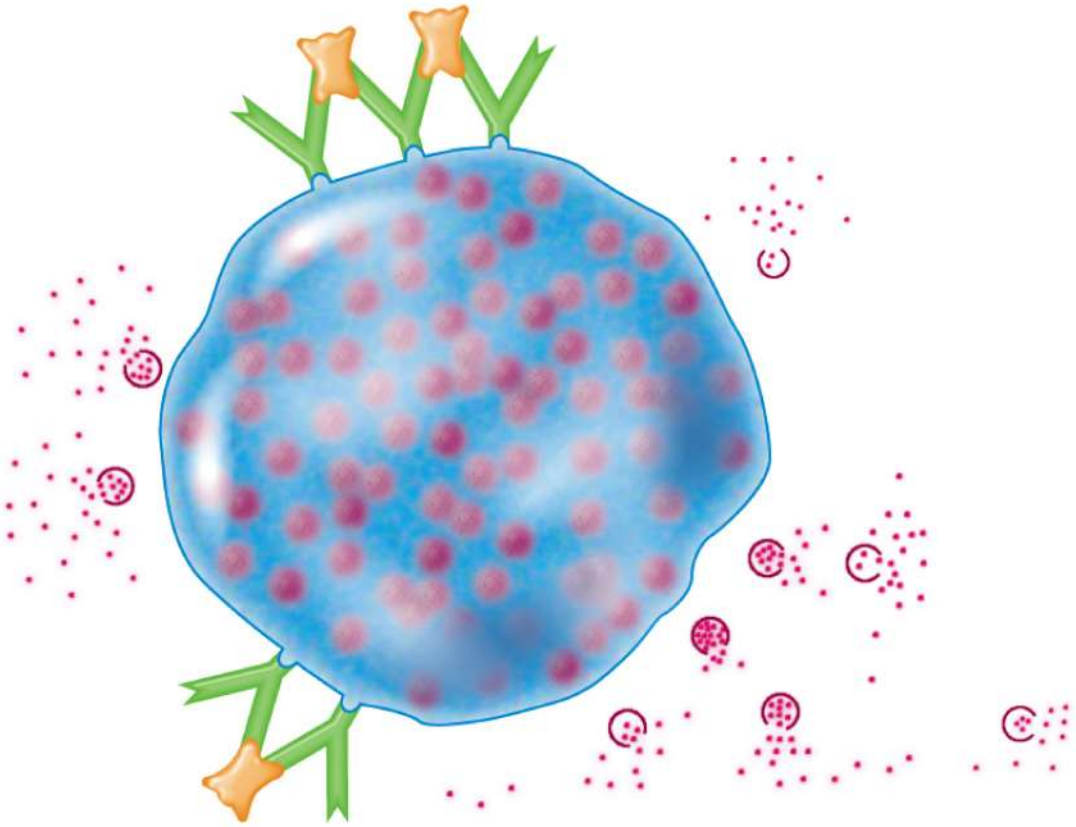
Hypersensitivity



What is hypersensitivity?

- **Hypersensitivity** – an excessive immune reaction against antigens that most people tolerate

- Hypersensitivity includes:
  - **alloimmunity** - reaction to transplanted tissue from another person
  - **autoimmunity** - abnormal reactions to one's own tissues
  - **allergies** – reactions to environmental antigens (**allergens**)
    - dust, mold, pollen, vaccines, bee and wasp venom, poison ivy and other plants, foods such as nuts, milk, eggs, and shellfish, drugs such as penicillin, tetracycline, and insulin

Four Different Types of Hypersensitivity

- Four kinds of hypersensitivity based on the type of immune agents involved (antibodies or T cells) and response to antigen
  - Type I acute (immediate) hypersensitivity /// very rapid response
  - Type II - sub-acute /// slower onset (1 – 3 hours after exposure /// last longer – 10 to 15 hrs)
  - Type III - sub-acute /// slower onset (1 – 3 hours after exposure /// last longer – 10 to 15 hrs)
  - Type IV - delayed /// Cell mediated response
  - Note: Types I, II, and III are antibody mediated responses

Type I Hypersensitivity (acute)

