

## THE NAIL - VARIOUS PHYSIOLOGICAL AND PATHOLOGICAL ASPECTS – REVIEW

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### Abstract

Nail research in recent decades has concerned most pharmacologists and dermatologists, as it offers a much safer and more concentrated alternative to conventional oral therapy. The understanding of the microstructure and composition of the nail is far from complete. The main objective of this article is to review the microstructure, composition and main diseases of the nails.

Keywords: nail, nail pathology, onychomycosis

### Introduction

The nail is a thin horny plate that grows on top of the last phalanx of the fingers and toes and covers the top of the end of the fingers. [1]

Over time, nails have been precise indicators of various diseases due to their shape and color, as well as indicators of iron, zinc (the lack of which causes irritation on the nails) and vitamin B complex (the lack of which makes the nails brittle ).

Nails occupy a very small area of the body and are considered dead structures, but they have attracted the medical world since the dawn of civilization. We find evidence about the nail in many documents belonging to ancient civilizations: the Mesopotamian clay tablets, various Egyptian papyri or the

ancient Indo-Iranian religio-social scripture, the Rik Veda

In the medieval period, the writings of famous authors such as Hally Abbas, Al Majusi, Albucassis and others mention the medical significance of nails. Modern scientific study began with the paper on the biochemical analysis of nails by Theophil Metecki (1837). Gustav Simon (1848), Kölliker (1852), Virchow (1854) and others did pioneering work on the anatomical and cellular aspects of nails.

Daniel Turner (1726) described ingrown toenails and Robert Willan (1808) wrote about psoriatic nail changes. Famous authorities such as Rayer (1835), Vidal (1855) and Hutchinson (1857) described eczematous changes, syphilitic affections and melanotic herpes respectively.

In the present era, the works of Zaias, Scher, Hashimto, Baran and others have put onychology on a solid footing. The subject has developed at a rapid pace over the past 100 years with subsequent advances in science and has become an important body of modern medical science. In the present era, the works of Zaias, Scher, Hashimto, Baran and others have put onychology on a solid footing.[2]

The subject has developed at a rapid pace over the past 100 years with subsequent advances in science and has become an important body of modern medical science.

Nails are a mirror that reflects a person's state of health, the multitude of changes in shape and appearance influencing their normal evolution. Any kind of abnormality is actually a sign of nail condition. Here are some examples:[3, 36-48]

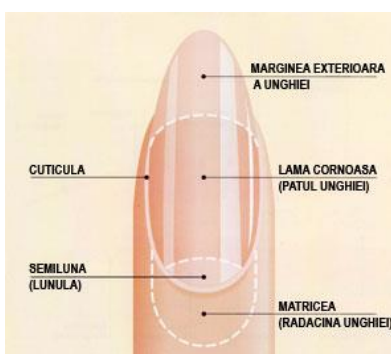
- curved nails are a sign of lung disease or emphysema
- small striations, or indentations, are a sign of arthritis, eczema or psoriasis
- horizontal lines are the result of stress, or chemotherapy, trauma, malnutrition, or are signs that appear in people who climb mountains
  - mountain climbers
  - vertical lines are signs of aging, or they can be genetic
- Convex nails are signs of iron deficiency
- half-white nails can be a sign of a kidney or liver disease.
- cardiovascular diseases and diabetes

- towards the tip, the nails have a dark shade, and semicircles can be seen on their surface;
- thyroid disorders
- brittle, brittle nails that break easily;
- psoriasis
- brittle nails, with striations on their surface;
- nasal polyps and chronic sinus infections
  - the nails are yellow;
  - bacterial infections
  - the nails have shades of green;
  - fungal infections (onychomycosis)
  - the nails are thickened, uneven, in shades of dark blue;
  - skin tumors
  - black or brown streaks may be present on the surface of the nail.

#### The structure of the nail

From an etiological point of view, nails appear from an epidermal bud represented by epidermal thickening at the level of the dorsal surface of the last phalanges, appearing towards the end of the third month. In intrauterine life, the nail remains covered by an epidermal blade that disappears only in the ninth month in the full-term newborn, the nail appears fully formed.[4]

Macroscopically, the nail has two parts: a visible part - the body of the nail or the limbus and a part hidden under the nail fold - the root. The lunula is the white portion of the body located near the root. [Fig.1]



**Fig.1** The structure of the nail

Bordul (marginea) liberă a unghiei este extremitatea unghiei care nu aderă pe patul unghial. Această porțiune este mai groasă decât la nivelul rădăcinii, deoarece aici sunt acumulate mai multe celule de keratină.

