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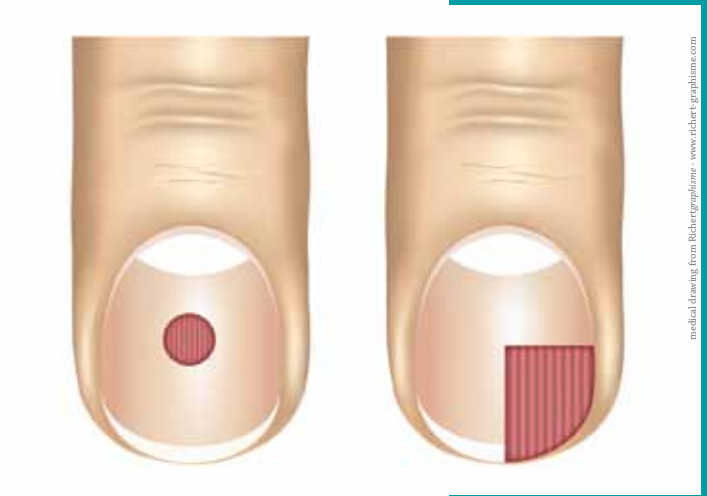
n°8

The nail



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What's new ?

ENS European Nail Society

The Official Journal of the European Nail Society

Pierre Fabre DERMATOLOGIE

The nail - What's new ? n°8

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The nail - What's new ? n° 8
THE OFFICIAL JOURNAL OF THE EUROPEAN NAIL SOCIETY
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EDITORIAL

2015 is the year of the World Congress of Dermatology. It takes place every five years and I therefore thought that it would be interesting to list a number of the innovations that have appeared in the nail field during this period. I accordingly put pen to paper and to my amazement my hand was not fast enough to write down everything that was popping out of my head!

The first fact that came to mind was that it has now been clearly demonstrated that UV light, whether A, B or C, does not cross the nail plate. Since I found this out, I have had trouble in understanding photoonycholysis! I admit this is not a common disease, but all nail doctors will come across several cases during their nail career.

As expected, the onychomycosis field progressed a good deal: new techniques have been developed to allow a fast and inexpensive diagnosis, its classification has been updated and a severity score is now available. We learned that dermatophytes are colonizing the world, as they are traveling by plane, and that they may hide for years in the lymph nodes and may later be discharged into the blood flow to once again reach the nail unit.

Medical imaging with high resolution devices has demonstrated the intimate link between the matrix and the joint, and this technique now allows us to state that absolutely no nail psoriasis is without joint involvement. Consequently, this has had an impact on the way biologics will soon be prescribed for nail psoriasis. Confocal microscopy ex vivo permits the diagnosis and treatment of suspicious longitudinal melanonychia in a single session.

Until a few years ago, lasers had not been tools for nail disorders. Even if their efficacy has not yet been proved and their mode of action is still poorly understood, their introduction in the treatment of onychomycosis is a new niche for laser companies. On the contrary, pulsed dye lasers have proved to be somewhat effective in nail psoriasis and are worth trying, especially in the onycholytic variant.

New diseases with ungual tropism have likewise been described. The emergence of the superficial fibromyxoma is surprising. Is this a really new entity, had we missed it or had the pathologists been calling it differently? Based on several clinical cases, geneticians acknowledged only an ungual variant of epidermolysis bullosa that may evolve over several generations, until full expression of the disease appears in a descendant.

Old diseases have evolved or been rediscovered. Yellow Nail Syndrome, as well as some cases

of nail lichen planus, may be linked to the presence of heavy metals (especially Titanium) in dental restorative substances, drug tablets and confectioneries. Correlation has been found and proved between the severity of the nail involvement in the YNS and the severity of lung disease.

Concerning nail lichen planus, we learned from two very large series that only 2/3 of the patients will respond to steroid systemic treatment and that about 2/3 of those will have a relapse. Alitretinoin is a new retinoid that has a more potent anti-inflammatory action than acitretin and has shown some promising results in a few cases. We were also informed of a very frightening side effect that every dermatologist should be aware of and which is that injection of crystals containing solutions at the proximal nail fold may be responsible for the Hoigné syndrome.

Nail surgery has also improved and has re-discovered some old procedures. The most exciting one is surely the tangential excision for longitudinal melanonychia. It has been established that this technique allows accurate diagnosis and leaves almost no post operative nail dystrophy. In ingrowing toenails, studies have demonstrated that alcohol does not neutralize, but dilutes phenol. The term "phenol-alcohol technique" should definitively be abandoned and saline should be preferred for rinsing the surgical field. A new promising cauterant has appeared: trichloracetic acid 100%. The main drawback of chemical cautery is that the oozing may last up to 4 weeks. However, it has been shown that debridement of the coagulated tissues dramatically shortens the oozing time. Howard and Dubois were the first ones to use debulking of the soft tissues many years ago. It has now resurfaced and the Vandenbos (a re-appearance from 1954), the Super U (a Brazilian variant of the previous one) and the Noel procedures (a vertical variant of the Dubois one) can also be added to the list. These are very effective in any type of hypertrophic ingrowing disease.

Treatment of malignant tumours has also dramatically changed. Mohs' surgery is now recognized as the gold standard therapy for squamous cell carcinoma of the nail unit. And even if there are still no guidelines for the treatment of melanoma of the nail unit, recent literature has offered hints in favour of "functional" excision for nail melanoma in situ and reserves distal amputation for invasive melanoma.

Nail cosmetics have also their brand new baby: UV gel cured nails! Its resistance has definitely won over women's hearts. The oncogenic concern about a regular exposure of the hands to UV nail lamps has been dropped, but gloves, cut at their extremity, remain recommended. In addition, NAC has become the ultimate solution for those who cannot stop biting or playing with their nails.

This list is surely incomplete, but it does however show how the nail field is dramatically evolving and attracting people. A telling example is the arrival of a third nail society: the Nail Society of India that will host the 3rd International Summit on Nail Disorders in Delhi in November 2015.

Bertrand Richert

Robert BARAN

DENTAL RESTORATIVE SUBSTANCES, DRUG TABLETS AND CONFECTIONERIES ARE RESPONSIBLE FOR SOME CASES OF YELLOW NAIL SYNDROME AND NAIL LICHEN PLANUS

In Décember 2014[1] and February 2015[2] two papers were published concerning an article of Berglund and Carlmark[3] on yellow nail syndrome where 4 patients with titanium implants showed complete resolution of their symptoms after the gold dental work was removed. In addition to their article, I remind readers that some authors have found other dental allergens responsible for nail lichen planus (NLP). Yellow nail syndrome (YNS) is characterized by nail changes, respiratory disorders, and lymphedema. The yellow nails are unsightly, discolored and hard, show transverse overcurvature, and are slow growing. Paronychia and onycholysis may be observed **(Fig 1)**.
Nail abnormalities may be the only pattern of this syndrome.

Fig1 - *Yellow nail syndrome. © R. Baran*

On the other hand, the diagnosis of lichen planus of the nails may be readily made when it exists together with typical cutaneous or mucous membrane disease. However, in those cases in which the nail is involved (about 10%) a definitive diagnosis must be rendered prior to instituting therapy. NLP alone is rare (1-2 %) and presents a difficult diagnostic challenge, because the clinical signs of NLP are dependent on the anatomic site of the nail unit that is involved in the process **(Fig 2)**.

Berglund and Carlmark[3,4] examined nail clippings from patients with one or more features of YNS. Their nails were analyzed by energy dispersive X-ray fluorescence: titanium (Ti) was regularly found in patients' fingernails, but not in control subjects.
The Ti ions were released through the galvanic action of dental gold or amalgam or through the oxidative action

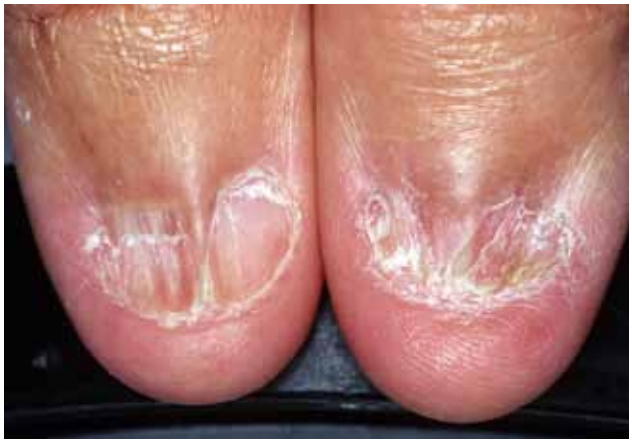

Fig2 - *Lichen planus, advanced type with pterygion. © R. Baran*

of fluorides. Stopping the galvanic release of Ti ions or cancelling exposure to Titanium dioxide led to recovery. In one patient with a Ti implant, the symptoms recurred after renewed exposure to Ti. In their initial paper, four men and four women had symptoms of YNS after exposure to Ti dioxide in drug tablets or confectioneries **(Table I)** and the dominant cause of yellow nails was the galvanic interaction between gold in the teeth and Ti implants and several publications mentioned the exposure to drugs (that usually contain Ti dioxide) preceding the development of yellow nails and also the return to normal conditions, months after withdrawal of the drugs.
Although metal allergy has also been considered to be one of the precipitating factors in lichen planus, only a few reports exist that show a clinical association between metal allergy and NLP. In the study of Nishizawa et al[5] "the prevalence of positive metal patch test (PT) results were higher in NLP as compared with oral lichen planus (OLP)". In addition, 60% of these NLP patients (6 of 10 cases) showed clinical improvement after, either removal of the dental materials, or systemic disodium cromoglycate therapy. Positive patch testing to metals, such as Cr, Ni and Au, carried out in patients, was detected in both dental fillings/braces and in the nail lesions in some of the authors' NLP patients. Kato et al[6] reported on a patient with lichen planus of the buccal mucosa (OLP) caused by mercury allergy, in which both the nails and the skin were affected. "Patch testing showed positive reactions to mercury 0.05%, ammoniated mercuric chloride 1.0, and thimerosal 0.1% in toothpaste that contained mercury, as a component of the patient's dental fillings. When these were replaced by the hard resin jacket crowns, the mucosal, and nail symptoms gradually improved".
A similar case of allergy due to mercury amalgam has been presented by Higashi[7] where a patient developed a systemic

Table 1 - *Exposure to titanium dioxide*

Decker A, Daly D, Scher RK (with permission of Skin Appendage Disord 2015; 1:28-30)

Foods	Chewing gum / Candy (especially the outer shell) / Chocolate / Products with icing or powdered / sugar topping / Powdered product mixed into foods
Personal care items	Sunscreen / Moisturizers / Deodorants / Shampoo / Lip balms / Toothpaste
Medications	Multivitamins / Oral capsules / Suspensions / Tablets

lichen planus, associated with NLP restricted to the toes.
Yokoseki et al[8] examined a 51-year-old man with "20-nail dystrophy" produced by lichen planus, histologically confirmed. The authors carried out patch-tests, which revealed positive reactions to both nickel and gold. After these fillings were replaced by hard resin jacket crowns, the nail symptoms dramatically improved.
Takeuchi et al[9] observed the case of a 57-year-old man, whose 10 fingernails were deformed for 18 months, before presentation and deformity of all 10 tœnails.
Histology showed lichen planus. The patient had worked as a tinsmith for over 30 years and had had dental metal on several teeth for approximately 20 years. The metal patch tests revealed positive reactions to chromate and tin. Treatment with systemic steroids was quite effective in treating the nail lesions.
Finally, the enigmatic yellow discoloration observed in some cases of isolated NLP10-13 may well be considered as a clinical bridge between LP and YNS **(Fig 3)**. However, above all, we have tried to demonstrate that a common culprit may be an important link for these quite different diseases.

Fig3 - *Lichen planus yellow 20 nail dystrophy. © R. Baran*

CAPSULE SUMMARY

- Yellow nail syndrome (YNS) is characterized by a triad: nail changes, respiratory disorders and lymphoedema.
- Nail lichen planus (NLP) may present with different features.
- Both conditions may be produced by dental restorative substances. This is demonstrated by metal patch tests, recovery after cancelling exposure to titanium dioxide and recurrence after renewed exposure to titanium.
- The yellow discoloration observed in some NLP especially the 20 nail dystrophy variant may well be considered as a clinical bridge between Lichen planus and YNS

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Marie CAUCANAS

THE PROXIMAL NAIL FOLD: A KEY IN SYSTEMIC DISEASES

Elmansour I, Chiheb S, Benchikhi H. Nail changes in connective tissue diseases: a study of 39 cases. Pan Afr Med J. 2014;18:150

This study aimed to identify nail unit changes associated with connective tissue diseases (CTD) and evaluate their frequency. The authors carried out a prospective trial over one year, enrolling 39 patients, with a mean age of 40 years and 6 years mean duration of the disease, suffering from systemic sclerosis (n=16), lupus erythematosus (n=14), dermatomyositis (n=8) and primary Sjögren's syndrome (n=1). A clinical examination of the fingernails was performed by the same dermatologist together with clinical pictures. Corresponding nail features were classified. 27 patients (69%) demonstrated nail unit abnormalities, as shown in **Table 1**. The proximal nail fold appeared as the most affected site **(Fig 1)**.
These results were similar to previous studies[1, 2]. The authors concluded that the knowledge of clinical features associated with CTD may provide clues to the diagnosis, in association with other tools, such as biopsy of the nail fold, capillaroscopy or dermoscopy.

Though this descriptive clinical study has a small sample of patients and has no control group, it confirms previous findings, emphasizes the importance of examining the nail apparatus in systemic disorders and allows the clinician to strengthen his knowledge about nail unit changes and current CTD, such as systemic sclerosis, systemic lupus erythematosus and dermatopolymyositis/ polymyositis. A high incidence of ventral pterygium in systemic sclerosis is to be noted in this study, as it has not been mentioned in bigger studies such as the one conducted by Tunc et al with 190 patients.[1] It would have been interesting to connect it to disease activity. Also readers would have benefited from a correlation between clinical and dermoscopic/ capillaroscopic findings, as these are available easy non-invasive techniques and were suggested as complementary tools in their conclusion.

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NAIL CHANGES (%)	SS (N=16)	SLE (N=14)	DPM/ PM(N=8)
Proximal Nail Fold			
Nail fold telangiectasia	**56**	/	25
Periungual erythema	/	**28.57**	**50**
Ragged/hypertrophic cuticle	**37.5**	/	**50**
Dyschromia of the proximal nail fold	18.75	/	/
Lunulae			
Macrolunulae	6.25	/	/
Red lunulae	/	7.1	/
Nail plate			
Longitudinal ridging	25	**28.5**	**37.5**
Increase of longitudinal curvature	25	/	/
Increase of transverse curvature and beaking of the nail	25	/	/
Nail plate pigmentation	12.5	7.1	/
Pseudoclubbing	6.25	/	/
Nail bed			
Splinter haemorrhages	/	**21.4**	/
Subungual hyperkeratosis	/	14.2	/
Onycholysis	/	14.2	/
Hyponychium and fingertips			
Fingertip scars	**56.2**	/	/
Ventral pterygium	12.5	/	/

Table 1. *Nails changes reported in Systemic Sclerosis (SS), Systemic lupus erythematosus (SLE) and Dermatopolymyositis-Polymyositis (DPM-PM).*

Fig1 - *Nail fold telangiectasias in systemic sclerosis. © B. Richert*

CAPSULE SUMMARY

- Nail unit changes are frequent in CTD
- The most affected site remains the proximal nail fold, showing telangiectasia in SS and DPM/PM, periungual erythema in SLE and DPM/PM, ragged/hypertrophic cuticles in SS and DPM/PM.

THE NAIL AT MEDICAL SPECIALITIES CROSSROADS

Yuksel S, Pancar Yuksel E, Yenercag M et al. Abnormal nail fold capillaroscopic findings in patients with coronary slow flow phenomenon. Int J Clin Exp Med. 2014;7(4):1052-8

The coronary slow flow phenomenon (CSFP) is an angiographic clinical entity defined by a delayed opacification of coronary arteries in the absence of significant stenosis. It occurs most commonly in young men and smokers, and patients admitted with acute coronary syndrome though the pathogenesis has not been fully determined yet. In this case-control study, the authors sought to investigate the nail fold capillaries of CSFP diagnosed patients (n=25) and make a comparison with those of a group of subjects with normal coronary flow (NCF, n=24). Demographic, clinical features and transthoracic echocardiographic parameters were similar in both groups. Nail fold capillary abnormalities including dilation, tortuosity and microhemorrhage were found to be 5.7 times higher in the CSFP group (60%) compared to the NCF patients (21%). The authors conclude that the results of their study, combined with the available data about CSFP, are in favour of a generalized vascular disease affecting different microvascular systems rather than a local abnormality affecting only the coronary blood flow.

This article has a very strong methodology and reflects close collaboration between the Cardiology and Dermatology Departments in Ondokuz Mayis University in Samsun, Turkey. Notably, the recruitment procedure was very strict, in order to select patients suffering from CSFP as was initially defined. The capillaroscopic findings are not specific of CSFP, but give a strong argument to classify CSFP as a more general vascular entity, rather than as a local coronary phenomenon. Where capillaroscopy remains a Dermatologic practiced skill, learning about CSFP allows cardiologists and dermatologists to collaborate better. Beyond these specialities, nail fold capillaroscopy is studied more and more, as it provides inestimable non-invasive information about many diseases with impaired microcirculation, with or without an inflammatory component.[1,2]

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CAPSULE SUMMARY

- CSFP patients were found to have nearly 6 times higher occurrence of microvascular dilation, tortuosity and microhemorrhages.
- Capillaroscopy is an easy and useful non-invasive technique allowing to explore the microvasculature reflecting the general vascular state.

YELLOW NAIL SYNDROME: NAILS, LUNGS AND LEGS

Piraccini BM, Urciuoli B, Starace M et al. Yellow nail syndrome: clinical experience in a series of 21 patients. J Dtsch Dermatol Ges. 2014;12(2):131-7

The Yellow Nail Syndrome (YNS) is a rare condition associating yellow nails **(Fig 2)**, respiratory disorders and lymphedema. The authors aimed to assess the clinical features, associated diseases and response to treatment of patients with YNS. A retrospective-transverse observational study was conducted out of a database of 15600 patients of the Outpatient Nail Clinic at the University of Bologna, over a period of 28 years. 21 patients who had been diagnosed

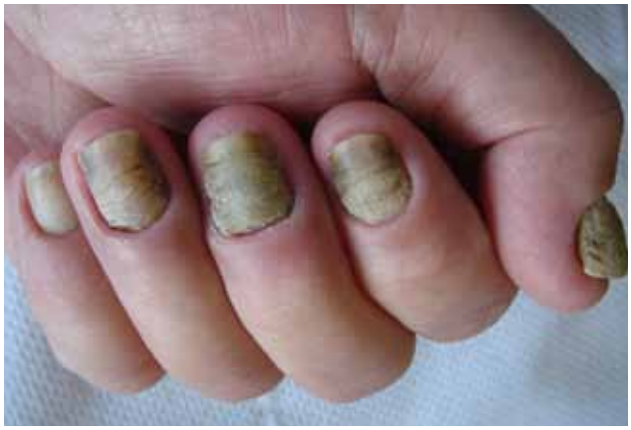

Fig2 - *Yellow Nail Syndrome. © B. Richert*

Marie CAUCANAS

Table 1. Results of the observational study assessing 21 patients with YNS.

Demographic data
• 11 men, 10 women • Mean age: 57±12 years (time of diagnosis); 53±11 years (onset of nail alterations)
Dermatologic findings
General nail features: progressive thickening, change of color (n=18); nail growth arrest (n=3) Nails involved: All of them (n=15); Fingernails only (n=6) Intensity of the nail alterations Mild (n=3): increased transverse curvature, onycholysis and yellow-green discoloration Moderate to severe, with impaired digital function (n=18): nail fold swelling, lack of the cuticle, yellow-green to black nail discoloration, severe onycholysis, nail plate shedding Mycological examination (n=12): *Trichophyton rubrum* positive culture in 5 patients Dermoscopic examination of the nail fold (n=15): dilated and tortuous capillary loops in 100%
Systemic involvement
Partial or complete syndrome • Complete triad: yellow nails, lymphedema, chronic respiratory diseases (n=6) • Nail involvement and respiratory diseases only (n=10)

Chronic obstructive lung disease	Chronic bronchitis	History of pleural effusion	Bronchiectasias
Chronic sinusitis	Recurrent pneumonia	Restrictive lung disease	Nasal septum deviation
Asthma	Nasal polyposis	Chronic rhinitis	

• Yellow nail alterations only (n=5) Associated diseases • 85% had varying concomitant diseases • 9% suffered from malignant tumours
Nail treatment
• Spontaneous recovery of the nail alterations in one patient • Vitamin E 1200 IU/day (n=11): complete recovery in 3, improvement in 3, no change in 5 • Vitamin E 1200 IU/day + Itraconazole 400 mg/day one week/month for 6 months (n=9): complete recovery in 1, improvement in 3, no change in 5 • Systemic signs not influenced by vitamin E treatment
Evolution of disease (mean follow-up: 38 months)
• Stable nail symptoms in 7/10 non-responders; worsening in 3 • Associated respiratory diseases progressed; diseases of other types remained stable • Death in 4 patients over 70: cardiac failure (n=3), acute pulmonary edema (n=1)

with YNS were identified and contacted to undergo a new clinical evaluation and to collect new pictures to compare with the previous ones. Videodermoscopy of the proximal nail fold was performed to investigate capillaries. Evolution of the nail condition was assessed following oral vitamin E and itraconazole treatment. The results are summarized in **Table 1**.

In the discussion, the authors highlight the main features about YNS, supported by the review of the literature:

YNS is a rare disorder, accounting for 0.13% of nail diseases seen over 28 years in this study. It usually affects male or female middle-age adults. The pathogenesis of YNS has not been elucidated yet. Lymphatic deficit has been evoked.

It is admitted that the typical clinical nail alterations suffice for the diagnosis. Other symptoms may develop at different times, but pulmonary abnormalities were found to precede nail lesions.

Main differential diagnoses are chronic paronychia for fingernails, onychomycosis, onychogryphosis and acquired pachyonychia for toenails.

All nails are more or less affected, usually in a severe way, causing cosmetic and functional impairment: yellow to brown discoloration, thickened nail plate, arrested growth, increased curvature, onycholysis, nail fold swelling, lack of cuticle and sometimes nail shedding.

Contrary to the data available in other case series, only 28% of the patients presented with lymphedema (vs 80%) and 81% with pleuropulmonary symptoms (vs 63%).[1,2] Chronic obstructive lung disease and chronic bronchitis were the most common respiratory disorders, in contrast with pleural effusions more commonly described.

Other underlying diseases have been associated with YNS, including malignant tumours. Considering the small sample of patients and the YNS average age of onset after 50, the authors did not make any correlation between YNS and the occurrence of neoplasia.

10 to 30% spontaneous remission has been reported[3,4] and no treatment has yet shown consensual results. Successful outcome rose nearly 50% with high dose vitamin E treatment in this study and no patient experienced any side effect. In case of severe subungual hyperkeratosis, onychomycosis should be ruled out.

The authors conclude that physicians should be aware about YNS nail signs and screen for lymphedema and respiratory diseases, as well as diagnosing associated onychomycosis. Although natural favourable evolution may happen, they encourage the use of oral high dose vitamin E treatment, always well tolerated.

With 0.13% incidence over 28 years within a specialised nail disease center, YNS is indeed a rare entity. Contrary to other diseases affecting millions of people like diabetes or hypertension, recruiting a series of 21 patients suffering from YNS appears to be a real performance. Medical science has been built up upon observation, so this study represents a strong contribution to a better understanding of this disorder and gives clues for its management and treatment, to the best of today's knowledge. In this case, prospective studies are almost impossible, because they would last too many decades, but it is interesting to notice that though this was a retrospective study, the authors called back their patients to allow a new clinical evaluation, thereby strengthening its scientific relevance.

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CAPSULE SUMMARY

- Typical nails alterations are enough to diagnose YNS, though respiratory symptoms and lymphedema may appear at different times.
- YNS work-up should include ultrasound examination of the lower limbs and chest X-ray.
- It is worth trying vitamin E therapy in all patients with YNS.

NAILS AND AMYLOIDOSIS

Renker T, Haneke E, Röcken C et al. Systemic light-chain amyloidosis revealed by progressive nail involvement, diffuse alopecia and sicca syndrome: report of an unusual case with a review of the literature. Dermatology. 2014;228(2):97-102

The authors report the case of a 66-year-old woman with a 15-year history of asymptomatic hand skin changes, nail abnormalities and hair loss, who then developed xerostomia, xerophtalmia **(Table 1)** and a propensity of easy ecchymoses and hematomas after trauma. The work-up included biopsy specimens of the scalp, nail apparatus, minor labial salivary glands and abdominal skin, revealing deposits of immunoglobulin light-chain (AL)

Marie CAUCANAS

Table 1. *Clinical findings of the skin, hair, nail and mucosae locations in the 66 year-old woman.*

Skin changes	Hair changes	Nail abnormalities	Mucosae changes
Yellow-orange discoloration (face, décolleté)	Reduced hair density, thin hair shaft (vertex, frontoparietal)	Fingernails: - Plate thinning - Loss of nail shine - Longitudinal ridging - Onychorrhexis	Dry, atrophic oral mucosae and tongue
Parchment-like and scleroatrophic appearance of the hands and fingers	Complete loss of axillary hair	Toenails: more discrete similar findings	Eye dryness
Firm abdominal skin	Sparse genital hair		

kappa-type amyloid. The urinary protein electrophoresis revealed a weak band of light chains of the kappa-type. This is a peculiar presentation of a systemic amyloidosis of the AL type with a very indolent course, associating nail involvement, diffuse hair loss, skin discoloration and parchment-like acral changes with sicca syndrome as the predominant clinical features over years. In the discussion, the authors point out that the most frequent mucocutaneous manifestations of AL amyloidosis include purpura, petechiae and ecchymoses in periorbital, flexures and traumatised areas. Other skin changes reported are waxy papules, nodules or plaques, pigmentary changes, scleroderma-like thickening of the skin and bullous lesions. Nail dystrophy, alopecia and sicca syndrome are rare manifestations of systemic amyloidosis. Nail dystrophy is due to amyloid deposition in the matrix, nail bed and nail fold, altering nail synthesis. Contrary to clinically similar nail abnormalities, amyloidosis nails are very soft and thin. Features include brittleness, longitudinal ridging **(Fig 3)**, crumbling, onycholysis and subungual thickening, striations and anonychia. The authors conclude that this observation highlights the importance of being aware of these rare mucocutaneous signs as a potential beginning of amyloidosis of the AL type, and as clues for early diagnosis and management of this multiorgan involvement disease.

This observation is richly illustrated, with histopathologic examination of four different locations (salivary gland, abdominal skin, scalp and lateral longitudinal nail biopsy) and an extensive review of the literature. Nail changes

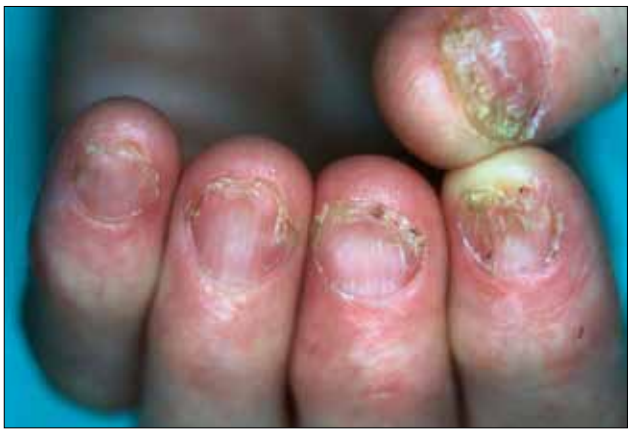

Fig3 - *Nail dystrophy in systemic amyloidosis. © J. André*

associated to amyloidosis have rarely been described, but can sometimes be the only cutaneous manifestation of systemic amyloidosis.[1] Therefore it appears essential to know both the frequent and less frequent mucocutaneous signs, in order to better diagnose and manage this disease.

Reference
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CAPSULE SUMMARY
- Amyloidosis nails are soft and thin.
- Mucocutaneous signs may represent a clue for the diagnosis of systemic amyloidosis.

NAILS AND CHEMO

Miller KK, Gorcey L, McLellan BN. Chemotherapy-induced hand-foot syndrome and nail changes: a review of clinical presentation, etiology, pathogenesis, and management. J Am Acad Dermatol. 2014;71(4):787-94

Hand-foot syndrome (HFS), also known as palmoplantar erythrodysesthesia or acral erythema, is a side-effect of multiple chemotherapeutic agents, such as pegylated liposomal doxorubicin (PLD), capecitabine, 5-fluorouracil (FU), cytarabine and docetaxel. Another entity has been named « Hand-foot skin reaction » (HFSR), more specifically related to the newest targeted multikinase inhibitors (MKIs) such as sorafenib, sunitinib, pazopanib, regorafenib, axitinib and vemurafenib. The main features of both affections are listed in **Table 1**.
Chemotherapeutic agents may also be responsible for nail changes as listed in **Table 2**.

Table 1. *Main features of HFS and HFSR.*

	HFS	HFSR
Incidence	• 6-64% • Influenced by: - Causative agent (PLD and capecitabine: ↗) - Combinations (eg. Doxorubicin + continuous 5-FU: ↗) - Dosage (drug formulations, continuous infusion) - Gender: ↗ in females - Genetic variations impacting drug metabolism	• 10-62% • ↗ risk if: female, normal pretreatment leucocytes, good performance status, liver metastases, several affected organs • Asian > Western patients (genetic polymorphisms)
Clinics	• Onset: 2-21 days, up to 10 months • **Palms >>> soles** • **Palmoplantar neuropathic pain, well demarcated erythema, edema: lateral aspect of the fingers and distal fat pads +++** • Possible blistering with ulceration • In African American patients, possible hyperpigmentation (capecitabine++)	• **Soles >>> palms** • **Hyperkeratosis, erythema over flexural and friction-prone areas:** fingertips, heels, joints, interdigital web spaces and lateral aspect of feet
Histo-pathology	• Basal layer vacuolar degeneration or full thickness necrosis; spongiosis, hyperkeratosis, parakeratosis	• Well-defined band of discohesive dyskeratotic keratinocytes
Diagnosis	• Clinical • Differential diagnosis: allergic drug eruptions, contact dermatitis, vasculitis, erythema multiforme, erythromelalgia, acral bleomycin toxicity, acute graft-versus-host-disease (GVHD)	
Pathogenesis	• Poorly understood	
Treatment	• No large controlled treatment trials • Treatment interruption or dosage decrease: improvement within 1-2 weeks • Supportive measures: high-potency topical corticosteroids, wound care for erosions and ulcerations to prevent infection, topical keratolytics to decrease hyperkeratosis, emollient, pain control	
	• Dexamethasone, celecoxib	• Topical heparin
Prevention	• Antiperspirant on palms and soles • Regional cooling (ice packs, ice-water immersion, frozen gloves or socks)	• Urea-based creams twice-daily

Table 2. *Nail disorders caused by chemotherapeutic agents.*

Chemotherapy	Nail Changes
Taxanes (docetaxel, paclitaxel)	• Onycholysis **(Fig 4)**: 0-44% • Taxane-specific form of HFS: « periarticular thenar erythema with onycholysis » • Beau lines, subungual hemorrhage, nail pigmentation, acute paronychia, splinter hemorrhage: up to 88% • Functional disability in 42% • Treatment: COX-2 inhibitor • Prevention: regional cooling
Anthracyclines (doxorubicin, daunorubicin, iadarubicin)	• Diffuse and banded patterns of nail pigmentation (also mucocutaneous) • Resolve after discontinuation of therapy
Epidermal growth factor receptor inhibitors	• Paronychia, pyogenic granuloma: 10-30% • Slowing or cessation of nail growth • Brittle nails, onycholysis

Marie CAUCANAS

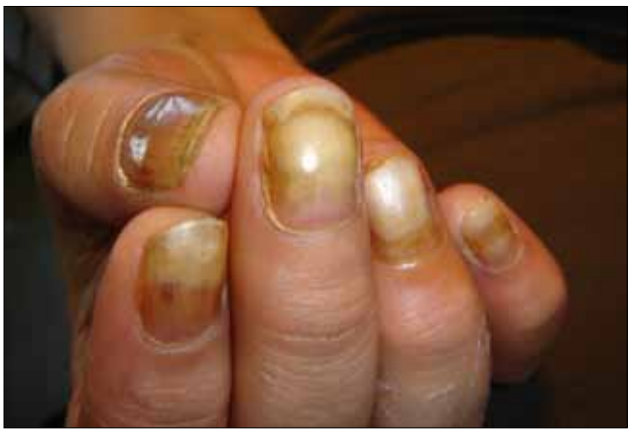

Fig4 - *Onycholysis induced by docetaxel. © B. Richert*

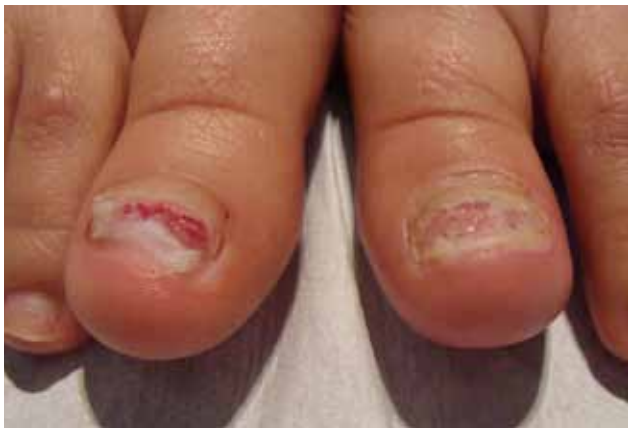

Fig5 - *Painful subungual pyogenic granulomas due to docetaxel. © B. Richert*

The authors conclude that though these side-effects are now well recognized and cause significant morbidity to the affected patients, little data is available to adequately manage these chemotherapy-induced toxicities. They highlight the need for further research and development of strategies for prevention and treatment.