- characterized by hypotension // vasodilatation
- includes most common allergies
- IgE-mediated reaction that begins within seconds of exposure
- usually subsides within 30 minutes, although it can be severe to fatal
- allergens bind to IgE on the membranes of mast cells
  - stimulate them to secrete histamine and other inflammatory and vasoactive chemicals
  - chemicals trigger glandular secretion, vasodilation, increased capillary permeability, smooth muscle spasms, and other effects

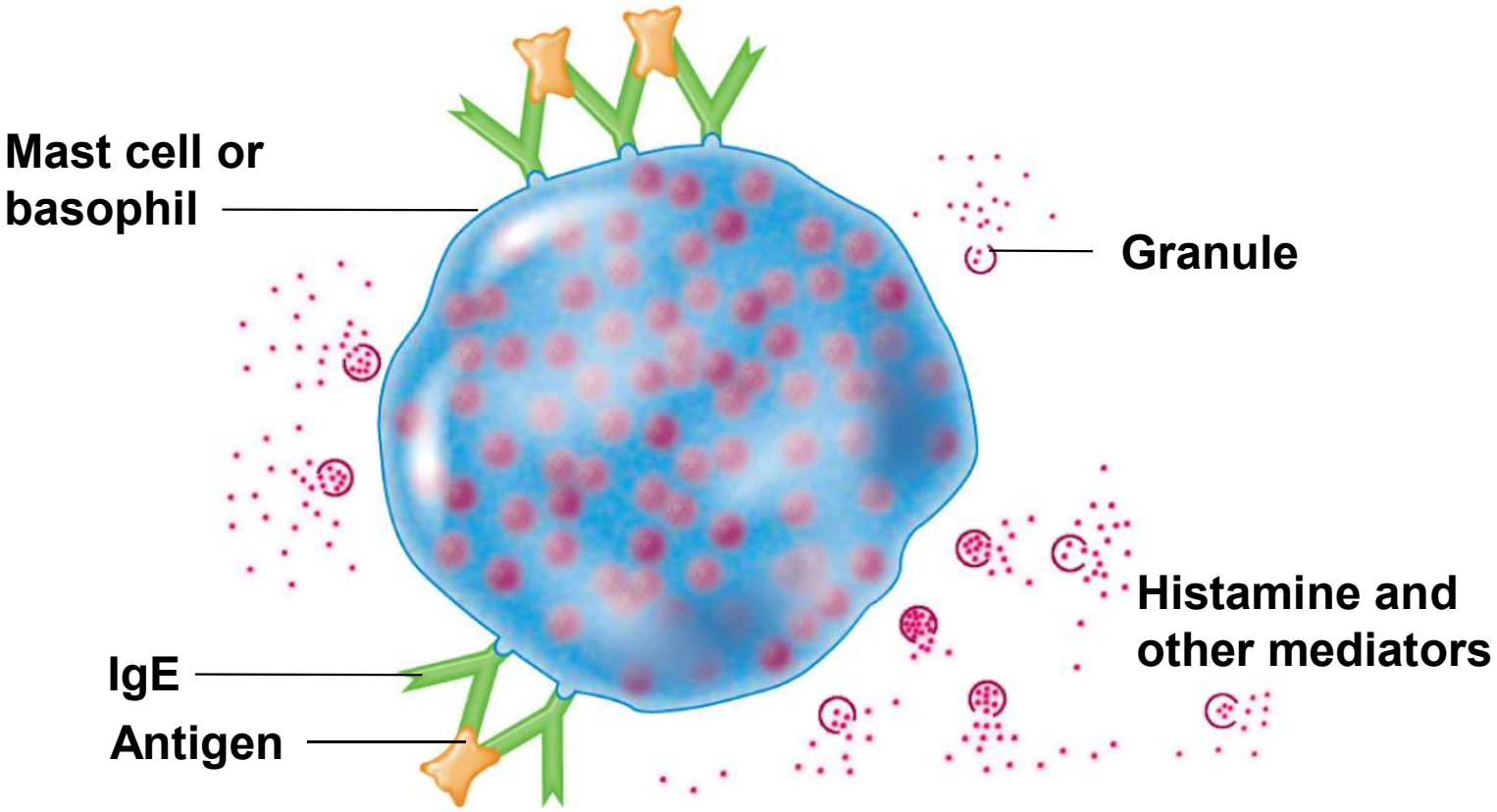
Type I Hypersensitivity (acute)

