INTRODUCTION

Eczema is histologically characterized by a lymphocytic epidermotropic inflammation with spongiosis; however, the latter varies in intensity from one eczema type to the other and depends on the acuity and cause of the eczema. Nails are often affected though frequently not specifically noted in clinical practice. Here, only non-infectious skin inflammations will be dealt with.

Allergic contact dermatitis of the nail unit

Allergic contact dermatitis is a type IV immunologic reaction due to a second contact with a substance, against which the body had developed an allergy upon the first contact.

Most allergic contact dermatitis cases of the nail unit develop in the course of hand or less frequently foot eczema (Figure 1). The periungual skin may react in the same way with reddening, swelling, appearance of tiny vesicles, which may lead to oozing. When the acute phase is over, i.e. there is no more any contact with the offending allergen, the oozing skin starts healing and being re-epithelialized and the former wet surface begin to desquamate. In the nail unit, the proximal nail fold is swollen, which makes its free margin thicker and round with consecutive disappearance of the cuticle. This is called paronychia. Particularly in chronic eczema, the developing space under the free margin of the proximal nail may harbor bacteria and yeasts.

The development of an allergic contact dermatitis primarily in the nail unit is rare, even when there is an allergy to nail cosmetics such as in allergy to acrylic monomers of artificial nails or gel nails or due to nail varnish ingredients (Figure 2); however, the volatile solvents of nail cosmetics may cause a so-called ectopic contact dermatitis of the face and anterior surface of the neck, which is a special type of an airborne contact dermatitis. If the allergic reaction involves the proximal nail fold it may spread along its undersurface to the matrix causing characteristic nail plate changes with surface irregularities. They may appear as irregular furrows, which are more pronounced medially than laterally in the nail plate (Figure 3). The nail may lose its shine due to a rough surface with innumerable tiny pits; this phenomenon is called trachyonychia. It may be thickened and intransparent as the spongiotic inflammation of the matrix leads to inclusion of serum and lymphocytes in the nail plate. The dermatitis may spread from the fingertip and hyponychium to the nail bed. Onycholysis then develops, often associated with subungual hyperkeratosis and sometimes with oozing (Figures 4 and 5). If this is caused by acrylic nails it may cause long-lasting pain. Severe acrylate allergic finger dermatitis may develop in dentists. Incapacitating dermatitis was observed in persons
working with industrial sealants, triple-cured hybrid glass ionomers, dentin bonding systems and in other jobs with contact with liquid monomer acrylics and even with acrylic vapor.

In chronic allergic dermatitis of the nail, the nail folds are thick, the skin is rough and hyperkeratotic, the cuticle is lacking, there is a split between the free margin of the nail fold and the nail plate in which exogenous substances and microbial organism may be trapped. They may, even if not primarily pathogenic, lead to a subchronic inflammation aggravating the paronychia (Figure 6). Allergy to acrylic nails may develop a few months after their application. Thumb, index and middle fingers may be scaling and fissuring in printing workers due to photopolymerizable acrylic resin.

Chronic paronychia may be a particular representation of a protein contact dermatitis although there is still a dispute whether this is a chronic Candida spp. may be grown in culture. Proof of the true nature of the origin of this type of paronychia may be seen in the way it reacts to potent topical steroids or antifungal therapy.

Tulip fingers are characterized by painful dry fissured eczema, irregular nail surface and onycholysis. It starts at the hyponychium extending to the nail bed, finger pulp and nail folds. Erosions may develop and in severe cases, hands, forearms, face, and genitals may be involved.

The management of allergic contact dermatitis consists of identifying the allergen, allergen avoidance and short term potent steroids. However, eczema of the nail bed and matrix is usually difficult to treat as the drug does not get to the site of inflammation. In nail bed dermatitis, the overlying nail plate is cut away to allow direct access for the topical preparation. Matrix involvement is even more recalcitrant as it is situated under the proximal nail fold and nail plate. A short course of oral steroids may be helpful. As mentioned before, allergic contact dermatitis of the nail bed due to acrylic nails may cause long-lasting pain not reacting to the topical treatment.

