Embryology of the Human Nail

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The nail anlage appears in fingers of embryos 9 weeks old.

Externally the earliest recognizable nail structure is the primary nail field which is present in embryos at 10 weeks.

The first nail structure to keratinize is the distal ridge and is seen in embryos as early as 11 weeks.

The earliest matrix was found in the area of the lunula in embryos of 13 weeks.

Differentiation of the matrix primordium cells into matrix cells occurs in a distal to proximal direction beginning from the lunula. This process is manifested by a vacuolation of the matrix primordium cells, which is seen first at the lunula and later moves proximally as the embryo matures. By 20 weeks all the matrix primordium cells have matured into matrix. Possibly a small cluster of primordial cells remains in adult life at the most proximal tip of the matrix.

The matrix produces nail plate by a parakeratosis-like process without keratohyaline granules.

In embryos 13 weeks old the keratinization of the nail bed involves the production of keratohyaline granules and a stratum corneum. The adult nail bed produces a horny layer by a process which does not involve keratohyaline granules and a stratum corneum but is parakeratotic-like. The change in the process of keratinization of the nail bed is seen as the nail plate grows over the nail bed in embryos 20 weeks and older. Sulfhydryl stains are strongly positive in the nail plate of embryos early in life. This reaction decreases in intensity as the fetus becomes older, and in the adult nail it is mildly to variably positive.

Disulfide stains are mildly positive in the nail plate of embryos early in life. This reaction becomes more intense as the embryo becomes older and in the adult nail is strongly positive.

Introduction

Interest in the nail began in the late 19th century. Zander,[27,28] Kölliker [13] and Unna [26] investigated the embryology of the human nail. At the same time, Boas [4,5] studied the comparative anatomy of the claws of reptiles, birds, and mammals. Henle [10] and Zander [28] also participated in the study of the comparative anatomy of nails of animals

After the initial spark of interest, the nail literature was enriched by many authors, both on the embryology and the anatomy of the human nail.[1,6,8,11-14] Among the outstanding studies of the early 20th century, the work of Felix Pinkus [22] stands today as a cornerstone of information on the nail. Also in the early 20th century, F. Bruhm's study on the nails of the higher apes [7] and LeGros Clark's work on the comparative anatomy of the claw-like nails of the lower primates [14] contributed much to knowledge of the structure in primates.

Most of the earlier investigators accurately described the developmental stages of the human nail, but they were handicapped by the technical shortcomings of their time.

In spite of confusion from the many synonyms in embryological nail terminology, the

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authors agreed that the nail plate is formed entirely by the matrix cells and that the nail bed does not contribute to the formation of the nail plate. In 1954, Barton Lewis [16,17] challenged this view and presented the concept of a nail unit consisting of a dorsal, intermediate, and ventral nail. The greater portion of this nail unit consisted of the intermediate nail or nail plate. Lewis based his differentiation of the nail unit on the use of the silver-proteinate stain.

The purpose of this study is to describe further the development of the human nail and to attempt to clarify the terminology of nail embryology.

Materials and Methods

Fingers and toes of human embryos of varying ages from 9 weeks (3 cm.) to full term (30 cm.) were prepared for histologic examination. The approximate age of the fetus was determined by crown-to-rump measurements.[18] Specimens were prepared for routine paraffin embedding and cut at 6 micra. Those used for special stain techniques to demonstrate sulfhydryl and disulfide groups in proteins were fixed in 1% trichloroacetic acid in 80% ethyl alcohol and cut at 10 micra.[8] All other specimens were fixed in 10% buffered formalin. No decalcification technique was employed, as fetal bone posed no technical difficulties during sectioning. Pollices and halluces were used to provide a control on the variations of nail growth in different fingers.[15]

Longitudinal, near midline and cross sections, as well as serial sections, were made of all material. Sections were floated in a solution of Meyer's albumin and water, 1 to 20, to expand the paraffin and adhere the section to the glass slide. Sections to be stained for sulfhydryl and disulfide were floated in the same solution; after expansion of the paraffin, the albumin solution was pipetted off because albumin gives a positive sulfhydryl and disulfide reaction.

Sections were stained with hematoxylin and Biebrich's scarlet, orcein-Giemsa,[23] periodic acid-Schiff stain, Feulgen, sulfhydryl, and disulfide stains.

The small dimensions of the fetal digits require careful orientation in order to obtain true longitudinal and cross sections.

The paraffin blocks of fingers of embryos 6 months or older were soaked in water for a few hours prior to sectioning, to soften the nail plate and facilitate cutting.[30]

Size and Ages of Embryos Used in the Study [18]

Size in Cm. Crown-Rump	Age, Wks.	Size in Cm. Crown-Rump	Age, Wks.
1.75	<4	11.25	15
2.75	9	(2)12.0	16
4.5	10	13.5	17
5.25	11	14.0	17+
5.50	11+	(3)15.0	18
5.70	11+	16.0	20
5.90	11+	17.0	20+
6.0	11+	(2)19.0	22
8.0	13	23.0	26
8.5	13+	24.0	27+
9.0	13+	26.0	30
10.0	14	(2)30.0	36
10.25	14	—	
		30 embryos	

Glossary

The present terminology in nail literature contains many synonyms and is confusing to the author. A glossary is presented to assure proper communication with the reader (Fig. 1).

The nail plate is a flat, roughly rectangular, slightly convex horny plate, the edges of which rest on depressions or grooves on the surface of the distal phalanx of fingers and toes. The nail plate has 2 lateral, 1 distal, and 1 proximal edge.

The nail folds: The nail plate edges are overlapped by cutaneous folds, except for the distal edge. Thus, there are 2 lateral nail folds and a proximal nail fold.

The distal free edge is the edge of the nail plate which extends beyond the attachment of the nail plate to the epidermis of the dorsum of the distal phalanx. The distal free edge is convex in the horizontal plane. The shape of this edge is determined by the shape of the distal edge of the matrix, the lunula.

The nail grooves: If the nail plate is avulsed, the grooves become visible where the nail plate rested. These are potential spaces and only become real spaces in abnormal conditions of the nail, as in paronychia. There are 2 lateral and 1 proximal groove. These grooves are made up by the overlapping of cutaneous folds over the nail plate edges, the so-called nail folds.

The lateral nail grooves: These grooves are shallower and smaller than the proximal nail groove. The epidermis lining these grooves does not contribute to the formation of the nail plate, except in the most proximal portions of these grooves, where it becomes continuous with the epidermis of the proximal groove or matrix.

The proximal nail groove: This is a wedge-shaped groove, the apex of which is directed proximally and obliquely toward the longitudinal axis of the digit. It is lined with 2 different types of epidermis. The ventral portion is lined by the matrix

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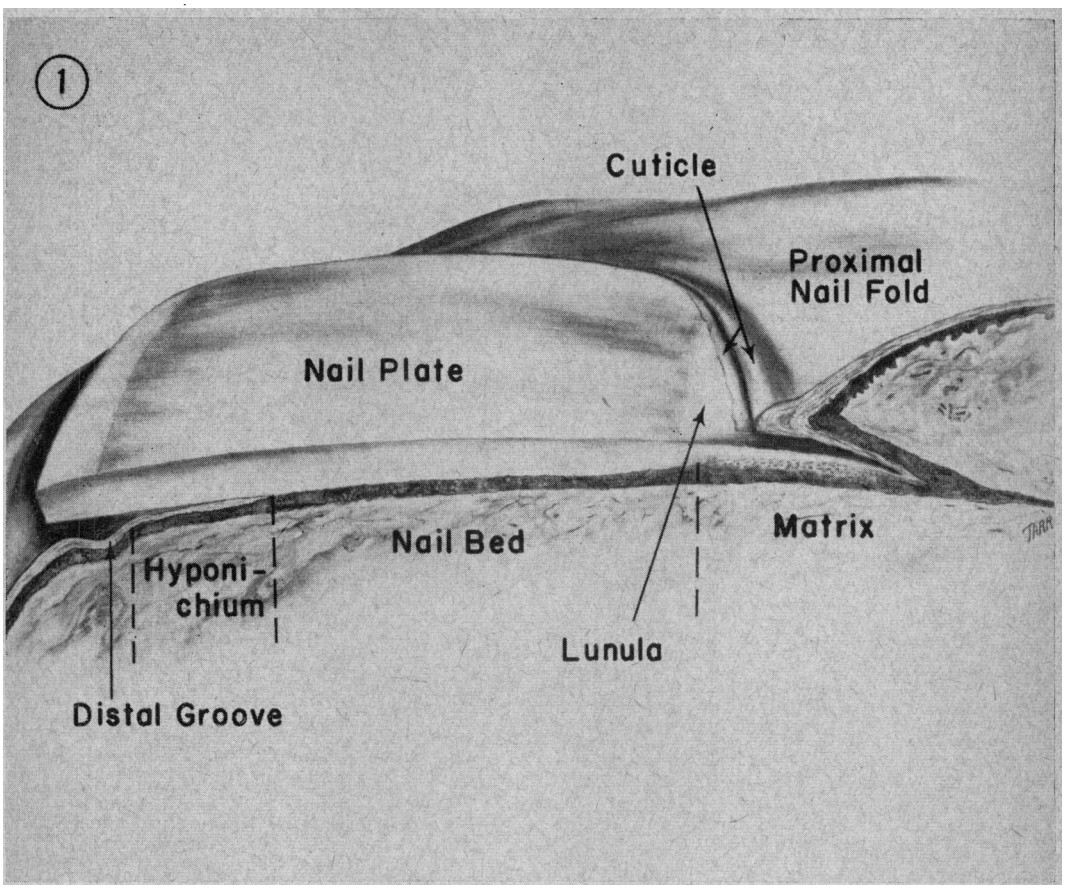


