Atlas of

Skin Cancer

ANTHONY DU VIVIER

Gower Medical Publishing

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Skin Cancer

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Preface

Skin cancer is on the increase. It affects Caucasians and is largely a result of the damaging cumulative effects of ultra-violet light on fair skin. It has become commonplace because of the dictates of fashion, the ease of access to sunlight, increased recreational activity, unprotected childhood exposure and longevity. The general public is aware of skin cancer through medical and media publicity, and is more conscious of lesions on the skin than previously. Patients therefore present frequently to their doctors for diagnosis.

This book illustrates and discusses the normal anatomy of the skin and common benign abnormalities including naevi. These serve as an essential introduction to the chapter on the diagnosis and management of malignant and premalignant disorders of the skin. The text is liberally complemented by illustrations that should help to improve diagnosis. Consequently, this book should be of interest to family practitioners, surgeons, oncologists and dermatologists, as well as to students.

Anthony du Vivier London

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Finally the atlas is dedicated to my wife, Judith, who makes everything worthwhile.

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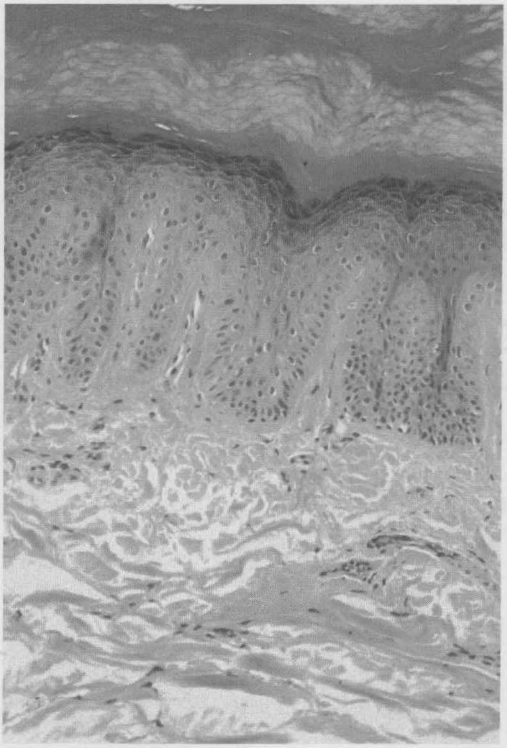
1

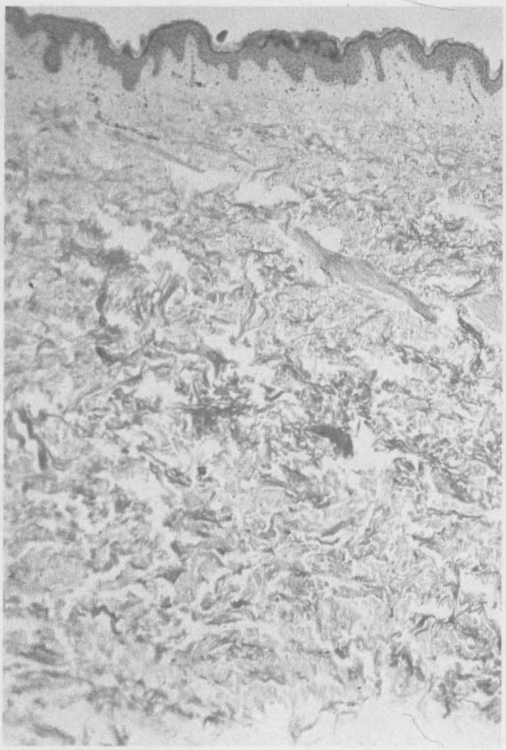
The Structure and Function of Normal Skin

PHILLIP H. McKEE
MB BCh BaO MRCPath

In addition to its obvious property of enveloping the body, the skin has a wide range of diverse functions including protection against injury, thermoregulation, waterproofing and fluid conservation. It is of considerable importance in the absorption of ultraviolet radiation and in the production of vitamin D; it acts as a barrier to pathogenic organisms and functions in the detection of sensory stimuli.

