Therapies for Psoriatic Nail Disease.
A Systematic Review

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**ABSTRACT.** Nail involvement is common in patients with psoriasis and psoriatic arthritis, affecting 80%–90% of patients at some time. It also has significant effects on quality of life. Psoriatic nail disease can be refractory to treatment, and different features may respond variably to different therapies. The lack of standardized outcome assessments hinders the interpretation of available data. In this systematic evidence-based review of the literature, we assess various treatments for psoriatic nail disease.

(First Release May 15 2006; J Rheumatol 2006;33:1452–6)

**Key Indexing Terms:**

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<th>PSORIATIC ARTHRITIS</th>
<th>PSORIASIS</th>
<th>NAIL</th>
<th>TREATMENT</th>
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</table>

**INTRODUCTION**

Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy characterized by the association of arthritis and psoriasis. There is substantial heterogeneity in both the extent and type of articular and dermatologic involvement. Nail involvement is common, estimated to affect 80%–90% of people with PsA at some time during their lives. It has been suggested that nail lesions occur more commonly in PsA than in uncomplicated psoriasis. Nail psoriasis significantly affects quality of life; one study of 1728 psoriatic patients found that 93% with nail psoriasis considered it to be a cosmetic handicap, 48% reported that it interfered with their jobs, and 52% described pain.

Psoriasis can affect all components of the nail. The nail plate is composed of hard, translucent, dead keratin. The matrix, at the proximal end of the nail, synthesizes 90% of the nail plate is composed of hard, translucent, dead keratin. The plate cells, much the same way psoriatic scale is shed, reflect psoriasis of the hyponychium with silver parakeratotic scale and absent granular lesion, similar to what is seen in psoriatic skin lesions.

Compared with skin psoriasis, nail bed psoriasis has the same layering of parakeratosis and polymorphonuclear leukocytes in the stratum corneum, but has more spongiosis in the epidermis and more serum accumulation in the stratum corneum. Nail disease can be refractory to treatment, and different features can respond variably to different treatments.

In our review, we assess the clinical effect on signs, symptoms, and quality of life and the toxicity of therapies for nail psoriasis in patients with PsA. Given the limited number of studies on nail disease in PsA, the search was broadened to include nail disease in patients with psoriasis, but not necessarily PsA.

**Search Strategy**

A comprehensive literature search of PubMed beginning in 1953 and limited to articles in English was performed. Titles, abstracts, and reference lists of selected trials were manually reviewed to identify additional studies.

Inclusion criteria: Psoriatic nail involvement in adults with psoriasis or PsA, clinical trials of agents for psoriatic nail disease, and for completeness, case series and observational studies.

Exclusion criteria: Studies or case reports with 5 or fewer...
patients, studies in which the number of patients was not clearly indicated.

Outcome Measures
There are no validated outcome tools for nail involvement with psoriasis. This and the lack of appropriate controls for many of the studies precluded meaningful determination of effect size or other quantitative assessments.

RESULTS
Using the MeSH terms “psoriatic arthritis” and “nail” and “treatment” we retrieved 19 articles. Crossing “psoriasis” and “nail” and “treatment” yielded an additional 148 articles. Twenty-one articles that met the inclusion and exclusion criteria are included in this review and are summarized in Table 1. Toxicities were reported variably; therefore we were unable to compare them. Several reported treatments (e.g., topical cyclosporine30, electron beam radiation31, grenz ray treatment12, superficial radiotherapy33) were not included in this review because they are not widely available.

Treatment Recommendations
Based on our interpretation of the data presented here, treatment recommendations are listed below.