Fig. 1.—Diagramatic drawing of an adult finger tip, showing nail structures through a longitudinal, midline plane.

cells which produce the nail plate. The dorsal portion of the groove does not partake in the formation of the nail plate.

The proximal nail fold and the cuticle: The proximal nail fold is wedge-shaped. The ventral surface is lined with an epidermis, the stratum corneum of which is closely applied to the dorsal surface of the newly formed nail plate and moves with the nail plate, as a sheet of cornified material, a short distance before it desquamates. The dorsal surface of the proximal nail fold consists of the epidermis of the dorsum of the digit. Its stratum corneum, near the tip of the wedge, rests on the cornified material produced by the ventral portion of the fold. These 2 cornified layers constitute the cuticle.

The matrix: The matrix is situated in the ventral portion of the proximal nail groove and is overlaid by the proximal nail fold, although separated from it by the newly formed nail plate. The distal portion of the matrix extends beyond the proximal nail fold and is seen through the nail plate as a whitish opacity with an arc-like border. This portion of the matrix is termed the lunula. The matrix cells form the nail plate.

The primary nail field: This is an area on the surface of the distal phalanx which is delineated by 2 lateral, 1 proximal, and 1 distal groove, all of which communicate with each other. It is termed the nail field in embryos from the ages of 9 to 13 weeks and is the site of the future nail.

The distal groove: In embryos of less than 13 weeks, the nail field is limited distally by a shallow depression termed the distal groove. After the 13th week this depression becomes more definite, deeper, and separates the nail structures from the volar epidermis. It is small and inconspicuous in humans, but in primates it is large and well-defined.

The distal ridge: This structure is a ridge situated parallel and just proximal to the distal groove and is apparent in embryos as early as the 11th week (5.5 cm.). The ridge represents a thickening of the stratum intermedium in this area. As the embryo becomes more mature, the ridge broadens. By the 6th or 7th month, as the nail plate begins to move distally over the nail bed, the distal ridge flattens and, in the adult, becomes what is termed the *hyponychium.*

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The hyponychium: This term will be used to describe the area in the adult nail which evolves from the distal ridge. Earlier investigators believed this structure to be of phylogenetic significance and termed it the "Sohlenhorn."[9] The hyponychium is limited proximally by the nail bed and distally by the distal groove.

The nail bed: This structure is first present in embryos of 13 weeks (7.5 cm.). It is located between the distal ridge and the matrix, or lunula. In adults and in embryos older than 8 months, the nail bed lies between the lunula and the hyponychium.

The matrix primordium: This term is given to the solid wedge of epithelial cells which originate from the most proximal portion of the nail field in embryos of 10 weeks (4.5 cm.). This wedge extends proximally and ventrally into the digit. The

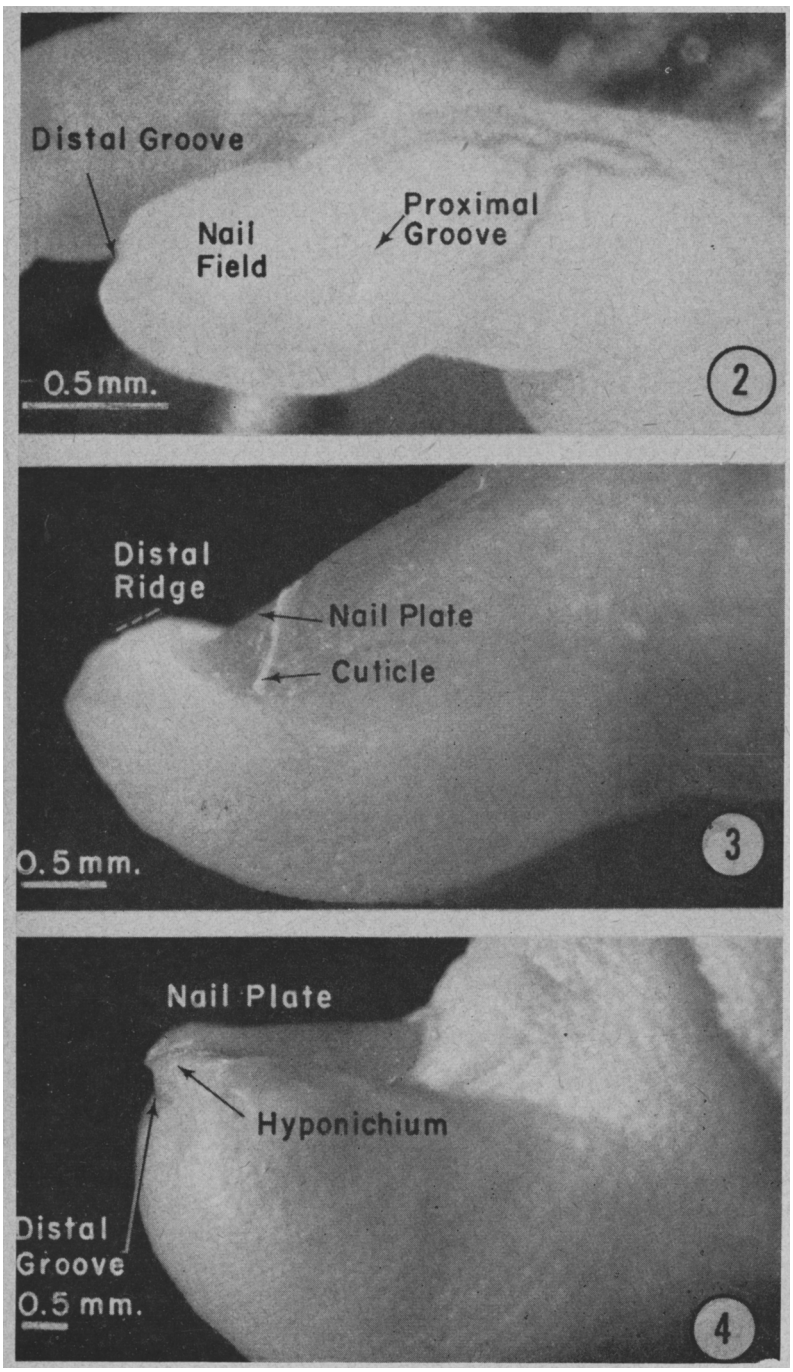


Fig. 2. — Dorsolateral view of a thumb of an embryo 11 weeks old. × 40.

Fig. 3.—Lateral view of a thumb from an embryo 14 weeks old. × 26.

Fig. 4.—Lateral view of a thumb from an embryo 32 weeks old. × 10.

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cells comprising the dorsal portion of the wedge give rise to the epidermis which lines the ventral surface of the proximal nail fold (or dorsal surface of the proximal nail groove). The cells of the ventral portions of the wedge differentiate into the matrix cells lining the ventral surface of the proximal nail groove. Maturation and differentiation of the ventral layer of the wedge into matrix cells occur in a distal to proximal direction, so that the lunula is the first portion of the matrix to differentiate. The most proximal portion of matrix is the last to differentiate into matrix cells.