The skin conveniently divides into two distinct layers, the epidermis and its appendages, derived from ectoderm, and the dermis with the underlying subcutaneous fat, derived from mesoderm. (The nerves and melanocytes are of neuroectodermal origin). The epidermis is a multilayered (stratified) squamous epithelium from which arises the pilosebaceous follicles, apocrine glands and eccrine sweat glands. The dermis consists of the ground substance plus a fibrous component (collagen and elastin).





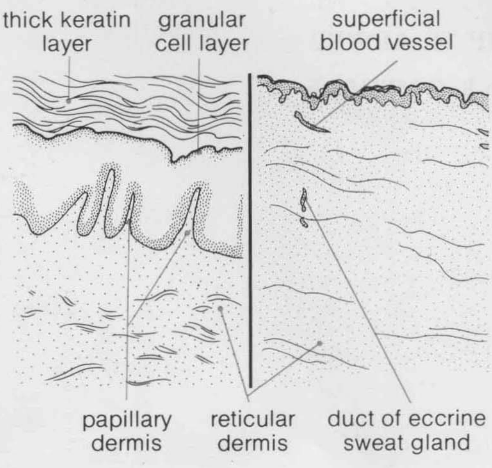
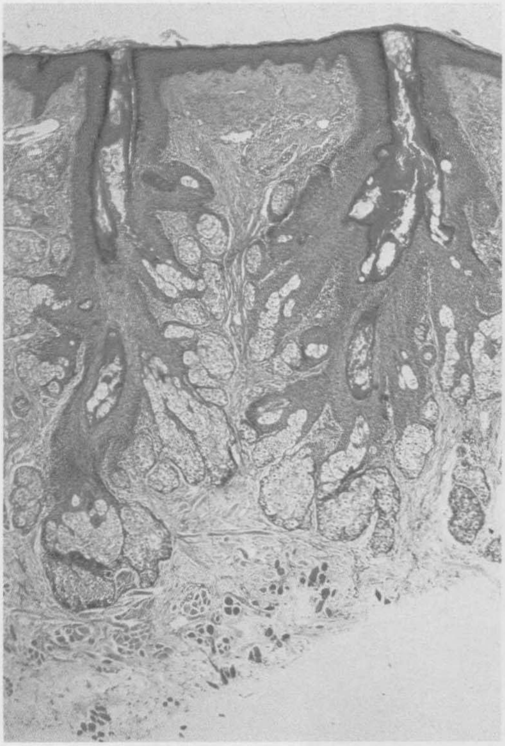


Fig. 1.1 Marked regional variations of normal skin structures as seen in sections from: (left) fingertip of young male and (right) abdomen of young female. Haematoxylin & eosin stains.

There is considerable regional variation in skin structure and to some extent function (Figs 1.1 & 1.2). Skin is divided into two types, glabrous and hairy. Glabrous skin (typified by a thick keratin layer) covers the surfaces of the palms and soles whilst hairy skin covers the rest of the body. Hair production is maximum about the head, the axillae and pubic regions, and on the face of males. Sebaceous glands are especially numerous about the face and nose whilst eccrine glands are most commonly found on the palms and soles. The surface of the skin is far from regular, being marked by a series of complex creases determined by the underlying epidermal ridge pattern. This is clearly demonstrated by the whorls, loops and arches that constitute fingerprints. Mucous membranes differ from skin by the absence of both granular and horny layers.



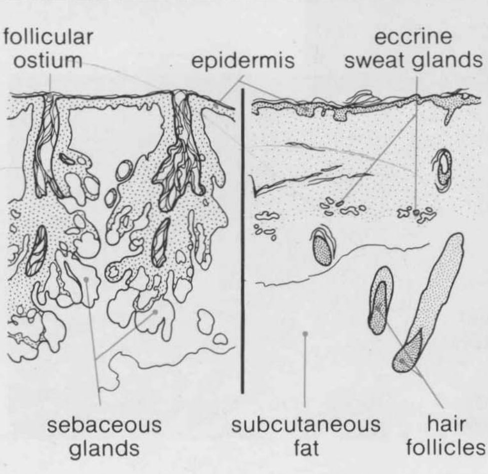


Fig. 1.2 Marked regional variations of normal skin structures as seen in sections from (left) nose of young female and (right) scalp of elderly female. H & E stains.

