Nail Therapeutics

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Conflicts of Interest

Accure Medical, LLC: Tri-Founder, Tri-Owner, Member Board of Directors
Diagnoses Seen Most Frequently In Nail Clinic:

- #1: Onychomycosis
- #2: Traumatic Onychodystrophy
- #3: Paronychia
- #4: DMC
- #5: Onycholysis
- #6: Psoriasis

- Also congenital malalignment of great toenails, LP, retronychia even though less common presenters
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Assumption for This Talk

• We have confirmed the clinical dx of onychomycosis by KOH, culture, DTM, PAS, or PCR

• Why must we confirm the dx by testing?
• Avoids unnecessary treatment
• Avoids disappointed pts that “fail” therapy
• Because trauma, LP, psoriasis, tumors etc. may mimic onychomycosis
“Don’t prescribe oral antifungal therapy for suspected nail fungus without confirmation of a fungal infection. Approximately half of all patients with suspected nail fungus do not have a fungal infection.”
Our Patient Has Decided They Want Treatment For Their Onychomycosis.
Tailor Treatment to the Individual Patient

- Pt is actively involved in deciding on their treatment plan
- Severity and number of nails involved
- Organism(s) causing the patients onychomycosis
- Co-morbidities
- Cost/insurance coverage
- Systemic drugs that may interact with oral antifungals
- Patient preferences
Stages of Treatment

- **Pre-Treatment**: discuss dx, expectations, options including RBA
- **During Treatment**: labs, Rx supplemental to antifungals
- **After Treatment**: prevention of recurrence
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Onychomycosis Pathogenesis

• Low prevalence of infection in spouses of pts w/onychomycosis compared to among their children suggests a genetic risk factor
• Inflammatory, traumatic, and neoplastic disorders all may cause nail dystrophy
• Dermatophyte (arthroconidia) in skin cornified layer use keratinases to invade a dystrophic nail plate
• Evidence that dermatophytes slow epithelial maturation

Therapeutic Options: May be Used Together

- Topical therapy
- Systemic therapy
- Devices
FDA Approved Rx for Treating Onychomycosis

**Adults**
- Terbinafine: continuous dose
- Itraconazole: continuous or pulsed dose
- Griseofulvin
- Ciclopirox
- Efinaconazole
- Tavaborole
- Lasers “temporary increase of clear nail in patients with onychomycosis”

**Children**
- None
FDA Definitions of Cure

- **Complete Cure:** Totally clear nail and neg KOH and neg cx

- **Mycologic Cure:** neg KOH and neg cx (sometimes neg KOH + neg PAS)

- **Clinical cure:** varies by study e.g. <10% clinical involvement + mycologic cure

Complete cure and clinical cure may not be possible due to nail bed/matrix injury or keratinization, underlying nail disease such as psoriasis, etc.
Therapeutic Options: May be Used Together

- Topical therapy
- Systemic therapy
- Devices
Topical Therapy for Onychomycosis

• Consider for mild to moderate distal subungual or superficial onycho in pts that can apply a med x 48 weeks
• Avoids the systemic risks of orals
• *Use as monotherapy: SWO, early DLSO when < 80% nail affected with lack of involvement of lunula, or systemics contraindicated
• Educate pt RE: Rx associated t. pedis, debride
• Then pt makes their educated choice

Specific Topicals

- All FDA approved in adults, applied qd x 48 weeks (toenails)
- 8% ciclopirox (Penlac®) lacquer, a hydroxypyridone derivative efficacy for dermatophytes, yeast, molds
- 10% efinaconazole (Jublia®) in alcohol, triazole, FDA approved 6/2014
- 5% Tavaborole (Kerydin®) in alcohol, first oxaborole, inhibits LeuRS to inhibit fungal protein synthesis, FDA approved 7/2014
- Clinical cure rates were greatest for efinaconazole >tavaborole>ciclopirox (not yet studied head to head)
- Efinaconazole & tavaborole seem to penetrate nail
Therapeutic Options: May be Used Together

- Topical therapy
- Systemic therapy: consider when >50% distal plate involved, >3-4 nails involved, proximal subungual onychomycosis, poor predictive factors
- Devices
Systemic Therapy for Onychomycosis

• *Terbinafine drug of choice: better cure rates, fewer drug interactions than itraconazole
• Lab monitoring: FDA recommends baseline liver transaminases
• **Debridement (manual or 20-40% urea) helps sx but not mycologic, clinical, complete cure

Included were 48 studies, total 10,200 patients with subungual ds.