• Topical steroids9-11
  – Alone: marginal response, grade C9
  – With salicylic acid: moderate response, grade C10
  – With topical calcipotriol: moderate response, Grade B11
• Topical tazarotene: moderate improvements in some features of psoriatic nail disease, grade A, C12,13
• Topical urea/propylene glycol (Belanyx): improvement of nail disease, grade C15
• Topical 5-fluorouracil
  – Alone: improvements of nail disease, grade C14,15
  – In combination with topical urea/propylene glycol (Belanyx): does not result in further improvements than Belanyx alone, grade A15
• Topical calcipotriol9,11,20
  – Alone: moderate improvements, grade B, C9,10
  – With topical steroid: moderate response, grade B11
  – With oral cyclosporine: moderate response, grade B20
• Topical anthralin16,21
  – Alone: moderate improvement, grade C16
  – After oral cyclosporine or etretinate: maintains and may increase improvements with those medications, grade B21
• Intravenous infliximab: improvement, grade A, C18,19
• Intramuscular alefacept: some improvement, grade C19
• Oral cyclosporine20,21
  – Alone: some benefits, grade A, C20,21
  – With topical calcipotriol: further benefits, grade C20
• Oral retinoids9,21
  – Alone: moderate improvement in pustular nail psoriasis, grade C9,21
  – Followed by anthralin: some improvement, grade B21
• Oral nimesulide: marginal improvements, grade C9
• Injectable steroids22-28
  – With needle and syringe: possible moderate benefits, but utility is questioned given side effects, grade C26-28
  – With needle-less device: possible moderate benefits, more for nail matrix disease; questionable side effects, grade C22-25
• Oral photochemotherapy: moderate benefits, grade C29

DISCUSSION
The lack of data on nail involvement in PsA studies requires that data be extrapolated from psoriasis studies. Interpretation of the data is difficult: Many studies have small patient numbers, most lacked appropriate controls, and no standard outcome measures were used, making it impossible to compare outcomes.

Recently, a psoriatic nail grading instrument, the Nail Psoriasis Severity Index (NAPSI) was developed to evaluate nail matrix disease (pitting, leukonychia, red spots in the lunula, and nail plate crumbling) and nail bed disease (oil drop discoloration, onycholysis, nail bed hyperkeratosis, and splinter hemorrhages)8. Validation of this instrument and modified versions of the NAPSI are in progress34.

Many of the trials reviewed had positive outcomes, but have questionable utility, in our opinion, because of side effects or the transient nature of the results.

Although there is a paucity of data regarding quality-of-life benefits of these therapies, patients report that psoriatic nail disease significantly affects their lives in terms of cosmetics, pain, and activities of daily living3. In one study, 77% of patients indicated they would like to undergo treatment for nail psoriasis3. Further investigations into safe, efficacious treatments for nail psoriasis are needed.

REFERENCES
Table 1. Treatments for nail disease.

