BP 605 T. Pharmaceutical Biotechnology (Theory)

Hypersensitivity reactions, Immune stimulation and Immune suppressions

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Overview

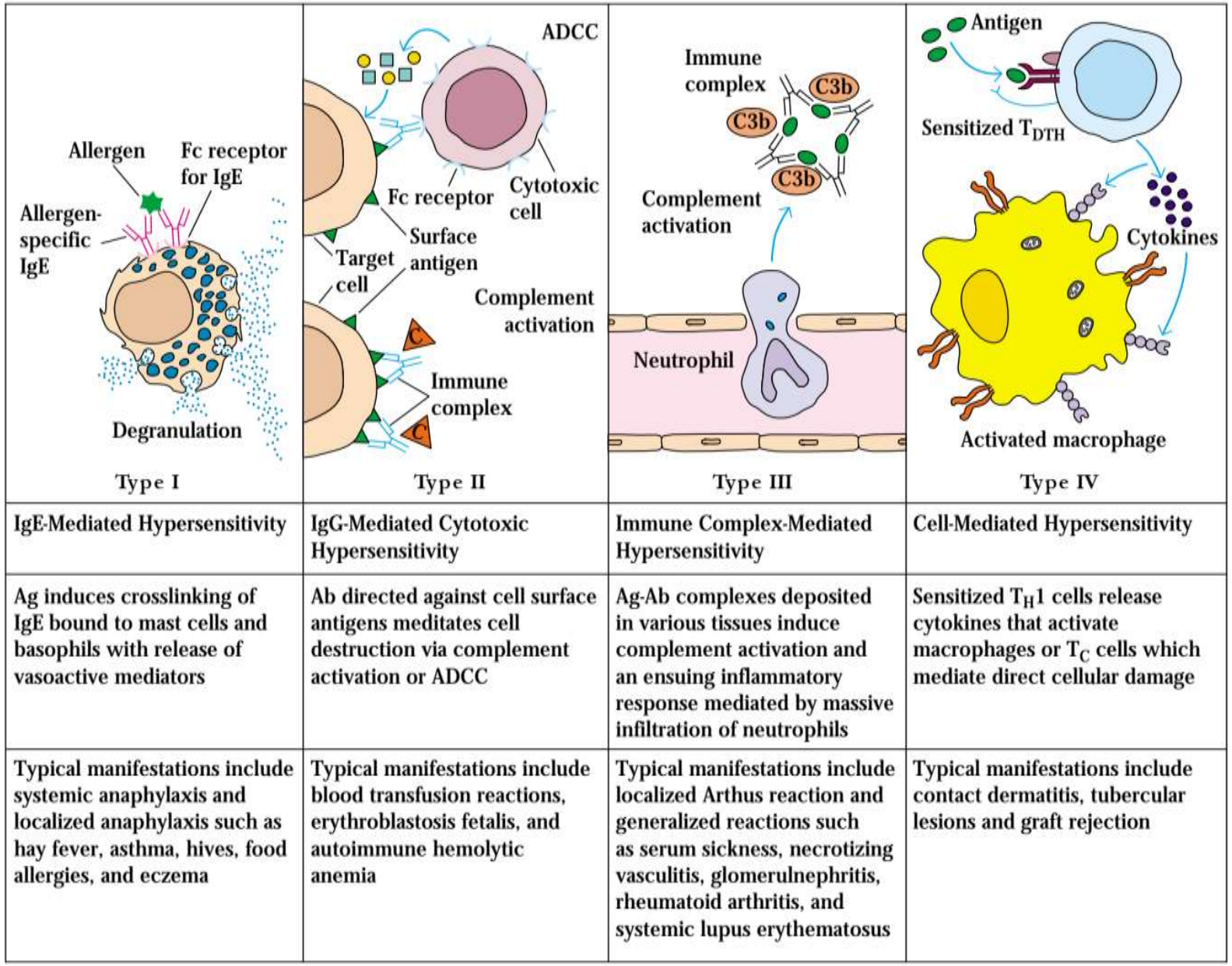
- Definition and Introduction
- Hypersensitivity reactions
- Immune stimulation and Immune suppression

Hypersensitivity Reactions

Definition:

- ✓ Excessive undesirable (damaging, discomfort producing and sometimes fatal) reactions produced by the normal immune system.
- ✓ Require a pre-sensitized (immune) state of the host.
- ✓ Hypersensitivity reactions can be divided into four types:

1. type I
2. type II
3. type III
4. type IV

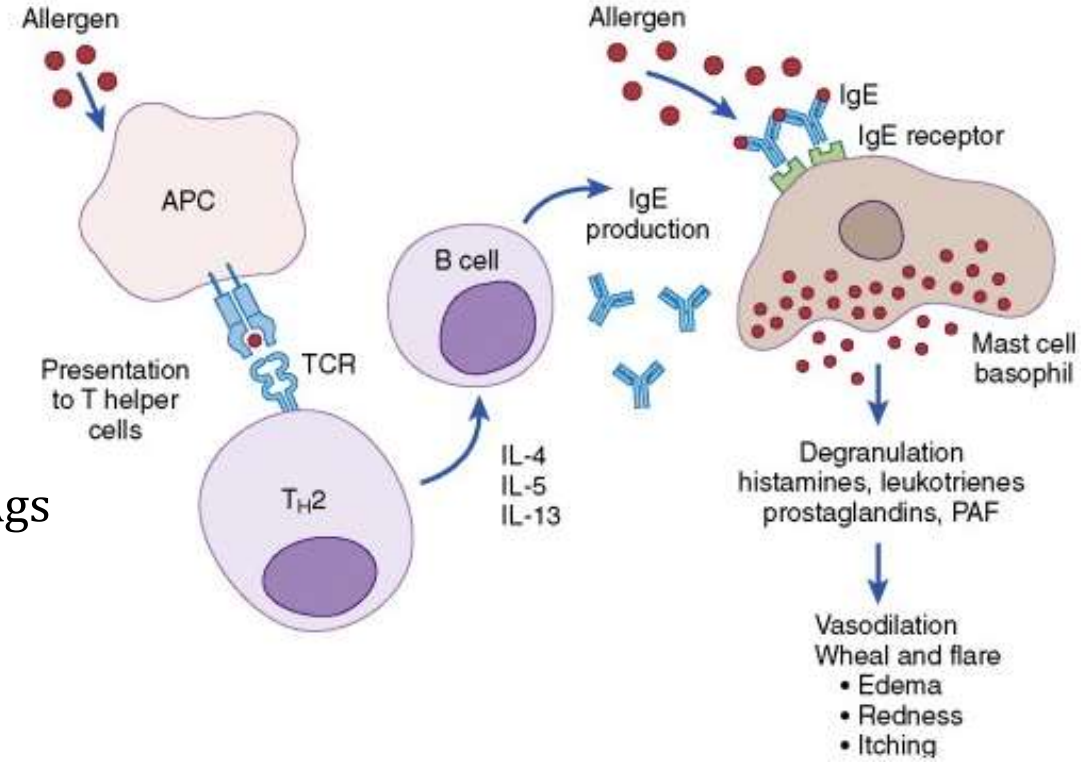


IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces crosslinking of IgE bound to mast cells and basophils with release of vasoactive mediators	Ab directed against cell surface antigens meditates cell destruction via complement activation or ADCC	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils	Sensitized T_H1 cells release cytokines that activate macrophages or T_C cells which mediate direct cellular damage
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulnephritis, rheumatoid arthritis, and systemic lupus erythematosus	Typical manifestations include contact dermatitis, tubercular lesions and graft rejection

Kuby; Immunology; Figure 16-1

Type I Hypersensitivity Reactions

- ✓ It is also known as **immediate or anaphylactic hypersensitivity**
- ✓ The reaction takes **minutes from the time of exposure to the antigen**. May sometimes be **delayed** (10-12 hours).
- ✓ The reaction may involve:
  - skin (urticaria and eczema)
  - eyes (conjunctivitis)
  - nasopharynx (allergic rhinitis)
  - bronchopulmonary tissues (asthma)
  - gastrointestinal tract (gastroenteritis)
  - Systemic: Anaphylactic shock from ingested or injected Ags (massive drop in blood pressure.)



Allergens : pollen, dust mite, insects etc.