Indeed, this review of the literature has the great merit to collect the data and help the clinician tidy up his knowledge about these seemingly close and resembling entities. However, one remark has to be made concerning the nail paragraph which is unfortunately incomplete, as the authors mentioned neither the occurrence of painful onycholysis, subungual abscesses and pyogenic granuloma **(Fig 5)** caused by taxanes and anthracyclines, nor considered their management, appreciably discussed in mainstay articles, such as the ones published by Piraccini et al.[1,2] HFS symptoms are well known and HFSR lesions may still evolve as more and more targeted therapies are released on the market each year. Yet the means for treatment and prevention remain very limited. Taking into account the wide spectrum of activity against solid tumours exhibited by taxanes[3] and the explosion of the use of present and future epidermal growth factor receptor inhibitors,[4] there is no need to be a statistician to expect an exponential increase of patients suffering from corresponding cutaneous and ungual side-effects in the near future. Hence the Dermatologist is, and will become even more, a pivotal link to handle the diagnosis and management of these patients.

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CAPSULE SUMMARY

- HFS and HFSR main differences reside in the nature of the causative agents and the clinical presentation.
- Taxanes will notably induce onycholysis and epidermal growth factor receptor inhibitors will be responsible for paronychia and pyogenic granuloma.
- Means of treatment and prevention remain very weak.

DRUGS, NAILS AND PYOGENIC GRANULOMAS

Piraccini BM, Venturi M, Patrizi A. Periungual pyogenic granulomas due to topical tazarotene for nail psoriasis. G Ital Dermatol Venereol. 2014;149(3):363-6

Pyogenic granuloma-like lesions are a well-known side effect of systemic retinoids, but topical retinoids are most commonly expected to produce burning, itching, stinging and erythema, following local skin irritation. To date, there has been only one reported case of pyogenic granuloma (PG) following topical application of tazarotene for scalp psoriasis.[1] In this article, the authors present two cases of periungual PGs following application of topical tazarotene on nail psoriasis. Patient 1 was a 77 year-old woman, who had been using tazarotene 0.1% once daily for 3 months, before numerous and painful periungual PG-like lesions appeared on the treated areas. The diagnosis was made clinically. Tazarotene was stopped and the lesions resolved after a two-week treatment with clobetasol propionate ointment under occlusion in the evening. Patient 2 was a 39 year-old man, who had been applying tazarotene 0.1% once daily for 2 months, before a mildly painful PG appeared on the second digit of his left hand. The features were suggestive of PG and the diagnosis was also made clinically. Once tazarotene was stopped, PG improved after two weeks and healed over the next 4 weeks. Nail PG is then discussed as summarized below:

PGs may be due to drugs, local mechanical trauma, peripheral nerve injury and inflammatory systemic diseases.

A biopsy should be performed when PG is single, especially if the nail bed is involved, to rule out malignant melanoma. First-line treatment includes application of topical steroids and antibiotics or curettage. For PGs due to drugs, topical medication or curettage may help, but it may be necessary to diminish the dosage of the drug or even interrupt it. Drugs mostly responsible for PGs are listed in **Table 1**.

Table 1

Systemic Retinoids	Anti-Retrovirals	Antineoplastic/ Immuno-Suppressive Drugs
- Isotretinoin - Etretinate - Acitretin	- Indinavir - Lamivudine	- Epidermal growth factor receptor inhibitors - Capecitabine - Cyclosporin - Docetaxel - Mitoxantrone

The authors describe the few cases reported in the literature where PGs developed after applying topical tretinoin[2-5] and retinoic acid combined with minoxidil.[6] They describe the first case series of 2 patients in relation to tazarotene 0.1% for treatment of nail psoriasis, since only one case had been reported with the same molecule as medication for scalp psoriasis.[1]

Dealing with the latency before onset of tazarotene-induced PGs, the delay was longer (2-3 months) in these two cases, compared to the observations in the literature (as soon as 2 weeks).[1] It was suggested that PGs due to topical retinoids seemed to develop earlier than those developed while under oral isotretinoin therapy.[5] The authors conclude that vigilance should be maintained during the whole treatment time and not only in the first weeks, as previously advised.

This 2-patient case series represents an original description of PGs induced by tazarotene gel. This side-effect, well known from systemic retinoids, should be kept in mind, at least in countries where tazarotene gel is still frequently prescribed. Retinoids are not always alike. For instance, the most recent one, alitretinoin in its topical form, was found interestingly to be efficient in treating... Pyogenic granuloma![7]

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CAPSULE SUMMARY

- PGs are classical oral retinoid side-effects, but may also be induced by a local retinoid treatment.
- PGs due to topical retinoids may occur after a few weeks, but the delay may be up to a few months.
- Treatment usually relies on drug suspension.

David de BERKER

This review of nail science publications over the last year provides articles in three main categories. The first concerns the chemical pollutants and biological markers that can be found in the nail **(Table 1)**. The second is about the biology of nail in evolutionary and growth terms. The third refers to nail penetration by topical agents, usually for therapeutic purposes.

Table 1. *Table illustrating different methods for analysing the nail and the applications of these methods.*

I. STRUCTURAL AND MINERAL CONSTITUENTS OR EXOGENOUS MATERIALS	
METHOD	ANALYSED COMPONENT
Raman Spectroscopy	Water, proteins and lipid
Immunohistochemistry	Keratin, collagen, BMZ components, trichohyalin
Polymerase chain reaction	Forensic, paternity, fungal
Electron Microscopy	Cystine
X-ray diffraction	Mg, Cl, Na, Ca, S, Cu
Colorimetry	Fe
Atomic Absorption Spectometry	Cd, Pb, Zn, Ca, Cr, Fe, Cu, Mn, Ni, Co, Na, K.
Mass Fragmentography	Metamphetamine
Gas Chromatography	Amphetamine, Cocaine
Flow Injection Hydride Generation Atomic Absorption Spectrometry	Arsenic
II. BIOLOGICAL MARKERS	
High Performance Liquid Chromatography	Furosine (Glycosilated keratin), terbinafine
Microscopy	Lipid: Triglyceride
Adsorption Differential Pulse Voltammetry	Nickel
Enzymic assay	Steroid Sulphatase
Neutron Activation analysis	Zinc, Selenium

THE NAIL AS A MARKER FOR HEAVY METAL POISONING

Bio-indicator in contamination monitoring of heavy metals in Dizajabaad, Zanjan province-Iran. J Environ Health Sci Eng. 2014;12(1):147

There continues to be a trickle of scientific papers examining the content of the nail for one of 2 or 3 reasons. The most common is a question about an environmental contaminant, where the authors are interested in a heavy metal or some other stable material that is deposited in the nail after involuntary ingestion or contact. The second is about whether something the person has ingested intentionally can be verified through nail analysis. This is usually a drug and can be part of pharmaceutical analysis in a trial or forensic analysis where the person (or corpse) is not willing (or able) to tell. The third pertains to the analysis of a physiological substance that might vary from one person to another, such as cholesterol or sugar or some biochemical proxy for these. Such markers can be used as a part of health screening or monitoring. I have chosen three papers from last year that include these points. The first relates to environmental pollution in northern Iran. The paper was written by academics from the Department of Environmental Sciences in the University of Zanjan and the first question I asked myself was how much academic freedom there is in Iran to publish papers that may be critical of the status quo. The structure and content of the paper suggests no obvious restriction. Zanjan is in the northwest of Iran and the study took place near the National Iranian Lead and Zinc company area of influence. Concern was expressed that local inhabitants were being exposed to excessive levels of lead, cadmium, zinc and nickel. Such materials can get into the water supply, earth,

food chain and sometimes the air. This can happen at the point of mining, smelting or transportation between the two locations. Three types of sample were collected from within the study area and outside for control. These were soil (30 samples from within a 16sq km zone), 18 leaf samples from three standard local plants and 29 fingernail samples taken from people with an age range of 9-65 years, with a median age of 35 years. The age selection is relevant, as it is quite possible that the rate of uptake varies in different age groups, as it concerns the way they handle the material, and based on age alone, the cumulative content may be different. All the samples have well tried methods of solvent extraction and analysis of the extract. In brief, the cadmium, lead and zinc levels were all substantially higher in the soil and where the soil levels were put into four quartiles of concentration of pollutants, there was a correlation with the level of leaf contamination. All pollutant concentrations in the nail were increased by (mean values) factors of between 2 (zinc) to 20 (arsenic). There was no outright p-value stated for these figures, which may reflect the wide standard deviation in the results. In human terms this means that there are some people with very high levels of exposure (arsenic level in fingernail 68x and lead levels 44x greater than mean of control area), although these risks may not be equal within the population. The clinical risks at high levels of contamination are neurological damage with lead, kidney damage and ultimately failure with cadmium and arsenic, causes of cardiovascular, skin changes and a range of malignancies. What this study cannot tell us is whether the high reported levels of contamination are due to humans mining and processing the materials, or if it arises as a natural event secondary to the presence of the materials in the earth.

Viana GF, de Carvalho CF, Nunes LS, Rodrigues JL, Ribeiro NS, de Almeida DA, Ferreira JR, Abreu N, Menezes-Filho JA. Noninvasive biomarkers of manganese exposure and neuropsychological effects in environmentally exposed adults in Brazil. Toxicol Lett. 2014;231(2):169-78

The evidence for pollution causing biological effects is offered from another nail analysis project undertaken in Brazil in connection with manganese. Manganese is used in a range of alloys, battery production and as an oxidizing agent. Viana and colleagues looked at manganese levels in hair, blood, saliva and nail to determine the level and then, in turn, to see if there was a correlation with the features of manganese toxicity. These features include poor performance on neuropsychological tests examining motor, cognitive and behavioural functions as measured by the Weschsler intelligence scale and the Rey auditory verbal learning test. The subjects were volunteers, who had lived in the area of a ferromanganese refinery for at least 5 years and were aged between 15 and 55. Manganese was measured using dete electrothermal absorption spectrometry. Significant correlation was observed between Mn in hair and fingernail with the performances in several neuropsychological tests. These effects were greatest in people of lower socioeconomic class. Blood managanese levels had no correlation. There was no control group in the study, but manganese levels were 8 times higher than national norms.

Both these papers illustrate a point about contamination and how the exposure of an individual and a population can be measured, sometimes with correlation with the expected toxicities. Nail is only one of biological samples which can be used for such studies, but it has the advantage of being very stable, like hair. Unlike hair, it does not disappear in some groups and is sometimes easier to sample. In addition, unlike blood, it represents a sample over time, or as JHS Beau would have said, it provides us with "retrospective semeiology".

If we want to apply retrospective analysis to a biological function, rather than a pollutant, it is possible to look at diabetic control through nail sampling.

CAPSULE SUMMARY

- The nail can carry a range of organic and inorganic constituents that are not structural, but reflect the physiology of an environmental exposure of the individual. With some environmental elements such as heavy metals, nail and hair both act like excretory organs, enabling the body to deposit unwanted materials into a bodily substance, which is shed.

THE NAIL AS A MARKER FOR DIABETES?

Kishabongo AS, Katchunga P, Van Aken EH, Speeckaert R, Lagniau S, Coopman R,Speeckaert MM, Delanghe JR. Glycation of nail proteins: from basic biochemical findings to a representative marker for diabetic glycation-associated target organ damage. PLoS One. 2015 Mar 17;10(3):e0120112. doi:10.1371/journal.pone.0120112. eCollection 2015

It has been known for over 20 years that glycated nail can be used as a means of measuring control of blood sugar in a diabetic over a prolonged period. Kishabongo used more recent tools to examine this question in more detail. Two hundred and sixteen patients undergoing cataract surgery were enrolled, of which approximately 30% were diabetic

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and 70% not. Fingernail clippings were collected. Glycation occurs through a non-enzymatic reaction of the carbonyl group of glucose, with a protein and the compound then bonds with the underside of the nail creating fructosamine. Nail was sampled through clippings processed initially by delipidization in chloroform and methanol, before further solvent extraction and separation using boronate affinity chromatography and gel electrophoresis. The main analysis revealed the ability to differentiate between diabetics and non-diabetics, as HbA1c and the level of fructosamine correlated well (p=0.01). Boring the nail in 2 phases to extract a superficial and deep sample demonstrated a further point, which was that the fructosamine content was significantly higher in the ventral layer of the nail than in the dorsal nail.

The authors claim that the methods are simple and appropriate for less affluent countries and enable transport of samples without degradation. The latter claim would need clarification, if the test relies on the less durable material found on the undersurface of nail. If the higher values seen on ventral nail are purely to do with apposition to a vascular nail bed, then it is unlikely to be lost with time and specimen transportation. However, if it is connected with the presence of t epidermal debris, sometimes found on the undersurface of nail, this could be partially lost, as the nail is transported. It is estimated that by 2030 most diabetics will be living in low income countries and simple tests of long term control will be important.

THE NAIL AS AN INDICATOR FOR OSTEOPOROSIS?

Mussatto JC, Perez MC, de Souza RA, Pacheco MT, Zângaro RA, Silveira L Jr. Could the bone mineral density (T-score) be correlated with the Raman spectral features of keratin from women's nails and be used to predict osteoporosis? Lasers Med Sci. 2015;30(1):287-94

I finish this review of science in last year's nail literature with a negative paper, which failed to prove what it had set out to prove. The clinical suspicion was that people with thin fingernails may have fragile bones, or more specifically, osteoporosis. I was pleased to come across this paper, as I had asked myself this question in the past and it was one that has been addressed to some extent in the literature. I had thought that a typical elderly lady with a light frame and thin nails was almost certain to have osteoporosis, compared to overweight ladies - who did not seem to present with thin nails. Mussatto thought the same, as did others before him, who established that there is a reduction in the disulphide bonds of nail as people get older. In the introduction it becomes clear that the biology of nail and bone have some significant differences, as one is composed of collagen and hydroxyapatite and the other of keratin and a little lipid. However, they both have disulphide bonds and they both seem to get thinner with time. 213 women had DEXA scans to obtain a T score (number of standard deviations from the normal 30 year-old adult) coupled with Raman spectroscopic analysis of nail disulphide bonds. To put it briefly, no connection was found. Does this mean that the clinical hunch is unfounded? Are we measuring the right thing?

NAIL PROTEINS AND MORPHOGENESIS

Mlitz V, Strasser B, Jaeger K, Hermann M, Ghannadan M, Buchberger M, Alibardi L, Tschachler E, Eckhart L. Trichohyalin-like proteins have evolutionarily conserved roles in the morphogenesis of skin appendages. J Invest Dermatol. 2014;134(11):2685-92

This article discusses S100 fused-type range of proteins (SFTP), to which filaggrin and trichohyalin belong. In mammals there are 7 in all; filaggrin 2, hornerin, repetin, trichohyalin-like 1, in addition to the first 2. The SFTP genes are on the epidermal differentiation complex (EDC). The broader aim of the paper was to look at the presence of SFTP in non-mammalian vertebrate species, such as lizards and chickens. Reverse transcription PCR was used to determine the presence of relevant genes and then mRNA *in situ* hybridization was used to detect expression of the proteins at different stages of differentiation of the 2 chosen non-mammals. The interesting finding with respect to nail science was that the chicken expresses an SFTP called scaffoldin at a range of sites, including the zone forming the tip of the chicken claw in embryogenesis. This probably corresponds to the site of human trichohyalin expression, as determined by immunohistochemistry, where positivity is found in the hyponychium. Cornulin is also found in a similar pattern. Scaffoldin was also found in the feather root sheath and associated with the egg tooth, with which the reptile breaks out of the egg.

CAPSULE SUMMARY

- Examination of the biology of hard keratinized structures in birds and reptiles illustrates analogous proteins in the different species, which enables durable extremities with modified functions, such as beaks, claws and nails. At these sites scaffoldin is found in chickens and reptile egg tooth, and trichohyalin is the corresponding protein for the human nail.

NAIL REGENERATION

Leung Y, Kandyba E, Chen YB, Ruffins S, Chuong CM, Kobielak K. Bifunctional ectodermal stem cells around the nail display dual fate homeostasis and adaptive wounding response toward nail regeneration. Proc Natl Acad Sci U S A. 2014;111(42):15114-9

Leung undertook work on mice with the aim of identifying and characterising a population of stem cells in the nail unit. She noted a ring of cells described as being located between the tip of the matrix and the proximal nail fold, which expressed keratin 15, also seen in hair follicle stem cells. These cells appeared to have two functional states, one of which was to contribute to the epithelial framework of the nail fold, but when a nail was avulsed, they changed function. At this point, the bone morphogenetic factor appeared to come into play and the cell group started to generate nail instead of nail fold. This group of cells was also characterised by retaining label and hence having a low mitotic turnover. They were consequently termed Label Retaining Cells (LRC). A slow turn over group of LRTs is also seen in the hair follicle and sweat glands. The relevance of this observation presents the classic questions:
Is the behaviour with wound repair the same as that seen during embryogenesis? Are the same molecules expressed and do the same sequence of events unfold?

TOPICALS FOR ONYCHOMYCOSIS

Elsayed MM. Development of topical therapeutics for management of onychomycosis and other nail disorders: a pharmaceutical perspective. J Control Release. 2015;199:132-44

Several articles were written last year about the science of nail penetration by topical agents. It is a technical topic that can, at times, seem remote from clinical practice. If you need a balanced view of the topic, then the review by Elsayed will help. He provides useful tables of many of the topical agents used in onychomycosis and other nail disorders and explains the roles of the different categories of ingredients. It is a good starting point for a general understanding of nail products.

Täuber A, Müller-Goymann CC. In vitro permeation and penetration of ciclopirox olamine from poloxamer 407-based formulations - comparison of isolated human stratum corneum, bovine hoof plates and keratin films. Int J Pharm. 2015;489 (1-2):73-82

The use of topical agents to treat nail fungal infection becomes increasingly attractive for older patients, as they are on more drugs. European demographics reflect an ageing population and risks of side effects of systemic agents become both more likely and less acceptable. The challenge is to find an agent that is pharmacologically effective and can penetrate the nail sufficiently to kill fungus. In some patterns of disease, subungual hyperkeratosis may also provide a barrier to penetration and hence success. In fact, the more the disease is present, the thicker the nail is likely to be in some instances, although when the integrity of the nail is disrupted by fungus, the thickness can be offset by fragility. The normal nail is a modified form of stratified corneum 80 to 90 cells thick **(Fig 1)**. It has a higher water content than skin and a lower lipid content and this means that it can act as a hydrophilic gel membrane or path into/through the nail. Drug penetration is a function of several variables, which include the physicochemical properties of the active pharmacological ingredient (API), the vehicle and the nail. Agents such as urea and actetylcysteine can act as penetration enhancers, when combined with the formulation. The ideal API would be a small molecule with no charge.

Fig1 - *Section of nail plate illustrating similarity with thickened stratum corneum. © D. de Berker*

David de BERKER

The authors were looking to enhance the penetration of ciclopiroxolamine through nail, where ciclopirox is already available in many European countries as a 8% nail lacquer and olamine salt as a 1% cream. The element under study in this project was the polaxamer, P407. Poloxamer 407 is a triblock copolymer consisting of a central hydrophobic block of polypropylene glycol flanked by two hydrophilic blocks of polyethylene glycol. Assessment of penetration was undertaken using three systems; keratin films, bovine hoof and human skin. Keratin films are made from dissolved hair, which is then reconstituted into films of controlled thickness (120 microns) and diameter (15 mm). Bovine hoof is cut into similar size plates, also of 120 micron thickness. Human skin was obtained from plastic surgery abdominal reductions and frozen, thawed and trypsinized according to an established technique. Typical thickness was 20 microns. The three barriers were used in Franz Diffusion cells, which is an industry standard for this form of evaluation. High performance liquid chromatography was used to establish concentrations either side of the barrier over time.

Results showed different levels of penetration across the three barriers with different formulations. Concentration of the drug was not the main determinant. For Keratin films less lipid, less drug and a greater aqueous element resulted in preferential penetration with lower viscosity to match. Bovine hoof showed a similar profile of penetration, although values overall were reduced in comparison to keratin film. Skin however, is more easily penetrated where there is a greater concentration of isopropyl alcohol and polyethylene glycol, illustrating the need to disrupt barriers which may contain lipid and keratin. Skin samples taken from a 52-year-old woman had more than 2x the level of penetration, than those taken from a 37-year-old person. Where the commercial 8% nail lacquer was used as control for the keratin films and bovine hoof, the optimum experimental preparation was 2 to 3 standard deviations better, indicating scope for improvement for clinical use. The superior results for the experimental preparations over commercial preparations were not seen with the skin samples in either of the ages of donor skin.

The conclusion of the study is that keratin films were a good substitute for bovine hoof as the results were similar in pattern, although different in extent. The real values of keratin film penetration may require substantial secondary interpretation to relate them to real life. However, this is not really important, if ultimately that conversion factor can be determined. The other point, is that when applied to diseased nails, the values may once again change by some substantial degree. This could even be that formulations that do not penetrate normal nails are good at penetrating abnormal nails, as seen in fungal nail infection. There are several examples in skin pharmacology, where penetration or biological effects are differential for diseased skin over normal skin and the nail could be identical. The other main finding was that the age of the skin donor made a substantial difference to the result of the penetration. Whilst this is not surprising, it also ties in with some other observations in Dermatology. The first question is if skin age is expected to make a difference to the responsiveness of people to topical antifungals? Is body site expected to make a difference also? The skin of the sole of the foot is likely to be quite different from that of the abdomen. The second point relates to the acknowledged change with age of the barrier function of the skin. Although this is normally expressed in terms of water loss, it works both ways and in pharmacological terms it may be something that can be exploited. If it gets too good, we may yet have to worry about systemic side effects of agents administered through the skin, such as flu-like symptoms sometimes experienced with imiquimod.

Baraldi A, Jones SA, Guesné S, Traynor MJ, McAuley WJ, Brown MB, Murdan S. Human nail plate modifications induced by onychomycosis: implications for topical therapy. Pharm Res. 2015;32(5):1626-33

Baraldi and colleagues move the topic on by aiming to establish the physical and penetration characteristics of abnormal fungal infected nail in comparison to normal nail, where the latter has been the previous laboratory standard. They obtained clippings of healthy and infected nails from volunteers (no mention of fungal confirmation - probably done on clinical grounds). Part of the healthy nail sample was artificially infected with trichophyton rubrum, according to an established method. All three groups of nails were then examined with scanning electron microscopy. Nail cell separation was greater in the real and artificial fungal nail infection, than in the normal controls. Desmosomes were retained so in this case, the separation did not result in disintegration. Tensile strength was reduced in the infected nail. Raman spectroscopy to assess sulphur-sulphur and sulphur-hydrogen bonds did not reveal any specific differences between the groups. It is of note that these bonds were more numerous on the dorsal aspect of nail, than on the ventral portion and this matches the observation that this surface is more rugged and that it is possible that fungus gains ingress through the ventral surface in many instances.

The final assessment was of the uptake and transport of rhodamine into and across the nail. An aqueous solution of rhodamine was applied to all the samples for 5 weeks, with wells of fluid on the ventral aspect to absorb the penetrating chemical. The rate of uptake into the nail was three-fold with the diseased nail, in comparison with the normal nail. Rhodamine is a relatively large molecule, and not an ideal one for measuring uptake by the nail where small molecules do better. Nevertheless, this makes the observation even more significant.

The Authors' work can be summarised by saying that the changes in the nail plate in connection with fungal infection may make it more able to absorb and benefit from antifungal treatments. Although such changes can increase the thickness of the nail, this effect might be offset. The study does not attempt to control for nail plate thickness, although they matched fingernail specimens with fingernail, and toenail with toenail.

It may be helpful to have a physical measure of brittleness or even something as simple as thickness?

CAPSULE SUMMARY

- Pharma continues to work to produce better nail penetration by pharmacologically active agents to treat fungal nail disease. The bonus is cheapness, less side effects and often greater access to the public. Small aqueous molecules are often the most suitable active molecules, but their evaluation can be undertaken in vitro using a range of techniques. Variables of concentration, lipid content and solvents are all open to analysis with each pharmacologically active agent, given how the different factors interact.

Nilton DI CHIACCHIO

Soto R, Aldunce MJ, Wortsman X, Sazunic I. Subungual schwannoma with clinical, sonographic and histologic correlation. J Am Podiatr Med Assoc. 2014;104(3):302-4

In this report, the authors show a subungual schwannoma case of the big toe with clinical features, color Doppler ultrasound imaging, and histologic findings.

Despite schwannoma being the most common neurogenic tumor, just a few cases with subungual location have been reported **(Fig 1)**, with none of them having color Doppler ultrasound findings.

Ultrasonography showed a 6 x 12-mm subungual mass of mixed echogenicity with a hypoechoic rim (solid) and an anechoic center (cystic) that displaced the nail plate upward and produced scalloping of the distal phalanx bony margin **(Fig 2)**. The mass involved the matrix region, and on color Doppler ultrasound, there were slow-flow arterial blood vessels in the periphery.

The gray-scale sonographic pattern was different from the one previously described (Moon et al), and the authors suggest that it could represent another form of presentation of this rare tumor. The authors consider that the color Doppler ultrasound can be useful for the differential diagnosis.

The histopathological analysis and immunohistochemical test (S-100 +) confirmed the schwannoma diagnosis.

The authors conclude that the support of pre-op ultrasound imaging should be considered when dealing with subungual tumors of the foot.

The ultrasound study of the nail unit tumors proves useful to locate the lesion, but studies with a larger number of cases are needed to try to define specific patterns able to suggest the diagnosis of tumor.[1]

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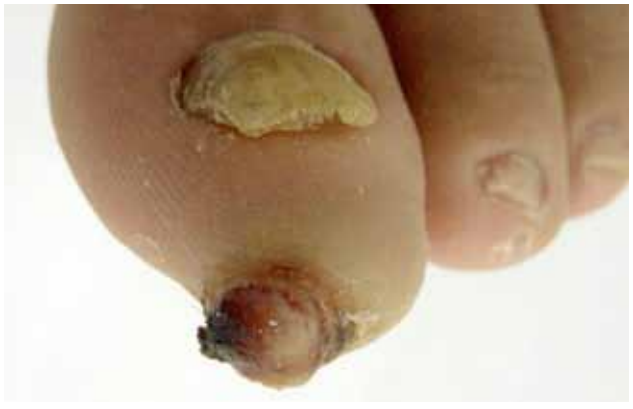

Fig1 - *Clinical picture of the lesion in the great toe. © X. Wortsman*

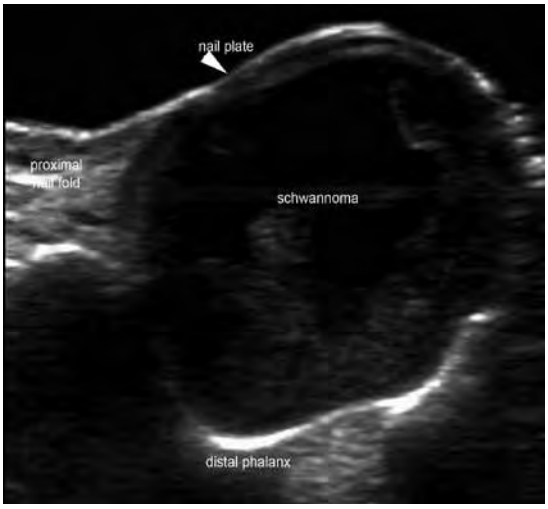

Fig2 - *Ultrasonography view of a big toe schwannoma. A subungual mass with a hypoechoic rim (solid) (gray) and an anechoic center (cystic) (black). © X. Wortsman*

Wortsman X, Alvarez S. Color Doppler ultrasound findings in the nail in cystic fibrosis. J Eur Acad Dermatol Venereol. 2014 July, ahead of print.

Cystic fibrosis (CF) is an autosomal recessive disease. The clinical manifestations are related to lung disease, pancreatic insufficiency, infertility, and skin changes. Digital clubbing is a common sign of CF. Although its pathophysiology is unclear, several factors such as hypoxia, platelet activation, release of platelet-derived growth factor, and vascular endothelial growth factor are involved. The clinical feature is due to a fibrovascular hyperplasia of the nail bed's underlying connective tissue.

The authors report a case of a 25-year-old male diagnosed with CF and clubbing in both hands.

The sonographic examination showed:

- diffusely increased nail bed thickness
- decreased echogenicity of the nail bed in the fingernails of both hands, especially thumbs
- the same change was observed in the matrix region of all nails
- an upward displacement of the nail plates
- absence of solid or cystic nodules.

The color Doppler ultrasound with spectral curve analysis showed:

- hypervascularity, mainly in the proximal part of the nail beds
- abundant arterial blood vessels in the nail beds reaching a thickness between 0.8 and 1,0 mm and showed a low speed flow with a peak systolic velocity of 10,5 cm/s, without any arteriovenous shunts **(Fig 3)**.

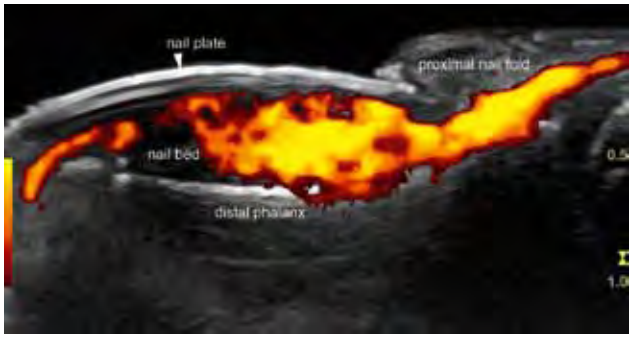

Fig3 - *Power Doppler ultrasound image demonstrating a prominent hypervascularity within the nail bed and a dilated digital artery and displacement of the nail plate. © X. Wortsman*

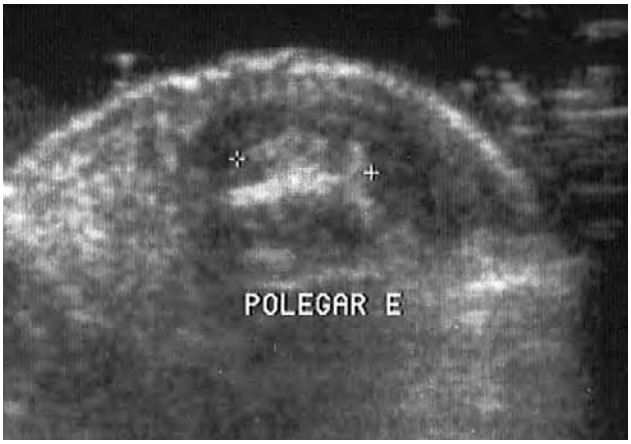

Fig4 - *An isoechoic well-circumscribed subungual glomus tumor. © N. Di Chiacchio*

Chiang YP, Hsu CY, Lien WC, Chang YJ. Ultrasonographic appearance of subungual glomus tumors. J Clin Ultrasound. 2014;42(6):336-40

This is a retrospective study describing the sonographic (US) features of 14 pathologically confirmed subungual glomus tumors of a tertiary hospital in Northern Taiwan. The tumor sizes ranged from 1.9 to 10,0 mm. Well-circumscribed tumors with clear margins were identified on US in 12 cases. The major part of the tumors (11) was hypoechoic and only one case was isoechoic. On power or color Doppler US, 11 showed hypervascularity within or adjacent to the masses, with or without bony erosion. Seven patients exhibited focal bony erosion in the underlying phalangeal bone, and the average tumor size was larger in patients with bony erosion, than in those without bony erosion.

The most common US findings of subungual glomus tumors were focal circumscribed hypoechoic or isoechoic masses on high-resolution gray-scale US **(Fig 4)** and hypervascularity on power or color Doppler imaging. Bony erosion is a common US feature of digital glomus tumors. Despite the US findings described in this paper, and also in medical literature[2,3] they are not pathognomonic. A clinical correlation and histopathological examination are mandatory.

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Mendonça JA. Differences of spectral Doppler in psoriatic arthritis and onychomycosis. Rev Bras Reumatol. 2014;54(6):490-3

The author evaluated the use of spectral Doppler (SDoppler) to quantify inflammatory activity and detect nail echotextural differences in patients with psoriatic arthritis and onychomycosis.

The gray-scale ultrasound study shows changes in the regular presence of echotexture at the nail insertion, nail bed thickening and loss of trilaminar nail pattern, and the spectral Doppler resistive index (RI) detects the inflammatory process in the nail enthesis. Two patients – one with psoriatic arthritis without clinical change to nails and one with onychomycosis and rheumatoid arthritis – were included. Seven distal interphalangeal (DIP) joints in both patients were evaluated in two planes, obtaining nine RI.

