Table 6-1 Mechanisms of Hypersensitivity Reactions

Type	Immune Mechanisms	Histopathologic Lesions	Prototypical Disorders
Immediate (type I) hypersensitivity	Production of IgE antibody → immediate release of vasoactive amines and other mediators from mast cells; later recruitment of inflammatory cells	Vascular dilation, edema, smooth muscle contraction, mucus production, tissue injury, inflammation	Anaphylaxis; allergies; bronchial asthma (atopic forms)
Antibody-mediated (type II) hypersensitivity	Production of IgG, IgM → binds to antigen on target cell or tissue → phagocytosis or lysis of target cell by activated complement or Fc receptors; recruitment of leukocytes	Phagocytosis and lysis of cells; inflammation; in some diseases, functional derangements without cell or tissue injury	Autoimmune hemolytic anemia; Goodpasture syndrome
Immune complex–mediated (type III) hypersensitivity	Deposition of antigen-antibody complexes → complement activation → recruitment of leukocytes by complement products and Fc receptors → release of enzymes and other toxic molecules	Inflammation, necrotizing vasculitis (fibrinoid necrosis)	Systemic lupus erythematosus; some forms of glomerulonephritis; serum sickness; Arthus reaction
Cell-mediated (type IV) hypersensitivity	Activated T lymphocytes → (1) release of cytokines, inflammation and macrophage activation; (2) T cell–mediated cytotoxicity	Perivascular cellular infiltrates; edema; granuloma formation; cell destruction	Contact dermatitis; multiple sclerosis; type 1 diabetes; tuberculosis

Ig, Immunoglobulin.

interfere with cellular functions and cause disease without tissue injury.

- **In immune complex–mediated disorders (type III hypersensitivity), IgG and IgM antibodies bind antigens usually in the circulation, and the antigen-antibody complexes deposit in tissues and induce inflammation.** The leukocytes that are recruited (neutrophils and monocytes) produce tissue damage by release of lysosomal enzymes and generation of toxic free radicals.
- **In cell-mediated immune disorders (type IV hypersensitivity), sensitized T lymphocytes (T_H1 and T_H17 cells and CTLs) are the cause of the tissue injury.** T_H2 cells induce lesions that are part of immediate hypersensitivity reactions and are not considered a form of type IV hypersensitivity.

Immediate (Type I) Hypersensitivity

Immediate, or type I, hypersensitivity is a rapid immunologic reaction occurring in a previously sensitized individual that is triggered by the binding of an antigen to IgE antibody on the surface of mast cells. These reactions are often called *allergy*, and the antigens that elicit them are *allergens*. Immediate hypersensitivity may occur as a systemic disorder or as a local reaction. The systemic reaction most often follows injection of an antigen into a sensitized individual (e.g., by a bee sting), but can also follow antigen ingestion (e.g., peanut allergens). Sometimes, within minutes the patient goes into a state of shock, which may be fatal. Local reactions are diverse and vary depending on the portal of entry of the allergen. They may take the form of localized cutaneous rash or blisters (skin allergy, hives), nasal and conjunctival discharge (allergic rhinitis and conjunctivitis), hay fever, bronchial asthma, or allergic gastroenteritis (food allergy).

Many local type I hypersensitivity reactions have two well-defined phases (Fig. 6-13). The *immediate reaction* is characterized by vasodilation, vascular leakage, and depending on the location, smooth muscle spasm or glandular secretions. These changes usually become evident within minutes after exposure to an allergen and tend to

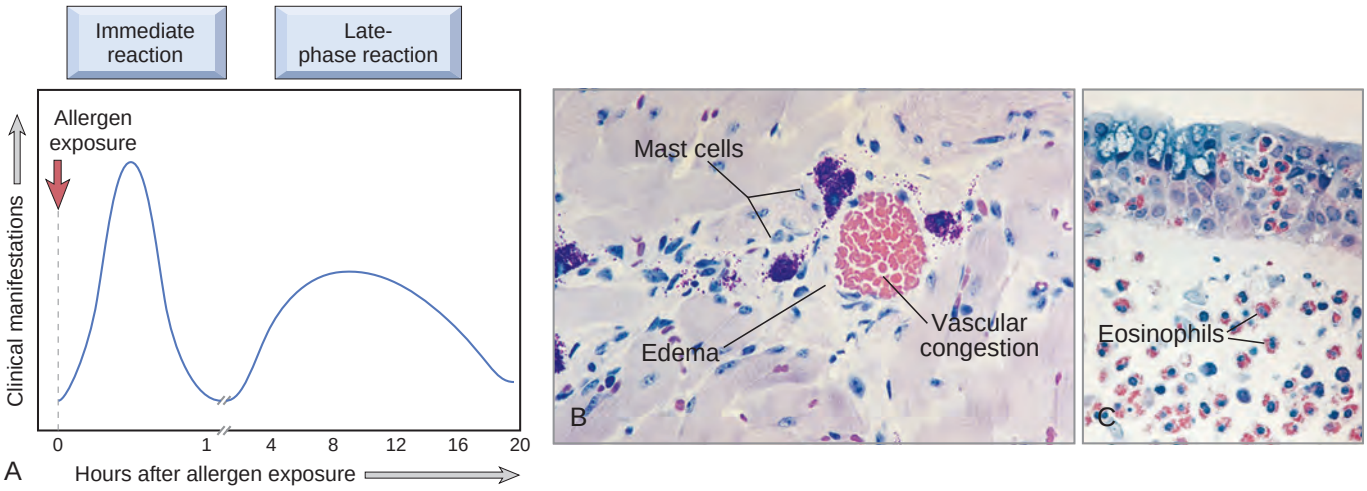

Figure 6-13 Phases of immediate hypersensitivity reactions. **A,** Kinetics of the immediate and late-phase reactions. The immediate vascular and smooth muscle reaction to allergen develops within minutes after challenge (allergen exposure in a previously sensitized individual), and the late-phase reaction develops 2 to 24 hours later. The immediate reaction **(B)** is characterized by vasodilation, congestion, and edema, and the late-phase reaction **(C)** is characterized by an inflammatory infiltrate rich in eosinophils, neutrophils, and T cells. (Courtesy Dr. Daniel Friend, Department of Pathology, Brigham and Women's Hospital, Boston, Mass.)

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