- ✓ mediated by **IgE.**
- ✓ The primary **cellular component is mast cell or basophil**.
- ✓ The reaction is **amplified and/or modified by other cells such as eosinophils.**

Mediators of Immediate Hypersensitivity

- ✓ It is not clear why some individuals are more prone to type-I hypersensitivity
- ✓ It has been shown that such individuals produce more of T_H2 cells that secrete IL-4, IL-5 and IL-13 which in turn favor IgE class switch.
- ✓ IgE has very high **affinity for its receptor (Fcε; CD23) on mast cells and basophils**.

Mediators of Immediate Hypersensitivity:

Histamine:

- Dilates and increases permeability of blood vessels (swelling and redness)
- increases mucus secretion (runny nose),
- Causes smooth muscle contraction (e.g. bronchi).

Prostaglandins:

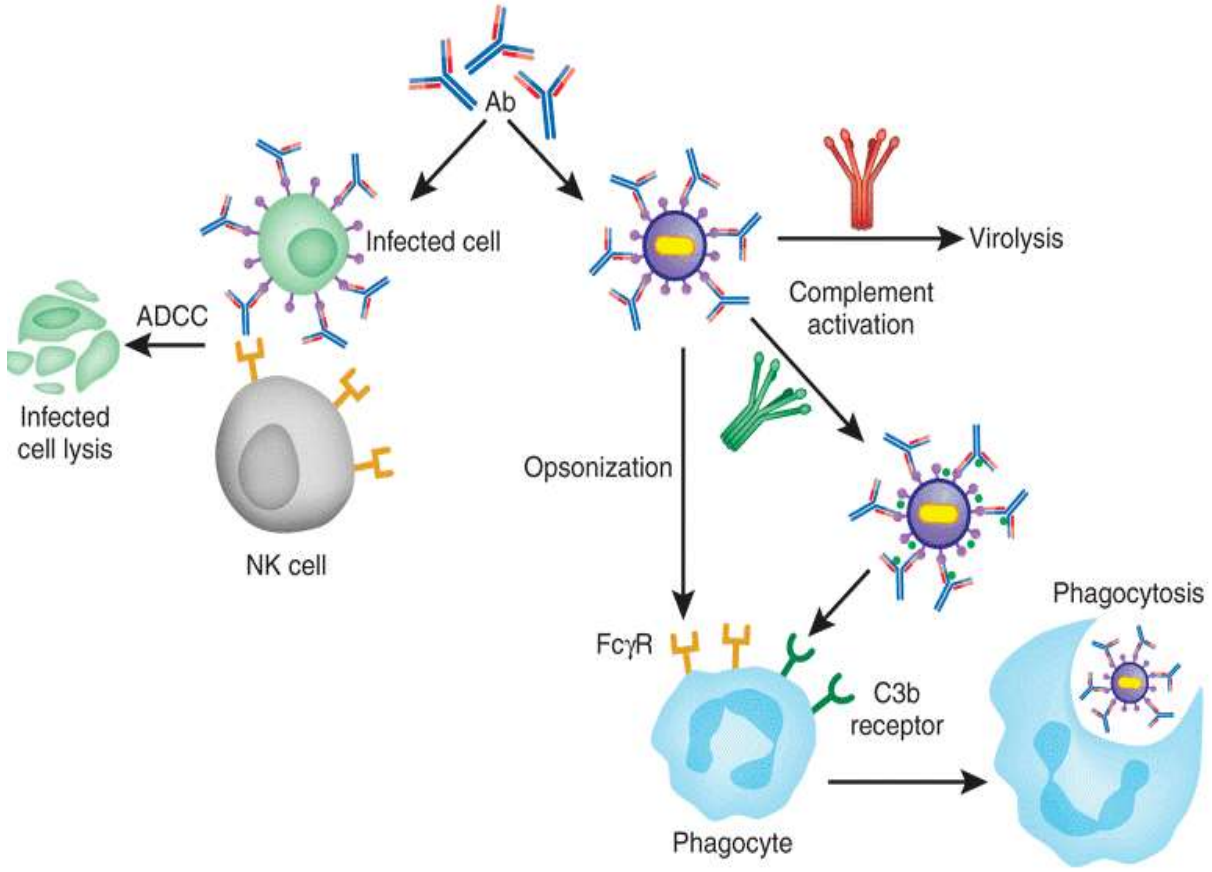
- Contraction of smooth muscle of respiratory system
- increased mucus secretion.

