HERMANN WERNER SIEMENS, M.D.

Translated by KURT WIENER, M.D.

GENERAL DIAGNOSIS AND THERAPY OF SKIN DISEASES

An Introduction to Dermatology for Students and Physicians

The first English translation of a recent German text which offers a new approach to the teaching of dermatology

With 375 illustrations

THE UNIVERSITY OF CHICAGO PRESS

General Diagnosis and Therapy of Skin Diseases

AN INTRODUCTION TO DERMATOLOGY
FOR STUDENTS AND PHYSICIANS

By

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Preface

IN THE Preface to the German edition of his book (1952), Hermann Werner Siemens states that the only excuse for a new textbook on dermatology can be a new approach to teaching dermatology. He has in mind concentration on the *fundamentals of dermatology* by thorough explanation and particularly by illustrations in close-up photography. Of course, most textbooks devote a certain amount of space to the fundamentals, namely, the definition of the lesions and also the principles of therapy, but these efforts have usually the character of a short introduction hurrying to the main part of the texts—the special pathology and therapy of the skin diseases. There, it is hoped, the beginner will also find the illustrations which are to clarify the definitions in words. Of course, it is most desirable to have these illustrations right next to the discussion of the lesions, eruptions, and therapy, and the photography should be taken with the purpose in mind of illustrating a written definition. Siemens has, in more than twenty-five years of teaching at the University Skin Clinic at Leiden, directed his photographer, Mr. J. J. van der Walle, to take pictures just as he found necessary for his way of teaching the elements of dermatology. On the basis of a very large number of such photographs, the book has been written independently of existing texts.

In the chapters on therapy, Siemens tries to inculcate in the student the fundamental rules of all therapy: Use for healing what experience has shown to be effective, but only that. Do not choose medications for reasons of tradition or pharmacological expectations that the method *should* be good, but because you know it is good. Carefully weigh effect against toxicity. Throw out "ruthlessly" what is honored only by time and not by merit. Be suspicious of complicated prescriptions, no matter how famous. Learn how to master a small, though sufficient, armamentarium and stick to it, instead of becoming a therapeutic butterfly that sips from one blossom today and tomorrow from another, never really familiar with anything. The chapter on the application of therapeutic agents is based entirely on Siemens' own clinical experiments. He is a man who is perfectly willing to spend much of his time and his great energy on the unglamorous work of investigating, evaluating, and often "debunking" famous recipes which have been handed down to us. He teaches that the student should not memorize ready-made prescriptions but, instead, learn the strengths of the agents so that he can prescribe them as the case requires. Of course, not too much of our so-called heritage survives this strict treatment, but what passes is better founded, simpler, and often better to work with than the weighty combinations of old. The therapeutic part of the book is written in a

spirit of scientific curiosity which changes everyday treatment from a monotonous routine to an interesting experiment. But Siemens, though sometimes tending to lean over backward in order to demonstrate his point to the beginner, is also a man of practical experience. Even the most experienced dermatologist will pick up sound advice on many pages, and he will enjoy the graphic descriptions and pictures. The best point, however, which the medical student can learn from the book is the spirit of intellectual discipline and honesty in which it is written.

Siemens, who comes from a famous German family of engineers, scientists, inventors, and industrialists, received his dermatological training at the clinics of Joseph Jadassohn in Breslau and Leo von Zumbusch in Munich, where he also taught. In 1929 he was offered the chair of dermatology at the famous University of Leiden, Holland, where he trained many Dutch and other dermatologists. During the occupation of the Netherlands by the Nazis, he courageously defended the academic freedom of his university. As could be expected, the invaders soon dismissed him from his position. For his opposition, the Germans took him twice as a hostage and imprisoned him in a concentration camp. After the defeat of Hitler and the liberation of the Netherlands, the grateful Dutch government immediately reinstated him, and his first lecture inspired a moving demonstration of respect for the German who, even under threat of death, had placed his convictions and human principles above everything else.

