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安德鲁斯皮肤病学

第 9 版

ANDREWS'

DISEASES OF THE SKIN

CLINICAL DERMATOLOGY

NINTH EDITION

RICHARD B. ODOM
WILLIAM D. JAMES
TIMOTHY G. BERGER

科学出版社 · Harcourt Asia · W.B. SAUNDERS

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Preface

Andrews' remains as it was from the beginning: an authored text that consists of one volume jam-packed with clinical signs, symptoms, diagnostic tests, and therapeutic pearls. The authors have remained general clinical dermatologists in an era of subspecialists in academia. They are committed to keeping *Andrews'* as a reference for anyone who needs help to diagnose a patient with a clinical conundrum or to treat a patient with a therapeutically challenging disease. The advantages of limited authorship are consistent, concise discussions without redundancy and an ability to bring to the text a unified philosophy in caring for patients with skin disease.

As with all previous editions of *Andrews'* our primary goal was to maintain it as a single volume so that it may be used in the clinical setting on the desktop, not as an after-the-fact, library resource. Its intended primary audience is the practicing dermatologist. Residents have always found it to be readily digestible for a yearly curriculum of study, and we are hopeful that another decade of trainees will learn clinical dermatology from the clinical descriptions, disease classifications, and treatment insights that define *Andrews'*. We believe that students, interns, residents, internists and other medical specialists, family practitioners, and other healthcare professionals who desire a comprehensive dermatology textbook will find that ours meets their needs in understanding and managing their patients.

Many major changes have been made in this edition. Harry Arnold died soon after the eighth edition was published. Tim Berger agreed to co-author this revision and has worked diligently to update and improve the organization of the text. Curt Samlaska also participated in revising several of the chapters, and his contributions have been invaluable. Finally, Kirsten Vin-Christian and Roy Grekin have combined the radiotherapy and dermatologic surgery chapters and added the vast array of new surgical techniques to their chapter.

Since our last edition was published a decade ago, medical science has advanced with meteoric speed. Molecular investigative techniques have been a major impetus in gaining insight into skin disease. Inherited conditions are understood at the subcellular level and give us a broader view of the mechanisms leading to tumor formation, immunologic responsiveness, and cell adhesion. Immunodiagnostics continue to sort tumor biology into new classification schemes, especially visible in lymphoma and bullous disease research. Technologic breakthroughs have given us lasers, narrowband ultraviolet therapy, and epiluminescence microscopy. New medications have found their place in the formulary: a multitude of retinoids, calcipitriol, mycophenolate mofetil, topical metronidazole, topical tacrolimus, the rebirth of thalidomide as an immunomodulator, finasteride, and

improved systemic antifungals, antivirals (and retrovirals), antibiotics, and antihistamines are some examples.

Extensive revision of the text was necessary to include the wealth of new information. Just as advances in understanding led to additions, older concepts needed to be selectively discarded. These offsetting alterations allow us to maintain the total volume of information constant. Old, oftentimes, classic references are not cited in favor of new ones. When available, references that can readily be found on the practicing dermatologist's shelf, such as recent volumes of the *Journal of the American Academy of Dermatology* and the *Archives of Dermatology,* are cited. The seminal but older references are to be found in these sources.

More than 75 new entities, numerous new diagnostic tests, several new infections, and many new associations appear for the first time in the ninth edition. This sea of new knowledge is presented to be navigated easily and enjoyed.

Many thank yous are in order on completion of a task of this magnitude. Judy Fletcher and Melissa (Dudlick) Messersmith at W.B. Saunders and Liz Fathman, Ellen Baker Geisel, and Anne Salmo at Mosby helped keep us on task and brought our ideas into print. Curt Samlaska's placing his second novel on hold to assist us with this ninth edition leaves us in his debt.

We hope you enjoy this edition of *Andrews'* as we begin to collect new knowledge from the year 2000 literature to present to you in the upcoming tenth edition!

Richard B. Odom, M.D.
William D. James, M.D.
Timothy G. Berger, M.D.

