

B. Epidermis

a. Structure and cells of the dermis

The epidermis is on average about 0.2 mm thick, and 95% of the cells composing it are epidermal keratinocytes that proliferate and divide in the epidermal basal layer and move up to the upper layers as they mature (to form cornified cells). In the epidermis, epidermal keratinocytes at different stages of maturation are arranged in layers that can be divided into four levels (Figs. 1.4 and 1.5). The period between the production of daughter epidermal cells and their exfoliation from the outer surface of the epidermis is called the turnover time, which is approximately 28 days in normal skin.

1. Basal cell layer

The basal cell layer is a single layer consisting of basal cells including the epidermal stem cell subpopulation. Basal cells vary in shape from cubic to columnar. They contain basophilic (or darkly staining) cytoplasm and an elliptical nucleus that is rich in chromatin. The basal cells have desmosomes (for cell attachment), gap junctions (for cell communication), and hemidesmosomes (for cell attachment to the basement membrane).

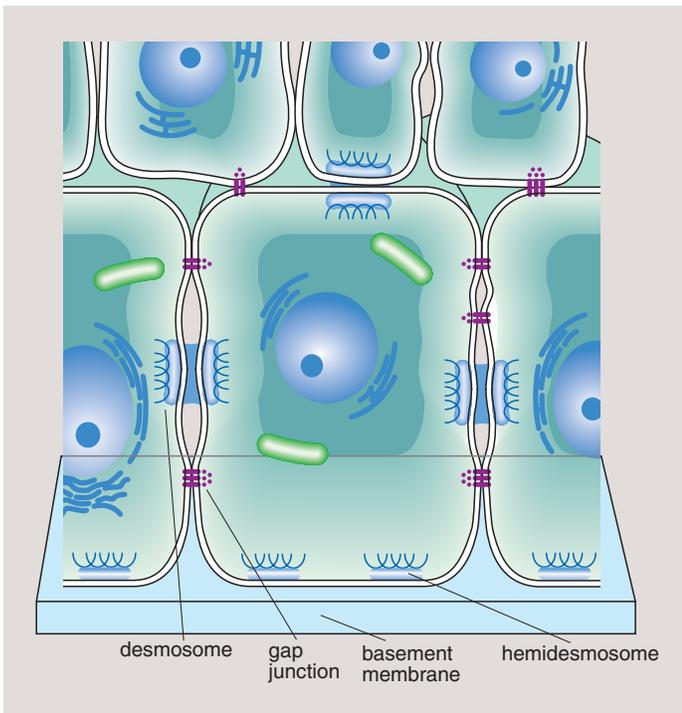


Fig. 1.6 Intracellular positions of desmosomes, gap junction and hemidesmosomes.

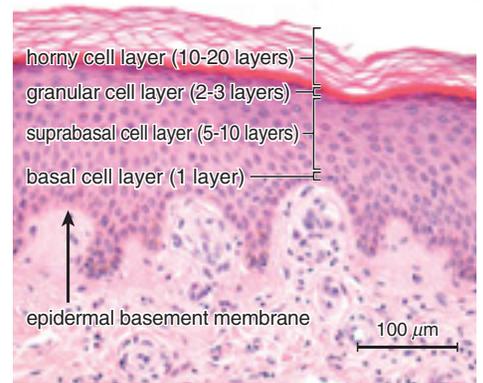


Fig. 1.4 The four layers of the epidermis: basal cell layer, suprabasal cell layer, granular cell layer and horny cell layer.

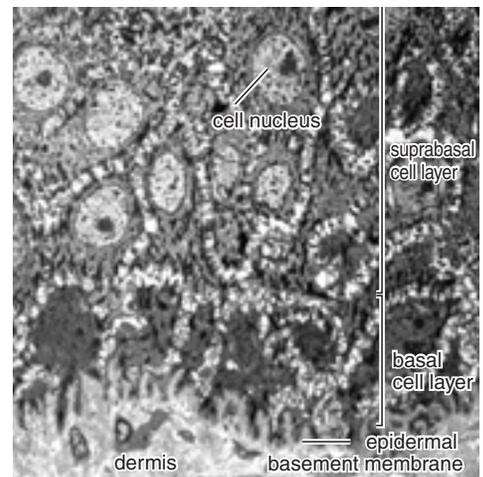


Fig. 1.5 Ultrastructural anatomy of the epidermis.

