

# THE BIOLOGY OF THE SKIN



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# Basic science of the nail unit

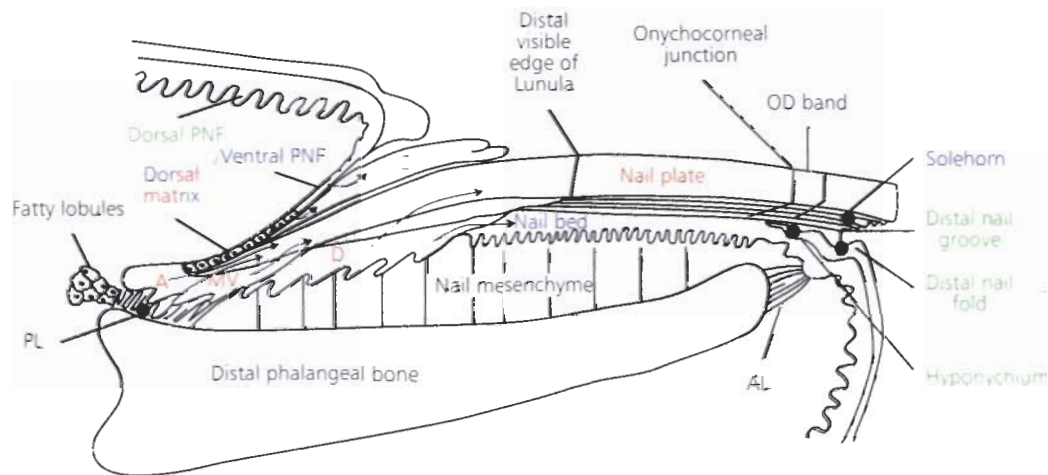
Eyal K. Levit and Richard K. Scher

## ANATOMY OF THE NAIL UNIT

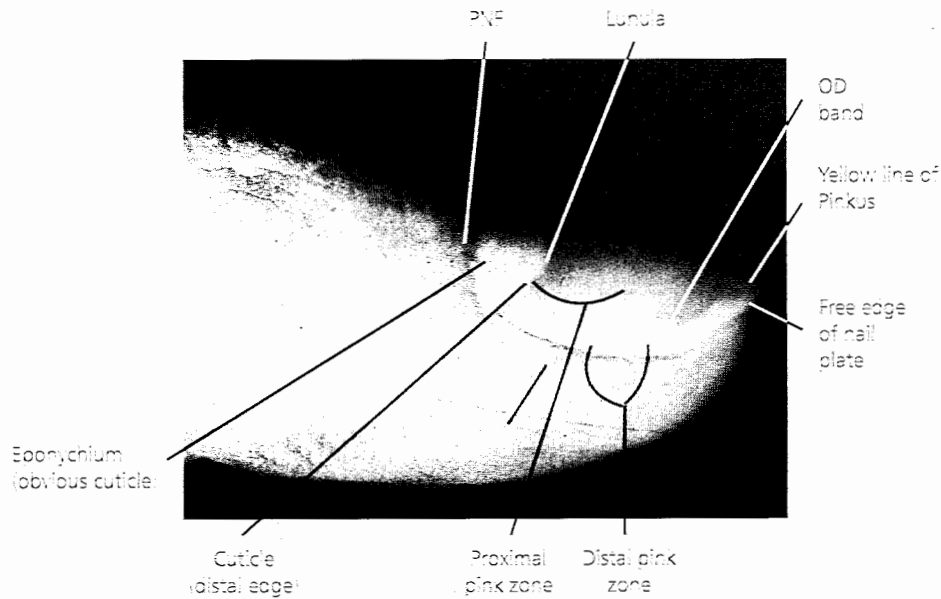
The nail unit has been classically divided by Zaias into six components<sup>1</sup>. We prefer to divide it here into seven components. A thorough understanding of these components is essential in understanding, diagnosing and treating disease states of the nail. The anatomical structures are grouped and subdivided according to their functional relationships (Figures 1 and 2).

### The matrix

The nail *matrix* ranges from 4 to 9 mm in length, with most or all of it located under the proximal nail fold<sup>2</sup>. The distal end of the nail matrix is visible in most people and is represented by the distal end of the lunula. A small portion of the nail matrix is located on the proximoventral part of the proximal nail fold, the dorsal nail matrix (Figure 1). A number of divisional systems have been proposed<sup>3,4</sup>.



