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Nutrition and nail disease

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Abstract The nail is a specialized keratinous skin appendage that grows approximately 2 to 3 mm per month, with complete replacement achieved in 6 to 9 months. Although this structure can be easily overlooked, nail disorders comprise approximately 10% of all dermatologic conditions. This contribution first provides an overview on the basic anatomy of the nail that will delineate between the nail unit (eg, hyponychium, nail bed, proximal nail fold, and matrix) and anatomic components not part of the nail unit (eg, lateral nail folds, nail plate, and eponychium). The function of each nail structure will also be presented. The chemical profile of the normal nail plate is reviewed with a discussion of its keratin content (hair type keratin vs epithelial type keratin), sulfur content, and mineral composition, including magnesium, calcium, iron, zinc, sodium, and copper. The remainder will focus on nail manifestations seen in states of malnutrition. Virtually every nutritional deficiency can affect the growth of the nail in some manner. Finally, the discussion will include anecdotal use of nutritional and dietary supplements in the setting of brittle nail syndrome as well as a brief overview of biotin and its promising utility in the treatment of nail disorders.

Introduction

Although skin might encompass a large portion of the field, dermatology also includes the study of its appendages, namely the nails and hair. These two skin appendages are often discussed together, or are at least compared with one another, in the literature. The dynamics of hair and nail growth control are related in several ways: both are skin appendages serving protective functions, and both are differentiated epithelial products, which consist of tightly bound cells made rigid by special intermediate filament proteins, the hard keratins.[1]

Basic anatomy of the nail unit

The nail is a specialized keratinous appendage produced by a germinative epithelium just as basal epidermal cells produce the stratum corneum of the skin. Nail keratinocytes contribute to nail cornification through the production of hard keratins, and hardness of the nail plate is due to a high concentration of sulfur matrix protein.[2] Although it can be grossly appreciated and show manifestations of various underlying pathologies, the nail plate is, surprisingly, not considered one of the four anatomic structures that comprise the nail unit[3]:

- nail bed
- hyponychium
- proximal nail fold
- matrix

The nail plate is made of anucleate keratinocytes oriented so that the cells are flattened in the plane of the plate, whereas

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the intermediate filaments are oriented perpendicular to its plane of growth. This unique orientation and the transverse and longitudinal curvature of the plate are thought to provide its structural rigidity.[4] Nail plates are roughly rectangular and flat but demonstrate considerable variation within the normal population. The plate is actually translucent; however, it appears pink on gross examination due to the rich underlying vascular network of capillaries weaving through the nail bed, which firmly adheres to the nail plate above.

The white, crescent-shaped area on the proximal nail plate is known as the lunula. It can be seen projecting from under the proximal nail fold and represents the most distal portion of the matrix, which ultimately determines the shape of the free edge of the nail plate. As the nail plate emerges from the matrix, it is bordered by three normal skin structures—two lateral nail folds and a proximal nail fold. The proximal nail fold is crucial in the formation of the nail plate. In fact, approximately 25% of the nail plate's total surface area is located under the proximal nail fold.[5]

The four epithelial components that comprise the nail unit serve vital functions necessary for maintaining the integrity of the nail plate. The matrix is a thick epithelium situated above the middle part of the distal phalanx of the digits.[6] It is bordered proximally by the proximal nail fold and distally by the lunula, generating the bulk of the nail plate. The proximal nail fold is an invaginated, wedge-shaped fold of skin on the dorsum of the distal digit[5] that protects much of the matrix and newly forming nail plate.

Not considered one of the four epithelial components of the nail unit, the eponychium (cuticle) is a part of the proximal nail fold. It serves as a sealant and protective barrier against entry of infectious organisms into the germinative matrix. Disruption of the eponychium allows irritants to enter, which subsequently leads to the inflammation seen in chronic paronychia.[7]

The hyponychium is a narrow zone of epidermis between the nail bed and the distal nail groove beneath the free edge of the nail plate.[5] Its function is very similar to that of the eponychium but in an inverted manner. It seals the undersurface of the nail plate, where it lifts off the tip of the digit. Disruption of this area results in the creation of a potential space between the nail plate and nail bed, as can be appreciated in onycholysis.[7]

Lastly, the nail bed begins where the distal matrix or lunula ends, extending to the hyponychium, where the free edge of the nail separates.[5]Its contribution to nail plate formation is still questioned. The nail bed keratinocytes contribute about 20% of ventral nail plate's thickness and mass.[6] The main function is keeping the nail plate attached to the nail unit.

