Nail psoriasis

R. Manhart[1], P. Rich[2]

[1]Oregon Dermatology and Research Center, Portland, Oregon, USA;
[2]Department of Dermatology, Oregon Health Science University, Portland, Oregon, USA.

Racheal Manhart, BS
Phoebe Rich, MD

Please address correspondence to:
Racheal Manhart,
Oregon Dermatology and Research Center
2565 NW Lovejoy, Suite 200
97210 Portland (OR), USA.
E-mail: racheal.manhart@gmail.com

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ABSTRACT

Nail psoriasis affects nearly 80% of patients with plaque psoriasis and is even more prevalent in patients with psoriatic arthritis. Nail psoriasis is not simply a cosmetic problem but one that effects the structure and function of the nail, resulting in negative psychological effects. The first level in management of nail psoriasis is patient education. The hierarchy of nail psoriasis therapy begins with topical medication followed by devices, intralesional injections, and small molecules. For nail psoriasis patients unresponsive to these treatments, and especially in patients with severe plaque psoriasis, biologics are safe and effective options.

Epidemiology and prevalence

Psoriasis is a chronic inflammatory disorder that affects nearly 2% of the population and can involve the skin, scalp, joints, mucous membranes and nails (1, 2). A large study of 1,738 patients with psoriasis showed that 79.2% of patients had involvement of the nails and estimated lifetime incidence of nail psoriasis up to 90% (3-5). At the time of presentation, psoriasis limited to the nails is uncommon and estimated to occur in 5% to 10% of patients with psoriasis (6). Many patients who present with psoriasis only in their nails later develop psoriasis of their skin and/or joints, thus, the absolute number of patients exclusively with nail psoriasis is not known. In patients with psoriasis, adults are more likely to have nail psoriasis than children. In the pediatric population, the prevalence of nail psoriasis ranges from 7% to 13% (7-9).

Psoriatic arthritis and nail psoriasis

The prevalence of psoriatic arthritis (PsA) in psoriatic patients ranges from 6% to 42% depending on the study (10, 11). The prevalence of nail psoriasis in patients with PsA is high ranging from 50% to 87% (12, 7). Psoriasis of the skin, scalp and/or nails often precedes the appearance of psoriatic arthritis by up to 12 years (7, 13). More severe plaque psoriasis as well as psoriasis of the nails, scalp and intertriginous areas have been associated with the likelihood of developing PsA. The highest correlation with PsA appears in patients with nail disease.

In a large retrospective study from Germany, 4,146 psoriatic patients were analysed for psoriasis history, clinical findings, PsA, and nail involvement using standardised questionnaires to seek possible predictive features for psoriatic arthritis. The strongest predictor for concomitant PsA was nail involvement. By contrast, scalp involvement was not a significant predictor of PsA (14).

Quality of life

Psoriasis can have a significant negative impact on a patient's quality of life (QOL) causing physical impairment and pain. Psoriasis of highly visible areas of the body (including face, hands, scalp and nails) affects the patients quality of life sometimes more when compared to other chronic diseases (8, 15-17). In a series of 1,369 patients with nail psoriasis, 90% reported the disease as cosmetically distressing, and had restrictions in their activities of daily living due to nail psoriasis (3). A study preformed in the Netherlands, reviewed 5,400 patients with psoriasis who completed a self-reported Dermatology Life Quality Index (DLQI) and Nail Psoriasis Quality of life 10 (NPQ10). Patients with nail psoriasis scored higher on the DLQI than patients without nail psoriasis. Furthermore, patients with nail bed psoriasis scored higher on the NPQ10, than patients with only nail matrix psoriasis. Overall NPQ10 scores were higher in females (18). These results underscore the negative impacts of nail psoriasis in patients' quality of life.