**Figure 1** The figure is not drawn to scale. Red, blue and green denote the different patterns of keratinization observed in the nail unit, representing onychokeratinization, onycholemmal and epidermoid keratinization, respectively. A, apical matrix; AL, anterior ligament; C, cuticle; D, distal ('lunular') matrix; E, eponychium; K, keratogenous zone; MV, mid-ventral matrix; OD band, onychodermal band; PL, posterior ligament; PNF, proximal nail fold. Reproduced after modification with permission from Gonzalez-Serva A. Structure and function. In Scher RK, Daniel CR III, eds. *Nails: Therapy, Diagnosis, Surgery*, 2nd edn. Philadelphia: W.B. Saunders Co., 1997:12-31



**Figure 2** Normal thumb nail showing the different anatomical landmarks observed: LNF, lateral nail fold; OD band, onychodermal band; PNE, proximal nail fold

including one calling the nail bed the ventral nail matrix<sup>4</sup>. The nail matrix is shaped as a ‘V’ on sagittal section, forming a folder-like lining around the proximal part of the nail plate, with a thin short dorsal wall and thicker, longer apical and ventral walls. While recent keratin studies give credence to dividing the nail matrix into apical, dorsal and ventral parts<sup>5</sup>, the gradual changes observed as one proceeds distally along the nail matrix may best be captured, for clinical–pathological correlation purposes, if one further divides the apical and ventral nail matrix continuum into three parts: apical, mid-ventral and distal<sup>3</sup>. The apical matrix, proximal third, gives rise to the superficial portion of the nail plate and has the highest rate of mitosis. The middle third, the mid-ventral matrix (excluding the ‘lunular’ matrix), gives rise to the middle third of the nail plate and has a slightly slower rate of cell division. The distal third of the ventral nail matrix (in most patients visible as and corresponding to the lunula) forms the bottom third of the nail

plate (contributing about 19% of the total nail plate cell number<sup>6</sup>). It divides more slowly than the other two regions. The purpose of the dorsal nail matrix is not exactly clear and while it probably adds to the superficial portion of the nail plate, recent keratin studies suggest a possible partial role in the formation of the cuticle (Figure 1)<sup>5</sup>.

### The nail plate

While the origin of the nail plate has been much debated, newer evidence supports its origin from the nail matrix<sup>6</sup>. Most of the disease processes affecting the nail plate can thus be traced back to its source – the nail matrix. For therapeutic and diagnostic purposes, the nail plate can be divided into thirds both in depth, vertically (as a curvilinear extension of the nail matrix), and in length, horizontally. The proximal portion overlying the nail matrix is usually white in color and is defined as the lunula. The middle section, firmly adhering to and

overlying the nail bed, terminates at the onychocorneal band, or junction, signifying the proximal portion of the onychodermal band (about 1 mm in length). The onychodermal band represents the most proximal point of attachment of the finger tip stratum corneum and the plate, and is located over the distal pink zone. The onychodermal band is bordered distally with a thin layer of the remaining distal pink zone followed by a barely perceptible yellow line 0.1 mm in length called the yellow line of Pinkus (Figures 1 and 2)<sup>2,7</sup>. The distal third section is represented by the free edge of the nail plate.

### The nail frame (perionychium)

This consists of three components. Proximally, the proximal nail fold, is responsible for molding the nail plate shape from above; it has a dorsal and a ventral component. The dorsal component gives rise to the eponychium (obvious cuticle) represented by the distalmost portion of the proximal nail fold<sup>3</sup>. The ventral component produces the cuticle<sup>3</sup>, either alone or with participation from the dorsal nail matrix (Figure 1). Laterally, the nail plate is supported by the medio-lateral and latero-lateral nail folds; and distally, the distal nail fold serves as the distal support (Figure 1). Unfortunately, worse than the debate upon a unified measuring system, is the confusion of terms such as eponychium and cuticle, which are defined by some<sup>2</sup> to represent the exact opposites of what has been accepted by others<sup>3,5</sup> and adopted above (see Figure 1).

### The cuticular system

This system ensheathes the nail plate from above (dorsally) and below (ventrally) serving both as attachments for and as barriers from the forces of the external environment. From above, those include proximally the eponychium and deeper and more distally the cuticle.

From below, it involves, proximally and in closer attachment, the bed horny layer overlying the solehorn. The hyponychium provides a less intimate and more superficial ensheathment that ends distally at the convex distal groove.