Siemens has written a very large number of articles, many of them the result of thorough scientific investigation. Besides dermatology, Siemens has, from his student days, been fascinated by the field of human genetics. Frequently, he applied his great knowledge of human genetics to dermatology. In 1923 the method of studying identical twins to confirm or rule out hereditary factors in disease was introduced by him and often applied to dermatoses. In 1924 he wrote a monograph on the method of "Twin Pathology,"[1] and much of his genetic work, as far as it has a bearing on skin diseases, is presented in Jadassohn's monumental Handbook,[2] for which he wrote the chapter on heredity in dermatology.

My translation was greatly helped by Drs. Harold L. Miller, Joel E. Taxman, and Roger Laubenheimer, all dermatologists of Milwaukee, who read the manuscript. Dr. Allan L. Lorincz, assistant professor of dermatology at the University of Chicago, also read the manuscript and suggested many improvements. Mr. Walter Hahn, a registered pharmacist of Milwaukee, checked the dosages and helped me to adapt some European prescriptions to American conditions. My secretary, Mrs. Gloria Kurtz, typed the manuscript. I am most grateful to every one of them.

KURT WIENER

1. *Die Zwillingspathologie, ihre Bedeutung, ihre Methodik, ihre bisherigen Ergebnisse* (Berlin: J. Springer, 1924).

2. Joseph Jadassohn, *Handbuch der Haut- und Geschlechtskrankheiten*, Vol. III (Berlin: J. Springer, 1929).

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Anatomic and Histopathologic Introduction

THE skin consists of three major layers: the *epidermis* in the outermost position, the *cutis*, or corium, in the middle, and the *subcutis*, or stratum subcutaneum, below. Besides these three layers, the skin possesses the so-called appendages, namely, sebaceous glands, sweat glands, hair, and nails.

The *epidermis* is of ectodermal origin. It is a covering epithelial mantle in which the cells are closely packed together. It contains no blood vessels and is nourished only by tissue fluid, which circulates among its cells. Terminal ramifications of sensory nerve fibers innervate this layer.

The *cutis* is of mesodermal origin. In contrast to the epidermis, the bulk of it consists of fibers produced by cells rather than of the cells themselves. Connective tissue cells are scattered only sparsely among their fibrous products. The cutis contains blood vessels, nerves, and also small, smooth muscle fibers.

The *subcutis*, which also contains vessels and nerves, consists of a fine network of connective tissue interspersed with fat cells.

The *epidermis* can be thought of as the spread-out parenchyma of the skin. Its entire thickness, as well as the thickness of its individual layers, varies on different parts of the body surface. In most areas the total thickness is less than 1 mm. The basal layer or the stratum germinativum is the deepest layer of the epidermis. Above this lie, in sequence, the stratum spinosum, the stratum granulosum, the stratum lucidum, and, finally, the stratum corneum, the outermost part of the latter being the actual skin surface. The basal cells at the bottom are cylindrically shaped and are arranged perpendicularly to the surface. The cells in the immediately overlying layers assume polyhedral shapes, while toward the surface they become flattened and are arranged parallel to the surface. In the topmost layers the cells lose their nuclei and are finally shed from the surface as thin, microscopic flakes.

The epidermis constantly renews itself by the formation of young cells in the basal cell layer. Mitoses are always found in this layer and become more numerous when the skin is irritated. *Melanin*, the iron-free, brown pigment of the skin, is found mainly in the upper parts of cylindrical basal cells as small granules grouped to form caps over the basal cell nuclei. Thus the skin pigment is situated mainly in the bottom layer of the epidermis but at the highest pole of each individual cell. From here it is carried upward as far as the horny layer, but also downward into the cutis. Scattered among the cylindrical cells in the basal cell layer there is also an interconnecting network of dendritic cells called

melanocytes (dendritic melanoblasts or Ehrmann's cells), which are believed to be the cells in which melanogenesis primarily occurs. The dendritic melanocytes extend upward into the entire layer of the stratum spinosum.