<table>
<thead>
<tr>
<th>Study</th>
<th>Agent</th>
<th>No. of Patients</th>
<th>Study Type</th>
<th>Outcome Measure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piraccini&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Topical steroid vs topical calcipotriol (5µg/g) vs oral retinoid (etretinate 0.5 mg/day or acitretin 0.5 mg/day) vs oral nimesulide (100 mg bid)</td>
<td>46 total (topical steroid: 18; topical calcipotriol: 15; oral retinoid: 12; oral nimesulide: 13)</td>
<td>Obs</td>
<td>Responder or nonresponder</td>
<td>Topical steroid: 4/18; calcipotriol: 9/15; oral retinoid: 6/12; oral nimesulide: 4/13</td>
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<tr>
<td>Tosti&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Topical calcipotriol (50 µg/g) vs topical betamethasone dipropionate (64 mg/g) and salicylic acid (0.03 g/g)</td>
<td>56</td>
<td>RCT</td>
<td>Nail thickness (mm) measured qmo</td>
<td>Calcipotriol: 41–49% reduction at 5 mo in responders; betamethasone dipropionate and salicylic acid: 52% reduction at 5 mo in responders c/w baseline; 2 treatments equally effective</td>
</tr>
<tr>
<td>Rigopoulos&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Topical calcipotriol + clobetasol propionate</td>
<td>62 (48 w/nail disease)</td>
<td>Open</td>
<td>Hyperkeratosis thickness</td>
<td>72% and 70% reduction in nail thickness (fingers and toes, respectively)</td>
</tr>
<tr>
<td>Scher&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Topical tazarotene 0.1% gel</td>
<td>31</td>
<td>RCT</td>
<td>7-point scale for pitting, onycholysis, subungual hyperkeratosis, leukonychia, nail plate crumbling, splinter hemorrhages, nail bed discoloration</td>
<td>Improved onycholysis in occluded at wk 4 &amp; 12 and nonoccluded wk 24; improved pitting at wk 24 in occluded ≤ 0.05 for those listed</td>
</tr>
<tr>
<td>Bianchi&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Topical tazarotene 0.1% gel</td>
<td>25</td>
<td>Open prospective</td>
<td>Visual assessment scale (0–2), specific (onycholysis, hyperkeratosis, oil spots, pitting) and nonspecific (thickened/brittle nails, paronychia, splinter hemorrhages) signs</td>
<td>Specific signs improved statistically significantly; nonspecific signs improved &lt; 0.0001</td>
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<tr>
<td>Fredriksson&lt;sup&gt;14&lt;/sup&gt;</td>
<td>1% topical fluorouracil</td>
<td>20</td>
<td>Open prospective</td>
<td>Improvement</td>
<td>17/20 improved; decreased pitting and hypertrophy (about 75% improvement c/w baseline); nail loss seen in treated pts w/onycholysis</td>
</tr>
<tr>
<td>De Jong&lt;sup&gt;15&lt;/sup&gt;</td>
<td>1% topical fluorouracil in Belanyx (urea, propylene glycol) lotion vs topical Belanyx lotion alone</td>
<td>57</td>
<td>RCT</td>
<td>Nail area severity score (0–4 score for pitting area, number of pits, subungual keratosis, onycholysis, oil spots) &amp; overall nail severity scores</td>
<td>Percent improvement with: fluorouracil: 32%/40% at wk 12/16; Belanyx: 39%/46% at wk 12/16 ≤ 0.05 c/w baseline, no difference between 2 treatment groups</td>
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<tr>
<td>Yamamoto&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Topical 0.4–2.0% anthralin in petrolatum followed by topical 10% triethanolamine</td>
<td>20</td>
<td>Open prospective</td>
<td>Improvement in: onycholysis: 4/7 pts: fair; thickening: 3/6 pts: fair; pitting: 4/8 pts: fair; longitudinal and transverse lines: none</td>
<td>Improvement in: onycholysis: 4/7 pts: fair; thickening: 3/6 pts: fair; pitting: 4/8 pts: fair; longitudinal and transverse lines: none</td>
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<tr>
<td>Reich&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Infliximab (5 mg/kg IV) at wks 0, 2, 6 and q8 wks thereafter vs placebo at wks 0, 2, 6, 14, 22, and crossing over in double-blind fashion to infliximab (5 mg/kg IV) at wks 24, 26, 30 and q8 wks thereafter</td>
<td>378 (w/nail psoriasis; placebo: 65; infliximab: 240)</td>
<td>RCT</td>
<td>Nail psoriasis severity index (NAPSI)&lt;sup&gt;8&lt;/sup&gt; at wks 10, 24, 50 (target nail divided into quadrants, scored for presence of 4 nail matrix and 4 nail bed features)</td>
<td>Percent improvement in NAPSI score: Wk 10: infliximab 26.0%, placebo –5.9%; wk 24: infliximab 56.3%, placebo –3.2%; wk 50: infliximab 56.3%, placebo crossing to infliximab 72.5% Wk 10: &lt; 0.0001; Wk 24: &lt; 0.0001</td>
</tr>
<tr>
<td>Bianchi&lt;sup&gt;18&lt;/sup&gt;</td>