The Nail Anlage

The earliest recognizable fingers are seen in embryos 42 to 45 days old (16 mm. crown-rump), while the toes lag somewhat and are seen at 52 to 54 days of age (18.5 mm.).[25]

The youngest embryo in this study is 9 weeks old (2.75 cm.). There is no visible external structure of a future nail site. In a longitudinal section of this embryo's thumb (Fig. 5), the distal digit consists of tightly packed undifferentiated mesenchymal cells, vascular channels, and an outer covering epidermis. The epidermis consists of 2 layers; a superficial layer, the periderm, and a deeper layer, the stratum germinativum. The periderm layers consist of 1 to 2 layers of flattened cells. They are incompletely cornified and protect the skin of the embryo.[26] With hematoxylin-Biebrich's scarlet, the periderm cells have a very basophilic nucleus and a slightly pink cytoplasm.

The deeper layer, or stratum germinativum, resembles cuboidal basal cells of adult skin. The epidermis of the dorsal and volar surfaces appears to be similar. The epidermis of the dorsal tip of the digit is called the nail anlage.

The Earliest Nail Structure: The Nail Field

At 10 weeks, the dorsal surface of the distal phalanx begins to show the earliest external changes in the development of the nail. There is a smooth, shiny quadrangular surface which is delineated by continuous shallow grooves. This surface of the phalanx is the "primary nail base" of Zander,[27] better called "primary nail field." At this age (Fig. 6), chondrocytes and young cartilage appear in the mesenchyme. The epidermis consists of 3 layers; a superficial periderm, a well-formed basal or stratum germinativum, and a layer 2 to 3 cells thick between these 2, termed the stratum intermedium. The cells of the intermediate layer have smaller and more oval nuclei than the cells of the stratum germinativum and a vacuolated fibrillar cytoplasm with prominent cell membranes. The matrix primordium is beginning to develop and grow downward as a solid wedge of cells.

The Development of the Distal Ridge: The Earliest Keratinization of the Nail Field

At 11 weeks, the fingers are well formed, with discernable interphalangeal joints (Fig. 2). There is swelling of the volar pads in the distal phalanges. On the surface of the distal phalanx the primary nail field, with well demarcated proximal and lateral grooves, is seen. The distal groove is enlarged and accentuated, partially due to the increased volar touch pads.

A longitudinal section of the thumb (Fig. 7) shows chondrocytes and young cartilage. The connective tissue cells are arranged in fascicles which later will form tendons, muscle, and other mesodermal structures. Nests of basal-like cells are seen in the epidermis of the volar surface of the distal phalanx. These nests represent the anlage of the primary epidermal rete and are first seen in the fingertips. Differentiation of the epidermis of the nail field, just proximal to the distal groove, occurs as a thickening of the stratum intermedium consisting of 6 to 8 cell layers. The uppermost cells have dispersed in their cytoplasm granules of varying size. This structure is the distal ridge and is the first to become keratinized in the nail field. The distal ridge and the volar touch pads accentuate the depth of the distal groove. The distal ridge was not seen to evolve from the "dorsal plume," a term introduced by Barton Lewis.[16,17] The matrix primordium is a

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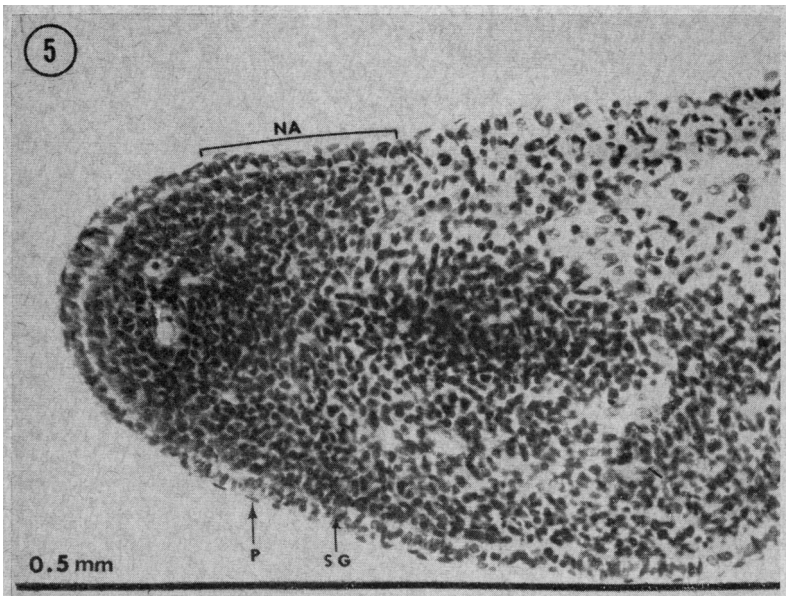


Fig. 5. — Longitudinal section of a thumb from an embryo 9 weeks old; fixed in formalin and stained with hematoxylin-Biebrich's scarlet. The epidermis consists of 2 layers: a superficial layer, the periderm (*P*), and a deep layer, the stratum germinativum (*SG*). The nail anlage (*NA*) can be differentiated from the dorsum epidermis by its closely placed stratum germinativum cells. × 210.

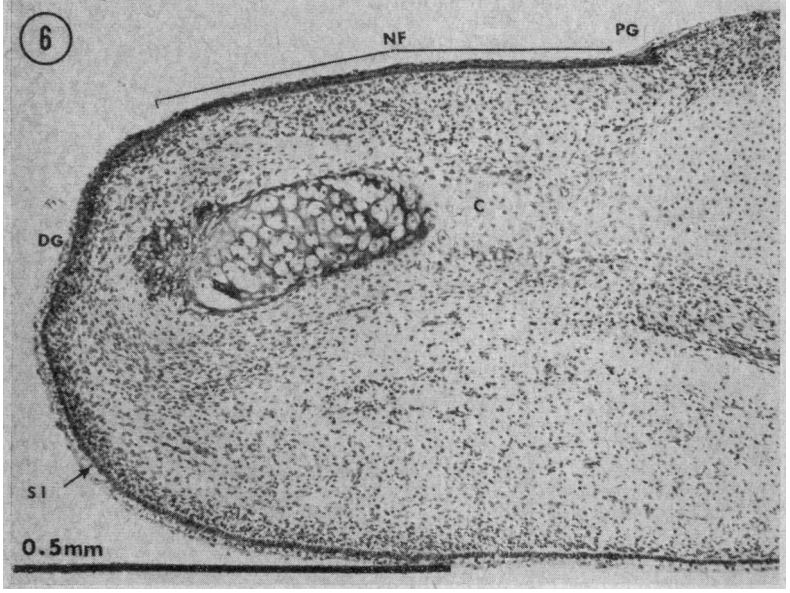


Fig. 6.—Longitudinal section of a thumb from an embryo 10 weeks old; fixed in 1% trichloroacetic acid and stained with hematoxylin - Biebrich's scarlet. The nail field (*NF*) on the dorsal surface of the digit is delineated by the distal groove (*DG*) and the proximal groove (*PG*). The epidermis consists of 3 layers. The stratum intermedium (*SI*) lies between the periderm and the stratum germinativum. Chondroblasts (*C*) are present. × 120.

wedge of cells derived from the epidermis of the proximal portion of the nail field and consists of a double layer of stratum germinativum cells between which is a layer of stratum intermedium cells. The matrix primordium has grown into the substance of the distal phalanx, thus isolating a wedge of dermis dorsal to it. This dermal wedge and its surrounding epidermis will develop into the proximal nail fold.

Stages Preceding Nail Plate Formation: Differentiation of the Nail Bed

At 13 weeks of age, the fingers have elongated, and the nail field lies distal, midway from the tips of the fingers to the distal interphalangeal joints. The nail field can be recognized by its smooth surface. The tips of the fingers have become pointed and a slight swelling is all that remains of the volar touch pads.

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A longitudinal section of the thumb (Fig. 8) shows the cartilaginous outline of the future bony phalanx with calcification distally. The volar epidermis is thicker and more primitive than the epidermis of the nail bed. The epidermal primary rete are present at the tips of the fingers before any other place in the digit.