In the *stratum spinosum* the cells have become polyhedral. Protoplasmic bridges appear to cross the intercellular spaces from cell to cell, giving, at first glance, the impression of prickles or spines. For this reason the cells of this layer have been called *prickle cells*, and this whole epidermal layer is named the *stratum spinosum* or *stratum acanthoticum* (Latin, *spina;* Greek, *akantha*, a "spine," "thorn," or "prickle").

The *stratum germinativum*, together with the stratum spinosum, forms the part of the epidermis which is actually living and capable of reaction. Therefore, one frequently is in need of a word which encompasses both layers. The terms *rete malpighii*, rete mucosum, or just rete for short are commonly used for this purpose. More precisely, it should be called the rete spinobasale. All rete cells are connected with one another by *epithelial fibers* (tonofibrils).

The *stratum granulosum*, which lies just above the rete, generally consists of one to two layers of flat and, in cross-section, *spindle-shaped cells* which are arranged parallel to the skin surface and contain rather large granules of *keratohyalin*. This material is a cellular product associated with keratinization, although it is not generally believed to be a direct precursor of keratin. Its exact relation to keratin formation is not understood. If the keratohyaline layer is very thick, it may become visible through the horny layer as a bluish-white substance. This phenomenon causes the so-called Wickham's striae in lichen planus, which will be described later.

The *stratum lucidum* is a narrow light band between the granular and the horny layers. It contains *eleidin*, a protein derivative which, like keratohyalin, is associated with keratinization, but its exact place in the process of keratin formation is not clear.

The *stratum corneum* is the outermost layer of the epidermis. It is composed of compressed, parallel, homogeneous keratinized lamellae which no longer possess stainable nuclei. The process of keratinization begins in the stratum spinosum, where keratinizing protoplasmic fibrils pervade the intercellular bridges in basket-like fashion. From the top of the horny layer, groups of keratinized and flattened cells are shed as microscopic scales, a process which goes on unnoticed, so to speak, as insensible desquamation. The smooth texture, dull sheen, and water resistance of the horny layer are qualities imparted by its content of lipoid substances derived from keratinizing cells as well as from secretion from the sebaceous glands.

Between the epidermis and the cutis lies a *border layer* of fine interwoven fibers in whose meshes circulates epithelial lymph. This layer is connected with the epidermis by footlike processes of the basal cells and with the cutis by fine collagenous and elastic connective tissue fibers.

The *cutis* consists of a network of *collagenous* (meaning "glue-generating") and spirally twisted *elastic fibers*. This composition from two types of fibrous elements makes the skin tough as well as expansible, so that structurally it can be likened to an elastic suspender. In the meshes of the fibrous elements are relatively few oblong *connective tissue cells*, and in pigmented skin areas also rather large, more or less star-shaped cells which contain coarse granules of pigment. This pigment, however, was not formed by these cells but was picked up from the basal layer of the epidermis and transported into the cutis. Thus they are merely *carriers* of pigment, called *melanophores* or *chromatophores*.

The connective tissue of the cutis projects finger-like processes called *papillae* into the epidermis above it. Since the epidermal rete fills the space between these digitations, a system of *rete ridges* develops. Therefore, in vertical cross-section, the border between epidermis and cutis appears to be wavy. One should, however, keep in mind that only the upward-directed curves represent actual individual projections, while the depressions between them form a continuous network of ridges. (Because of the appearance in cross-section, the erroneous term *rete pegs* is often used rather than the correct term, *rete ridge*.) All papillae—i.e., the cutis projections—as a whole form the important uppermost part of the cutis, called the *papillary body* or the *stratum papillare*. The zone beneath the papillae is termed *stratum reticulare*. The histopathologist frequently needs a special word for the uppermost part of the stratum reticulare which adjoins the papillae and forms their common base. The term *stratum subpapillare* is used for this structure.