I would just like to dedicate my professional efforts to my family members and thank the many patients who extended the privilege of allowing me to participate in their care.

RBO

My wife, Ann, and my children, Dan and Becca, have supported this effort and my career with their love and patience; the faculty, residents, and patients at Walter Reed and the University of Pennsylvania continued to teach me every day over the years. Dick Odom and Tim Berger continue to provide me with examples to emulate.

WDJ

My efforts in this text are dedicated to Dr. Richard B. Odom, my mentor, colleague, and friend in dermatology for a quarter century. And to Jessica, the love of my life.

TGB

ANDREWS'

DISEASES *of the* SKIN

CLINICAL DERMATOLOGY

Contents

CHAPTER 1

The Skin: Basic Structure and Function

The skin is composed of three layers: epidermis, dermis, and subcutaneous tissue (fat). The epidermis, the outermost layer, is directly contiguous with the environment. It is formed by an ordered arrangement of cells called *keratinocytes,* whose basic function is to synthesize keratin, a filamentous protein that serves a protective function. The dermis is the middle layer. Its principal constituent is the fibrillar structural protein collagen. The dermis lies on the panniculus of subcutaneous tissue, which is composed principally of lobules of lipocytes (Fig. 1-1).

All skin sites are composed of these three anatomically distinct layers, although there is considerable regional variation in their relative thickness. The epidermis is thickest on the palms and soles, measuring approximately 1.5 mm. It is very thin on the eyelid, where it measures less than 0.1 mm. The dermis is thickest on the back, where it is 30 to 40 times as thick as the overlying epidermis. The amount of subcutaneous fat is generous on the abdomen and buttocks compared with the nose and sternum, where it is meager.

EPIDERMIS

During the first weeks of fetal life, the epidermis consists of a single sheet of contiguous, undifferentiated cells that subsequently assume the characteristics of keratinocytes. Adnexal structures, particularly follicles and eccrine sweat units, originate during the third month of fetal life as downgrowths from the developing epidermis. Later, apocrine sweat units develop from the upper portion of the follicular epithelium and sebaceous glands and ducts from the midregion of the follicle. The development of adnexal structures at specific skin sites, such as the regional variation in thickness of the three skin layers, is genetically modulated.

The adult epidermis is composed of three basic cell types: keratinocytes, melanocytes, and Langerhans' cells (Fig. 1-2). An additional cell, the Merkel cell, can be found in the basal layer of the palms and soles, the oral and genital mucosa, the nail bed, and the follicular infundibula. The Merkel cells, located directly above the basement membrane, contain intracytoplasmic neurosecretory-like granules, and, through their association with neurites, act as slow adapting touch receptors. They have direct connections with adjacent keratinocytes by desmosomes and contain intermediate filaments composed of low–molecular-weight keratin. Whether these cells originate from the neural crest or from within the epidermis is still unknown.

Keratinocyte

The keratinocyte, or squamous cell, is the principal cell of the epidermis. It is a cell of ectodermal origin that has the specialized function of producing keratin, a complex filamentous protein that not only forms the surface coat (stratum corneum) of the epidermis but also is the structural protein of hair and nails. Multiple distinct keratin genes have been identified and consist of two subfamilies, acidic and basic. The product of one basic and one acidic keratin gene combines to form the multiple keratins that occur in many tissues. The mixture of these keratins vary with cell type and degree of differentiation.

The epidermis may be divided into the following zones, beginning with the innermost layer: basal layer, malpighian or prickle layer, granular layer, and horny layer, or stratum corneum (Fig. 1-3). These names reflect the changing appearance of the keratinocyte as it differentiates into a cornified cell.

A proportion of the basal cells proliferate, differentiate, and move in a stepwise fashion through the full thickness of the epidermis. As the cell moves upward through the epidermis, it changes morphologically. It flattens out, and eventually the nucleus disappears.

Just as there is regional variation in the thickness of the anatomic layers of the skin, so also is there variation in the thickness of the different zones of the epidermis according to skin site. The horny layer and granular layer are thickest on the palms and soles, and virtually absent on the more delicate skin of the flexor aspect of the forearms and the abdomen. The basal layer, however, is generally one cell thick, regardless of the skin site examined.