EPIDERMIS

Histologically the epidermis consists of at least four cell types (keratinocytes, melanocytes, Merkel cells and Langerhans cells) and has four clearly defined layers, the basal cell, prickle cell, granular cell and keratin layers. A fifth layer may be interposed between the granular and keratin layers on the palms and soles. The basal cell layer is the germinative layer of the epidermis. With each division, approximately fifty percent of the daughter population contributes to the developing epidermis. It is thought that the epidermal transit time is approximately thirty days. Maturation consists of the conversion of columnar basal cells into the fully keratinized cells of the epidermal horn and involves a transformation of cellular polarity, basal cells being arranged at right angles to the basement membrane whilst

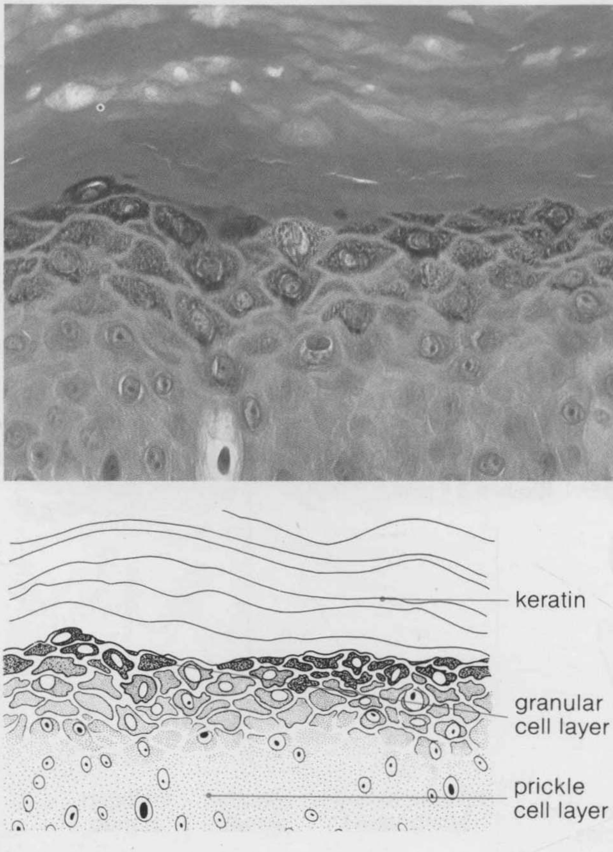


Fig. 1.3 Normal skin from the palm showing basophilic granular cell layer. H & E stain.

the cellular residues of the keratin layer lie parallel.

These perpendicularly-orientated columnar cells have basophilic cytoplasm and round to oval hyperchromatic nuclei and, when mature, acquire the polyhedral outline of the prickle cell layer. The acquisition of keratohyalin granules (Fig. 1.3) characterizes the granular cell layer. Further maturation leads to loss of nuclei and flattening of the cellular outline until the flattened plates of the keratin layer are fully formed. The keratinocytes are united at their free borders by intercellular bridges (desmosomes) best seen in the prickle cell layer. They are much more conspicuous in the disease states of the skin involving intercellular oedema (Fig. 1.4). The epidermis lies on a thin basement membrane, clearly visualized by periodic acid-Schiff staining (Fig. 1.5).

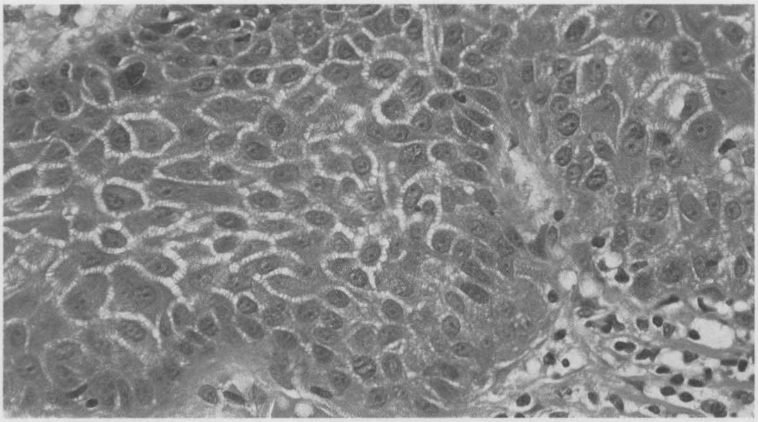


Fig. 1.4 Epidermis showing slight intercellular oedema, thus exaggerating the intercellular junctions (desmosomes). H & E stain.