Like the epidermis, the cutis is also of widely varying *thickness* on different parts of the body surface. Its tissue structure may be *loose* or *dense*, to give widely varying degrees of firmness or toughness to the skin. The cutis is particularly loose on the eyelids, the dorsa of the hands, and the genitalia. For this reason, these sites are liable to form excessive and even giant accumulations of fluid (edemas). In contrast to the epidermis, the cutis is everywhere well supplied with blood and lymphatic vessels.

The *blood vessels* of the cutis form a superficial (subpapillary) vascular network beneath the papillae and a deep (deep-reticular) one at the border between cutis and subcutis. Both vascular networks run parallel to the surface of the skin and are connected by anastomoses, which also supply the appendages of the skin (hair follicles, sebaceous and sweat glands). The upper network sends capillary loops vertically into the papillae.

In addition to the blood vessels, the cutis contains a lymphatic system. In the epidermis, lymph circulates between the rete cells and fills the *intercellular spaces*. Lymph also collects in the border between epidermis and cutis. In the cutis and subcutis there occur actual *lymphatic capillaries and vessels* which frequently accompany the veins.

The skin is supplied by the autonomic, as well as the cerebrospinal, *nervous*

system. The autonomic, *vegetative nerves*, which are non-medullated, run in the cutis, there supplying the blood vessels, the smooth muscles, the glands, and the hairs. The *cerebrospinal nerves* ascend into the epidermis almost as far as the horny layer. They are medullated but lose their medullae before entering the epithelium. Some of these nerves terminate as free nerve fibrils, while others form complicated terminal apparatuses which represent perceptive organs of sensation. These include Merkel's tactile cells around the hair follicles and a whole series of different nerve corpuscles in the cutis, all of which have been named after their discoverers (Meissner, Krause, Ruffini, Vater-Paccini, Golgi-Mazzoni).

The *subcutis* consists of a tenuous network of connective tissues which carry blood vessels and nerves. Its meshes are filled with grapelike clusters of fat tissue. This skin layer is also of variable thickness in different regions of the body. The thickness of this fat-containing layer obviously also depends, to a large extent, on the general nutritional status. This layer has manifold functions, such as mechanical padding, thermal insulation, and storage of reserve food and water. The rounding of body form which it accomplishes lends beauty to the female figure. The amount of subcutaneous fat under given nutritional conditions is determined locally by influences intrinsic in the skin. Thus abdominal skin, if transplanted without fat to the dorsum or palm of the hand, will develop subcutaneous fat tissue along with any general weight increase as if it were still part of the paunch.

Appendages (adnexa) of the skin are oil and sweat glands, hair, and nails. They all are of ectodermal origin.

The *sebaceous glands* (glandulae sebaceae) are situated in the upper part of the cutis and open mostly into a follicle, thus forming, in general, a lateral annex of the hair follicle. Generally, where the gland is very large, the associated hair and its follicle are small and vice versa. Certain areas, however, have *free* sebaceous glands which have no connection with the follicle. These free glands can be found in the vermilion border of the lips, in the inner laminae of the foreskin, and in the labia minora. The sebaceous glands are *acinous* ("grapelike") in type, having sacculated lobes. They consist of large cells whose cytoplasm in cross-section presents a honeycomb-like appearance by a process of fatty degeneration. The entire cells become converted into sebum. Thus their secretion is of the holocrine type. These glands occur most numerously on the nose and ears and along the anterior and posterior upper mid-line of the body. These latter areas also tend to accumulate sweat when it is profuse and are hence called the *sweat furrows*. The palms and soles are devoid of sebaceous glands.

