Brittle Nails

10

Solomon Geizhals and Shari R. Lipner

Abbreviations

FDA	Food and Drug Administration
HPCH	Hydroxypropyl chitosan
TOWL	Transonychial water loss

Anatomy of the Nail

The nail plate is a fully keratinized structure that is 0.5–1 mm thick and is produced by the germinative epithelium of the nail matrix. Under normal conditions, the mean growth rate of a fingernail is 3 mm/month and that of a toenail is 1 mm/month. The matrix consists of an epithelium that keratinizes without the formation of a granular layer and is made up of three distinct layers:

- The dorsal nail plate (0.08–0.1 mm thick) is produced by the proximal portion of the nail matrix and gives the nail plate its characteristic hardness and smoothness.
- The intermediate nail plate (0.3–0.5 mm thick) is produced by the distal matrix and gives the nail flexibility.
- The ventral nail plate (0.06–0.08 mm thick) is produced by the nail bed and is necessary for the adhesion to the nail plate [1].

Nail plate keratinocytes consist of 80–90% hard, hair-type keratin filaments and 10–20% soft, epithelial-type keratin filaments that are orientated in multiple directions. In the α-keratin filament predominant middle layer, the filaments are oriented perpendicularly to the growth axis. The dorsal and ventral layers are composed of epidermis-type keratin filaments which are oriented parallel and perpendicular to the growth axis [2].

Sulfur makes up approximately 10% and calcium makes up 0.2% of the nail plate by weight, respectively. The remaining principal minerals include magnesium, calcium, iron, zinc, sodium, and copper [3]. Healthy nails contain up to 5% lipids filling certain ampullar dilations of the dorsal plate and intercellular spaces in the ventral plate [1]. These lipids, particularly acylceramides, coupled with the disulfide bonds of cystine and desmosomes, are considered the main contributors to nail hardness and are referred to as the intercellular "cement" [4, 5]. They work in sync via cross-linking α-helix keratin fibers together between the corneocytes, all held together by hydrophobic interactions, forming a water-impermeable layer [6].

S. Geizhals
SUNY Downstate Medical School,
Brooklyn, NY, USA

S. R. Lipner (✉)
Weill Cornell Medicine, Department of Dermatology,
New York, NY, USA
e-mail: shl9032@med.cornell.edu

R. L. Baran (ed.), *Advances in Nail Disease and Management*, Updates in Clinical Dermatology,
https://doi.org/10.1007/978-3-030-59997-3_10

Risk Factors and Pathogenesis

The factors that are critical to the integrity of the nail plate include the following:

1. The intracellular skeleton structure of keratin fibrils
2. Keratin-associated proteins that form the matrix between keratin filaments
3. Lipid bilayers
4. Desmosomes

Epithelial growth and keratinization occur in both the nail matrix and nail bed and are responsible for creating a normal nail plate. Environmental factors, both chemical and mechanical, may damage intercellular adhesion of the nail plate corneocytes, causing lamellar peeling known as onychoschizia (Fig. 10.1). The longitudinal ridges and splits, known as onychorrhexis (Fig. 10.2), are caused by fluctuations in nail plate production by the matrix. Nail matrix vascularization and oxygenation are crucial for normal keratinization [7]. The primary pathology of brittle nails is believed to be secondary to nail plate hydration and/or nail matrix or corneocyte abnormalities. Family history and genetic predisposition contribute to the pathogenesis [8, 9].

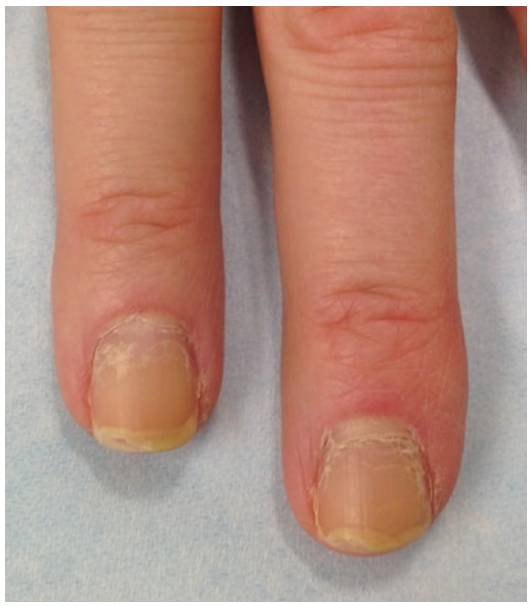

Fig. 10.1 Onychoschizia: lamellar splitting of the free edge of the nail plate generally attributed to intercellular fractures of nail plate corneocytes

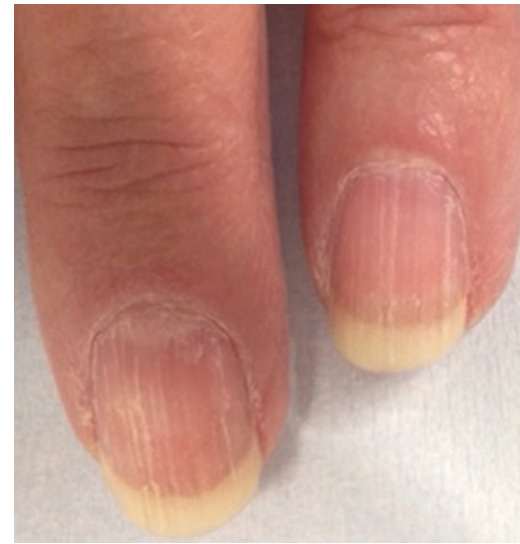

Fig. 10.2 Onychorrhexis: fissuring of the longitudinal nail plate generally attributed to nail matrix dysfunction

Nail plate hydration is thought to be a significant factor in the pathogenesis of brittle nails [10]. It was generally accepted that baseline nail water content is approximately 16–18%, and the nail becomes brittle when it becomes less than 16% and soft when greater than 25% [11]. Transonychial water loss (TOWL), defined as water escape through the nail plate, is relatively high compared to the stratum corneum, although this has been challenged [12–14]. It is difficult to replace water lost from the nail plate because extensive soaking paradoxically results in enhanced water loss, not rehydration [15].

