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We hope that making available the relevant information on Pachyonychia Congenita will be a means of furthering research to find effective therapies and a cure for PC.
The SKIN

A CLINICOPATHOLOGIC TREATISE

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With 495 Full-Page Illustrations

Frontispiece in Color

ST. LOUIS • THE C. V. MOSBY COMPANY

1954
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nderlying the nail is the hyponychium. The nail matrix is the posterior nail fold continuous with the eponychium. The nail plate or true nail rests on the nail bed. Normally, fine longitudinal lines traverse the nail plate and fit into corresponding grooves (and the dermal papillae) of the nail bed. These lines, which become more pronounced with age, may be observed on both surfaces of the nail. The dermal papillae are flattened over the nail bed but cylindrical at the root and the free edge (Plate 15 D). The dermis is directly fused with the periosteum of the phalanx (Plate 15 B and C).

ReGENERation.—Regeneration of a lost fingernail takes from 100 to 160 days. The period of regeneration is about three times as long for the toenails. The nail regenerates by growing forward from the nail root. The nail plate immediately underlyng the dorsal portion of the nail bed grows simultaneously from behind forward, as can be judged not only from the changing position of a subungual blood clot, but also from the anteriorly advancing mark such as a blotch of silver nitrate placed on the bed after a nail plate has been removed. In other words, the nail plate does not grow by "gilding" over or covering a static nail bed but in conjunction with corresponding growth. There is a type of leukonychia due to a fungus (leukonychia trichophytica) in which the involved white portion remains stationary and does not advance to the free edge. In this form the fungus involves the lower portion of nail which originates not from the matrix but the keratinized nail bed.

Many types of changes that occur in the nail plate furnish important clues in the diagnosis of disease. These changes include fine pitting of the surface, Beau's lines, discolorations, dysplasias, thickenings, and spontaneous loss of the nails. General debilitation, psoriasis, reaction to Atubrine, fungi, congenital disorders, idiopathic pigmentary disturbances, and neoplasia may produce characteristic changes in the nails which are discussed in the appropriate sections.

Nerves

The cutaneous nerves, particularly the sensory components, constitute a complex system in contrast to the sensory innervation of other organs. This complexity of nerve fibers and nerve endings subserves the wide variety of stimuli received from both the external and internal environment. The stimuli include heat, cold, pain, touch, and pressure. These are predominantly external stimuli, but the internal environment with psychic stimuli, as well as controlled or involuntary excitation of the cutaneous vessels and glands as in blushing, shock, and many other aspects of homeostatic readjustment, is also involved in the neural activities of the skin. The cutaneous structures concerned with neural influence include not only blood vessels, sweat glands, arrectores pilorum, and hair follicles, but also the epidermis and even the collagen of the dermis by virtue of cholinergic, urticarial, and serotonergic trophic responses among others. Clearly, the comprehension, control, or modification of the responses to this broad and potent gamut of stimuli is of pivotal importance in the ultimate therapy of a tremendous number of eruptions, particularly the psychodynamic and allergic varieties.

The segmental distribution of the cutaneous sensory nerves is fairly constant in all individuals so that from the location of an anesthetic area the particular nerve involved can be indicated, although some overlapping of the sensory innervation exists. This overlapping of innervation is greater in some areas (the forearm) than in others (the fingertips). Moreover, the concentration of sensory nerves varies, there being many more nerve endings in the region of the lips, the nipples, the glans penis, and the finger pads than in the skin generally. In any area of skin the branches of nerves, both medullated and nonmedullated, ramify as plexuses into the skin from radial directions, so that the likelihood of anesthesia from a surgical incision is minimized. The recovery of sensation in split-thickness grafts has been found to be partial and patchy, usually appearing between the seventh and ninth postoperative week. Naturally the degree of recovery of sensation is dependent on the relative absence of scar tissue and the integrity of the nerves in the recipient area.