During keratinization, the keratinocyte first passes through a synthetic and then a degradative phase on its way to becoming a horn cell. In the synthetic phase, the

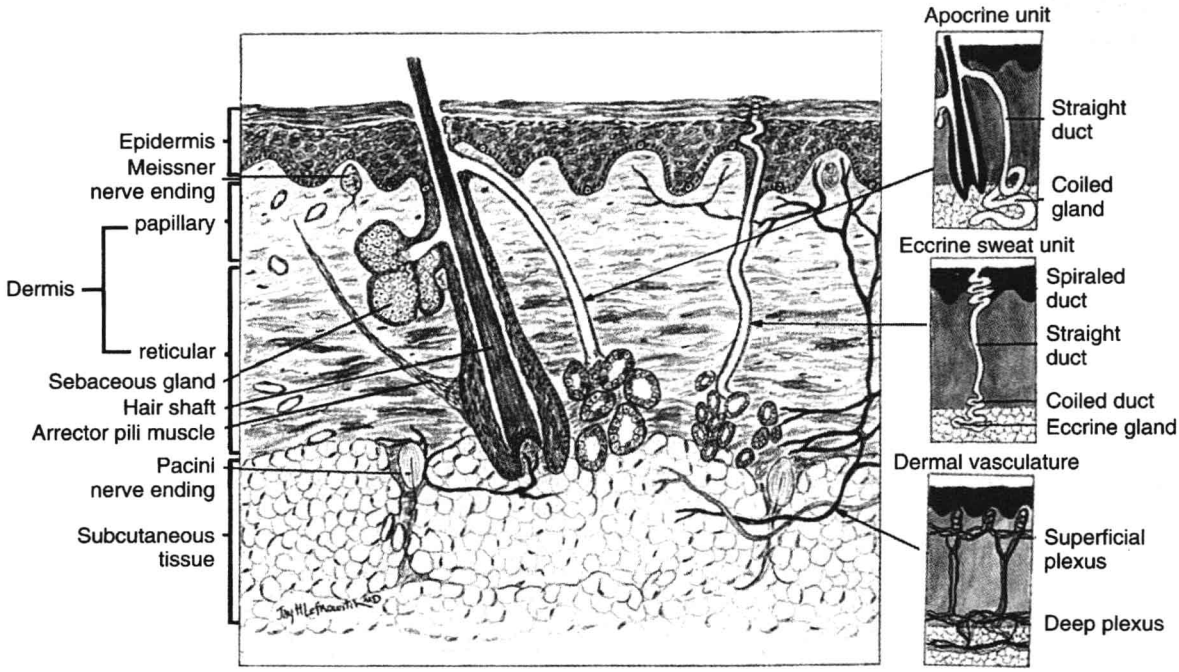

Fig. 1-1 Diagrammatic cross section of the skin and panniculus.