In the psoriatic arthritis patient, the author's findings included loss of the normal aspect of the trilaminar nail plate and preserved nail beds and DIP joint capsules. The SDoppler showed RI < 1 (mean ± SD = 0.50 ± 0.75) in the microcirculation at nail enthesis, with characterization of bone erosion in the third left DIP joint and RI = 0.38 and 0.63 in the transverse and longitudinal planes, respectively. The onychomycosis patient showed the following changes: hypoechogenicity at nail insertion, loss of nail shape, and SDoppler at nail enthesis with RI > 1 (mean ± SD = 1.71 ± 0.98).

The author concludes that SDoppler can be considered as an important tool for the diagnosis of subclinical inflammatory lesion at nail enthesis.

Nilton DI CHIACCHIO

The most interesting detail of this article is the possibility of diagnosis of a subclinical inflammatory lesion at nail enthesis by SDoppler. Recent studies have suggested that inflammation in psoriatic arthritis arises in the enthesis. This is based on imaging and anatomical data and could be important data for the treatment of psoriasis.[4]

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MAGNETIC RESONANCE IMAGING

Nakamura J, Halliday NA, Fukuba E, Radjenovic A, Tanner SF, Emery P, McGonagle D, Tan AL. The microanatomic basis of finger clubbing - a high-resolution magnetic resonance imaging study. J Rheumatol. 2014;41(3):523-7

In this pilot study the authors compared the microanatomic basis of 4 patients with finger clubbing and 4 healthy subjects using magnetic resonance imaging (MRI). This is the first study using high-resolution MRI to investigate the microanatomic basis for finger clubbing **(Fig 5)**.
The measurements of fingers showed that the profile angle, phalangeal depth ratio, and thickness of the nail bed were greater in patients with finger clubbing, than in healthy subjects. The median angle was 186° in finger clubbing and 176° in healthy subjects.
Median phalangeal depth ratio was 1.04 in finger clubbing and in healthy subjects. The median thickness of the nail bed was higher (3,4 mm/1,8 mm) in finger clubbing when compared with healthy subjects.
Nail bed changes were observed in all clubbed fingers.

Fig5 - *Clubbed fingers in a patient with lymphoma.* © *N. Di Chiacchio*

The soft tissue edema and hypertrophy with contrast enhancement was extensive and completely involved the nail bed in finger clubbing, and in 3 of them the nail roots adjacent to the extensor tendon enthesis were involved.
In 3 out of 4 patients with finger clubbing, bone edema was observed. One of them had a diffuse bone edema, involving the distal phalanx and had focal bone edema around enthesophytes at the extensor tendon insertion and at the collateral ligament insertion.
Entheseal change was observed in one clubbed finger. The collateral ligaments were thickened, but without contrast enhancement.
The findings suggested the possible role of increased blood flow in the nail bed with tissue hypertrophy and secondary curvature of the nail in clubbing.
Digital clubbing was first described by Hippocrates in 400 BC in a patient with empyema. It is associated with a number of neoplastic, pulmonary, cardiac, gastrointestinal, infectious, endocrine, psychiatric, and multisystem diseases, but the knowledge of its pathophysiology and microanatomy is still incomplete.[5,6]
Despite only a small number of cases, both previous papers allow a better understanding of this important sign.

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CONFOCAL MICROSCOPY

Cinotti E, Fouilloux B, Perrot JL, Labeille B, Douchet C, Cambazard F. Confocal microscopy for healthy and pathological nail. J Eur Acad Dermatol Venereol. 2014;28(7):853-8

This paper is a systematic review of the literature on confocal microscopy for the study of either healthy or pathological nail. The review was performed by PubMed database searching the terms: 'nail', 'reflectance confocal microscopy','confocal microscopy' and 'onychomycosis'. The authors reported the use of confocal laser-scanning microscopy (CLSM) in normal nails, onychomycosis, melanonychias, inflammatory diseases of the nails, leukonychias, and nail research applications.
In normal nails CLSM is able to:
- Display single corneocytes and the integrity of their borders.
- Scan nail plate from the surface to the lower part adjacent to the underlying nail bed.

- Distinguish three different layers. The superficial layer shows a brighter reflection, followed by a zone with a slightly poorer signal, followed again by a brighter zone in the deepest part.
- Observe the transition to the underlying nail bed, visible only in thin nails and displayed in wave-like structures.
- Observe the transition between the skin and the proximal part of the nail plate, characterized by a stripe corresponding to the cuticle, and by stellate figures corresponding to the membranes of keratinocytes sectioned obliquely on the skin side.

In onychomycosis:
- Dermatophytes can be easily observed in the nail plate as a network of lengthy structures with high reflection and the typical shape of hyphae.
- Only a paper reporting aspect of yeasts.
- Moulds have not been described in nails yet.

In melanonychias:
- Can image melanocytes of Hutchinson's sign
- Cannot penetrate in the nail matrix *in vivo*, to allow a diagnosis of sub-ungueal melanoma.
- Is a promising tool for the intraoperative diagnosis of melanonychia because it combines the advantages of dermoscopy and histopathology.
- Can differentiate pigmented squamous cell carcinoma presenting as melanonychia striata from melanoma.

In leukonychias:
- CLSM showed a detachment of single hyper-reflective corneocytes
- There are no reports about the features of different conditions (trauma, lichen planus, onychomycosis and drug intake)

In inflammatory disorders of the nails:
- There are no studies about CLSM diagnosis of inflammatory disorders of the nail.

In nail research applications can be used to evaluate drug delivery of topical nail therapies and measure nail plate thickness

The authors also reported the limitations of confocal microscopy for nail imaging:
- A wide use of this technology is limited due to cost.
- The limited penetration depth that does not allow to clearly image in vivo the nail bed and reach the nail matrix.
- The convex surface of the nail and the concavity of the transition between the nail plate and the surrounding skin make it difficult to place and hold the device during in vivo imaging.

Despite the fact that confocal laser-scanning microscopy is a promising technique for the diagnosis of some nail diseases, the cost of the device, and anatomical aspects of the nail, make this method unsuitable for routine use.

Rothmund G, Sattler EC, Kaestle R, Fischer C, Haas CJ, Starz H, Welzel J. Confocal laser scanning microscopy as a new valuable tool in the diagnosis of onychomycosis - comparison of six diagnostic methods. Mycoses. 2013;56(1):47-55

Onycomycosis always need confirmation of the diagnosis. Several diagnostic methods are described to confirm the diagnosis and species differentiation. In this paper the authors evaluate the use of confocal laser scanning microscopy (CLSM) and optical coherence tomography (OCT) as new non-invasive diagnostic tools in onychomycosis, and also compare it with KOH preparation, culture, PAS-staining and Polymerase chain reaction (PCR).
It was a prospective study with 60 patients (50 clinically suspected of having onychomycosis – all types) - and 10 patients having other nail diseases – psoriasis, lichen planus, eczema and nail dystrophy.
KOH and direct examination, fungal culture, PCR, histopathology with PAS staining, confocal laser scanning microscopy (CLSM) and optical coherence tomography (OCT) were performed.
Sensitivity and specificity were calculated for each diagnostic method. According to sensitivity, polymerase chain reaction offered the best sensitivity (94.9%), followed by OCT (92.3%), CLSM (79.5%), KOH-preparation (74.4%), histopathology (PAS-staining) (69.2%) and fungal culture with 20.5%. PCR, culture and histopathology – considered as gold standard - showed a specificity of 100%. CLSM showed the best value for specificity with 81%, followed by KOH-preparation with 76.2% and lastly, way below, the OCT with only 42.9%.
The authors concluded that CLSM was comparable to PAS staining and superior to KOH preparation and despite the fact that optical coherence tomography has a high enough resolution for measuring nail thickness and displaying the different layers of the nail organ, it is not useful as a standard method in the diagnosis of onychomycosis.

Despite CLSM being considered as non-invasive and a good method for the diagnosis of onychomycosis, it remains an expensive method and is inaccessible to the daily practice of dermatologists.[7]

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Nilton DI CHIACCHIO

Sanchez M, Hu S, Miteva M, Tosti A. Onychomatricoma has channel-like structures on in vivo reflectance confocal microscopy. J Eur Acad Dermatol Venereol. 2014;28(11):1560-2

It is the first report of *in vivo* reflectance confocal microscopy (RCM) being used in the evaluation of onychomatricoma. A RCM VivaBlock mode was used, which allows to reach deeper structures than the conventional mode.
The authors evaluated the affected nail and the contralateral unaffected nail (control) of each patient.
The affected nails showed longitudinal dark areas and bright/grey lines, forming channel structures within the distal intermediate nail plate. The channels (observed from 186 to 505 lm of depth) were outlined by bright circular lines with grey dot centres. The splinter hemorrhages showed black structureless areas. The unaffected nails showed homogenous, white/grey structureless areas. The image features of affected nails correlated well with histology. The channel-like structures within the nail plate observed on RCM correspond to the tunnelled cavities in the nail plate, that are lined by matrix epithelium and contain PAS-positive serum. On RCM, the matrix epithelium cells outlining the channels appear as circular bright lines with a dark dot centre (corresponding to their nuclei). The channels are dark, most likely representing serum and blood, which have low refraction of light on RCM. Splinter hemorrhages were seen on RCM as dark structureless areas that correlated with the low refraction of blood clots.
Based on these findings the authors say that onychomycosis can be differentiated from onychomatricoma and also consider that the depth of visualization, need for training, and equipment are the main limitations.
Onychomatricoma is a benign tumor of the nail matrix and is often unknown, even for general dermatologists.[8] Several reports on clinical features[8] **(Fig 6)**, nail plate dermoscopy[8], nail clipping[9], ultrasonography[10], MRI[11] **(Fig 7)**, and histopathology[12] show that diagnosis of onychomatricoma is not so difficult. This first report on RCM contributes to a better understanding of this tumor and also adds a new diagnostic tool.

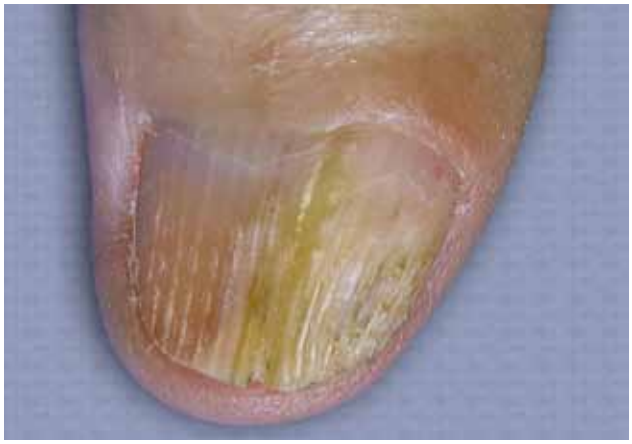

Fig6 - *Onychomatricoma of the right thumb showing splinter hemorrhages longitudinal xanthonychia (yellow), transverse and longitudinal over-curvature, thickening of the nail plate, and periungual erythema and swelling. © N. Di Chiacchio*

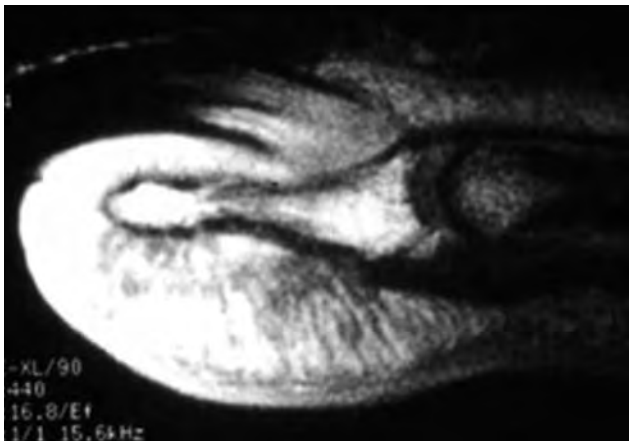

Fig7 - *MRI showing a filamentous tufted tumor. © B. Richert*

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DERMATOSCOPY

Mazzotti NG, Bredemeier M, Brenol CV, Xavier RM, Cestari TF. Assessment of nail fold capillaroscopy in systemic sclerosis by different optical magnification methods. Clin Exp Dermatol. 2014;39(2):135-41

The authors studied 45 patients with Systemic sclerosis (SSc), comparing capillaroscopy images taken with three devices, the gold-standard method (conventional stereomicroscope nailfold capillaroscopy; SNFC), with polarized light noncontact dermoscopy (PNCD) and nonpolarized light contact dermoscopy (NPCD), and evaluated their accuracy in diagnosing characteristic SSc-related alterations. The images were randomly analysed by a blinded observer.

Patients were diagnosed with SSc based on the criteria of the American College of Rheumatology (ACR) or the criteria proposed by LeRoy and Medsger for the diagnosis of early forms of SSc.

The examination was performed on the fourth finger of the left hand and the structures were analysed for the presence of haemorrhage, ectasia (loops with diameters about 4 or more times the normal size), giant capillaries (giant capillary loops, with a diameter about 10 or more times the normal size) bush-shaped vessels, and vessels with bizarre morphology and folding.

The scleroderma pattern was found in 83% of patients. PNCD and NPCD were highly sensitive in identifying the presence of focal capillary loss (96.4% and 100%, respectively), haemorrhage (96.2% and 92%, respectively), and scleroderma (91.9%, 94.6%), and showed high specificity for haemorrhage and enlarged loops. The intra-observer kappa values for detection of the scleroderma pattern by SNFC images, NPCD and PNCD were moderate to good: j=0.71 (95% CI 0.44–0.95), j=0.60 (95% CI 0.35–0.83) andj=0.60 (95% CI 0.32–0.86), respectively. Evaluation of haemorrhage presence gave high kappa values for all methods:j=0.77 (95% CI 0.57–0.95),j=0.90 (95% CI 0.76–1.00) andj=0.95 (95% CI 0.85–1.00), respectively.

The results showed that both polarized and nonpolarized dermoscopy are reliable methods for the evaluation of nailfold capillaroscopy of patients and can be compared with traditional capillaroscopy.

Conventional capillaroscopy and dermoscopy of proximal nail folds have been reported as important tools for the diagnosis of rheumatologic diseases.[13,14,15] Only a few dermatologists have access to the apparatus needed for performing conventional capillaroscopy, but portable handheld dermoscopes (polarized or not) are a frequent tool in most dermatology offices. Thus the possibility to study capillaroscopy in patients with systemic sclerosis has become easier.

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CAPSULE SUMMARY

- Subungual schwannoma is a rare condition. Doppler ultrasound may help in the differential diagnosis.
- Clubbing is common in patients with cystic fibrosis. The color Doppler ultrasound findings allow a better knowledge of the physiopathology of clubbing. Sonography is useful to define the hypertrophy of ungual connective tissue and inflammatory components.
- Edema and hypertrophy with increased blood flow of nail bed soft tissue and entheseal changes are observed in clubbed fingers by a high-resolution magnetic resonance imaging study.
- Spectral Doppler is an important tool for the diagnosis of subclinical inflammatory lesions at nail entheses. An inflammatory process can be detected in patients with nail psoriatic arthritis, even without nail changes.
- Longitudinal melanonychia may represent an early stage of nail melanoma. An automated evaluation system of dermoscopic images based on color variation is useful for a better diagnose of nail melanoma.
- Confocal microscopy is a useful tool for a better knowledge of healthy nail and also some nail diseases, especially onychomycosis.
- Dermoscopy of proximal nail folds are reliable when compared with traditional capillaroscopy for evaluation of systemic sclerosis.
- Ultrasonography associated with power or color Doppler is useful for the diagnosis of glomus tumor. Focal circumscribed hypoechoic or isoechoic masses, hypervascularity and bony erosion is a common US feature of digital glomus tumors.
- Reflectance confocal microscopy can contribute to the diagnosis of onychomatricoma.

Eckart HANEKE

NAIL REGROWTH AFTER AVULSION

Mefford AM, Kasdan ML, Wilhelmi B. Photo-documentation of thumbnail regrowth after surgical avulsion: case report and literature review. ePlasty 2014;14:202-205

Nails have important functions and are of great cosmetic concern. A study on the outcome of 33 nail avulsion procedures in subjects between 27 and 86 years of age reported periods of full regrowth ranging from 5 to 10 months, including fingernails and toenails.[1] The authors present here a 9-month photo-record of nail regrowth after complete nail avulsion and nail bed biopsy in a 76-year-old non-smoking male surgeon. After the procedure, the original nail was curetted, irrigated, and replaced. The nail remained in place for 10 days before falling off. Naftifine 2% cream was applied twice a day for 33 weeks. The nail required 33 weeks to regrow to a length of 18 mm. The regrowth of the nail was photo-documented and compiled into a time-progression video.

Nails are often avulsed for both diagnostic and therapeutic purposes. Regrowth takes 4 - 5 months for fingernails and 10 - 18 months for toenails.[2,3] More precise growth rates have been measured in healthy non-avulsed nails with 0.094 to 0,124 mm/day and some variability can be explained by the nutritional status.[4] Another study found 0.05 to 0,15 mm/d.[5] This nail grew 0,078 mm/d. Age, nutritional status, environmental temperature (faster growth in warm months), trauma, handedness (faster growth in dominant hand), finger length (middle finger grows fastest), pregnancy, acute illness, and pre-existing skin conditions all influence nail growth.

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PINCER NAIL

Sano H, Ogawa R. A novel nonsurgical treatment for pincer nail that involves mechanical force control. Plast Reconstr Surg Glob Open 2015;3:e311; doi:10.1097/GOX.0000000000000220; Published online 19 February 2015

The authors speculate that mechanical forces influence nail configuration and may be involved in the development of nail deformities. Nails have an automatic curvature feature and their normal flat shape is maintained by the daily upward mechanical forces from the finger/toe pad. Thus, under normal conditions, the upward daily mechanical force and the automatic curvature force are well balanced, and an imbalance between these two forces would cause nail deformation. Pincer nails are believed to be caused by the absence of the upward mechanical forces and/or by a genetically driven over-strong automatic curvature force, whereas koilonychias occur when the upward mechanical force exceeds the automatic curvature force. Consequently, this hypothesis then led the authors to propose that nail deformities can be treated by improving the balance between the automatic nail curvature force and the upward mechanical forces from the finger/toe pad. They treated a pincer nail by reducing the automatic curvature force by thinning the nail with a grinder from 1.4 to 0,9 mm thickness. Judging from the figures, the curvature decreased from > 270° to about 210° and the pain disappeared. This nonsurgical approach is said to obviate the need for surgery.

As all too often, the disadvantages of surgery are stressed as being complex, painful, time-consuming, requiring anaesthesia, and risking a cosmetic deformity. Elastic wire and plastic braces are mentioned as conservative alternatives to reinforce the upward daily mechanical force. However, all these methods, including shape-memory alloy nail clips, do not reinforce the upward forces, as they do not act on the longitudinal axis of the nail plate, but directly counteract the transverse over-curvature. Furthermore, the principle of softening the nail is not new concerning the treatment of pincer nails. **Figure 1** shows the big toenails of a 2-year-old girl with both malalignment and overcurvature, the base of the distal phalanx is very wide and the nail grows obliquely up. It is the wide base of the distal phalanx that uncurves the nail proximally leading to overcurvature distally.

Figure 2 demonstrates the big toenail of a 24-year-old man with lateral deviation and overcurvature of the nail. **Figures 3** depict the nails of a 44-year-old man with Alport syndrome and overcurvature of the toenails becoming less and less marked from the big to the fifth toenails.

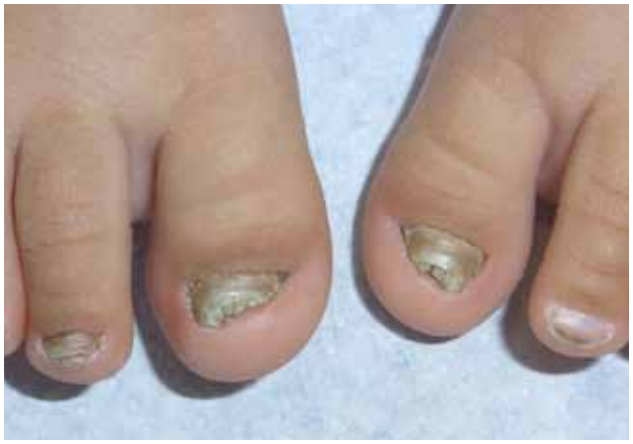


Fig1 - *Congenital malalignment and overcurvature of the big toenails in a 2-year-old girl. © E. Haneke*

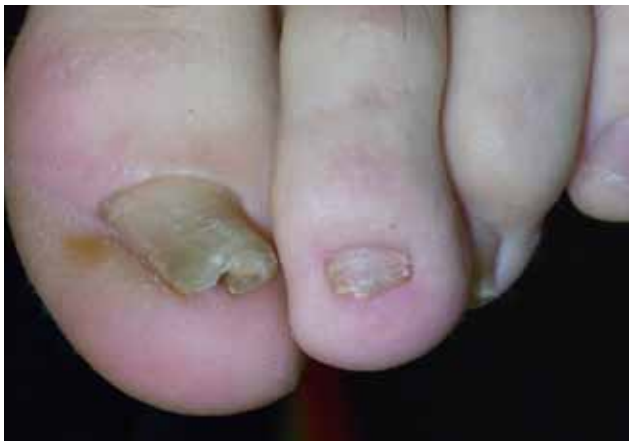


Fig2 - *Pincer nail with marked thickening of the nail plate in a 24-year-old man. © E. Haneke*

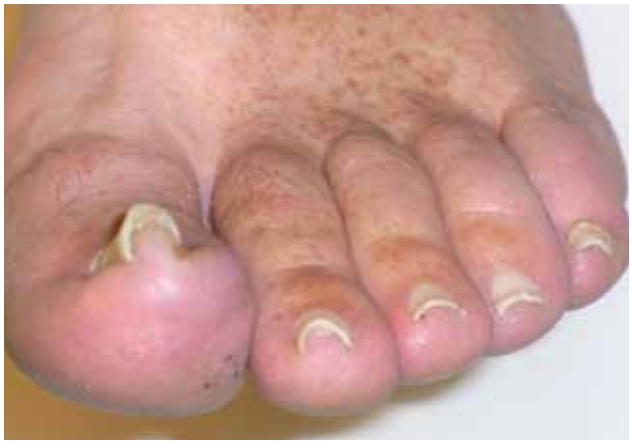
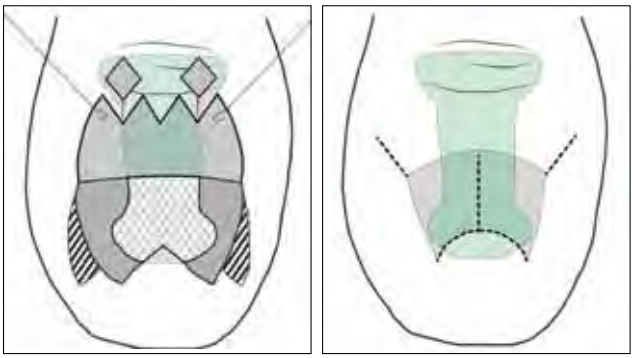


Fig3 - *Pincer nails with diffuse subtotal leukonychia in a 44-year-old man with Alport syndrome. © E. Haneke*

Jung DJ, Kim JH, Lee HY, Kim DC, Lee SI, Kim TY. Anatomical characteristics and surgical treatments of pincer nail deformity. Arch Plast Surg 2015;42:207-213

The authors conducted a retrospective review of 14 cases with 21 pincer nails of the great toe and compared them with thirty controls without pincer nail or history of foot trauma. Width and height indices were calculated, and interphalangeal angles and base widths of the distal phalanx were measured with radiography. Surgical treatment methods were chosen, taking into account age, diabetes mellitus, kidney disease, and peripheral vascular disease. The zigzag nail bed flap method (9 nails) and the inverted T incision method (11 nails) were used to repair the deformities **(Schematic illustration)**. The outcome of 20 nails was evaluated 6 months after surgery.



The interphalangeal angle (deviation of the long axis of the distal phalanx from that of the proximal phalanx) was significantly greater in the preoperative patient group (14.0°±3.6°) than in the control group (7.9°±3.0°) ($P < 0.05$); this is a common observation in virtually all pincer nail patients. The base width of the distal phalanx was claimed to be almost the same in the pincer nail and control groups; however, the measurements were not performed where the medial basal osteophytes - present in 70% of the cases - were located, but more proximally, and this is not the site where the matrix horns are localized **(Figs. 4a-d)**. This is also true for fingers **(Fig. 5)**.

The distal dorsal osteophyte was removed with a diamond burr. The postoperative width and height indices improved very close to the control group, and most patients were satisfied with the outcome; this is also our experience. One patient with diabetes, who was operated with the zigzag nailbed flap, did not show satisfying nail growth and was excluded from the evaluation. The mechanism of over-curvature is not explained by these authors; they assume

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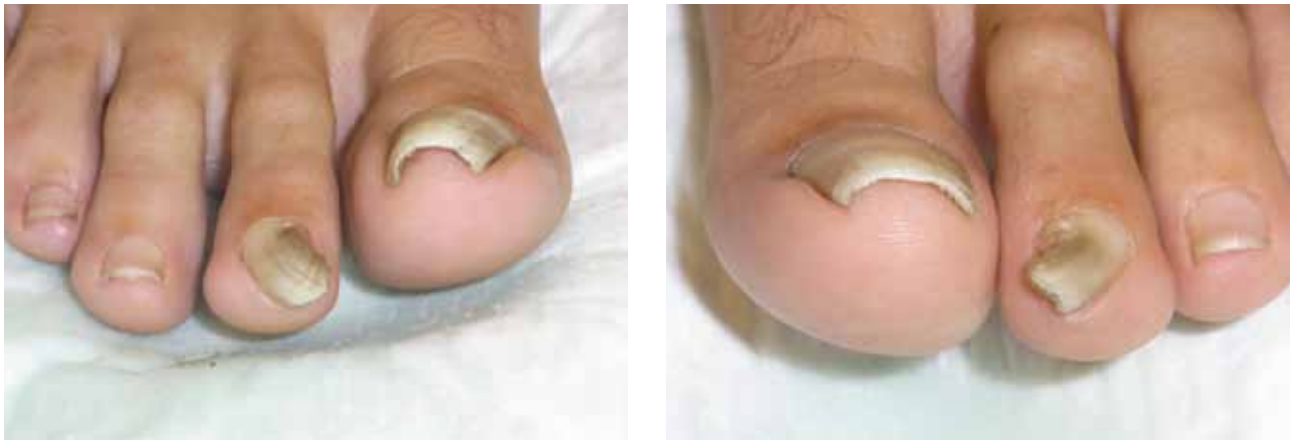

Fig 4a, b: *Pincer nails of a 51-year-old woman. The big toenails show overcurvature while the 2nd toenails display a medial deviation with inward torsion of the nail plate. © E. Haneke*

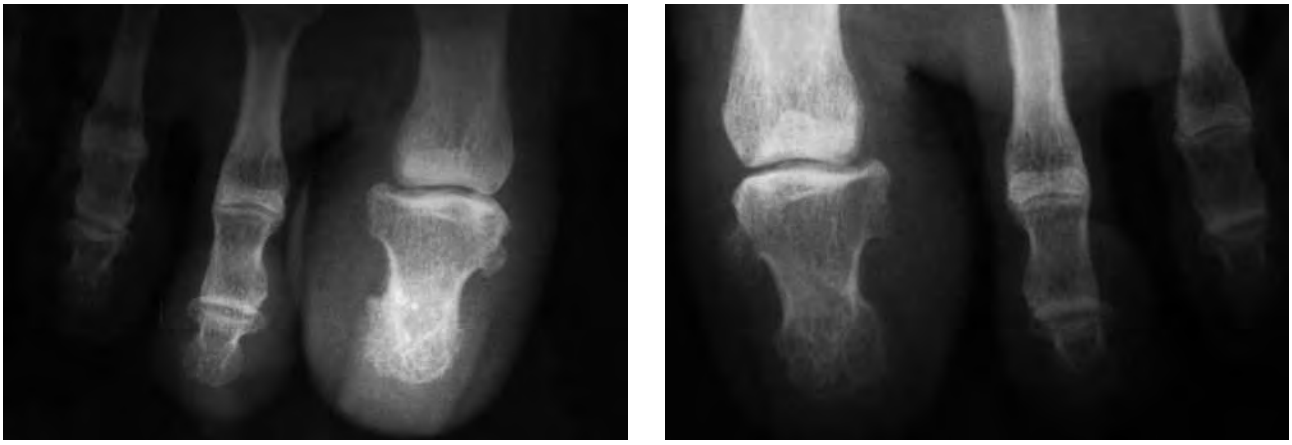

Fig 4c: *Right first three toes. © E. Haneke*

Fig 4d: *Left first three toes. © E. Haneke*

that the distal dorsal osteophyte is secondary to the overcurvature, which is consistent with our findings; however, they cite Kosaka et al[1], who only looked for these dorsal osteophytes and not for the basal medial ones, which are, in fact, responsible **(Figs. 4a-d)**.

The authors believe that the width and height indices are useful for evaluation of the deformity and outcome of surgery. Two different surgical methods for the two patient groups with respect to perfusion-related factors were used and both found to be satisfactory. Consequently, they recommend considering the circulatory condition of the foot, when deciding upon the surgical method for pincer nail deformity: the inverted T incision is less invasive and therefore safer for patients with potential vascular compromise. The zigzag flap elevates the entire nail bed at the sub-periosteal level and de-epithelializes the lateral nail folds, whereas the inverted T incision is a distal rectangular extension of our median longitudinal nail bed incision.[2] They did not use tie-over sutures to keep the nail bed flat on the phalanx bone; instead they fixed a silicone sheet on the nail bed. Antibiotics were administered for 5 days. Patient satisfaction was requested by questionnaire after 6 months.

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SURGERY OF THE NAIL UNIT (LM and melanoma excluded)

INGROWING NAILS

Bryant A, Knox A. Ingrown toenails: the role of the GP. Aust Fam Physician 2015;44:102-105

Ingrown toenails are a painful condition that can become infected and may require surgical treatment. The epidemiology of onychocryptosis is difficult to determine, as it is often considered to be a minor medical problem and as such has been somewhat neglected in the literature. There is a slightly higher male-to-female ratio, particularly in the 14–25 age group, but it can affect patients of any age. Multiple reasons may cause an ingrown toenail - improper nail cutting, tight-fitting footwear, trauma, anatomical factors such as thickening of the nail plate, pincer-shaped toenail, pressure from abutting digits caused by hallux valgus or lesser toe deformities, the presence of a subungual exostosis and, occasionally, the use of isotretinoin in the treatment of severe acne being the most frequently mentioned factors. This overview by professors from a podiatric medicine unit stresses the role of nail incurvation and careful nail trimming in the conservative treatment of an early ingrown toenail. This may be combined with antiseptic soaks and the application of 25% silver nitrate. Sharp nail spicules must be avoided and small inserts of cotton wool may prevent the nail edge from digging into the flesh. Once the nail has penetrated the skin of the nail sulcus, the offending border of the nail and hypergranulation tissue are removed. A haemostatic and antiseptic dressing is applied and home care consists of twice daily antiseptic soaks. When this treatment is unsatisfactory, definitive surgical cure is required, either with the sharp technique of Winograd or phenolization. A digital ring block with 0.5% or 0.75% ropivacaine is used. The surgical technique is as follows: Use a nail splitter to split 2–3 mm of the affected side of the nail longitudinally; make two skin incisions: the first is made deeply through the split nail to include the nail bed extending proximally and the dorsal skin over the nail matrix, the final incision is to excise the lateral nailfold, connecting the proximal and distal ends of the initial incision. Excise the nail section, bed and matrix tissue totally and then curette gently to remove any remaining matrix tissue. This technique yielded 96.3% satisfactory results of 239 patients in one series and 91.2% success in another series of 224 patients with revisional surgery required in 7.1%. Phenol matricectomy is described as an alternative with less risk of infection and less postoperative pain. The success rate is better than the sharp technique. The lateral nail strip is removed and the matrix curetted before the liquefied phenol BP is rubbed in for 3x20 seconds. Daily showering is advised, until healing is complete after 2 - 3 weeks.
This overview, although written by podiatry professors, describes the same mistakes concerning the Winograd technique as do many other articles, because the excision of the matrix horn is not stressed and, in fact, is not feasible with the incision lines shown. Nevertheless, we admit that the percentage of recurrence may be acceptable when performed by an experienced podiatric surgeon, although it is disappointing to see that old mistakes are still being made. It is also surprising that the authors mention the phenol matrix ablation as an alternative with a lower risk of infection and less pain and nevertheless emphasize the Winograd method first instead of omitting it.
It would have been more logical to briefly describe other chemical ablation methods of the lateral matrix horns like 80 - 100% trichloracetic acid or 10 - 20% sodium hydroxide.

Ince B, Dadaci M, Altuntas Z. Knot technique: A new treatment for ingrown nails. Dermatol Surg 2015;41: in press.