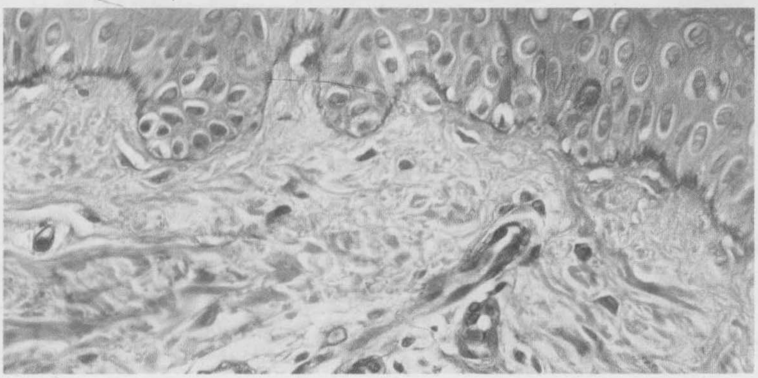
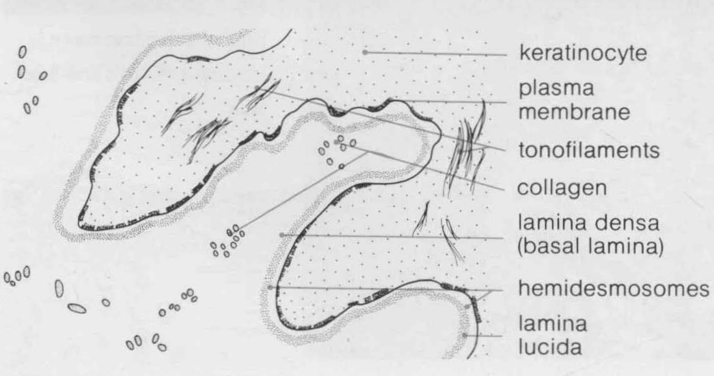


Fig. 1.5. Normal skin showing purple-staining basement membrane. Periodic acid-Schiff stain.

Under the electron microscope the basement membrane of the epidermis is no longer the homogeneous entity suggested by light microscopic examination but instead is seen to be quite a heterogeneous structure (Fig. 1.6).

Hemidesmosomes are seen at intervals along the basal cell plasma membrane and, beneath this, a clear zone intervenes before the electron-dense lamina densa (basal lamina). Anchoring filaments adjoin the hemidesmosomes to the lamina densa and its fibrils may be seen spreading from the lamina densa into the papillary dermis. Basal cells contain tonofilaments loosely aggregated into bundles or tonofibrils while in the prickle cell layer the tonofibrils form an interlacing network occupying much of the cytoplasm (Fig. 1.7). The cytoplasmic membrane is infolded and shows numerous

Fig. 1.6. Basement membrane region of normal epidermis. Note conspicuous hemidesmosomes, lamina lucida and lamina densa. EM, × 20,200.



desmosomes (Fig. 1.8). The prickle cells also contain lamellated oval structures known as membrane-coating granules or Odland bodies, measuring 100–500nm in diameter. Covered by a double-layered membrane, they contain parallel lamellae about 20Å thick orientated along the short axis of the granule and are located particularly in the region of the plasma membrane (Fig. 1.9). In addition to the membrane-coating granules, the granular cells contain keratohyalin granules which are not membrane-bound and consist of closely packed amorphous particles (Fig. 1.9). The cells of the keratin layer contain tonofibrils embedded in an amorphous matrix and are characterized by a thickened cytoplasmic membrane. The intercellular spaces contain a material probably derived from the membrane-coating granules which functions as an intercellular cement.