Irritant contact dermatitis

Chronic irritation from mechanical and chemical damage is a common cause for hand dermatitis and may be the forerunner of allergic contact dermatitis, then called two-phase eczema. Wet work damages the barrier of the skin and permits the penetration of potential allergens. This is also seen in the nail unit although usually in association with hand dermatitis. Acute inflammation is rarely seen. The skin is dry, fissuring, scaling and often hyperkeratotic. The proximal nail fold’s free margin is thickened and rounded, the cuticle is absent. The nail plate itself is rough, without shine, shows an irregularly wavy surface, the free margin is often broken (Figures 7 and 8).

Chronic skin picking and onychotillomania may be seen as a particular type of irritant dermatitis (Figure 9)

The management of irritant contact dermatitis comprises meticulous skin care and avoidance of the etiologic agents. Fourth-generation topical steroids, which are inactivated as soon as they penetrate the basal membrane of the epidermis are often indicated and needed for extended periods. Systemic treatment with alitretinoin is often successful [11].

Atopic dermatitis

This condition is also called atopic eczema, endogenous
use [15] Crisaborole, a new phosphodiesterase 4 inhibitor, has also shown promise in the long-term topical treatment of mild to moderate atopic dermatitis [16]. However, the treatment of nail lesions in atopic dermatitis has seen a tremendous change due to the development of IL13/31 inhibitors [17] and more recently of small molecules and Janus kinase (JAK) inhibitors [18] Topical JAK inhibitors are being developed and shown their efficacy in clinical trials [19] Trachyonychia was reported to benefit from systemic altretinoin [20,21].

**Nummular eczema**

This condition, also called nummular dermatitis, discoid eczema, and microbial eczema, is commonly seen on the lower legs, forearms, dorsa of the feet and hands and not so rarely on the proximal nail fold. It may occur in the course of asthenotic eczema, atopic dermatitis, or stasis dermatitis. A number of triggering factors are postulated, such as contact allergy to certain substances, environmental factors such as frequent hot baths, skin irritation by rough fabrics. Clinically, red patches and plaques with tiny erosive points and hemorrhagic crusts are seen. Swabs taken from the oozing lesions usually yield *Staphylococcus aureus*, hence the synonym microbial eczema. Hyperpigmented patches are seen in skin types IV – VI after resolution.

The treatment consists of skin care measures such as frequent application of moisturizers, avoidance of hot showers, use of mild relipidizing soaps and topical steroids, often in an alternating regime with calcineurin inhibitors [22] The prognosis is said to be very good, however, in alcoholics, this type of eczema may be extremely recalcitrant.

**Figure 7** Chronic irritant contact dermatitis of the distal finger and periungual skin. There is also longitudinal melanonychia due to repeated irritation of the matrix.

**Figure 8** Toxic-irritant dermatitis after manicure-induced onycholysis semilunaris and attempts at cleansing the nail with household chemicals.

**Figure 9** Chronic skin picking: Perionychotillomania and onychotillomania. A. Overview. B. Close-up.

**Figure 10** Chronic atopic dermatitis with giant lichenification of the toes.

**Figure 11** Trachyonychia in a 12-year-old atopic girl.
Seborrheic dermatitis

This particular type of dermatitis is not characteristic for the nail unit as this does virtually not have sebaceous glands [23].

Nail psoriasis

Psoriasis is a chronic inflammatory disease affecting the skin of about 2% of the world population. Both genetic and environmental factors play an important rule; they vary between cutaneous and nail involvement [24]. Psoriasis is the dermatosis with the most frequent nail involvement [25]. Roughly 1 - 5% of the psoriasis patients have isolated nail involvement [26]. Between 30 and 50% of the psoriasis patients show some specific nail changes at any given time and up to 90% will develop nail psoriasis over lifetime [27]. Nail psoriasis patients are at greater risk to develop psoriatic arthritis and 80% of individuals with psoriatic arthritis have nail changes. Discomfort, pain, functional impairment, negative impact on work and social life, and psychologic stress are commonplace. Nevertheless it is often neglected and most countries have not included it into their psoriasis guidelines. Most psoriatic nail alterations are characteristic enough to allow the clinical diagnosis to be made right away [28]. Depending on where within the nail unit the psoriasis is located very different lesions are observed.