Utilizing a "nail flexometer" on cadaver nails, Finlay et al. noted the increased flexibility of the nail plate after immersion in water, implying increased moisture content is a significant factor for flexibility. Moreover, they noted that the nail maintained its enhanced flexibility after the application of mineral oil or phospholipids on the nail, implying that one can trap the increased moisture with a hydrophobic seal [16]. Raman spectroscopic studies on the nail plate confirmed that mechanical properties are directly related to nail plate water content [17].

The importance of nail plate water content in the pathology of brittle nails has been challenged. In one study (n = 102), the authors found that there was no statistically significant difference in water content between patients with brittle nails (11.9%) and healthy patients (12.5%). Moreover, participants of the study who used hand moisturizers frequently had 6.57 greater odds to suffer from brittle nails (95% CI 1.35, 32.10) than those with healthy nails [8]. Nevertheless, while water content in it of itself may not be a risk factor for brittle nails, excessive hydration and desiccation likely disrupt intercellular lipid lamellae [18, 19]. Wetting and drying cycles of the nail plate can result in contraction and expansion of the nail, damaging corneocyte adhesion, specifically manifesting itself as in onychoschizia, in women, in thumb-sucking infants, and during the changing seasons [20–24]. This is supported by the finding of decreased sulfur content in 77.3% of patients (n = 55) with dystrophic nails, implying a paucity of disulfide bridges weakening the corneocyte-based infrastructure of the nail plate [25].

Occupational exposure to chemicals, thioglycolates, cement, solvents, alkalis, acids, anilines, salt, and sugar solutions can all dissolve intercellular lipids, causing fractures between corneocytes leading to brittle nails [26]. Although nail lacquer alone is not deemed a risk factor in and of itself, excessive use of polish removers, hardeners especially those containing formaldehyde, cuticle removers; special nail procedures such as nail wrapping, sculpturing, premixed acrylics, and gel polish; and the improper use of manicure tools can all create intercellular fissures in the nail plate [27–30]. Occupational contact with a variety of solutions and solvents can lead to progressive dehydration of the nail plate and is found in shoemakers, carpenters, and even tea pickers [31, 32].

The prevalence of brittle nails in these occupations may also be attributed to repetitive bouts of microtrauma, which may account for the increased prevalence found in chemical and medical personnel, photographers, painters, and musicians [1, 33]. Normal activities of daily living may also contribute to traumatic brittle nails such as typing, dialing, improper nail clipping, onychotillomania, and onychophagia [1, 34, 35]. Although the increased prevalence of brittle nails in women has been attributed to a heightened cosmetic consciousnesses, other factors are likely involved including household chores (either due to increased water exposure or microtrauma) [1], a constitutional fragility relative to males [23] (possibly due to their thinner nail matrix [36]), slower nail growth rates relative to men, [37] decreased lipid content in aging women [38], or possibly to postmenopausal changes [39].

Fungal infections can traumatize the nail plate, fracturing both intracellular and intercellular via fungal proteolytic activity, crumbling the nail plate, and increasing the susceptibility of idiopathic nail brittleness [21]. Although other dermatological conditions may cause brittleness, they often present in a variety of ways other than onychorrhexis and onychoschizia. These include the thinning, longitudinal ridging, and distal splitting of lichen planus [40] and lichen striatus; the longitudinal streak with distal splitting at the nail's free edge of Darier's disease [1]; the lamellar exfoliation of eczema; the rough, sandpapered nails of trachyonychia [41]; the grid-like and superficial pitting of alopecia areata [42]; and the irregular and deep pits of nail psoriasis [43]. The overlapping features of these pathologies led to the hypothesis that chronic inflammation contributes to brittleness [44].

Secondary nail brittleness can be caused by a variety of systemic diseases, nutritional deficiencies, and drug intake. Systemic diseases generally cause brittle nails via effects on nail keratinization. Arteriopathy, vasculopathy, and neuropathy may lead to poor perfusion of the nail matrix, producing a weak nail plate. This can be seen in diabetes, Raynaud's phenomenon, polycythemia vera [45], and systemic sclerosis [46]. Thyroid disease, more commonly in hypo- than hyperthyroid, can cause both soft and brittle nails but is often reversible following successful therapy [47]. Increased nail fragility, onycholysis, and longitudinal ridging can all occur in Sézary syndrome [48], amyloidosis [49], graft-versus-host disease, and rheumatoid arthritis [50]. Syphilis [51] and leprosy [52] have been associated with nail thinning, fragility, and brittleness. Liver disease, such as cirrhosis, HBV,

and HCV, can all cause a variety of nail changes including brittle nails [53]. Chronic infectious diseases including pulmonary tuberculosis, empyema, bronchiectasis, and sarcoidosis can impair nail formation causing brittleness [9]. A case of recurrent malignant glucagonoma was diagnosed due to brittle nails and dyspareunia [54]. Nail pathologies, including trachyonychia [55], melanoma, squamous cell carcinoma, warts, onychopapillomas, and pyogenic granulomas, may present with longitudinal abnormalities that can present as fragile nails [56].