### The supporting system

This comprises three components: the nail bed, nail mesenchyme and phalangeal bone. The nail bed, which lacks a granular layer as does the nail matrix, extends from the distal edge of the lunula to the onychodermal band. The nail mesenchyme (dermis of the nail bed) extends from the proximalmost portion of the nail matrix to the end of the nail bed. This mesenchyme is composed of an abundant connective tissue network radiating vertically from the periosteum of the distal phalanx to the nail bed epithelium, binding the two together. It bears no resemblance to dermis anywhere else in the skin and has been likened in texture to a tendon; it is thus also considered as part of the anchoring system. The nail mesenchyme has been divided on sagittal section into three portions: the posterior ligament, located between the matrix and the proximal portion of the distal phalanx, the nail bed dermis, and the anterior ligament connecting the hyponychium to the tip of the distal phalanx<sup>3</sup>. The phalangeal bone immediately follows below the thin nail mesenchyme. It is responsible for molding the nail plate shape from below.

### The anchoring system

This provides the attachment between the nail plate and its supporting structures. It consists of ligamentous-type collagen fibers positioned in a vertical distribution. Proximally it joins the phalanx to the nail matrix and distally to the lateral and distal nail grooves (Figure 1).

### The vascular (arterial, venous, lymphatic) and nervous supply of the nail unit

The vascular supply is closely followed by the sensory enervation. Two lateral digital arteries course along the lateral finger giving rise to dorsal branches at the junction between the middle and terminal phalanges. These branches divide, forming the distal and proximal arcs that supply the matrix and proximal nail fold with their smaller rami<sup>8</sup>.

## HISTOLOGY OF THE NORMAL NAIL UNIT

This section follows the anatomical divisions discussed above and is not meant to be exhaustive. It includes information as it relates to the understanding of the basic science of the nail unit in health and disease.

### The matrix

The nail matrix is formed from a thick epithelium consisting mostly of matrix cells lacking a granular layer. The rete ridges of the apical and ventral matrix form club-shaped projections, directed downward and proximally, into the nail mesenchyme (Figure 1)<sup>9</sup>. Melanocytes are present in the matrix, but are poorly developed and fewer in number than elsewhere in the skin. They are most abundant in the distal (mid-ventral and 'lunular') matrix, with an increased number of melanocytes seen in darker pigmented races. The melanocytes are located in the basal and suprabasal layers as single cells and as small clusters of three and four cells<sup>10</sup>. Langerhans and rare Merkel cells have both been observed throughout the nail matrix<sup>11,12</sup>. The distal portion of the ventral nail matrix (lunular matrix) has a keratogenous zone overlying its dorsal surface and adhering tenaciously to the overlying plate (Figure 1). This zone consists of a multilayered band of epithelial cells with flattened dark nuclei and

eosinophilic cytoplasm, and is believed to explain the white appearance of the lunular matrix, persisting on the undersurface of the nail plate even after it is avulsed<sup>9,12</sup>. A thin, short portion of the nail matrix is located on the proximoventral part of the proximal nail fold, the dorsal nail matrix. It lacks rete ridges, dermal papillae and melanocytes, and unlike the rest of the nail matrix, the dorsal matrix, has a granular layer (Figure 1)<sup>4</sup>.

### The nail plate

The nail plate consists of closely packed, fully keratinized, multilayered lamellae of cornified cells. It is dorsally smooth. Upon avulsion, the ventral surface of the nail plate shows longitudinal folds and grooves. The folds and grooves are formed by the nail bed horny layer overlying the solehorn, both adhering tightly to the nail plate and 'sliding' along with the nail plate and nail bed, as the nail plate grows distally<sup>3</sup>. The nail plate thickness varies from about 0.6 to 1 mm<sup>5</sup> (see physiology section below for discussion). As one examines the nail plate sagittally along its depth, one appreciates larger and broader onychocytes in the deep portions of the plate and smaller onychocytes as one moves toward the dorsal surface of the nail plate<sup>13</sup>. At the onychocorneal band, or junction, the bed horny layer disappears and the solehorn attaches directly to the undersurface of the nail plate, continuing to unsheath it up to and including its free edge.