Chemical make-up of the nail plate

Most the nail plate is made of keratin and contains both hair-type ("hard") keratin and epithelial-type ("soft") keratin.[8] In addition to these keratins, intermediate filament-associated proteins high in sulfur or tyrosine/glycine moieties and the protein trichohyalin are also expressed throughout the nail unit. Different types of keratin are variably expressed in separate areas of the nail unit. Keratin expression in the proximal nail fold and the fingertip epidermis consists of normal interfollicular epidermis. More specifically, keratins K5 and K14 are expressed in basal keratinocytes, K1 and K10 are expressed in suprabasal keratinocytes, and K2E is expressed by keratinocytes high in the spinous layer.[1] The nail matrix also expresses normal interfollicular keratins similar to the proximal nail fold and fingertip epidermis; however, unlike the proximal nail fold, the nail matrix sporadically expresses hard keratins and trichohyalin in its suprabasal layers. Finally, the nail bed epithelium also expresses the basal keratins, K5 and K14, and keratins K6, K16, and K17 are expressed in its suprabasal layers.[1]

Hair-type keratin constitutes 80% to 90% and the epithelial type keratin comprises 10% of 20% of the nail plate. Its overall sulfur content is approximately 10% by weight. The disulfide bonds of cystine in the matrix proteins are thought to contribute largely to nail hardness by acting as glue that holds the keratin fibers together, thereby creating the nail plate's tensile strength. Contrary to popular belief, calcium does not contribute to nail hardness and makes up only 0.2% of the nail plate by weight.[9] The lipid content is relatively low, especially compared with the amount of lipids found in the stratum corneum. Glycolic and stearic acids are types of lipids found in the nail plate, and their presence likely explains the nail plate's water resistance. Despite this feature, the nail plate's water content can vary greatly, with normal content being 18%.[10] Its hydration state is thought to contribute to nail hardness. For example, nails become brittle when the water content is less than 16% and become soft when greater than 25%.[11] Although the major contribution of nail plate hardness is unclear, it is likely due to both the high concentration of sulfur matrix protein and the current hydration state.

Minerals are another important aspect of the nail plate's composition. The principal minerals include magnesium, calcium, iron, zinc, sodium, and copper.

Patients with soft, flaky nails that are inclined to break or split may have significantly reduced plasma and nail plate magnesium levels.[12] A second study revealed that selenium is an essential trace element with a significant effect on nail health. This report described a young boy whose fingernails turned white approximately 2 years after starting total parental nutrition (TPN). Close examination of these nails and dermatologic consultation revealed that the nails were fully developed and normal, but virtually the entire nail bed was white except for a distal zone of normal pink. The boy's nail findings, of approximately 12 months' duration, resolved dramatically after selenium therapy was instituted.[13]

The specific mineral content of a given individual's nail plate varies greatly between different populations.

Higher levels of calcium and zinc are found in men, higher levels of magnesium are found in women, and the level of iron is equal between them. Levels of calcium are higher in older people than in younger individuals. Children have higher levels of magnesium, sodium, and iron than adults, and iron is actually highest amongst neonates across all groups. Children with kwashiorkor disease have higher levels of calcium and sodium and healthy children have higher levels of magnesium. Two final examples that might seem more intuitive include lower levels of iron in nail plates of patients with iron-deficiency anemia and higher levels of copper in nails of patients with Wilson disease.[9]

Malnutrition and the nail

Several systemic diseases can lead to nail changes that clinicians can visually appreciate; however, not all gross changes are secondary to malnutrition alone. Those nail changes solely due to malnutrition and other systemic diseases that could manifest secondary to a deficiency in a particular vitamin, mineral, or other trace element (eg, iron-deficiency anemia) will be outlined systematically by which part of the nail unit is affected. The exception will be the first section on chromonychia, because this particular nail change can affect three different parts of the nail unit.