Leukotrienes:

- Bronchial spasms.

Type II Hypersensitivity Reactions

- ✓ It is also known as cytotoxic hypersensitivity
- ✓ The antigens(allergens) are normally endogenous.
- ✓ Exogenous chemicals (haptens) which can attach to cell membranes can also lead to type II hypersensitivity.
- ✓ Involve activation of complement by IgG or IgM binding to an antigenic cell, antigenic cell is then lysed
- ✓ ADCC is also involved, through NK cells



Examples of type II hypersensitivity reaction

1) **Transfusion reaction :**

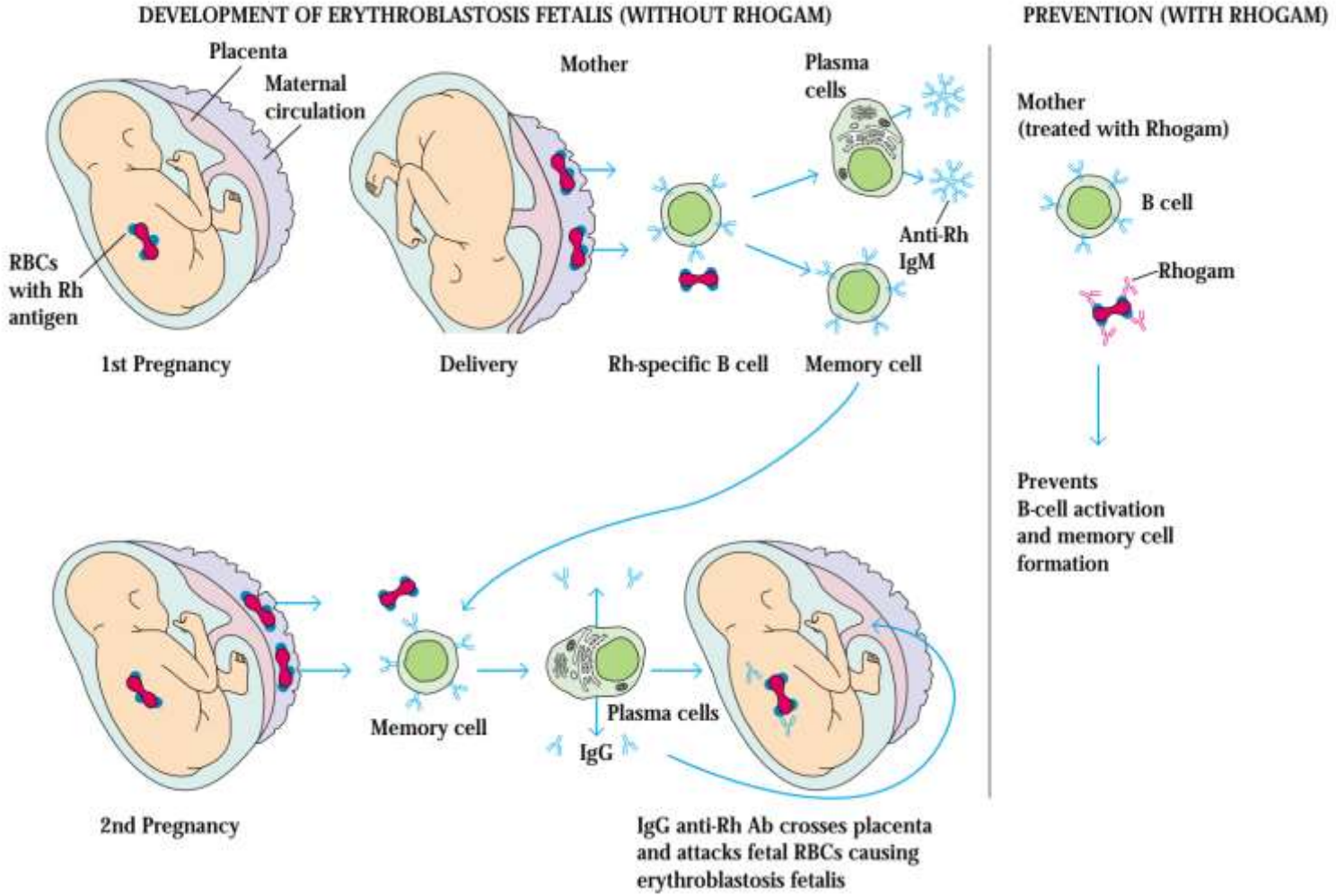
✓ hemolysis : mismatch of ABO blood group