Nutritional deficiencies may result to nail fragility and thinning. Vitamin A, vitamin B6, vitamin B12, vitamin C, vitamin D, and vitamin H (biotin) are all integral to nail growth and improve nail strength while reducing moisture loss [1]. Although the pathogenesis is unknown,the concentration of these elements in brittle nails is not significantly different from the concentration in normal nails; however, a deficiency of iron, zinc, calcium, and magnesium can all lead to brittle nails and onycholysis [57, 58]. As such, a decreased dietary water or food intake, a common phenomenon among and those suffering from anorexia nervosa [59], bulimia [60], and the elderly [3], can all lead to an increased prevalence of brittle nails.

Systemic drugs such as chemotherapeutics, antiretrovirals, and retinoids can all contribute to the pathology of brittle nails [61–63]. Patients treated with MEKIs, EGFRIs, mTOR inhibitors, and ibrutinib have all been noted to cause onychodystrophy including brittle nails and possibly a slower nail growth rate [64]. With antiretrovirals and retinoids, most notably etretinate [65] and oral isotretinoin [66], it is common for the nail plate to break easily and give rise to tiny spicules that penetrate the periungual furrows causing the formation of pseudo-pyogenic granulomas [1]. Abnormal keratinization may result from previous irradiation or arsenic use, leading to brittle nails as well [3].

Pregnancy can also induce nail changes including transverse grooving, brittleness, and softening. These changes may occur as early as the sixth week of pregnancy. These changes can be attributed to rapid nail growth causing delayed keratin maturation due to increased estrogen [67]. On the other hand, the slow linear growth of nails has also been implicated by some as a cause for the greater prevalence of brittle nails in the elderly, whose nails grow much more slowly than in the young [68], and in women in general [37], leaving the status of nail growth as an impetus for brittleness unclear and may merit further investigation.

Epidemiology

In 1940, Silver et al., in a comprehensive cross-sectional study of brittle nails, showed that 18.4% (n = 994) of the general population were affected by brittle nails. Similar prevalence of 19.6% was later confirmed by Lubach et al. in 1986 (n = 1584) [27, 31]. Silver and Lubach both noted that women were affected in a 2:1 ratio compared to men, with similar findings replicated in a cross-sectional study of patients wearing daily occlusive gloves [27, 31, 69]. Gequelim et al. observed that 57% of female dermatological patients suffered from brittle nails but commented that the higher percentage may be due to selection bias, as the patient population was limited to dermatological patients, as opposed to the prior studies which included a more generalized populace. Additionally, the methodology used by Gequelim employed the van de Kerkhof criteria for brittle nails, while the older studies utilized subjective analysis [7, 34].

Those greater than 60 years old have a greater prevalence of brittle nails [70], with one study (n = 200) finding that 67.5% of elderly Egyptians were affected compared to 5% under the age of 60 ($p < 0.001$) [71]. Lubach found this discrepancy more pronounced in males; only 12% of younger males were affected compared to 31% of elderly males, while 29% of younger females reported brittle nails compared to 36% of elderly females [12]. Women between the ages of 40–60 most frequently suffer from brittle nails, with one study finding that it affected up to 30% of women over 50 years old [1]. Lubach noted that 35% of women aged 31–40 (n = 113) also suffered from brittle nails [31]. Although not statistically sig-

nificant, two studies found an increased prevalence of brittle nails, specifically onychoschizia, in infants [20, 72].

Brittle nails are more common in fingernails compared to toenails, with one study having 94% and 6% affected, respectively [34]. Increased frequency of involvement of the first three digits of the dominant hand has been reported with Gequelim reproducing these findings albeit without differentiating between dominant and nondominant hands [34, 73]. However, Weistenhöfer et al. only found increased prevalence in the first digit [69]. Increased prevalence of brittleness in the hands relative to feet, as well as to the first three digits, can be attributed to increased exposure to the environment and trauma of those areas, specifically in those presenting with onychoschizia [22, 74]. In contrast, onychorrhexis is a phenomenon largely associated with aging [1].

One survey-based study found that patients who were black/mixed race, were atopic, or had a depressed mood had an increased perception of nail fragility even though there was no evidence of such according to clinical definitions [34]. Patients tend to perceive brittle nails differently from physicians, often skewing survey data and potentially underreporting true prevalence; hence, physical examination is crucial for data records [8].

History and Clinical Presentation

Brittle nails are generally presumed to be a cosmetic problem, but when dystrophy is severe, functional capabilities can be affected as well. Patients generally complain of soft, nongrowing, dry, weak, and easily breakable nails [9]. Although some have proposed as many as six clinical findings of brittle nails [65], much of the literature tends to emphasize two pathologic variants [8]:

1. Onychorrhexis—superficial, parallel longitudinal ridging in the nail surface that can often result in splitting on the distal free edge (see Fig. 10.2). It may also present with multiple crenulated splits, characterized by triangular fragments at the free edge that are easily torn off [7]. Onychorrhexis has been reported as the strongest association with nail fragility perception [34].
2. Onychoschizia—horizontal layering frequently seen in the form of lamellar splitting of the distal free edge of the nail plate (see Fig. 10.1). Onychoschizia may also include breaking of the lateral edges, causing transverse splitting which can lead to loosening of at least one-third of the distal nail plate [7].