Chromonychia and the nail matrix, nail bed, and nail plate

Chromonychia can occur in the lunula (the most distal portion of the nail matrix), the nail bed, or the nail plate. The word is defined as any color (excluding white) that abnormally discolors a part of the nail unit. Because white is not necessarily considered a distinct color, whitened areas of the nail unit define the term leukonychia. Chromonychia of the lunula has been reported as a bluish discoloration in copper overload from Wilson disease.[14] Argyria—a chronic elevation of silver salts in the body—has been associated with a blackish-gray discoloration of the lunula and is thought to be photoinduced.[15]

Color changes in the nail bed are more diffuse than focal chromonychia of the lunula. For example, diffusely bluish discoloration of the nail bed is characteristically associated with ingestion of silver and does not need light exposure to manifest itself.[16] The differential diagnosis of a patient who presents with a bluish, discolored nail bed includes a glomus tumor, especially when associated with pain. Although nonspecific, pallor of the nail bed can be a sign of anemia and an indication that iron body stores may be low.

Chromonychia of the nail plate can occur due to increased melanogenesis in the matrix or to a melanocytic neoplasm.[17] Longitudinal melanonychia of the nail plate secondary to increased melanin production in the matrix has been reported in malnutrition, vitamin D and vitamin B_{12} deficiencies, and hemochromatosis.[16]

The nail bed

The nail bed can display signs of nutritional imbalances. Physical signs of nail bed disease include splinter hemorrhages, Terry nails, Muehrcke lines, and onycholysis. Splinter hemorrhages are formed by extravasation of red blood cells from longitudinally oriented nail bed vessels into adjacent longitudinally oriented troughs.[17] Although classically associated with subacute bacterial endocarditis, these are most frequently seen as a result of trauma and have been associated with a slew of systemic illnesses. Among the nutrition-related conditions are scurvy and hemochromatosis.

Despite its classical association with chronic liver disease, Terry nails can also be seen in malnutritive states, especially in the elderly.[10] Terry nails are described as any 0.5- to 3.0-mm wide, distal, brown-to-pink nail bed bands with proximal pallor.[16] Muehrcke lines are characterized by two transverse white bands of pallor. When pressure is applied to the distal plate, the narrow transverse bands disappear, confirming a nail bed change.[16,18] Leukonychia, the term used to describe whitened areas of the nail unit, can be applied to Muehrcke lines. In fact, leukonychia can be further classified as true or apparent. Muehrcke lines are an example of the latter, as evidenced by disappearing white bands with applied pressure to the distal plate. Although Muehrcke initially associated this finding with hypoalbuminemia, this nail change has also been associated with malnutrition and acrodermatitis enteropathica, an autosomal-recessive metabolic disorder that affects zinc absorption.

Onycholysis is defined as separation of the nail plate from the underlying nail bed, causing a proximal extension of free air.[17] It is the third most common nail disorder seen, after onychomycosis and verrucae vulgaris.[16] Although classically a sign of thyroid disease, the correlation of onycholysis with systemic illness is overrated and more likely to be associated with common local conditions such as trauma, allergic contact dermatitis, or irritant reactions.[17] Onycholysis may be due to exogenous or endogenous causes, with the former representing most cases seen in the clinic. Some endogenous causes of onycholysis related to nutritional imbalances include iron-deficiency anemia, pellagra, and Cronkhite-Canada syndrome, an extremely rare nonfamilial syndrome characterized by marked epithelial disturbances in the gastrointestinal tract and epidermis. The abnormal mucosal proliferation leads to fluid and electrolyte abnormalities, malabsorption, and malnutrition.[19]