They assessed 18 of these studies to be at high risk of bias, 1 was low

Moderate quality evidence that terbinafine more effective than itraconazole (RR 0.82, 95% CI 0.72-0.95, 15 studies, 2168 patients)

Seems to be no difference in side effects nor recurrence rate between terbinafine and itraconazole

Moderate evidence that itra and griseofulvin equally effective but griseofulvin has higher risk of side effects i.e. GI, allergy
Treatment of Onychomycosis in Children

- *Children seem to respond better to topicals than adults*
- **Systematic review of 7 studies (either randomized controlled trial, clinical trial, or retrospective analysis w/clin & mycologic confirmed onycho of >5 pts=itraconazole had highest (94%) clinical cure rate followed by ciclopirox (70%). No studies of terbinafine fit the authors definitions of cure so “other cure (80%)” was published.*


Itraconazole

• FDA approved for treatment of onychomycosis in adults
• Package insert: mycologic cure rate 61%, 54% and complete cure rates 47%, 14% for fingernails and toenails, respectively
• Black box warnings: Do not use in pts with ventricular dysfunction i.e. CHF; Do not use concomitant w/taking CYP2D6 inhibitors (colchicine…) as may lead to QT prolongation & ventricular tachycardia
Itraconazole: Better Coverage of Non-Dermatophytes than Terbinafine

**Children**
- 10mg/mL suspension
- 5mg/kg/day divided qd-BID
- Itraconazole tablets can be crushed and added to nonacidic food

**Adults**
- 200mg po qd OR
- Pulsed 200mg po BID x 7d/mo
- Renal dosing
- Many drug interactions, inhibitor of CYP3A4
Griseofulvin: liver failure, minor photosensitivity
500mg tabs, 125mg/5mL suspension

**Children**
- >2y/o
- 10-20 mg/kg/day po divided qd-qid, max 1g/d
- Take with high fat meal
- Fingernails=treat for >4 mo
- Toenails=treat for >6 mo

**Adults**
- 1000mg/day po divided qd-qid
- Many drug interactions including warfarin (↓ INR), ethinyl estradiol & levonorgestrel among others (↓hormonal contraceptive levels), - statins (reduced statin levels), tamoxifen (↓ levels), induced metabolism of kinase inhibitors e.g. erlotinib
Fluconazole: Off-label for Adults and Children

**Children**
- >2y/o
- 10mg/mL or 40mg/mL suspension
- Suppository: 10mg/kg, 200mg pulverized tablet in polyethylene glycol base
- 3-6mg/kg po qwk x 12-16wk
- 3-6mg/kg po qwk x 18-26wk

**Adults**
- Fingernails 150-450mg po qwk x 3-6 mo
- Toenails 150-450mg po qwk x 6-12mo
- Many drug interactions to consider
- *No stat significant improvement in mycologic cure over topicals

Fluconazole: Off Label for Adults & Children

- When taken for more than one dose it is Pregnancy D
- *Double blind randomized study (n=362), complete cure rates for toenails at 12 months=37%, 46%, and 48%, in subjects receiving 150 mg, 300 mg or 450 mg once per week, respectively
- **Recommended dosing=150 mg qwk x 6-9 months for fingernails, 12-18 months for toenails (↓concentration in nails)


Oral Antifungals On the Horizon

• Viamet VT-1161 is an inhibitor of CYP51 a metalloenzyme important in cell wall synthesis, phase II trials, may have better side effect profile

• Posaconazole: Phase IIB trial

Therapeutic Options: May be Used Together

- Topical therapy
- Systemic therapy
- Devices
Devices

- Lasers are FDA approved for temporary improvement in clear nail
- *Review of 2 laser studies: lower mycological cure rates (11%) than FDA approved oral & topical therapies (29-61%).
- **MOE Medical atmospheric plasma device, pilot study 19 enrolled, 13 completed study, 3 weekly Rx, 15.3% mycologic cure, 54.8% clinical cure defined as 3-5mm of clear nail