Clinical features of nail psoriasis

The clinical features of nail psoriasis depend on the location of the psori-

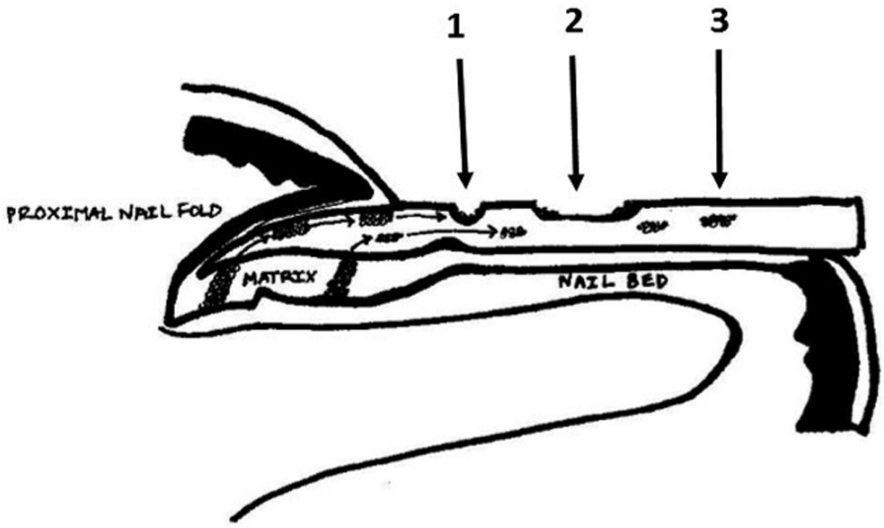

Fig. 1. The location and duration of psoriatic inflammation causes the nail matrix psoriasis features. These features include: pits, crumbling and psoriatic leukonychia. The proximal matrix which forms the superficial layers of the nail plate is responsible for pitting (1). Crumbling is confluent pitting that results from broad foci of inflammation in the proximal matrix for a longer duration (2). Leukonychia is caused by psoriasis in the mid and distal nail matrix which forms the deeper layers of the nail plate. This causes the parakeratotic cells to be trapped within the substance of the nail plate (3). Leukonychia looks like pitting however, the surface of the nail plate is smooth rather than pitted. During the minimum time it takes for the nail to grow out, if the smooth surface of the nail plate overlying leukonychia is worn away, the deeper parakeratotic cells of leukonychia become more superficial and may even evolve into pitting. Drawing modified from Zaias 1969. Archives Dermatology.

atic Inflammation within the nail unit. The scientific basis of our current knowledge of the clinical features of nail psoriasis comes from the research of Nardo Zaias done in 1969. He described the pathophysiology of the clinical features of nail matrix and nail bed psoriasis (19, 20).

The nail unit is composed of four epithelial structures; the nail bed, nail matrix, hyponychium and nail folds. Any or all of these structures can be affected with nail psoriasis. Generally, psoriasis of the nail matrix and nail bed result in most of the observed pathologic changes, whereas psoriasis of the hyponychium and nail folds contribute less to the pathologic changes (Fig. 2A-B). None of the features of nail psoriasis are unique to psoriasis. It is the collection of features that allow us to recognise a diseased nail as psoriatic.

Nail matrix signs

The nail matrix is responsible for the formation of the nail plate. When the nail matrix is affected by psoriatic inflammation, changes in the nail plate include pitting, crumbling, psoriatic leukonychia (white spots), and red macules in the lunula. Occurrence of these features depend on the duration and location of psoriasis within the distal or proximal matrix (Fig. 1). For example, foci of psoriasis in the proximal matrix cause pitting, whereas the same process in the mid or distal matrix results in psoriatic leukonychia. The mid and distal areas of leukonychia resemble pitting, but these abnormal cells are trapped in the nail plate resulting in white spots (leukonychia) rather than a pitted surface. Crumbling represents confluent pitting due to a longer duration of nail psoriasis in the proximal nail matrix.

Nail bed signs

The nail bed is responsible for the firm attachment of the nail plate. Psoriasis in the nail, and results in changes of oil drop/salmon patch dyschromia, nail bed hyperkeratosis, and splinter haemorrhages, which disrupts the connection of the nail bed and nail plate resulting in onycholysis.

Assessment and grading of nail psoriasis

There are many valid and useful nail psoriasis assessment tools, including: NAPSI, modified NAPSI, Target NAPSI,