Kerkhof et al. and Sherber et al. each proposed their own semiquantitative grading system that allows for the calculation of an average score reflecting the level of severity, thereby allowing an objective means of following progression because in many patients, brittle nail changes are mostly subjective [7, 75]. Although primarily a clinical diagnosis, dermoscopy is a useful tool in diagnosing brittle nails. It can assist in identifying longitudinal ridges, superficial pits, and lamellar splitting especially in early stages of mild disease [76].

Treatment and Management

Therapeutic approaches to brittle nails should first be targeted to eliminating eliciting factors followed by general measures and more specific therapies. If possible, it is important to determine and treat brittle nail etiology, such as nutritional deficiency and dermatological, infectious, or a systemic condition, as that may improve or even cure the nail brittleness [9]. Secondary nail brittleness often damages the nail matrix and tends to involve the entire nail plate. However, most patients with brittle nails have an idiopathic nail fragility, usually caused by internal or external damage to the intercellular keratinocytes causing onychorrhexis and onychoschizia. Physicians should always inquire if both the fingernails and toenails are brittle. In majority of the cases, only the fingernails are affected. It is therefore integral to stress that external factors play a pivotal role [56]. As mentioned above, onychorrhexis is more

associated with older age and onychoschizia with water exposure; however, this is not absolute.

Some general measures focus on increasing the water content of the nail, especially in onychoschizia, as well as minimizing trauma (Table 10.1). Frequent hydration by soaking in lukewarm water for 15 minutes daily is helpful [77]. Gloves are recommended to reduce prolonged water immersion and avoidance of irritants, although extensive use of occlusive gloves can also lead to softened and brittle nails [69]. Avoidance of hand sanitizers that contain triclosan is preferred as triclosan eliminates water from the nail plate to a greater extent than traditional washing [56]. Patients are also advised to limit the use of nail polish removers (especially those that are acetone based), nail prostheses, and gel and acrylic nails. Identifying and subsequently minimizing microtrauma that includes any rubbing, friction, and drying are recommended. This is especially common during improper and repetitive manipulations in nail salons where multiple risk factors are commonplace. Patients should remain vigilant in avoiding cuticle tampering and the use of sharp instruments under the nail plate surface for cleaning, as well as having nails filed in only one direction [56]. The nails should be kept short and squared to minimize trauma, and after any soaking, nails can be rehydrated with topical moisturizers [1].

Many supplements including a multitude of vitamins, oligo-elements, and amino acids claim to improve brittle nails. These include biotin (vitamin H), application of essential fatty acids, ingestion of vitamin C, vitamin D, primrose oil, ascorbic acid, pyridoxine, amino acids, silicon [78] and gelatin [79], L-methionine, keratin, pantothenic acid, salt, millet, yeast, chromium, and rhodanates [80, 81]. Topical gelatin and botanical extracts are promoted to strengthen brittle nails, but no clear evidence exists [76]. Iron supplementation may be considered when systemic ferritin levels are below 10 ng/mL [1]. Oral γ-linolenic acid (GLA)-rich borage oil has been promoted for treating brittle nails based on anecdotal evidence that prostaglandin E1 helps improves the strength of keratin-dependent tissues [21]. One recent study (n = 25) found that after ingestion of 2.5 g of a specific bioactive collagen peptides (BCP, VERISOL®), brittle nails improved by 88% via clinical assessment, as well as causing a notable decrease in frequency of broken nails. It was hypothesized that the improvement was due to increased protein intake and the stimulatory effects of collagen peptides on epidermal and dermal metabolism [82]. As an open, non-controlled trial, certain inherent biases should not be discounted, including potential behavioral changes of some of the patients.

Marked biotin deficiency is associated with poor nail quality [80]. After it was discovered that biotin improved the hardness of pig claws and horse hoofs [83], there was interest in this vitamin for treating human brittle nails, which are also keratin based. Biotin, an important regulator of lipid synthesis, is believed to be beneficial by improving the quality of intercellular lipids [21]. Subsequent trials and studies were done which showed some improvement in firmness and hardness of the nail after taking varying dosages of oral biotin [84, 85]; however, the parameters of these studies were not ideal, including small sample size and unknown baseline biotin levels. Likely due to its low cost, over-the-counter availability, and glamorization in the media, biotin has become an overwhelmingly popular recommendation from physicians to improve skin, hair, and nails [86]. However, a recent warning issued by the Food and Drug Administration (FDA) stated that ingestion of biotin can significantly interfere with laboratory tests [87], including some

Table 10.1 Recommendations for treatment of brittle nails: general measures

General measures
Soaking nails in lukewarm water for 15 min daily
Wearing gloves (avoiding prolonged water and irritant exposure)—ideally cotton gloves worn inside rubber gloves
Avoidance of triclosan-based hand sanitizers
Limit nail cosmetics (nail paint removers, prostheses, gels, and acrylics)
Minimizing nail trauma (overzealous manicurists, nails should be kept short and squared, avoiding shattering/chipping of free edge via nail filing in only one direction and using sharp nail cutters)
Moisturizing the proximal nail plate and cuticle

immunoassays, troponins, and thyroid function tests. As the evidence supporting biotin is weak and may have adverse health effects [80], the risks and benefit of treatment with biotin for nail diseases should be carefully weighed for each nail patient [88, 89].