2) **Hemolytic disease of newborn**

✓ Mother Rh- : first baby Rh+(Ab), second baby Rh+, fetal RBCs destroyed

3) **Autoimmune hemolytic anemia and type II drug reaction**

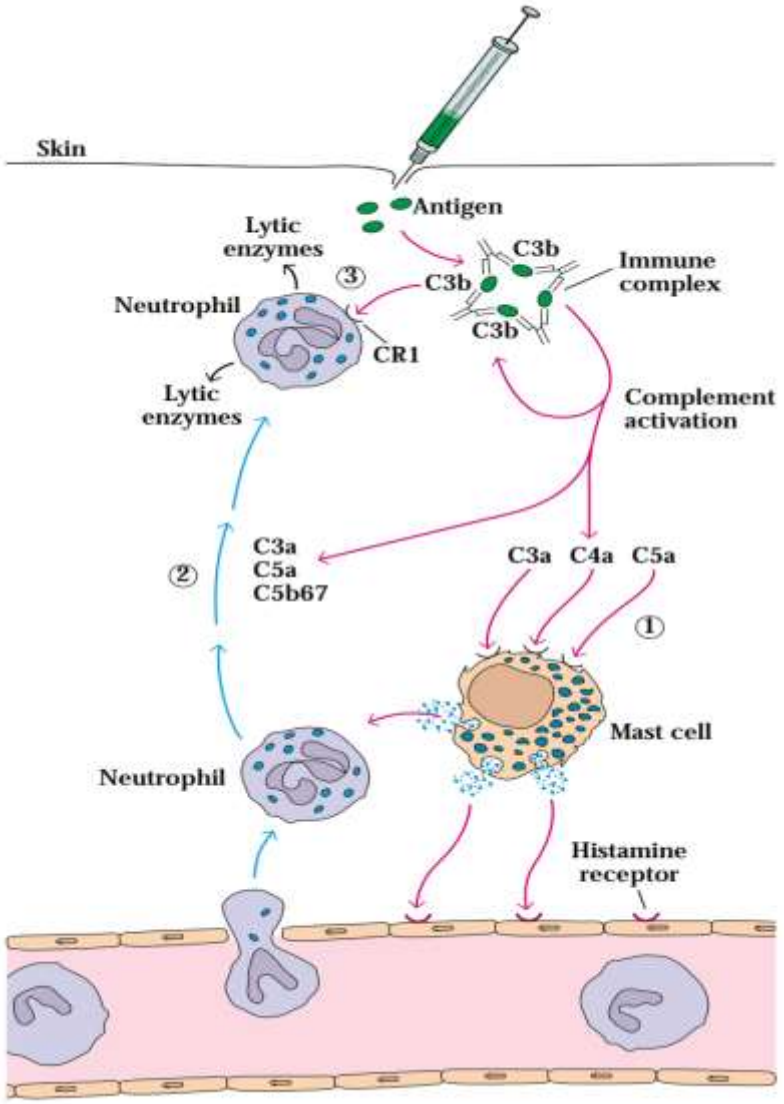
4) **Autoimmune thrombocytopenia**



Kuby; Immunology; Figure 16-14

Type III Hypersensitivity Reactions

- ✓ Known as immune complex reactions
- ✓ Abs are mostly of the IgG class, although IgM may also be involved.
- ✓ The antigens may be
- Exogenous: chronic bacterial, viral or parasitic infections
- Endogenous: non-organ specific autoimmunity: e.g., systemic lupus erythematosus, SLE.
- ✓ Antibody-Antigen immune complexes are deposited in organs, activate complement, and cause inflammatory damage.