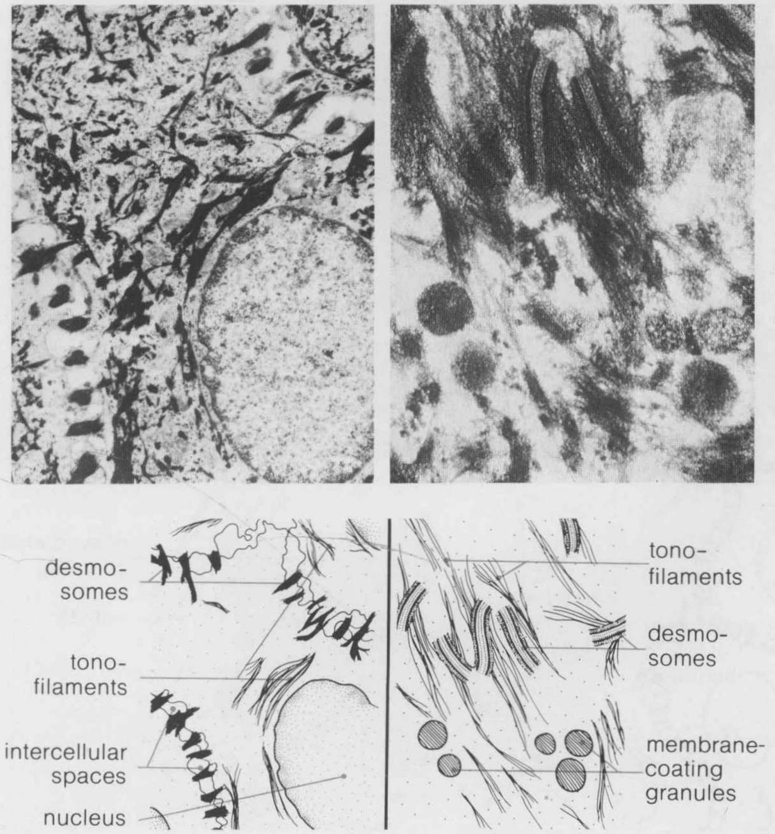


Fig. 1.7 Lower prickle cell layer of normal skin showing (left) tonofilaments and dilated intercellular spaces; (right) tonofilaments inserting into desmosomes. EMs, × 5200 (left), × 30,300 (right).

Tonofilaments and keratohyalin granules are largely composed of protein whilst membrane-coating granules contain large amounts of lipids and hydrolytic enzymes (possibly involved in exocytosis of the granules).

Keratinization is the process of epidermal differentiation by which basal cells are converted into the protective membranous horny layer. Its exact mechanism is not fully understood but it depends on the development and interplay of the three intracellular organelles, namely tonifibrils, keratohyalin granules and membrane-coating granules.

Maturation of the epidermis involves an increase in the number of tonofibrils followed by their incorporation by the