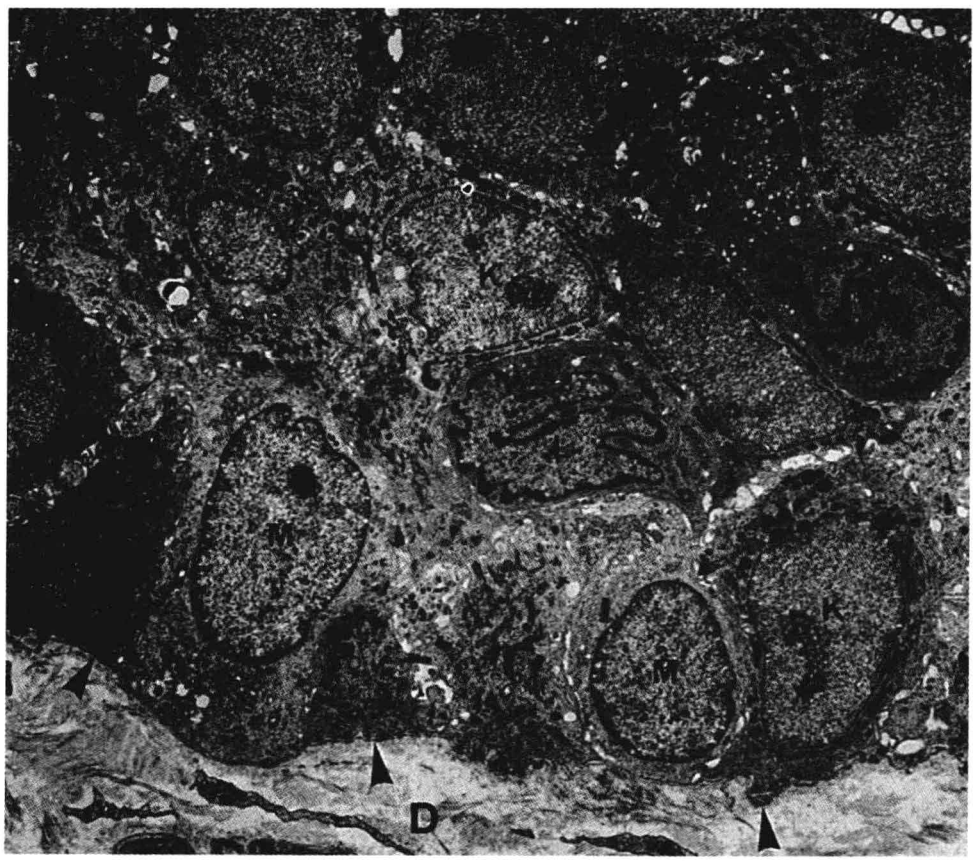

Fig. 1-2 Electron micrograph illustrating the three basic cell types in the epidermis and their relationships. Most of the cells are keratinocytes (prickle cells and basal cells), some labeled *(K)*. Langerhans' cells *(L)* with their characteristic cribriform nuclei are distributed among the keratinocytes in the malpighian layer. Melanocytes *(M)* are located in the basal layer of the epidermis, which is separated from (and attached to) the dermis *(D)* by the basement membrane zone *(arrows)*.

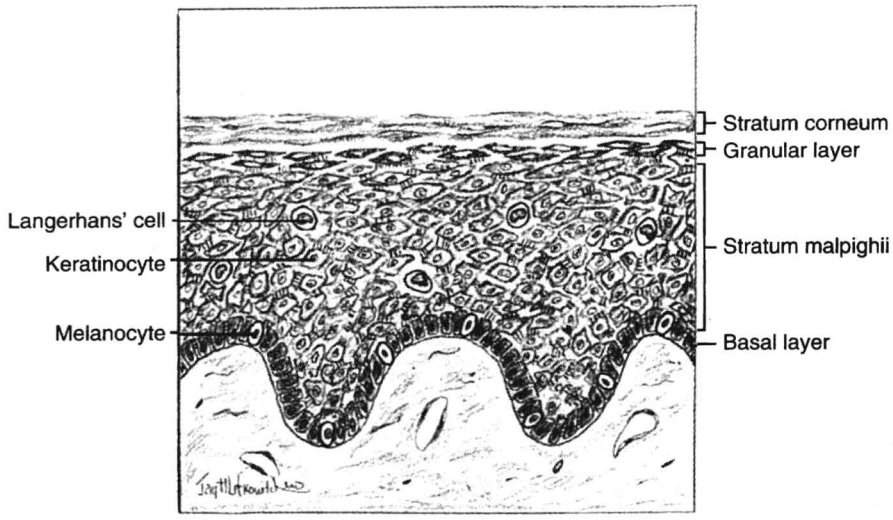

Fig. 1-3 The layers of the epidermis.

keratinocyte accumulates within its cytoplasm intermediate filaments composed of a fibrous protein, keratin, arranged in an alpha-helical coiled-coil pattern. These tonofilaments are fashioned into bundles, which converge on and terminate at the plasma membrane, where they end in specialized attachment plates called *desmosomes* (Fig. 1-4). The degradative phase of keratinization is characterized by the disappearance of cell organelles and the consolidation of all contents into a mixture of filaments and amorphous cell envelopes (Fig. 1-5).