- clinical signs include:
  - local edema, mucus hypersecretion and congestion, watery eyes, runny nose, hives, and sometimes cramps, diarrhea and vomiting
- examples: food allergies and asthma – local inflammatory reaction to inhaled allergens

Type I Hypersensitivity (local vs systemic)

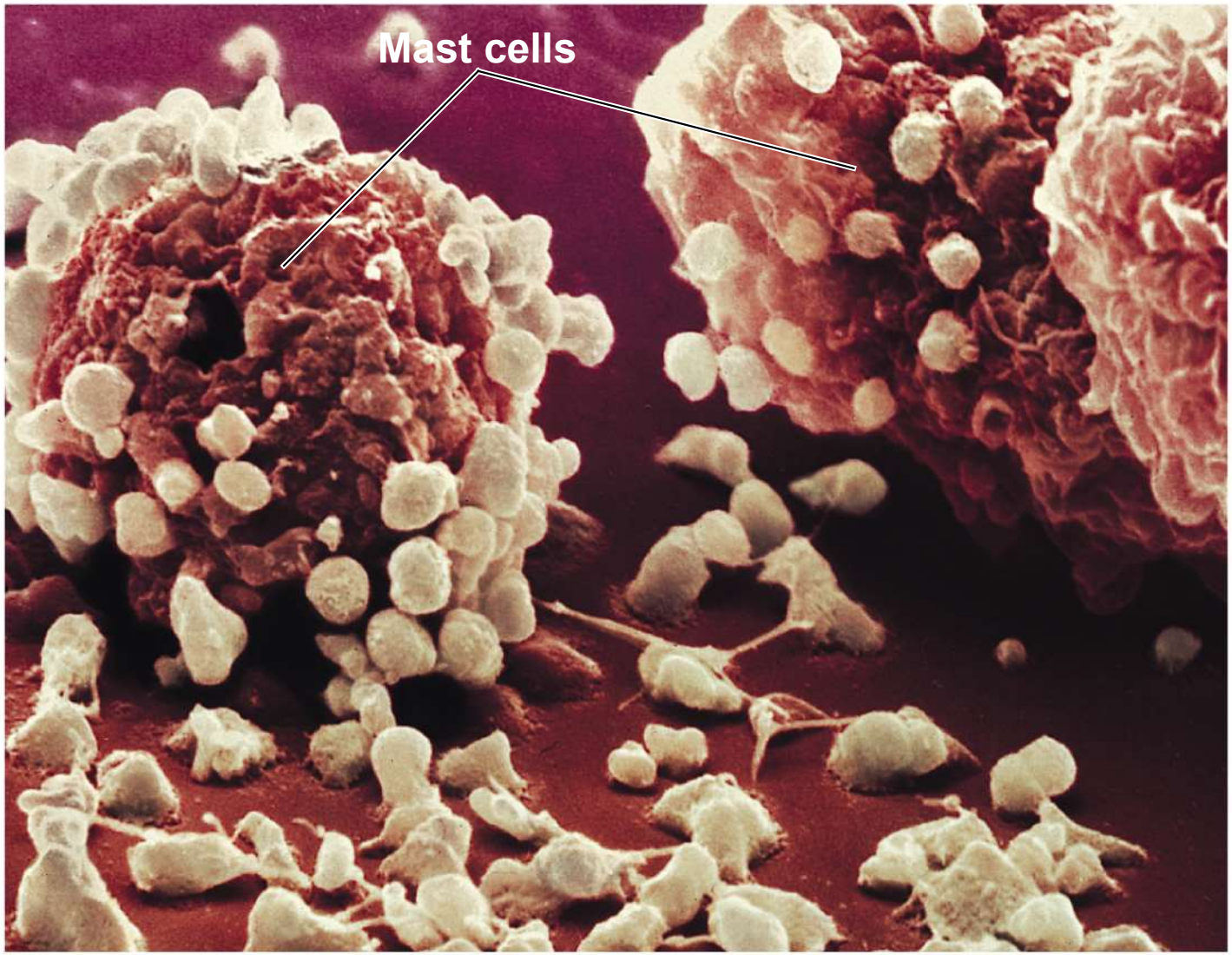
- Anaphylaxis (local)
  - immediate, severe reaction Type I reaction
  - local anaphylaxis can be relieved with antihistamines
- Anaphylactic shock (systemic - e.g. in response to a bee sting)
  - severe, widespread acute hypersensitivity that occurs when an allergen is introduced to the bloodstream of an allergic individual
  - characterized by bronchoconstriction, dyspnea (labored breathing), widespread vasodilation, circulatory shock, and sometimes death
  - antihistamines are inadequate by themselves
  - epinephrine relieves the symptoms by dilating bronchioles, increasing cardiac output, and restoring blood pressure
  - fluid therapy and respiratory support are sometimes required