### The nail frame (perionychium)

The proximal nail fold has a dorsal and ventral epithelial surface. The dorsal surface epithelium is an extension of the dorsal skin of the digit and as such has a similar histological appearance, with a four-layer epidermis interdigitating with the dermal papilla. It has melanocytes and sweat glands, but lacks pilosebaceous units. Its

cornified layer extends distally as the eponychium. The ventral surface also has similar epidermis, but is thinner, lacks the interdigitating rete-dermal papilla arrangement and has no epidermal appendages and no melanocytes<sup>3,4</sup>. Its cornified layer extends as a thin transparent vest under the nail eponychium in direct apposition to the proximal nail plate. The lateral and distal nail folds represent overhanging skin extending from the ventral side of the digit and have a similar histological appearance to this volar skin.

### The cuticular system

This system represents thin layers of enucleated corneocytes formed through different modes of keratinization from their corresponding counterparts. The hyponychium represents an extension of the fingertip skin lacking adenexae and a fingerprint.

### The supporting system

The nail bed lacks a granular layer, as does the nail matrix. It has a thin, two- to three-layer, epidermis made with few parakeratotic cells that adhere closely to the undersurface of the nail plate. The nail bed is firmly attached to the underlying dermis (mesenchyme) by long, narrow, comb-like epithelial rete ridges that are interlocked with dermal papilla forming regular longitudinal folds along the nail bed, extending from the distal edge of the lunula to the onychodermal band. The nail mesenchyme is a thin layer of dermis immediately overlying the terminal phalanx composed of elastin and collagen with a rich vascular network tracking through it. The dermal region underneath the middle and lunular matrix contains rare glomus bodies, but no pilosebaceous units and no fat. Between the apical nail matrix and the periosteum is a thin layer of connective tissue infiltrated with fatty lobules extending from the hypodermis of the dorsal surface of the phalanx (Figure 1)<sup>1</sup>.

### The anchoring system

This is discussed under mesenchyme above.

### The vascular supply of the nail unit

The different nail unit components have a different vascular network. The capillary loops of the proximal nail fold are arranged horizontally in tiers of uniform size located equidistantly from the base of the eponychium. The toenail folds, unlike the finger folds, have a reduced flow rate but a greater density of capillaries<sup>4</sup>. The mid-ventral and lunular nail matrix has a pseudopapillary network composed of long, waved and flattened capillary loops projecting distally, parallel to the axis of the finger in grooves between the nail plate and matrix. The reticular network lying beneath it has a thick proximal network that thins down as it approaches the mesenchyme of the distal end of the lunula; this is barely distinguished from the subdermal network lying below it. The nail bed has a papillary network consisting of short, fine capillary loops arranged in longitudinal lines lying perpendicular to the axis of the nail plate growth. These represent tributaries of the underlying reticular network. Unlike the nail matrix, the nail bed reticular network involves more vascular meshes distributed in a narrower plane. This is distinguished from the subdermal network, which has a denser and more irregular architecture<sup>2</sup>.

Glomus bodies are found abundantly in the nail bed. They represent neurovascular bodies forming an encapsulated oval organ acting as an arteriovenous anastomosis<sup>4</sup>.

## EMBRYOLOGY

A number of morphogens (substances involved in formation and differentiation of tissues) have recently been identified, namely retinoic acid and homeobox genes ('master' genes)<sup>14</sup>. The morphogens activate and control cells

located at the base of the limb, called the zone of polarizing activity<sup>15</sup>, which leads to the normal organization and adult formation of the nail unit<sup>16</sup>. The limb bud formation of the hand and foot appears first during the fourth and eighth weeks of gestation respectively, and arises from the ectoderm and lateral plate mesoderm<sup>17</sup>. From the fifth week of gestation until the 23rd week, the epidermis undergoes transformation from a two-cell layer surface composed of periderm that bathes with its microvilli in the amniotic fluid and the germinative layer, into a multilayer surface with shedding of the periderm and its substitution with the stratum corneum.

The basement membrane appears structurally mature by the middle of the second trimester<sup>18</sup>, and perhaps even earlier<sup>19</sup>. By the eighth week, bone formation can be observed, followed by the formation of blood vessels during the 12th week. At 10 weeks of gestation, a distinct region with clear proximal, lateral and distal grooves is identified and is termed the nail field. This primary nail field, representing the dorsal epidermis of the digit, forms the matrix primordium through its proximal ventral surface invagination, which ultimately gives rise to the nail group<sup>14</sup>.