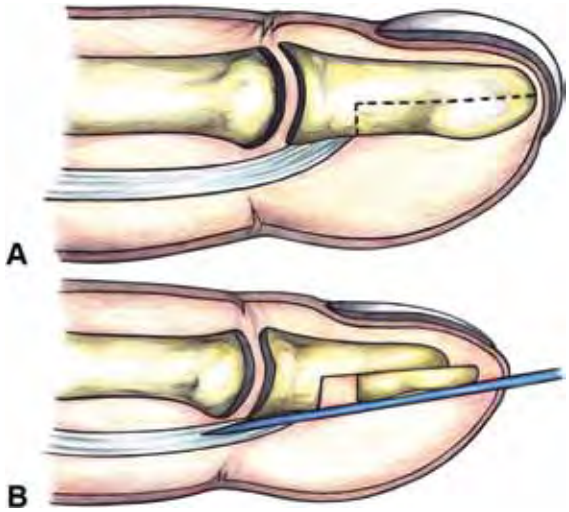
Thirty patients with stage 2 and 3 ingrown nails were operated by the same surgeon. Under local anaesthesia, a wedge excision of the upper and lower soft tissues of the nail was performed. The wound margins were simply sutured with 2/0 sharp polypropylene. Approximately, 8-10 knots were tied without cutting the stitches under the nail. These knots were used to push the soft tissue down and to raise the nail edge. This was achieved by placing a knot under the nail after the needle had been passed inside the nail, without cutting the suture before another knot was tied above the nail.
Therefore, the ingrown part of the nail was raised. They were careful during the procedure to avoid passing the stitch through the proximal part of the ingrown nail because in general, this area is weaker and more fragile than other parts of the nail. Stitches were removed after the nail had grown past the ingrown part (approximately 3-5 weeks later). Patients were advised not to cut their nails for 2 months after surgery, to cut their nails straight across, and to avoid wearing tight shoes.
This is a valuable method for a subset of ingrown nails where the distal part of the lateral nail fold is continuous with the hyponychium and thus is an obstacle for the outgrowth of the nail. The abundant soft tissue is removed by a wedge excision, which is sutured distally with the series of knots that elevate the nail plate corner. Our own first patients have shown good results.

Eckart HANEKE

HOOK NAIL

García-López A, Laredo C, Rojas A. Oblique triangular neurovascular osteocutaneous flap for hook nail deformity correction. J Hand Surg Am 2014;39:1415-1418

Hook nails are defined by an exaggerated longitudinal curvature. They are often the result of a distal amputation of the terminal phalanx leading to loss of bone support of the nail. Previous techniques mainly sought to add more soft tissue to the pulp defect. However, this was rarely enough to solve the problem definitely. The authors recommend careful removal of the nail plate and to leave the nail bed intact. A distally based triangular oblique flap on one side of the distal phalanx is designed using a modified Venkataswami technique. This yields a compound flap including half of the osteotomized distal phalanx. The base of the flap corresponds to the zone where the nail bed ends. At the flap base, an incision is made to expose the phalanx bone. The mediolateral incision is made dorsal to the neurovascular pedicle. The flap is dissected without detaching septa that insert on the periosteum; however, it is separated from the flexor tendon sheath. An oblique incision is made until the subcutaneous fat is herniated. Collateral vascular pedicles and digital nerves are preserved and included in the flap. All the cutaneous ligaments of the flap to the adjacent structures are divided, except for those that attach to the periosteum on the volar aspect of the phalanx. An osteotomy of the phalanx is made dorsally with an oscillating microsaw **(Schema A)** as shown by the dotted line. A transverse cut is made distal to the insertion of the flexor digitorum profundus tendon. It is necessary to cut the distal fibers of the tendon insertion to fully mobilize the bone distally. Once the osteotomy is performed, the bone and the finger pulp flap can be advanced to reconstruct and elongate the phalanx **(Schema B)**. Because the bone is thin and cannot be perforated, a subcutaneous needle or a Kirschner wire are used as a ledge for the bone. The needle holds the skin and spikes through the periosteal soft tissue as far as the flexor tendon and the joint capsule, providing sufficient stability **(Schema B)**. Placing the raised nail bed over the advanced bone completes the reconstruction and simple interrupted sutures close the skin. The needle remains in place for 4 weeks and the patient can then start full range of motion. In contrast to free bone grafts that are often resorbed, the osteotomy fragment remains and gives support to the nail bed. Radiographs after 2 years no longer showed any bone defect.



Scheme of the authors':
A Preoperative phalanx osteotomy planning.
B Scheme of completed reconstruction.

FROM THE SURGICAL THEATER TO THE LAB

Reinig E, Rich P, Thompson CT. How to submit a nail specimen. Dermatol Clin 2015;33:303-307

Laboratory technicians and pathologists are often afraid of receiving a nail unit specimen, because they pose two significant challenges: the first to get the nail plate to adhere to a glass slide and the second because the soft tissue specimens of the nail unit matrix and bed are often small and fragmented. Interpretation by the pathologist is challenging, not only because of the often difficult nature of the specimen, but also because orientation at the microscopic level is tricky, especially when examining a diseased nail unit. Placing nail biopsy specimens free in formaldehyde results in both loss of orientation and frequent loss of critical tissue needed to make a diagnosis. Thus, in the clinic, nail unit specimens require additional work to preserve tissue integrity and orientation.
Good communication with the laboratory is important in nail unit specimen submission. The laboratory has to pay close attention to small fragments of tissue. The clinician must submit reasonable differential diagnoses to guide the laboratory.
For specimen orientation, the epithelial surface may be marked with ink before placing it into the fixative, or the

specimen may be put on cardboard with a nail diagram and covered with filter paper and both are then stapled together. This keeps the specimen flat and also oriented in a proximal-to-distal direction. The authors' technique is to place the specimen on a cartoon printout of the nail in exactly the same position as it was taken. It may then be inked with blue or green colour at one or more margins to further improve orientation. This is placed into a tissue cassette, together with a sponge to secure the specimen, which is then put into a formalin container. Fixation is done overnight. The direction of sectioning is crucial for many diagnoses and must be either indicated by the surgeon beforehand or by the pathologist. The lab is informed to cut 5 to 10 unstained sections and mount them on positively charged slides to be used for additional stains. In contrast to our habit, the authors recommend separating the nail plate from the soft tissue part of the nail biopsy, in order to avoid loss of the more important soft tissue of the matrix and nail bed. It is not clear how much of the epithelium remains attached to the nail plate. The plate should always be stained with PAS, as secondary fungal infection over a pathological lesion is not infrequent.

Nail plate adherence to the glass slide is a challenge. Gelatin coating is usually effective, and adding gelatin to the water bath is very easy. Diastase treatment makes the section float off the slide. For the diagnosis of a pigmented band, Fontana-Masson, PAS stain and MelanA immunohistochemistry are recommended.

This protocol is similar to the one published by the Belgian nail group.[1] It is evident that different opinions and experiences exist. For instance, in contrast to the authors we found that transverse sections of onychopapilloma specimens with the nail plate attached, give much more information than longitudinal ones without the overlying nail, and we also find longitudinal sections of onychomatricoma very useful.

Reference

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SURGERY AND INFECTIONS

Leonel Fierro-Arias L, Silvia Marinne Ramírez-Dovala SM, Javier Araiza-Santibáñez J, Peniche-Castellanos A, Bonifaz A. Frecuencia de infecciones micóticas oportunistas tras intervención quirúrgica del aparato ungueal en la Unidad de Dermato-Oncología y Cirugía Dermatológica del Hospital General de México Dr. Eduardo Liceaga (Frequency of opportunistic fungal infections after a nail unit surgical event in the Dermato-Oncology and Dermatologic Surgery Department of the General Hospital of Mexico Dr. Eduardo Liceaga). Dermatol Rev Mex 2015;59:19-25

Nail diseases are common in dermatological practice and surgical procedures may be performed for both diagnostic and therapeutic purposes. Surgery is usually well tolerated. Complications are rare, but due to the intense handling and contamination, secondary fungal infection is possible; the former condition may influence surgery failure as well. The frequency of these infections in postoperative patients has not been established, and screening tests are not performed as a routine protocol.

In order to evaluate the frequency of opportunistic fungal infections in patients who received nail surgery, a single center, prospective, observational and descriptive clinical trial was performed during six months in the Dermato-Oncology and Dermatologic Surgery Department of the General Hospital of Mexico. Examinations and fungal cultures were made during pre-surgical evaluation, and at week 1 and month 1 of the post-surgical period.

3 of the 26 patients studied were excluded (11.5%), because they had onychomycosis before surgery. In two patients, 8.6%, a postoperative fungal infection was confirmed. In one patient *Aspergillus fumigatus* was identified by direct examination and culture one month post-surgery; in the other patient *Fusarium chlamydosporum* infection was diagnosed seven days postoperatively.

The results thus show that the risk of a secondary fungal infection after nail surgery was not statistically significant; however, the authors believe it to be imperative to monitor postoperative clinical changes that might suggest the development of a fungal infection.

Whereas bacterial infections after nail surgery are not rare, fungal infections have not been systematically investigated. It is our experience that they are rare and in most cases already present before surgery. On the other hand, we have repeatedly seen that a (distal-) lateral onychomycosis cleared after segmental phenolization.

Eckart HANEKE

SURGERY OF THE NAIL UNIT (LM and melanoma excluded)

Tessari G, Cagalli A, Girolomoni G. Opportunistic deep cutaneous mycoses in solid organ transplant recipients. G It Dermatol Venereol 2014;149:417-422

Effective immunosuppression is a prerequisite for long-term organ transplant such as heart, lung and liver. Despite considerable progress in managing solid organ transplant recipients, life-threatening infections still pose a major risk for them. Whereas superficial fungal infections due to *Candida* species, dermatophytes and *Malassezia* spp may be effectively treated, deep fungal cutaneous infections are often the sign of a systemic infection spreading. The most common pathogenic agents are *Aspergillus* spp, non-Aspergillus moulds, *Cryptococcus neoformans*, zygomycetes, *Fusarium*, *Scedosporium* and Pseudoallescheria spp. They are notoriously difficult to diagnose and treat, although liposomal amphotericin and new azole compounds are often active.

Lesions often occur on the hand and fingers, possibly because of their particular vascular conditions. They start as an inflammatory nodule with subsequent ulceration, an unspecific aspect often misdiagnosed as a common boil. The authors demonstrate cases of opportunistic deep mycoses on the hand and distal phalanx and show their histopathology. Therapeutically, liposomal amphotericin B is given in a dose of 3 mg/kg/d over a period of 1/2 weeks, but the dose may be increased in severe cases. Fluconazole is a triazole with an excellent long-term safety profile for yeast infections, whereas itraconazole is effective against aspergillosis and other endemic mycoses. Voriconazole is indicated for fusarium and scedosporium infections, as well as for aspergillosis resistant to intraconazole. Posaconazole is also active against zygomycosis. Surgical debridement and/or excision of single lesions are helpful in all cases.

Al-Qattan MM, Helmi AA. Chronic Hand Infections. J Hand Surg Am 2014;39:1636-1645

The distal phalanx, together with the nail unit, are often involved in hand infections. The authors describe an example of orf (ecthyma contagiosum), a parapox virus infection acquired from sheep and goat, on the proximal nail fold. This infection develops at the inoculation site as a papule that later acquires a halo and finally dries and disappears. The entire duration of the disease is usually 8 weeks, but healing can be hastened considerably by application of imiquimod cream over a week. Non-healing lesions in immunocompromised subjects require surgical removal.

CAPSULE SUMMARY

- Nail growth is different from person to person and depends on the individual's age. It was measured over a period of 33 weeks where it grew 18 mm.
- Pincer nails are due to an unbending of the proximally curved nail resulting in a compensatory distal hyper-curvature. The authors claim that there is an imbalance of an automatic horizontal curvature force and a counteracting upward force from the digital pad.
- To study the mechanics of pincer nail formation, the correct points of the distal phalanx have to be measured. These points are where the lateral matrix horns sit on the lateral condyles.
- Ingrown nails are easily and effectively treated with selective matrix horn phenolization.
- Excision of a spindle from the corner of the hyperplastic distal portion of the lateral nail fold and placing a series of knots, so that they push up the lateral corner of the nail plate, is an easy method to operate an ingrown nail.
- Hook nail development is usually due to lack of bony support of the nail bed. This can be achieved with an elongation of the distal phalangeal bone.
- Opportunistic fungal infections after nail surgery do occur, although rarely. In solid organ transplant recipients, infections of the hands and digits may be of a fungal nature and are notoriously difficult to treat.
- The submission of surgical nail specimens to a histopathology laboratory is a delicate issue, and care must be taken to ensure a good diagnostic result.

Matilde IORIZZO

PEDIATRIC NAIL DISORDERS

Piraccini BM, Starace M. Nail disorders in infants and children. Curr Opin Pediatr 2014; 26:440-5

As stated by the Authors in the title page, this is a review of nail disorders most commonly observed in infants and children, starting from basic details of anatomy and biology of the nail in order to explain nail morphology and development. This paper is a well-executed review addressed to dermatologists who wish to refresh their knowledge about pediatric nail disorders. Congenital nail disorders are mentioned first and particular attention is given to misalignment of the big toenail, nail-patella syndrome, epidermolysis bullosa and pachyonychia congenita. Acquired nail disorders comprise the following set of topics and are described according to their pathogenesis. Inflammatory nail disorders (parakeratosis pustulosa, psoriasis, twenty nail dystrophy, lichen striatus and lichen planus) are described first, followed by infections (warts, acute paronychia and onychomycosis) and tumors (nail matrix nevi and exostoses). The clinical characteristics of each disorder are described in detail in order to help non-nail experts with the diagnosis of the disorder they are dealing with. Examination techniques that facilitate the diagnosis are fully reviewed. Treatment aspects are also described in a practical way. The Authors' conclusion is that, although rare, nail disorders in children are a source of anxiety, especially for the patients' parents, and for this reason they should be promptly recognized and treated. Treatment, when possible, should take into account the age of the patient and the severity of the condition. Unfortunately there are a very limited number of treatments that can be used for nail disorders in children as topical drugs are often not effective and many systemic treatments are not always appropriate for administration in childhood.

CAPSULE SUMMARY

- Nail disorders in children should be promptly recognized and treated as they are a source of anxiety.
- A complete picture of the patient could be helpful in performing a diagnosis of a nail disorder.

Chu DH, Rubin AI. Diagnosis and management of nail disorders in children. Pediatr Clin N Am 2014;61:293-308

This paper focuses on a limited number of diseases. Only the most common nail disorders and signs encountered in a general pediatric practice are discussed including: onychomycosis, melanonychia, trachyonychia, onychomadesis and pitting. The Authors want to help clinicians with diagnosis and let them know when referral to a specialist is appropriate. Compared to the previous review, this article is mostly addressed to pediatricians rather than to dermatologists. Since nail disorders in children may be associated with mucocutaneous or systemic manifestations, a complete picture of the patient could be helpful in performing the diagnosis. Diagnostic considerations and treatment options are discussed. Onychomycosis is discussed in detail, in all its clinical forms, followed by diagnostic methods and treatment options. Each diagnostic method and treatment is compared with presentation of the pros and cons in a table. Melanonychia is discussed next. The Authors state that a pediatrician is usually confronted with the scenario of evaluating a single nail with pigmentation. The major anxiety produced with melanin pigmentation is the exclusion of melanoma, but the Authors underline how very rare this event is. Nevertheless it can occur and, since nail biopsy is not so easy to perform in a child, differential diagnosis must be accurate. The differential diagnosis of melanonychia includes exogenous pigment deposition, subungual hematoma and pigmented bacterial or fungal infections of the nail unit. A practical algorithm is presented in order to help with the approach to melanonychia. Melanonychia, trachyonychia, onychomadesis and pitting are then discussed and described in their clinical presentations and within the context of associated systemic and dermatologic conditions.

Löser C. Pediatric nail surgery. Hautarzt 2014; 65:321-6

This manuscript is published in German. It is included because it reviews surgical approaches to different pediatric nail conditions. The Author states that it is first mandatory to recognize the condition and only then decide if it is feasible and worthwhile to perform the surgical operation. Inappropriate interventions on nails can, in fact, lead to irreparable damage to fingers and toes. Conscious sedation or even general anesthesia is required with infants and toddlers and this is often difficult for

Matilde IORIZZO

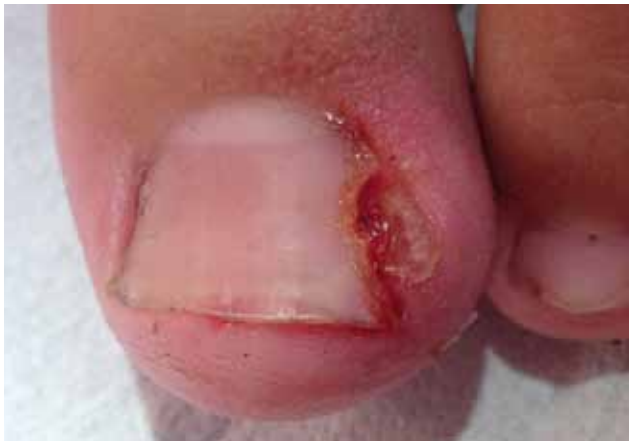

Fig1 - *Ingrown toenail referred for surgery due to painful lateral inflammation. © M. Iorizzo*

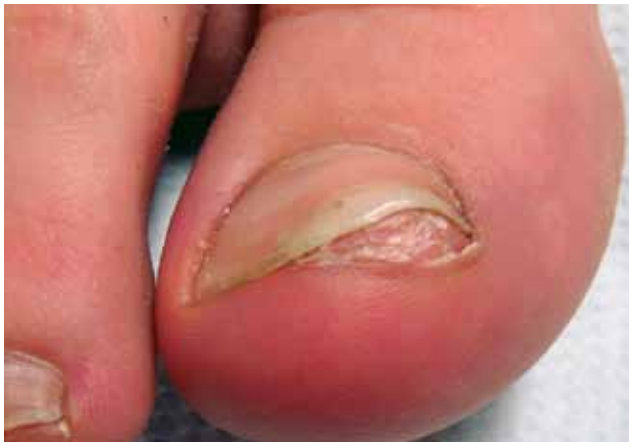

Fig2 - *Exostosis referred to surgery due to pain and uplifting of the nail plate. © M. Iorizzo*

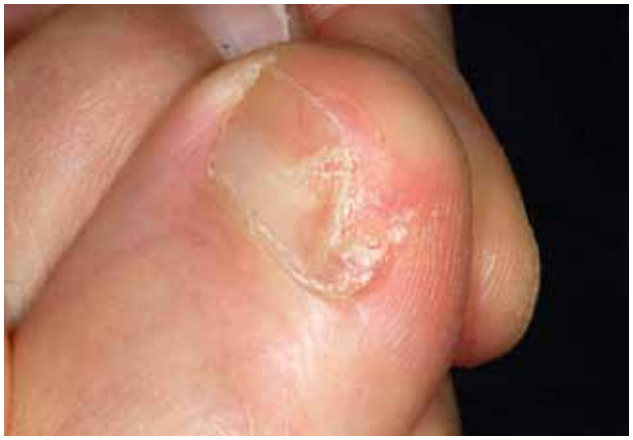

Fig3 - *Regrowth of a nail spicule resulting from an incomplete matricectomy performed by a general surgeon, not expert in nail disorders. © M. Iorizzo*

parents to accept. Regional anesthesia can be used in teenagers. Melanonychia, ingrown toenails, exostoses and onychogryphosis are the most common reasons for nail surgery consultation in children **(Figs 1-2)**. When facing melanonychia the first question should be to inquire if there is an on-going malignancy. It is then important to decide whether the risk of possible aesthetic/functional damage to the nail justifies surgery (biopsy or excision). Severe and persistent inflammation may require surgical intervention for an ingrown toenail. Permanent narrowing of the nail plate is the objective of surgery. Phenolization is less painful than surgical matricectomy, with a shorter recovery time, but higher recurrence rates. Despite the Author's description of a very practical way to approach pediatric nail disorders referred to dermatologists for surgery, it must be said that nail surgery is not so common or easy to perform for most dermatologists, even in adult patients. Detailed knowledge of nail anatomy and physiology are mandatory before performing nail surgical procedures, as otherwise severe side effects and/or nail dystrophies may occur **(Fig 3)**. Among all nail disorders affecting children and requiring surgery, melanonychia is the most important due to the issue of melanoma. Disorders like ingrown toenails, exostosis and nail plate abnormalities might require surgery when the patient is significantly affected and when no other treatment is feasible. Psoriasis, lichen planus and other inflammatory disorders might require surgery (biopsy) if the clinical diagnosis is difficult.

CAPSULE SUMMARY

- Nail surgery in children is difficult and can lead to severe dystrophies if not performed by an expert.

NAIL MELANOMA IN CHILDREN

Cooper C, Arva NC, Lee C, et al. A clinical, histopathologic and outcome study of melanonychia striata in childhood. J Am Acad Dermatol 2015;72(5):773-9

In this review the Authors share their experience with longitudinal melanonychia clinically and histologically diagnosed in 30 children from 2 to18 years of age (median age 6 years). They compare their data to that previously published[1,2] and report that in children very few cases of longitudinal melanonychia result from melanoma and in those instances it was melanoma in situ. The cases of malignant melanoma of the nail unit in children reported in the literature[3,4] do not come from longitudinal

melanonychia. Among the 30 cases observed in Chicago, 20 were diagnosed as lentigo, 5 as nevi and 5 as atypical junctional melanocytic hyperplasia. Ten selected cases with atypical clinical features had nail matrix biopsy performed and 20 patients, where the concern for melanoma existed after expert review, had complete excision of the band. Clinically, 8 patients had a band ≥ 3 mm and, in 5 patients, the band was ≥ half of the nail bed. Hutchinson's sign was present in 4 patients and pseudo Hutchinson's in another 4. Nail dystrophy was detected in 2 patients. In 10 cases the lesion was noted to have changed or evolved with respect to width or colour. Clinical characteristics which raised the concern of malignancy, were bands ≥ 3 mm, rapid changes of the width or colour of the pigmentation (blurred lateral borders, absence of parallelism, different colours at the same time), presence of nail dystrophy and Hutchinson's sign. Despite this, when facing a band of melanonychia, the clinical diagnosis might be difficult even for nail experts. The use of a dermatoscope is very helpful **(Fig 4)** and adds useful information to the clinical examination, but sometimes this device is insufficient and surgery must be performed. Surgery in children is often complicated because it requires conscious sedation or general anesthesia, and due to the possibility of permanent nail dystrophy as a consequence and also as there is still not a definite consensus on biopsy or excision of a band of melanonychia. Usually, when clinically worrisome features are present, total excision of the pigmented lesion is recommended. On the contrary, for small doubtful lesions, a simple biopsy can be performed. A transverse biopsy of the nail matrix is preferable to a punch biopsy; the latter is generally performed when the band is less than 3 mm. A punch biopsy sample is often incomplete and if the histology reports a benign lesion it may be a false negative.[5]

Fig4 - *Longitudinal melanonychia seen at dermoscopy. © M. Iorizzo*

The correct specimen should include nail matrix, nail plate and periungual normal appearing skin. The pathologist should be familiar with nail disorders in order to perform a correct diagnosis. Nuclear atypia of a few melanocytes and a mild degree of transepidermal melanocytic migration, in single cells or in clusters, may be seen without being a sign of malignancy. These characteristics are particularly prominent in the proximal matrix and can lead to over diagnosis of melanoma *in situ*.

Instead the presence of an increased number of atypical melanocytes irregularly distributed in solitary units at the dermo-epithelial junction, and at different levels in the epithelium of the nail matrix and nail bed, support the diagnosis of melanoma.

The clinical and histologic results of the cases reported in this paper are similar to those reported in the literature, with the exception of the clinical presentation. The Authors reported a high percentage of changing bands (33% compared to the 3% reported in the literature). For this reason they more frequently performed surgery in their patients. Compared to other Authors, they diagnosed more cases of atypical melanocytic hyperplasia as compared to diagnosis of melanoma *in situ* underlying the fact that, histopathologically, the differential diagnosis between these two conditions is very difficult. The Authors state that since some conditions in children (Spitz, Reed, congenital nevi) are considered as benign and in adults they raise the suspicion of melanoma, the same could be true with atypical melanocytic hyperplasia. Obviously this is just a hypothesis, because no one exactly knows the biologic capacity of atypical melanocytic hyperplasia evolving into malignant melanoma.

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CAPSULE SUMMARY

- In children, longitudinal melanonychia result exceptionnally from melanoma that is, generally, an in situ melanoma. Differential diagnosis between atypical melanocytic hyperplasia and melanoma in situ may be difficult even for expert nail pathologists.

Matilde IORIZZO

RETRONYCHIA IN CHILDREN

Piraccini BM, Richert B, de Berker DA, et al. Retronychia in children, adolescents and young adults: A case series. J Am Acad Dermatol 2014;70:388-90

Retronychia describes the embedding of a detached proximal nail plate into the proximal nail fold.[1] Usually, when an insult temporarily interrupts nail matrix activity (with or without complete onychomadesis), the new growing nail pushes forward the old nail plate. When the alignment is not maintained the new nail may push the old nail upwards and backwards favouring proximal ingrowing with subsequent paronychia and pyogenic granulomas. Causes of this disrupted alignment are persistent minor trauma from sports or from ill-fitting shoes, which push against the free edge of the detached nail plate that is not removed from the nail bed. Usually this condition is reported in adults,[2] but the Authors of this paper reported its occurrence in 15 patients under 24 years of age. Among these patients were a not quantified group under 12 years of age. The clinical presentation of the disease and the causative agents are the same as in adults. The therapeutic approach in children should then be the same, i.e. complete avulsion of the detached nail plate. During surgery it is not uncommon to find more than one nail plate overlapping another. The avulsion should not involve the new growing nail. Retronychia, unlike lateral ingrown nails, resolves with one surgery[3] **(Figs 5-6)**. When patients refuse surgery, a course of topical clobetasol propionate 0.05% is usually prescribed, even if this is almost always associated with recurrences. Permanent nail dystrophy might be a consequence of retronychia in 30% of patients, even after surgery. The Authors state that, in their experience, this condition is under-reported in the literature especially in young patients, because of a faster growth rate of their nail plate. In young patients trauma, sport and the wearing of soft shoes is usually more frequent than in adults. In conclusion retronychia should be suspected in every instance of persistent, treatment resistant paronychia, with or without granulation tissue.

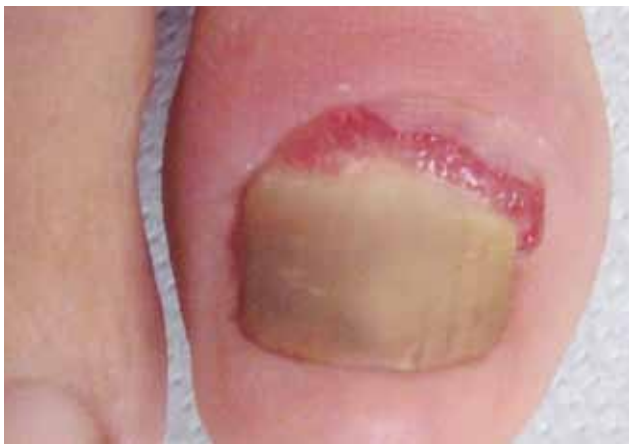

Fig5 - *Retronychia with periungual pyogenic granuloma in a dancer. © M. Iorizzo*

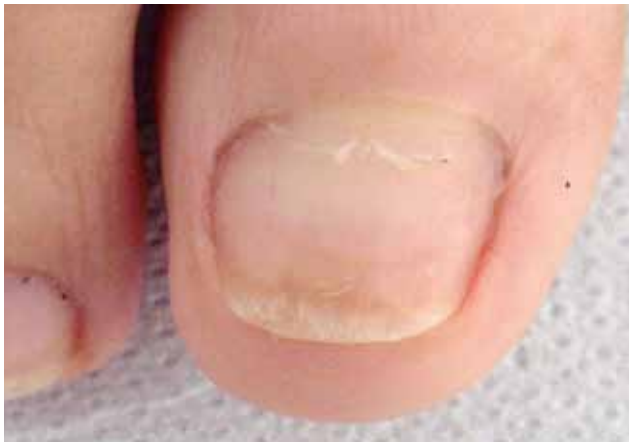

Fig6 - *The same patient of Fig. 5 after surgery. © M. Iorizzo*

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3. Richert B, Caucanas M, André J. La rétronychie. Ann Derm Venereol 2014 ;141 :799-804.

CAPSULE SUMMARY

- Retronychia should be suspected in every instance of persistent, treatment resistant paronychia, with or without granulation tissue. The condition is probably under-reported or misdiagnosed in young patients, due to a faster growth rate of their nail plate.

TRACHYONYCHIA

Kumar MG, Ciliberto H, Bayliss SJ. Long-term follow-up of pediatric trachyonychia. Pediatr Dermatol 2015;32:198-200

The Authors report 11 children, between the ages of 2 and 7, with trachyonychia of 20 nails (only 1 patient had trachyonychia of 13 nails). The children were all in good health, had no family history of nail disorders and no biopsies were performed, because they were not necessary for the diagnosis due to the lack of a uniform pathologic picture. They followed these children for an average of 6 years (10-126 months) and they treated 9 patients with topical corticosteroids (fluocinonide in 8 patients and triamcinolone in 1 patient), 1 patient with petrolatum and 1 patient with a not specified vitamin supplement. Almost all patients discontinued treatment soon after the baseline visit (loss of compliance) and almost all of them (82%) were improved or cured at the end of follow- up. This data demonstrated, once again, that trachyonychia improves within several years, regardless of treatment. Nevertheless children with trachyonychia may subsequently develop psoriasis, lichen planus or alopecia areata in adulthood. In this case series only 1 patient developed alopecia areata of the eyebrows during the follow-up period. These Authors reported a long-term follow-up of patients with trachyonychia confirming the already available data in the literature.[1-3] Trachyonychia is an acquired benign inflammatory disease of the proximal nail matrix, which produces diffuse homogeneous roughness only of the dorsal nail plate that tends to improve over time, despite a lack of treatment **(Fig 7)**. The extent and distribution of nail plate abnormalities depends on the severity and course of the inflammatory insult. Severe and persistent inflammation produces opaque trachyonychia. Milder and more intermittent inflammation is responsible for the shiny variant. The insult to the proximal nail matrix keratinocytes impairs their maturative and differentiative activity, without interrupting the mitotic activity, which is why trachyonychia is not a scarring disorder.[4] Most commonly it is due to spongiotic changes in the proximal nail matrix, but nail psoriasis and lichen planus may be found histopathologically. To identify the underlying inflammatory disorder a biopsy is mandatory, but this is not usually recommended, due to its invasiveness and irrelevance to the course of the disease. Generally no treatment is prescribed for this disorder, except for mild emollients or cosmetic camouflage.

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CAPSULE SUMMARY

- Trachyonychia improves within several years, regardless of treatment or etiology. Nail biopsy is irrelevant. Affected children could subsequently develop psoriasis, lichen planus or alopecia areata.

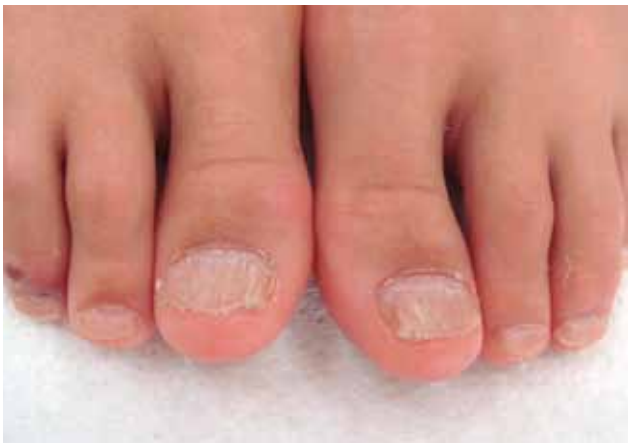

Fig7 - *Trachyonychia in a young boy. © M. Iorizzo*

Matilde IORIZZO

NAIL PSORIASIS IN CHILDREN

Piraccini BM, Triantafyllopoulou I, Prevezas C, et al. Nail psoriasis in children: common or un common? Results from a 10-year double center study. Skin Appendage Disord 2015; 1:43-48

The aim of this paper has been to estimate the prevalence of nail psoriasis in the pediatric population and compare it to a double center 10 years data. The Authors performed an extensive literature search and collected data, ranging from 2004 to 2013, concerning the number of children seen in pediatric dermatology consultations in Athens, Greece and in Bologna, Italy (University Hospitals), with the diagnosis of psoriasis and nail psoriasis.

After reviewing the literature they reported that nail psoriasis rarely occurs in children suffering from skin psoriasis, the incidence being lower than in adults. Pediatric nail psoriasis is not related to the type/severity of skin psoriasis and is independent from psoriatic arthritis. As in adults, nail abnormalities may be the only manifestation of the disease. In the literature the prevalence of pediatric nail psoriasis in Caucasian patients was evaluated by selecting papers from Europe, the USA and Australia. A total of 343 children out of 3,355 patients affected by psoriasis had nail involvement (10.2%).