Common disease of type III hypersensitivity

1) Local immune complex disease

✓ Arthus reaction e.g. after vaccination against diphtheria and tetanus

2) Acute systemic immune complex disease

✓ Serum sickness: Anti-serum ➡ Ab+Ag ➡ systemic tissue injury ➡ fever, arthritis, skin rash

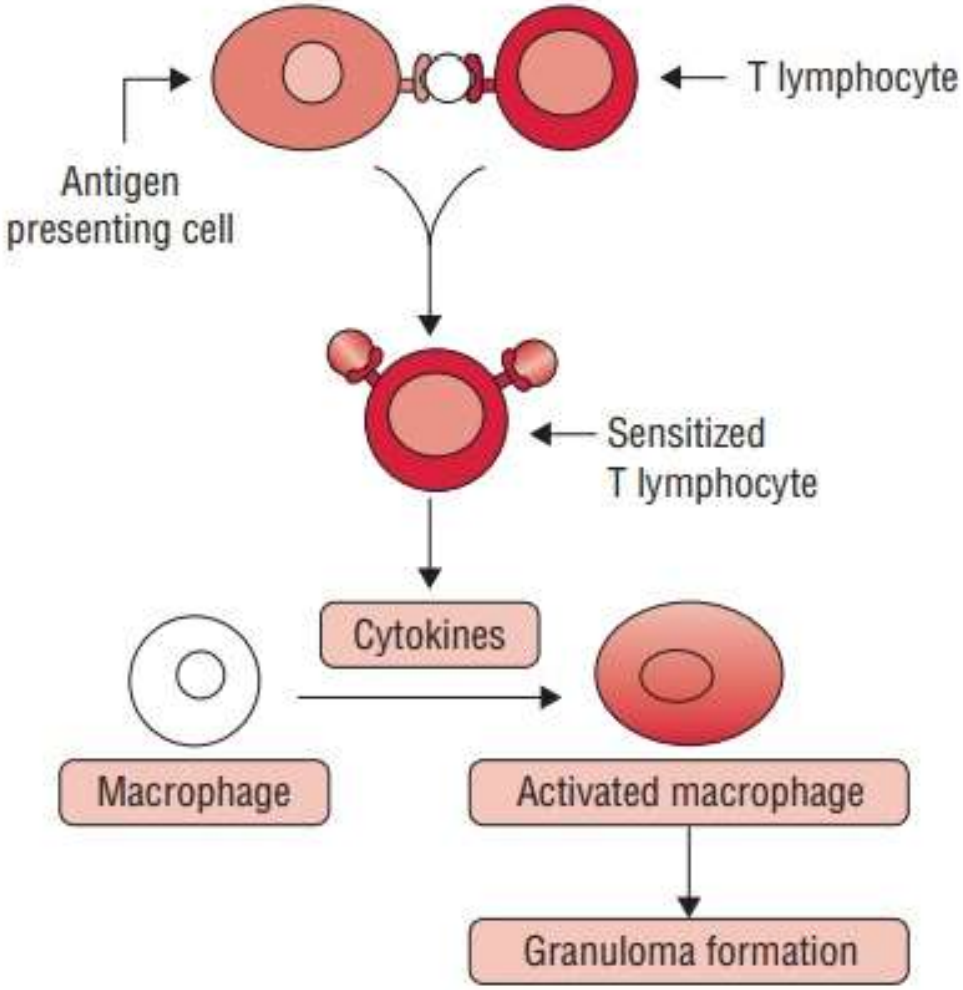
3) Chronic immune complex disease

✓ Systemic lupus erythematosus (SLE)

✓ Rheumatoid arthritis : RF + IgG ➡ Deposit on synovial membrane

Type IV Hypersensitivity Reactions

- ✓ Also known as **cell mediated or delayed type hypersensitivity**
- ✓ Involve reactions by **T_D memory cells.**
  - **First contact sensitizes person.**
  - **Subsequent contacts elicit a reaction.**
- ✓ **Inflammation and tissue injury mediated by $CD4^+$ Th1**
  - **Release cytokines which attract macrophages**
- ✓ **Cytotoxicity** of **$CD8^+$ CTL**
- ✓ **Infectious delayed type hypersensitivity**