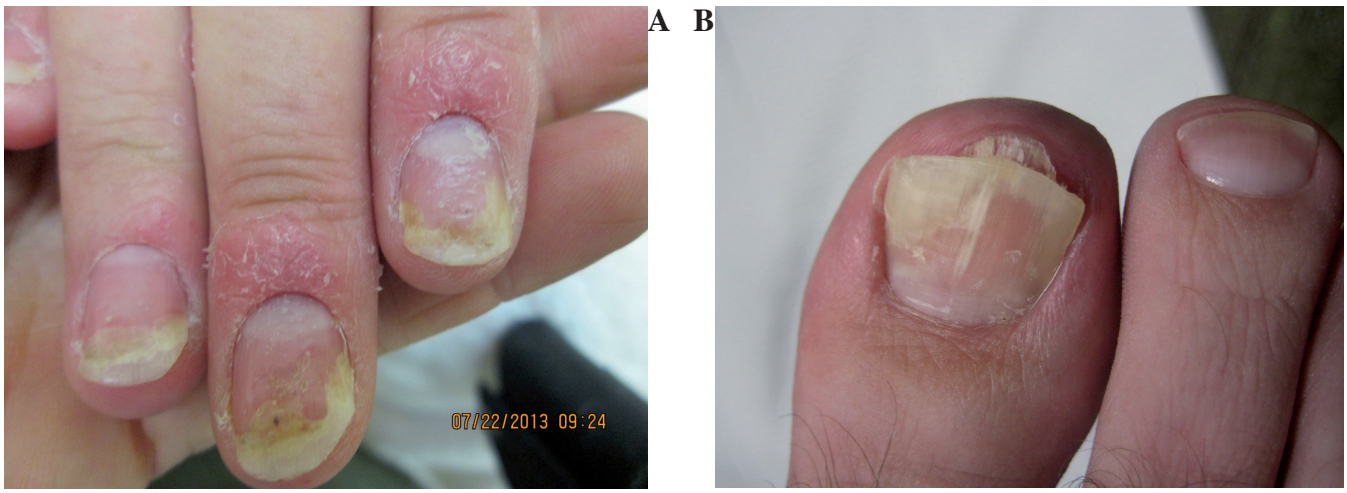

Fig. 2. A Psoriasis involving the proximal nail fold results in nail plate surface irregularities similar to forms of paronychia;
B Psoriasis of the hyponychium causes hyperkeratosis and distal onycholysis.