<td>Infliximab (5 mg/kg IV) at wks 0, 2, 6, 14, 22</td>
<td>9 psoriasis pts; 16 arthropathic pts</td>
<td>Open prospective</td>
<td>NAPSI&lt;sup&gt;8&lt;/sup&gt; at wks 0, 2, 6, 14, 16, 22</td>
<td>Steady improvement of NAPSI score in both groups; wk 22 mean NAPSI score in both groups was 0 At wk 22 &lt; 0.0001</td>
</tr>
<tr>
<td>Study</td>
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<tr>
<td>Cassetty&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Alefacept (15 mg IM) qwk × 12 wks</td>
<td>12 (only 6 w/nail psoriasis)</td>
<td>Open</td>
<td>NAPSI&lt;sup&gt;4&lt;/sup&gt;; 30% improvement at 12 wks</td>
<td>At 12 wks, 3/6 pts w/30% improvement NAPSI score</td>
</tr>
<tr>
<td>Feliciani&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Oral CsA vs oral CsA w/topical calcipotriol (50 µg/g)</td>
<td>54</td>
<td>Single-blind comparative</td>
<td>Improvement on 3-point scale based on area involved</td>
<td>Improvement at 3 mo: combined: 79% pts; alone: 48% pts</td>
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<tr>
<td>Mahrle&lt;sup&gt;21&lt;/sup&gt;</td>
<td>Oral CsA (2.5 mg/kg/day) at 10 wks, followed by oral CsA taper or topical anthralin vs oral etritinate (0.5 mg/kg/day) at 10 wks, followed by topical anthralin</td>
<td>210 (66.5% pts w/nail involvement)</td>
<td>RCT</td>
<td>4-point scale</td>
<td>Improvement in score at 10 wks (no statistically significant difference); CsA: 17.5% (90/137 improved); etritinate: 9.2% (47/60 improved); reduced score after second phase: CsA/CsA: 46.0%; CsA/anthralin: 26.2%; etretinate/anthralin: 24.1%</td>
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<td>Abell&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Needle-less-injected triamcinolone acetonide (5 mg/ml) 0.1 ml × 1–10 qwk × 3</td>
<td>7</td>
<td>Open</td>
<td>Improvement</td>
<td>5/7 improved</td>
</tr>
<tr>
<td>Abell&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Needle-less-injected triamcinolone acetonide (5 mg/ml) 0.1 ml qwk × 2–4</td>
<td>24 matrix only, 20 matrix &amp; onycholysis, 14 onycholysis only</td>
<td>Open</td>
<td>Improvement</td>
<td>21/24 improved (matrix only); 19/20 combined improved (matrix features more); 3/14 good results (onycholysis only)</td>
</tr>
<tr>
<td>Bleeker&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Needle-less-injected triamcinolone acetonide q2-3 wks × 3</td>
<td>92 (569 nails)</td>
<td>Open</td>
<td>Cure, improvement, status quo</td>
<td>In 225 pts w/involvement of matrix only, 197 w/improvement (86 recur); in 155 pts w/onycholysis only, 81 w/improvement (49 recur); In 167 pts w/involvement of matrix and onycholysis, 155 w/improvement in matrix and 78 w/improvement in onycholysis; 5/19 pts w/improvement in thickened nails (3 recur)</td>
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<tr>
<td>Bedi&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Injected triamcinolone acetonide qmo (0.1 ml of 10 mg/ml) using needle</td>
<td>7</td>
<td>Open</td>
<td>Graded improvement 0–3 (none to complete recovery)</td>
<td>4/7 complete recovery but relapsed (3 w/matrix involvement only); 2 w/moderate improvement had mixed disease: 1 no response</td>
</tr>
<tr>
<td>De Berker&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Triamcinolone acetonide (0.1 ml of 10 mg/ml × 4) after ring block w/lidocaine</td>
<td>19 (46 digits)</td>
<td>Open</td>
<td>Improvement in onycholysis, pitting, subungual hyperkeratosis, ridging, thickening</td>
<td>Onycholysis: 18/36 digits improved, 12 resolved; pitting: 9/20 digits improved, 4 resolved; hyperkeratosis: 16/16 digits improved, 4 resolved; ridging: 15/16 digits improved, 7 resolved; thickening: 10/12 digits improved, 8 resolved</td>
</tr>
<tr>
<td>Bleeker&lt;sup&gt;28&lt;/sup&gt;</td>
<td>Injected triamcinolone acetonide (5 mg/ml)</td>
<td>3 (treated w/needle-less-injector and syringe and needle) + 6 more pts</td>
<td>Open</td>
<td>Observed Improvement</td>
<td>In 3 pts treated w/both: similar results; w/needle-less: 80% success rate</td>
</tr>
<tr>
<td>Marx&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Oral methoxysalen (0.6 mg/kg) and UVA (320–300 nm) light × 2–3/wk</td>
<td>10</td>
<td>Open</td>
<td>Graded by 25% increment improvement in psoriatic nail features</td>
<td>Onycholysis, proximal nailfold, oil drop, crumbling improved; pitting did not improve</td>
</tr>
</tbody>
</table>

CsA: cyclosporine; c/w: compared with; mo: month; Obs: observation; RCT: double-blind randomized study; w/: with; wk: week; pt: patient; recur: recurrence.