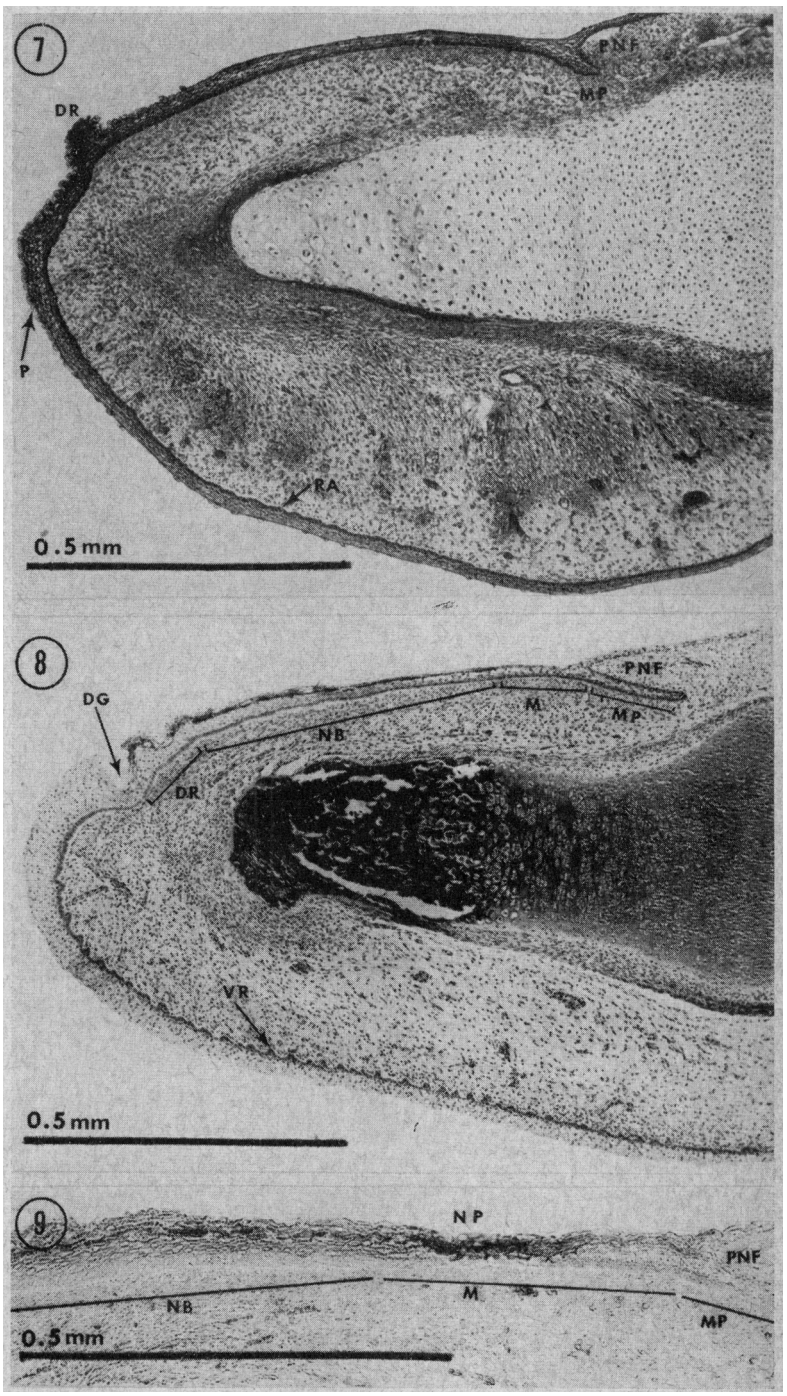
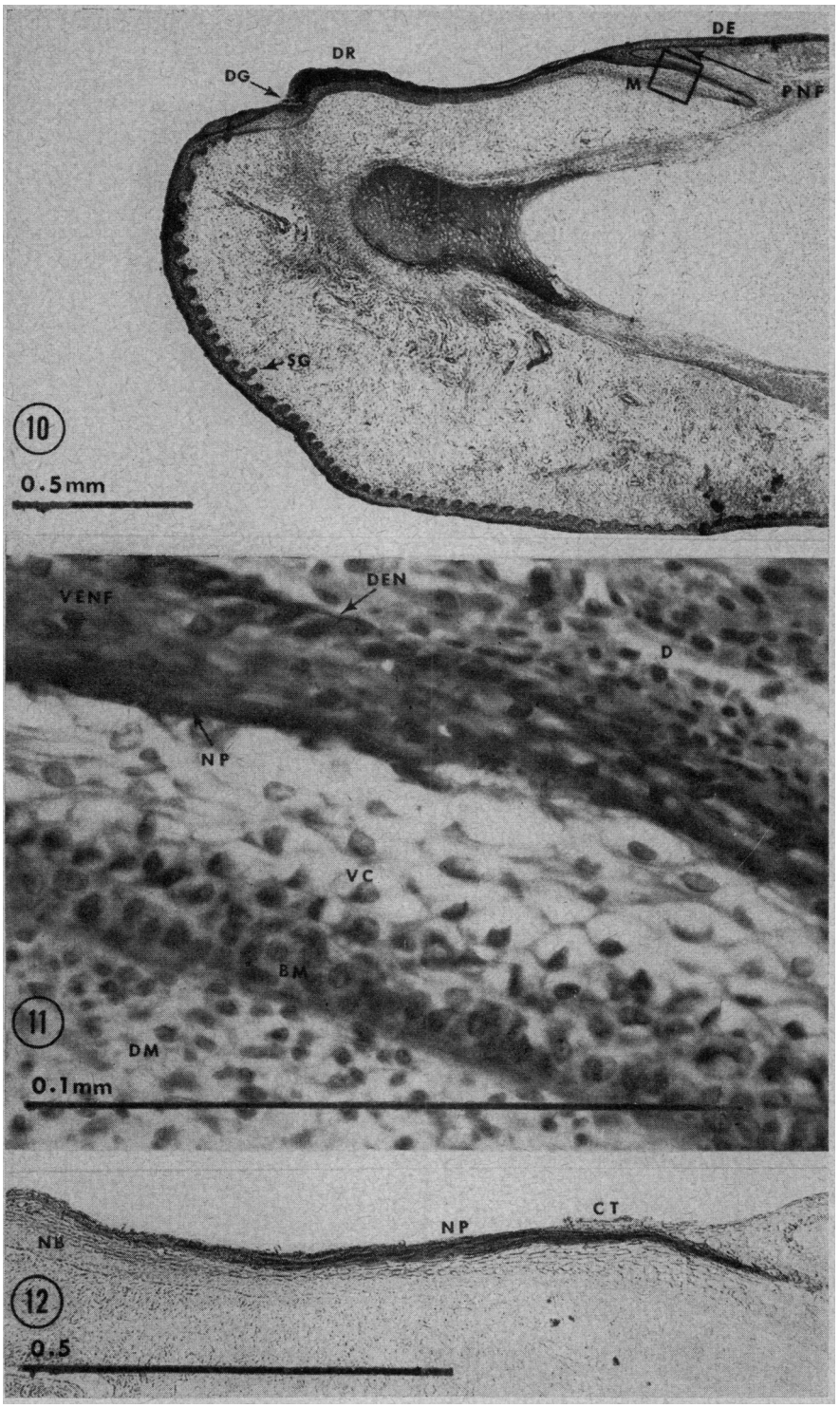


Fig. 7. — Longitudinal section of a thumb from an embryo 11 weeks old; fixed in 1% trichloroacetic acid and stained with hematoxylin - Biebrich's scarlet. The distal ridge (*DR*) is the result of thickening of the stratum intermedium at the distal portion of the nail field. The matrix primordium (*MP*), a proliferating wedge of epidermal cells, creates a wedge of dermis which evolves into the proximal nail fold (*PNF*). Nests of cells proliferating from the basal layer of the volar epidermis represent the primary epidermal rete anlage (*RA*). Periderm (*P*) cells are often lifted from the surface of the epidermis creating the impression of projecting cells. This phenomenon is artefactual. × 80.

Fig. 8. — Longitudinal section of a thumb from an embryo 13 weeks old; formalin-fixed and stained with hematoxylin-Biebrich's scarlet. Differentiation of the nail bed is seen in 3 areas. The distal ridge (*DR*) epidermis has a cornified layer similar to that seen in the nail bed, but the underlying epidermal cells resemble the stratum intermedium of the volar epidermis. The distal groove (*DG*) separates the volar epidermis from the distal ridge. The nail bed (*NB*) epidermis consists of all the layers seen in adult skin. The earliest matrix (*M*) is present just distal to the proximal nail fold (*PNF*) and is characterized by the presence of a parakeratotic-like horny layer. The cells of the matrix have a vacuolated appearance. The rete of the volar epidermis are prominent. ×80.