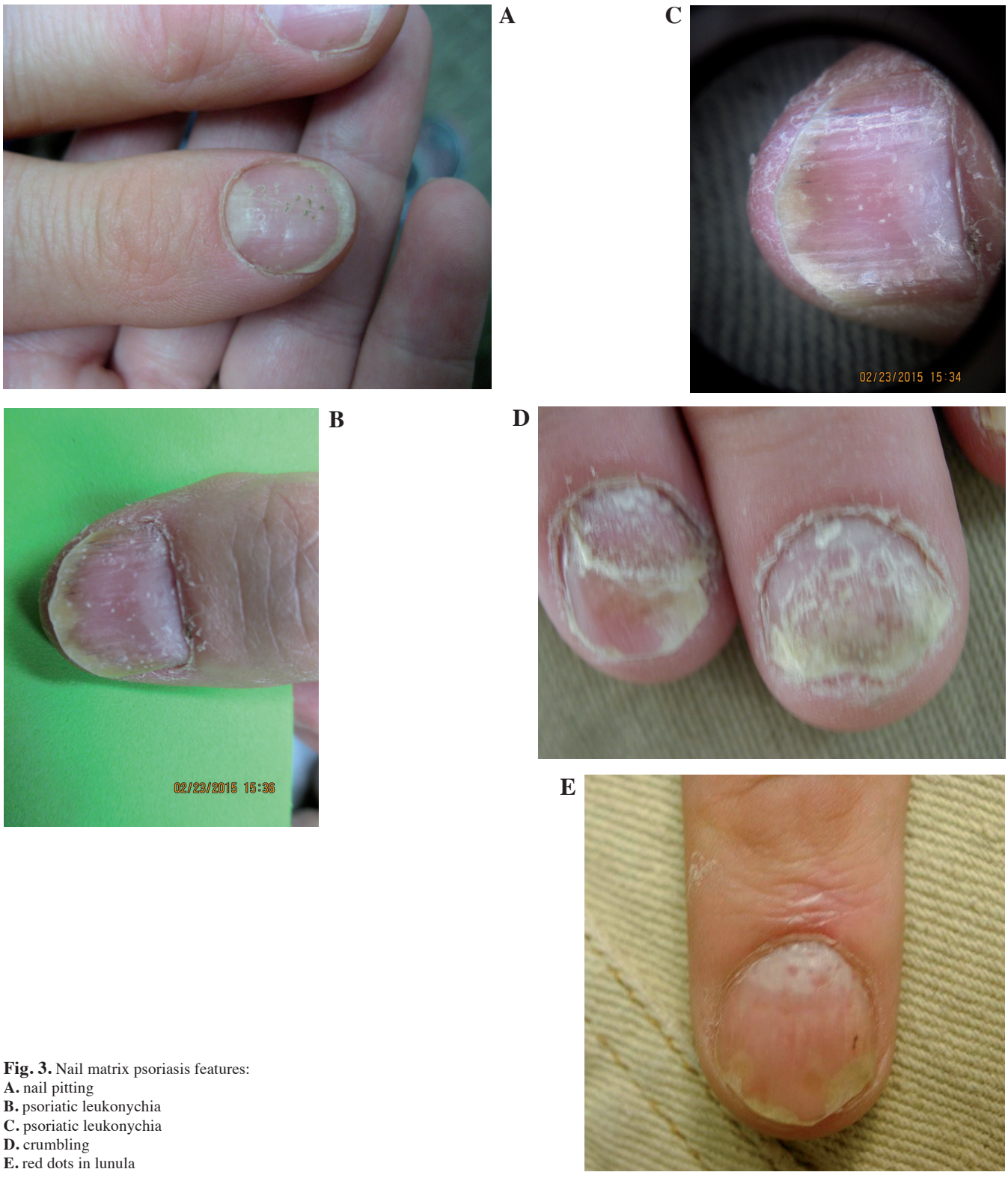

Fig. 3. Nail matrix psoriasis features:
A. nail pitting
B. psoriatic leukonychia
C. psoriatic leukonychia
D. crumbling
E. red dots in lunula

Baran, N-Nail, Cannavo, PNSS, NASS and others (21). None of these tools are perfect, and all have benefits and limitations which, are summarised in an excellent review of nail psoriasis assessment methods by Kaalssen *et al.* (21).

NAPSI was the first quantitative nail assessment tool published in 2003, and has been used in nearly all large pharmaceutical trials in which nail psoriasis was evaluated (22). This includes more than 800 published reports, posters, and abstracts over the past decade. The principles of NAPSI are based firmly in Zaias' research. His research explains the pathogenesis of nail pitting, crumbling, and psoriatic leukonychia in nail matrix, and of oil drop / salmon patch, hyperkeratosis and the resultant onycholysis in the nail bed (20). NAPSI divides the nail into imaginary quadrants