The *sweat glands* (glandulae sudoriferae) mostly lie deep in the cutis or even in the subcutis. They are fundamentally coiled, double-layered, blind tubules. Their long ducts run upward more or less vertically and then wind themselves

like corkscrews through the epidermis, to end finally on the surface in tiny openings called *sweat pores*. The sweat gland cells actively secrete sweat, a watery, acid fluid. All sweat glands are merocrine, which means that their products consist of a secretion only and not of parts of cells. The cells of the sweat glands do not die in the process of secretion. The ordinary small sweat glands are called *eccrine*, to indicate that no cellular protoplasm is shed with the secretion. Besides these eccrine sweat glands, there exist in the axillary and pubic areas and also around the nipples larger *apocrine* coil glands which, like sebaceous glands, empty their secretion into the hair follicles. Apocrine sweat is mixed with fragments of protoplasm from the larger glandular cells and is a weakly acid to slightly alkaline milky secretion. Anatomically as well as functionally, the mammary glands are related to the apocrine sweat glands.

The *hairs* and their follicles are implanted obliquely into the cutis. They are arranged in streams and whorls. The part of the hair which protrudes from the skin is called the *hair shaft*. It has a roughly cylindrical shape and consists of long, spindle-shaped, horny fibers, which, according to the race, contain more or less melanin. The hair shaft contains a main *cortex* and is covered by a *cuticle*, whose scales are arranged like shingles on a roof. The shafts of stronger hairs also contain central medullae. That part of the hair which lies within the cutis is misleadingly called the hair *root*. It is surrounded by the follicular sheaths, which, on the surface, continue into the epidermis and cutis. The hair root has a swelling at the base, called the hair *bulb*. Large hairs reach deep down into the cutis or even into the subcutis. The hair bulb, which represents the generative tissue of the hair and contains many mitoses, overlies and partially envelops the hair papilla. This hair *papilla* consists of connective tissue and carries blood vessels, from which the hair bulb derives its nourishment. On the average, a hair grows almost 1.5 cm. ($\frac{5}{8}$ inch) per month or about 15 cm. (6 inches) per year. After a certain period, which amounts to approximately 3 years for the long hairs, the hair separates from the bulb but still contains a club-shaped end (club hair) and is then finally expelled by a developing new hair. Thus a continuous *change of all hairs is constantly* in progress.

The hair root is incased in the *hair follicle*, which consists of several layers. The innermost layer is the *inner root sheath*, a thin epidermal stratum of cells. It forms a cuticular sheath, the cells of which tightly interlock with the cells of the hair cuticle. It is, in turn, surrounded by the *outer root sheath*, which represents a continuation of the epidermal rete into the mouth of the hair follicle. This epidermal layer is coated by the *hyaline or vitreous layer*. The whole epidermal structure is surrounded by a relatively dense connective tissue, *the connective tissue hair follicle*, in which the arrector pili muscle is anchored.

The arrectores pilorum muscles consist of smooth muscle fibers and, like the other appendages of the skin, are subserved by the autonomic nervous system. The muscle fibers run from the uppermost layers of the cutis obliquely down to

the hair follicle, so that their contraction raises the hair. Their action becomes visible on the surface of the skin by the formation of transient little bulges which simulate papules, a phenomenon generally known as "goose flesh" or "cutis anserina." Contraction of these muscles also enhances the delivery of sebum. Besides the muscles of the follicular apparatus, one finds smooth muscle fibers in certain areas of the cutis (e.g., scrotum, nipples) which form coherent muscular layers.

There are various types of hairs, including the *long hairs* (scalp, bearded area, axillae, pubes), the *bristle hairs* (eyebrows, lashes, vibrissae of the ear and nose openings), and the *downy hairs* (lanugo) which cover almost the entire body except the palms and soles, the fingertips, and the foreskin. In the fetus they form a dense growth of downy hairs (*primitive or fetal hair growth*), which, however, either sometime before or shortly after birth starts being shed. At the time of birth, the development of the secondary (*permanent*) hair growth is already in progress, and fetal hairs are gradually replaced by terminal hairs. In the hair covering of infancy, both types, fetal and terminal, are simultaneously present. At puberty, terminal hair development is everywhere completed. The hairy covering then consists of the *diffuse hairy coat*, which has replaced the fetal lanugo, and the sexual hair growth, which, under the influence of the sex hormones, appears only in certain regions (face, axillae, mons pubis).