The nerves may be identified even with routine stains (hematoxylin and eosin) as far as the level of the junction of the upper and middle thirds of the dermis (Plate 20 C). Beyond this level special nerve stains are necessary for the demonstration of the terminal axon fibers as they enmesh and innervate hair follicles, sweat glands, sebaceous glands, arrectores pilorum, and vessels.
A. NAIL OF ADULT with central focus of common form of leukonychia.

B. LONGITUDINAL SECTION OF NAIL from 3-month human fetus.

C. LONGITUDINAL SECTION OF NAIL from 4-month human fetus.

D. MATRIX and ROOT OF NAIL. Disturbances in this critical area are responsible for many types of changes in the nail plate. (From 4-month fetus.)
They are necessary also for certain of the nerve endings, particularly those beaded endings which subserve pain (and itching), the Ruffini spindles, and also the Merkel-Ranvier corpuscles. However, special stains are not at all necessary for the demonstration of such endings as Pacinian corpuscles, Meissner corpuscles, the end bulbs of Krause, taste buds, and neuromuscular spindles, all of which are quickly detectable with simple hematoxylin and eosin or other routine stains (Plate 16). The nerve endings are found in the upper cutis and epidermis, except for the Pacinian corpuscles, which are usually located in the subcutaneous fat. The individual nerve endings are considered in the following paragraphs.

**Meissner Corpuscles.**—The Meissner corpuscles, which average about 100 microns in diameter (0.02 to 0.045 mm.), are located in the immediate subepidermal portion of most of the papillae of the skin particularly of the ball of the digits (about 23 per square millimeter) and also of the palms and soles. They may be easily recognized in routinely prepared sections colored with ordinary stains such as hematoxylin and eosin (Plate 16 A). Silver stains emphasize details of the transverse nerve fibers. These fibers, interspersed with vesicular nuclei, are nearly folded like a packet of wool, forming the terminus of a medullated nerve fiber. The capsule of the corpuscle appears to be formed from the nerve sheath, but the nerve enters the corpuscle as a naked axon cylinder. Somewhat similar formations (lamines folliculaires) are noted in the depths of intradermal nevi and have been specifically interpreted, in our opinion, as evidence of the neurogenic nature of these nevi (Plate 392 C and D). The Meissner corpuscles receive sensations of touch.

**Merkel-Ranvier Corpuscles.**—The Merkel-Ranvier corpuscles are poorly defined, meniscus-shaped nerve endings which are stated to be located directly within the epidermis as the arborization of a dermal nerve fiber. They appear to be invisible with ordinary stains but are said to be argyrophilic. Their precise function is not known, but they are thought to represent tactile nerve endings. There has been much confusion regarding the relationship of the Merkel-Ranvier corpuscles to the cellules claires of Masson. The evidence currently suggests that these clear cells are not nerve endings but are simply modified basal cells. There are also controverted interpretations of the so-called Langerhans' cells, which are referred to by Masson (1951) as "worn-out melanoblasts" (worn out "clear cells") but about which there is considerable doubt as to even their cellular nature (Maximov and Bloom, 1953).

**Pacinian Corpuscles.**—The Pacinian corpuscles measure approximately 1 to 4.5 mm. in diameter, so that they may actually be seen grossly. They are found predominantly not only in the lower cutis and subcutis, but also in muscles, tendons, joints, and the serosa of abdominal viscera, and even within the parenchyma of the pancreas. The mesentery of the rat contains so many of them that this tissue is used for the demonstration of the corpuscles to students. They are easily detected with routine stains (Plate 16 C). The structure consists of thin, concentrically arranged collagenous fibers, separated by layers of fluid, surrounding a fluid-filled central cavity into which a medullated nerve penetrates as an axon fiber and to which changes of pressure are transmitted. The medullary sheath is lost after it pierces the capsule, and the axon fiber terminates into two or three swollen branch endings. The nerve itself is demonstrable with silver stains (Bieleskowsky's stain). The Pacinian corpuscles are assumed to receive deep pressure and to effect proprioceptive sensations. The end bulbs of Krause are club-shaped structures somewhat similar to the Pacinian corpuscles but are a good deal smaller, averaging about 0.03 mm. in length. They are located in greatest numbers in the glans penis and clitoris but are also found at the edge of the eyelids, the soles of the feet, and in oral