The most frequent ungual alterations are pits and subungual hyperkeratosis. The pits develop from minute psoriasis lesions in the apical matrix leading to parakeratosis of the cells in the most superficial layer of the nail plate (Figure 12). The parakeratosis may either break out from the nail after emerging from under the proximal nail fold leaving a small depression, the pit, or may be retained and then appear as a tiny ivory colored round spot. More than 10 pits in one nail or more than 50 pits or dots in all nails are taken as diagnostic for psoriasis. So-called pseudo-pits may be seen in pustular psoriasis [29]. Nail bed psoriasis is either seen as a salmon or oil spot or may cause subungual hyperkeratosis. Psoriatic onycholysis represents distal nail bed psoriasis (Figure 13). If a small psoriasis lesion is located in the mid-matrix a psoriatic leukonychia develops as the parakeratosis in the nail plate is optically inhomogeneous and causes the white aspect due to light scattering. Involvement of most of the matrix leads to nail destruction and nail crumbling (Figure 14). Psoriasis of the proximal nail fold causes psoriatic paronychia (Figure 15). Hyponychium and pulp affection is reflected by intense reddening of the fingertip (Figure 16). As all these psoriasis signs may be variably expressed the clinical appearance of the nails varies from nail to nail within the same patient and between patients (Table 2). Further, psoriasis and onychomycosis may co-exist (Figure 17). The distribution and degree of the nail signs are used for the NAPSI score, which is a helpful tool to determine the severity and course of the nail involvement.

The treatment of nail psoriasis is still a challenge [30]. Topical therapy is not very successful as the antipsoriatic drug has to penetrate through the nail plate to reach the nail bed and through the nail fold and underlying nail to get to the matrix. Nevertheless, topicals are recommended for the beginning and in children [31]. Usually high-potency steroids are used. If not more than 3 nails are involved perimatrical injection of steroid crystal suspension may be performed, 0.5 mg per each side of the proximal nail fold to be repeated very 4-6 weeks. Systemic steroids are not recommended. If this treatment is unsuccessful methotrexate 15-20 mg per week or oral cyclosporin 3 -5) mg/d to a serum concentration of 3.5 mg may be given. Internal contraindications have to be considered, and for cyclosporin, no longer than 6-12 months are recommended. If these treatments fail to achieve improvement either biologics or small molecules are indicated. In most countries they are reimbursed when this “therapeutic ladder” had been tried before. Which of the new agents is used depends on the experience of the treating physician, the preference for certain drugs, their side effects spectrum and not
Table 1: Causes of allergic contact dermatitis of the nail unit.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Allergen</th>
<th>Particularities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nail lacquer</td>
<td>Toluene sulfonamide formaldehyde resin</td>
<td>Often chronic eczema and ectopic skin lesions</td>
</tr>
<tr>
<td>Antifungal nail varnish</td>
<td>Undecylenic acid</td>
<td>Used for treatment of onychomycosis</td>
</tr>
<tr>
<td>Artificial nails</td>
<td>Acrylate monomers,\textsuperscript{1,2} ethylcyanoacrylate</td>
<td>May cause long-lasting excruciating pain</td>
</tr>
<tr>
<td>Dentin bonding system</td>
<td>Acrylate monomers</td>
<td></td>
</tr>
<tr>
<td>Tulip fingers</td>
<td>a-Methylene-g-butyrolactone</td>
<td>Allergen is in the tulip bulbs</td>
</tr>
<tr>
<td>Abrosermeria dermatitis (Peruvian lily, lily of the Incas)</td>
<td>Tuliposide A and B\textsuperscript{2,3}</td>
<td>Allergen mainly in flowers, passes through vinyl gloves.</td>
</tr>
<tr>
<td>Hydrangea dermatitis</td>
<td>Hydrangenol</td>
<td>Flowers and stem.</td>
</tr>
<tr>
<td>Tabernaemontana coronaria</td>
<td>Various alkaloids</td>
<td>Alkaloids are antimutagenic</td>
</tr>
<tr>
<td>Turpentine</td>
<td>Oleoresin of pine trees</td>
<td>Professional allergy in certain crafts workers</td>
</tr>
<tr>
<td>Toxicodendron spp: poison ivy, poison oak, poison sumac, Chinese lacquer tree</td>
<td>Urushiol\textsuperscript{1,8}</td>
<td>Rhus dermatitis, urushiol-induced contact dermatitis, Toxicodendron dermatitis.</td>
</tr>
<tr>
<td>Hevea brasiliensis: Latex. Type I allergy to natural latex.\textsuperscript{9}</td>
<td>Hevein (Hev b6.02), less frequently Hev b2, Hev b7, Hev b8, Hev b12 \textsuperscript{10}</td>
<td>Be aware of latex-fruit syndrome: avocado, kiwi, bananas, chestnut, less frequent: apple, carrot, celery, melon, papaya, potato, tomato</td>
</tr>
<tr>
<td>Epoxy resin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gloves, medical equipment. Type IV allergy mainly to additives</td>
<td>Antioxidants and accelerators in production</td>
<td>Often confused with true latex allergy. Powdered gloves may be more potent sensitizers.</td>
</tr>
<tr>
<td>Hair dyes (illegal), color intensifier (henna skin painting 	extquotedblright henna tattoos	extquotedblright)</td>
<td>Paraphenylenediamine</td>
<td>May cause group allergy of many so-called para substances</td>
</tr>
<tr>
<td>Cement</td>
<td>Dichromate</td>
<td>Professional allergen of brick layers; associated with chronic hand eczema.</td>
</tr>
<tr>
<td>Cobalt, some printing colors</td>
<td>Cobalt</td>
<td>Often not clear whether it is an allergic or toxic reaction</td>
</tr>
<tr>
<td>Nickel-containing jewelry, piercings</td>
<td>Nickel</td>
<td>Most frequent allergen in atopics</td>
</tr>
</tbody>
</table>