The *nails* consist of the *nail plates*, which are intimately connected with the epidermis of the *nail bed* (hyponychium). The nail plates are more or less convex, smooth, translucent, and horny. The nail bed has no part in the formation of the nail plate except for its most proximal portion, the *matrix*, which underlies the so-called nail root, the imbedded posterior edge of the plate. The matrix is actually the productive part of the nail bed, from which originates the growth of the nail. It extends from the proximal end of the nail to the distal border of the *lunula*, a milky-colored, crescent-shaped zone of the nail, which indicates the area where the nail plate is still connected with the matrix. Posteriorly and laterally, the edges of the nail plates are inserted into the *nail grooves*. They are covered by the *nail fold* or *nail wall*. The stratum corneum of the nail fold extends over the nail plate, forming the *nail cuticle*, which gradually detaches itself from the growing nail. At the free edge, the nail plate detaches itself from the nail bed. From the matrix, where it grows, the nail plate moves distally at an even rate of almost 1 mm. per week or 3–4 mm. per month.

Pathological processes in the skin may, of course, take place in various layers. Most of them are epidermo-cutaneous in nature so as to cause changes simultaneously in the epidermis and in the cutis.

EPIDERMIS

In the epidermis, either single or multiple layers may show pathologic changes. The stratum corneum may be thinned or thickened. In the latter

case the thickening may consist of normal keratin (*hyperkeratosis*) or of an abnormal keratin in which the cellular nuclei are retained and are stainable (*parakeratosis*). In the latter case the stratum granulosum, which is increased in hyperkeratosis, is usually lacking, as is also the stratum lucidum. Hyperkeratosis and parakeratosis may be seen side by side in the same histologic section. Another form of abnormal keratinization, called *dyskeratosis*, is characterized by premature formation of individual, double-contoured, rounded, and enlarged keratinizing cells (*corps ronds*) and their shrunken end-product granules (grains). These three types of pathological keratinization will be more fully described later.

The horny layer may be thickened as well as loosened (scaling); it may be excessively saturated with sebum; it may contain pigment granules (in hypermelanotic conditions); or it may show accumulations of transmigrating leukocytes or their pyknotic nuclear residues (so-called micro-abscesses, especially in psoriasis).

If the stratum granulosum is thickened, as is usually the case in hyperkeratosis, the condition is called *granulosis*. In lichen planus, the granulosis is often so marked that the areas of increased accumulation of granulosum cells can be recognized with the naked eye as bluish-white, little stripes and rings (Wickham's striae). Analogously to the terms *hyperkeratosis* and *granulosis*, a thickening of the rete, caused by an actual increase in rete cells and not merely by edema, is called *acanthosis*, so as to refer to the stratum acanthoticum or spinosum. In this condition the number of cellular layers is increased, and the rete ridges, therefore, may appear elongated. Acanthosis is encountered in a great variety of dermatoses, especially in those marked by inflammations. Conversely, the rete may be thinned, and the entire epidermis reduced to a very few layers of cells. In this case the rete ridges are usually absent, as is the case in scars (see p. 3 and Fig. 155). Intercellular edema in the epidermis may deform and push apart the epithelial cells to such a degree that the intercellular bridges tear, giving rise to microscopic vesicles which give the rete a spongy appearance (*spongiosis*). These microscopic vesicles may coalesce and form macroscopic vesicles (*vesiculae*). Vesicles may also be caused by *intracellular edema*, starting with unicellular vesicles which later coalesce (*altération cavitaire*) or by necrobiotic processes (*ballooning* or *reticular degenerations*). The significance of these different types of vesicle formation will be discussed later on page 44.