The Mechanism of Anaphylaxis



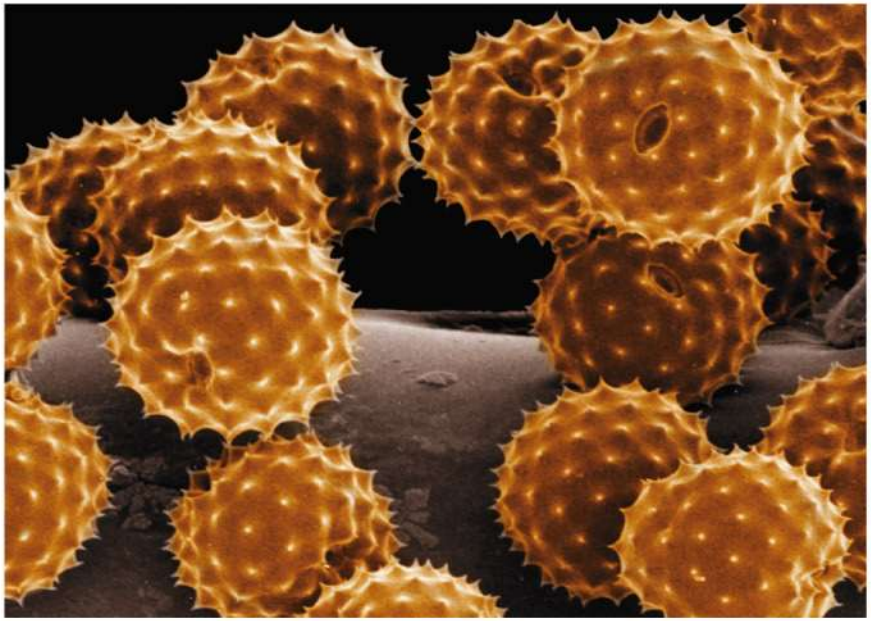
(a) IgE antibodies, produced in response to an antigen, coat mast cells and basophils. When an antigen bridges the gap between two adjacent antibody molecules of the same specificity, the cell undergoes degranulation and releases histamine and other mediators.

The mechanism of anaphylaxis.



A degranulated mast cell that has reacted with an antigen and released granules of histamine and other reactive mediators

Localized anaphylaxis.