The plasma membranes of adjacent cells are separated by an intercellular space. Electron microscopic histochemical studies have shown that this interspace contains glycoproteins and lipids. Lamellar granules function in this space, primarily at the interface between the granular and cornified cell layers.

Keratinocytes of the granular zone contain, in addition to the keratin filament system, keratohyaline granules, composed of amorphous particulate material of high sulphur-protein content. This material, called profilaggrin, is a precursor to filaggrin, so named because it is thought to be responsible for keratin filament aggregation. Conversion to filaggrin takes place in the granular layer, and this forms the electron-dense interfilamentous protein matrix of mature epidermal keratin.

Lamellated organelles called *Odland bodies,* also referred to as membrane-coating granules or keratinosomes, are found intracellularly in upper-level keratinocytes. Their contents are discharged into the extracellular space at the junction of the granular and horny layers. This establishes a barrier to water loss and, with filaggrin, mediate stratum corneum cell cohesion.

Keratinocytes play a role in the immune function of the skin, and they participate in communication, interaction, and regulation of cell systems collaborating in the induction of the immune response. Keratinocytes secrete a wide array of cytokines and inflammatory mediators. They also can express molecules on their surface such as ICAM-1 and MHC Class II molecules, which demonstrates that keratinocytes actively respond to immune effector signals.

Melanocyte

The melanocyte is the pigment-producing cell of the epidermis. It is derived from the neural crest, and by the eighth week of development can be found within the fetal epidermis. In normal adult epidermis, melanocytes reside in the basal layer at a frequency of approximately 1 for every 10 basal keratinocytes. The number of melanocytes in the epidermis is the same, regardless of the person's race or color; it is the number and size of the melanosomes or pigment granules, continuously synthesized by these melanocytes, that determine differences in skin color (Fig. 1-6).

In histologic sections of skin routinely stained by hematoxylin and eosin, the melanocyte appears as a clear cell in the basal layer of the epidermis. The apparent halo is an artefact caused by separation of the melanocyte from adjacent keratinocytes during fixation of the specimen. This occurs because the melanocyte, lacking tonofilaments, cannot form desmosomal attachments with keratinocytes.

The melanocyte is actually a dendritic cell, a feature rarely appreciated at the light-microscope level. Its dendrites extend for long distances within the epidermis, and any one melanocyte is therefore in contact with a great number of keratinocytes; together they form the so-called epidermal melanin unit.

Melanosomes are synthesized in the Golgi zone of the cell and pass through a series of stages in which the enzyme tyrosinase acts on melanin precursors to produce the densely pigmented granules. While this is occurring, the melanosome migrates to the tip of a dendrite, where it is transferred to an adjacent keratinocyte. Keratinocytes are the reservoir for melanin in the skin.

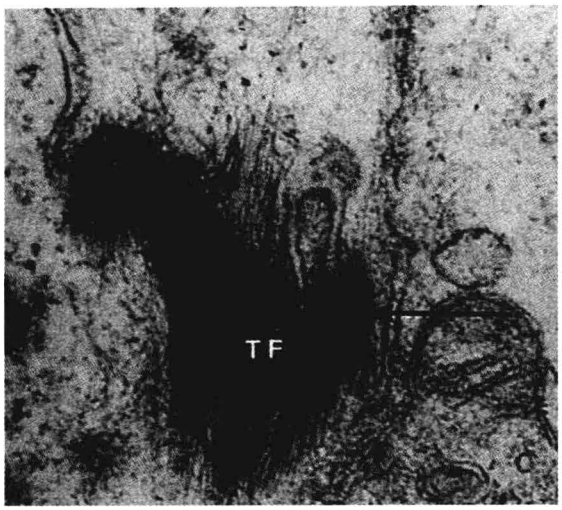

Fig. 1-4 Ultrastructural appearance of the desmosome *(arrow),* the specialized attachment plate between adjacent keratinocytes. Tonofilaments *(TF)* within the cytoplasm of adjacent keratinocytes converge on the plasma membrane of each cell, where they condense to form an electron-dense zone.

