Skin is a major organ where immune/allergic reactions occur. Various skin diseases have been increasingly understood by the concept of immunity and allergic reactions, which are generally classified into the four categories established by Coombs & Gell (Table 3.4).

### Type I allergy

Type I allergy is caused mainly by mast cells. Since a reaction occurs 5 to 15 minutes after an antigen (allergen) is administered, it is also called an immediate hypersensitivity. Mast cells with IgE on the surface react to antigens, and chemical mediators such as histamines and leukotrienes are then secreted by the mast cells (Chapter 8). These chemical mediators enhance vascular permeability, to produce edema; in addition, they induce migration of...
eosinophils, to evoke inflammation. Therefore, nasal discharge, pruritus, and bronchial asthma are induced, and blood pressure is decreased, by vascular dilatation. A patient with these symptoms may undergo anaphylactic shock in serious cases. The symptoms are transient and usually subside within several hours.

Typical skin diseases caused by type I allergy are urticaria and certain types of drug eruptions (urticarial reaction). Other factors are involved in atopic dermatitis; however, IgE plays a pivotal or even solo role in the pathogenetic process. Additionally, allergic rhinitis (hay fever) and allergic bronchial asthma are common diseases caused by type I allergy.

2. Type II allergy

In type II allergy, antibodies are produced against the antigen on the cell surface to which complements and cytotoxic T cells have been activated, thereby injuring the cells. Type II allergy induces cutaneous diseases such as autoimmune blistering diseases. In bullous pemphigoid, autoantibodies bind to BP180 (BPAG2) in the basal cell hemidesmosomes, and the basal cells are injured by Type II allergy, resulting in blisters (Chapter 14).

A drug may function as a hapten to bind with epidermal cells or blood cells to cause Type II allergy. Drug-induced hemolytic anemia, thrombocytopenic purpura, and toxic epidermal necrolysis (TEN) occur by this mechanism.
Blood group incompatibility from transfusion, autoimmune hemolytic anemia, and Goodpasture syndrome are also Type II allergies.

3. Type III allergy

Type III allergy occurs when antigen-antibody complexes (immune complexes) deposit in the blood vessels and specific sites of tissue. An infection or a drug induces immune complex deposition, where an allergic reaction causes fibrinoid degeneration and neutrophilic infiltration; this is called cutaneous small-vessel vasculitis (Chapter 11).

Serum sickness disease, glomerular nephritis and lupus nephritis are also type III allergies.

4. Type IV allergy

Type IV allergy is inflammation caused by a reaction between an antigen and the corresponding T cells (Th1 in particular). There are two stages in type IV allergy: sensitization, and an effector phase. After an initial invasion, the antigen is engulfed by antigen-presenting cells to activate T cells in the regional lymph nodes. At this time, memory T cells along with effector T cells are produced in order to enable them to respond promptly to the secondary invasion of the antigen (sensitization). In the secondary and later invasions, memory T cells are activated by the antigen-presenting cells, and inflammation is evoked that peaks 48 hours after antigenic challenge (effector phase). Since it takes a long time for the reaction to occur, Type IV allergy is also

Hapten

Phagocytic cells engulf antigens that contain proteins of 10,000 molecular weight or greater (complete antigen) and carry the information of the antigens to lymphocytes. That is, non-protein substances of small molecular weight (e.g., carbohydrates, fats, organic compounds, metallic molecules) cannot be antigens themselves; they are called haptens, or incomplete antigens. Although antibodies react to haptens individually, lymphocytes produce such antibodies only in combination with other proteins.

Fig. 3.9 Mechanism of allergic contact dermatitis.
called delayed hypersensitivity (Fig. 3.9).
Typical lesions caused by type IV allergy are allergic contact dermatitis and graft-versus-host disease (GVHD).

D. Immune abnormality

1. Autoimmune diseases

Immunity is a mechanism whereby self is distinguished from non-self to exclude non-self. Therefore, autologous proteins do not usually induce immune reactions. If there is a disturbance in the body, antibodies (autoantibodies) are produced against autologous proteins and the immune mechanism tries to exclude self; this phenomenon is called autoimmunity, and the diseases caused by it are called autoimmune diseases. Autoantibodies are thought to appear by the following mechanisms.

● Organs that have been isolated from the immune system since the embryonic phase are exposed to the immune system for an unknown reason and are recognized as non-self (e.g., sympathetic ophthalmia, azoospermia).

● Normal tissues are degenerated by viruses or bacteria, and antibodies are produced against the degenerated proteins (e.g., mycoplasma pneumonia).

● Antibodies that have been produced against specific bacteria react with similar self antigens (cross-reaction) (e.g., rheumatic fever).

● Immunologic homeostasis becomes dysfunctional somehow, and lymphocytes that react against autoantigens (forbidden clones), which are excluded in a normal state, are not excluded (some autoimmune diseases, including systemic lupus erythematosus (SLE)).

● Regulatory T cells suffer reduced function for some reason, and immune reactions to self become uncontrolled (some autoimmune diseases, including SLE).

The major autoimmune diseases that are treated in dermatological practice include SLE, systemic sclerosis (SSc) and autoimmune blistering diseases such as pemphigus and pemphigoides.

2. Immunodeficiency

Immunodeficiency is subclassified into congenital and acquired. In congenital immunodeficiency, the immune factors are congenitally lacking. In acquired immunodeficiency the cause is secondary – the result of a disease or treatment. Different factors are dysfunctional in each disease, resulting in immunodeficiencies such as hypogammaglobulinemia, lymphocytopenia and the decrease of compliment titer.

In congenital immunodeficiency diseases, the infection is often