Fig. 9. — Longitudinal section from the thumb of the embryo in Figure 8; stained for the demonstration of sulfhydryl groups. The nail plate (*NP*) is strongly positive, while the nail bed (*NB*) and the proximal nail fold (*PNF*) are negligible. The matrix (*M*) producing the nail plate is just distal to the proximal nail fold. × 96.

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The nail field has changed in character, and differentiation is seen in 3 areas; the epidermis of the distal ridge, the nail bed epidermis, and the epidermis distal to the matrix primordium. The distal ridge consists of 2 or more ridges with the distal ridge usually more developed. In this area the basal and intermediate layers resemble those layers in

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volar epidermis, while the granular layers and the cornified layers resemble those layers in the nail bed epidermis.

The distal groove separates the volar epidermis from the distal ridge. The epidermis of the nail bed consists of a basal, spinosum, granular, and cornified layer. The cells comprising the spinous layer have denser cytoplasm than those cells in the intermediate layer of the volar epidermis. The epidermis distal to the matrix primordium differs microscopically from the remainder of the nail bed epidermis in the absence of the granular and cornified layers and by the presence of a parakeratotic-like layer in their stead. This parakeratotic-like layer is not the remnant of the periderm layer. The epidermis of this area shows an organized process of nuclear retention and flattening of the cells as they differentiate from the basal layer. In hematoxylin-Biebrich's scarlet-stained sections the basal cells are situated closer together and are more basophilic than basal cells in other areas.

Sections stained for the sulfhydryl groups [21] show a positive reaction in the parakeratotic-like epidermis just distal to the matrix primordium (Fig. 9) and a mildly positive reaction in the area between the granular and cornified layers of the nail bed. In sections stained for the demonstration of disulfide groups [28] only, a midly positive reaction was noted in the entire cornified layer of the distal ridge and nail bed epidermis and a negligible positive reaction in the parakeratotic-like area just distal to the matrix primordium entrance.

The Early Stages of the Nail Plate Formation

At 14 weeks the nail plate is recognizable by its smooth surface which extends distally from under the proximal nail fold (Fig. 3). The distal ridge is broader and flatter.

A section of a thumb of an embryo 14 weeks of age (Fig. 10) shows the phalanx with calcification of its distal tip. Muscle, tendons, and subcutaneous tissues are more organized. Collagen bundles are present in the dermis. In the volar epidermis the primary epidermal rete are present, and cords of epithelial cells extend from these into the dermis. These cords represent the forerunners of the sweat glands. Volar epidermis consists of all the layers seen in the adult. No spiral sweat ducts are seen in the stratum corneum. Neither epidermal rete or sweat gland anlage are present in the epidermis of the dorsum of the digit.

In the nail field there is further differentiation of the epidermis of the nail bed and the distal ridge. There is evidence of nail plate formation by the matrix in the distal portion of the matrix primordium.

The distal ridge and the nail bed will be described first. The distal ridge is a flattened broad ridge. Its stratum corneum is more

Fig. 10.—Longitudinal section of a thumb from an embryo 14 weeks old; fixed in 1% trichloroacetic acid and stained with hematoxylin-Biebrich's scarlet. The distal ridge (*DR*) is broader than in earlier embryos. The distal groove (*DG*) separates it from the volar epidermis. The primary rete are present. The earliest signs of sweat glands are seen (*SG*). The epidermis of the dorsum (*DE*) or the digit has no rete. The proximal nail fold (*PNF*) consists of a wedge of dermis covered by epidermis. The dorsal surface of the fold is covered by the epidermis of the dorsum of the digit, while the ventral surface of the fold is covered by an epidermis which evolved from the matrix primordium. The matrix which also evolved from the matrix primordium extends from just distal to the proximal nail fold to about three-quarters of the length beneath the fold. The distal fourth remains as the matrix primordium. × 48.

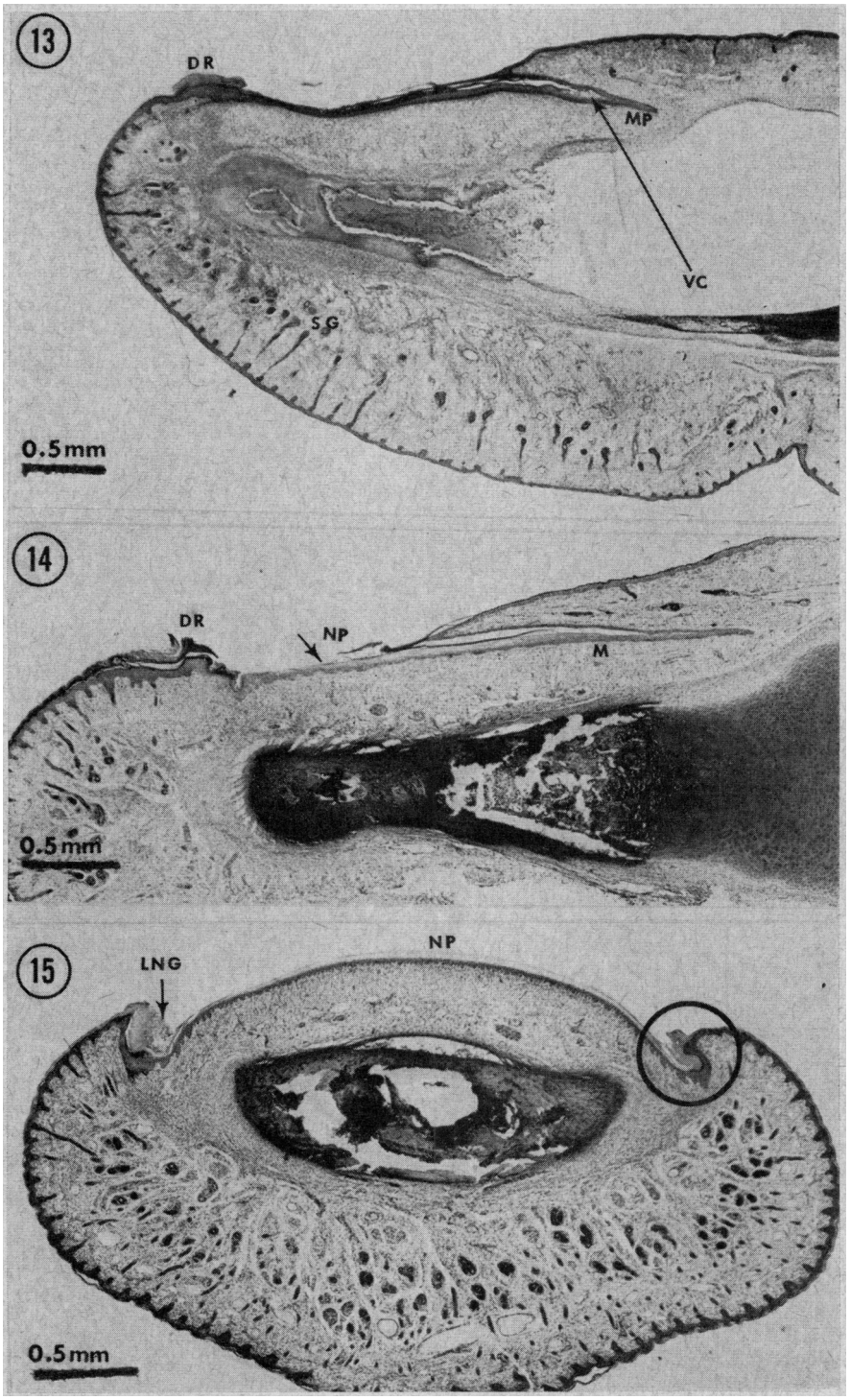
Fig. 11.—Enlarged matrix area enclosed by square from Figure 10. The matrix primordium differentiates into the matrix in a distal to proximal direction. Newly differentiated matrix exhibits the phenomenon of cell vacuolation. The vacuolated cells (*VC*) are derived from the basal layer of the matrix (*BM*). The columnar basal cells exhibit a vacuolation of the cytoplasm and a general flattening of the cell. As the vacuolated cell differentiates into the nail plate cell (*NP*) it undergoes further flattening with nuclear fragmentation. These compressed cells are strongly adherent to each other and form a sheet of cells whch becomes incorporated as a unit and forms the nail plate. The horny layer produced by the ventral surface of the proximal nail fold (*VENF*) becomes adherent to the dorsal surface of the newly formed nail plate. Melanocytes are present in the ventral epidermis of the fold in Negro embryos. A dendrite (*DEN*) of a melanocyte is shown. × 1,000.