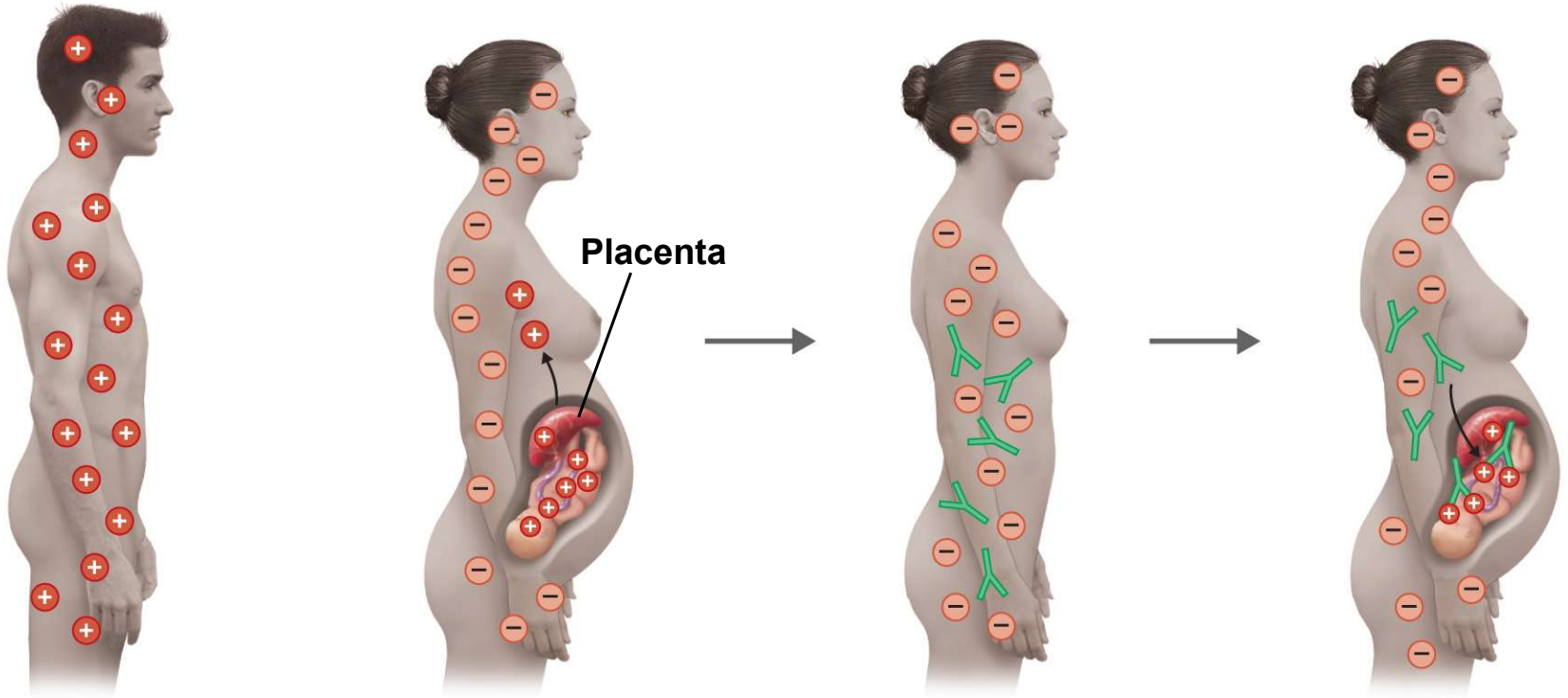
(a) A micrograph of pollen grains

(b) A micrograph of a house mite on fabric

Type II Hypersensitivity (Antibody-Dependent Cytotoxic)