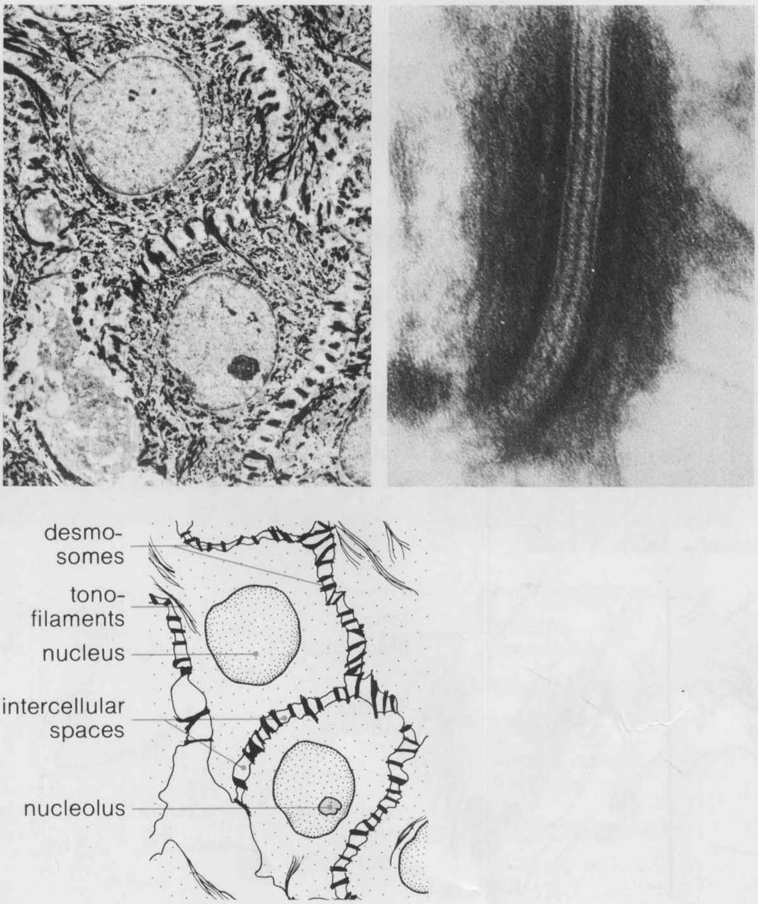


Fig. 1.8 Prickle cell layer showing conspicuous desmosomes (left); the multilayered nature of the desmosome (intercellular bridge) is clearly seen (right). EMs, × 2200 (left), × 71,000 (right).

amorphous substance of the keratohyalin granules. There is some evidence suggesting that desmosomes play an important role in keratinization, possibly functioning as attachment sites for tonofilament orientation. The cells of the horny layer are cemented together to form a tough and flexible membrane, the superficial aspect of which is continuously being shed as large clusters of squames. The keratin layer prevents the loss of body fluids and influx of water into the skin by means of lipid deposits between the horny cells. The strength and integrity of the horny layer is believed to be due to the presence of disulphide bonds between adjacent keratin molecules.

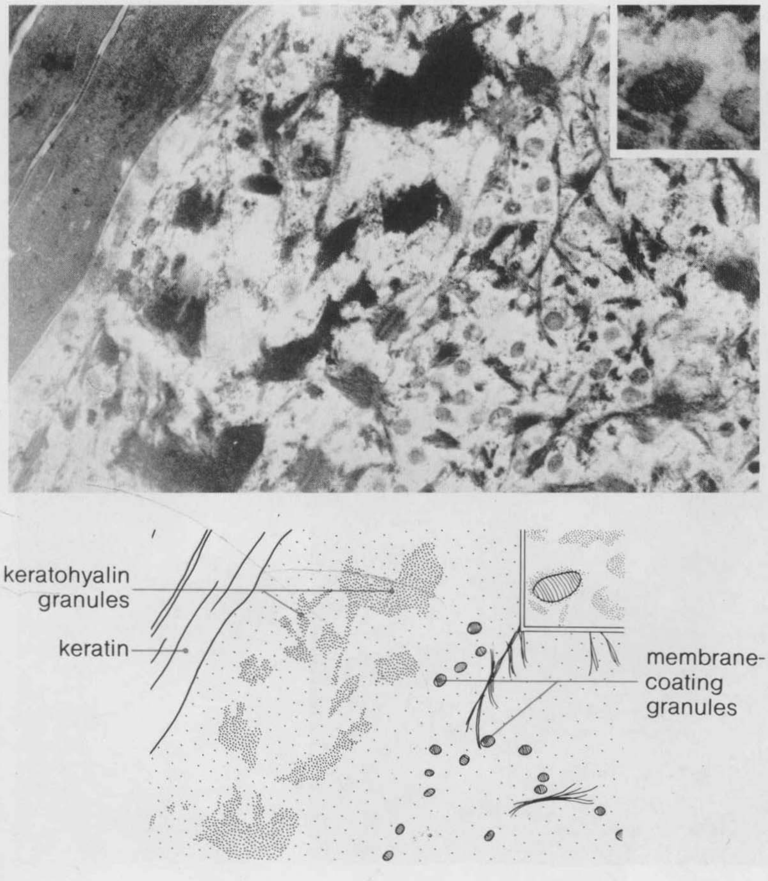


Fig. 1.9 Keratohyalin and membrane-coating granules are present in the granular cell layer, the lamellated structure of membrane-coating granules is seen (inset). EM, × 17,500, (inset) × 48,000.