In the subgroup of European patients, 165 patients (12.5 %) out of 1,318 children with psoriasis were diagnosed with nail psoriasis. The 2 center data revealed that 68,839 patients, aged 6-17 years, were seen in pediatric dermatology consultations between 2004 and 2013 at both clinics [30,044 (GR) and 38,795 (IT)]. Among them, 406 had skin psoriasis (0.6%) and 74 had nail psoriasis (0.11%): 55 in Greece (0.18%) and 19 in Italy (0.05%). In children with skin psoriasis, the rate of children affected by nail psoriasis was 19.4% in Greece and 15.5% in Italy. Considering the total number of the sample, this is the retrospective study with the largest number of cases of nail psoriasis in a pediatric population. It confirms the European prevalence data regarding skin psoriasis in children, estimated between 1.01 and 0.71%.[1] Moreover nail psoriasis is confirmed to be uncommon. The rate of children with nail psoriasis among children with psoriasis is slightly higher in comparison to the European rate published (12.5%). This is probably because the patients received a diagnosis in a nail unit consultation, where dermatology experts in nail disorders were more accurate than pediatricians or non-nail experts. The diagnosis of nail psoriasis in children, especially in the very young, might be difficult. The condition could be over-estimated as other diseases that induce similar nail signs may be missed. These diseases include onychomycosis, parakeratosis pustolosa, trachyonychia, alopecia areata limited to the nails, eczema and trauma.

A wide experience of nail diseases is required to be able to distinguish between these disorders. According to the literature the most common clinical sign of nail psoriasis in children is pitting, which is not pathognomonic of the disease. Pits are typically large, deep and irregularly distributed. Pits in the toenails, which are exceptional in adults, may occur. Other signs of nail psoriasis include onycholysis with erythematous border and nail thickening due to subungual hyperkeratosis **(Fig 8)**. Nail psoriasis is a chronic condition and complete remission is uncommon. Sunlight and hot weather are less effective remedies than in skin psoriasis. Prompt and correct diagnosis is necessary before starting treatment.

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Fig8 - *Nail psoriasis in a teenager. © M. Iorizzo*

CAPSULE SUMMARY

- Nail psoriasis rarely occurs in children affected by skin psoriasis and, as in adults, it can be the only manifestation of the disease. The condition is often unrecognized, as presenting signs are not pathognomonic of the disease, or over-estimated as other disorders induce similar nail signs.

NAIL LICHEN PLANUS IN CHILDREN

Chiheb S, Haim H, Ouakkadi A, Benchikhi H. Clinical characteristics of nail lichen planus and follow-up: a descriptive study of 20 patients. Ann Dermatol Venereol 2015;142:21-5

This paper, written in French, describes clinical features, response to treatment and a 2 year follow-up of nail lichen planus diagnosed in 20 patients at the University Hospital of Casablanca, Morocco. Among these patients 8 were children ≥ 9 years old. In this series no family history of lichen planus was reported and no gender preponderance, contrary to the literature where a male predisposition is usually reported. Only 5 patients had extra nail lichen planus, but they were all adults.

Unfortunately the Authors made no distinction between adults and children in describing their clinical findings and, for this reason, it is impossible to understand which characteristics are typical of children and which ones are typical of adults. All twenty nails were affected in 55% of patients, nail matrix involvement was observed in 85% of patients (onychorrexis, trachyonychia, pterigium, anonychia) and nail bed involvement was reported in 55% of patients (onycholysis, hyperkeratosis).

Generally in children the disease manifested as trachyonychia, but it was not specified in how many patients. As a treatment they prescribed intramuscular triamcinolone acetonide 0,5 mg/kg/month for 3 to 6 months to 10 patients, those with matrix involvement or severe cases. In 80% of them, the disease improved or regressed after the 3rd injection. In the remaining 10 patients, those with nail bed lichen planus or those with limited disease, the Authors prescribed clobetasol propionate cream and the disease improved or regressed quickly. No patient reported recurrences after 2 years of follow up.

According to the Authors early diagnosis of the disease, especially in children, allows initiation of adequate treatment that could limit the risk of sequelae (the relationship between early diagnosis and response to treatment is however not reported). They confirm intramuscular corticosteroids as being safe and effective in the treatment of this disorder.[1] This case series has a high percentage of children (40%) compared to other reports.[2,3] Unfortunately the follow up is too short to state that the disease will not result in recurrences in the future. More extensive reported follow ups (mean 10 years) demonstrated that recurrences are common (60% in the first year after discontinuation of treatment).[2]

Nail lichen planus is considered to be a rare disease in children, but recent reviews show that this is not always the case.[4] A case series of 316 children, aged between 2 and 14, with lichen planus included 14% of patients with nail involvement. Nail lichen planus in children may be underestimated for three main reasons:

1- Lack of skin/mucosal lesions makes the diagnosis difficult for non-nail experts;
2- Lichen planus is not considered in patients with trachyonychia. There are no clinical criteria, in fact, that permit diagnosis of the inflammatory disorder responsible for trachyonychia (lichen or psoriasis or alopecia areata) and the clinical association with alopecia areata, lichen planus or psoriasis is not helpful: the nail pathology may suggest lichen planus or psoriasis in patients with trachyonychia clinically associated with alopecia areata.
3- Reluctance in performing nail biopsies in children.

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CAPSULE SUMMARY

- Nail disorders in children should be promptly recognized and treated as they are a source of anxiety.
- A complete picture of the patient could be helpful in performing a diagnosis of a nail disorder.
- Nail surgery in children is difficult and can lead to severe dystrophies if not performed by an expert.
- In children, longitudinal melanonychia result exceptionally from melanoma that is, generally, an in situ melanoma. Differential diagnosis between atypical melanocytic hyperplasia and melanoma in situ may be difficult even for expert nail pathologists.
- Retronychia should be suspected in every instance of persistent, treatment resistant paronychia, with or without granulation tissue. The condition is probably under-reported or misdiagnosed in young patients, due to a faster growth rate of their nail plate.
- Trachyonychia improves within several years, regardless of treatment or etiology. Nail biopsy is irrelevant. Affected children could subsequently develop psoriasis, lichen planus or alopecia areata.
- Nail psoriasis rarely occurs in children affected by skin psoriasis and, as in adults, it can be the only manifestation of the disease. The condition is often unrecognized, as presenting signs are not pathognomonic of the disease, or over-estimated as other disorders induce similar nail signs.

André LENCASTRE

For this review, PubMed and Google Scholar databases were searched for all articles written in English, Portuguese, French, Spanish or German and published in 2014. The following keywords were used: Nail, Cosmetics, Rejuvenation, Prosthetic, Polish, Gel, Lacquer, Shellac, Varnish, Manicure, Pedicure, Peeling, Aesthetics, Fiberglass, Silk, Art, Linen, Sculpture, Artificial and Cuticle.

UV AND NAIL CANCER

O'Sullivan NA, Tait CP. Tanning bed and nail lamp use and the risk of cutaneous malignancy: A review of the literature. Australas J Dermatol 2014; 55(2): 99-106

Tanning bed and nail lamp use and the risk of skin cancer.

This is a narrative review of 82 articles searched from PubMed (1966 - present), Embase (1974 - present) and Google with the keywords: tanning beds, sunlamps, solarium, melanoma, cutaneous malignancy, non-melanoma skin cancer, NMSC, BCC and SCC.

This paper mainly concerns skin cancer risk with the use of tanning beds. Of the papers reviewed, only 3 are cited on the topic of UV nail lamp exposure and related skin cancer: an anecdotal report of 2009, on dorsal hand SCC in two patients with previous UV nail lamp exposure that raised safety concerns on these devices; a 2012 mathematical model study that found a very low risk of developing SCC with UVA nail lamp use, when compared to typical sun exposure; and a 2013 study that concluded that 250 years of weekly exposure to nail lamps would be required to reach the same UV dose as that found in one course of narrowband UVB treatment (15-30 treatments). The authors of the 2012 study also recommended the use of fingerless gloves during curing to reduce cancer risk to almost nothing.

One can only conclude, as did the authors of this review, that there remains a scarcity of evidence in this area and further research is prompted. Undoubtedly my fellow colleagues are aware of these papers. A nail expert should nevertheless be aware of the current evidence on this subject, in order to properly advise those mentioning the use of UV nail lamps and/or expressing fears of UV-related skin cancer.

FRENCH AND NAIL COSMETICS

Ficheux AS, Morisset T, Chevillotte G, Postic C, Roudot AC. Probabilistic assessment of exposure to nail cosmetics in French consumers. Food Chem Toxicol. 2014;66:36-43

Exposure to nail cosmetics.

The aim of this study was to assess the exposure to cosmetics on finger nails including base coat, polish, top coat and nail polish remover in French child and adult consumers. A national web questionnaire, volunteer and lab experiments were conducted.

In March 2013, the authors conducted a national web questionnaire survey to collect information on usage patterns of base coat, polish and top coat on finger nails (i. e. percentage of users, frequency of use, wearing time and number of coats applied). The percentage of users and frequency of use were also obtained for polish remover. Participants from this questionnaire group were asked about their bodyweight and if they practiced onychophagia in the presence of nail cosmetics. Data was obtained from 1512 French women aged 18-85 years and mothers of 301 children (0-17 years) to determine the percentage of users and the frequency of application.

110 Volunteers (aged over 18) were asked to participate in the experimental part of this study. Information was obtained concerning products habitually used (base coat, polish, top coat and/or polish remover) and to collect personal data: age, place of residence, socio-professional category, body weight and height. Products habitually used by the volunteer were offered with instructions to adhere to personal habits of use. During testing, setting and drying time of base coat, polish and top coat used were measured and the number of coats applied was noted. The time of use of nail polish remover was also measured. The quantity of each nail cosmetic used was determined by differential weighing before and after use. Participant hands were photographed and analysed to estimate the surface and width of fingernails, and nail wall area was estimated. The findings obtained were used to deduce results for the wider population.

In the lab, the breathable fractions of base coat, polish, top coat and nail polish remover were assessed, calculating their evaporation rates by weighing a fraction of these products at regular intervals.

Probabilistic assessment exposure was made using the Monte Carlo probabilistic method on computer software. Dermal, inhalation and oral routes (in case of onychophagia) were taken into account for base coat, polish and top coat. Exposure was assessed by inhalation for nail polish remover.

Among the 1512 female adults interviewed (18-85 y. o.), 88% of women reported using cosmetics on finger nails at least once a year, as well as 69% of children aged 0-17 years. 12% of adults and 31% of 0-17 year-olds never use nail cosmetics.

Only women and children classified as regular consumers were taken into account in the exposure assessment. Regular use was considered as frequency of use was greater than 0.188 times a week - i. e. more than 1.5 times every 2 months (this value corresponds to the 10th percentile of the distribution of frequency). Hence, regular consumers of nail cosmetics were 58% of 35-85 year-olds, 73% of 18-34 year-olds, 80% of 13-17 year-olds and 22% of 0-12 year-olds. Among the regular adult consumers, 88% reported getting their manicures at home, 11% at home and at nail salon and 1% at nail salon only. The frequency of use of nail cosmetics was equal to 1.11 week (35-85 years), 1.27 week (18-34 years), 1.40 week (13-17 years) and 0.91 week (0-12 years). The wearing time was on average equal to 1.02 weeks for adults aged 18-34, and equal to 0.89 weeks for women aged 35-85 years.

Nail polish was used by 98% of regular adult consumers. Base coat was applied by 60% of 18-34 year-olds and by 63% of 35-85 year-olds. Top coat was used by 43% of 18-34 year-olds and by 32% of 35-85 year-olds. Products were applied in one or two coats. Nail polish remover was used by 98% of adult consumers. 28% of women aged 18-34 years and 11% of women aged 35-85 years reported practicing onychophagia in the presence of varnishes.

Consumption data for toenails were also obtained for 1512 adults and 301 children. 84% of 18-34 year-olds and 78% of 35-84 year-olds reported using cosmetics on toenails at least once a year. 61% of 301 children aged 0-17 years wore nail products on toenails at least once a year. Apparently not enough experimental data was collected from the volunteer group regarding toenail cosmetic use. Consequently, the authors did not assess exposure to nail cosmetics on toenails.

For base coat, nail polish and top coat the main route of exposure was ungual. Inhalation was the secondary route of exposure, followed by dermal ("nail wall") and oral routes. For these cosmetics, life-long exposure values measured in mg (kg bw week)^{1} were obtained. Polish contributed most to exposure, regardless of the route of exposure. Among age classes, children aged 0-12 years were the most exposed to polish by ungual route. Children aged 13-17 years were the most exposed to polish by inhalation and oral route. Children aged 13-17 years were also the most exposed to top coat, regardless of the way of exposure. Among age classes, children aged 13-17 years were the most exposed to base coat, regardless of the route of exposure. Young people aged 0-12 years were the most exposed to remover. Some selection bias, data bias and lack of information on some parameters are promptly reported in the paper and should be reviewed in case of interest.

The authors note that no exposure data have been published for nail cosmetics and consumption data for nail cosmetics are very limited in Europe. They claim this paper to be the first assessment of exposure to nail cosmetics. Through this work, the authors aimed to create a national database containing current consumption and exposure data for nail cosmetics in order to provide a basis for future toxicological studies of the uptake of substances contained in them.

This work provided data regarding the usage patterns of four nail cosmetics consumed by adult French women: base coat, polish, top coat and polish remover. Different parameters including the percentage of users, frequency of use, wearing time and number of coats of varnishes applied were obtained by a national enquiry. The amount of use, time of use, and application area were obtained by laboratory experiments.

Ungual exposure to nail cosmetics does not seem trivial. The nail plate is lowly permeable to diffusing substances. Transfer through the nail should be lower according to molecules and consequently, systemic exposure could be limited. In my personal opinion, dermal absorption through the surrounding nail folds should perhaps be given more relevance, as is the case for the oral route in case of onychophagia. Inhalation has been documented as an easy and fast means of exposure. Physicians should be aware of these routes of exposure.

Although this study may appear to perhaps be of greater interest for toxicologists, pharmacologists and cosmetovigilance authorities, it still provides important data for the nail expert. I highlighted some of it in text.

It provides (albeit for the population of French women) an estimate on the percentage of nail cosmetic consumers. It indicates habitual frequency of use and how consumers use these products. Of note, the highest percentage of regular users was among adolescents. Bearing in mind that in this study, some data for young children had to be estimated or inferred from other age groups, children were found to be the age group with the highest life-long exposure values for types of all nail cosmetics. There is no discussion or appreciation on the potential local or systemic side-effects associated with nail cosmetic use, important topics for the nail clinician. However, there is some good information that can be used in a consultation when safety concerns are risen. I also consider it to be a good paper to quote on nail cosmetic usage practices in the future.

André LENCASTRE

WHEN NOTHING ELSE CAN BE DONE

Nanda S, Grover C. Utility of gel nails in improving the appearance of cosmetically disfigured nails: Experience with 25 cases. J Cutan Aesthet Surg 2014;7:26-31

Utility of Gel Nails in Improving Disfigured Nails.

In this prospective, uncontrolled, open-label study, 25 patients with cosmetically disfigured, KOH-negative nails, received gel nail application with a Ranara gel nail kit®. Patients had: trachyonychia (n=8); superficial pitting (n=6); onychorrhexis (n=4); superficial pitting with onychoschizia (n=3); Beau's lines (n=3) and pterygium (n=1). Standard pre- and post-treatment photographs were taken. Patients received an in-office specific study protocol of gel nail application, and were instructed to keep them for a 4 week period and return for removal. Scores of patient satisfaction and global assessment of improvement, and any side effects were recorded.

A total of 69 nails (average of 2.76 nails treated per patient; range 1-8 nails). Majority of the patients had involvement of finger nails, with only three patients seeking treatment for their toe nails. Post-procedure, the average patient satisfaction score was 9.08 ± 0.86 (range 7-10). The global assessment done by two independent physicians on the basis of serial photographs showed excellent improvement in 40% cases (n=10); good improvement in 56% cases (n=14) and mild improvement in the single case of pterygium.

A slight roughness was noted in some patients that responded to moisturizers.

The authors express their (perhaps reasonable) assumption that dermatologists have demurred gel nail usage to their reported side effects **(Fig 1, 2)**. They propose the use of this cosmetic procedure when avoiding other treatments such as intralesional steroid injections or systemic medication, themselves not devoid of potential side effects. They also make a point that offering no treatment is also not very acceptable.

Artificial nails (e.g. acrylic) have already been used in the management of a few nail conditions. Bringing gel nail making, from the nail salon into the dermatologist's office, will perhaps command further arguments. I must admit a skeptical approach at first. However, in the case of the patient whose risk-benefit relationship draws one away from conventional pharmacological therapies (or when these have failed), one can only admit that other techniques might be in order.

Several precautions (provided in text) such as the minimal buffing of the nail plate, application of one single layer of gel nail, and consequently its easier removal, were perhaps considered "crucial" (sic) for having no relevant side-effects reported (to be further studied, of course).

These precautions could perhaps be transmitted to a patient's manicurist in the case of only mild to moderate disease, with a short follow-up period.

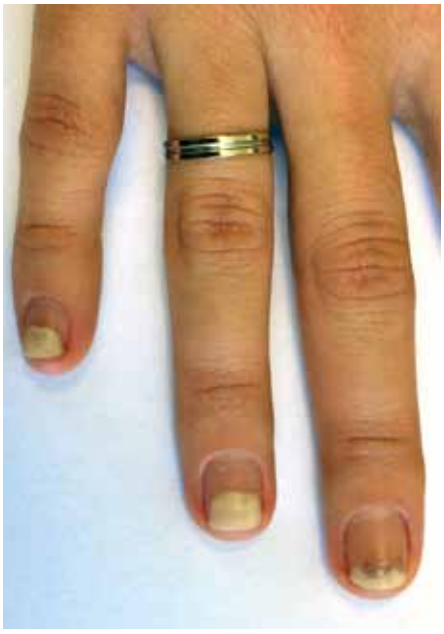

Fig1 - *Onycholysis following gel nail application. © A. Lencastre*

Fig2 - *Allergic contact dermatitis to acrylate gel nails that persisted shortly after removal. © A. Lencastre*

NAILS MAY BE REJUVENATED TOO

Banga G, Patel K. Glycolic acid peels for nail rejuvenation. J Cutan Aesthet Surg 2014; 7: 198-201

Glycolic Acid Peels for Nail Rejuvenation.

In this article the authors report their results in a prospective, single-center, uncontrolled, open-label trial on the application of 70% glycolic acid (GA) to improve the cosmetic appearance of nail diseases. Thirty-one patients were included, 22 with dry, rough and discolored nails due to "chemical abuse" (sic), and 9 with hyperkeratotic nails - 7 post-onychomycosis (OM) and 2 with lichen planus (LP). Hypersensitivity to GA, very thin nails and active infection or inflammation in or around the nails were among the exclusion criteria.

Treatment consisted of:

1- cleansing the nail with plain water;

2- periungual application of petroleum jelly;

3- application of 70% GA with a pH of 1,5 with the help of a cotton bud.

Patients were divided in:

• Group 1 (22 patients) - single coat, for dry and dull nails;

• Group 2 (9 patients) - 2-3 coats, depending on nail plate damage, for pathologic nail conditions.

The peel was left on for 45 minutes and rinsed off with plain water. Patient sessions varied according to nail condition. Follow up occurred 2 weeks after treatment, except for hyperkeratotic nail patients, who were treated and followed up weekly up to 6-12 weeks. Patients with hyperkeratotic nails were allowed to continue their usual nail disease treatments, remaining patients were advised to liberally apply an urea/lactic acid-free, aloe vera based moisturizer. Only a patient satisfaction scale of 0-5 was used.

For Group 1, 18 patients (82%) reported good results, whereas for group 2, 6 showed good results (all with onychomycosis).

There was mild burning sensation, dryness and peeling in and around the cuticle in three patients.

This trial uses two different protocols of GA for the cosmetic improvement of nail appearance in two different settings. Unfortunately, there were some limitations in this study. No demographic characteristics were provided. Two distinct nail patient groups were evaluated. The majority was described as having, dry, rough and discolored nails. The term "dryness" appears to be confusing and the meaning of "discoloration" can only be subjectively assumed. An unspecified number of these patients had alterations caused by "chemical abuse", also unspecified. Others had nail changes brought on by aging or nutritional deficiency. The remaining patients had nail disease. No impression of disease type or severity is provided although all patients with OM were under systemic antifungals. The number of sessions for patients in this group remained undisclosed. Regrettably, no physician assessment scale or objective evaluation was reported.

Further studies should be made, to confirm this study's suggestion of a beneficial "cosmetic" effect on the nails with a GA peel. An increased "nail drying" effect with GA peel cannot be excluded. I also wonder how many of these patients may have actually improved on the liberal application of moisturizer only.

In the future, investigators interested in the use of nail acid peels should focus on a specified nail alteration/disease, provide either a control group or control untreated nail unit, and have longer follow-up times. Nail disease severity scales and patient demographics should be employed.

CAPSULE SUMMARY

- There is a dearth of knowledge that can substantiate a link between skin cancer risk and nail lamp use.
- A novel questionnaire based and experimental study, reveals that French female adolescents and children are frequent users of nail cosmetics. Among age groups, regular usage of these products in children implies the highest life-long exposure for all types of nail cosmetics. Despite an absence of mention of its potential for local or systemic disease, physicians should be aware of the prevalence of such habits.
- Mildly disfigured nails may improve from a delicate protocol of gel nail application
- Glycolic acid may improve patients with nail changes. Future studies are required.

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TREATMENT OF NAIL PSORIASIS: NEW EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

Introduction

Treatment of patients with nail psoriasis has always been a time-consuming challenge with an insecure outcome. Many clinical trials have been performed in order to optimize this treatment. In 2013 the first Cochrane review appeared focussed on interventions for nail psoriasis. In this review, all randomized controlled clinical trials (RCTs) focussing on clinical improvement were subjected to an extensive analysis in order to assess evidence for efficacy and safety.[1] Eighteen RCTs, involving 1266 participants, were included and analysed. These were comprised of ten studies assessing topical treatments (clobetasol, cyclosporine in maize oil, hyaluronic acid with chondroitin sulphates, 5-fluorouracil, a combination of dithranol with salicylic and UVB, tazarotene, and calcipotriol); five studies assessing systemic treatments, (golimumab, infliximab, ustekinumab, cyclosporine, and methotrexate); and three studies assessing radiotherapy (electron beam, grenz ray, and superficial radiotherapy). The results of this evidence based approach were more disappointing than convincing: only infliximab, golimumab, superficial radiotherapy, grenz rays, and electronbeam caused significant nail improvement when compared to a comparative treatment. All these treatments are not, or only rarely, used in daily practice, while no RCTs had been carried out for other, more commonly used treatments for nail psoriasis.

Since the publication of this Cochrane review several new publications on the treatment of nail psoriasis have appeared. Not only systemic therapies with biologics were the subjects of these trials, but topical treatments were fortunately also investigated. All twelve published RCTs on nail psoriasis with 1469 patients and these will be discussed in the following pages, in order to find out if their data can contribute to the unmet needs of our patients.

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NAIL LACQUER BASED ON CHITIN EXTRACTED FROM CRAB CARAPACE

Cantoresi F, Caserini M, Bidoli A, Maggio F, Marino R, Carnevale C, et al. Randomized controlled trial of a water-soluble nail lacquer based on hydroxypropyl-chitosan (HPCH), in the management of nail psoriasis. Clinical, cosmetic and investigational dermatology. 2014;7:185-90

Many patients confronted with a nail disease first try an OTC product, rather than visit their physician. One of the OTC products they may encounter is a hydroxypropyl chitosan (HPCH)-based nail solution, based on aminosaccharide chitin extracted from crab carapace. Two other components, methyl sulfonyl methane and Equisetum arvense (a herbaceous perennial plant commonly known as horsetail), provide sulphur and silica, which are claimed to contribute to the strengthening of the nail and provide minerals to form "the collagen that cements the onychocytes". This water-based HPCH solution should form a protective film that, according to the communication of the company, remineralises and restructures nails, protects keratin, and maintains hydration. However, the company that markets this product (Polichem S.A. Lugano, Switzerland) appears to have ambitions that reach further than formulating appealing slogans; they want to substantiate their claims with trials in several nail disorders, including nail psoriasis. In this randomized, double-blind, vehicle controlled, parallel-group trial, 87 patients were included with mild to moderate psoriasis of the nail bed and/or nail matrix of at least one finger nail (modified target NAPSI ≥2). Patients were treated once daily for 24 weeks. Clinical features were evaluated every 4 weeks. The primary end-point was clinical cure, defined as a mNAPSI score ≤4 at the end of the treatment. Based upon intention-to-treat, the clinical cure rate among the patients treated with the active compound was 55%, and 31.7% among the patients treated with the vehicle (P=0.0445). The proportion of patients with improvement in mNAPSI of ≥50% was rather low (20-25%), and there was no significant difference at week 24 between the patients treated with HPCH-containing nail lacquer or vehicle. Unfortunately, the mean NAPSI is only presented at baseline and cannot be derived from the published data. No local adverse events were reported in either treatment group.

The authors' conclusion was that they had demonstrated that HPCH nail lacquer could be an effective and safe option for decreasing the signs of nail dystrophy in psoriatic patients. And indeed, clinical signs in a number of patients with nail psoriasis had improved during the 24

weeks of treatment. The suggested clinical cure rate of 55% is somewhat misleading, because patients with a mNAPSI at baseline of ≥2 were considered as having nail psoriasis and were included in the trial. However, during the phase of analysis patients with a mNAPSI ≤4 were considered clinically cured. So patients with unchanged or worsened mNAPSI, between 2 and 4, were considered cured during this trial. The reason for these biases may be that the study was entirely supported by the manufacturer and that two of the authors are employees of this company. New analysis of the obtained data by an uninvolved party could help remove any residual distrust concerning the efficacy of this treatment.

TACROLIMUS OINTMENT IN NAIL PSORIASIS

Wang C, Lin A. Efficacy of topical calcineurin inhibitors in psoriasis. Journal of Cutaneous Medicine and Surgery. 2014;18(1):8-14

The topical calcineurin inhibitor tacrolimus has been shown to be effective in facial, genital, and intertriginous psoriasis. This is the first randomized trial investigating its efficacy in fingernail psoriasis, and was designed as a controlled, open label, intraindividual study. Tacrolimus 0,1% ointment was prescribed to 21 psoriatic patients for application once daily on the nail folds of affected nails of one hand for 12 weeks, whereas nails of the other hand did not receive any treatment. Patients were instructed to apply the ointment at bedtime and not to wash their hands till the next morning. At baseline, after 6,and after 12 weeks of treatment, NAPSI (range 0 to 80) and target NAPSI (range 0 to 8) were calculated. Physician Global Assessment (PGA) was also assessed, to compensate for the lack of correlation between the magnitude of the NAPSI score and the experienced severity of nail disease.[2]

The primary end-point of the study was to compare the mean absolute change in NAPSI score at week 12. A statistical significant ($P < 0.001$) improvement was obtained in the treated hands compared to the untreated hands. The average total NAPSI dropped from 23.0 at baseline to 10.0 at week 12 in the tacrolimus treated hand, while the average total NAPSI in the untreated hand remained almost unchanged (19.3 at baseline, 16.3 at week 12). Both nail bed and nail matrix appeared to have improved during the tacrolimus treatment. Also the PGA had improved significantly more in the tacrolimus treated hands. One patient was withdrawn from the tacrolimus application after 9 weeks, because of the appearance of acute paronychia, while no side-effects were reported from the untreated hands.

The authors' conclusion is that tacrolimus 0.1% ointment may be an efficacious and safe therapeutic opportunity in the treatment of nail psoriasis. They advise confirmation of these results by a double-blind study with a larger sample of patients. Since the results are very promising one might hope that this double-blind study will be carried out soon, and that new results will confirm this study. However, browsing through the five major clinical trials registers did not show any current ongoing trial focussing on tacrolimus and nail psoriasis.

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CLOBETASOL 0.05%, 1% AND 8% NAIL LACQUER IN NAIL PSORIASIS TREATMENT

Nakamura RC, Abreu L, Duque-Estrada B, Tamler C, Leverone AP. Comparison of nail lacquer clobetasol efficacy at 0.05%, 1% and 8% in nail psoriasis treatment: prospective, controlled and randomized pilot study. Anais brasileiros de dermatologia. 2012;87(2):203-11

Corticosteroids as powerful and safe anti-inflammatory compounds are the cornerstone of every dermatology practice. They are able to improve quality of life for numerous patients with itching and stigmatizing skin diseases. They have also been used extensively and successfully for many decades in the treatment of psoriasis. Remarkably, no randomized studies on corticosteroids in nail psoriasis had been published before Nakamura et al. published their study on clobetasol nail lacquer in 2012. Three different concentrations were investigated (0.05%, 1%, and 8%) in fifteen psoriatic patients with nail abnormalities on both hands. The left hand was the treated hand in all patients, while the right hand served as control. The severity of the nail psoriasis was assessed thoroughly every 4 weeks. Not only the NAPSI and target NAPSI were used, but also a pachymeter to assess subungual keratosis, and patients' satisfaction were measured. No primary end-point was defined, which makes it harder to estimate the value of the presented results, particularly since rather unusual end-points are highlighted, like "NAPSI variation 25". The potentially interesting pachymeter data and the

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data regarding the patients' satisfaction are not presented or discussed.
None of the three tested concentrations was individually able to induce a significant improvement. However, one must consider that each of these groups contained only five patients. The claimed result in the abstract and conclusion, namely that clobetasol 8% nail lacquer showed a statistically relevant clinical response compared to the other groups, cannot be derived from the data or tables in the full text. Another remarkable finding is the claimed improvement in nail matrix features of nail psoriasis, which is unlikely for a nail lacquer that is applied on the nail plate, quite distally from the nail matrix.

Response of nail psoriasis to topically applied corticosteroids is rather disappointing, according to many dermatologists involved in nail diseases. The abstract of this study indicated positive results of a clobetasol 8% nail lacquer but, unfortunately, the data do not convince.

CALCITRIOL OINTMENT COMPARED TO BETAMETHASONE DIPROPRIONATE OINTMENT IN NAIL PSORIASIS

Kole L, Cantrell W, Elewski B. A randomized, double-blinded trial evaluating the efficacy and tolerability of vectical ointment (calcitriol 3 mcg/g ointment) when compared to betamethasone diproprionate ointment (64 mg/g) in patients with nail psoriasis. Journal of Drugs in Dermatology: JDD. 2014;13(8):912-5

Not only corticosteroids, but also vitamin D3 (calcitriol) and its more powerful derivate calcipotriol (US: calcipotriene), have been proven to be useful topical treatments for plaque psoriasis. In particular calcipotriol has been shown to combine good efficacy with safety for long-term application in psoriatic skin conditions. In many countries calcipotriol is no longer available as a monotherapy. Therefore, for patients who want to reduce their use of topical steroids, calcitriol is often the only topical vitamin D3 compound that can be prescribed. Calcitriol might be therapeutically less potent than calcipotriol, but is known as also being safe after prolonged use.[3] In this recent study Kole et al. investigated the efficacy and tolerability of calcitriol ointment compared to betamethasone diproprionate ointment in ten patients with nail psoriasis of the fingernails and/or toenails. From uncontrolled trials of Tosti et al. and of Zakeri et al. it was suggested that calcipotriol was as effective as corticosteroid preparations at reducing subungual hyperkeratosis in nail psoriasis.[4,5] However, several patients in those studies complained of localized burning and irritation with calcipotriol therapy. The aim of this study was to evaluate the efficacy and safety of 20 weeks use of calcitriol ointment (3 ug/g, b.i.d.) for treatment of nail bed psoriasis. Results with calcitriol were compared to betamethasone diproprionate ointment. An absolute reduction of nail thickness (or rather subungual hyperkeratosis) was the primary efficacy outcome, but surprisingly the technique used to measure the nail thickness was not described or indicated.
All patients in both betamethasone diproprionate and calcitriol treatment groups demonstrated a reduction in target nail thickness.
However, this reduction just failed to be significant in the calcitriol group: after 20 weeks of treatment, average thickness was reduced from 2,52 mm to 1,45 mm in the calcitriol group (P=0.06), and from 1,62 mm to 1,02 mm in the betamethasone diproprionate group (P=0.01). The differences in reduction of the hyperkeratosis and also in physician global assessment (PGA) between the two groups turned out not to be significantly different. Data on onycholysis were not given. Throughout the study, there were no complaints of erythema or irritation during treatment.

The conclusion is that this small study indicates that both calcitriol and betamethasone might be able to reduce subungual hyperkeratosis in nail psoriasis. Subungual hyperkeratosis and its sequel onycholysis are important clinical features for patients suffering from nail psoriasis. The results on subungual hyperkeratosis should encourage the authors to start a study with enough power to get significant statistical results in order to remove any remaining doubts.

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INDIGO NATURALIS EXTRACT IN OIL (LINDIOIL) IN TREATING NAIL PSORIASIS

Lin YK, See LC, Huang YH, Chang YC, Tsou TC, Lin TY, et al. Efficacy and safety of Indigo naturalis extract in oil (Lindioil) in treating nail psoriasis: a randomized, observer-blind, vehicle-controlled trial. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology. 2014;21(7):1015-20

Indigo naturalis is used in traditional Chinese medicine because of the antipyretic, anti-inflammatory, antiviral, antimicrobial, and detoxifying effects that are attributed to it. Indigo naturalis and its active compound indirubin, have been used for decades in China for systemic treatment of psoriasis. The topical use is limited due to dark blue stains on the applied area.