Pielea care acoperă rădăcina constituie bureletul unghial a cărui extremitate liberă, foarte keratinizată, se numește *epionichium* sau cuticula, pe când regiunea situată sub marginea liberă a unghiei se numește *hiponichium*.

În secțiune longitudinală se disting de la suprafață spre profunzime:

- platoul unghial care este echivalentul stratului cornos al epidermului interfolicular este format din celule cornoase;
- patul unghial este un epiteliu pavimentos stratificat;
- dermul care în dreptul lunulei și la nivelul zonei de colorație roză, este atașat periostului falangei distale.

În spate, rădăcina unghiei se înfundă profund în derm. atingând articulația interfalangiană distală. În față, epidermul patului unghial se continuă cu extremitatea

degetului.[5]

The free border (edge) of the nail is the extremity of the nail that does not adhere to the nail bed. This portion is thicker than at the root level, because more keratin cells are accumulated here.

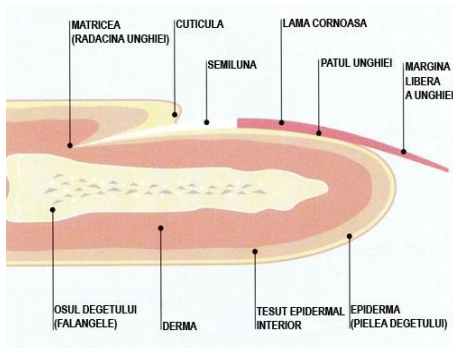
The skin covering the root constitutes the nail sponge whose free extremity, highly keratinized, is called epionychium or cuticle, while the region located below the free edge of the nail is called hyponychium.

In the longitudinal section, from the surface to the depth:

- the nail plate, which is the equivalent of the corneous layer of the interfollicular epidermis, is made up of corneous cells;
- the nail bed is a stratified squamous epithelium;
- the dermis that is attached to the periosteum of the distal phalanx near the lunule and at the level of the pink colored area.

At the back, the root of the nail digs

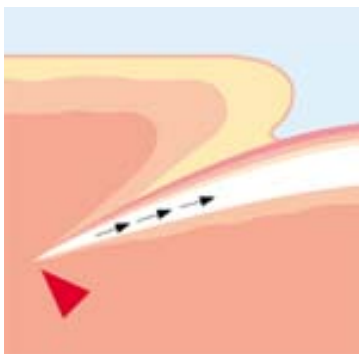
deep into the dermis, touching the distal interphalangeal joint. In front, the epidermis of the nail bed continues with the extremity of the finger.[5]



**Fig.2** Nail structure – cross section

The growth of the nail is done by the proliferation and differentiation of the epithelium of the nail root and lunule, called the nail matrix. The matrix produces the nail plate at a rate of 1 mm/week on the hands and 0.25 mm/week on the feet.

The matrix [fig.3] is what gives rise to the nail and comes from the germinative basal layer that contains large voluminous, young cells capable of regenerating skin, hair and nails. Starting from the matrix, the blade (plate) is formed, also called the horny tongue.



**Fig.3** Nail matrix

Melanocytes are present not only in the basal layer as in the interfollicular

epidermis, throughout the height of the epithelium. Langerhans cells are also present.

At the level of the nail bed and palmo-plantar regions (hands, feet, fingers) there are arterio-venous anastomoses, with or without glomus. They play an important role in thermoregulation.

The glomus is a special vascular organ present in the dermis, more frequently at the extremities of the fingers and the nail bed. It consists of a direct arterio-venous anastomosis (not via arterial and venous capillaries), respectively of an afferent arteriole with a narrowed lumen and an efferent vein with a widened lumen, surrounded by glomerular (myoepithelial) cells.

The vascularization of the nail depends on distal arteries that branch into several branches irrigating the nail, matrix, and overlying nail fold.

The nervous system of the nail includes free and encapsulated sensory nerves of cerebral-spinal origin and nerves of sympathetic origin. The origin of these nerves is at the level of the spine - the cervical area.[5]

Chemically, the nail is made up of hard keratin or scleroproteins rich in sulfur, cysteine and arginine.