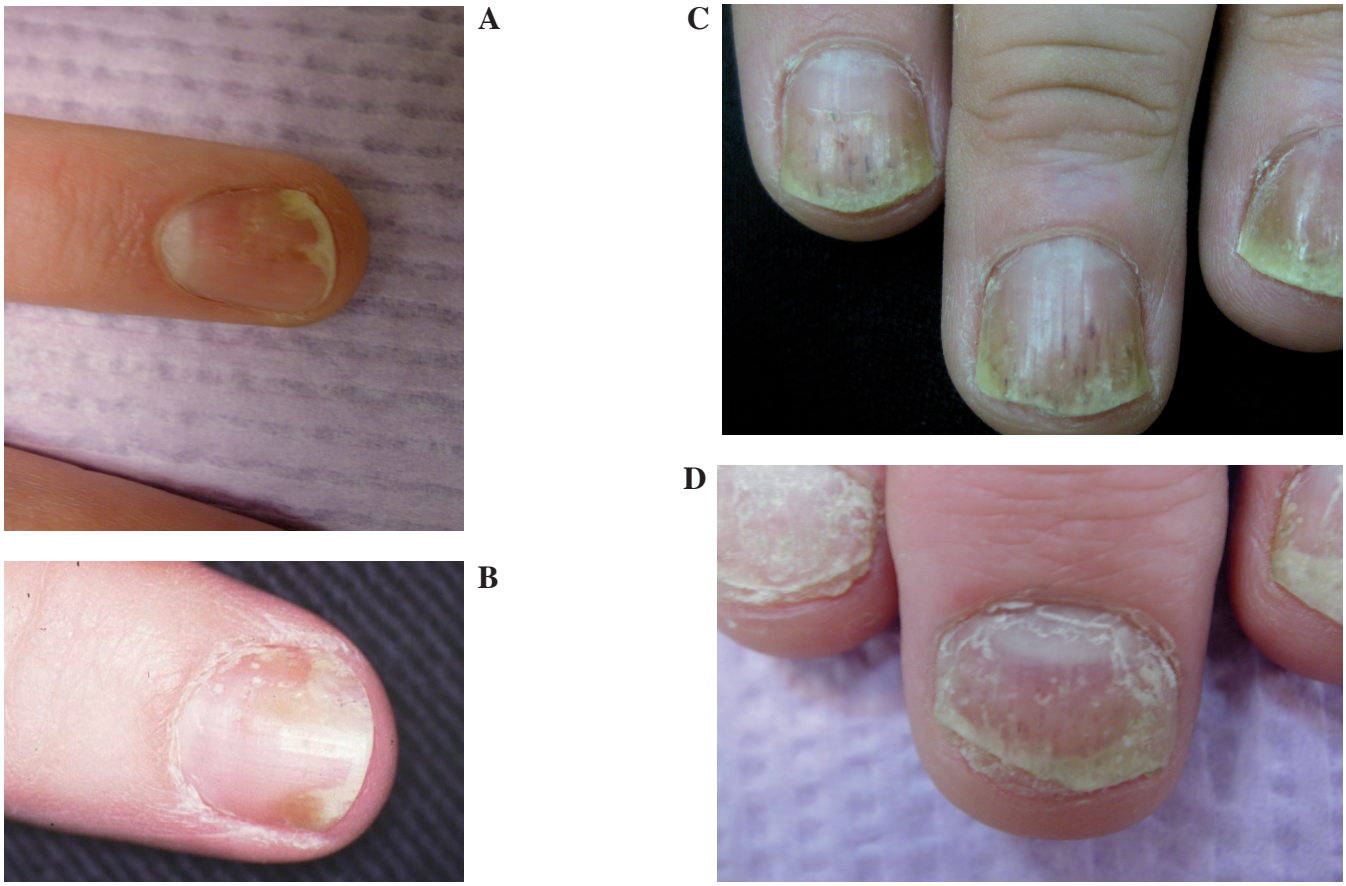

Fig. 4. Nail bed psoriasis features: **A.** onycholysis, oil drop dyschromia; **B.** oil drop dyschromia, onycholysis; **C.** splinter haemorrhages, onycholysis; **D.** splinter haemorrhages, nail bed hyperkeratosis, onycholysis.

and records the number of quadrants in which any of the interchangeable features of nail matrix psoriasis and any of the features of nail bed psoriasis are seen. The composite score for each nail is between 0–8. There are other quality assessments scales that are scientifically sound, and are listed at the beginning of this section (21). However, some scales count pits and estimate percent of involvement of various features rather than the binary system of quadrants (21).

Patient education

The first level in the management of nail psoriasis is to instruct patients about nail care. For example, it is important to instruct patients on how to avoid activities that may result in Koebner (isomorphic) reaction where localised trauma including minor repetitive trauma to the skin or nails induces or exacerbates psoriasis at the site of injury. Simple advice includes, avoiding minor repetitive nail trauma by wearing gloves for household chores and gardening, and keeping diseased nails short when fingertip activities like typing and piano playing are performed. Patient should avoid excessive nail grooming, picking, and filing or buffing the surface of the nail plate. Woman can attempt to disguise unsightly psoriatic nails by using nail polish (lacquer, enamel), but nail enhancements such as acrylic nails are not advised. Patients should be counseled that nail improvement occurs slowly and clearing often requires 6 or more months for fingernails, and up to 12 months for toenails. Few studies show significant nail improvement before 12 weeks, and several studies with infliximab, etanercept, and ustekinumab demonstrate continued improvement beyond 6 months (23-25).

Approximately 30% of psoriatic toenails have concomitant onychomycosis. Treating the fungal infection may be helpful in some cases of thick dystrophic psoriatic nails prone to Koebner reactions.

Treatment of nail psoriasis

Physician/provider prescribed therapies are numerous and are selected based on many individual factors including disease severity, comorbidities, and the impact of psoriatic nail dystrophy on the patient's QOL due to impaired function, pain and aesthetics. Patient motivation, adherence, and out of pocket cost of medications are additional factors. The usual hierarchy of treatment of nail psoriasis parallels treatment of plaque psoriasis. Topical therapies such as corticosteroid, calcipotriol, corticosteroids, tazarotene, and tacrolimus creams and ointments may be helpful in mild or early nail psoriasis (Table I). A Chinese botanical, Indigo Naturalis (Lindioil) is a newly described topical botanical treatments for psoriatic nails (26). Intralesional triamcinolone and light based devices such as excimer and pulse dye are sometimes useful when few nails are involved and before systemic medications are considered.

Table I. Management of nail psoriasis.