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**PLATE 16. ANATOMY NERVES**

A. **MEISSNER CORPUSCLE**, from skin of foot, which transmits the sensation of touch.

B. **TASTE BUD** incorporated in epithelium of tongue.

C. **PACINIAN CORPUSCLE** which suberves pressure.

D and E. **NEUROMUSCULAR SPINDLES** of skeletal muscle which have a proprioceptive function.
and other genital mucose membranes. They are stated to transmit sensations of heat and cold.

**Ruffini Spindles.**—The spindles of Ruffini are found chiefly in the lower dermis and subcutis of the palms and soles. They are made up of a network of nerve fibrils derived from a nonmedullated fiber and enclosed in an elastic and collogenous capsule. They are about the size of Krause’s end bulbs and are detectable only with special stains. They are assumed to receive sensations of heat (Plate 1).

**Taste Buds.**—Taste buds are still another form of nerve ending readily visible with ordinary stains (Plate 16 B). They are found predominantly in the tongue but are present also in the mucose of the epiglottis and larynx. The taste buds are ovoid collections of crescentic supportive or sustentacular cells, among which are intermingled long, narrow, gustatory or neuroepithelial cells. These latter cells extend to the pit or pore of the bud which opens on to the surface. Axon fibers reach the buds of the anterior two-thirds of the tongue from the chorda tympani of the facial nerve and by way of the glossopharyngeal nerve for the posterior third. It is presumed that each of the tastes (salt, sweet, sour, and bitter) is subserved by specialized receptors.

**Muscle Spindles.**—Another type of nerve ending might be mentioned even though it is not found in the skin or mucose membrane. It is the neuromuscular spindle found scattered in skeletal muscles, including the extraocular muscles. The endings have a proprioceptive function. They are variable in size, from 100 to 2,000 microns in length and 20 to 100 microns in width. They are easily detectable with routine stains by their oval or circular cross sections with a delicate capsule enclosing loosely disposed nerve fibers enmeshed about several muscle bundles (Plate 16 D and E) (Cooper and Daniel, 1949).

**Glomera.**—The precise anatomic relationship between nerve twigs and capillaries is still not entirely clarified, although the contact must be intimate. In addition to these vasomotor nerve plexuses, there is a specialized apparatus known as a glomus which serves also to regulate the blood flow through the skin. The glomus consists of a nonmedullated nerve in association with an afferent arteriole and an efferent nerve, linked by a sinuosoidal channel called the Suequet-Hoyer canal. So-called glomus cells, round uniform structures of about the size and shape and appearance of nonpigmented intradermal nerve cells, cuff the vessels in several layers. These cells are presumed to have the capacity of contractility for purposes of altering the caliber of the vessels they surround. Glomera, which average about 150 to 300 microns in diameter, are particularly abundant in the finger tips, where their concentration is about 500 per square centimeter in the nail bed. They may also be found in the skin of other parts of the body, in joints, and in viscera. Clinically and histologically, characteristic tumors arise from glomera (Plate 18 A and B).

**Blood Vessels**

The blood vessels of the skin are different in certain basic respects from those of the viscera. In the first place, the cutaneous vessels are exposed to rapid and wide variations of external heat and cold, to ultraviolet radiation, to trauma, and to widespread alteration by disease of their overlying epidermis. Second, there is in reality a relative paucity of cutaneous capillaries in contrast to their number in other organs, such as muscle, kidney, or intestine. For example, the concentration of capillaries may average 18 to 65 per square millimeter of skin, whereas that of skeletal muscle may be 1 to 2 thousand per square millimeter (Krogh, 1929; Zotterman and Witzel, 1926). Third, the vascular system of the skin is critically important in the homeostatic regulation of blood volume in the more vital areas of the body. This homeostatic control of the over-all body economy is on occasion achieved at the expense of the skin through neglect of its metabolic requirements. Psychosomatic reactions (blush-