The authors of this article have a changed formulation for indigo naturalis (Lindioil) so that it can be easily washed off and does not leave visible stains on the skin or nails. In order to test if Lindioil is effective and safe in nail psoriasis this randomized, observer-blind, vehicle-controlled, intra-subject trial was performed. Lindioil was applied twice daily for 12 weeks on the fingernails of one hand of 31 subjects, while the other hand was treated with olive oil. At the beginning of week 13, Lindioil was applied to all affected nails on both hands for another 12 weeks. Every 4 weeks a single hand NAPSI, modified target NAPSI, subject global assessment, and PGA were measured.
At week 12 the Lindioil treated fingernails had significantly lower single hand NAPSI (-49.8% vs -22.9%), modified target NAPSI (-59.3% vs -16.3%), subject global assessment, and PGA than the contralateral fingernails. From week 13 Lindioil was also applied on the control hands, which resulted in improvement of the nail psoriasis and disappearance of the differences in single hand NAPSI (-61.0%), modified target NAPSI (-76.6%), subject global assessment, and PGA at week 24. The authors did not record any side effects. Regardless of these impressive results, the study has two limitations. The first is that the colour of the substance is slightly purple-red, making it impossible to blind the subjects. Another limitation is that the author himself has developed the investigated compound, making unintended bias a serious risk. However, the methodology of the study is robust and the results are promising. One might hope that larger studies can confirm these results and the safety of the product.

Very recently, the same authors published a randomised controlled study in which they compared Lindioil to calcipotriol scalp lotion in nail psoriasis. They found Lindioil superior over calcipotriol in single hand NAPSI and modified target NAPSI.[6]

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6. Lin YK, Chang YC, Hui RC, See LC, Chang CJ, Yang CH, et al. A Chinese Herb, Indigo Naturalis, Extracted in Oil (Lindioil) Used Topically to Treat Psoriatic Nails: A Randomized Clinical Trial. JAMA Dermatology. 2015.

DIFFERENT PULSE DURATIONS IN THE TREATMENT OF NAIL PSORIASIS WITH PULSED DYE LASER

Treewittayapoom C, Singvahanont P, Chanprapaph K, Haneke E. The effect of different pulse durations in the treatment of nail psoriasis with 595-nm pulsed dye laser: a randomized, double-blind, intrapatient left-to-right study. Journal of the American Academy of Dermatology. 2012;66(5):807-12

Several studies have proven the efficacy of pulsed dye laser (PDL) in the treatment of plaque psoriasis. To treat plaque psoriasis pulse durations between 0.35 and 1.5 milliseconds are used, which are supposed to improve psoriatic lesions by the obliteration of their supporting vasculature. Studies indicating the effectiveness of PDL on nail psoriasis have been discussed in the previous issue of this journal. The current paper from Bangkok describes the results of the first randomized, double-blind study comparing two pulse durations with a 595-nm PDL. The proximal and lateral nail folds of one hand of twenty patients were treated with 6-millisecond pulse duration and 9 J/cm^2, while the opposite hands of the same patients were treated with 0.45-milliseconds pulse duration and 6 J/cm2. Spot size in both protocols was 7 mm. These protocols were based upon other publications using PDL to treat nail psoriasis.[7,8] Forty nails were treated with the first protocol and 39 nails were treated with the second protocol. Treatments were performed every 4 weeks for 24 weeks. Nail matrix NAPSI, nail bed NAPSI, total NAPSI scores, and level of pain using a visual analogue score (VAS: 0 = no pain and 10 = maximum pain) were determined at baseline and at every monthly visit. The average total NAPSI was about ten at baseline, indicating only mild nail psoriasis, and NAPSI had dropped to about five after three months of PDL treatment. There was no significant difference in improvement between the longer and shorter pulse duration treatment groups. In particular the matrix features of nail psoriasis improved, while the nail bed features were rather refractory to PDL treatment. After this initial rapid decrease in nail matrix and total NAPSI, NAPSI scores increased significantly after the third month of treatment in both treatment groups,

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despite ongoing treatment. Patients experienced relevant levels of pain with both treatment protocols (mean VAS 4 to 5), but a significantly higher level of pain was found in the longer pulse duration group. Other adverse events were hyperpigmentation and petechiae. Hyperpigmentation occurred in both groups in about 30% of patients, while petechiae occurred more frequently in the longer pulse duration groups, 42.5% and 33.3%, respectively.

The conclusion from this first randomized, double-blind study of PDL for the treatment of nail psoriasis is that both treatments had similar effects on the severity of nail disease. The longer pulse duration had a worse profile regarding the occurrence and severity of adverse effects. The lack of a placebo group is the major limitation of this study, in particular because no differences in the efficacy of the two investigated protocols could be found and the positive results faded away after three months, in spite of ongoing treatment. A randomized study comparing PDL treatment with sham laser treatment is urgently needed to justify this painful treatment in patients with nail psoriasis.

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EFFECT OF CERTOLIZUMAB PEGOL ON NAIL PSORIASIS IN PATIENTS WITH PSORIATIC ARTHRITIS

Mease PJ, Fleischmann R, Deodhar AA, Wollenhaupt J, Khraishi M, Kielar D, et al. Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA). Annals of the rheumatic diseases. 2014;73(1):48-55

Certolizumab pegol (CZP) belongs to the family of monoclonal antibodies to tumour necrosis factor alpha (TNF-α) and has an European registration for the treatment of rheumatoid arthritis, spondylitis ankylopoetica, and psoriatic arthritis. Mease et al. published data from a phase 3 randomised study in patients with psoriatic arthritis (RAPID-PsA) in which the effects on nail psoriasis were secondary outcomes. The trial was double-blind and placebo-controlled to week 24, dose-blind to week 48, and then open label to week 216. Patients were randomised 1:1:1 to placebo, or 400 mg CZP at week 0, 2 and 4 followed by 200 mg CZP every 2 weeks or 400 mg CZP every 4 weeks. Concomitant methotrexate (in over 60% of patients), sulfasalazine, leflunomide, or oral corticosteroids ≤ 10 mg/day prednisolone equivalent was allowed.
409 patients were randomised for the study, three hundred (73.3%) of them having nail involvement. Analysis of nail data was based on the modified NAPSI of the most affected nail at baseline (range 0-8), which in average was between 3 and 3.5 in the three groups. At week 24, the NAPSI change was -1.6 with CZP 200 mg every two weeks and -2.0 with CZP 400 mg every 4 weeks versus -1.1 with placebo ($p=0.003$ and $p<0.001$, respectively). More detailed information, as well as information concerning the follow up till week 216, is missing in this publication. Only mild adverse events were reported.
The conclusion from this publication is that after infliximab and golimumab, CPZ is the third anti-TNF treatment that is potentially effective for nail psoriasis. CPZ is able to reduce nail psoriasis, as measured by modified target NAPSI, by about 50%. However, even though those powerful systemic treatments have been shown to be beneficial, they are not a realistic option for most people troubled with nail psoriasis, unless the patient is prescribed these systemic treatments because of cutaneous psoriasis or psoriatic arthritis or if the nail psoriasis is severe, refractory to other treatments, or has a major impact on the person's quality of life.

TWO DOSES OF ETANERCEPT IN NAIL PSORIASIS

Ortonne JP, Paul C, Berardesca E, Marino V, Gallo G, Brault Y, et al. A 24-week randomized clinical trial investgating the efficacy and safety of two doses of etanercept in nail psoriasis. The British Journal of Dermatology. 2013;168(5):1080-7

It has just been seen that certolizumab pegol, infliximab and golimumab are anti-TNF treatments that have positive effects on clinical signs of nail psoriasis. However, two other anti-TNF compounds, etanercept and adalimimab, are at least as widely used to treat psoriasis patients as the aforementioned three. In their study, Ortonne et al. tried to assess the efficacy and safety of etanercept (ETN) on nail psoriasis in patients with moderate-to-severe plaque psoriasis. In this randomised open-label study 72 patients

with moderate-to-severe plaque psoriasis were randomized to receive open-label ETN 50 mg twice weekly for 12 weeks followed by once weekly for 12 weeks (BIW/QW group) or ETN 50 mg twice weekly for 24 weeks (QW/QW group). All patients had previously failed at least one form of systemic therapy for nail psoriasis, but had never used any biologic therapy. In contrast to the study of Mease et al. on certolizumab pegol no concomitant use of methotrexate or any other systemic anti-psoriasis therapy was allowed in this study. Patients were required to have at least mild to moderate nail psoriasis, with a target NAPSI ≥ 2 (range 0-8) and overall NAPSI > 14 (range 0-64), and moderate to severe plaque psoriasis. For some reason the thumbs were excluded in the overall NAPSI. The primary endpoint was similar to the study of Mease et al.: mean improvement in the target NAPSI measured over 24 weeks in the fingernail with the most severe abnormalities. Secondary end-points were the NAPSI 50 and NAPSI 75 (50% and 75% improvement, respectively) and the overall NAPSI, the number of patients without remaining signs of nail psoriasis (NAPSI = 0) at week 24, and changes from baseline in physician's and patients' assessment of nail psoriasis activity (visual analogue scale; range 0-100). A quality of life questionnaire was also included. In both treatment groups the target NAPSI and overall NAPSI significantly decreased. In the BIW/QW group the mean target NAPSI improved from 6.0 at baseline to 3.3 at week 12, and to 1.7 at week 24. In the QW/QW groups the mean target NAPSI improved from 5.8 at baseline to 2.9 at week 12, and to 1.4 at week 24 (all P values < 0.0001). The mean overall NAPSI in the BIW/QW group improved from 34.8 at baseline to 21.2 at week 12, and to 12.2 at week 24. In the QW/QW groups the mean overall NAPSI improved from 31.4 at baseline to 15.7 at week 12, and to 8.8 at week 24 (all P values < 0.0001). The physician assessment of nail psoriasis (VAS) improved from 62.7 at baseline to 18.0 at week 24 (BIW/QW group), and from 61.4 at baseline to 20.4 at week 24 (QW/QW group). The assessment of the patients themselves (VAS) improved from 70.6 at baseline to 21.7 at week 24 (BIW/QW group), and from 67.5 at baseline to 25.8 at week 24 (QW/QW group; all P values < 0.0001). Also the quality of life score improved significantly in both groups. However it is not sure how much this was caused by the improvement of the nail psoriasis, since patients at baseline had moderate to severe plaque psoriasis which also improved significantly. Nasopharyngitis (11-12%) and headache (9-11%) were the most reported adverse events in both groups.

The conclusion is that both ETN treatment regimens could benefit patients with nail psoriasis. The study has some limitations because of its design. A placebo control group was not included as a comparator, which potentially could have confirmed that the improvement of the nail psoriasis was due to ETN treatment and not due to a bias in the study. One of the inclusion criteria was that patients had to be naïve of biologic therapy, restricting the scope of the study to a subset of patients. However, the major reduction of the nail psoriasis in all outcome parameters appears to justify the conclusion that ETN is an efficacious therapy for nail psoriasis.

ADALIMUMAB IN PATIENTS WITH NAIL PSORIASIS AND MODERATE-TO-SEVERE CHRONIC PLAQUE PSORIASIS OF THE HANDS AND/OR FEET

Leonardi C, Langley RG, Papp K, Tyring SK, Wasel N, Vender R, et al. Adalimumab for treatment of moderate to severe chronic plaque psoriasis of the hands and feet: efficacy and safety results from REACH, a randomized, placebo-controlled, double-blind trial. Archives of Dermatology. 2011;147(4):429-36

Adalimumab is currently the most widely used anti-TNF treatment in plaque psoriasis patients. Contrary to some other anti-TNF treatments it has never been the subject of a randomized trial in nail psoriasis patients. Considering the increasing interest in nail psoriasis, the manufacturer of adalimumab has reanalysed nail psoriasis data from the REACH study. The major topic of the original REACH study was to assess the value of adalimumab for treatment of moderate to severe chronic plaque psoriasis of the hands and feet. Poulin et al have published a post hoc analysis of the data from this study. Thirty-one of the seventy-two patients in the REACH study had signs from nail psoriasis at baseline and were analysed at week 16. The outcome was a target NAPSI 50 (at least a 50% improvement from baseline in NAPSI score) response at this time point; those who achieved or did not achieve NAPSI 50 were defined as 'responders' or 'non-responders' respectively. No statistical data on significance were shown throughout the publication, most likely because of the low number of patients in both groups.

A greater percentage of adalimumab-treated patients (56.5%) compared with placebo-treated patients (12.5%) achieved NAPSI 50 at week 16. Also data concerning quality of life were investigated (DLQI). Responders, that is adalimumab-treated patients achieving a NAPSI 50, demonstrated greater mean percent improvement in DLQI score (74%) compared with NAPSI 50 non-responders

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(53.6%). However, since these results are derived from a post hoc analysis of patients with moderate to severe plaque psoriasis of the hands and the feet, it is reasonable to assume that part of the improvement of the DLQI is the result of improvement of the hands and feet.
The most attractive part of this study is the presence of a placebo branch. However, the study gives rise to some comments with respect to its design. It is important to use accepted outcome measures when doing a post hoc analysis, otherwise one might get the impression that an author is working towards certain results. The authors of this publication decided to introduce outcome measures (target NAPSI 50) that had never been used before. Unfortunately, the mean change of the target NAPSI or total NAPSI in the adalimumab-group and placebo-group are missing.
Considering the post hoc design with its unusual outcome measure, it is impossible to translate differences between placebo and adalimimab to clinical relevant differences. Another limitation of this study is that it was carried out in a subgroup of psoriasis patients with plaque psoriasis of the hands or feet. It is unclear if these results can be extrapolated to all patients with nail psoriasis. Nevertheless, it appears reasonable to accept the conclusion of this publication that adalimimab is most likely to be efficacious in treating psoriatic nail disease.

COMPARISON OF THREE TUMOUR NECROSIS FACTOR-ALPHA BLOCKER AGENTS IN NAIL PSORIASIS

Ozmen I, Erbil AH, Koc E, Tunca M. Treatment of nail psoriasis with tumor necrosis factor-alpha blocker agents: an open-label, unblinded, comparative study. The Journal of Dermatology. 2013;40(9):755-6

This small open-label randomized controlled trial was published by Ozmen et al. as a letter to the editor in The Journal of Dermatology. A total of 28 patients with nail psoriasis was randomized into three treatment groups. Nine patients received etanercept 50 mg twice a week for the first 12 weeks and once weekly thereafter. Eight patients were treated with adalimumab, initially 80 mg, and 40 mg at week 1, then 40 mg every other week thereafter. Eleven patients received infliximab infusions (5 mg/kg) at weeks 0, 2, and 6, and every 8 weeks through weeks 46. Patients were evaluated for NAPSI and modified NAPSI at baseline, and then every twelve weeks, up to 48 weeks of treatment.

At the end of 48 weeks of treatment, NAPSI improvements were 53.8%, 57.3% and 40.4%, and modified NAPSI improvements were 48.6%, 59.6% and 40,4% in adalimumab, etanercept and infliximab treatment groups, respectively. Each treatment was found effective in comparison with baseline and there were no statistically significant differences between the three groups in terms of effectiveness.

The conclusion of the study was that adalimumab, etanercept and infliximab are effective in psoriatic patients with nail involvement. It is obvious that a letter to the editor about this small study with 28 patients cannot supply a reviewer with all the desired information concerning study design, blinding and other potential biases. The absence of a placebo group is a pity, but regarding the small number of patients is an understandable choice. Studies investigating one anti-TNF compound are almost never comparable with each other because of differences in patient selection, follow-up, severity of nail psoriasis or used scoring system. The great advantage of this study is that it compared three anti-TNF treatments in the same population using the same protocol of analysis. Therefore, it is reasonable to conclude from this study that there are no major differences in the efficacy of adalimumab, etanercept and infliximab in treating nail psoriasis.

USTEKINUMAB IN PSORIATIC NAIL DISEASE: RESULTS FROM PHOENIX

Rich P, Bourcier M, Sofen H, Fakharzadeh S, Wasfi Y, Wang Y, et al. Ustekinumab improves nail disease in patients with moderate-to-severe psoriasis: results from PHOENIX 1. The British Journal of Dermatology. 2014;170(2):398-407

Anti-TNF treatments were the first safe and powerful biologics with registration for the treatment of plaque psoriasis. Randomised trials with infliximab, etanercept, adalimumab, certolizumab pegol, and golimumab have shown that efficacy against nail psoriasis should probably also be considered a group characteristic of all anti-TNF compounds. Ustekinumab is another biologic available for the treatment of plaque psoriasis, but with a different mode of action. It is a monoclonal antibody against the p40 subunit shared by interleukin 12 and interleukin 23. The PHOENIX 1 is a phase 3, double-blind randomized, placebo-controlled trial that evaluated the efficacy and safety of ustekinumab in patients with moderate to severe

plaque psoriasis.[9] All patients were assessed at entry in the PHOENIX 1 study to determine whether nail psoriasis was present. This was the case in 545 out of 766 patients (71.1%). Those with nail involvement were included in an analysis of the efficacy of ustekinumab in the treatment of nail psoriasis. The PHOENIX study had a complicated study design, which included four distinct treatment periods: placebo-controlled (weeks 0-12), placebo crossover and active treatment (weeks 12-40), randomized withdrawal (weeks 40-76) and long-term extension for up to 5 years. Target NAPSI scores, number of affected fingers and PGA of a target finger (range 1 to 5) were assessed at baseline and at weeks 12 and 24 (before rerandomisation at week 40) for all patients with nail involvement and also at week 52 for initial responders. A decrease of at least 1 point on the PGA was considered improvement in nail psoriasis.
The mean target NAPSI score at baseline was 4.4, and PGA indicated mild, moderate, and (very) severe disease in approximately 50%, 40%, and 10% of patients, respectively. NAPSI scores were significantly improved from baseline as early as week 12 for both ustekinumab 45 mg (-26.7%; $P < 0.001$ vs. placebo) and 90 mg (-24.9%; $P = 0.001$ vs. placebo), compared with placebo (-11.8%). Percentage improvements in NAPSI score from baseline continued to improve through to week 24 in ustekinumab-treated patients on 45 mg (-46.5%) and 90 mg (-48.7%), but given the design of the study no data on placebo are available at this time point. Among patients receiving placebo who crossed over to receive ustekinumab at week 12, percentage improvements in NAPSI scores at week 24 were generally comparable with the week 12 results for patients initially randomized to receive ustekinumab. The highly significant improvement in NAPSI in the ustekinumab treated patients was not reflected in a change in PGA at week 12, but was at week 24. There was also a reduction in the number of fingers involved in the patients treated with ustekinumab, but most involved fingers retained one or more signs of nail psoriasis. Full clearing was only achieved in a small minority of patients. Overall, patients with greater skin responses also demonstrated better nail responses. For that reason, results beyond week 24 are not discussed here, because patients with a PASI < 50 response were withdrawn from the study, which introduces a major bias.

The conclusion is that the combination of results of the PGA with that of the target NAPSI shows that positive nail responses can be observed with ustekinumab treatment. However, data from the PGA show that it may take half a year before improvement can be noticed clinically. Direct comparison between anti-TNF and ustekinumab on nail disease is lacking. It appears that the choice between anti-TNF or ustekinumab in a given plaque psoriasis patient should not be based upon the presence of nail disease.

Reference

9. Leonardi CL, Kimball AB, Papp KA, Yeilding N, Guzzo C, Wang Y, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). Lancet. 2008;371(9625):1665-74.

SECUKINUMAB IN HAND, FOOT AND NAIL LESIONS IN MODERATE-TO-SEVERE PLAQUE PSORIASIS

Paul C, Reich K, Gottlieb AB, Mrowietz U, Philipp S, Nakayama J, et al. Secukinumab improves hand, foot and nail lesions in moderate-to-severe plaque psoriasis: subanalysis of a randomized, double-blind, placebo-controlled, regimen-finding phase 2 trial. Journal of the European Academy of Dermatology and Venereology : JEADV. 2014;28(12):1670-5

Secukinumab belongs to another new family of drugs for the treatment of psoriasis. It is a fully human monoclonal antibody that selectively binds and neutralizes interleukin 17A. Although the drug was originally intended to treat rheumatoid arthritis, phase II clinical trials for this condition yielded disappointing results. Similarly, while patients in a phase II clinical trial for psoriatic arthritis did show improvement over placebo, the improvement did not meet adequate endpoints. Several studies in moderate to severe plaque psoriasis showed more encouraging results, resulting in FDA and EMA approval for this indication. One post hoc analysis describing a randomised, double-blind, placebo-controlled trial of secukinumab in nail psoriasis has been published, based upon data from a phase II study on plaque psoriasis.[10] In the original study 404 subjects were randomized (1 h 2 mn 2 s : 1) to one of three subcutaneous secukinumab 150-mg induction regimens [Single (Week 0), Monthly (Weeks 0, 4, 8), Early (Weeks 0, 1, 2, 4)] or placebo. In the subgroup (n = 304) with fingernail psoriasis, efficacy was assessed as mean percentage change from baseline to week 12. Scoring was done using a composite fingernail score (range 0 to 20), based on the affected area of all ten fingernails.
At baseline the mean composite fingernail score was 8.9. At week 12, the composite fingernail score improved significantly with the early and monthly regimens, whereas it worsened with placebo (mean change from baseline: -19.1% and -10.6% vs. +14.4%). There were no substantial

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differences with the single regimen vs. placebo (-3.7%). No data on commonly used scoring systems like NAPSI, target NAPSI, PGA, or patient satisfaction were given. This is the major limitation of the study, making comparison of the results with other studies even more complicated than in other studies.

However, from these data it is likely that ustekinumab has some efficacy in nail psoriasis. It cannot be excluded that this efficacy is less than that of anti-TNF treatments, which would be in line with current opinion that nail psoriasis and psoriatic arthritis are anatomical and pathophysiological related. It is still hypothetical, but also results from studies with biologics suggest that efficacy of a drug against psoriatic arthritis could be predictive for efficacy against psoriatic nail disease.

Reference

10. Rich P, Sigurgeirsson B, Thaci D, Ortonne JP, Paul C, Schopf RE, et al. Secukinumab induction and maintenance therapy in moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled, phase II regimen-finding study. The British Journal of Dermatology. 2013;168(2):402-11.

Conclusion

A randomised controlled trial is the most convincing single study to prove efficacy of any treatment. The increasing number of RCTs focussing on nail psoriasis will eventually make it possible to define in evidence-based treatment regimens. In particular systemic treatments with anti-TNF, but also with anti IL17 and anti IL12/23, have shown attractive results. Nevertheless, these drugs are beyond reach for the majority of patients suffering from nail psoriasis without major skin or joint involvement. Fortunately, also RCTs with topical treatments have been published recently. These studies differ in quality, but show the path to follow. The study using a nail lacquer based on chitin extracted from crab carapace has major limitations, and the results from the study using clobetasol nail lacquer do not convince. Two of the presented studies compare two treatments: one study compared calcitriol ointment with betamethasone diproprionate ointment, and one study compared two different PDL pulse durations. Comparing two treatments is a useful approach if one of the treatments is an accepted or gold standard treatment.

However, treatments without sufficiently proven efficacy were used as the comparator in these two trials. The unfortunate consequence is that it remains unclear if the investigated treatments do have any real efficacy, because no differences in efficacy could be shown between the two compared treatments. Data from vehicle-controlled or placebo-controlled trials are more convincing. In this light the positive results with tacrolimus 0.1% ointment and with Lindioil are very interesting and deserve confirmation.

A major concern with regard to all these studies is the incomparability of the results. Not only do the inclusion criteria and concomitant use of other treatments differ between the studies. Likewise the used scoring systems differ between almost all the studies. Among the used clinical scoring systems were NAPSI, single hand NAPSI, eight finger NAPSI, modified NAPSI, target NAPSI, modified target NAPSI, nail matrix NAPSI, nail bed NAPSI, NAPSI variation 25, NAPSI 50, NAPSI 75, physician global assessment, subject global assessment, pachymeter data, and subungual hyperkeratosis. So, almost every study used a unique scoring system. In order to obtain data which are at least somewhat comparable, it is essential to have one scoring system for nail psoriasis, and this should include clinical features of nail bed and nail matrix, patient satisfaction data, and data concerning quality of life. Since the number of RCTs concerning nail psoriasis is increasing, it is urgent to work towards such a uniform scoring system. Please have a look at the website www.nailinitiative.org. The initiative has been taken, so please join if you are interested in this matter.

CAPSULE SUMMARY

- Treatment of nail psoriasis is challenging and has an insecure outcome. From an evidence based approach we only knew that infliximab, golimumab, superficial radiotherapy, grenz rays, and electronbeam caused significant nail improvement compared to a comparative treatment.
- Over the past couple of years several new randomised controlled trials on nail psoriasis have been published.
- Systemic treatments with anti-TNF, anti IL17, and anti IL12/23 have shown positive results.
- Topical treatments have also been the subject of RCTs: a nail lacquer based on chitin extracted from crab carapace, clobetasol nail lacquer, a comparison of calcitriol ointment with betamethasone diproprionate ointment, a comparison of two different PDL pulse durations, and two vehicle-controlled or placebo-controlled trials: tacrolimus 0.1% ointment and a changed formulation of a drug used in traditional Chinese medicine: Lindioil.
- In particular the trials with tacrolimus ointment and Lindioil showed promising results.

Bianca Maria PIRACCINI

INFECTIOUS DISEASES

The healthy nail is protected from microbial invasion: the nail plate surface is smooth and adherent to the nail bed; the cuticle seals the skin of the proximal nail fold to the nail plate, and nail growth permits elimination of exogenous material deposited above or below. Nail infections occur when the biological agent has a strong invading capacity (as in the case of non dermatophyte molds), or, more commonly, when the nail is predisposed to invasion since it is damaged in some way, or when there are systemic or genetic diseases or conditions that favor infection.

Nails infected by microorganisms are often contagious, and may cause diffusion of the infection to other nails or body sites (as, for example, in the case of onychomycosis by *T. rubrum*, where the fungus may spread to other nails, as well as to the skin of the palms, soles and groin) or to other persons, as can occur in viral infections (i. e. periungual warts). Nails affected by fungal infections may also spread microorganisms in the environment when drilled, with diffusion in the air of organic microparticles that can be inhaled.

PODIATRISTS WHO USE HIGH SPEED DRILLS DURING THEIR WORK HAVE A GREAT RANGE OF MICROBES IN THEIR NASAL CAVITIES

Tinley PD, Eddy K, Collier P. Contaminants in human nail dust: an occupational hazard in podiatry? J Foot Ankle Res. 2014;7(1):15

A nail with onychomycosis may act as a reservoir of fungi that may then colonize other skin sites, such as the soles and groins, or be diffused in the environment when walking barefoot,[1] but may also diffuse the fungi in the air when pulverized by drilling.

Podiatrists commonly use high-speed nail drills in their clinical practice, to reduce thickened toenails, to remove parts of nail plates affected by onychomycosis, and also to treat foot calluses and corns. Drilling produces particles of organic dust **(Fig 1)** that remains airborne for long periods and are largely respirable, with >80% of the particles within a 0.8-1,6 µm particle size range, and are thus capable of penetrating the lower lung. Nail dust may carry microbes that, when inhaled, colonize the nose and may induce chronic infections, particularly worrisome in the immunosuppressed. Toenail dust generated from the treatment of onychomycotic nails is rich in fungi species, including dermatophytes, non-dermatophytes and yeasts, but also in bacteria and endotoxin. For this reason, even if podiatrists should regularly utilize protective measures (disposable gloves, dust masks, eyeglasses), have a room mechanical ventilation system and use a variety of disinfectants for cleaning, the use of nail drills is considered an occupational hazard for developing respiratory diseases such as asthma, sinusitis, bronchitis, chest infections, and nasal irritation.

Reference

1. Yenişehirli G, Karat E, Bulut Y, Savcı U. Dermatophytes isolated from the mosques in Tokat, Turkey. Mycopathologia. 2012;174: 327-30.

Fig1 - *Removal of the nail plate affected by onychomycosis using a high speed nail drill. Note the numerous scales scattered on all surfaces: a similar amount of visible and invisible scales are carried in the air. © BM. Piraccini*

CAPSULE SUMMARY

- Onychomycosis treated by drilling may diffuse infected microparticles in the air that can be inhaled by podiatrists.

Bianca Maria PIRACCINI

The study by Tinley and Collier evaluated the presence of microbes in the nasal cavities of podiatrists, compared to those of controls not exposed to airborne human nail dust particles. Each participant self-administered a nasal swab that was utilized for culture and filled out a questionnaire about the frequency of exposure to nail dust in time and the protective measures utilized in their office. The results show that podiatrists had more types of microbes in their noses compared to the control group, and had more pathogenic species, including *Aspergillus fumigatus*. The questionnaire showed that several of the protective measures required in a podiatrist's office were not adequate in most cases.

EVEN NORMAL NAILS MAY CONSTITUTE A HAZARD!

Recent evidence shows that even apparently healthy nails may act as carriers for different pathogens, as different types of microbial agents may be harbored in normal nails. This finding, which has been shown possible for some bacteria, fungi and parasites, has various possible consequences, which are discussed in the following part of this review.

UNTRIMMED FINGERNAILS AND LACK OF HAND WASHING ARE ASSOCIATED WITH INTESTINAL PARASITIC INFECTIONS IN FOOD HANDLERS

Tefera T, Mebrie G. Prevalence and predictors of intestinal parasites among food handlers in Yebu Town, southwest Ethiopia. PLoS One. 2014 Oct 17;9(10):e110621. doi: 10.1371/journal.pone.0110621

Infection with intestinal parasite is one among the most significant factors affecting public health related issues globally. The infection may cause acute or chronic diarrhea and other intestinal problems and death is a possible outcome. It is estimated that about 1/3 of the global population is infected by intestinal parasites, especially in tropical and subtropical parts of the world. This problem is in fact particularly high in developing countries, due to low levels of education and the difficulty of adopting optimal hygienic practices during food handling. Most of the intestinal parasites of medical importance are transmitted by ingestion of food or water contaminated with the infective stages of the parasite. Increasing travel in poorly developed countries, and the frequent attitude to mix with the local population and adopt its eating style, has caused a rise of intestinal problems due to parasitic infection in Europe.[2]

The study by Tefera & Mebrie evaluated the prevalence of intestinal parasites and its relation to hygienic procedures among food handlers in a small town in Ethiopia, where food handlers are appointed without screening for hygiene related infections. One hundred and eighteen adults, male and female, were screened for intestinal parasitic infection by parasitological assessment of the feces and were asked to answer questions about personal habits and routine hygienic measures. The prevalence of intestinal parasitic infections in food handlers was 44.1%, with persons over 35 being more frequently infected and *Ascaris lumbricoides* was the predominant parasite. Individuals who did not wash their hands regularly before a meal were 7 times more likely to be infected than those who did. The practice of not washing the hands after using the toilet was also associated with parasitic infection. People with intestinal parasites frequently had untrimmed nails, and those with long nails were infected 14 times more frequently then those with trimmed nails. Although this study did not attempt to assess the parasite carriage of the fingernails, the presence of intestinal parasites under the nail plate free margin in food handlers with intestinal parasites and poor hygienic practices has already been shown.[3] This study adds the length of the fingernails as an additional risk factor for parasite carriage by food handlers.

References
2- Soonawala D, van Lieshout L, den Boer MA, et al. Post-travel screening of asymptomatic long-term travelers to the tropics for intestinal parasites using molecular diagnostics. Am J Trop Med Hyg. 2014; 90: 835-9.
3- Ifeadike CO, Ironkwe OC, Adogu PO, et al. Prevalence and pattern of bacteria and intestinal parasites among food handlers in the Federal Capital Territory of Nigeria. Niger Med J. 2012; 53: 166-71.

CAPSULE SUMMARY

- Long fingernails of food handlers with poor hygienic practices are a risk factor for parasite carriage and transmission of intestinal parasites.

THERE IS NO EVIDENCE TO DETERMINE WHETHER WEARING NAIL POLISH AFFECTS THE NUMBER OF BACTERIA IN THE SKIN POST SCRUB, AND MAY BE A RISK FACTOR FOR SURGICAL INFECTION

Arrowsmith VA, Taylor R. Removal of nail polish and finger rings to prevent surgical infection. Cochrane Database Syst Rev. 2014 Aug 4;8:CD003325. doi: 10.1002/14651858.CD003325.pub3. Review.

Surgical wound infection is quite common, and it occurs because of microbial contamination of the wound during surgery. The hands of hospital staff are the most common vehicles by which microorganisms are transmitted. The risk of wound infections after surgery is therefore greatly decreased by the intensive scrub procedure of the hands carried out by operating theatre staff (doctors, nurses, and assistants) prior to surgical procedure. Several studies over the years have dealt with the possibility that wearing artificial nails or nail polish may increase the number of bacteria in the hands after scrub and lead to an increased rate of surgical wound infections. Nail polish and artificial nails may reduce the efficacy of the scrub, because an increased number of bacteria are harbored in the microscopic imperfections on the surface of these nails. There is evidence that artificial fingernails, which are usually long and polished, harbor higher microbial populations than natural nails and that pathogen carriage after hand cleansing with antimicrobial soap or gel remains higher in health care workers wearing artificial nails, than in controls.[4] Thus, nurses working in surgery centers are strongly discouraged from wearing artificial nails.