The nail plate emerges beneath the proximal nail fold from the matrix primordium at 14 weeks of gestation, with its free edge extending beyond the hyponychium by the 32nd week. By the 20th week the matrix has achieved its mature adult form. From 20 weeks of gestation, the nail plate abuts the distal ridge, growing in tandem with the finger<sup>4</sup>. As the nail plate moves distally, tucking under the overhanging lateral nail folds, it shears off the distal ridge, its remnant represented by the hyponychium (the first site of the nail unit to keratinize<sup>20</sup>), and leads to the concomitant loss of the granular layer of the nail bed epithelium. Merkel cells appear during the ninth week, but recede during the 22nd week and are only rarely found in the adult nail matrix<sup>21</sup>. The development of the human toenail

follows a similar program, but lags fingernail development by about 4 weeks<sup>1</sup>.

## CELL BIOLOGY AND PHYSIOLOGY OF THE NORMAL NAIL UNIT

As nail matrix cells proceed to differentiate into the nail plate by broadening, flattening and nuclear fragmentation, there is an accumulation of cytoplasmic microfibrils. These intermediate filaments form the keratin pattern observed during the differentiation of nail matrix cells into nail plate cells. This transformation occurs in the absence of keratohyalin granules. Odland bodies (lamellar granules) are formed within the differentiating cells, their contents (neutral sugars, hydrolytic enzymes and free sterols)<sup>22</sup> extruded into the extracellular space of the transitional zone. They are believed to contribute to the thickness of the plasma membrane and adherence among the corneocytes.

### Nail unit keratinization

Three forms of keratinization exist in the nail unit: epidermoid, onycholemmal and onychokeratinization<sup>3</sup>. Onychokeratinization, observed in the nail matrix, is characterized by a prominent keratogenous zone not preceded by a granular layer. Onycholemmal keratinization consists of the keratinization process of the nail bed and of the ventral part of the proximal nail fold, both devoid of a keratogenous zone. Epidermal keratinization is the typical basket-weave orthokeratinization observed in the rest of the skin epidermis, with a typical granular layer preceding it<sup>3</sup>. Figure 1 delineates the different keratinization process and the nail unit section they give rise to.

### Nail rigidity

Numerous factors have been suggested to be responsible, by their presence or absence, for the rigidity ('hardness') of the nail plate. Unlike

bones, nail plate rigidity is not dependent on calcium levels<sup>23</sup>. A high sulfur content is provided in the nail plate through the sulfur bonds of cystine making up the hard keratins of the nail. Desmosomes, along with finger-like interdigitations between corneocytes and their glycoprotein cement, may also play a role in the nail plate cohesiveness and thus in its rigidity<sup>24</sup>. Physical properties of the nail plate, such as its curvature and the orientation of its fibers perpendicular to the direction of the nail plate growth, have also been suggested to decrease the brittleness of nails. Last but not least, water has been shown to help improve nail plate flexibility and elasticity together helping to decrease its brittleness<sup>22</sup>.

### Nail kinetics

The rate of nail growth is affected by a multitude of factors<sup>2</sup>. The fingernail grows on average at a rate of 0.1 mm day, with about 2 months required to expose itself from beneath the proximal nail fold. The toenail grows at half this speed. As the nail plate grows outwardly, it glides along with the nail bed over the longitudinal interdigitations it forms with the nail bed mesenchyme. It has long been puzzling how the nail plate moves forward over the nail bed mesenchyme yet remains firmly adherent to the nail bed. Recent evidence has shown that mature nail matrix cells may change their *in vivo* keratin production depending upon their *in vitro* conditions<sup>5</sup>. This may lend itself to explain why previous studies found tritiated thymidine originally incorporated into the nail matrix, appearing in the nail bed<sup>25</sup>. It may be that the nail matrix produces the nail bed epithelium and as the nail matrix migrates to the nail bed area the different milieu leads to the different keratin production and the slightly varied histological and biochemical appearance between the nail bed and matrix; thus the nail plate and bed, both products of the matrix, will grow outwardly in tandem.

The apical, mid-ventral and lunular matrix, forming the different layers of the nail plate, have different growth rates, thus leading to centripetal and centrifugal vectors. These vectors are in turn molded by forces of adhesion of the nail plate to the nail bed and pressures from the proximal nail fold and distal phalanx<sup>3</sup>. Together these lead to the observed overall shape and thickness of the nail plate<sup>3</sup>.