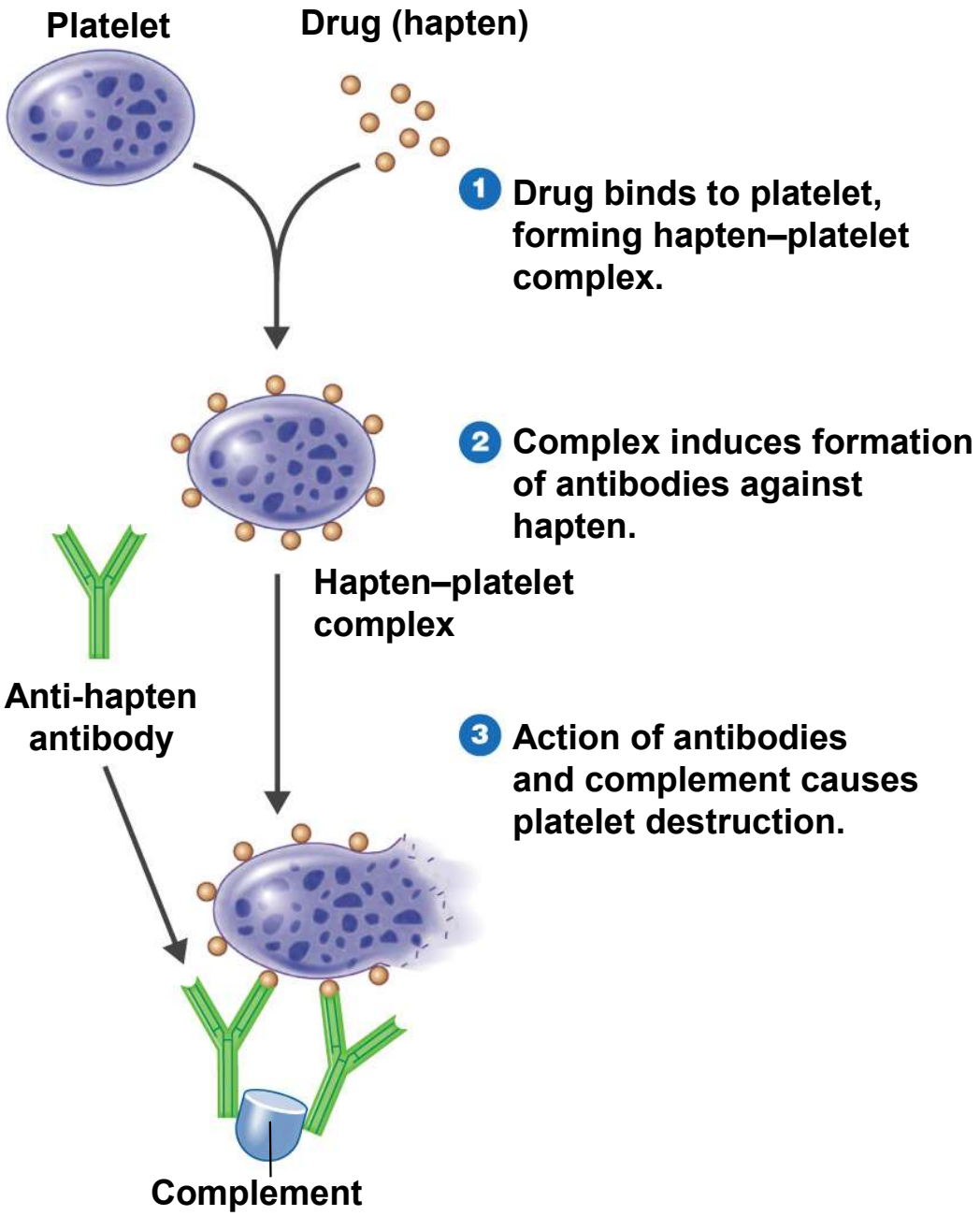
- occurs when IgG or IgM attacks antigens bound to cell surfaces
  - reaction leads to complement activation
  - and lysis or opsonization of the target cell
  - macrophages phagocytize and destroy opsonized platelets, erythrocytes, or other cells
- examples: blood transfusion reaction, pemphigus vulgaris, and some drug reactions

Hemolytic disease of the newborn.



1. Rh^+ father.
2. Rh^- mother carrying her first Rh^+ fetus. Rh antigens from the developing fetus can enter the mother's blood during delivery.
3. In response to the fetal Rh antigens, the mother will produce anti-Rh antibodies.
4. If the woman becomes pregnant with another Rh^+ fetus, her anti-Rh antibodies will cross the placenta and damage fetal red blood cells.