It also contains water, lipids such as cholesterol and fatty acids (oleic acid), calcium, the main mineral constituent of the nail, iron and phosphorus.

The thickness of the nails is about 0.5 mm, the nails of the toes being always thicker. Nail growth is perpetual, around 1 mm per week, renewing completely in 5-6 months. Nails do not exfoliate under normal

medical conditions, and growth is from the matrix to the free edge.

The nail protects the distal extremities of the fingers, plays an important role in grasping small objects, and participates in the sensitivity of the phalanges.

The nail folds hold the nail in place and anchor it to the skin, forming the cuticle. This prevents microbial organisms from entering the nail bed and also prevents moisture. It also has a social and aesthetic role, it is an indicator of health status and sometimes of social status.[6]

### **Aspects of nail pathology**

Nails, even if they are appendages, are very important, because changes at their level can indicate systemic diseases. Healthy nails are usually smooth, pink, uniform, with a white lunula (this is the pale area at the base of the nail).

Discoloration and specific changes in shape can signal various lung diseases, cardiovascular, kidney and liver diseases or diabetes and anemia. White dots and vertical grooves are usually without serious pathological significance.

The nail pathology that raises therapeutic approach problems is represented by:

- bacterial infections;
- fungal infections; ingrown nails;
- tumors.

However, if the nails are cut on time and properly cared for, a series of problems can be avoided.

**Nail diseases vary in etiology and morphology.**

Nail disorders are numerous and can be classified as follows:

- acquired conditions;
- due to aging;
- congenital conditions.

Nail pathology that raises therapeutic approach problems can be classified according to the cause: bacterial infections, fungal infections, ingrown nails, tumors.

The most common nail changes include:

- consistency changes;
- changes in pigmentation and coloring;
- shape and texture changes;
- other changes

### **Consistency changes**

Exfoliation (onychoschizia) or lamellar dystrophy is a condition characterized by the detachment of horizontal fragments from the surface of the nail.

Exfoliation is accompanied by onychorrexia - the appearance of longitudinal bumps on the surface of the nail.

The most common causes of this type of problem are exposure of the hands to the aggression of chemicals, very strong soaps or hard water. That is why onychoschizia appears among nurses, hairdressers, housekeepers.

Exfoliation can also be caused by certain nail polishes, special care products, solvents, manicure/pedicure procedures, professional exposure to various chemicals (acids, alkalis, cement, salts, sugar solutions). Trauma can be responsible for the same effect.

The systemic pathologies often incriminated in the occurrence of these manifestations are: endocrine disorders,

tuberculosis, malnutrition, Sjogren's syndrome. Other causes of onychoschisis are lichen planus, psoriasis and oral administration of vitamin A. The problem can be prevented if patients use hand creams and avoid contact with aggressive agents.[7]

#### **Pigmentation and coloring changes**

Leukonychia are small whitish spots that are visible on the surface of minor lesions. It usually persists for a few weeks or months and then goes away on its own.

Cyanosis of the nails occurs in diseases with accentuated peripheral vasospasm, such as Raynaud's disease characterized by arteriolar vasoconstriction, in exposure to cold, cold water or in trauma. Following trauma, extravasated blood accumulates under the nail, which will give the nail its characteristic appearance. As the lesions heal, the coloration will also change.

Also, melanoma can change the color of the nail, from purple to black, but such localization is rarer.[7]

#### **Changes in shape and texture**

They can occur in a wide variety of diseases. Some changes are normal and appear as part of the body's aging process, when some protrusions appear at the nail level, but others are of a pathological nature: thickening of the nail, its crumbling and color change, symptoms characteristic of adults with poor circulation in the extremities .

**Ingrown toenails** are often caused by improper trimming, tight footwear, or can occur as a hereditary trait. The nail can grow in the thickness of the periungual integuments, causing pain, swelling, edema and infection. In rare cases, abscesses can also form under the nail.

**Onycholysis** is the spontaneous detachment of the nail from the surface of the nail bed either from the side or from the distal end. By lifting some areas, a space is created in which debridement tissues accumulate, mainly made up of keratin that normally peels off the surface of the nails. If water also gets under the nails, bacteria can populate the area, causing infections.