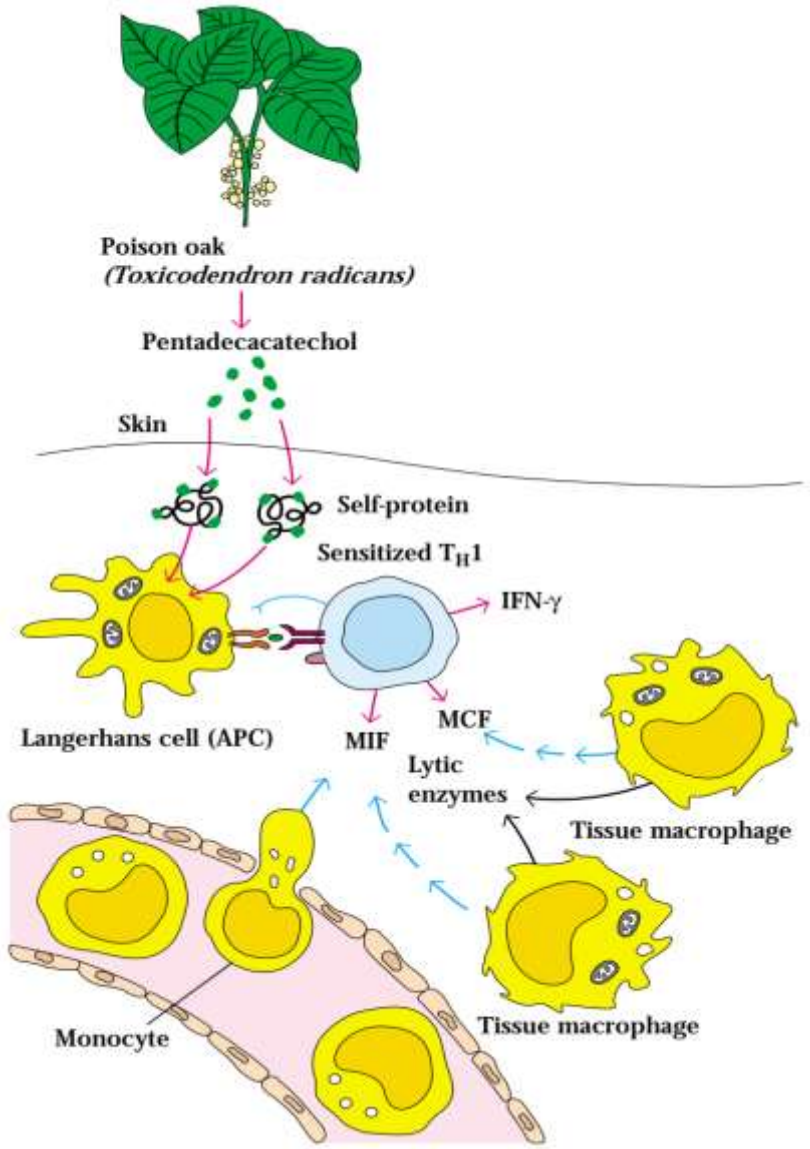


Common disease of type IV hypersensitivity

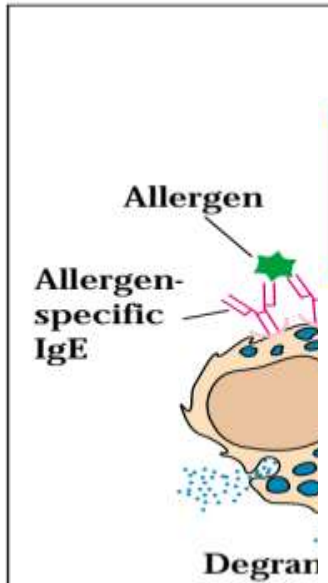
1) Infectious delayed type hypersensitivity
   - Mantoux: OT(Old Tuberculin) test
2) Contact dermatitis :
   - Paint, drug ➡red rash, water blister, dermatitis

TABLE 16-6 Intracellular pathogens and contact antigens that induce delayed-type (type IV) hypersensitivity

Intracellular bacteria	Intracellular viruses
Mycobacterium tuberculosis	Herpes simplex virus
Mycobacterium leprae	Variola (smallpox)
Listeria monocytogenes	Measles virus
Brucella abortus	
Intracellular fungi	Contact antigens
Pneumocystis carinii	Picrylchloride
Candida albicans	Hair dyes
Histoplasma capsulatum	Nickel salts
Cryptococcus neoformans	Poison ivy
Intracellular parasites	Poison oak
Leishmania sp.	