Table 2: Psoriasis lesions of the matrix nail bed and periungual skin.

<table>
<thead>
<tr>
<th>Matrix</th>
<th>Nail bed</th>
<th>Periungual skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pits</td>
<td>Salmon/oil spots</td>
<td>Paronychia</td>
</tr>
<tr>
<td>Ivory spot</td>
<td>Subungual hyperkeratosis</td>
<td>Psissing of digital tip</td>
</tr>
<tr>
<td>Red dots of the lunula</td>
<td>Onycholysis</td>
<td></td>
</tr>
<tr>
<td>Leukonychia</td>
<td>Splinter hemorrhages</td>
<td></td>
</tr>
<tr>
<td>Nail plate thickening</td>
<td></td>
<td></td>
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<tr>
<td>Nail crumbling and destruction</td>
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</tbody>
</table>

Table 3: Differential diagnosis of psoriasis and onychomycosis (adapted from [25], with permission of the author).

<table>
<thead>
<tr>
<th>Psoriasis</th>
<th>Onychomycosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Most frequent dermatosis with nail involvement; 80% of patients with psoriasis will develop nail psoriasis during lifetime.</td>
</tr>
<tr>
<td>Course</td>
<td>Chronic to chronic-recurrent, often with intermittent improvement.</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Chronic progressive, but also often stable over years.</td>
</tr>
<tr>
<td>Signs</td>
<td>Embarrassment, often painful, and restricting daily activities.</td>
</tr>
<tr>
<td>Pits</td>
<td>Embarrassment, potentially painful.</td>
</tr>
<tr>
<td>Onycholysis</td>
<td>Subungual hyperkeratosis, yellowish discoloration, onycholysis.</td>
</tr>
<tr>
<td>Frequent.</td>
<td>Rare, irregular size.</td>
</tr>
<tr>
<td>Frequent.</td>
<td>Frequent.</td>
</tr>
<tr>
<td>Discoloration</td>
<td>None or yellowish.</td>
</tr>
<tr>
<td>Spores and hyphae</td>
<td>Yellow to brown.</td>
</tr>
<tr>
<td>Transverse ridges</td>
<td>Rare.</td>
</tr>
<tr>
<td>Trauma</td>
<td>Very frequent: spores and hyphae.</td>
</tr>
<tr>
<td>Important predisposing factor.</td>
<td>Very rare.</td>
</tr>
</tbody>
</table>
Strong genetic component. Lesions elsewhere

Psoriatic plaques often present in typical localization. Susceptibility to develop onychomycosis is inherited as an autosomal dominant trait

Hyperkeratosis with parakeratosis and included neutrophils and serum globules.

Marked hyperkeratosis with neutrophils and serum inclusions contains most of the pathogenic fungi. Leukocytes in subungual hyperkeratosis and surrounding by parakeratosis (Munro's microabscesses). Focal hypergranulosis. Papillomatous nail bed. Spongiosis, mononuclear, and neutrophil exocytosis. Hyphae and spores in the subungual hyperkeratosis and underside of the nail plate.