Stages of Treatment

- **Pre-Treatment:** discuss dx, expectations, options including RBA
- **During Treatment:** labs, Rx supplemental to antifungals
- **After Treatment:** prevention of recurrence
Rx Supplemental to Antifungals

- Keep nails short to debride infection, limit trauma and improve access of topicals to infection
- No cleaning under nails with sharp tools
- Treat footwear to limit reinfection & limit spread to other nails
- Treat associated tinea pedis esp. if using only topicals to nails
- Debridement: options inc. clippers, urea cream
Stages of Treatment

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Prevention of Recurrence of Onychomycosis

• Risk of recurrence=approx. 50%
• *Preventative strategies are important to attempt
• Keep nails short so that skin not nail hits surface first
• Do not clean under nails with sharp tools
• *Treat feet with topical antifungal (and treat shoes)
• Shoe treatment with ozone light and more typical is spray
• Educate to RTC early for signs of recurrence

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Acute Paronychia

- Pus, inflammation
- Cx pus
- Rx soaks +/- abx, remove spicule
- If proximal & persistent >24-48h despite Rx then release
- Epidermal growth factor inhibitors
Table 2. Proposed grading of severity of EGFR-associated cutaneous toxicity.

<table>
<thead>
<tr>
<th>Contributing factors</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact on patient’s quality of life</td>
<td>Not limiting day-to-day life activities</td>
<td>Limiting certain daily activities</td>
<td>Intolerable to patient</td>
</tr>
<tr>
<td>Intervention needed</td>
<td>Can be self-managed by the patient</td>
<td>Requires several treatments to manage</td>
<td>Requires intensive local and possibly systemic treatment to manage</td>
</tr>
<tr>
<td>Ability to continue EGFR treatment</td>
<td>No dose modification required</td>
<td>No dose modification required</td>
<td>Treatment discontinuation until symptoms improve to mild, and possible dose reduction</td>
</tr>
<tr>
<td>Example appearance</td>
<td>Skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Redness and flushing only, with or without itch</td>
<td>Papules, pustules and irritation (acneiform)</td>
<td>Crusted, eroded purulent acneiform lesions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Example of a severe EGFR-induced acneiform rash:</td>
</tr>
<tr>
<td></td>
<td>Nails</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nail-fold edema or erythema; disruption of the cuticle</td>
<td>Edema or erythema with discharge or nail-plate separation resulting in discomfort</td>
<td>Edema or erythema with discharge or nail-plate separation resulting in severe pain and reduced mobility</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Example of mild EGFR-induced paronychia</td>
<td>Example of moderate EGFR-induced paronychia</td>
<td>Example of severe EGFR-induced paronychia</td>
</tr>
</tbody>
</table>

Figure 1. Illustration indicating usual timeline of most common cutaneous toxicities.

Cycle 2 onwards
Skin toxicity assessment and management for patients continuing EGFRi treatment (cycle 2 onwards)

Is skin toxicity evident?
- Xerosis
- Eczema
- Acneiform rash
- Paronychia

Yes
- Continue to follow prophylactic advice, including the daily use of emollient cream and antiseptic soap substitute
- Treat aggressively and manage as follows depending on grading of severity, with review at every treatment cycle

No
- Record skin toxicity assessment in notes and continue to review at every treatment cycle
- Continue preventative treatment and advice as per cycle 1

Mild
Continue EGFRi and assess adherence to current supportive treatment. If adherence is poor, advise on correct use; if good, intensity treatment as follows:
- For acneiform rash: mild topical steroid +/- antifungal TDS until clinical improvement or review; and continue oral tetracycline (e.g. tetracycline or doxycycline) once daily for at least 12 weeks
- For scalp involvement: betamethasone 0.1% scalp application used daily until clinical improvement

Moderate
Treat as per mild and intensity treatment as follows:
- For acneiform rash: increase dose of oral tetracycline to BD for 4 weeks where appropriate
- For scalp involvement: potent topical steroid +/- antifungal TDS until clinical improvement or review
- For xerosis or eczema: consider switching emollient to a more greasy preparation (ointment)
- For pruritus: anti-histamine, such as hydroxyzine, once daily before bed where pruritus is disruptive to sleep
- For paronychia: potent topical steroid cream (betamethasone 0.1%) applied under occlusion until clinical improvement or review. If purulent, culture and prescribe oral antibiotic based on sensitivity