Stern et al. reported that those that applied hand emollients frequently had a high prevalence of brittle nails [8]; nevertheless, moisturizing the periungual area has been recommended, especially with emollients containing phospholipids [16]. Since TOWL is high during water immersion, nail water content may be increased with a hydrophobic seal [90] or moisturizer. Urea (5–20%) and alpha hydroxy acid (5–10%)-based moisturizers are both efficacious options in increasing water-holding capacity of the nail. The hydration is only temporary, however requiring two applications per day, but too frequent applications can wear away the nail plate. Moisturizers rich in glycerin and petrolatum should be applied more frequently than twice per day [15]. Moisturizing while occluding with cotton gloves or saran wrap is helpful, preferably at bedtime for at least three months, to help increase emollient penetration [91].

Cosmetic treatments may camouflage nail abnormalities but do not address the underlying issue and may cause adverse reactions. These include nail polishes, hardeners, strengthening agents, builders, wraps, and artificial nails. Lacquers or polishes typically enhance nail hardness and prevent contact of detergents with the nail. Nail polish slows down water vapor loss from 1.4 to about 0.6 mg/cm^2/h, stabilizing water content, although this is variable depending on the type of polish used [92, 93]. However, the continuous use of nail polish can damage the superficial layers of the nail plate, resulting in fine and scaling white spots on the nail plate. Hardeners are theoretically ideal for soft nails; however, they contain formaldehydes. Formaldehydes strengthen the nail plate by creating more keratin cross-links but are also drying. Strengtheners are recommended for fully developed nails that are prone to splitting, while builders for thin, poorly formed nails. Gel nails, wraps, and artificial nails are mainly meant to afford protection and camouflage [91, 94]. Although these cosmetics have some utility, use of nail polish remover causes increased nail dehydration and increased risk of brittleness [15]. Some precautions may be instituted with gel nails to avoid these adverse effects, including only applying one layer of gel and decreasing acetone nail remover exposure if feasible [94].

Prescription medications are also utilized to treat brittle nails, with most based on the principle of restoring the affected nail and maintaining a normal degree of hydration (Table 10.2). Since it was believed that chronic inflammation plays a role in brittle nails, a randomized controlled study (n = 24) was performed utilizing topical cyclosporine to treat this condition. There was no statistically significant difference between cyclosporine with emulsion and emulsion alone ($p < 0.05$ each) when comparing each with untreated brittle nails [95]. In an open-label study (n = 20), patients with brittle nails applied tazarotene 0.1% cream twice daily for 24 weeks. A 89.5% subjective improvement was endorsed by the patients in surveys, and a semiquantitative grading system showed a 73.7% overall improvement in brittleness [75]. Genadur® is a hydrosoluble lacquer formulated from *Equisetum arvense*, or horsetail, extract, methylsulfonylmethane and hydroxypropyl chitosan (HPCH) [96]. When applied to the nails, it forms a highly elastic, smooth, and almost invisible film that adheres to the nail structures, protecting them against physical injuries [4]. In a comparative study (n = 34) between HPCH-based lacquer and another lacquer of a similar composite-lacking HPCH, there was a 74% overall clinical improvement and an 80% improvement in cases of severe onychoschizia noted by the investigators [97]. Another available topical is a lacquer made of 16% polyurea urethane, marketed as Nuvail™, that, when applied to the nails, adheres tightly to the surface providing a protective layer that prevents direct injury, provides mechanical support, and possibly augments the formation of new, healthy nail from the nail matrix by improving cellular migration [98].

Table 10.2 Medical treatment of brittle nails and supporting evidence

Topical medication	Supporting study	Proposed mechanism of action	Treatment regimen
Topical cyclosporine emulsion 0.05%	Mackay-Wiggan et al. [95] 36-week, single-center, double-blind, randomized study *n* = 24 90% improvement based on patient surveys	Anti-inflammatory action coupled with moisturizing emulsion	Twice daily for 24 weeks
Tazarotene cream 0.1%	Sherber et al. [75] 36-week, open-label, single-center, investigator-initiated trial *n* = 20 73.7% clinical improvement	Receptor-selective synthetic retinoid Normalizes epidermal differentiation and reduces inflammation	Twice daily for 24 weeks
Hydroxypropyl chitosan-based lacquer	Sparavigna et al. [97] 4-week, open label, randomized hand selection to either HPCH-based or non-HPCH-based, single-center trial *n* = 34 Clinical improvement in 80% in those with severe onychoschizia	Combination of horsetail extract, methylsulfonylmethane, and hydroxypropyl chitosan Strengthen the nail, supports nail growth, and improves hydration	Once daily application at bedtime
16% polyurea-urethane	None to date Anecdotal evidence	Adheres to the surface providing a protective layer and mechanical support Enhances cellular migration	Once daily application at bedtime

Conclusion

Brittle nails are a common, yet complex problem that is distressing for patients and physicians alike. Currently, there is a lack of consensus regarding multiple aspects of brittle nails including degree of physical manifestations, pathophysiology, and treatment regimens. If an underlying cause cannot be found, then the brittle nails is most likely multifactorial, caused by a combination of intrinsic nail fragility and environmental exposure to damaging substances. General preventative measures including minimizing nail trauma, avoiding prolonged water exposure, limiting nail cosmetics, and moisturizing should always be advised, and tazarotene cream, HPCH-based lacquer, or 16% polyurea-urethane can also be helpful.