This Cochrane Review by Arrowsmith & Taylor is the fifth update on this topic, which is to determine whether there is a relationship between the presence of nail polish on the hands of the surgical scrub team and the rate of postoperative wound infections. The Authors only looked at studies concerned with bacteria harbored in nails with nail polish and did not take artificial nails into consideration. No new trial was found, and the main results are similar to the previous reviews: there is insufficient evidence to determine whether wearing nail polish affects the number of bacteria on the skin post-scrub.
The only randomized controlled study on the topic, which dates back to 1994,[5] compared the number of bacteria isolated from the nails of the dominant hand after surgical hand scrubs in 3 groups: nurses with fresh nail polish (applied within 2 days); nurses with chipped nail polish (applied 4 days before); nurses with natural nails. Although chipped fingernail polish or fingernail polish worn longer than four days fostered increased numbers of bacteria, the results were not statistically significant. There were no significant correlations between fingernail length and the number of bacterial colonies found after scrub.
However, the lack of scientific evidence does not imply that the surgical team should wear fingernails short and without nail polish as a hygienic measure.

References
4- McNeil SA, Foster CL, Hedderwick SA, Kauffman CA. Effect of hand cleansing with antimicrobial soap or alcohol-based gel on microbial colonization of artificial fingernails worn by health care workers. Clin Infect Dis. 2001; 32: 367-72.
5- Wynd CA, Samstag DE, Lapp AM. Bacterial carriage on the fingernails of OR nurses. AORN J. 1994; 60: 796, 799-805.

CAPSULE SUMMARY

- There is no evidence that wearing nail polish increases the number of bacteria on the hands after scrub and leads to an increased rate of surgical wound infections.

Bianca Maria PIRACCINI

NORMAL APPEARING NAILS MAY HARBOUR FUNGI: CAN THEY BE CONSIDERED AS A PRECLINICAL ONYCHOMYCOSIS?

Shemer A, Gupta AK, Farhi R, Daigle D, Amichai B. When is onychomycosis onychomycosis? A cross-sectional study of fungi in normal-appearing nails. Br J Dermatol. 2015;172(2):380-3

The Authors performed mycology from healthy looking nails and from the plantar skin of 585 healthy adults. The criteria included were absence of onychodystrophy and healthy foot skin, without scaling or erythema of the plantar skin and interdigital spaces. Subungual scrapings from the distal edge of the great toenail were processed by 20% KOH and cultured in Sabouraud's dextrose agar with cycloheximide. Mycology was also performed on skin samples collected from the edge of the heel. A positive KOH, revealing septate branching hyphae was found in 9.2% of the nail samples and in 7% of the plantar skin samples. Cultures were positive in a smaller percentage of persons and both techniques revealed the presence of fungi in 3,1 and 1.4% of the nail and skin samples, respectively. *Trichophyton rubrum* was the predominant infecting organism in both toenail and foot infections. Other anthropophylic dermatophytes, less commonly isolated, included *T. mentagrophytes* and *E. floccosum* (only found on the soles). *Scopulariopsis brevicaulis* was found in 2 toenails, but not in the skin. There was a significant association between the presence of fungal organisms in normal-appearing toenails and on the soles of the feet.

The possibility that fungi may reside in the skin or under the nail, without giving clinical signs, has also been proven by other studies. The first was carried out by Baran and Badillet in 1983.[6] Sakka et al.[7] recently showed that 14% of adults carry dermatophytes in apparently healthy soles (they called it "occult" tinea pedis): the carrier status is more common in males with a mean age of 43 years and anthropophylic dermatophytes (*T. rubrum, E. floccosum* and *T. mentagrophytes*) are the isolated agents. Foot odor and personal or family history for dermatophyte infections were significantly more common in the dermatophyte carriers compared to controls, as was the presence of clinically evident onychomycosis. Walling[8] looked for the presence of dermatophytes in apparently healthy nails in subjects with and without tinea pedis, using periodic acid–Schiff (PAS) staining of the great toenail clippings, and found that subjects with tinea pedis were harboring fungi significantly more frequently, probably dermatophytes, in normal looking nails than in controls. In fact fungal organisms were detected in 17% of clinically normal toenails of subjects with tinea pedis.

The presence of fungi in normal appearing nails and/or on the plantar skin possibly represents a subclinical infection where fungi are not active, probably due to the host reaction to the invasion. In time, these cases are likely to evolve into clinically evident onychomycosis and/or tinea pedis, when predisposing factors, including changes in the host's reaction to fungi, age and local factors will facilitate fungal growth and diffusion.

The issue is: should we change our clinical practice after this evidence?

In particular, should fungal presence be looked for in the plantar skin and in the nail of every person, in order to eradicate fungi early, when the infection is not clinically evident? This would avoid spreading fungi in the environment and the diffusion of the infection to other people or body sites. An alternative could be to look for fungi in healthy nails, only in persons with clinically evident tinea pedis, and prescribe antifungal nail lacquers in case of evidence of fungal presence in the nail plate, in order to block nail invasion from the beginning.

Follow-up studies are required to ascertain the percentage of carriers who will develop a true onychomycosis, in order to provide additional data to correctly modify our current approach.

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CAPSULE SUMMARY

- Clinically normal nails may carry a dermatophyte: a preclinical onychomycosis?

POSITIVE KOH AT THE END OF CLINICAL TRIALS: IS IT A SIGN OF TREATMENT FAILURE?

Ghannoum M, Isham N, Catalano V. A second look at efficacy criteria for onychomycosis: clinical and mycological cure. Br J Dermatol. 2014;170(1):182-7. doi: 10.1111/bjd.12594. Review.

Most of the randomized, double blind placebo-controlled trials performed to assess drug efficacy in the treatment of onychomycosis, the mycological cure (primary endpoint), was defined as a negative direct KOH (Potassium hydroxide) examination and a negative dermatophyte culture. However, at the end of the trial a high percentage of clinically cured patients often had a positive KOH examination associated with a negative culture. This finding, which is considered as a sign of treatment failure, may indeed not be a true indicator of persistence of the infection.

Ghannoum and co-workers reviewed the mycology data from seven international onychomycosis trials of topical antifungals, for which their Center for Medical Mycology served as the central mycology laboratory. All these trials had a 48 week period of treatment, and a further follow-up visit at week 52. The seven studies included a total of 3054 samples collected at the end of the trials: among the 2414 specimens that were culture negative, 1879 specimens (77,8%) showed fungal hyphae at KOH examination and, were finally considered as mycologically positive. The specimens taken at week 52 showed a similar distribution. Without knowing which specimen had been treated with a drug and which with placebo, the Authors looked at the hyphae morphology and found that 60% of the specimens diagnosed as positive for fungal infection contained damaged and most likely non-viable fungi.

This finding supports the hypothesis that, in these specimens, fungal filaments are non-viable though still visible, as the KOH preparation does not differentiate between viable and non-viable cells **(Fig 2)**. The hypothesis that negative cultures associated with positive KOH could be caused by retention of drug in the subungual debris, with inhibition of the growth of fungi in culture is therefore not valid, as it is most likely that the drug is effective in killing fungi, but does not mechanically destroy them.

The final suggestion of the Authors is to verify drug efficacy in onychomycosis trials by performing a mycological evaluation 3-6 months after the end of treatment, in order to allow enough time for nail growth to eliminate the residual subungual debris harboring dead fungi. At that time, a positive KOH would not be attributable to non-viable fungi, but rather to persistence of the infection and would likely be associated with a positive culture.

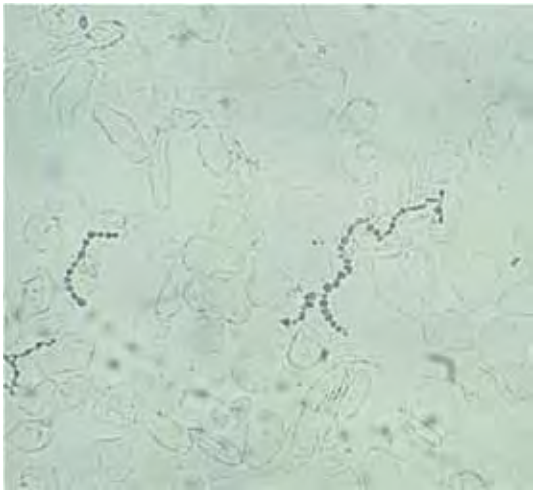

Fig2 - *KOH preparation of subungual debris of a nail with onychomycosis showing keratinized cells and fungal hyphae. Hyphae appear as septate branching filaments; there are no clues to determine if they are viable or not. © BM. Piraccini*

Evaluation of cure 3 to 6 months after the end of therapy would also enable a better clinical evaluation of cure, as the nail would have had more time to grow back to normal, without the residual distal dystrophies that are often reported at the end of trials.[9]

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CAPSULE SUMMARY

Clinically cured nails after an antifungal treatment may show hyphae at direct microscopic examination, but have negative culture: are these fungi dead or alive?

Bianca Maria PIRACCINI

CAN BETA-PAPILLOMAVIRUS HAVE A ROLE IN CHRONIC ONYCHOLYSIS?

Umanoff N, Werner B, Rady PL, Tyring S, Carlson JA. Persistent Toenail Onycholysis Associated With Beta-Papillomavirus Infection of the Nail Bed. Am J Dermatopathol. 2014 Jul 3. [Epub ahead of print]

This single case report is about a persistent onycholysis of the great toenail that was biopsied and found to be infected by beta-papillomavirus (Beta-PV) by PCR. The patient was a healthy 27-year-old female who had chronic traumas from shoes that could have caused the long-lasting onycholysis, which was negative at mycology. A nail bed biopsy showed psoriasiform hyperplasia of the epithelium with marked hyperkeratosis, hypergranulosis, and acanthosis and a fibrotic dermis. The spinous layer showed scattered koilocytes, a finding that lead to immunohistochemical studies and PCR, which identified 6 Beta- PV genotypes, including some oncogenic types: HPV 5, HPV 8, HPV 20, HPV 37, HPV 23 and one novel HPV genotype FA25.
The authors postulated that this Beta-PV infection could have been introduced by recent trauma or represent an activation of commensal infection, as these viruses are thought to be possible commensals on our skin.[10] Beta-PV infection could have induced persistent onycholysis, as these viruses induce a disruption of epithelial cells terminal differentiation and hyperkeratosis which, in the nail bed, result in acanthosis and appearance of a granular layer.
Is the patient reported in this article an isolated case, or would we find Beta-PV if we took a nail bed biopsy in chronic onycholysis **(Fig 3)**? Perhaps a pilot study, looking for Beta-PV infection in a small series of patients with chronic onycholysis should be carried out, to verify the presence of these viruses.

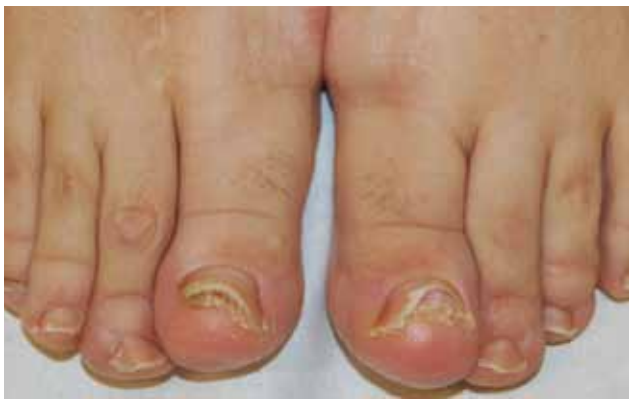

Fig3 - *Persistent onycholysis of the great toes. Mycology is negative and the digits are continuously exposed to trauma by shoes. © BM. Piraccini*

Reference
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CAPSULE SUMMARY
- Beta-papillomavirus (Beta-PV) in nails with chronic onycholysis: coincidence or causality?

NEW AND OLD DIAGNOSTIC TECHNIQUES FOR INFECTIVE NAIL DISORDERS

The diagnosis of infective nail disorders is a step-by step path, starting from the clinical examination, moving onto onychoscopy, which enhances visualization of nail signs, and then onto specific tests that are chosen on the base of the suspected infection. New methods of investigation, more or less specific for nail infections, are introduced every year, with pro and contra that make them better or not than the current standard tests.
An ideal diagnostic method should be easy to perform, give results in a short time, be performable by every doctor, without the need of proper skills or training, and have a low cost. Sensitivity and specificity should also be high, in order to avoid false positive and false negative results.

REFLECTANCE CONFOCAL MICROSCOPY FOR DIAGNOSIS OF ONYCHOMYCOSIS

Pharaon M, Gari-Toussaint M, Khemis A, Zorzi K, Petit L, Martel P, Baran R, Ortonne JP, Passeron T, Lacour JP, Bahadoran P. Diagnosis and treatment monitoring of toenail onychomycosis by reflectance confocal microscopy: prospective cohort study in 58 patients. J Am Acad Dermatol. 2014;71(1):56-61

Two non-invasive techniques have been applied to the nails in the last years: reflectance confocal microscopy (RCM, confocal laser scanning microscopy, CLSM) and optical coherence tomography (OCT). In nails affected by onychomycosis **(Fig 4a)**, RCM shows white lengthy or thread-like structures with high reflection and typical shape, or spore-like bright aggregates. Images of nails invaded by fungi at OCT show a loss of the differentiation of the different scattering parallel layers of the nail plate and, both inside the thickened nail plate and below it, signal intense structures surrounded by low scattering areas **(Fig 4b)**. Pharaon and colleagues evaluated sensitivity and specificity of reflectance confocal microscopy (RCM) for the diagnosis of onychomycosis, compared to direct microscopy in KOH and fungal culture. They also evaluated the ability of RCM to assess treatment outcome. Patients with suspected distal subungual onychomycosis involving 10-75% of the great toenail were examined by RCM and then underwent nail sampling for KOH and cultures. The RCM diagnosis of onychomycosis was based on the presence, on at least three consecutive images, of bright filamentous branching structures corresponding to septate hyphae. Patients who proved positive for onychomycosis underwent the same testing procedures after 24 weeks of therapy with terbinafine 250 mg/day. RCM had a sensitivity of 52.9% and a specificity of 90.2%, as it showed hyphae in 9 of the 17 patients with onychomycosis proven by KOH and cultures and gave false positive results in 4 of the 41 negative patients. At the end of treatment, RCM showed a normal nail plate in all the cured patients.

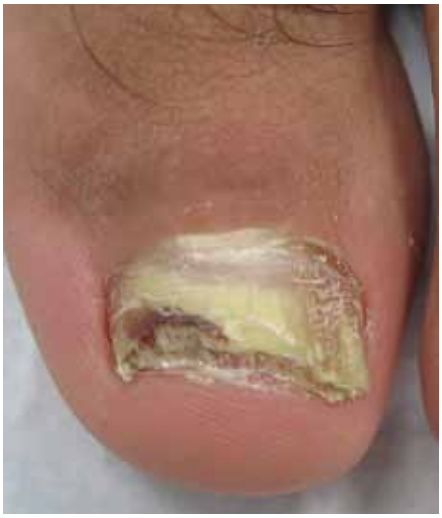

Fig4a - *Distal subungual onychomycosis. © Dr Mandel*

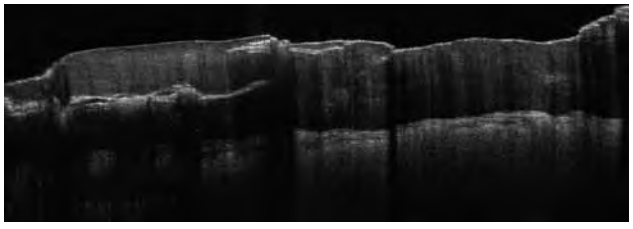

Fig4b - *Optical coherence tomography (OCT) shows lengthy structures with high reflection below the nail plate. © Dr Mandel*

RCM sensitivity and specificity found in this paper are different from those reported by Rothmund and colleagues[11] that found a sensitivity and a specificity of RCM of 79.5% of 81%, respectively. The Rothmund study compared different diagnostic methods for onychomycosis and showed that polymerase chain reaction (PCR) offered the best sensitivity (94.9%), followed by Optical Coherence Tomography (OCT) (92.3%), RCM (79.5%), KOH examination (74.4%), histopathology (with PAS staining) (69.2%) and culture (20.5%). PCR, culture and histopathology had the highest specificity. The comparison of the costs of the techniques, which took several factors into account, including waiting time for final results, costs of the device and the materials utilized, need of trained personnel, etc., showed that only KOH and cultures are considered low cost techniques, while the others are expensive, with OCT and RCM requiring high expenses for the device and needing experienced examiners.

The conclusion is that although these new techniques are intriguing and give rapid results, the sensitivity and specificity are too low to replace other diagnostic methods. This, together with the high cost, precludes their use as solitary screening tools, and suggests their utilization only for study purposes.

Referrence

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CAPSULE SUMMARY

Diagnosis of onychomycosis: reflectance confocal microscopy (RCM) and optical coherence tomography (OCT) cannot replace conventional mycology (KOH and cultures).

Bianca Maria PIRACCINI

CYTOLOGY (TZANCK SMEAR): A FORGOTTEN SIMPLE TEST MAY HELP DIAGNOSIS IN ACUTE PARONYCHIA RESISTANT TO SYSTEMIC ANTIBIOTICS

Durdu M, Ruocco V. Clinical and cytologic features of antibiotic-resistant acute paronychia. J Am Acad Dermatol. 2014;70(1): 120-6.e1

This article recommends the use of this forgotten technique to evaluate systemic antibiotic-resistant acute paronychia, before any further use of antibiotics and before performing a surgical drainage procedure.

The results of cytology (Tzanck smear) in a series of patients with acute paronychia that was resistant to systemic antibiotics were analyzed retrospectively. Exclusion criteria were paronychia due to ingrowing nail, chronic paronychia with nail dystrophy and untreated acute paronychia. Tzanck smear was performed by scraping the affected periungual area after a superficial incision and spreading the obtained tissue pieces on a microscopic slide that was left to dry and then stained with May-Grunwald-Giemsa. Additional staining was done in the case of presence of cocci and bacilli (Gram stain) and direct immonufluorescence was performed if the slide only showed acantholytic cells. Tzanck smear showed diagnostic findings in 54 (93%) of the 58 patients examined: the most common cause of antibiotic-resistant paronychia was bacterial infection **(Fig 5)** (cocci or bacilli), most commonly *Staphylococcus aureus*, followed by viral infections **(Fig 6)** (herpes simplex in children and Orf in adults). Fungi were found in the fingernails of thumb-sucking children (*Candida*) and in the great toenail of an adult with chronic tinea pedis (dermatophytes).

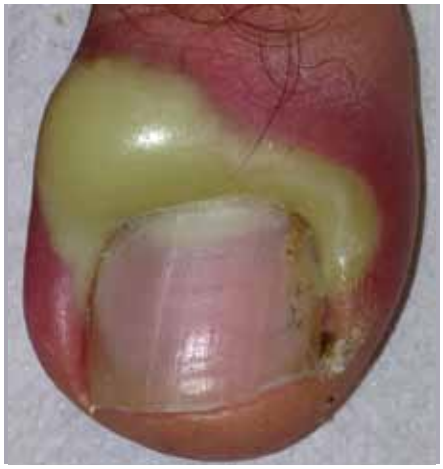

Fig5 - *Acute purulent paronychia of the right great toenail after 2 weeks of systemic antibiotics. Drainage and cultures revealed methicillin-resistant Staphylococcus aureus. © BM. Piraccini*

Cytology also permitted to diagnose three cases of acute paronychia, due to pemphigus vulgaris, in 3 patients who had other oral and cutaneous lesions of the disease.

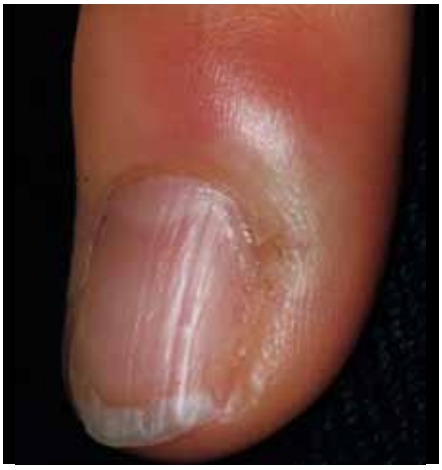

Fig6 - *Acute purulent paronychia of the 2nd right fingernail after 2 weeks of systemic antibiotics. Tzanck smear revealed multinucleated giant cells allowing the diagnosis of herpes simplex infection. © BM. Piraccini*

CAPSULE SUMMARY

- An old technique to improve the diagnosis of paronychia resistant to systemic antibiotics: Tzanck smear.

These results are very interesting and should lead to an increased use of Tzanck smear in the evaluation of inflamed nails. Although the technique requires time and trained personnel, as examining a cytological specimen at the microscope can be done only with some experience, it is performed quickly and has a low cost.

CICLOPIROX IN ONYCHOMYCOSIS

Proofs of efficacy and tolerability of ciclopirox nail lacquer in the treatment of onychomycosis is annually increasing with evidences that confirm the topical drug as firstline therapy in mild to moderate distal subungual onychomycosis involving 1-3 nails.[12]

Permeation data suggested that there was systemic absorption of ciclopirox olamine from the studied formulations, proving the optimal tolerability of the drug.[13]

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Bertrand RICHERT

LONGITUDINAL MELANONYCHIA and MELANOMA

Longitudinal melanonychia (LM) remains a challenge for dermatologists and even for nail doctors. Indeed, the prognosis of melanoma at the nail apparatus is poor, mainly due to its late diagnosis.[1] The reason for the delay is twofold: first the patient does not suspect the possibility of cancer at that site and second, the overall accuracy of dermatologists, even nail experts, in the diagnosis of nail melanoma is still poor.[2] Up to now, early diagnosis and excision of the tumor is the only treatment known to increase survival.[1] There are no evidence-based studies determining precise criteria that can be used to decide if an LM should be biopsied or not.[3]

Nail apparatus melanoma is rare and accounts for 0.7 to 3% in Caucasians,[3] but in Japan this rate climbs to 20%. This may be the reason why Japanese researchers are looking for acute techniques that may diagnose early melanoma *in situ*.

A CLASSIFICATION OF LONGITUDINAL MELANONYCHIA?

Sawada M, Yokota K, Matsumoto T, Shibata S, Yasue S, Sakakibara A, Kono M, Akiyama M. Proposed classification of longitudinal melanonychia based on clinical and dermoscopic criteria. Int J Dermatol. 2014;53(5):581-5.

In this study, the authors examined 137 longitudinal melanonychias and classified them according to naked eye features and dermatoscopic criteria. They evaluated both the nail plate and the periungual skin.

Type I corresponded to a brown or grayish background with thin regular gray lines in the plate. No periungual pigmentation was noted. In **Type II**, the background was still brown or grayish, but the lines were darker and still regular. A pseudo-Hutchinson sign might be observed. In **Type III**, the background was brown or grayish with darker, irregular lines.

The Authors decided to observe LM Type I (72 lesions) every six months with a dermatoscope. Lesions classified as Type III (13), were totally excised (nail apparatus ablation). For the Type II lesions (52), a strict dermatoscopic follow-up every 3 months was performed and, in cases in which the pigmented band enlarged or changed (5 cases), the lesions were surgically removed completely.

All lesions classified Type III were histologically confirmed as melanoma *in situ*. LM Type II that changed with time and that were removed were proven to be lentigo or benign melanocyte hyperplasia. No biopsy was performed for Type I or stable Type II LM. After a follow-up of a median 5.5 years, no lesion showed any modification. They were thus retrospectively considered as benign.

It is pleasing to see that nowadays the management of LM is much better unified. The recommendation of the authors, according to the clinical aspect of the LM in a Table, is very clear for the novice. The LM should indeed be evaluated with the naked eye, as well as with the dermatoscope and the color of the background should be determined together with the regularity and parallelism of the pigmented lines. The International Study Group on Melanonychia recently published a paper stressing that the most important point is the homogeneity of color and width of each individual longitudinal line.[4]

Nevertheless, there is nothing new in this study! It is simply a summary of what has been done in many nail centers and published in textbooks. Their classification is only a renaming of the initial proposal from Ronger et al.[5] and Braun et al.[6] The authors do not give a proper definition of the pseudo-Hutchinson sign, which is not a pigmentation of the surrounding skin, but means that the most proximal part of the pigmented band is visible through the cuticle, and this is very clear on their clinical pictures.

Even if the dermatologist may find it very convenient to have a table to guide him/her when dealing with a LM, the frame remains too restrictive. The approach should be somewhat more holistic and less rigid. The International Study Group on Melanonychia has also specified that any decision to excise a pigmented band should be based on established clinical criteria (history and physical exam) and not on nail plate dermoscopy patterns only. New techniques have even been developed to increase the sensibility and sensitivity of the diagnosis:

- *intraoperative nail matrix dermatoscopy* using immersion with a sterile gel has been shown to increase the diagnosis, as it directly examines the pigment in the matrix without interposition of the nail plate,[7]
- *intraoperative reflection confocal microscopy* examination of the nail matrix has enabled one-step surgical management of *in situ* melanoma: diagnosis and surgical removal.[8]

Bertrand RICHERT

DOTS AND GLOBULES: A SUSPICIOUS SIGN IN LONGITUDINAL MELANONYCHIA

Inoue Y, Menzies SW, Fukushima S, Nishi-Kogushi H, Miyashita A, Masukuchi S, Muchemwa F, Kageshita T, Ihn H. Dots/globules on dermoscopy in nail-apparatus melanoma. Int J Dermatol. 2014;53(1):88-92

This (once again) Japanese paper originates from a clinical case. A 35-year-old man presented with a 9 mm wide LM which had been evolving for about 5 years. The nail plate was not dystrophic. Dermatoscopy showed a black brown background, irregular lines, no Hutchinson sign and dots/globules. The appearance was highly suggestive of melanoma and the whole nail apparatus was excised en bloc. The diagnosis was a 1,1 mm thick melanoma. On histological examination, some atypical melanocytes rich in melanin were found clumped together within the nail plate. They corresponded to the dots/globules seen on dermatoscopy. These dermatoscopic features are not described in the initial publication of Ronger[5] or Tosti.[9] This prompted the Authors to review all the melanomas they had observed over the last seven years. They collected 242 melanomas with 20% of them involving the fingers or the toenails. This high percentage is similar to the rate of nail apparatus melanoma in other Japanese publications. As in other studies, the first digit (thumb or great toenail) was affected in 67 % of cases and the median age was 65. The Authors collected retrospectively the following dermatoscopic features from all the nail melanomas without plate destruction (31 patients): blood spots, grayish background, brownish background, regular lines, irregular lines, Hutchinson's sign, grooves and dots/globules. The brownish background and irregular lines were the most common features, followed by the micro Hutchinson's sign. They found dots and globules in 25% of the cases (8 patients). They did not find any significant difference between invasive and *in situ* melanomas. Dots and globules were indifferently present in invasive or *in situ* melanomas. Another Japanese dermatologist reported that dots/globules are often seen in LM in children, but rarely in adults. The authors conclude that dots/globules should increase the suspicion of melanoma in adults.

We were personally very interested in this publication, as we had a case of nail melanoma *in situ* with an unusual dermatoscopy: a grayish background, no well individualized longitudinal lines, a tiny groove running along the whole length of the LM and dots and globules on the lateral side **(Fig 1a, 1b)**. Nail avulsion for matrix biopsy revealed an irregular pigmentation pattern on the matrix highly suggestive of melanoma **(Fig 1c)**. Indeed, dots and globules

Fig1a - *Longitudinal melanonychia on the second toe of a 52 year-old lady. © B. Richert*

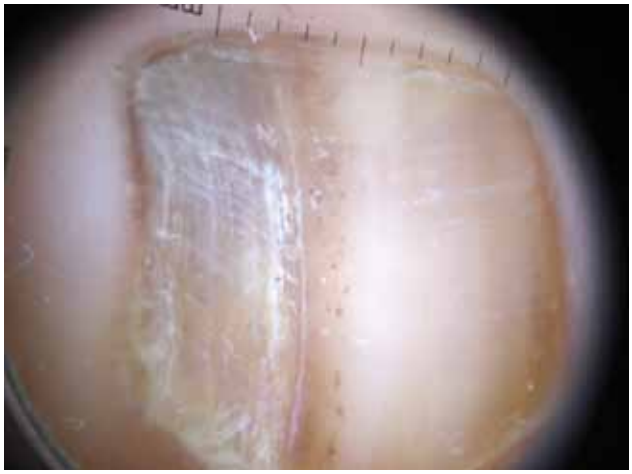

Fig1b - *Dermatoscopy shows no longitudinal lines but a diffuse brown grayish discoloration. Note the superficial dystrophy and the globules and dots on the lateral part of the band. © B. Richert*

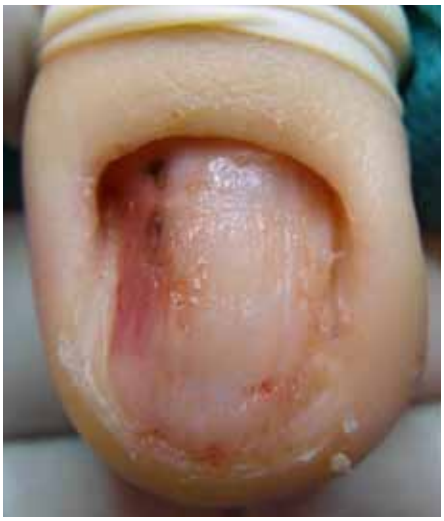

Fig1c - *Avulsion demonstrates that the irregular pigmentation spreads from the matrix into the nailbed. © B. Richert*

were not reported as a suspicious sign of nail melanoma in adults in the Ronger criteria. Hirata et al. established and validated 4 patterns for matrix intraoperative dermatoscopy. Dots and globules were observed in both nevus and melanoma.[7] This demonstrates once again that all information that might be collected during clinical examination with the naked eye, the dermatoscope and even an intraoperative dermatoscopy (and even confocal dermatoscopy) are useful to diagnose the cause of a LM. And even with these, in many cases the help of histopathology is required, as it holds the final diagnosis.

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Yamamoto S, Harada K, Ando N, Kawamura T, Shibagaki N, Tanaka M, Shimada S. Nodular melanoma on the hyponychium: clinical and dermoscopic features. J Dermatol. 2014;41(3):277-8

This letter to the Editor, reports the case of a nodular melanoma of the distal nail bed **(Fig 2)**. An important feature was noted in dermatoscopy: there was a thick negative pigment network with irregular blue brown dots/globules. The latter were entirely distributed on the surface of the lesion and dense globules were observed at the periphery. The central area showed a structureless white area with blue-gray dots. Histology revealed a 6 mm thick melanoma. The dot and globules corresponded to melanophages in the papillary dermis, sheet-like proliferation of atypical melanocytes and dermal fibrosis. The authors stress that only 3 cases of nodular nail bed melanoma had been reported in the Japanese literature. In these cases, the dermatoscopic findings were totally different and included a blue-white veil, atypical vascular pattern and a homogenous blue pigmentation.

This publication emphasizes that irregular dots and globules observed in a pigmented lesion of the nail, either a longitudinal melanonychia or a nodule, should seriously raise the suspicion for melanoma. As stated previously, dots and globules were not reported as a suspicious sign of nail melanoma in adults in the original publications on dermatoscopy of longitudinal melanonychia. Although rare, they should definitely be added to the list of suspicious criteria along with irregular and interrupted pigmented lines. Hopefully, we are getting used to recognizing globules and dots in skin melanoma.

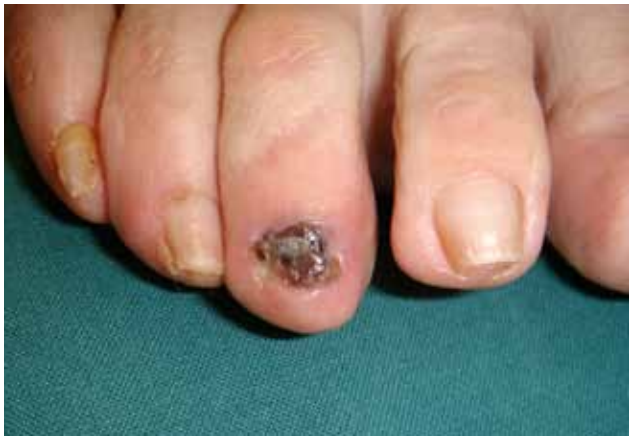

Fig2 - *Nodular melanoma of the nail bed. Dermatoscopy was not performed but it would maybe have shown irregular dots and globules. © B. Richert*

Bertrand RICHERT

A COMPUTER PROGRAMME TO EVALUATE LONGITUDINAL MELANONYCHIA

Koga H, Yoshikawa S, Sekiguchi A, Fujii J, Saida T, Sota T. Automated evaluation system of dermoscopic images of longitudinal melanonychia: proposition of a discrimination index for detecting early nail apparatus melanoma. J Dermatol. 2014;41(10):867-71

The aim of this study was to develop an automated dermoscopic screening system for LM, allowing discrimination between benign origin and melanoma. It took me quite some time to understand the method, as this article comes from the Department of Electrical Engineering... To summarize: they studied 31 LM and took digital pictures of each of the LM. For each digital dermatoscopic image, the pixels belonging to the nail plate were retained and the ones from the nail folds and hyponychium were excluded. The areas of Hutchinson's sign were excluded from the study. They analyzed the RGB information of each pixel, paying particular attention to color variation. What is RGB? It is not specified anywhere in the article, but I finally discovered that this simply stands for Red, Green and Blue. They used some very complicated calculations, which, after a discussion (very nebulous to me) allowed them to conclude that in melanoma *in situ*, there are some portions of the dermatoscopic images where the red dominates over the green and blue and this suggests either a decrease in the eumelanin/pheomelanin ratio in the nail apparatus melanoma cells (as in the uveal melanoma) or the rich vasculature in melanoma tissues. These RGB color variegations were already reported in an automated screening system for melanoma of non-glabrous skin. They may reflect changes in the pigment at a molecular level.
This fact may be very interesting, but even if the authors develop an original computer program that can easily be used by clinicians, there are some gaps. The sample size of the study was small. They worked in an incomplete manner: they clinically decided that 6 LM were melanomas and excised them surgically. The diagnosis was pathologically proven. The 25 remaining bands were not biopsied and were considered as benign, as they did not turn out to be melanomas in the five year follow-up (!). This means that they worked on only 6 histologically proven LM. Their methodology ruined their work. They should have taken pictures of all LM and performed either an excision, if the lesion was suspicious, or a tangential biopsy of lesions that appeared to be benign. Unfortunately, even if the idea is extremely seducing, it remains statistically inconclusive.

