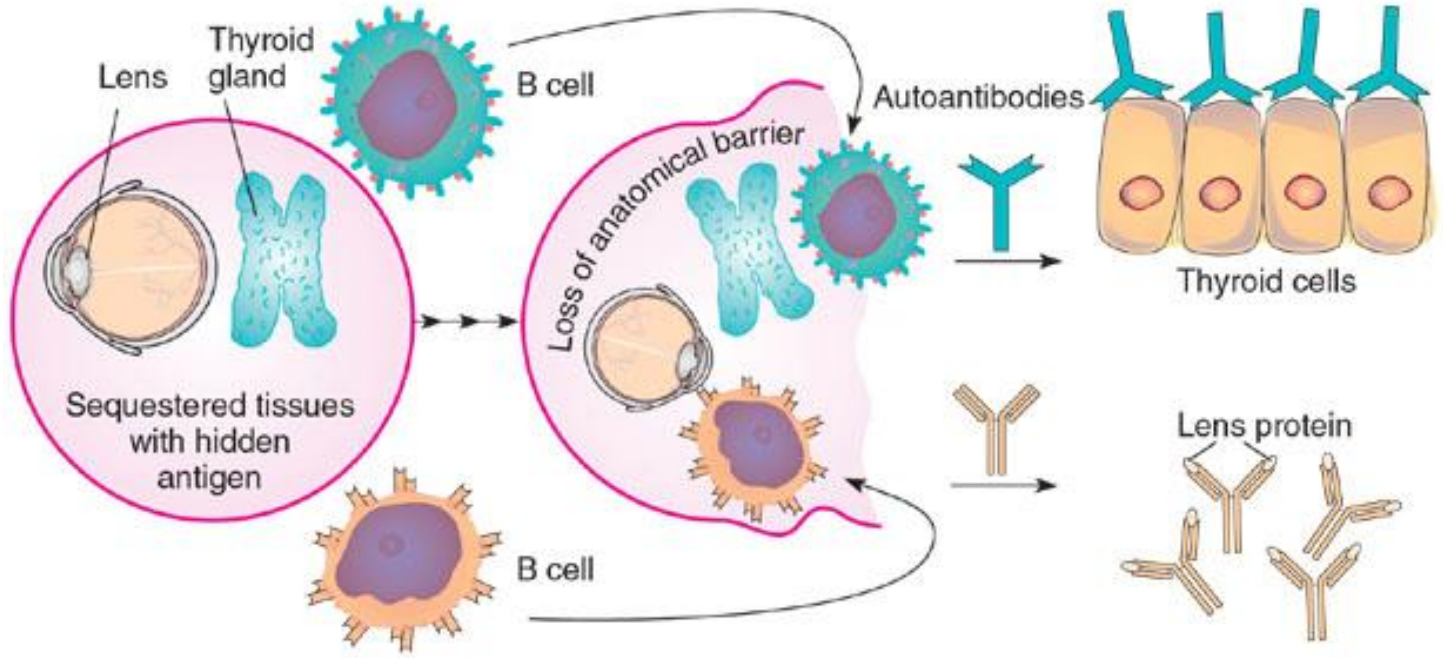
Major organs that can be targets of immune complex deposition

Steps:

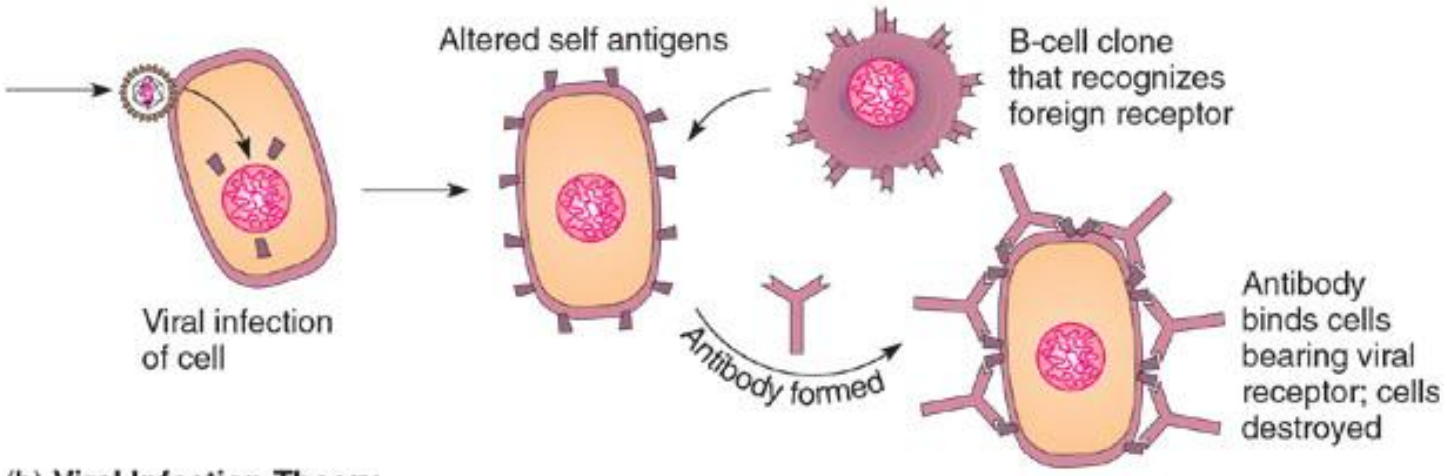
1. Antibody combines with excess soluble antigen, forming large quantities of Ab/Ag complexes.
2. Circulating immune complexes become lodged in the basement membrane of epithelia in sites such as kidney, lungs, joints, skin.
3. Fragments of complement cause release of histamine and other mediator substances.
4. Neutrophils migrate to the site of immune complex deposition and release enzymes that cause severe damage in the tissues and organs involved.

Autoimmunity

- In certain type I & II hypersensitivities, the immune system has lost tolerance to self molecules and forms autoantibodies and sensitized T cells against them.
- More common in females
- Disruption of function can be systemic or organic specific
  - Systemic lupus erythematosus
  - Rheumatoid arthritis
  - Endocrine autoimmunities
  - Myasthenia gravis
  - Multiple sclerosis