Severe
Defer EGFRi until symptoms have resolved to mild and consider dose reduction according to licence.
Treat as per moderate and intensity treatment as follows:
- For xerosis or eczema: switch to a more potent topical steroid +/- antifungal and use ointment preparation instead of cream.
  Advise more frequent application of emollient and switch to a more greasy preparation (ointment) if not already done so.
  Prescribe oral steroid (e.g. prednisolone), with or without gastroprotection; titrate down, for example from 20 mg to 5 mg OD over 14 days, and review (monitor blood sugars).
- For acneiform rash: switch to a lighter emollient.
  Switch to a moderate intensity topical steroid, e.g. 0.025% betamethasone valerate
  As for severe xerosis or eczema, prescribe oral steroid.
- For all severe cutaneous reactions, including paronychia: swab lesions for culture and susceptibility testing and prescribe antibiotic accordingly

Seek advice from dermatology department.
Chronic paronychia

- Chronic: inflammation & hyperplasia nail fold(s), confirm typical
- Rx=eliminate causes, gloves for wet/friction work, address any issues of pressure/gait, restore cuticle, topical antifungals/steroids, ILK prn, po fluconazole prn, rarely remove hypertrophied fold(s)
- Educate that nail plate changes grow out slowly
- Consider cx, bx, Xray esp. if recalcitrant & l nail
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Intraoperative: Digital Mucous Cyst

- No standard treatment, may recur after any/all
- Needling, scarification, other conservative methods, surgery
- Needling: <50% effective, 21 or 25 or other gauge needle
- Cryosurgery: <50% effective, I&D cyst then make ice ball freeze 15-30sec inc. 2mm around, thaw 60-90 sec.
- IL injection=highest rate recurrence (kenalog, sclerosants polidochenol or sodium tetradecyl sulfate)
## Digital Mucous Cysts

<table>
<thead>
<tr>
<th>Class</th>
<th>Recurrence Rate (%)</th>
<th>Tolerance</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeated needling</td>
<td>28–50</td>
<td>Painful; may decrease patient compliance(^70)</td>
<td>2–3% infection rate</td>
</tr>
<tr>
<td>Steroid/sclerosant injection</td>
<td>30–70</td>
<td>For some, only procedure to achieve long-term resolution</td>
<td>Risk of skin atrophy, pigmented changes(^11)</td>
</tr>
<tr>
<td>Cryosurgery</td>
<td>14–44</td>
<td>Painful</td>
<td>Possible significant scarring(^71); notching of proximal nail fold</td>
</tr>
<tr>
<td>Carbon dioxide laser</td>
<td>33</td>
<td>Quick procedure; low risk of infection</td>
<td>Possible injury to underlying nail matrix</td>
</tr>
<tr>
<td>Simple excision</td>
<td>&gt; 25</td>
<td>Higher theoretical chance of cure</td>
<td>Possible minor scarring</td>
</tr>
<tr>
<td>Infrared coagulation</td>
<td>14–22</td>
<td>Quick procedure; good cosmesis; minimal superficial tissue destruction(^68)</td>
<td>29% risk of blistering, pain, posttreatment erythema</td>
</tr>
</tbody>
</table>

Digital Mucous Cysts

- Few studies and those that exist have small numbers of pts
- Your approach?
- One surgical approach is creation of various flaps
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Treatment of Onycholysis

- Confirm no other dx i.e. associated onychomycosis, tumor
- Rx=keep nail short, limit irritants, gloves for wet work, role of candida controversial, pts usually expect Rx besides irritant avoidance, do not clean out under the nail (water only)
- If present >6-12 mos. likely permanent
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Treatment of Nail Psoriasis

• Lifetime incidence of nail involvement=80-90%
• Approx 5% of patients with psoriasis present with nail only ds
• Evaluate for psoriatic arthritis: in one study psoriatic nail changes were able to predict the onset of psoriatic arthritis with a risk ratio of 2.24¹