Summary



Type I

IgE-Mediated Hyp

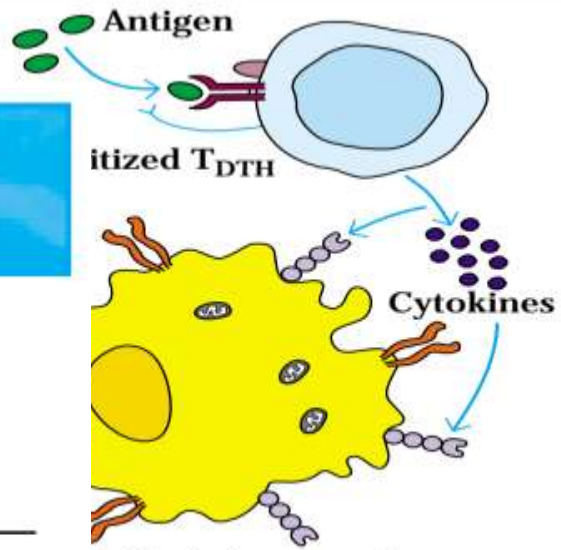
Ag induces crossl
IgE bound to mas
basophils with rel
vasoactive mediat

Typical manifesta
systemic anaphyla
localized anaphyl
hay fever, asthma
allergies, and ecz

ADCC

Immune

rheumatoid arthritis, and systemic lupus erythematosus



Type IV

Mediated Hypersensitivity

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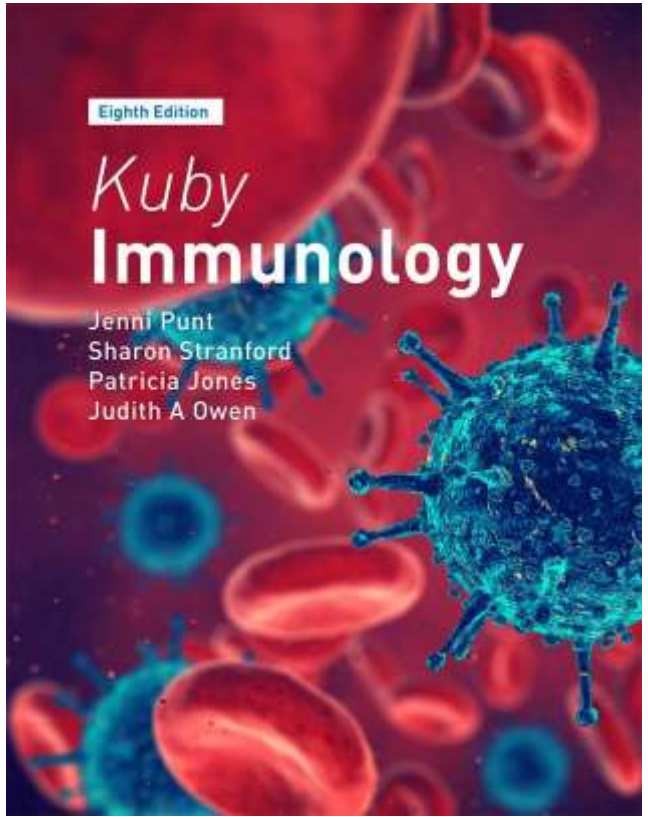
ines that activate
ophages or T_C cells which
te direct cellular damage

al manifestations include
ct dermatitis, tubercular
s and graft rejection

TABLE 16-5 Penicillin-induced hypersensitive reactions

Type of reaction	Antibody or lymphocytes induced	Clinical manifestations
I	IgE	Urticaria, systemic anaphylaxis
II	IgM, IgG	Hemolytic anemia
III	IgG	Serum sickness, glomerulonephritis
IV	T_{DTH} cells	Contact dermatitis

Next Class on Monday



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