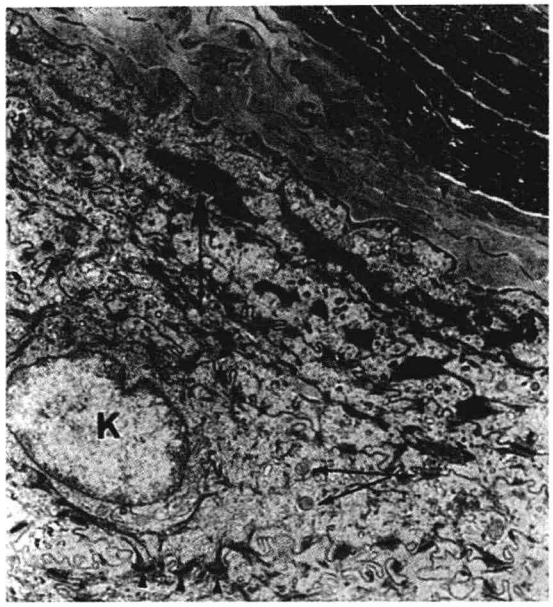

Fig. 1-5 The upper portion of the epidermis. Keratinocytes *(K)* are flatter than those of the lower portion (see Fig. 1-2), and contain keratinosomes *(thin arrows).* Desmosomes *(short arrows)* become more obvious as the ratio of nucleus to cytoplasm increases. Keratinocytes of the granular layer have developed keratohyalin granules *(broad, long arrow).* The stratum corneum *(SC)* is composed of horny plates that retain only filaments and amorphous material enveloped in a thickened cell membrane. Horny cells, like other keratinocytes, are joined by desmosomes *(short arrowheads).*

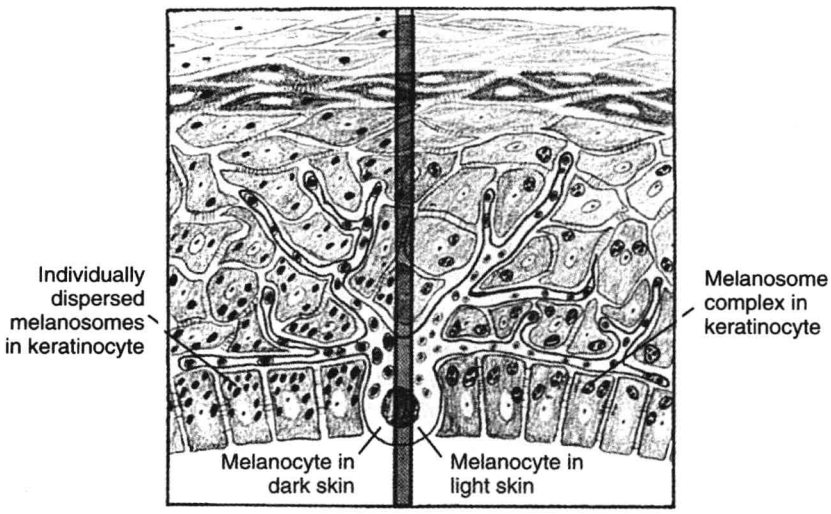

Fig. 1-6 The epidermal melanin unit in dark *(left)* and light *(right)* skin.