### Nail shape

The breadth of the nail plate and its transverse axis are directly related to the breadth and degree of arching, respectively, of the matrix forming it. The length and longitudinal convexity of the nail plate are dependent upon the length and convexity (height), respectively, of the nail bed to which the plate is firmly attached. The outline of the free edge of the nail plate is directly dependent on the outline of the onychodermal band, which in turn parallels the shape of the lunula<sup>3</sup>. After the above factors interplay in the nail plate conception, its development is molded by the external forces of the proximal nail fold from above and to a greater degree by the phalangeal bone from below.

### Nail thickness

The nail thickness varies from about 0.6 to 1 mm according to the nail matrix size and the variable speed of growth of its components<sup>5</sup>, paralleling the higher rate of mitosis in the proximal nail matrix that decreases distally, contributing the three different layers (see discussion of nail plate anatomy) of the nail plate<sup>3</sup>. Over 80% of the nail plate production (defined as total mean cell number) is formed from the proximal 50% of the nail matrix (dorsal, apical and mid-ventral matrix cells)<sup>6</sup>. The rest of the nail cell number is added by the lunular matrix, together accounting for the final mean total



cell number, but only 90% of the mean nail plate thickness. While the mean nail plate cell thickness continues to expand distally, with the maximum reached at the onychocorneal band (the pathogenesis of which is unclear<sup>6</sup>), the mean cell number shows a decrease between the onychocytes of the lunular nail plate and the ones located over the onychocorneal band<sup>6</sup>.

### Nail colors

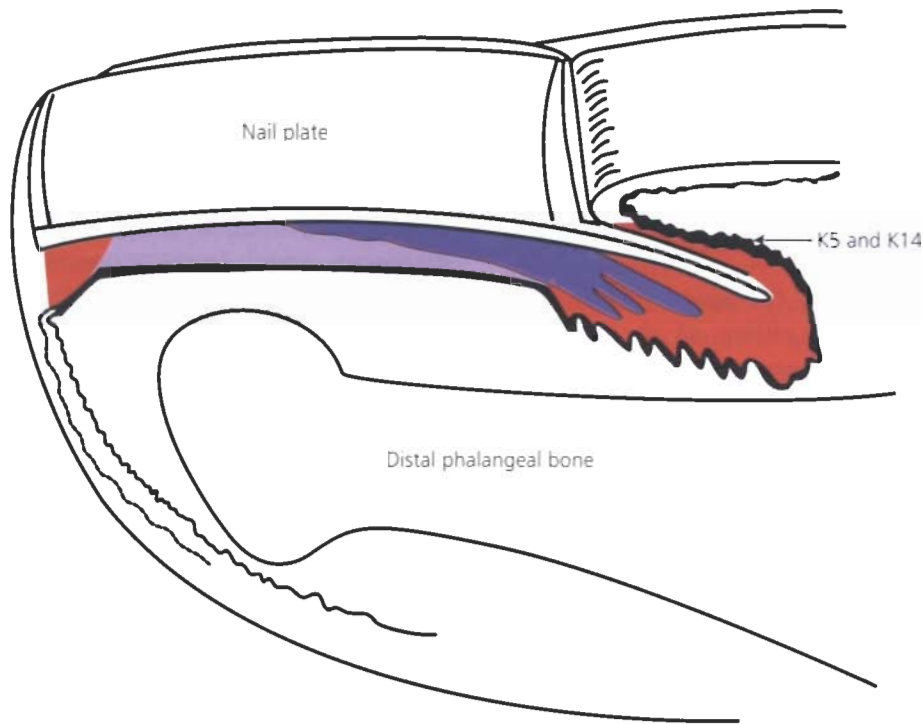
The nail plate is translucent and the color variations observed through it represent the scattered light absorbed and reflected by the variably thickened plate and epidermis, the presence or absence of the keratogenous zone and the degree of vascularization within the mesenchyme<sup>3</sup>. Together this interplay leads to eight color bands observed along the normal nail plate (Figures 1 and 2). Proximal to distal they include: the pearly white color of the *lunula*, a light violaceous color fading into pink (*proximal pink zone*), a poorly defined blanched out band, a shorter pink zone (*distal pink zone*) that is traversed on its distal edge by a well defined off-white band in Caucasians or a gray-brown band in darker skin races (onychodermal band), leaving a thin rim of the distal pink zone distal to it; this is followed by a thin yellow strip (Yellow line of Pinkus) and a white colored band overlying the free edge of the nail plate<sup>3,4</sup>.