Onycholysis can occur in several conditions, such as lichen planus, psoriasis or various types of dermatitis (eczema) but also endocrine diseases (especially thyroid), infections, some forms of cancer and pregnancy.

Drugs that cause this manifestation frequently as an adverse reaction are chemotherapeutics and vitamin A derivatives. Some substances, such as tetracyclines, can interact with ultraviolet radiation and can cause this effect to occur. Once the nail detaches from the nail bed, it will not reattach. The restoration of the nails takes place in 6 months from tomorrow, and those of the feet in 18 months.

**Onychomycosis** or ringworm of the nails, are mycotic infections of the nails and are caused by fungi. They represent approximately 50% of all nail diseases. In general, mycosis initially develops under the nail, between it and the nail bed, then spreads to the proximal region, towards the finger, along the nail bed to the sides. Most of the time the appearance varies depending on the particular type of infection or location.

Infections and allergic reactions are complications of artificial nails. Bacterial infections are due to the occurrence of traumatic lesions with continuity solution that are gateways for germs.

This type of nail infection becomes more common with age, most people over 70 suffering from this condition at least once over time. Onychomycosis is rarely found in children.[8]

**Paronychia or panaritium** is inflammation of the nail fold, i.e. from the proximal region of the phalanx. Inflammations can be acute or chronic (recurrent or permanent). Acute paronychia occurs by continuity solution and is more frequently located on the lateral areas. The most common are bacterial infections, but they can also be viral, for example herpes.

Chronic paronychia occurs most often in patients who spend a long time with wet hands or use hand cream excessively. Chronic paronychia also occurs in contact dermatitis. The infection bacterial infection can be complicated by fungal infections, often *Candida*. Panaritium or paronychia is the most well-known infection of the nail, which affects its basal part, the cuticle, but also the pulp of the finger or the outline of the nail. It is manifested by an inflammation that evolves in a few hours, and that leads to redness and an increase in the size of the affected area[9]

**Chip hemorrhages** are injuries to the blood vessels in the nail bed that can cause fine red-purple lines to appear under the nails. These hemorrhages are due to injuries determined by certain drugs, or occur in the context of certain diseases, characteristically in bacterial endocarditis. These hemorrhages do not require specialized treatment, disappearing in time, together with the process that was the basis of their appearance, with the treatment of bacterial endocarditis. [10]

**Nail hippocratism** is characterized by curvature of the nail and swelling of its root. Hippocratic nail is found in chronic bronchopulmonary diseases, pulmonary suppurations, in congenital heart diseases, but also in ulcerohemorrhagic rectocolitis or in paraneoplastic manifestations of lung cancer. Certain people have congenitally deformed nails, without associating a pathological significance.[11]

#### **The Beau lines are and**

Beau lines are horizontal grooves on the surface of the nail, parallel to the lunula. They appear as a result of processes that disrupt keratin production. As the nail grows, the lines disappear.

Their causes are multiple and can be represented by trauma or local conditions involving the nail fold. Depending on the duration and severity of the initial condition, the lines are also formed, deeper or more numerous). If Beau's lines appear on all nails, having similar characteristics, this fact most likely reflects a growth disorder as a result of some systemic pathologies such as: serious infections, febrile conditions, metabolic disorders, inflammatory diseases.[12]

**Paronychia** is inflammation of the periungual integuments, when the integuments become swollen, painful and reddened.

**Nail growth disorders** are due to certain drugs, such as chemotherapy in particular and antimalarials.

**Anonychia**, the complete absence of the nail, appears as a post-traumatic manifestation, following surgical interventions or may be congenital.

**Onychogryphosis**, a condition in which the nails are curved, similar to claws,

occurs in burns, frostbite or other physical trauma, as well as in chronic oxygen deprivation.

Modified nails can be the result of dermatological conditions such as: eczema, psoriasis, lichen planus, virus infections, the development of nail growths such as warts, cysts. Infection with certain viral strains of HPV can cause changes in the shape and thickness of the nail, but also the appearance of periungual warts. Characteristic nail changes may occur in HIV infection, Addison's disease or peripheral arterial ischemia, alopecia areata, and others.

Tumors can appear in any area of the nail, and the aspects are different, from changes in color to total destruction of the nail.