The nail plate

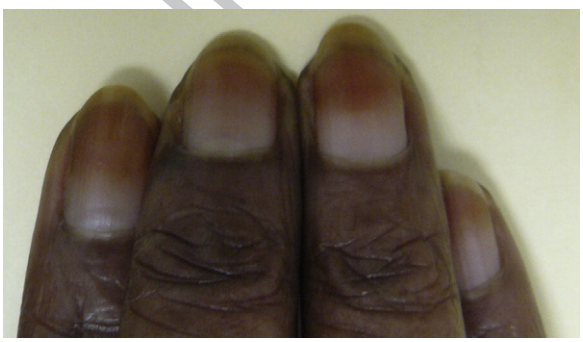
The nail plate is the last portion of the nail apparatus affected by nutritional imbalances that often result in grossly visible signs. Examples of observed nail plate changes

include transverse leukonychia, clubbing, koilonychia, hapalonychia, Beau lines, onychomadesis, onychorrhexis, and trachyonychia. Transverse leukonychia is distinguished by transverse, opaque white bands that tend to occur in the same relative position in multiple nails.[17] These bands mimic the contour of the lunula and grow out with the nail plate (Figure 1). Measuring the distance of the line from the proximal nail fold gives the clinician a time reference from when nail insult occurred, because fingernails grow about 0.10 to 0.15 mm/d. Although transverse leukonychia is typically associated with deficiency states like acrodermatitis enteropathica, pellagra (deficient niacin/vitamin B_3), and low calcium levels, it is additionally associated with overabundant states such as the increased blood iron levels that occur in hemochromatosis.

Mees line is a descriptive term used to specify transverse leukonychia with arsenic deposition in the plate secondary to arsenic poisoning.[20] Mees line is a classic example of true leukonychia, because the transverse white bands are truly deposited in the nail plate and will not disappear with applied pressure to the distal plate, unlike Muehrcke lines (apparent leukonychia), whose lines do disappear.

Clubbing (Figure 2) is a long-recognized nail sign that Hippocrates first described in 5th century BCE .[21] The term is used when the Lovibond angle (the normal 160° angle between the proximal nail fold and the nail plate) exceeds 180°. Clubbing can be inherited or acquired. An inherited type of clubbing that falls under the purview of nutritional imbalances includes citrullinemia, a rare autosomal-recessive disorder of the hepatic urea cycle that leads to an accumulation of nitrogenous waste compounds and other toxic substances, including citrulline, in the blood.[22] Acquired clubbing secondary to nutritional imbalances may be due to several different combinations of substances and pathologies, including phosphorus, arsenic, alcohol, mercury or beryllium poisoning, hypervitaminosis A, and cretinism caused by iodine deficiency.[16]

Koilonychia is defined as spoon-shaped nail plates. It is thought to occur due to a relatively low-set distal matrix compared with the proximal matrix that causes nail plate growth to occur in a downward direction as it grows toward the nail bed.[23] When present, it is usually more severe on the index and third fingernails.[24] Almost all cases of koilonychia



Q5 **Fig. 1** Apparent leukonychia.

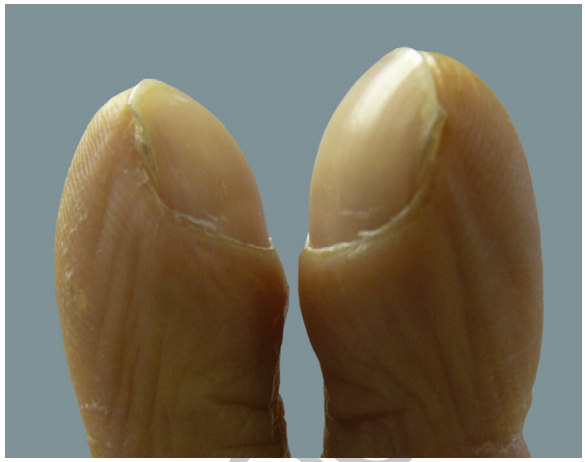


Fig. 2 Clubbing.