References

1. Iorizzo M, Pazzaglia M, M Piraccini B, Tullo S, Tosti A. Brittle nails. J Cosmet Dermatol. 2004;3(3):138–44.
2. Garson J, Baltenneck F, Leroy F, Riekel C, Müller M. Histological structure of human nail as studied by synchrotron X-ray microdiffraction. Cell Mol Biol (Noisy-le-Grand, France). 2000;46(6):1025–34.
3. Cashman MW, Sloan SB. Nutrition and nail disease. Clin Dermatol. 2010;28(4):420–5.
4. Iorizzo M. Tips to treat the 5 most common nail disorders: brittle nails, onycholysis, paronychia, psoriasis, onychomycosis. Dermatol Clin. 2015;33(2):175–83.
5. Wertz PW, Swartzendruber DC, Abraham W, Madison KC, Downing DT. Essential fatty acids and epidermal integrity. Arch Dermatol. 1987;123(10):1381–4.
6. Gniadecka M, Nielsen OF, Christensen DH, Wulf HC. Structure of water, proteins, and lipids in intact human skin, hair, and nail. J Investig Dermatol. 1998;110(4):393–8.
7. van de Kerkhof PC, Pasch MC, Scher RK, Kerscher M, Gieler U, Haneke E, et al. Brittle nail syndrome: a pathogenesis-based approach with a proposed grading system. J Am Acad Dermatol. 2005;53(4):644–51.
8. Stern DK, Diamantis S, Smith E, Wei H, Gordon M, Muigai W, et al. Water content and other aspects of brittle versus normal fingernails. J Am Acad Dermatol. 2007;57(1):31–6.
9. Shemer A, Daniel CR III. Common nail disorders. Clin Dermatol. 2013;31(5):578–86.
10. Samman P. Nail formation and some nail disorders. J Soc Cosmet Chem. 1972;23:405–13.
11. Scher RK. Brittle nails. Int J Dermatol. 1989;28(8):515–6.
12. Murdan S. Nail disorders in older people, and aspects of their pharmaceutical treatment. Int J Pharm. 2016;512(2):405–11.

13. Jemec G, Agner T, Serup J. Transonychial water loss: relation to sex, age and nail-plate thickness. Br J Dermatol. 1989;121(4):443–6.
14. Walters K, Flynn G. Permeability characteristics of the human nail plate. Int J Cosmet Sci. 1983;5(6):231–46.
15. Draelos ZD. Cosmetic consultation understanding and treating brittle nails. Cosmet Dermatol. 2009;22(12):598–609.
16. Finlay AY, Frost P, Keith AD, Snipes W. An assessment of factors influencing flexibility of human fingernails. Br J Dermatol. 1980;103(4):357–65.
17. Wessel S, Gniadecka M, Jemec GB, Wulf HC. Hydration of human nails investigated by NIR-FT-Raman spectroscopy. Biochim Biophys Acta. 1999;1433(1–2):210–6.
18. Warner RR, Stone KJ, Boissy YL. Hydration disrupts human stratum corneum ultrastructure. J Investig Dermatol. 2003;120(2):275–84.
19. Farran L, Ennos AR, Eichhorn SJ. The effect of humidity on the fracture properties of human fingernails. J Exp Biol. 2008;211(23):3677–81.
20. Sarifakioglu E, Yilmaz A, Gorpelioglu C. Nail alterations in 250 infant patients: a clinical study. J Eur Acad Dermatol Venereol. 2008;22(6):741–4.
21. Duarte AF, Correia O, Baran R. Nail plate cohesion seems to be water independent. Int J Dermatol. 2009;48(2):193–5.
22. Wallis MS, Bowen WR, Guin JD. Pathogenesis of onychoschizia (lamellar dystrophy). J Am Acad Dermatol. 1991;24(1):44–8.
23. Lubach D, Beckers P. Wet working conditions increase brittleness of nails, but do not cause it. Dermatology. 1992;185(2):120–2.
24. Egawa M, Ozaki Y, Takahashi M. In vivo measurement of water content of the fingernail and its seasonal change. Skin Res Technol. 2006;12(2):126–32.
25. Klauder JV, Brown H. Sulphur content of hair and of nails in abnormal states: II. Nails. Arch Dermatol Syphilol. 1935;31(1):26–34.
26. Runne U, Orfanos C. The human nail: structure, growth and pathological changes. Curr Probl Dermatol. 1981;9:102.