Nail tumors can be malignant or benign, as is the case with warts. Nail changes, with accompanying signs and symptoms, may affect the patient's ability to grasp small objects, make fine movements, walk, and palpate.[7]

If the nails change color or texture, one of the most common causes is a fungal infection. Also, common diseases, such as thyroid diseases, can cause pathological changes in the nails, they become dry, brittle and with multiple striations. The blue tint of the nails[13] is an indicator of chronic obstructive pulmonary disease (COPD), emphysema, or other lung diseases.

**The blue tint of the nails** is a type of cyanosis due to a low level of oxygen circulating in the red blood cells. These may represent a high level of hemoglobin in the bloodstream.

If the nails return to their natural color after heating and/or massage, the cause of this

sign is blood circulation disorder caused by exposure to cold, constriction or other reasons.

If the nails retain their blue tint, then there may be a condition or structural abnormality that interferes with the body's ability to oxygenate red blood cells.

**Dark, towards black** shade is an indicator for anemia, vitamin B12 deficiency, bacterial infections, chronic kidney disease, adrenal gland disorders, liver disease, cancer or melanoma, poisoning with silver or other heavy metals, trauma.

**The light**, white shade of the nails indicates kidney disease, liver disease or anemia. White lines positioned horizontally on the nails can signal protein deficiency.

**White spots** sometimes appear due to a deficiency of zinc, iron or damage to the nails. These white spots on the nail bed can also indicate certain internal conditions, such as arthritis or poisoning.

**White areas** under the nails, especially at the tip of the nail, indicate a fungal infection that requires medical treatment. If half of the nail has a light shade and the other half has a darker shade, especially towards the tip of the nail, then there is a possibility that the patient is suffering from kidney disease.

**The shade of grey, gray** suggests conditions such as rheumatoid arthritis, edema, malnutrition, complications after surgery, glaucoma, lung disease, emphysema or cardiovascular disease.

**The green tint** of the nails[fig.4] is associated with the existence of an allergy, bacterial infection, localized fungal infection or severe emphysema.





**Fig.4** The shade of green of the nail

**The yellow tint of the nails**[14][Fig.5] is an indicator for ailments



**Fig.5** The yellow shade of the nail

specific to the lymphatic system, diseases of the respiratory system, diabetes or liver diseases. Yellowing of the nails can occur due to respiratory conditions, such as acute bronchitis or lymphedema In the case of yellow nail syndrome, they thicken, grow with difficulty and lead to color changes. Nails affected by this disease may lack cuticles and detach from the tissue in certain areas.

**Purple shades of the nails** signify oxygen deprivation, circulatory disorders, congenital malformations[15]

**Red shades of nails** can indicate cerebral hemorrhage, cardiovascular disease, high blood pressure, lung disease, heart attack, carbon monoxide poisoning. **Lines in shades of red or brown** along the length of the nails[fig.6] can be caused by endocarditis or trichinellosis. Red nodules are seen in collagen vascular disease, heart failure, chronic obstructive pulmonary disease (COPD), cirrhosis, chronic urticaria, psoriasis, and CO poisoning.



**Fig. 6** - lines in brown shades

It can merge with the nail bed in the distal part of the lunule or it can be delimited. by a pale line and can be erased by pressure on the nail plate.[16]

The existence of a single line, in the shade of dark blue, is a sign of skin cancer. Dark black stripes on the surface of the nails indicate the existence of a heart condition (coronary atherosclerosis), and thin lines in shades of black indicate a heart condition.

**Brown spots under the nails** indicate common skin conditions such as psoriasis. Reddish-brown spots indicate a deficiency of folic acid, protein or vitamin C.

The texture of the nails is also a sign of some ailments of the body. Thus, the existence of small striations on the surface of the nail indicates iron deficiency in the body. If these striations are wavy then they indicate conditions such as psoriasis or inflammatory arthritis. If the nails are dry and brittle, it indicates the existence of a thyroid disease, and the presence of horizontal lines on the surface of the nail are signs of diabetes, circulatory diseases, fever manifested in the past or malnutrition.