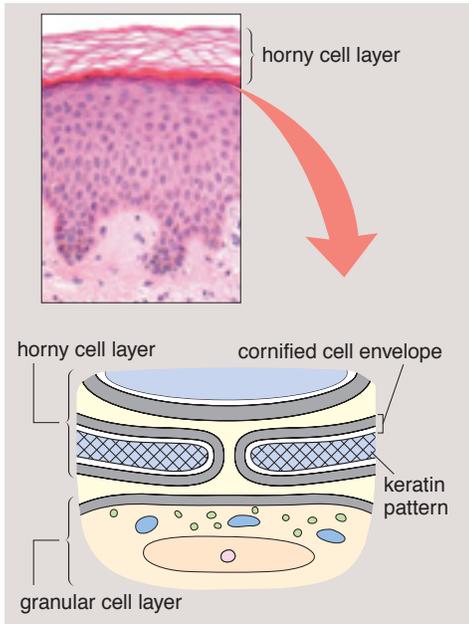


Fig. 1.7 Horny cell layer.

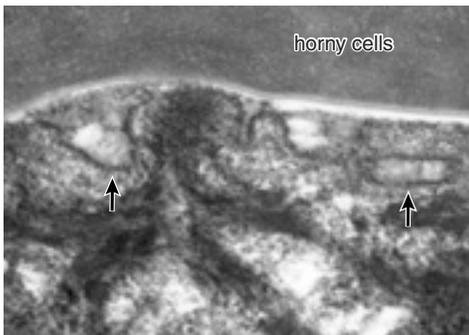


Fig. 1.8 Ultrastructural image of the epidermis between the granular cell layer and the horny cell layer, with cornified cell envelopes and lamellar granules (arrows).

hemidesmosomes (for connection with the extracellular matrix and underlying basal membrane) (Fig. 1.6). Cell cytokeratins (keratin filaments, tonofilaments) are abundant in the cytoplasm of many epidermal keratinocytes and are distributed in bundles at the periphery of the nucleus, from where they distally connect with hemidesmosomes and desmosomes to form a rigid and robust cellular cytoskeleton.

2. Suprabasal cell layer ★★

The suprabasal cell layer is composed of five to ten layers that appear connected to each other by prickle-like structures. Suprabasal (prickle) cells are polygonal in the lower layer and flattened in the upper layers. They are larger than basal cells and contain a small amount of chromatin in their circular nucleus. The part that gives the appearance of a prickle corresponds to the desmosome (a form of intercellular bridge).

3. Granular cell layer ★★

The granular cell layer is composed of two or three layers of cells containing basophilic keratohyalin granules. The cells and nuclei in the granular cell layers are even flatter than those in the suprabasal layer. Spherical lamellar granules, each with a diameter of approximately 300 nm (also known as Odland bodies or ketatosomes), can be observed in the granular cell layers by electron microscopy. The main component of lamellar granules is released into the intercellular space of horny cells as stratum corneum lipid.

4. Horny cell layer ★★

The horny cell layer, also called the stratum corneum, is composed of about ten sub-layers. Enucleated dead keratinocytes become membranous and multilayered, resembling fallen leaves, and exfoliate sequentially, beginning with the outer layer, in what is commonly called grime. The horny cell layer is very thick in the palms and soles. Horny cells are flat, and their cytoplasm is filled with aggregated keratin fibers. Directly above the granular cell layer, the horny cell structure appears as an eosinophilic layer. The horny cells gradually change into membranous structures in the upper layers. By electron microscopy, the contrast between electron-dense interfibrous substance and the low-electron-dense keratin fibers is clear; this contrast is called the keratin pattern.

The cell membranes are thicker in the horny cell layer than in the other layers. The lining structure is called a cornified cell envelope or a marginal band (Figs. 1.7 and 1.8). The protein, component of the cornified cell envelope, is extremely stable against physicochemical degradation.