Fig. 12.—Longitudinal section of the thumb from the embryo in Figure 10; stained for the demonstration of sulfhydryl groups. The nail plate (*NP*) is strongly positive while the adjacent cornified material of the cuticle (*CT*), and the nail bed (*NB*) is negligible. × 128.

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abundant than that of the nail bed. Both of these structures consist of all the layers found in adult epidermis.

To facilitate the description of the development and differentiation of the matrix and the epidermis lining the ventral surface of the proximal nail fold, these structures will be described in relation to the proximal nail groove (see glossary). This groove is a potential space, becoming real when the nail



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plate is absent. The space resulting from this absence is in effect the proximal nail groove. This space is limited dorsally by the proximal nail fold and ventrally by the matrix. It is well to remember that the epidermis lining the ventral surface of the proximal nail fold is the same as that which lines the dorsal surface of the proximal nail groove.

The matrix primordium (Fig. 8, *MP*), a wedge consisting of 2 types of epidermal cells, has differentiated further. Its dorsal layer has differentiated in the epidermis lining the dorsal surface of the slit-like groove. The ventral layer of the original wedge differentiates into the matrix epidermis lining the ventral surface of the groove.

In embryos 14 weeks of age, the matrix occupies the distal portions of the groove and extends for some distance outside of the groove. The latter portion is the lunula. The matrix area consists of 3 parts. Outside the groove is the lunula, proximal to it is an area of matrix which is characterized by vacuolation of its cells, referred to as the vacuolated cells, and proximal to this is the remainder of the matrix primordium.

In the lunula, nail plate is formed by a process which involves flattening of the basal cells of the matrix, followed by fragmentation of the nuclei and a condensation of the cytoplasms, forming a flat cell which is incorporated into one unit and forms the nail plate. The amount of nuclear material which remains in the nail plate cell varies, being greater early in embryonic life as compared to adult life. In Negro embryos, melanin granules can be seen in the nail plate. These granules are contributed by melanocytes present in the matrix epidermis. Pigmentation of Negro nails is not uncommon.[19] The vacuolated cells do not produce a characteristic nail plate but a horny material which is not as compact. These cells exhibit a vacuolation of their cytoplasm which can be severe, leaving the cell with a nucleus surrounded by its cell membrane. There is flattening of these cells as they mature and form a loose horny layer.

The epidermis lining the dorsal aspect of the groove is similar to the dorsum of the digit epidermis. It does not contribute to the formation of the nail plate in humans. Its stratum corneum lies on the surface of the newly formed nail plate and is seen as sheet extending from under the proximal nail fold. This horny layer is the ventral component of the cuticle. In Negro embryos this epidermis contains many more epidermal melanocytes than the nail bed and matrix. Epidermal melanocytes have been reported to be present in the epidermis of Negro embryos as early as 13 weeks of embryonic life.[29]

In hematoxylin-Biebrich's scarlet-stained sections of 14 week embryos, the nail plate, the stratum corneum of the nail bed, and the cuticle cannot be differentiated. Sections stained for the demonstration of sulfhydryl groups (Fig. 12) show a strongly positive reaction of the superficial horny layer corresponding to the flattened horny cells produced by the matrix and vacuolated cells. There is a negligible reaction of the cuticle and the stratum corneum of the nail bed. The presence of sulfhydryl groups differentiates the nail plate from the cornified layers of the adjacent epidermis.

Sections stained for the demonstration of disulfide groups show a weakly positive reaction of the nail plate as well as the epidermis and cornified layer of the adjacent structures.

Fig. 13.—Longitudinal section of a thumb from an embryo 16 weeks old; fixed in 1% trichloroacetic acid and stained with hematoxylin-Biebrich's scarlet. The distal ridge (*DR*) has an abundant stratum corneum. The sweat glands (*SG*) are present in the dermis. The matrix primordium (*MP*) continues to differentiate into matrix. A small cluster of vacuolated cells are present at the proximal portion of the matrix (*VC*). × 26.

Fig. 14.—Longitudinal, near midline section of a thumb from an embryo 17 weeks old. Fixed in formalin and stained with hematoxylin-Biebrich's scarlet. The nail plate (*NP*) is distinguishable by its staining qualities and by the lamellation phenomenon. The latter is artefactual, probably due to sectoning. The nail plate extends half way over the nail bed. The matrix does not exhibit vacuolation of its most proximal cells. × 28.

Fig. 15.—Cross section of a thumb at the level of the nail bed from the embryo in Figure 14; fixed in formalin and stained with hematoxylin-Biebrich's scarlet. The rete are more prominent in the epidermis lining the laterial nail grooves (*LNG*) than in the nail bed. × 28.

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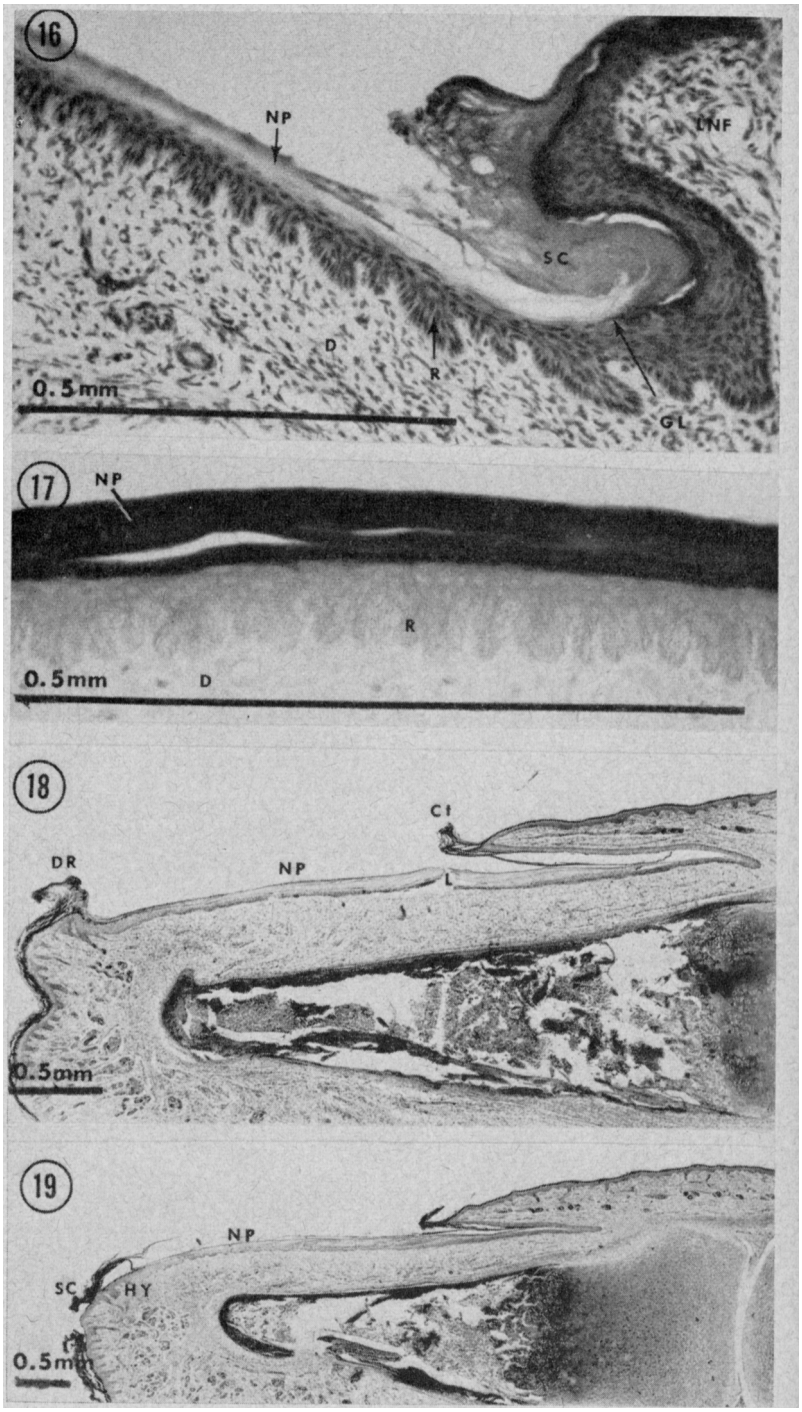


Fig. 16.—Enlarged nail fold encircled in Figure 15. The epidermis of the lateral nail fold (*LNF*) consists of all the layers seen in the adult skin of the dorsum of the digit. The granular layer (*GL*) ends where the epidermis of the nail bed meets the lateral nail fold epidermis. The stratum corneum (*SC*) of the nail fold overlies the nail plate (*NP*) in the lateral nail groove. The rete of the epidermis lining the lateral nail groove are larger than those in the nail bed. × 122.