are acquired, but it also may be idiopathic or inherited. Koilonychia is classically a sign of iron-deficiency anemia and has not been observed in any other type of anemia[24]; however, a few published cases have reported koilonychia in postgastrectomy patients and in patients diagnosed with Plummer-Vinson syndrome. These clinical syndromes still fall under the purview of iron-deficiency anemia (eg, iron malabsorption in postgastrectomy patients and iron-deficiency anemia as one criterion of the Plummer-Vinson syndrome clinical triad) and support the notion that koilonychia is observed only in sideropenic anemia and not in other anemias. Iron-deficiency anemia may be the only anemia strongly correlated with koilonychia, but other nutrition states such as riboflavin deficiency, pellagra, and more commonly, vitamin C deficiency have all been implicated in the development of koilonychia.

Hapalonychia, or soft nails, have been associated with occupational diseases, eczematous dermatides, and certain systemic diseases. Female gender and advancing age are two predisposing factors that influence the development of hapalonychia. Some systemic causes include hypochromic anemia, rheumatoid arthritis, and arsenic poisoning. Nutritional deficiencies involving vitamins A, B_6 (pyridoxine), C, and D, in addition to low serum calcium, have all been implicated in causing hapalonychia.[16]

Beau lines are defined as transverse grooves or depression of the nail plate seen in acute systemic disorders.[25] It is one of the most common signs encountered in clinical practice, but is the least specific. Acute illnesses are thought to cause a temporary arrest of the matrix. The width of the furrow is an indicator of the given ailment's duration.[16] Measuring the distance from the furrow to proximal nail fold gives an approximate time that the insult may have occurred, as can also be done with transverse leukonychia. If the entire activity of the matrix is inhibited for 1 to 2 weeks, a Beau line will reach its maximum depth, causing a total division of the nail plate (ie, onychomadesis).[26] Nutritional disorders associated with Beau lines include protein deficiency and pellagra. Dysregulated blood mineral levels, such as

hypocalcemia, chronic alcoholism (another source of malnutrition and malabsorption), and arsenic toxicity, can also play a role in the development of Beau lines.[16]

Onychomadesis (Figure 3) is the term used to describe complete onycholysis, beginning at the nail plate's proximal end, which is also known as complete nail shedding. The most common cause of onychomadesis is neurovascular change. Examples would be repeated episodes of drops in blood calcium levels or a chronic state of hypocalcemia with arteriolar spasm. This underlying pathophysiology leads to an abrupt separation of the nail plate from the underlying nail matrix and nail bed and results in the clinical manifestation of onychomadesis. Other associations that can lead to the development of onychomadesis include arsenic and lead poisoning.[16]

Onychorrhexis, or senile nail, describes longitudinal ridges in the nail plate that are most often associated with the aging process. This nail change can be inherited, and the pattern has been described as specific enough to distinguish between identical twins and can be useful in forensic identification.[26] It is most strongly correlated with rheumatoid arthritis, but other systemic disturbances can also contribute to its development. Mineral imbalances leading to onychorrhexis include iron-deficiency anemia, arsenic poisoning, and zinc deficiency.[16]

The term trachyonychia (Figure 4) describes rough nail plates with a characteristic gray opacity, brittle (fragilitas unguium) and split free ends, longitudinal ridging, and a rough sandpaperlike surface.[27] Brittle nails and trachyonychia are relatively common in persons aged older than 60 years. Causes often include repeated cycles of hydration and dehydration as occur in excessive domestic wet work and overuse of dehydrating agents such as nail enamel and cuticle removers. Another typical offender is poor or decreased dietary water and food intake, an especially common phenomenon in the elderly. Any of these may contribute to and precipitate brittle nails and subsequent trachyonychia seen in the elderly.[2]

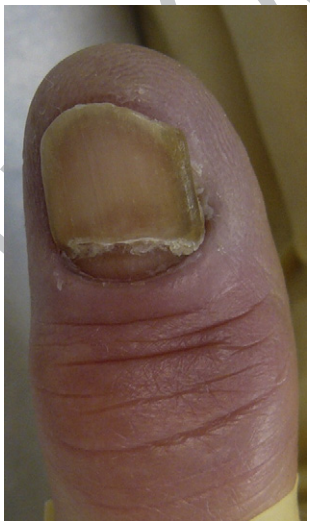


Fig. 3 Onychomadesis.