27. Silver H, Chiego B. Nails and nail changes: III. Brittleness of nails (fragilitas unguium). J Investig Dermatol. 1940;3(5):357–74.
28. Chen AF, Chimento SM, Hu S, Sanchez M, Zaiac M, Tosti A. Nail damage from gel polish manicure. J Cosmet Dermatol. 2012;11(1):27–9.
29. Baran R. Nail cosmetics. Am J Clin Dermatol. 2002;3(8):547–55.
30. Rieder EA, Tosti A. Cosmetically induced disorders of the nail with update on contemporary nail manicures. J Clin Aesthet Dermatol. 2016;9(4):39.
31. Lubach D, Cohrs W, Wurzinger R. Incidence of brittle nails. Dermatologica. 1986;172(3):144–7.
32. Tan C, Zhu WY. Thumbnail lamellar onychoschizia in a tea-picker. Int J Dermatol. 2006;45(11):1390–1.
33. Piraccini BM, Antonucci A, Iorizzo M, Pazzaglia M, Tosti A. Occupational nail fragility in a professional violist. Contact Dermatitis. 2004;51(1):35–6.
34. Gequelim GC, Kubota CY, Sanches S, Dranka D, Mejia MM, Sumiya FM, et al. Perception of brittle nails in dermatologic patients: a cross-sectional study. An Bras Dermatol. 2013;88(6):1022–5.
35. Baran R, Moulin G. The bidet nail: a French variant of the worn-down nail syndrome. Br J Dermatol. 1999;140(2):377.
36. Wollina U, Berger M, Karte K. Calculation of nail plate and nail matrix parameters by 20 MHz ultrasound in healthy volunteers and patients with skin disease. Skin Res Technol. 2001;7(1):60–4.
37. Dahdah MJ, Scher RK. Nail diseases related to nail cosmetics. Dermatol Clin. 2006;24(2):233–9, vii.
38. Brosche T, Dressler S, Platt D. Age-associated changes in integral cholesterol and cholesterol sulfate concentrations in human scalp hair and finger nail clippings. Aging Clin Exp Res. 2001;13(2):131–8.
39. Helmdach M, Thielitz A, Röpke E-M, Gollnick H. Age and sex variation in lipid composition of human fingernail plates1. Skin Pharmacol Physiol. 2000;13(2):111–9.
40. Tziotzios C, Lee JY, Brier T, Saito R, Hsu C-K, Bhargava K, et al. Lichen planus and lichenoid dermatoses: clinical overview and molecular basis. J Am Acad Dermatol. 2018;79(5):789–804.
41. Jacobsen AA, Tosti A. Trachyonychia and twenty-nail dystrophy: a comprehensive review and discussion of diagnostic accuracy. Skin Appendage Disord. 2016;2(1–2):7–13.
42. Chelidze K, Lipner SR. Nail changes in alopecia areata: an update and review. Int J Dermatol. 2018;57(7):776–83.
43. Choi JW, Kim BR, Seo E, Youn SW. Identification of nail features associated with psoriasis severity. J Dermatol. 2017;44(2):147–53.
44. Kechijian P. Brittle fingernails. Dermatol Clin. 1985;3(3):421–9.
45. Singal A, Arora R. Nail as a window of systemic diseases. Indian Dermatol Online J. 2015;6(2):67.
46. Marie I, Gremain V, Nassermadji K, Richard L, Joly P, Menard J-F, et al. Nail involvement in systemic sclerosis. J Am Acad Dermatol. 2017;76(6):1115–23.
47. Jabbour SA. Cutaneous manifestations of endocrine disorders. Am J Clin Dermatol. 2003;4(5):315–31.
48. Damasco FM, Geskin LJ, Akilov OE. Nail changes in Sezary syndrome: a single-center study and review of the literature. J Cutan Med Surg. 2019;23:380–7.
49. Fanti P, Tosti A, Morelli R, Galbiati G. Nail changes as the first sign of systemic amyloidosis. Dermatology. 1991;183(1):44–6.
50. Motswaledi MH, Mayayise M. Nail changes in systemic diseases. S Afr Fam Pract. 2010;52(5):409–13.
51. Noriega L, Di Chiacchio NG, Rezende FC, Di Chiacchio N. Periungual lesion due to secondary syphilis. Skin Appendage Disord. 2016;2(3–4):116–9.
52. Kaur I, Chakrabarti A, Dogra S, Rai R, Kumar B. Nail involvement in leprosy: a study of 300 patients. Int J Lepr Other Mycobact Dis. 2003;71(4):320–7.