Treatment of Nail Psoriasis

• Topical steroids and calcipotriene
• ILK 2.5mg/mL-10mg/mL monthly to matrix &/or bed
• Systemic therapy as indicated for skin psoriasis can be tried weighing risks/benefits/alternatives
• NPF Medical Board Recs based on PubMed search 1947-2014, treatment recommendations made based on 4 clinical nail psoriasis scenarios

Recommendations of the NPF Medical Board

- Tx should balance skin ds, psoriatic arthritis, nail severity, QOL
- All pts should be evaluated for onychomycosis
- For nail only disease: topical steroids +/- dovonex initially
- If fail topicals, then adalimumab, etanercept, ILK, ustekinumab, MTX, acetretin are recommended
- For skin + nail ds: adalimumab, etanercept, ustekinumab
- For nail + joint ds: adalimumab, etanercept, ustekinumab, infliximab, MTX, apremilast, golimumab

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Congenital Malalignment of Great Toenails

• The reason to remember this dx is so we do not miss it & unnecessarily treat them with antifungals, etc.
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Clues to Distinguish Nail LP From Mimics

- Findings from skin examination i.e. LP vs psoriasis…elsewhere

- Clues of nail LP in patients with disease limited to the nails:
  - Abrupt onset
  - Multiple nails
  - Slow growth of nails*
  - Asymptomatic
  - Pain (pterygium)

- Often clues are not enough. Biopsy to confirm diagnosis of LP.
Biopsy

• Matrix vs Bed depending on examination
• Confirm dx with 3mm punch bx or lat. longitudinal bx
• Soaks BID
• Path should be typical, rarely +++plasma cells
Nail lichen planus: Clinical and pathologic study of twenty-four patients

Antonella Tosti, MD, Anna Maria Peluso, MD, Pier Alessandro Fanti, MD, and Bianca Maria Piraccini, MD Bologna, Italy

Background: We studied a large series of patients with lichen planus (LP) limited to the nails.

Objective: Our purpose was to review the clinical and histopathologic features of 24 patients with LP limited to the nails and to discuss treatment and long-term prognosis.

Methods: The records of 24 patients with biopsy-confirmed nail LP were analyzed. Clinical and follow-up data were obtained.

Results: Nail LP usually appears during the fifth or sixth decade of life. Neither gender-associated susceptibility nor seasonal influences were detected. In most cases, nail LP is self-limiting or promptly regresses with treatment. Recurrences of nail lesions as well as development of LP in other regions of the body are possible. The development of severe and early destruction of the nail matrix characterizes a small subset of patients with nail LP.

Conclusion: Approximately 25% of patients with nail LP have LP in other sites before or after the onset of nail lesions. Long-term observation indicates that permanent damage to the nail is rare even in patients with diffuse involvement of the matrix.

(J Am Acad Dermatol 1993;28:724-30.)

Clinical report

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Michela STARACE
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Nail lichen planus: response to treatment and long term follow-up

In our twenty years’ experience of dermatological visits specifically for nail diseases, we saw 105 patients with pathologically proven nail lichen planus. We prescribed treatment to 75 of these patients and we report here the results of treatment. Twenty-seven of these patients were followed-up for more than 5 years (mean follow-up was 10 years): 9 of them (9/27 = 33.3%) did not respond to treatment with steroids (intramuscular or intralesional), 18 were cured (18/27 = 66.7%), 11 relapsed (11/27 = 40.7%). This study is important for the fact that no one has previously published the results of such a long follow-up of patients with nail lichen planus.
When to Initiate Treatment?

1. After a histologic diagnosis of LP has been established
2. When the patient decides they will undertake the risks of the medical option(s)
3. When the patient understands that treatment will not reverse pterygium & may not completely reverse damage done
4. When the patient understands that nail LP may recur regardless of the treatment utilized
Before Start Rx: Establish Expectations

- May not totally normalize nails with any therapy
- Potential for recurrence after all therapies is well-established
- Topical therapies are ineffective
- Pterygium are irreversible
- IL steroids and systemic therapy are first line
- Risks IL steroids: pain, hematoma, skin atrophy, dyspigmentation
IL Steroids: Best As An Option When ≤3 Nails Involved