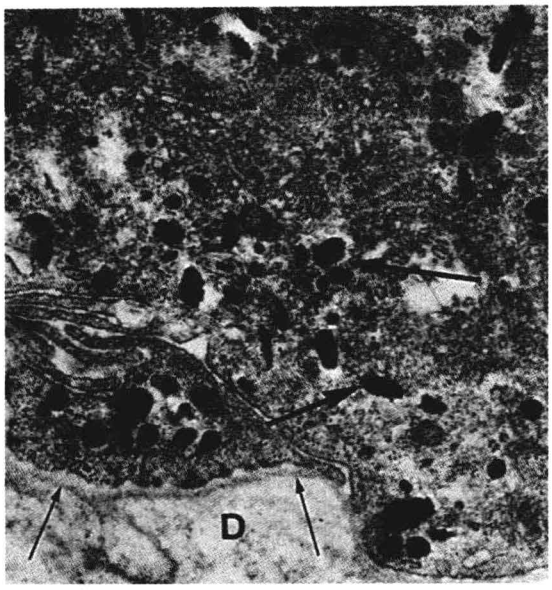

Fig. 1-7 Portion of a melanocyte from dark skin, illustrating melanosomes *(broad arrows)* at various stages of development. Basement membrane zone *(thin arrow)* and dermis *(D)* are also seen.

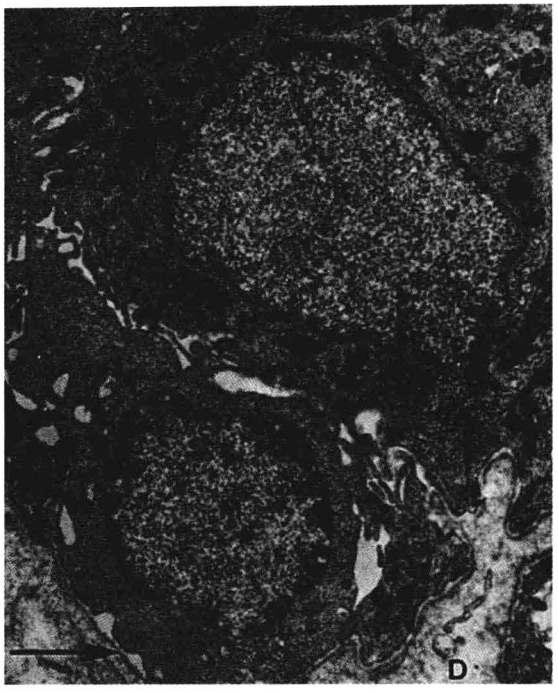

Fig. 1-8 The relationship between melanocytes *(M)* and basal keratinocytes *(K)* in light skin. Melanocytes synthesize pigment granules (melanosomes), which are transferred to keratinocytes, where they are contained within membrane-bound melanosome complexes *(small arrowheads)*. Bundles of tonofilaments *(broad arrowhead)* identify the cell as a keratinocyte. The basement membrane zone *(arrow)* separates epidermis from dermis *(D)*.

Melanocytes of dark skin synthesize melanosomes larger than those produced in light skin. The size of the melanosome is the principal factor in determining how the melanosomes will be distributed within the keratinocytes. The larger melanosomes of dark skin are individually dispersed within the cytoplasm of keratinocytes; smaller melanosomes of light skin are packaged in membrane-bound complexes within the keratinocyte (Figs. 1-7 and 1-8). Chronic sun exposure can stimulate the melanocyte to produce larger melanosomes, thereby making the distribution of melanosomes within keratinocytes resemble the pattern seen in dark-skinned individuals.

Areas of leukoderma or whitening of skin can be caused by very different phenomena. In vitiligo, the affected skin becomes white because of destruction of melanocytes. In albinism, the number of melanocytes is normal; however, they are unable to synthesize fully pigmented melanosomes because of defects in the enzymatic formation of melanin. Local areas of increased pigmentation can result from a variety of causes. The typical freckle results from a localized increase in production of pigment by a normal number of melanocytes. Nevi are benign proliferations of melanocytes. Melanomas are their malignant counterpart. Frequently, though, skin lesions are not pigmented because of hyperplasia or hyperactivity of melanocytes. Rather, they are colored by pigment within the keratinocyte. Seborrheic keratosis is a common example of such a benign pigmented epithelial neoplasm.