5. Other cells

Keratinocytes account for 95% of the cells within the epidermis. The remaining 5% are melanocytes, Langerhans cells, α -dendritic cells and Merkel cells, which are involved in melanin formation, antigen presentation, and sensation, respectively.

b. Adhesion of keratinocytes

The epidermal basement membrane plays a key role in dermal-epidermal adhesion. Even when normal skin is rubbed, the epidermal basement membrane keeps the epidermis and dermis from separating.

The epidermal basement membrane zone, which lies immediately under the epidermis, stains by periodic acid Schiff (PAS) under the light microscope. The complicated structure of the basal membrane includes the lamina densa (LD) and the lamina lucida (LL), which are observed by electron microscopy (Figs. 1.9 and 1.10).

The lamina densa is 60 to 80 nm thick and consists mainly of fibronectins, heparan sulphate proteoglycan, type IV collagen and laminin 5 (including laminin 332). Under the electron microscope, it appears to be an electron-dense lattice network structure. Hemidesmosomes play an important role in adhesion between the basal cells and the lamina densa. Although the hemidesmosome resembles a desmosome that has been cut in half, the molecular components of hemidesmosomes and desmosomes are very different. Keratin fibers within basal cells link hemidesmosomes, to maintain and anchor the structure of the cell (Fig. 1.11).

The lamina lucida includes the component laminin 332. Type XVII collagen (BP180; 180kDa bullous pemphigoid antigen) bridges the lamina lucida to connect hemidesmosomes directly with the lamina densa.

Anchoring fibrils, which form semi-circular loop structures, form firmly connections around type I and III collagens in the dermis linking it to the lamina densa.

1. Adhesion between keratinocytes ★

Epidermal keratinocytes adhere to each other by desmosomes and structures such as adherens junctions, gap junctions and tight junctions.

The desmosome is composed of an attachment plaque (comprising inner and outer plaques), a structure that penetrates membranes to connect cells. The attachment plaque is mainly composed of desmoplakin, to which keratin fibers connect, to strengthen the cytoskeleton. Transmembrane proteins such as desmogleins and desmocollins are homophilically connected to the same molecules by a calcium ion dependent mechanism, which makes connections between cells possible (Fig. 1.12).

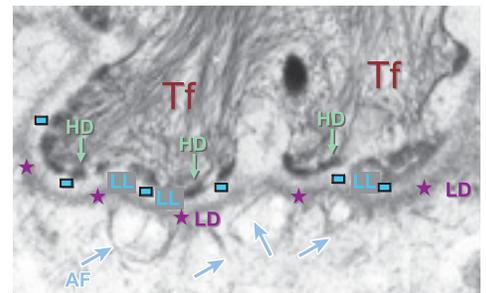


Fig. 1.9 Ultrastructural anatomy of the basement membrane zone.

TF: tonofilament. HD: hemidesmosome. LL: lamina lucida. LD: lamina densa. AF: anchoring fibril.

Blister formation caused by congenital change or autoantibody deposition MEMO

A congenital change or attachment of an autoantibody to the peripheral basal membrane may weaken the dermal-epidermal junction, leading to blister formation. When autoantibodies are produced against BP180 and BP230, which comprise hemidesmosomes, the disease bullous pemphigoid occurs. If a congenital abnormality is caused in K5, K14, BP180, laminin 332, or collagen type VII by genetic mutation, then epidermolysis bullosa occurs (Chapter 14). Blisters easily form after weakened epidermal intercellular adhesion resulting from production of autoantibodies against desmogleins, which are structural proteins of desmosomes; this is an autoimmune bullous disease called pemphigus.