1. Patient education
   a. Avoidance of minor repetitive nail trauma from typing and chores to prevent Koebner (isomorphic) reactions that may exacerbate nail psoriasis.
   b. Manage expectations about the time necessary for to nail clearing
   c. Discuss nail cosmetics and other factors that may interfere with therapy
   d. Discuss prevention and treatment of concomitant fungal infection in psoriatic nails
2. Topical products applied to the involved nails
   a. Pharmaceutical creams, solutions, ointments: calcipotriol, tazarotene, tacrolimus, etc.
   b. Botanicals Indigo naturalis (Lindioil)
   c. Treat concomitant fungal nail involvement, if present, with topical and/or systemic antifungals as indicated.
3. Intralesional corticosteroids (when single or few nails are involved)
4. Devices
   a. Light energy based devices: excimer laser, PDL, Grenz Ray
5. Systemic therapy with small molecules
   a. Traditional small molecule medications- methotrexate, acitretin , cyclosporine A
   b. Newer small molecules - apremilast, tofacitinib
6. Systemic therapy with biologic agents
   a. Adalimumab (ADA), Etanercept (ETN), Infliximab (IFN), Certolizumab pegol (CZP), Golimumab, Ustekinumab (UST), Ixekizumab (IXE), Secukinumab (SEC)

Table II. Therapy of nail psoriasis including references.

Therapeutic options for nail psoriasis	Reference
Topical agents	
Topial calcipotriol + betamethasone	60, 61
Topical clobetasol lacquer 0.05%, 0.1%, 8%	62
Tacrolimus ointment 0.1%	63
Tazarotene gel .1% daily	64
Topical Cyclosporine A 70% in corn oil	65
Indigo naturalis lindioil	66
Topical calcipotriol + betamethasone+ salicylic acid	67
Devices and Procedural Interventions	
Pulse Dye laser (PDL) 595 nm	68
Excimer laser	69
Intense pulse light (IPL)	70
Photodynamic therapy PDT, PDL plus MAL	71
Grenz Ray	72
Intralesional (IL) corticosteroids 5 mg/cc triamcinolone with injector monthly x4	73
IL triamcinolone injection with needleless injector	74
Combination Therapies	
Phototherapy with psoralen / acitretin	29
PDL + 0.1% tazarotene	75
Traditional Small Molecule Medications	
Methotrexate	28, 29, 32, 33, 34
Cyclosporine A (CsA)	28, 29, 30, 31
Acitretin	29, 35
Leflunomide	36
Newer Small Molecule Medications	
Apremilast	76
Tofacitinib	77
Biologic Agents	
Adalimumab (ADA)	31, 37, 38, 39, 40, 41, 43, 44
Etanercept (ETN)	43, 44, 45, 46
Infliximab (IFN)	29, 34, 44
Certolizumab pegol (CZP)	47
Golimumab	78, 79
Ustekinumab (UST)	54, 55, 56, 25, 57
Ixekizumab (IXE)	80, 58
Secukinumab (SEC)	81, 59

When lower level therapy fails or when there is concomitant extensive plaque psoriasis, systemic treatment may be employed. For nail psoriasis alone, traditional systemic medications such as Cyclosporine A (CsA), methotrexate, and acetritin appear to be more effective in clearing cutaneous plaque psoriasis than they are in clearing nail psoriasis. Cyclosporine A is associated with minimal improvement in nail psoriasis (27-31). Methotrexate is effective in psoriasis and psoriatic arthritis but efficacy in nail psoriasis is not compelling (28, 29, 32-34). Acitretin, a retinoid showed modest effect for improving nail psoriasis (27, 29, 34, 35). Leflunomide showed limited efficacy in nail psoriasis in a European trial (36).

Dozens of clinical trials have been conducted of biologic agents for moderate to severe plaque psoriasis, and many of these trials evaluated efficacy in nail psoriasis as a secondary endpoint of treatment. In addition, there have been numerous small trials specifically evaluating efficacy of the investigational product in nail psoriasis. Some of the nail-specific trials included small molecules and biologic agents as monotherapy, combination therapy. Some of these aforementioned trials were open-label, some blinded, and some with comparators. Several excellent recent publications review the data concerning these clinical trials in nail psoriasis (Table II). Biologics have been shown to be effective in the treatment of nail psoriasis in a number of well controlled studies with the tumour necrosis factor alpha (TNF-α) antagonists, Adalimumab (29, 31, 34, 37-44), Etanercept (29, 34, 42-46), Cergtolizumab pegol (47), and Infliximab (27, 29, 34, 42-44, 48-53). Ustekinumab is very effective in treating nail psoriasis, with weight based dosing (25, 54-57). Phase 3 data with Secukinumab and phase 2 studies with Ixekizumab showed very good nail improvement (58, 59, 80, 81).

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