**The appearance of the nails** is an indicator of some ailments of various organs. Thus, if the nails seem to curve around the finger it is a sign of lung disease, liver disease or inflammatory bowel disease, and if a line appears on the surface of the nail that divides the nail in two it indicates a thyroid condition.[17]

## Onychomycosis

Fungi, along with various types of bacteria, are found naturally in the body and on the skin. When they spread in excess, they can cause infections. Most skin infections are caused by the homogeneous group of keratinophilic fungi known as dermatophytes.

The dermatophyte *Trichophyton rubrum* is the major cause of tinea pedis and onychomycosis

The term onychomycosis traditionally referred to a non-dermatophytic infection of the nail, but today it is used as a general term to denote any fungal infection of the nail. *Tinea unguium* specifically describes a dermatophytic invasion of the nail plate.[18]

Onychomycosis or nail fungus is a fungal infection caused by three classes of fungi: dermatophytes, fungi, and nondermatophytic fungi. Onychomycosis can affect fingernails and toenails. Toenails are more at risk of infection, men being considered more vulnerable.

Dermatophytoses of the stratum corneum, hair, and nails are common, while infection of the dermis and subcutaneous tissue by these agents is rare. Although dermatophyte infections are rarely life-threatening, their high incidence and prevalence and associated morbidity make them an important public health problem.[19]

Other factors that increase the risk of onychomycosis are direct trauma to the nail, including that resulting from certain tic disorders, for example, nail biting.[20,21]

Four types of onychomycosis are recognized, characterized by clinical presentation and route of invasion. Distal

subungual onychomycosis It is the most common form of onychomycosis. It is characterized by the invasion of the nail bed and the lower part of the nail plate. [Fig.7]



**Fig.7-Distal subungual onychomycosis**

Distal subungual onychomycosis can develop on the fingernails, toenails, or both, with toenail infection being much more common than fingernail infection.[22]

Proximal subungual onychomycosis[Fig.8] It is also known as proximal white subungual onychomycosis and occurs when organisms invade the nail unit through the proximal nail fold through the cuticle area, penetrate the newly formed nail plate and migrate distal



**Fig.8 Proximal subungual onychomycosis**

Clinically, this type of onychomycosis includes subungual hyperkeratosis, proximal onycholysis, leukonychia, and destruction of the proximal nail plate. The growth pattern is from the

proximal nail fold to the distal lunula area, involving all layers of the nail.[23]

Although proximal subungual onychomycosis is the least common form of onychomycosis in the general population, it is common in AIDS patients and is considered an early clinical marker of HIV infection.[24]

**Superficial white onychomycosis**[Fig.9] It is a less common mycosis than distal subungual onychomycosis and occurs when certain fungi directly invade the superficial layers of the nail plate.[25]



**Fig.9** Superficial white onychomycosis

The infection can move through the nail plate to infect the cornified layer of the nail bed. It is characterized by the presence of well-defined opaque white spots on the external nail plate, which coalesce and spread as the disease progresses. The nail becomes rough, soft and crumbly. The inflammation is usually minimal and occurs mainly in the toenails.[26] The most common etiologic agent in this type of onychomycosis is *T. mentagrophytes*, but it can also be caused by nondermatophyte molds, including

*Aspergillus terreus*, *Acremonium roseogrisum*, and *Fusarium oxysporum*.[25]

### **Total dystrophic onychomycosis**

It is end-stage nail disease, although some clinicians consider it a distinct subtype. It can be the end result of any of the four main patterns of onychomycosis. The entire nail becomes thick and dystrophic[27]



**Fig.10** Total dystrophic onychomycosis

### **Conclusions**

The nail has an important role in the function of the hand, facilitating pinching and increasing the sensitivity of the fingertip. Therefore, an immediate and appropriate strategy in treating nail lesions is essential to avoid aesthetic and functional damage. The evolution of pharmaceutical forms with applicability on the nail, can take into account, on the one hand, the action of some medicinal plants with spectacular effects on fungi[28,29,30,31] or the anti-inflammatory, antimicrobial action[32,33], but also the pharmaceutical forms delay like liposomes, microcapsules, or nanocapsules[34,35]

Preservation of maximum function and appearance of the finger may be the most important goal of each patient. The appearance of the nail, maintaining a good

state of health, is paramount, which is why it is good to know how to act on the smallest signs of alteration of the good functionality of the nail.

The purpose of this review was to recall the main aspects regarding the structure of the nail, and the main diseases of the nail, so that it is an easy guide for every patient to follow.

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