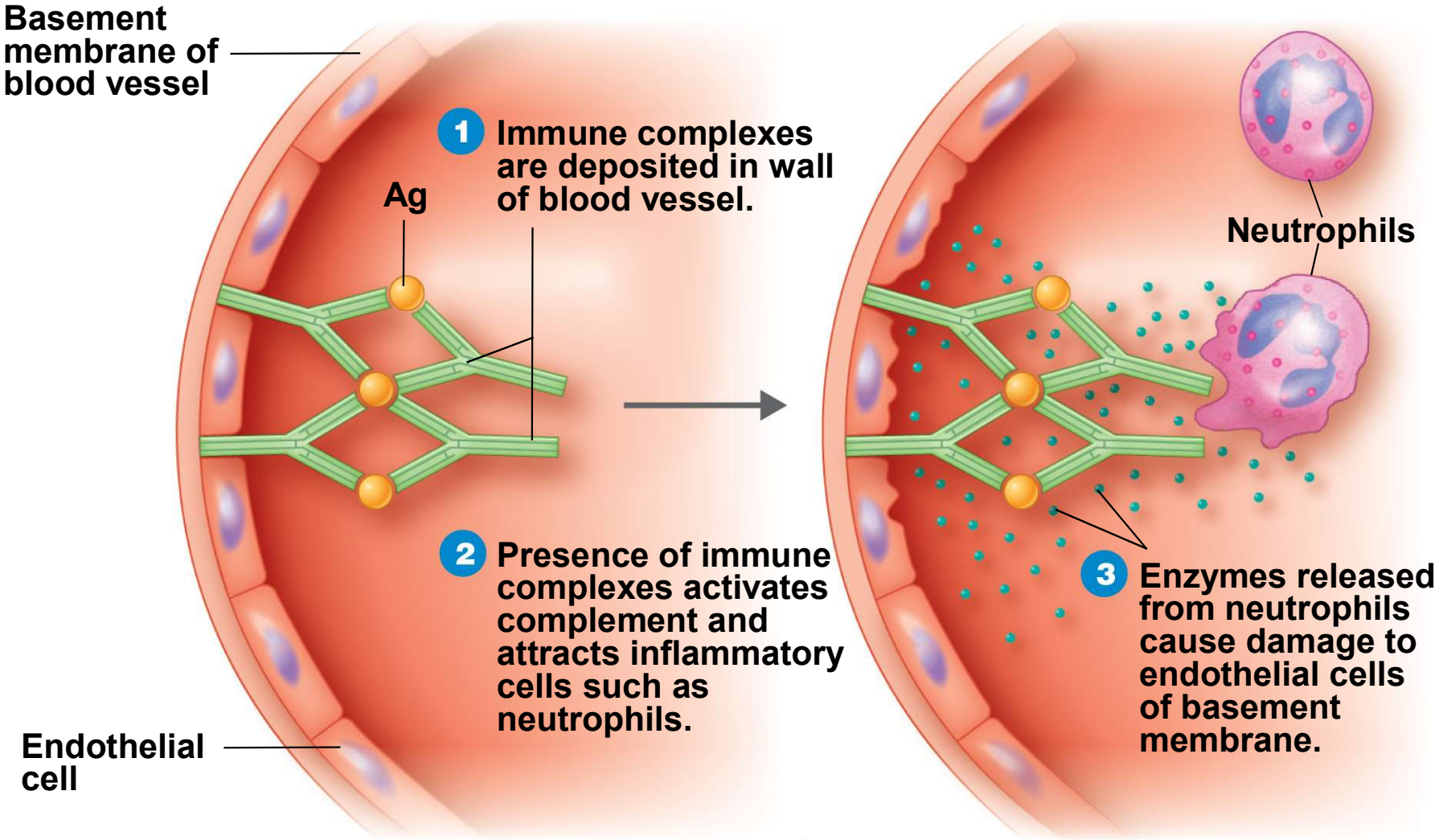
Drug-induced thrombocytopenic purpura.



Type III Hypersensitivity (Immune Complex)