Histopathology

Histopathology

Heredity.

Marked hyperkeratosis and subungual hyperkeratosis. Myriads of scabies mites inhabit these hyperkeratoses and recurrences are frequent because they are not killed by topical treatment. Paronychia with violaceous skin, linear and verrucous hyperkeratoses, onycholyisis, nail bed hyperkeratosis and occasional splinter hemorrhages as well as nail plate thickening, fragmentation, overcurvature and yellow-brown discoloration are characteristic signs of the rare keratosis lichenoides chronica now classified as an autoinflammatory keratinization disorder. In chilblain lupus erythematosus, the distal digits are often violaceous red (Figure 19). Raynaud's syndrome is characterized by periods of bluish-red discoloration of the digits that may slowly turn white; this is called digitus mortuus (dead finger), often associated with pain upon re-warming. In long-standing Raynaud's, the nail may become dystrophic (Figure 20). Both bullous pemphigoid (Figure 21) and pemphigus vulgaris may affect the nail unit and lead to paronychia-like inflammation.

Periungual inflammation is a sign of many acute infections, such as digital herpes simplex, bullous impetigo (run-around), erysipelas, erysipeloid, and ingrown nails (Figures 22-24). Their distinction from early acute contact dermatitis may be sometimes difficult. In skin types V and VI, more intense pigmentation is often the consequence of a previous inflammation (Figure 25).

Drug reactions

Drug reactions involving the nail unit are not rare although often neglected, particularly in severe widespread cutaneous disease. Depending on the specific localization of the lesions within the nail apparatus, variable clinical features may prevail. Matrix involvement may cause Beau's lines reflecting a short-term reduction of the nail growth rate, onychomadesis after complete stop of nail growth, or surface defects (Figure 26). Loss of the nail is characteristic after Stevens-Johnson syndrome/toxic epidermal necrolysis and severe erythema multiforme. Transverse leukonychia is another sign. Onychoschizia and onychorrhexis develop later. Nail bed affection may cause subungual hyperkeratosis, onycholyisis, sometimes photoonycholysis and apparent leukonychia due to vessel contraction or obstruction. Acute paronychia of several digits with granulation tissue is a characteristic adverse effect of synthetic retinoids, reverse transcriptase inhibitors and particularly epidermal growth factor receptor inhibitors [37]. This is often so severe and painful
Figure 15 Psoriasis unguium. Involvement of the proximal nail fold causes its thickening and spontaneous loss of the cuticle.

Figure 16 Intense reddening of the fingertip and hyponychium in distal digital psoriasis.

Figure 17 Periungual inflammation in a psoriatic patient with onychomycosis.

Figure 18 Papular and vesicular scabies with involvement of the fingers and periungual skin. A. Clinical aspect. B. Dermatoscopy.

Figure 19 Violaceous red toes and small dystrophic nails in chilblain lupus.

Figure 20 Onycholysis and receding nail bed in a patient with longstanding Raynaud’s syndrome.

Figure 21 Bullous pemphigoid of the left big toe in a 63-year-old female patient.

that the anti-cancer treatment had to be reduced or completely stopped. Acute contact dermatitis due to topical preparations also occurs on the nail apparatus. Chronic cutaneous graft-versus-host disease may cause eczema- and psoriasis-like skin lesions [38] although the common features of cutaneous GvHD are a lichen planus-like nail dystrophy.

CONCLUSION

Any type of dermatitis may involve the nail. Nail alterations depend on the specific disease and particularly on the particular structure of, and site within, the nail unit. Thus, understanding the anatomy and physiology of the nail is a prerequisite for a correct diagnosis and treatment.
Figure 22 Reddening of the lateral-proximal portion of the left toe nail fold in a 24-year-old patient with circumscribed paronychia due to an incipient growing nail.

Figure 23 Diffuse dermatitis of the periungual tissues in an acute ingrowing nail.

Figure 24 Periungual erythema in retronychia (A and B).

Figure 25 Postinflammatory pigmentation in a patient with skin type V and non-dermatophyte onychomycosis; mold infections of the nail apparatus are characteristically associated with periungual inflammation and paronychia.

Figure 26 Residual erythema around the nails after a multiform drug reaction. Note the surface defects of the ring fingernail plate.

REFERENCES


13. Chung BY, Choi YW, Kim HO, Park CW. Nail dystrophy in patients


