Type IV (Delayed Cell-Mediated) Reactions

up to this point we have discussed humoral immune responses involving IgE, IgG, or IgM. Type IV reactions involve cell-mediated immune responses and are caused mainly by T cells. Instead of occurring within a few minutes or hours after a sensitized individual is again exposed to an antigen, these **delayed cell-mediated reactions**, (or **delayed hypersensitivity)** are not apparent for a day or more. A major factor in the delay is the time required for the participating T cells and macrophages to migrate to and accumulate near the foreign antigens. Transplant rejection is most commonly mediated by cytotoxic T lymphocytes .

Causes of Delayed Cell-Mediated Reactions

Sensitization for delayed hypersensitivity reactions occurs when certain foreign antigens, particularly those that bind to tissue cells, are phagocytized by macrophages and then presented to receptors on the T-cell surface. Contact between the antigenic determinant sites and the appropriate T cell causes the T cell to proliferate into mature differentiated T cells and memory cells. When a person sensitized in this way is reexposed to the same antigen, a delayed hypersensitivity reaction might result.

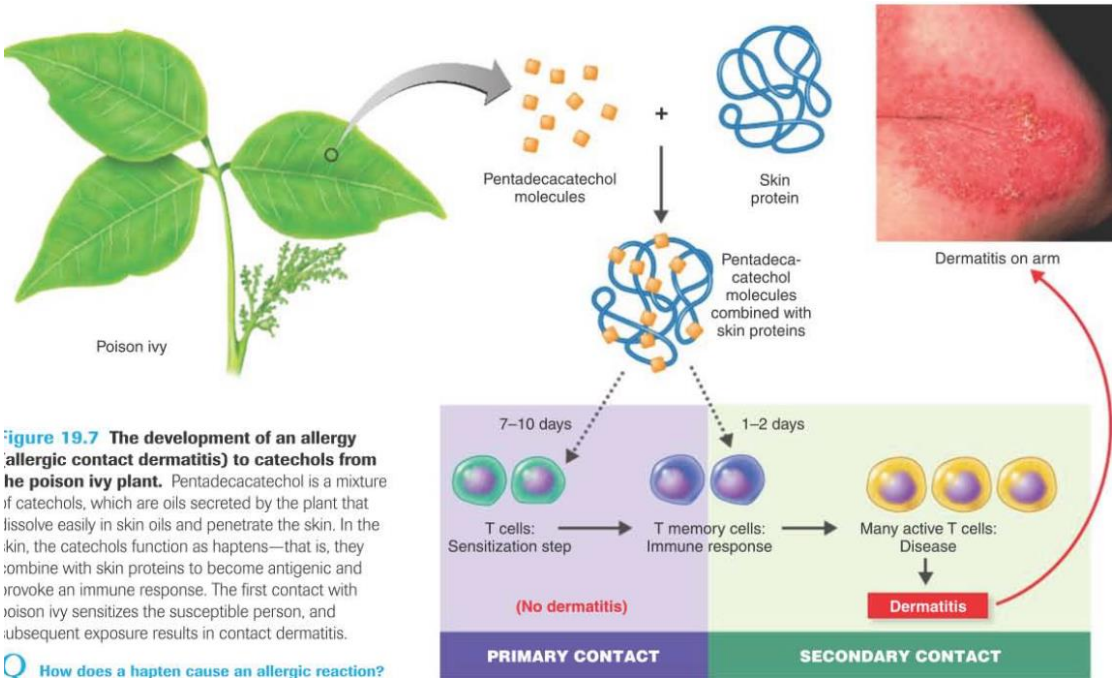
Memory cells from the initial exposure activate T cells, which release destructive cytokines in their interaction with the target antigen. In addition, some cytokines contribute to the inflammatory reaction to the foreign antigen by attracting macrophages to the site and activating them.

Delayed Cell-Mediated Hypersensitivity

Reactions of the Skin

We have seen that hypersensitivity symptoms are frequently displayed on the skin . One delayed hypersensitivity reaction that involves the skin is the familiar skin test for tuberculosis. Because Mycobacterium tuberculosis is often located within macrophages, this organism can stimulate a delayed cell - mediated immune response. As a screening test, protein components of the bacteria are injected into the skin. If the recipient has (or has had) a previous infection by tuberculosis bacteria, an inflammatory reaction to the injection of these antigens will appear on the skin in I to 2 days; this interval is typical of delayed hypersensitivity

reactions. **Allergic contact dermatitis**, another common manifestation of delayed cell -mediated hypersensitivity, is usually caused by haptens that combine with proteins (particularly the amino acid lysine) in the skin of some people to produce an immune response. Reactions to poison ivy (Figure 19.7), cosmetics, and the metals in jewelry (especially nickel) are familiar examples of these allergies.



igure 19.7 The development of an allergy allergic contact dermatitis) to catechols from he poison ivy plant. Pentadecacatechol is a mixture f catechols, which are oils secreted by the plant that lissolve easily in skin oils and penetrate the skin. In the kin, the catechols function as haptens—that is, they ombine with skin proteins to become antigenic and rovoke an immune response. The first contact with oison ivy sensitizes the susceptible person, and ubsequent exposure results in contact dermatitis.

How does a hapten cause an allergic reaction?

T-Cell-Mediated Recognition of Foreign MHC Receptors

Host Rejection of Graft When certain T cells of a host recognize foreign class I MHC markers on the surface of grafted cells, they release interleukin-2 as part of a general immune mobilization. The effect is to expand the helper and cytotoxic T cells specific to the antigens displayed by the donated cells. The cytotoxic cells bind to the grafted tissue and secrete lymphokines that begin the rejection process within 2 weeks of transplantation. Late in this process, antibodies formed against the graft tissue contribute to immune damage. A final blow is the destruction of the vascular supply, promoting death of the grafted tissue.