A META ANALYSIS OF TREATMENT FOR NAIL MELANOMA

Cochran AM, Buchanan PJ, Bueno RA Jr, Neumeister MW. Subungual melanoma: a review of current treatment. Plast Reconstr Surg. 2014;134(2):259-73

If you have time to read just one review article on nail apparatus melanoma (NAM), - this is the one. The Authors, plastic surgeons, conducted a complete review of all cases in the literature involving amputation and/or wide local excision for the treatment of NAM. This huge work spreads over 13 pages, with tables containing all the data from published cases. They go back to the very beginning in 1886 (Hutchinson) when aggressive treatment guided the management of NAM until the 2000s. They demonstrate that studies in the literature involving amputation for the treatment of NAM could not prove a significant benefit of prognosis and/or survival rate over the more conservative excision treatment. The level of evidence of the vast majority of articles on the treatment of NAM is relatively poor. However, they are able to conclude that collective data suggest that NAM *in situ* can likely be treated adequately with wide local excision. For invasive melanoma, a balance between tumor thickness and conservation of function should guide the level of amputation. However, there is definitely a lack of randomized prospective studies.

CAPSULE SUMMARY:

- Longitudinal melanonychia should be evaluated with both the naked eye and the dermatoscope. Any decision to excise it should be based on established clinical criteria (history and physical exam) and not only on nail plate dermoscopy patterns. The most important point is the homogeneity of color and width of each individual longitudinal line.

FUNCTIONAL SURGERY FOR NAIL MELANOMA *IN SITU*

Neczyporenko F, André J, Torosian K, Theunis A, Richert B. Management of in situ melanoma of the nail apparatus with functional surgery: report of 11 cases and review of the literature. J Eur Acad Dermatol Venereol. 2014;28(5):550-7

It is delicate to comment on an article that you have written yourself. It was published just after the article from Cochran, so it could not be included in their references, which is the reason why I wanted to add it here. In this retrospective study, we collected all data from all nail apparatus melanoma *in situ* (NAMIS) that had presented to our department over the last 13 years and that were treated with conservative treatment (ablation of the nail unit en bloc plus 6 mm safety margins) **(Fig 3a, b)**.

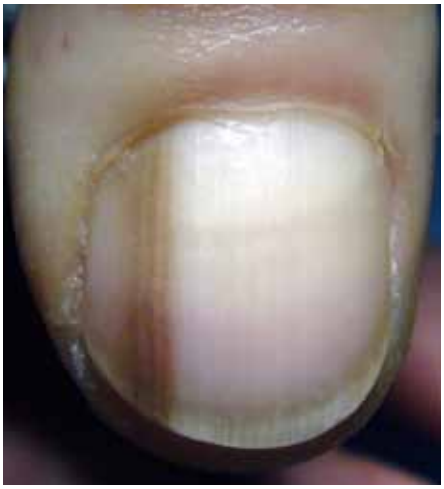

Fig3a - *Longitudinal melanonychia in a 43 year-old man. 3 mm wide. Dermatoscopy showed 2 severely interrupted lines and 3 globules (visible with the naked eye). The lesion was punched out in the matrix and showed an in situ melanoma. © B. Richert*

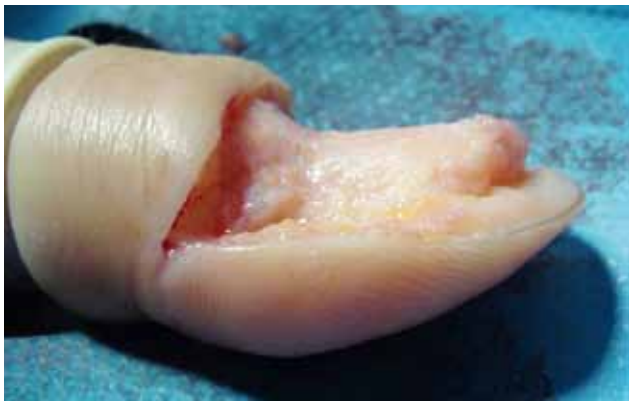

Fig3b - *Functional surgery was performed with 6 mm margins all around the boundaries of the nail apparatus, ending in what is called "skeletization". The defect was covered with a full thickness graft. © B. Richert*

We found 11 patients (the largest series up to now) with a median follow-up duration of 65 months. This study confirms that functional surgery is a rational approach for the management on NAMIS, with a 100% survival rate. One thing to remember is that a lifetime follow-up is mandatory, as recurrences may occur much later (7 and 11 years in our series) as well as a new melanoma in another location (1 case).

CAPSULE SUMMARY:

- Collective data from the literature suggest that nail unit melanoma *in situ* can likely be treated adequately with wide local excision. However, a lifetime follow-up is mandatory as recurrences may occur after a long period.

LYMPH NODE BIOPSY: WHEN?

Ito T, Wada M, Nagae K, Nakano-Nakamura M, Nakahara T, Hagihara A, Furue M, Uchi H. Acral lentiginous melanoma: who benefits from sentinel lymph node biopsy? J Am Acad Dermatol. 2015;72(1):71-7.

We also selected this article on the indications of sentinel lymph node biopsy (SLN) in acral lentiginous melanomas (ALM). This is a large series of 116 patients, all Japanese, but no nail melanoma was selected or they may have been included in "hand" or "foot" melanomas. However, this is interesting, as we know that melanomas of the nail unit are mainly ALM and that this type of melanoma has a different genetic background, especially infrequent BRAF mutations and frequent KIT mutations, suggesting a possible different biological behavior from non-ALM.[10] This study confirms the 2009 AJCC (American Joint Committee on Cancer) recommendations that SLN biopsy should be confined to patients with thick melanomas (>1 mm) or ulcerated ALM.[11]

References

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11. Balch CM, Gershenwald JE, Soong S-J, Thompson JF, Atkins MB, Byrd DR, et al. Final version of 2009 AJCC melanoma staging and classification. J. Clin. Oncol. 2009;27(36):6199-206.

CAPSULE SUMMARY

- Sentinel lymph node biopsy should be confined to patients with thick lesions (>1 mm) or ulcerated acral lentiginous melanomas.

Bertrand RICHERT

NAIL MELANOMA IN CHILDREN

Bonamonte D, Arpaia N, Cimmino A, Vestita M. In situ melanoma of the nail unit presenting as a rapid growing longitudinal melanonychia in a 9-year-old white boy. Dermatol Surg. 2014;40(10):1154-7

This case that appeared as a letter to the editor, has generated considerable discussion by nail experts from the nail societies. For those dealing with bands in children almost daily, the clinical image and the histological pictures are in favour of a pigmented nævus. LM in children may clinically appear terrible and the diagnosis of melanoma would be immediate in an adult **(Fig 4)**. This is a fact that was acknowledged some years ago by the International Study Group on Melanonychia: in children brown bands with lines irregular in color, width and spacing are not indicative of melanoma.[12] There has also been a very recent publication in the JAAD of a study on 30 LM in children: benign melanonychia striata in children can have clinical and histopathologic features that raise concern for melanoma in adults.[13] And performing a 3 mm punch in such a wide band does not reflect the reality of the lesion, as it only shows a tiny piece of the matrix. How can one propose nail apparatus excision based on such a minute specimen? It has been demonstrated that tangential excision is the best indication for such wide bands.[14] "Aggressive surgery, such as complete excision involving the entire length of the nail matrix can be reserved for cases in which melanoma cannot be excluded after expert review of the clinical and histopathologic findings".[13]

It is a pity that the Authors did not ask both clinician and histologist nail experts for further advice. And it is clear that the reviewer was not a nail expert either. This is how erroneous diagnosis comes to publication.

At the last meeting of the Council for Nail Disorders in San Francisco last March, Bianca Maria Piraccini presented a review of nail melanoma in children. 12 cases have currently been reported, including the one from this publication. Five of them are considered as being debatable, this case numbering among them. All cases where *in situ*, there was no invasive melanoma. Melanoma in children remains exceedingly rare and one should remember that the clinical, dermatoscopic, histological appearance should not be compared to that observed in adults. The ABCD rule cannot be applied to children. Only dark phototype (>V) may be considered as being at risk. And if a biopsy remains indicated, tangential excision is the gold standard. Careful examination, with advice from nail experts, is highly recommended in all cases.

References

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13. Cooper C, Arva NC, Lee C, Yélamos O, Obregon R, Sholl LM, et al. A clinical, histopathologic, and outcome study of melanonychia striata in childhood. J. Am. Acad. Dermatol. 2015;72(5):773-9.
14. Richert B, Theunis A, Norrenberg S, André J. Tangential excision of pigmented nail matrix lesions responsible for longitudinal melanonychia: evaluation of the technique on a series of 30 patients. J. Am. Acad. Dermatol. 2013;69(1):96-104.

CAPSULE SUMMARY:

- Benign melanonychia striata in children can have clinical and histopathologic features that raise concern for melanoma in adults. The ABCD rule cannot be applied to children.

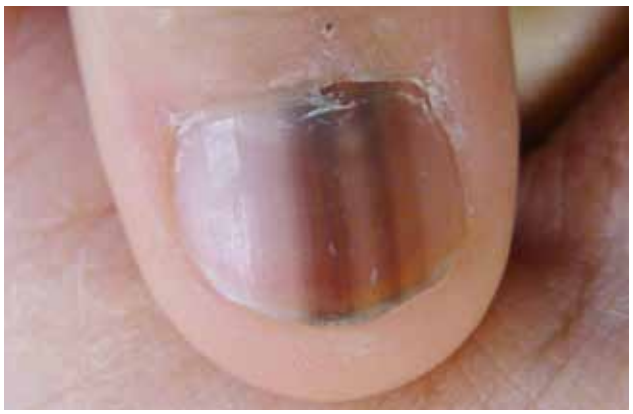

Fig4 - *Wide irregular longitudinal melanonychia in a 3 year-old child. This aspect should suggest melanoma in an adult but much more likely a nevus in a child. The lesion was tangentially excised and confirmed the diagnosis of a nevus. © B. Richert*

NAIL MELANOMA MIMICKER

Adnan A, Bajuri MY, Shukur MH, Subanesh S, Das S. Malignant melanoma masqueraded as ingrown toe nail. Clin Ter. 2014;165(1):41-5

A 62 year-old lady consulted for a year history of dull aching pain on the left big toe with tissue proliferation on one lateral side. The diagnosis made was ingrowing toenail with pyogenic granuloma. She benefitted from a classical wedge excision. Infection complicated healing several times and needed wound debridement. Tissue biopsy was carried out after 10 months, showing a melanoma with a Breslow index of 13 mm and a Clark level V. X-rays were normal. Amputation was performed. Post-operative CT scan showed enlargement of the inguinal lymph nodes that were removed surgically. Four months later, the patient developed lung metastasis and died from infection due to chemotherapy.

The lesson to retain from this terrible case from Malaysia is that no specimen should ever be thrown away. It is the same as when an appendix or tonsils are removed and sent to the pathologist: any specimen collected from skin or nail surgery should be sent to the lab. In our department, like in many others, we do send the specimen from curettage in ingrowing toenails to our lab, even if it really looks like granulation tissue. Several times we were very surprised to receive an unexpected result of melanoma or squamous-cell carcinoma **(Fig 5)**. This allowed quick diagnosis and adequate management.

The second point to remember is that 20 to 30% of melanomas of the nail unit are amelanotic. Thus, any subungual pinkish/bleeding mass in adults should be considered as a melanoma, until proven otherwise.

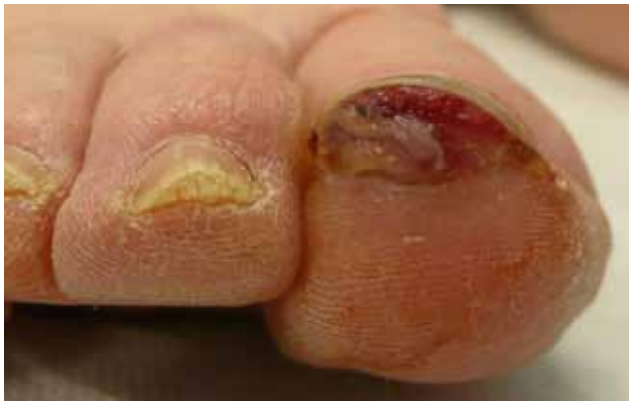

Fig5 - *Fragile bleeding tumour under the nail plate of a nun. She wore sandals all year round (see callosities at the tip of the toes). The lesion was suspected to be a pyogenic granuloma. It was removed tangentially but histology demonstrated an amelanotic melanoma. © M. CAucanas*

LONGITUDINAL MELANONYCHIA WITH DISTAL SPLITTING

Dika E, Piraccini BM, Fanti PA. A gray pigmented band of the third fingernail with distal splitting. JAMA Dermatol. 2014;150(2): 199-200

And finally this case report. Nice pictures of a LM with distal splitting. The short commentary will remind you of everything you need to know about nail melanoma. Short and concise. An excellent summary.

Dimitris RIGOPOULOS

Medical literature regarding inflammatory nail disorders, besides psoriasis, was rather limited in 2014. Therapeutically, novel publications investigating treatment of psoriasis, dominate dermatology therapy literature and nail disorder treatment is no exception. Literature regarding pathogenesis of inflammatory nail disorders is also extremely poor. This is probably due to the fact that few scientists do basic research on the nail unit, despite the fact that pathogenetic mechanisms of inflammatory nail disorders are far from being adequately illuminated. A possible remedy for this situation should include more active pursuit of grant-supported basic research by nail experts with adequately equipped research laboratories.
PubMed was searched for "inflammatory nail diseases", "nail lichen", "alopecia areata", and "chronic paronychia" in 2013, 2014 and 2015. The most interesting findings are presented herewith.

ALITRETINOIN FOR NAIL LICHEN PLANUS

Alsenaid A, I Eder, Ruzicka T, Braun-Falco T, Wolf R. Successful treatment of nail lichen planus with Alitretinoin: report of 2 cases and review of the literature. Dermatology 2014; 229: 293-296.

M Iorizzo. Nail lichen planus- a possible new indication for oral Alitretinoin. J Eur Acad Dermatol Venereol. 2014 Dec 2. doi: 10.1111/jdv.12904. [Epub ahead of print]

Alitretinoin is a retinoid with an on-label indication for chronic severe hand eczema. Even though alitretinoin has been available as a topical formulation for many years, it has not been investigated as a treatment option for nail lichen planus, probably due to its high cost and off-label use. The availability of alitretinoin taken orally kindled the investigation of a possible therapeutic effect in patients with nail lichen planus. Two publications appeared from Germany and Switzerland in 2014, as limited case series.
Alsenaid and colleagues treated two patients with Nail Lichen Planus (a male in his 50s and a female in her 60s) refractory to all previous treatment modalities (topical application of high-potency steroids, topical tacrolimus 0, 1% ointment), with oral alitretinoin, 30 mg/day, for 9 and 8 months respectively.[1]
The male patient started to improve after 2 months of treatment and a significant improvement was seen after 5 months of therapy (pterygium was the only symptom that remained unchanged). Alitretinoin was continued to 9 months, without any side-effects and topical mometasone solution was added in order to continue with the good response. One year follow-up revealed a stable nail condition.
The female patient was initiated with Alitretinoin 10 mg/day and after 3 months 30 mg/day. Treatment was discontinued after a total of 8 months of therapy due to side-effects (headache, elevated liver enzymes, and abdominal pain most likely unrelated to the medication), which the patient could not tolerate. Nail symptoms started to improve after 4 months from the beginning of treatment and remained stable, although pterygium was unchanged. This patient refused long follow-up.

Matilde Iorizzo reported three patients (2 males and 1 female) with nail changes consistent with the ones seen in Nail Lichen Planus treated with oral Alitretinoin 30 mg/day, as they refused IM steroids, and intralesional injections was not an option due to the large number of nails affected (two patients had all their fingernails and the third had all 20 nails).[2] All three patients presented with a remarkable improvement after 3 months of treatment and they asked to maintain their medication **(Fig 1, 2)**. Alitretinoin was

Fig1 - *Male patient before treatment with Alitretinoin. © M. Iorizzo*

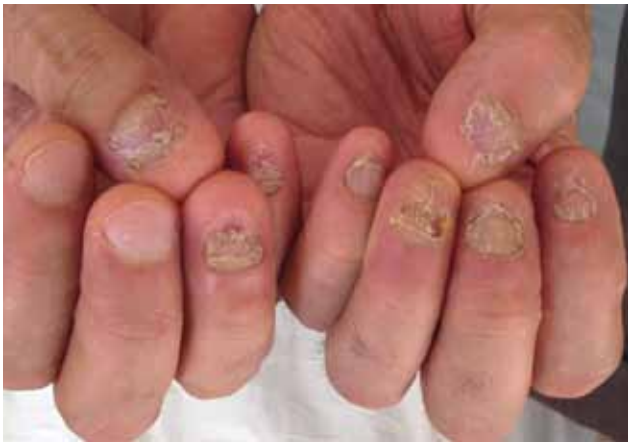

Fig2 - *Same patient 6 months after treatment with Alitretinoin. © M. Iorizzo*

decreased to 10 mg/day and was prescribed for 3 more months.
Nail lichen planus is an inflammatory disease with a still obscure pathogenesis. Relapses are common. The first fingers attacked are usually the most severely affected. It affects skin, mucous membranes, hair follicles and also nails in 10% of the cases, Fingernails are most commonly affected, but the disease can affect both finger and toenails. Symptoms depend on the area of the nail unit which is attacked. If the nail matrix is affected, then the commonest symptoms are thinning of the nail plate, longitudinal ridges, irregular pitting, longitudinal melanonychia and fissuring. If the nail bed is involved, which is not so common, then subungual hyperkeratosis, longitudinal erythronychia and onycholysis are commonly found.
Since etiology is unknown, treatment is symptomatic and has to start as soon as possible and in any case before the formation of dorsal ptergium, which is not reversible. It is important to stress the lack of any treatment guidelines.
Topical steroids applied to the involved sites appear to be effective in some cases and especially under occlusive dressings. Intralesional injections with triamcinolone acetonide 0, 5-0, 1 mg/nail every 2 months can also be used with good results in cases of involvement of up to three nails. Oral prednisone 0, 5 mg/kgr for 3 weeks is also successful in cases when more than three nails are involved. Acitretine as monotherapy or combined with topical steroids, tacrolimus ointment 0, 1% twice a day have also been proven to be effective, as well as antimalarials (chloroquine phosphate 250 mg three times a day). Etanercept was also reported to be effective in treating cases of nail lichen planus, although the medication has been reported to trigger the appearance of lichen planus.

In 2011 Pinter et al reported the successful use of Alitretinoin in cases of nail lichen planus.[3] Alitretinoin (9-cis-retinoic acid) is an endogenous derivative of vitamin A, which regulates cell proliferation and diffentiation. It controls the pro-inflammatory cytokine production by keratinocytes and the modulation of leukocytes activity and through these effects it has anti-inflammatory and immune-modulating actions. Its main and only indication is severe chronic hand dermatitis unresponsive to treatment with potent topical steroids. The treatment course is between 12 and 24 weeks and this depends on response. Its positive effect in the alterations of nail lichen planus, are possibly based on the anti-proliferative mode of action mediated by binding to the retinoid receptors of the nucleus and such indications of expression of nucleus retinoid receptors at the nail matrix, seems to exist. Moreover Alitretinoin seems to reduce the susceptibility of the epidermis to friction, a fact which probably negatively influences the growth of the normal nail in nail lichen planus.

These two new publications of 5 new cases, which are either refractory to conventional treatment or non compliant with the existing therapies, suggest the effectiveness of this treatment modality in cases of nail lichen planus. What is also important to point out is the rapidity of the positive result and the long lasting effect, at least concerning the case that was followed out. Of course it is necessary to mention that larger studies, with a long period of patients follow-up, are needed. A fact which is not easy to perform as this is an off-label use of Alitretinoin.

References.
1. Alsenaid A, I Eder, Ruzicka T, Braun-Falco T, Wolf R. Successful treatment of nail lichen planus with Alitretinoin: report of 2 cases and review of the literature. Dermatology 2014; 229: 293-296.
2. M Iorizzo. Nail lichen planus- a possible new indication for oral Alitretinoin. J Eur Acad Dermatol Venereol. 2014 Dec 2. doi: 10.1111/jdv.12904. [Epub ahead of print]
3. Pinter A, Pätzold S, Kaufmann R. Lichen planus of nails - successful treatment with Alitretinoin. J Dtsch Dermatol Ges. 2011 Dec;9 (12):1033-4

CAPSULE SUMMARY

- Alitretinoin can be an alternative off-label treatment for refractory nail lichen planus. It is characterised by the rapidity of the result and the possible long lasting effect.
- Alitretinoin used for severe chronic hand dermatitis can improve the nail symptoms resulting from the inflammation of the nail matrix.

Dimitris RIGOPOULOS

NAIL IMPROVEMENT DURING ALITRETINOIN TREATMENT OF CHRONIC HAND DERMATITIS

Milanesi N, D'Erme AM, Gola M. Nail improvement during alitretinoin treatment: three case reports and review of the literature. Clin Exp Dermatol. 2015 Feb 16. doi: 10.1111/ced.12584. [Epub ahead of print]

Milanesi and colleagues treated three patients (two male and one female) suffering from severe chronic hand eczema with alitretinoin 30 mg/day for 6 months.[4] Two of the patients had an atopic history, while one was non-atopic. Median nail dystrophy on both thumbnails and Beau's lines on the 3rd and 4th fingers (first patient), yellowish colour and nail plate thickness (second patient) and paronychia, subungual hyperkeratosis, onychoschizia and onychodystrophy (third patient), were the nail signs in the three patients. Besides medication, patients were instructed to follow preventive and protective measures before, during and after the treatment period with Alitretinoin. A complete resolution was observed in all three patients at the end of therapy and one year later, the patients were still free of any nail signs. The authors suggest that the positive results depend on the fact of the stronger anti-inflammatory and immunomodulating effect of Alitretinoin, by regulating keratinocyte proliferation and differentiation, cytokine production, leukocyte activity and antigen presentation.

It is very well known that hand dermatitis, which is a chronic inflammatory skin disease can cause erythema, scales, fissuring, vesicles, papules pruritus and pain, is frequently accompanied by nail symptoms, due to the inflammation of the periungual skin and consequential alteration of the nail matrix, which is situated underneath. In acute eczema, vesicles and erythema are seen surrounding the nail apparatus skin, which results in alterations of the nail plate. In chronic hand eczema, the chronic periungual dermatitis also results in Beau's lines, nail plate pitting and subungual hyperkaratosis. However, when the periungual skin is free of any symptoms, the cause must be looked for elsewhere.

What is of interest and supports the authors' opinion, is the fact that in one patient improvement was first noticed one month after treatment was initiated and in the other two, this was noticed respectively 4 and 5 months later. It was the female patient with a history of atopic dermatitis who improved after one month and she was the only patient with dermatitis of the surrounding skin.

Despite this, it should be emphasized that the protective measures prevent nail matrix inflammation and might possibly be the only measure needed when dealing with nail signs and hand dermatitis.

Reference

4. Milanesi N, D'Erme AM, Gola M. Nail improvement during alitretinoin treatment: three case reports and review of the literature. Clin Exp Dermatol. 2015 Feb 16. doi: 10.1111/ced.12584.

CLINICAL STUDY OF NAIL CHANGES IN VITILIGO

Anbar T, Hay RA, Abdel-Rahman AT, Moftah NH, Al-Kayyat MA Clinical study of nail changes in vitiligo. J Cosmet Dermatol 2013; 12(1):67-72

Based on the fact that alopecia areata is an autoimmune disorder with well known nail changes (multiple small superficial pits regularly distributed in a geometric pattern along longitudinal or transverse lines, twenty nail dystrophy, spotting of the lunula, onycholysis, onychomadesis, etc), Anbar and colleagues, hypothesized that nail changes should be taken into account in vitiligo too, which is another autoimmune disease.[5] Until this study, only nail dystrophy and red lunula have been described in the literature as nail signs associated with vitiligo. The authors therefore carried out this multi-centre study which included 91 vitiligo patients (45 male and 46 female, aged between 3 and 65) and 91 healthy controls with non inflammatory skin disease, age and sex matched. What is of interest is the fact that 68,1% of the vitiligo patients appeared with nail changes, in comparison with the 50,5% of the healthy controls (significant statistical difference). The most common symptoms in the patients' group, were longitudinal ridges (43, 9% vs 20,9% in the controls- significant statistical), punctuate leukonychia (19,8% vs 15,4%) and absence of the lunula (16,5% vs 6,6% - significant statistical). Pitting, transverse ridging, nails with flag sign, distal onycholysis, chronic paronychia and Terry's nails were the remaining reported nail signs.

Concerning the most common sign, longitudinal ridging, autoimmunity, trauma and aging are the possible causes reported. Hence, when the authors subdivided patients according to their age, there was no significant statistical difference in either group. Absent lunula, the second most frequently encountered sign, had not been reported before as a sign possibly related to vitiligo.
This is the first controlled study to report nail signs in association with vitiligo and it might possibly be the basis for further registry studies with a larger sample of patients.

Reference

5. Anbar T, Hay RA, Abdel-Rahman AT, Moftah NH, Al-Kayyat MA Clinical study of nail changes in vitiligo. J Cosmet Dermatol 2013; 12(1):67-72

CAPSULE SUMMARY:

- Vitiligo patients can present with a higher percentage of nail abnormalities than previously believed.

SKIN FEATURES IN MYOTONIC DYSTROPHY TYPE 1: AN OBSERVATIONAL STUDY

Campanati A, Giannoni M, Buratti L, Cagnetti C, Giulodori K, Ganzetti G, Silvestrin M, Provincialy L, Offidani A. Skin features in myotonic dystrophy type 1: an observational study. Neuromuscul Disrd 2015; 25 (5): 409-413

In order to record prevalence and types of skin changes in patients with Myotonic Dystrophy type 1 (Steinert disease), Campanati and colleagues conducted this observational study, including fifty-five patients with the above-mentioned disease and one hundred age and sex matched healthy controls.[6]
Among other symptoms, nail pitting was recorded significantly more frequently among patients than in healthy controls and this cause should be added to the numerous others; frequent (psoriasis, lichen planus, alopecia areata, etc) or uncommon (secondary syphilis-very large pits, sarcoidosis, dermatomyosistis, etc) conditions leading to this non-specific symptom.
It should be mentioned that nail pits found in the nails are due to the clusters of parakeratotic cells that appear in the proximal part of the nail matrix probably due to the inflammation. Consequently as the nail grows out, these parakeratotic cells are shed and the depressions appear.

Reference

6. Campanati A, Giannoni M, Buratti L, Cagnetti C, Giulodori K, Ganzetti G, Silvestrin M, Provincialy L, Offidani A. Skin features in myotonic dystrophy type 1: an observational study. Neuromuscul Disrd 2015; 25 (5): 409-413

CAPSULE SUMMARY:

- Myotonic dystrophy type 1 can be one of the causes of nail pitting.

Dimitris RIGOPOULOS

UPDATES ON YELLOW NAIL SYNDROME

8. Decker A, Daly A, Scher R. Role of Titanium in the development of Yellow Nail Syndrome. Skin Appendage Disorders 2015:1:28-30

Yellow nail syndrome is a rather uncommon disorder of obscure aetiology usually, affecting both finger and toenails. The condition is associated with a slow growth rate of nails and nail signs include thickened nail plate with over-curvature and pale yellow to dark yellow-green discoloration and the nails are usually opaque with no lunula visible. YNS is accompanied by lymphedema and respiratory tract involvement. These symptoms may precede nail symptoms by months or years.
In 2011 Berglund and Calmark proposed that titanium dioxide, - which was found to be elevated in nail clippings of 30 YNS patients, while it was not found in healthy ones, - might play a role in the yellow discoloration of the nails of a certain subgroup of patients.[7] These patients had been exposed to titanium from medication (multivitamins, suspensions, and tablets), confectioneries (chewing gum) and titanium implants with concurrent gold dental implants.

In the paper by Decker and colleagues, the case of a female patient is presented.[8] The 67-year-old lady presented with an 18 month history of yellow nail discoloration and "loosening", along with absence of the lunula, loss of cuticles and marked reduction of the growth rate of all her nails, together with a five year history of bronchitis and sinusitis. She had 8 silver amalgams, reported daily use of toothpaste containing fluoride and regularly ingested titanium dioxide though the daily use of 4 to 8 pieces of chewing gum and cetirizine tablets 10 mg/day. Titanium dioxide was elevated in her nail clippings.

It is stated in a review paper by Baran, that the exposure to drugs that actually contain titanium dioxide or dental restorative materials, can precede the development of YNS, and what is of most interest is that nails can return to normal a few months after the withdrawal of these drugs.[9] Of course, if we consider the numerous patients that have dental implants or are exposed daily to titanium dioxide through medication or food intake and, on the other hand the rarity of YNS, it should be emphasized that there must be other conditions that influence the induction of this syndrome.

References
7. Berglund F, Carlmark B. Titanium, sinusitis, and the yellow nail syndrome. Biol Trace Elem Res. 2011 Oct; 143(1):1-7.
8. Decker A, Daly A, Scher R. Role of Titanium in the development of Yellow Nail Syndrome. Skin Appendage Disorders 2015:1:28-30
9. Baran LB. Yellow Nail Syndrome and nail lichen planus may be induced by a common culprit. Focus on dental restorative substances. Frontiers in Medicine, Dermatology 2014; 1(46):1-3

CAPSULE SUMMARY

- Titanium dioxide, which can be found in medication, dental implants and confectioneries, may possibly be implicated in the Yellow Nail Syndrome pathogenesis.

QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY NAIL DISORDERS VS THE REST OF THE NAIL DISORDERS

Belyayeva E, Gregoriou S, Chalikias J, Kontochristopoulos G, Koumantaki E, Makris M, Koti I, Katoulis A, Katsambas A, Rigopoulos D. The impact of nail disorders on quality of life. Eur J Dermatol. 2013;23(3):366-71

Published literature tends to focus on the impact of nail psoriasis and onychomycosis on patients' quality of life (QoL). However, there have been very few publications concerning the impact of all the other nail disorders on QoL. We published an evaluation of the quality of life of all patients presenting in our nail clinic and we tried to compare the burden resulting from different nail disorders, including inflammatory nail disorders,[10] on their Quality of life.

One thousand and sixty three patients with nail disorders completed an anonymous nail specific QoL questionnaire, consisting of 24 and 16 questions respectively, for fingernails and toenails with five possible responses to each question.[11] A score of 1-5 was given to each response and the final score was adjusted on a percentile scale. The subjects were classified in groups according to nail disorders. Statistical analysis was carried out using the Pearson product moment correlation coefficient and regression analysis.

Comparison between groups showed that inflammatory nail disorders, such as trauma, onychomycosis, other infections besides onychomycosis, nail structure abnormalities, nail psoriasis, and paronychia had similar impact on patients' QoL. All the above mentioned disorders had higher impact on QoL, compared to chromonychias and tumours (p=0.000091). A possible explanation for the lower impact on QoL of chromonychias and tumours might be the more recent development of the initial lesion and consequently shorter duration of the disease before seeking medical counsel. As was to be expected, QoL patients with multiple nails involved (p=0.000017), were statistically more significantly affected, as well as women (p=0.03) and people in the 60-79 years old group (p=0.005). There was no statistically significant difference on the QoL impact between patients having only fingernails or only toenails involved. (p=0.137). A probable explanation for the similar burden of Quality of life in fingernails and toenails might be that the majority of the population were women, living in countries with very long summers, when they had the opportunity to wear open-ended shoes allowing toenails to be visible for many months.

There are several limitations in our study. The Greek version of the questionnaire was in the process of validation at the time. This was an onychomycosis-specific questionnaire not validated for other nail disorders. Even though our population was homogenous, it was still a population referring to a tertiary academic nail unit, so one should expect that previous consultations had not resolved the problem adding to their burden on Qol. Lack of a control group, and QoL after treatment, might also be considered as limitations.

What we do consider as important is that our results show that most nail disorder results are similarly distressing to patients and this is what incites them to seek medical counsel from experts.

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11. Drake LA, Patrick DL, Fleckman P, et al. The impact of onychomycosis on quality of life: development of an international onychomycosis-specific questionnaire to measure patient quality of life. J Am Acad Dermatol. 1999; 41:189-96.

CAPSULE SUMMARY

- Inflammatory nail disorders can affect quality of life in a manner similar to trauma, onychomycosis and other infections, nail psoriasis, nail structure abnormalities and paronychia, and have a higher impact than nail tumours and chromonychias.

notes

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