- Triamcinolone acetonide 2.5-5mg/mL total 0.5mL/nail
- Pain minimization techniques: vibration, cooling, distraction
- Repeat monthly x 2-6 months
- Discuss potential side effects including hemorrhage, pigmentary changes

Treatment Multiple (≥3) Nails

- 1st Line: triamcinolone acetonide 0.5-1mg/kg IM qmonth x 2-6 months
- Treat until proximal half of nail normalized
- If not improved by 6 months then stop
- Acetretin/etretinate, azathioprine
Assessment/Plan

- Clinical-path correlation=end stage LP
- Discussed working diagnosis
- Discussed Rx almost surely would not make any improvement
- Pt requested 3 mos IM Kenalog (dosed 1mg/kg/month)
- No improvement at 6 month follow-up
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What is the Optimal Next Intervention?

A. Topical class I steroid
B. Topical –azole plus topical class I steroid
C. Oral fluconazole plus topical class I steroid
D. Intralesional Kenalog
E. Nail plate avulsion
Diagnosis: Retronychia

- AKA Proximal Ingrowing of the Nail, Posterior Embedding of the Nail
- Trauma disturbs the longitudinal growth of the plate
- Results in multiple generations of nail plate misaligned beneath the proximal plate
- Presents as PNF paronychia, pain, granulation tissue
- Treatment: Avulsions, anti-inflammatory medication
- Culture if any concern for secondary infection
Retronychia: Proximal ingrowing of the nail plate

David A. de Berker, MRCP, Bertrand Richert, MD, PhD, Edith Duhard, MD, Bianca Maria Piraccini, MD, PhD, Josette André, MD, and Robert Baran, MD
Bristol, United Kingdom; Liège, Belgium; Tours and Cannes, France; and Bologna, Italy

- 2008 case series
- 19 cases over an 8 yr period
- Mean age=39 (range 14-71)
- 11/19 (58%) gave hx preceding trauma or systemic illness w/Beau’s lines
- 16/19 (85%) were women
- 16/19 were toes all of which were great toe, 3/19 were bilateral
- 3/19 were hand, 2 of those 3 were thumb only, 1 of 3 was thumb + index
- All w/cardinal features of proximal paronychia, elevation of proximal plate such that it was higher than distal edge
- In most the plate was thickened and yellow
- Granulation tissue present in 6/19 (32%), most often at lateral horn
Fig 4. The evolution and features of retronychia.

Figure 1. (a) Swelling deformity with tender paronychia, after injury of the three middle fingers of the right hand. (b) The three middle fingers of the left hand, without injury.

It is interesting to note the pathogenesis suggested by the few authors who have dealt with retronychia. In most cases affecting the big toes, it is likely that the precipitating event is pressure against the free edge, which pushes the nail backwards. This force could be repetitive as in jogging or hiking. Poorly fitting or tight-fitting footwear, such as high heels, can also be a causal factor.

Figure 2. (a) 3D sonographic anatomy of the normal nail. Longitudinal axis reconstruction shows the normal structures that compose the nail unit. The white line indicates the normal distance between the origin of the nail plate and the base of the distal phalanx (distal interphalangeal joint level). (b) 3D sonographic imaging in retronychia. Longitudinal axis reconstruction shows thickening of the proximal nail bed and proximal nail fold. Notice the location of the origin of the nail plate closer to the level of the distal interphalangeal joint. The white line indicating the distance between the origin of the nail plate and the base of the distal phalanx is dramatically shortened. PL, plate; NB, nail bed; Dph, distal phalanx; PNF, proximal nail fold; DIPJ, distal interphalangeal joint.
Take Home Points: Retronychia

- Painful proximal ingrowing of the nail plate
- Pathophysiology: trauma that separates matrix & plate
- Then as a new nail grows it pushes old one upward
- This causes inflammation of the PNF, Mimics paronychia
- Unlike paronychia the nail is yellow & the proximal plate higher than distal
- Observations by surgical authors=tighter than usual adherence of plate to bed and laxity of PNF
- Treatment=complete nail avulsion
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- #3: Paronychia
- #4: DMC
- #5: Onycholysis
- #6: Psoriasis

Also congenital malalignment of great toenails, LP, retronychia even though less common presenters
Thank you!
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