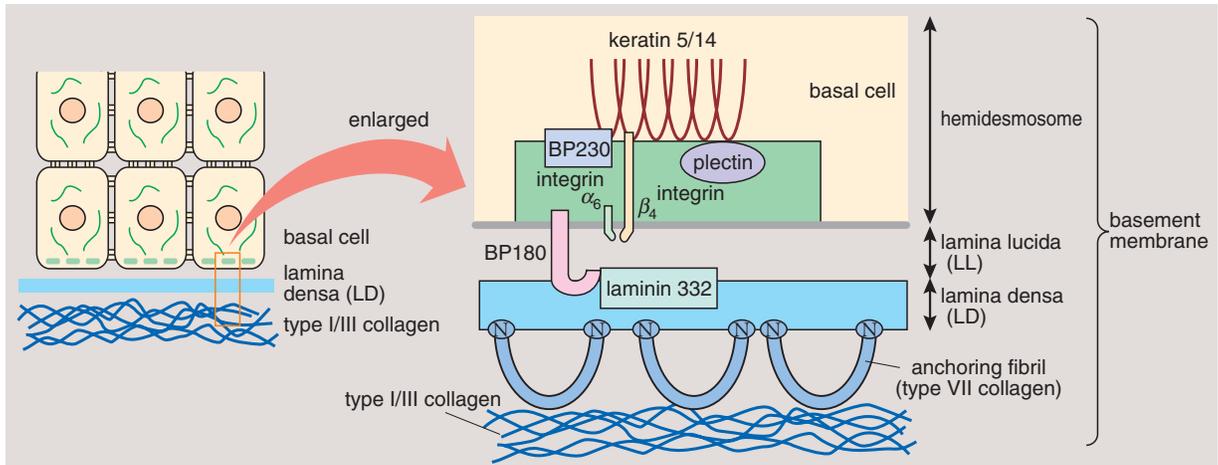


Fig. 1.10 Microstructure of the basement membrane zone.

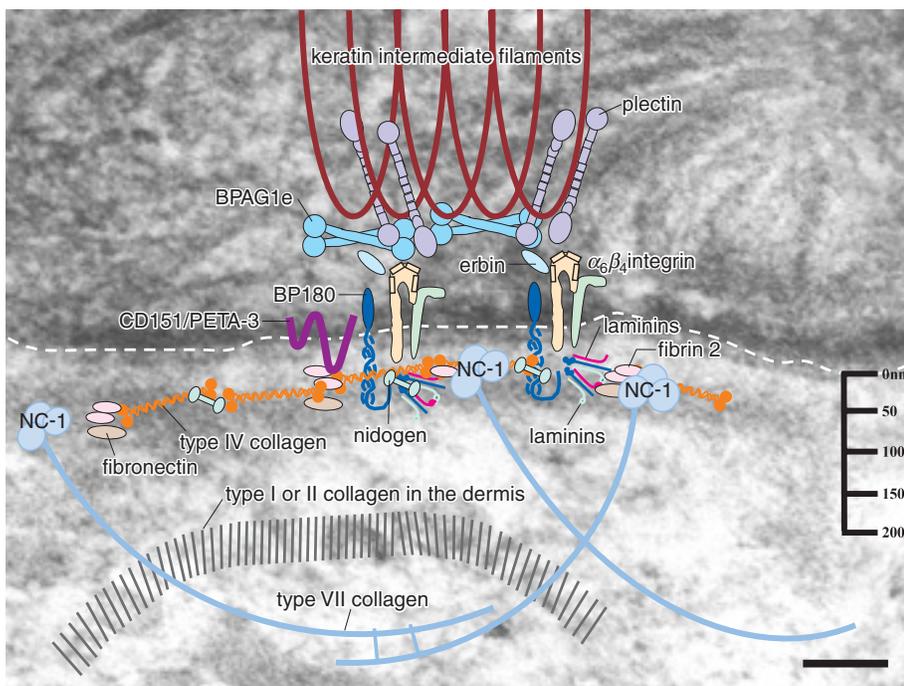


Fig. 1.11 Electron microscopy of the basement membrane zone.

The gap junction which is composed of connexin subunits, mechanism, has a structure in which cell plasma membranes associate with each other such as to leave a 2- to 3-nm space. Connexin is involved not only in connecting cells but also in transporting small molecules and ions between cells (**Fig. 1.13**).

The cell membranes of keratinocytes in the granular cell layers are connected to each other by a tight junction network characterized by membrane proteins called occludins and claudins, to prevent bodily fluids from leaking between cells in that the layer (tight conjugation).