



Figure 25-1 *Left*, The skin is composed of an epidermal layer (e) from which specialized adnexa (hair follicles, h; sweat glands, g; and sebaceous glands, s) descend into the underlying dermis (d). *Inset*, This projection of the epidermal layer (e) and underlying superficial dermis demonstrates the progressive upward maturation of basal cells (b) into cornified squamous epithelial cells of the stratum corneum (sc). Melanin-containing dendritic melanocytes (m) (and rare Merkel cells containing neurosecretory granules) and mid-epidermal dendritic Langerhans cells (lc) are also present. The underlying dermis contains small vessels (v), fibroblasts (f), perivascular mast cells (mc), and dendrocytes (dc), which participate in dermal immune responses and repair.

- **Dendritic cells.** Skin serves as one of the first lines of defense against microorganisms and is constantly exposed to microbial and nonmicrobial antigens, which are processed by intraepidermal dendritic cells known as *Langerhans cells*. Langerhans cells secrete factors that augment innate immune responses, and migrate from the skin to regional lymph nodes where they present their antigenic cargoes to T lymphocytes, thereby stimulating the adaptive immune system. Specialized *dendrocytes*, another type of dendritic cell found within the dermis, perform similar functions.
- **Lymphocytes.** Following their stimulation by dendritic cells in regional lymph nodes, T cells expressing an adhesion molecule called cutaneous lymphocyte-associated antigen (CLA) and chemokine receptors such as CCR4 and CCR10 leave the lymph node and home back to the dermis, a process that is directed in part by chemokines secreted by activated keratinocytes. The infiltrating T cells usually include helper (CD4+), cytotoxic (CD8+), and regulatory (Treg) T cells (Chapter 6). Cytokines produced by these T cells mediate the microscopic patterns and clinical expressions of cutaneous inflammatory and infectious diseases. In addition, small numbers of B cells are found in the dermis that can participate in humoral responses to antigens encountered in the skin.
- Like the gut (Chapter 17), there is increasing appreciation that the skin is a large and complex ecosystem that

provides niches for a broad spectrum of organisms, including bacteria, fungi, viruses, and mites. These organisms have evolved symbiotic relationships with their human hosts and appear to contribute to health in a number of ways. By occupying skin niches, the normal “zoo” of skin organisms prevents colonization of the skin by other potentially harmful organisms. In addition, the skin fauna primes and “educates” the cutaneous immune system in a manner that is believed to enhance immune responses to potential pathogens. This story is just in its infancy, and it is likely that the role of the skin microbiome in health and disease will continue to expand in the coming years.

- **Afferent nerve fibers** and a diverse set of associated specialized structures referred to as *neural end organs* are responsible for physical sensations that run that gamut from pleasurable to painful, including touch, vibration, itchiness, cold, and heat. In addition, *autonomic efferent nerve fibers* regulate adnexal components such as sweat glands and effector pili muscles (see later) and can also influence the function of innate and adaptive immune cells in the dermis. Another cell type found in skin that remains cloaked in mystery is the *Merkel cell*; these cells are located in epithelial basal cell layer and may have neuroendocrine or mechanoreceptor functions.
- **Adnexal components.** *Sweat glands* guard against deleterious variations in body temperature, and *hair follicles*, in addition to manufacturing hair shafts, have protected