Fig. 17.—Cross section of the same thumb from the embryo of Figure 15 at the level of the nail bed, stained for the demonstration of sulfhydryl groups. The nail plate (*NP*) is strongly positive while the nail bed epidermis is moderately so and that of the dermis (*D*) is negligible. × 200.

Fig. 18.—Longitudinal section of a thumb from an embryo 20 weeks old; fixed in formalin and stained with hematoxylin-Biebrich's scarlet. The nail plate (*NP*) has grown and is in contact with the stratum corneum of the distal ridge (*DR*). The increase in height of the distal ridge is due to its stratum corneum. The distal border of the lunula (*L*) is marked by a notch in the nail plate. The distal border of the lunula coincided with the distal border of the matrix. (*Ct*) Cuticle. × 25.

Fig. 19.—Longitudinal section of a thumb from an embryo 21 weeks old; fixed in formalin and stained with hematoxylin-Biebrich's scarlet. The nail plate has sheared off the stratum corneum (*SC*) of the distal ridge and has left the epidermis of the ridge which is now called the hyponichium (*HY*). × 15.

Cross sections of the thumb at the level of the matrix, nail bed, and the distal ridge of embryos 14 weeks of age show nests of basal-like cells aggregated at the dermal side of the basal layer of these sites. These nests represent the anlage of the epidermal rete.

Further Differentiation of the Matrix: The Formation of the Epidermal Rete of the Nail Area

At 16 weeks, the nail plate is thin and covers half of the nail bed. The proximal nail

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fold, cuticle, and the distal groove are well formed. The distal ridge is flat.

A longitudinal section of a thumb (Fig. 13) shows the phalanx with calcification of its distal tip. Marrow cells are present. Volar epidermis consists of primary and secondary epidermal rete. The sweat glands are beginning to coil in the dermis. The epidermis of the dorsum of the digit shows an occasional sweat gland, but epidermal rete are scanty.

The matrix has enlarged, and the vacuolated cells seen in earlier embryos are present only in the proximal portion of the matrix primordium. In the Biebrich's scarlet stains the nail plate is less acidophilic than the other cornified structures neighboring it and can barely be differentiated. Proximal to the vacuolated cells is the matrix primordium.

The epidermal rete of the matrix, nail bed, and the distal ridge are present in cross sections of the thumb. The rete of the epidermis of the lateral grooves and distal ridge are more prominent than in the matrix epidermis.

Sulfhydryl stains show a strongly positive reaction only in the nail plate. The stratum corneum of the nail bed, the volar epidermis, and the cuticle have a mildly positive reaction. Disulfide stains show a mildly positive reaction of the nail plate, the cornified layers of the epidermis, cuticle, and nail bed.

At 17 weeks the nail plate almost covers the entire nail bed. The distal ridge is flat and barely discernible. A longitudinal section of the thumb (Fig. 14) shows the phalanx entirely calcified. Volar epidermis has well formed primary rete, secondary rete, and sweat glands. The epidermis of the dorsum of the digit has rete, but they are not as arranged as those in the volar epidermis. Sweat glands are present.

The nail area looks adult. The distal ridge is small and flattened. The nail bed epidermis produces a horny layer which is parakeratotic-like and has no keratohyaline granules. The horny cells produced are added to the overlying nail plate and are more acidophilic than nail plate cells.

The matrix primordium has differentiated into matrix cells except for a small cluster at the most proximal tip.

Sulfhydryl stains (Fig. 17) show a strongly positive reaction in the nail plate. Disulfide stains show a positive reaction of the nail plate. Sulfhydryl and disulfide reactions of the epidermis elsewhere are mildly positive and variable.

The matrix, nail bed, and the distal ridge epidermis have well developed rete. The rete of the lateral grooves and the distal ridge are the longest and best developed (Figs. 15 and 16).

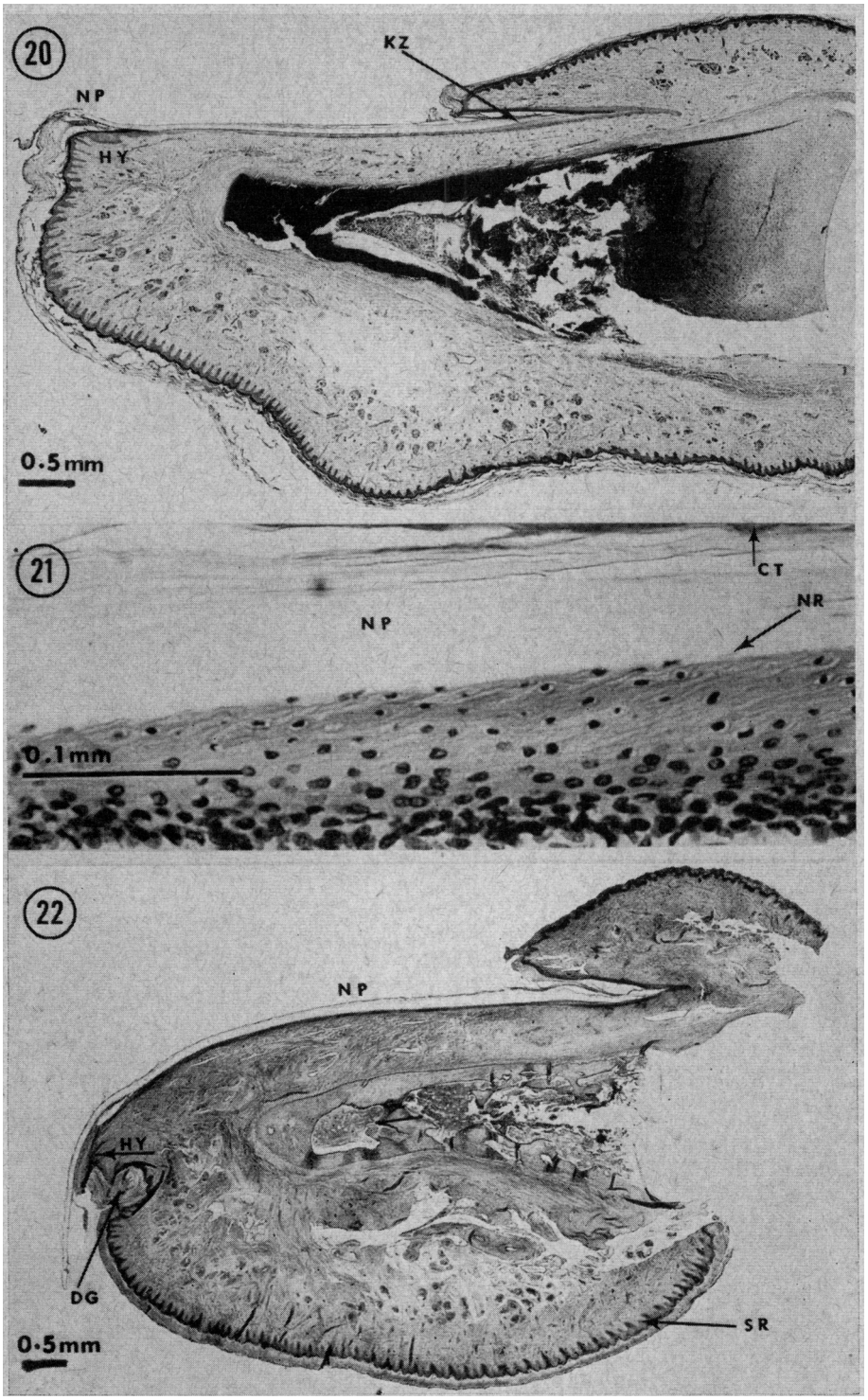
The Hyponychium

The changes of the nail from 17 weeks to newborn are mainly those of growth. The matrix extends over a larger area as the finger enlarges; this results in the production of a broader nail plate. The nail bed also enlarges proportionally. The dermis underlying the matrix and the nail bed is adult in character and is outstanding in the absence of sweat glands and other adnexal structures. Glomus bodies and venous channels are commonly seen.