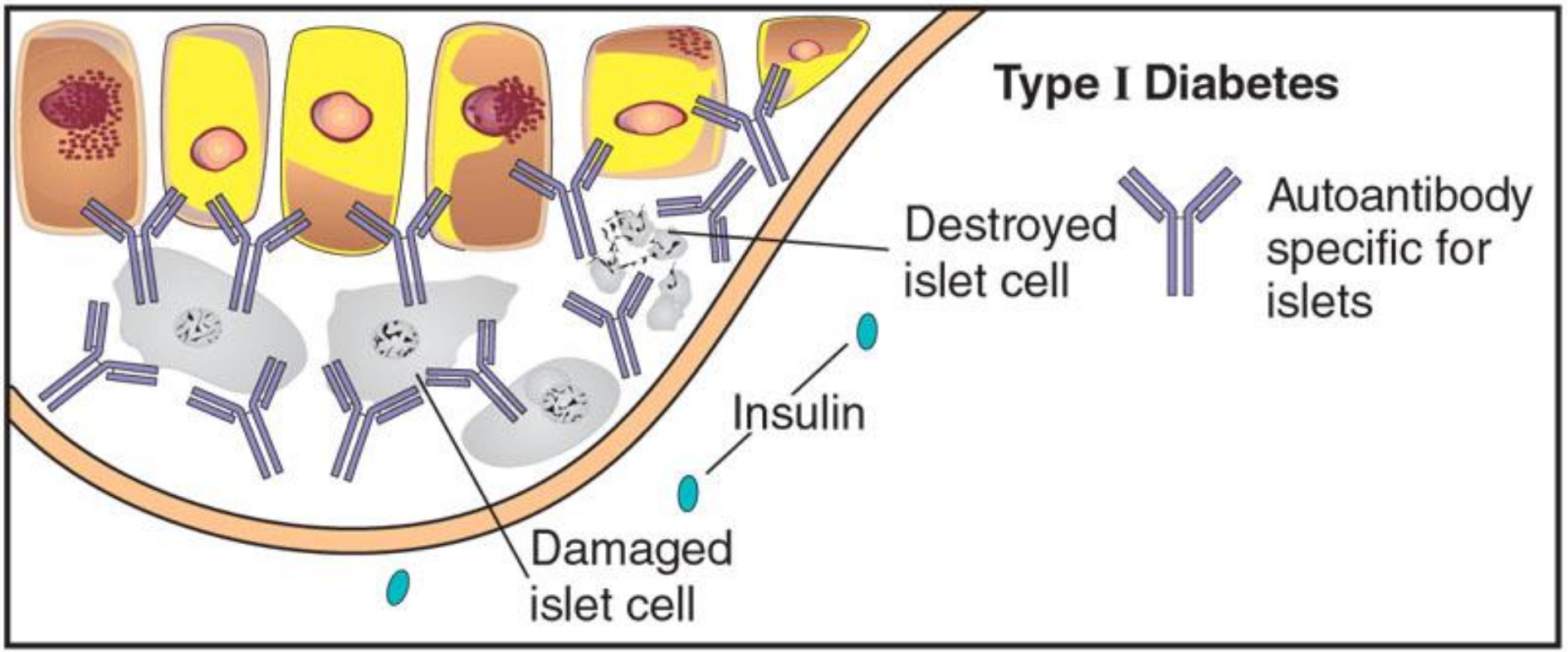
(a) **Sequestered Antigen Theory**

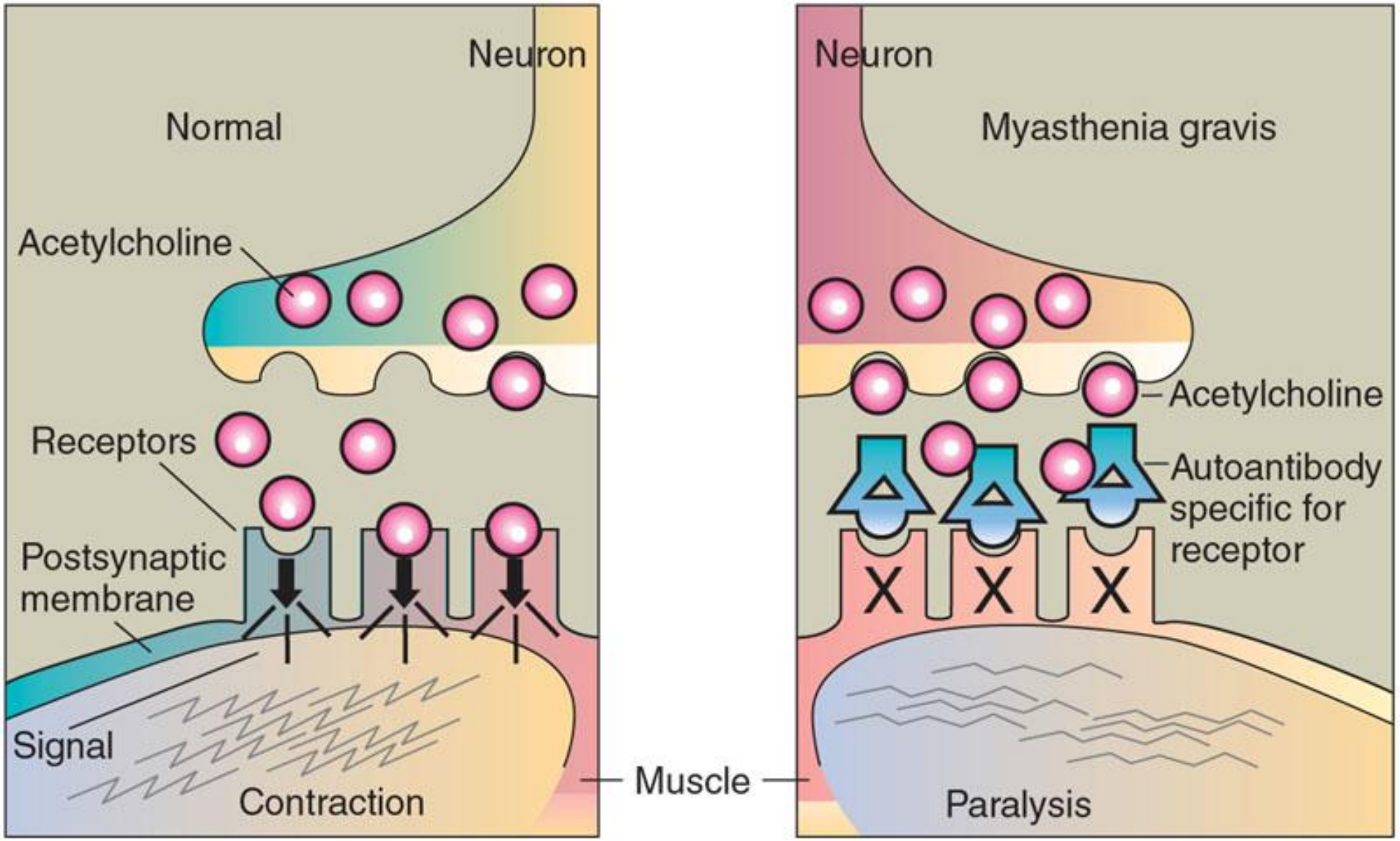


(b) **Viral Infection Theory**

(a)

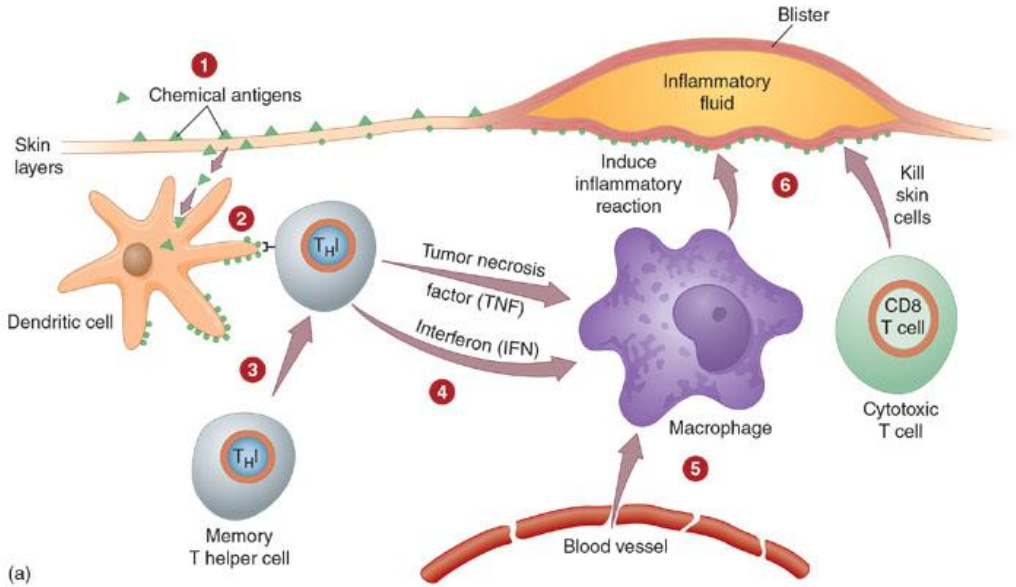
(b)





Type IV Hypersensitivity

- Cell-mediated
- A delayed response to Ag involving activation of and damage by T cells
- Delayed allergic response – skin response to allergens – tuberculin skin test, contact dermititis from plants, metals, cosmetics **Video**
- Graft rejection – reaction of cytotoxic T cells directed against foreign cells of a grafted tissue; involves recognition of foreign HLA



(a)

1. Lipid-soluble chemicals are absorbed by the skin.
2. Dendritic cells close to the epithelium pick up the allergen, process it, and display it on MHC receptors.
3. Previously sensitized T_Hl cells recognize the presented allergen.
4. Sensitized T_Hl cells are activated to secrete cytokines (IFN, TNF) that attract macrophages and cytotoxic T cells to the site. 5
6. Macrophage releases mediators that stimulate a strong, local inflammatory reaction. Cytotoxic T cells directly kill cells and damage the skin. Fluid-filled blisters result.

(b)

"Is it my imagination or are the allergens becoming more agressive?"