### BIOCHEMISTRY OF THE NORMAL NAIL UNIT

The nail plate is composed of both organic and inorganic components. The organic components include carbon and two trace elements found almost exclusively in amino acids (sulfur and nitrogen). The inorganic components include trace elements and electrolytes (for a detailed discussion of these refer to Table 4.1 of reference 4). Water is an important constituent of the nail

plate, responsible in part for its physical properties. It makes up 10–30% of the nail plate, directly dependent on the relative humidity<sup>24</sup>.

The nail plate is composed of keratins believed to be held in place by the surrounding globular matrix proteins with high concentration cystine disulfide bonds. Keratins are a group of intermediate filament proteins that contribute to the cytoskeleton of the cell; they are expressed not only in cornified cells as the nail plate but also in non-squamous cells. During the course of epithelial maturation, different keratins are expressed<sup>25</sup>. Keratins have been divided according to their isoelectric points into acidic or type I (K10–20) and basic or type II (K1–9) keratins. These keratins have been found in the epidermis of skin and also in the cells of hair and nail. More recently, additional keratins have been found that are uniquely expressed in hair, nail, filiform papillae of the tongue and thymic epithelium, and are responsible for the 'hard' keratinization observed in them. They have been called 'hard' keratins because they are almost completely insoluble under conditions that solubilize the epidermal ('soft') keratins. The hard keratins have also been divided, according to their isoelectric points, into acidic (Ha1–4, Hax) and basic (Hb2–4, Hbx) type keratins<sup>26</sup>. Ten to twenty percent of the nail plate keratins consist of epidermal keratins<sup>27</sup>. The keratins are expressed in specific pairs, one acidic and one basic, and their expression varies among the nail unit components<sup>24</sup>, and between their epithelial layers (Figure 3)<sup>25</sup>, in disease states and keratin mutations (e.g. epidermolysis bullosa [keratins 5 and 14], pachyonychia congenita type I [keratins 6a and 16] and type II [keratin 17])<sup>28</sup>. The Ha1 along with the other hard keratins of the nail unit have been localized to the suprabasal layers of the nail matrix and are absent from the nail bed. While some studies have failed to show these keratins in the nail plate, their absence has been attributed to the mechanical difficulties involved in studying



**Figure 3** This figure represents the presumed localization of the nail unit keratins (K). From the proximal to the distal and the periphery to the center of the nail bed they include: the solid black line represents K5 and K14 localized to the basal layer of the nail matrix, nail bed and, as with epidermis elsewhere, to the proximal nail fold and hyponychium. The red area represents K1 and K10 expressed in the suprabasal layer of the proximal nail fold, nail matrix and hyponychium. The blue area represents hard keratins (including Ha1) that are expressed sporadically throughout the suprabasal layer of the nail matrix. The purple area represents K6, K16 and K17, expressed over the suprabasal layer of the nail bed. Figure reproduced after modification with permission from Fleckman P. Basic science of the nail unit. In Scher RK, Daniel CR III, eds. *Nails: Therapy, Diagnosis, Surgery*, 2nd edn. Philadelphia: W.B. Saunders Co., 1997:37–54

the nail plate<sup>24,29</sup>. Keratins 5 and 14 have been localized, similarly to epidermis elsewhere, to the basal layer of the nail matrix and nail bed. Keratins 1 and 10 have been localized to the suprabasal layers of the nail matrix as well as to the proximal nail fold and hyponychium<sup>24</sup> as expected based on findings in epidermis elsewhere<sup>26</sup>. Lastly keratins 6, 16 and 17 have been localized to the suprabasal layers of the nail matrix<sup>24</sup>. The keratin intermediate filaments are arranged with their longitudinal axis along the plane of the nail plate<sup>24,26</sup>.

Another component providing chemical resistance, found both in epidermal stratum

corneum and nail, is the cornified envelope composed of high concentrations of proline<sup>30</sup>.

The basement membrane zone (BMZ) of the nail unit basal layer is uniform throughout and is identical to the BMZ of other epithelia<sup>31</sup>.

## COMMON DISEASES OF THE NAIL UNIT

In evaluating diseases of the nail unit, just as with skin diseases elsewhere, one is often reminded that a single morphology, such as subungual hyperkeratosis of the nail or morbilliform rash of the skin, may be a presenting sign

for many conditions. We will discuss here one or more disease processes affecting a single anatomical unit, their morphological presentation and, wherever possible, the presumed mechanism.