Of course, the rete cells may become *tumor cells* and send invading extensions into the structures beneath (epithelioma). In other instances, the entire epidermis or only one or more upper layers of it may be lacking (erosions, excoriations). In the stratum basale, the number of mitoses may be increased or the amount of pigment in this layer may be greater or less than normal. In a considerable number of inflammatory skin diseases there occurs edematous destruction of the basal layer with removal of the pigment (mostly by pigment-laden migratory cells, called *melanophores*) into the cutis (*incontinentia pig-*

menti). This phenomenon is most marked in the pigmentary dermatosis of Siemens and Bloch.

CUTIS

The *papillae* of the cutis may show dilated blood vessels, or they may be extended with edema and shaped like mushrooms (lichen planus). In other conditions, they are thinned, elongated, and finger-like, so that the adjoining rete ridges reach far down (psoriasis). Very frequently, there is a *cellular infiltrate* in the cutis. The infiltrate may be restricted to the stratum reticulare (papillae and subpapillary zone), ending sharply at its lower border. Or it may extend far deeper, with a marked tendency to follow blood vessels (*perivascular infiltrate*).

The types of *cells* forming the infiltrate may vary widely. In many acute inflammations, an infiltrate of *polymorphonuclear leukocytes* may be found. Under other circumstances, especially in subacute and chronic inflammation, *lymphocytes* may predominate. Sometimes connective tissue cells which resemble epithelial cells (*epithelioid cells*) may accumulate and be surrounded by a fringe zone of lymphocytes, while centrally there may be multinucleated *giant cells* of the Langhans type. There may also be caseation. This so-called tuberculoid structure is encountered not only in tuberculosis of the skin but also in a great variety of other granulomatous diseases. *Eosinophils* may be increased in number, or the picture may be dominated by *fibroblasts* and *histiocytes*. Besides the Langhans type of giant cell, other types are known, including Dorothy Reed–Sternberg cells in Hodgkin's disease, Touton giant cells in xanthomas, foreign-body giant cells, nevus giant cells, and epithelial giant cells such as occur in Bowen's disease. In common intradermal nevi, there occur *nevus cells*, which represent another type of epithelioid cell believed to derive primordially from the embryonic neural crest. In deeper chronic inflammations one frequently finds an increase in *plasma cells*, a non-granulated type of leukocyte with an eccentric, often cart-wheel-shaped, nucleus. In most inflammatory lesions and in the vicinity of tumors, the so-called *mast cells* are increased. This is most marked in urticaria pigmentosa, which, therefore, may be looked upon as a mast cell granuloma. The mast cells can be recognized by their coarse basophilic granules. Certain macrocytic cells, the so-called *melanophores* or chromatophores, may gorge themselves with melanin pigment from the basal layer, as in melanoses and the pigmentary dermatosis of Siemens and Bloch. Accumulation of dermal melanocytes may also occur and give rise to visible blue lesions (Mongolian spot, blue nevus). There may also be found *degenerated* cells and *cellular nuclei* distorted by pyknosis or karyorrhexis or *deposits* of blood, blood pigment (hemosiderin), cholesterol (xanthoma cells), calcium, amyloid, mucin, foreign bodies, etc. The cutis may also be invaded by *tumor cells* of variable types and origin.

The connective tissue itself may undergo changes. The *elastic fibers* especially may be changed in their configuration, or they may be scarce or entirely absent

(scars). The collagenous fibers may be subject to a variety of chemical degenerative changes which give rise to altered staining reactions (*collacin, collastin,* and *elacin degenerations*). Such degenerative processes, which make the connective tissue flaccid and non-elastic, form the histopathologic basis of senile skin wrinkling.

SUBCUTIS

Pathologic changes in the subcutis play a part in but few dermatoses and include *sclerotic processes, Wucher atrophy* of the fat tissue, and *fat necrosis.*

In the *blood vessels,* wall changes and thromboses, especially leukocytic ones, may be seen.

GENERAL DIAGNOSIS