Melanocytes

These cells are derived from the neural crest and are found only along the basal layers of the epidermis. They appear as clear cells on haematoxylin and eosin staining (Fig. 1.10, left). Melanin is readily identified by silver techniques such as the Masson–Fontanna reaction (Fig. 1.10, right) or by the dopa reaction. The ratio of melanocytes to basal cells varies considerably, 1:4 in the cheek to 1:10 in the arms. Melanocytes are dendritic cells and the melanin granules are transferred along the dendritic processes to adjacent kera-

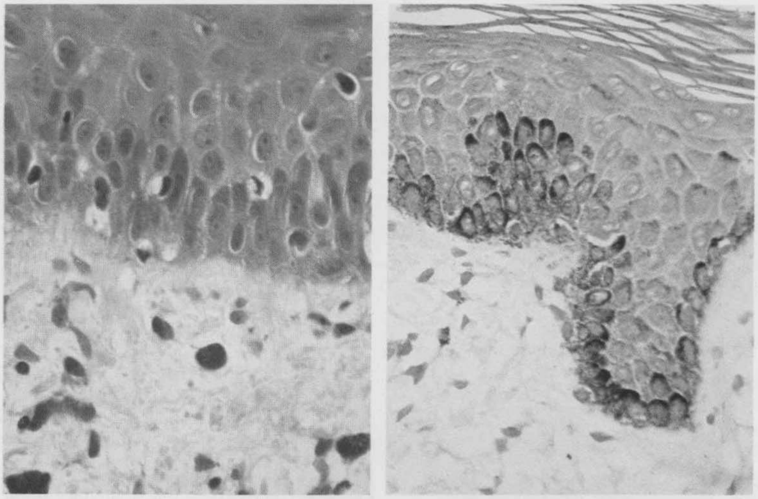


Fig. 1.10 Melanocytes appear as clear cells in the basal layer of the epidermis. Pigment is abundant in this section of skin from a black African (left). Positive staining of melanin pigment in a biopsy of simple lentigo from a young female (right). H & E (left), Masson–Fontanna (right) stains.

Fig. 1.11 Melanocyte typified by intracytoplasmic electron-dense melanosomes. EM, × 14,000.

tinocytes where they are actively phagocytosed. In addition to skin and hair colouration, melanin pigment is of extreme importance as protection against the injurious properties of ultraviolet radiation. Electron-microscopically the melanocyte is characterized by pale cytoplasm and an absence of both tonofilaments and desmosomes (Fig. 1.11) but with the presence of electron-dense melanosomes. These tyrosinase-containing granules, believed to be formed in the Golgi apparatus, have an oval structure measuring about 400nm in its greatest dimension. Partially developed melanosomes show a lamellated internal structure (Fig. 1.12) which is obscured by a pigment production in the mature granule. The quantity of melanin determines colouration; the degree of skin colour is dependent upon the total number, size and distribution of melanin granules.

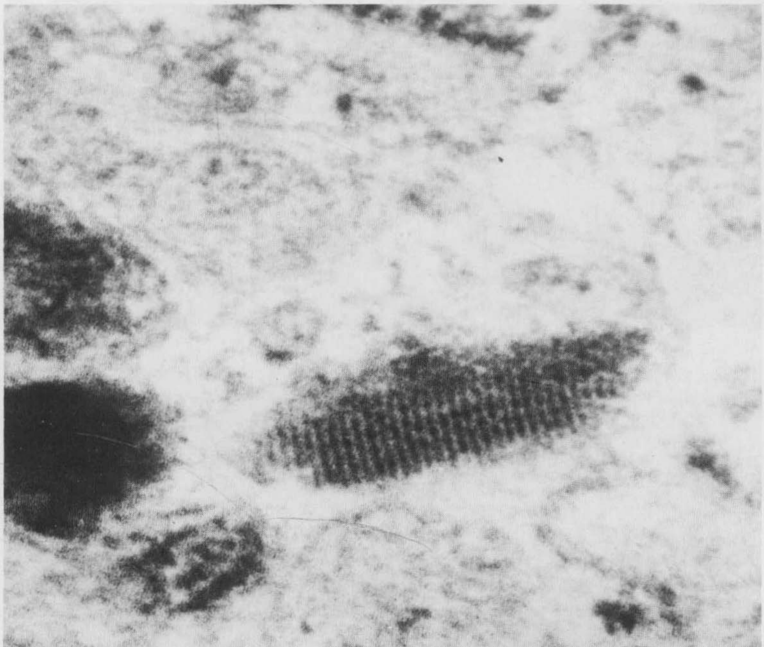


Fig. 1.12 Melanosomes from a case of malignant melanoma showing their lamellated internal structures. EM, × 200,000.