### Diseases of the nail matrix and nail plate

Psoriasis involving the apical and/or dorsal matrix results in pitting of the nail plate through the loss of parakeratotic cells from the upper layer of the nail plate<sup>9</sup>. White spots in the nail plate are the result of psoriasis involving the mid-ventral and/or apical nail matrix leading to light scattering from parakeratotic cells involving the middle corneocytes of the nail plate<sup>9</sup>. When parakeratotic cells appear in the distal third 'lunular' matrix, onycholysis may ensue<sup>9</sup>.

Melanonychia striata appears when melanocytic pigmentation occurs in the nail plate and usually represents involvement of the melanocytes in the distal lunular or mid-ventral nail matrix.

Sudden onset of a chronic illness or intermittent direct trauma (as with runners) may often lead to arrest of the apical nail matrix growth, resulting in Beau's line, a transverse depression along the nail plate.

As with the evaluation of hair for toxic exposure or nutritional deficiencies one may examine the nail plate to diagnose different nutritional deficiencies<sup>24</sup>, toxic exposures<sup>22</sup> or even duration of illness<sup>23</sup>.

### Diseases involving the nail frame (perionychium)

Tumors or cysts cradled in the proximal nail fold, such as mucous cyst, may present as thinning or even ridging of the proximal nail plate (through continuous external 'molding' pressure exerted over the nail matrix and plate) with variable degrees of erythema and swelling of the proximal nail fold.

Pterygium may appear when lichen planus involves large portions of the nail matrix with secondary scarring of most of the matrix that leads to thinning of the nail plate. The proximal nail fold, in the absence of an intervening plate, may grow onto the 'lunular' matrix and nail bed, forming a pterygium (scar). The pterygium extends from the proximal nail fold to the nail bed, dividing the plate into two parts, thus forming the pathognomonic wing-like deformity.

The proximal, lateral and distal nail folds may show manifestations similar in morphology to those seen on skin elsewhere, for instance in psoriasis.

### Diseases involving the cuticular system

The eponychium and the cuticle are often cut or pushed back during manicuring preparations, resulting in the undermining of the protective sheath around the nail plate with subsequent penetration of irritants and/or bacteria, producing acute or chronic paronychia. Absent eponychium is a pathognomonic sign for yellow nail syndrome.

The hyponychium is the site of invasion of distal subungual onychomycosis, the most common type of onychomycosis. Any cause that will help undermine the tight adhesion formed between the hyponychium and the undersurface of the nail plate will predispose to the development of onychomycosis, as with secondary onychomycosis in patients with traumatic onycholysis or psoriasis-induced onycholysis.

### Diseases involving the supporting system

Trauma to the nail plate, psoriasis or subacute bacterial endocarditis may result in minor capillary damage with blood extravasation from the nail bed supply. The blood collects in the

longitudinal grooves formed between the nail bed and the nail plate, presenting as longitudinal collections of blood, called splinter hemorrhages, that travel with the nail plate distally. In psoriasis, Darier's disease, as well as pachyonychia congenita, various degrees of subungual hyperkeratosis and secondary onycholysis are usually present. It may be that, as with the increase in the keratin types associated with hyperproliferative states (keratins 6 and 16)<sup>22</sup> normally expressed in the suprabasal portions of the nail bed<sup>24</sup> that lead to the manifested clinical findings of psoriasis, so too this may occur in the nail bed epithelium of pachyonychia congenita, due to overproduction of these keratins in order to compensate for the mutations.

The phalangeal bone may be affected with osteomyelitis with secondary periungual erythema, swelling, tenderness and even destruction of the nail plate, with bony exostosis resulting in

changes in the shape of the nail plate, and with psoriasis through psoriatic arthritis.

### Diseases involving the vascular supply of the nail unit

Glomus tumor results from hyperplasia of the glomus bodies that are normally found in the nail bed mesenchyme. This can be observed as a bluish-red discoloration seen through the nail plate with pain upon pressure or cold exposure. The continuous pressure on the overlying nail plate may manifest as thinning of the nail plate.

In scleroderma, by looking with an ophthalmoscope through an oil drop over the proximal nail fold, one can diagnose the early signs of scleroderma manifesting as avascular areas interrupting abnormally dilated capillary loops of the proximal nail fold (see histology section for discussion of normal vascular distribution).

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