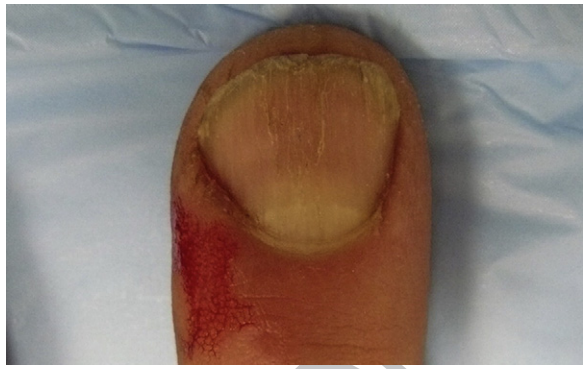


Fig. 4 Trachyonychia. Q6

Nutritional supplements and the nail

Little information is available on how nutritional supplements can affect different nail disorders; however, brittle nail syndrome is one nail disorder often found in what minimal literature exists. Brittle nail syndrome is a disease characterized by soft, dry, weak, easily breakable nails that show onychorrhexis and onychoschizia.[10] Brittle fingernails are an all-too-common complaint seen in the dermatologist's office. As many as 60 million people in the United States of America may experience this disorder, with women predominantly affected.[28] The causes are believed to be traumatic, vascular, or physical. Damage to the nails because of deficient production of intercellular cement substance may also be related to systemic diseases, nutritional deficiencies, endocrine or metabolic disorders, and dermatologic conditions.[28,29] The intercellular cement substance is mostly made of phospholipids, mucopolysaccharides, and acid phosphatases, and is found in high concentrations around cell junctions, known as the zonula occludens and gap junctions, and firmly adheres nail cells together.[30] Q3

A multitude of regimens exist for treatment of brittle nails, including buffing and moisturizing, application of essential fatty acids, and ingestion of vitamin C and pyridoxine, iron, vitamin D, calcium, amino acids, and gelatin.[28] One nutritional supplement that has been seriously investigated and has recently shown promise is biotin, or vitamin H. Biotin use to abate pathologic horse hoofs in veterinary medicine suggested it could be used to treat human nail disease.[31] A role for biotin in nail disorders is also indicated by its favorable effect on other skin disorders, such as seborrheic dermatitis, Leiner disease, and disorders of hair growth. Biotin deficiency may be caused by insufficient intake, ingestion of raw eggs, absorption disorders, production of biotin antagonists by intestinal bacteria, or disturbance in the intestinal flora by oral therapy with sulfonamides, antibiotics, or anticonvulsant agents.[29]

One study demonstrated a 25% increase in the thickness of the nail plate in patients diagnosed with brittle nails of unknown cause and treated with biotin (2.5 mg daily) for 6 to 15 months.[28] Another study showed that biotin was not equally effective in all patients, but a definite trend toward benefit was noted in most of those who took between 1.0 and 3.0 mg daily, with 2 months being the average time before clinically noticeable results. This same study also showed that approximately 10 weeks after biotin was discontinued, nail ridging gradually returned and the nail brittleness recurred.[29] Both studies provide clinical evidence that biotin is possibly effective in treating patients with nail brittleness. The next step in biotin investigation is to determine whether vitamin H supplementation is legitimately correcting an underlying deficiency or whether improvement in nail brittleness is through some other mechanism that has yet to be elucidated.

Conclusions

Nails as a skin appendage are considered ancillary and may be neglected by the nondermatologist in an examination; however, there are a myriad of recognizable patterns that can alter each individual part of the nail apparatus. Because systemic illness can manifest through subtle changes in the nail, clinicians may need to be reminded of these physical findings in determining the cause of nail complaints.

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