The Langerhans' Cell

Langerhans' cells are normally found scattered among keratinocytes of the stratum spinosum, or prickle cell layer of the epidermis. They constitute 3% to 5% of the cells in this layer. Like the melanocyte, they are not connected to adjacent keratinocytes by the desmosomes. At the light-microscopic level, Langerhans' cells are difficult to detect in routinely stained sections; however, they appear as dendritic cells in sections impregnated with gold chloride, a stain specific for Langerhans' cells. They can also be stained with peroxidase-labeled monoclonal antibody CDla or S100. Ultrastructurally they are characterized by a folded nucleus and distinct intracytoplasmic organelles called *Langerhans'* or *Birbeck granules* (Fig. 1-9). In their fully developed form, the organelles are rod shaped with a vacuole at one end and resemble a tennis racquet.

Functionally, Langerhans' cells are of the monocyte-macrophage lineage and originate in bone marrow. They play a role in induction of graft rejection, primary contact sensitization, and immunosurveillance. If skin is depleted of them by exposure to ultraviolet radiation, it loses the ability

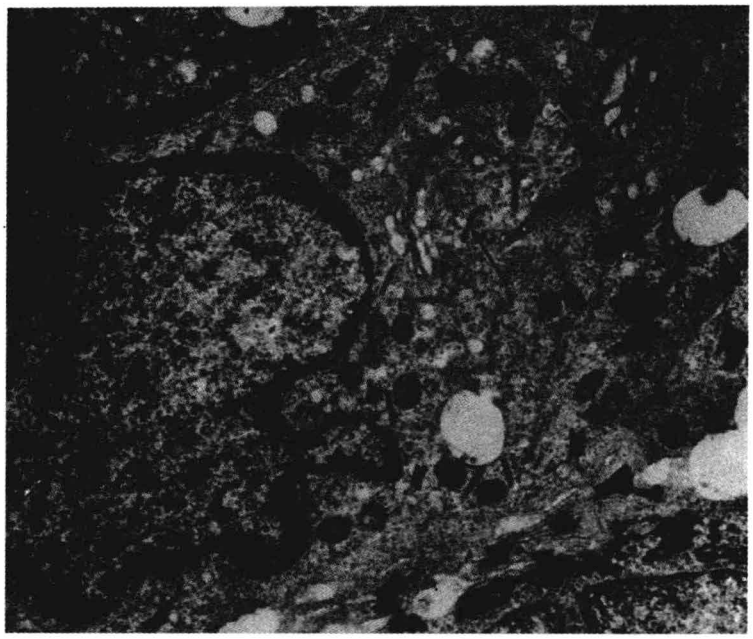

Fig. 1-9 Ultrastructural appearance of the Langerhans' cell *(L)*. The characteristic intracytoplasmic Langerhans' (Birbeck) granules have a rod-shaped handle *(thin arrow)* and a wide head *(broad arrowhead)*. The Langerhans' cell is not connected to adjacent keratinocytes *(K)* by desmosomes.

to be sensitized until its population of Langerhans' cells is replenished. Langerhans' cells function primarily in the afferent limb of the immune response by providing for the recognition, uptake, processing, and presentation of antigens to sensitized T lymphocytes.

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THE EPIDERMAL-DERMAL JUNCTION

The junction of epidermis and dermis is formed by the basement membrane zone (see Fig. 1-2). Ultrastructurally, this zone is composed of four components: the plasma membranes of the basal cells with the specialized attachment plates (hemidesmosomes); an electron-lucent zone called the lamina lucida; the basal lamina; and the fibrous components associated with the basal lamina, including anchoring fibrils, dermal microfibrils, and collagen fibers (Fig. 1-10). At the light-microscopic level, the so-called PAS-positive basement membrane is composed of the fibrous components. The basal lamina is synthesized by the basal cells of the epidermis. Uitto et al and Fine have reviewed in detail the many component layers of the basement membrane zone, the ultrastructural localization of the various immunoreactants in the chronic bullous dermatoses, and the abnormalities of the molecular structural proteins in both acquired and inherited blistering diseases.

The basement membrane zone is considered to be a porous semipermeable filter, which permits exchange of cells and fluid between the epidermis and dermis. It further serves as a structural support for the epidermis and holds the epidermis and dermis together. The basement membrane zone serves the same functions for the skin appendages.