The distal ridge becomes the hyponychium through changes mediated by the growing nail plate. At 17 weeks the distal ridge is barely visible. At 20 weeks (Fig. 18) the advancing nail plate abuts the cornified layer of the distal ridge producing a separation of this layer from its underlying epidermis. The separation of the cornified layer is seen externally as a ridge. At 24 weeks (Figs. 19 and 20) the nail plate has grown over the cornified layer of the distal ridge, removing most of it. The remaining epidermis of the distal ridge is termed the hyponychium. The cornified material produced by the hyponychium accumulates under the free edge of the nail plate and is the debris present in normal adult nails.

The process of the nail plate formation is adult in character (Fig. 21). This process involves: a progressive flattening of the columnar basal cells of the matrix as they move to the surface and become nail plate cells; a fragmentation and lysis of the nucleus of the basal cells as differentiation occurs, with retention of nuclear membranes, or portions, in the nail plate cells; a progressive cytoplasmic

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basophilia exhibited by the basal cells which in a defined zone just prior to the formation of the nail plate is very intense and which is lost as they become nail plate cells. The area of intense basophilia is termed the keratogenous zone. Nail plate cells are mildly acidophilic. Sulfhydryl stains show a positive and variable reaction in the nail plate and a negli-

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gible and variable reaction in the keratogenous zone.

The Newborn Nail

The newborn fingers are adult-like but smaller in size. Externally, the nail plate is thin and flexible. It extends beyond the tip of the finger, where it is strongly flexed toward the volar surface of the finger. Its edge is sharply pointed. The lunula is present in some fingers. In a longitudinal section of a thumb of the newborn (36 weeks) (Fig. 22), the phalanx, muscles, tendons, periosteum, and subcutaneous connective tissues are well developed and are adult in characteristics. The volar epidermis has well developed sweat glands in the dermis and intraepidermal sweat ducts. The epidermis of the dorsum of the digit does not have the organized pattern of the epidermal rete associated with the volar epidermis.

The matrix extends from the proximal tip of the floor of the proximal nail groove to the distal border of the lunula.

The matrix and the nail bed produce cornified layers by a parakeratotic-like process, while the epidermis of the hyponychium does so by a process involving a granular layer and a stratum corneum.

The distal groove is prominent at birth but becomes inconspicuous as the finger grows.

The epidermal rete of the matrix are smaller and more branched than those of the nail bed. The rete of the nail bed are more developed in areas adjacent to, or forming, the lateral nail grooves. These rete are not polygonal or branched and extend in a longitudinal direction parallel to each other for the entire length of the nail bed, from the lunula to the hyponychium. At the hyponychium the rete become very large and penetrate deeper into the dermis. Here they lose their parallel, longitudinal arrangement and become polygonal for a short distance, terminating at the distal groove. The rete of the volar epidermis are arranged to form the fingerprint pattern.

The cuticle which is formed by the stratum corneum of the proximal nail fold consists of a deep and superficial layer. The deeper layer is produced by the more proximal portions of the proximal nail fold epidermis. This cornified layer is seen adherent to the surface of the newly formed plate. It does not desquamate as easily as the more superficial layer of the cuticle which is produced by the distal and apical epidermis of the proximal nail fold.

Comment

In the adult finger the parallel longitudinal rete of the nail bed epidermis and the arching parallel rete of the volar epidermis, which forms the fingerprint pattern, are more alike than the polygonally arranged rete of the epidermis of the dorsum of the digit. This similarity is striking in the finger of the 9-week-old embryo. Here the nail anlage epidermis and the volar epidermis consist of similar basal germinativum cells which are different from those seen in the dorsal epidermis (Fig. 5).

The first structure to form in the nail field is the distal ridge (Fig. 7). This ridge does not evolve from a structure designated by Lewis as the "dorsal plume".[16,17] Seven embryos ranging in ages from 9 weeks (2.75 cm. crown to rump) to 11 weeks (6 cm.

Fig. 20.—Longitudinal section of a thumb from an embryo 32 weeks old; fixed in formalin and stained with hematoxylin-Biebrich's scarlet. The nail plate (*NP*) extends over the hyponychium (*HY*) and projects beyond the tip of the digit as the free distal edge. The process of nail plate formation is best seen in the keratogenous zone (*KZ*). × 13.

Fig. 21.—Enlarged keratogenous zone from Figure 20. The matrix basal cells as they differentiate and become nail plate cells (*NP*) undergo a process of flattening and of nuclear fragmentation. By this process the cytoplasm of the flattened cell exhibits a basophilia up until the final transformation is made into a nail plate cell. The nail plate cells are slightly acidophilic. The nail plate contains nail plate cells with some retained nuclear material and, in Negro embryos, melanin granules (*NR*). The cuticle can be seen (*CT*) on the surface of the nail plate. × 230.

Fig. 22.—Longitudinal section of a thumb from newborn child; fixed in 1% trichloroacetic acid and stained with hematoxylin-Biebrich's scarlet. The nail plate is thin and strongly flexed ventrally. The distal groove is accentuated but will diminish in size as the finger enlarges with age. In the volar epidermis there are secondary epidermal rete (*SR*). × 9.

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crown to rump) did not exhibit any structure which could be called a "dorsal plume". In the author's opinion, the "dorsal plume" of Lewis is an artefact produced by a sheet of periderm cells which lifted from the surface of the digit and were lying parallel to the plane of sectioning.

Cornification in the nail field first occurs in the distal ridge. The earliest signs of this appear to be granules of variable sizes in the upper layers of the stratum intermedium of the distal ridge in embryos 10 weeks old. These granules have been described by Zander [28] and other investigators as occurring wherever large appendage structures are being formed, as in the mucous membranes of the nasal area and around the mammary glands.[12]

Cornification of the nail field begins at the distal ridge and extends proximally over the nail bed as the embryo becomes older. At 14 weeks the entire nail bed is covered with a horny layer. In the cornification process keratohyaline and stratum corneum layers are produced. As the nail plate is formed and grows over the nail bed, the cornification process seen in the nail bed changes in that there is an absence of a granular and stratum corneum layers and cornification takes place with a process which involves the production of a parakeratotic-like horny layer. The cause of the change in the cornification process from hyperkeratosis to parakeratosis-like in the nail bed is not known, but it is seen coincidentally with the growth of the nail plate over the nail bed.

Differentiation and maturation of the matrix primordium cells into matrix cells occurs in a distal to proximal direction beginning at the lunula. This is suggested by a vacuolation of the matrix primordium cells first seen in the lunula area in embryos 13 weeks of age, which in later ages is seen in the more proximal portions of the matrix primordium (Figs. 10, *M* and 13, *VC*). The matrix primordium cells which lie distal to the vacuolated cells are mature matrix cells and produce nail plate. At 20 weeks of age, the vacuolation of the matrix primordium cells is no longer seen. Nail plate is formed by the matrix cells.

The vacuolated matrix cell is interpreted to be a transitional state of a matrix primordium cell undergoing maturity into a matrix cell. The presence of sulfhydryl groups in the horny layer of the vacuolated cells in greater amounts than in the matrix primordium cells suggests an early attempt to form nail plate by the vacuolated cells. This suggests that the matrix primordium differentiates into matrix cells in a distal to proximal direction. The characteristic strongly positive sulfhydryl reaction of the embryonic nail plate is never seen in the matrix primordium proximally to the vacuolated cells.

The nail plate early in embryonic life is strongly positive for sulfhydryl groups and mildly positive for disulfide groups. Later in embryonic life the strongly positive sulfhydryl reaction lessens and becomes variable, as in the adult nail plate. The disulfide reaction increases in intensity from a slight positive to a strong positive as in the adult nail plate.

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