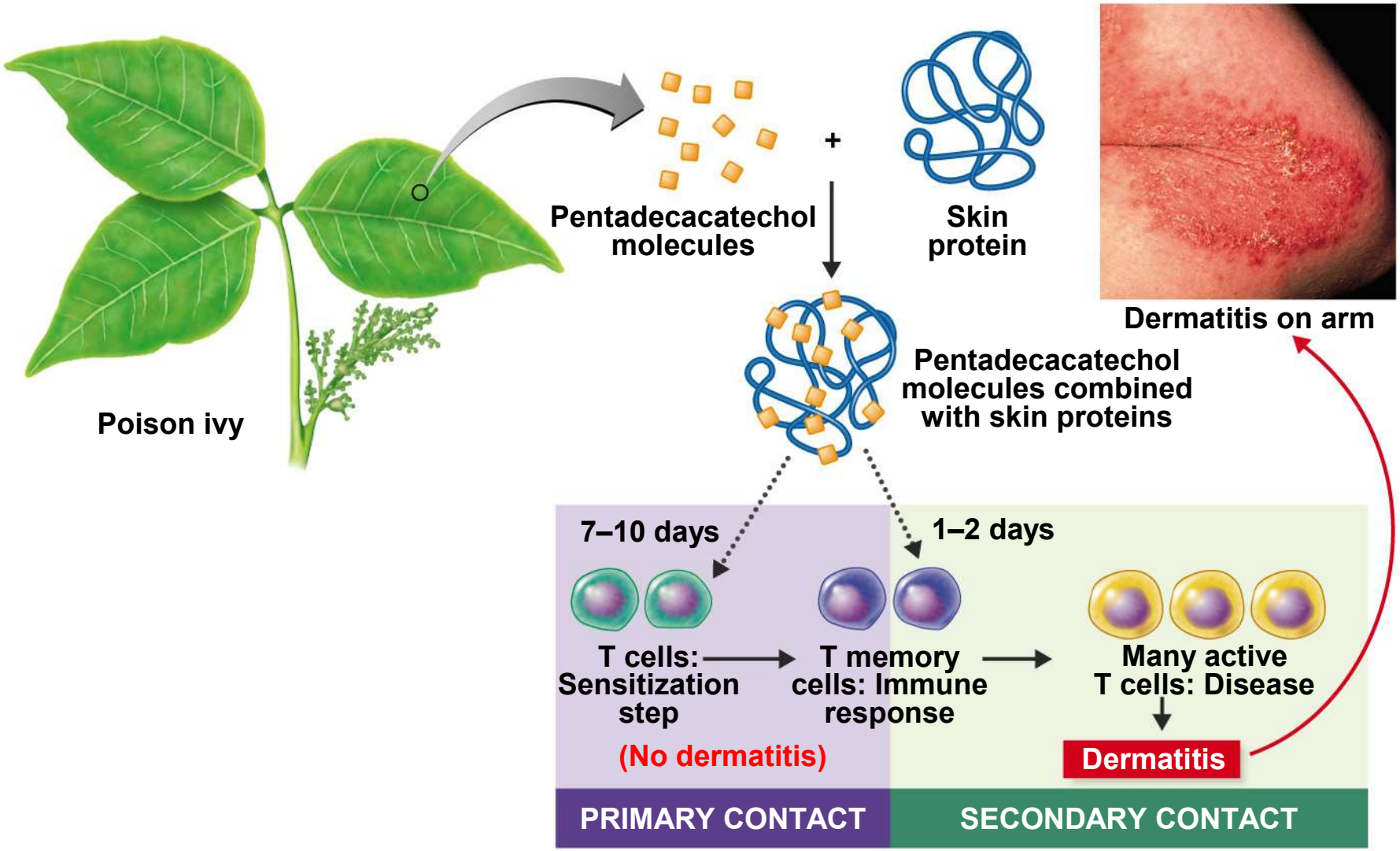
- occurs when IgG or IgM form antigen-antibody complexes with soluble antigen (toxins)
- antibodies and antigens form immune complexes that lodge in basement membranes
  - precipitate beneath endothelium of blood vessels and other tissues
  - at site, activate complement and trigger intense inflammation
  - examples: autoimmune diseases
    - acute glomerulonephritis
    - systemic lupus erythematosus // widespread inflammation of the connective tissues

Immune complex–mediated hypersensitivity.



Type IV Hypersensitivity (Delayed)

- Delayed-type hypersensitivities due to T cells
- Cytokines attract macrophages and T_C cells // Initiate tissue damage
- Cell-mediated reaction in which the signs appear 12 to 72 hour after exposure // following 2^{nd} exposure! – see next slide
  - begins with APCs in lymph nodes display antigens to helper T cells
  - TH cells secrete interferon and cytokines that activate cytotoxic T cells and macrophages
  - result is a mixture of nonspecific and Tc immune responses
- examples: haptens in cosmetics, poison ivy, graft rejection, TB skin test, beta cell destruction that causes type I diabetes mellitus



The development of an allergy (allergic contact dermatitis) to catechols from the poison ivy plant.

Allergic contact dermatitis.