53. Salem A, Gamil H, Hamed M, Galal S. Nail changes in patients with liver disease. J Eur Acad Dermatol Venereol. 2010;24(6):649–54.
54. Chao SC, Lee JY. Brittle nails and dyspareunia as first clues to recurrences of malignant glucagonoma. Br J Dermatol. 2002;146(6):1071–4.
55. Gordon KA, Vega JM, Tosti A. Trachyonychia: a comprehensive review. Indian J Dermatol Venereol Leprol. 2011;77(6):640–5.
56. Dimitris R, Ralph D. Management of simple brittle nails. Dermatol Ther. 2012;25(6):569–73.
57. Lubach D, Wurzinger R. Trace elements in samples of brittle and nonbrittle finger nails. Derm Beruf Umwelt. 1986;34(2):37–9.
58. Seshadri D, De D. Nails in nutritional deficiencies. Indian J Dermatol Venereol Leprol. 2012;78(3):237.
59. Swenne I, Engström I. Medical assessment of adolescent girls with eating disorders: an evaluation of symptoms and signs of starvation. Acta Paediatr. 2005;94(10):1363–71.
60. Schulze UM, Pettke-Rank CV, Kreienkamp M, Hamm H, Bröcker EB, Wewetzer C, et al. Dermatologic findings in anorexia and bulimia nervosa of childhood and adolescence. Pediatr Dermatol. 1999;16(2):90–4.
61. Bitar C, Farooqui MZ, Valdez J, Saba NS, Soto S, Bray A, et al. Hair and nail changes during long-term therapy with ibrutinib for chronic lymphocytic leukemia. JAMA Dermatol. 2016;152(6):698–701.
62. Dika E, Patrizi A, Ribero S, Fanti PA, Starace M, Melotti B, et al. Hair and nail adverse events during treatment with targeted therapies for metastatic melanoma. Eur J Dermatol. 2016;26(3):232–9.
63. Piraccini BM, Iorizzo M, Antonucci A, Tosti A. Drug-induced nail abnormalities. Expert Opin Drug Saf. 2004;3(1):57–65.
64. Lacouture M, Sibaud V. Toxic side effects of targeted therapies and immunotherapies affecting the skin, oral mucosa, hair, and nails. Am J Clin Dermatol. 2018;19(Suppl 1):31–9.
65. Baran R, Schoon D. Nail fragility syndrome and its treatment. J Cosmet Dermatol. 2004;3(3):131–7.
66. Önder M, Öztas MO, Öztas P. Isotretinoin-induced nail fragility and onycholysis. J Dermatol Treat. 2001;12(2):115–6.
67. Erpolat S, Eser A, Kaygusuz I, Balci H, Kosus A, Kosus N. Nail alterations during pregnancy: a clinical study. Int J Dermatol. 2016;55(10):1172–5.
68. Geyer AS, Onumah N, Uyttendaele H, Scher RK. Modulation of linear nail growth to treat diseases of the nail. J Am Acad Dermatol. 2004;50(2):229–34.
69. Weistenhöfer W, Uter W, Drexler H. Protection during production: problems due to prevention? Nail and skin condition after prolonged wearing of occlusive gloves. J Toxic Environ Health A. 2017;80(7–8):396–404.
70. Abdullah L, Abbas O. Common nail changes and disorders in older people: diagnosis and management. Can Fam Physician. 2011;57(2):173–81.
71. El-Domyati M, Abdel-Wahab H, Abdel-Azim E. Nail changes and disorders in elderly Egyptians. J Cosmet Dermatol. 2014;13(4):269–76.
72. Chinazzo M, Lorette G, Baran R, Finon A, Saliba E, Maruani A. Nail features in healthy term newborns: a single-centre observational study of 52 cases. J Eur Acad Dermatol Venereol. 2017;31(2):371–5.
73. Singh G, Haneef NS, Uday A. Nail changes and disorders among the elderly. Indian J Dermatol Venereol Leprol. 2005;71(6):386.
74. Oranges T, Aleid N, Faleri S, Tosti A. Patch test nails. Contact Dermatitis. 2016;75(6):394–5.
75. Sherber NS, Hoch AM, Coppola CA, Carter EL, Chang HL, Barsanti FR, et al. Efficacy and safety study of tazarotene cream 0.1% for the treatment of brittle nail syndrome. Cutis. 2011;87(2):96–103.
76. Tosti A, Piraccini BM. Nail disorders. St. Louis: Elsevier; 2018.
77. Maddy AJ, Tosti A. Hair and nail diseases in the mature patient. Clin Dermatol. 2018;36(2):159–66.
78. Lassus A. Colloidal silicic acid for oral and topical treatment of aged skin, fragile hair and brittle nails in females. J Int Med Res. 1993;21(4):209–15.
79. Rosenberg S, Oster KA, Kallos A, Burroughs W. Further studies in the use of gelatin in the treatment of brittle nails. AMA Arch Derm. 1957;76(3):330–5.
80. Haneke E. Onychocosmeceuticals. J Cosmet Dermatol. 2006;5(1):95–100.
81. Scheinfeld N, Dahdah MJ, Scher R. Vitamins and minerals: their role in nail health and disease. J Drugs Dermatol. 2007;6(8):782–7.
82. Hexsel D, Zague V, Schunck M, Siega C, Camozzato FO, Oesser S. Oral supplementation with specific bioactive collagen peptides improves nail growth and reduces symptoms of brittle nails. J Cosmet Dermatol. 2017;16(4):520–6.
83. Comben N, Clark R, Sutherland D. Clinical observations on the response of equine hoof defects to dietary supplementation with biotin. Vet Rec. 1984;115(25–26):642–5.
84. Colombo VE, Gerber F, Bronhofer M, Floersheim GL. Treatment of brittle fingernails and onychoschizia with biotin: scanning electron microscopy. J Am Acad Dermatol. 1990;23(6):1127–32.
85. Hochman L, Scher R, Meyerson M. Brittle nails: response to daily biotin supplementation. Cutis. 1993;51(4):303–5.
86. Soleymani T, Lo KS, Shapiro J. The infatuation with biotin supplementation: is there truth behind its rising popularity? A comparative analysis of clinical efficacy versus social popularity. J Drugs Dermatol. 2017;16(5):496–500.
87. Administration FDA. The FDA warns that biotin may interfere with lab tests: FDA safety communication 2017. Available from: https://www.fda.gov/medical-devices/safety-communications/fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication
88. Patel DP, Swink SM, Castelo-Soccio L. A review of the use of biotin for hair loss. Skin Appendage Disord. 2017;3(3):166–9.
89. Lipner SR. Rethinking biotin therapy for hair, nail, and skin disorders. J Am Acad Dermatol. 2018;78(6):1236–8.

90. De Berker D. The physical basis of cosmetic defects of the nail plate. J Cosmet Dermatol. 2002;1(1):35–42.
91. Iorizzo M, Piraccini BM, Tosti A. Nail cosmetics in nail disorders. J Cosmet Dermatol. 2007;6(1):53–8.
92. Batory M, Namieciński P, Rotsztejn H. Evaluation of structural damage and pH of nail plates of hands after applying different methods of decorating. Int J Dermatol. 2019;58(3):311–8.
93. Batory M, Wołowiec-Korecka E, Rotsztejn H. The effect of various primers improving adhesiveness of gel polish hybrids on pH, TOWL and overall nail plates condition. J Cosmet Dermatol. 2019;18:1529–38.
94. 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(1):26.
95. Mackay-Wiggan J, Marji J, Walt JG, Campbell A, Coppola C, Chakraborty B, et al. Topical cyclosporine versus emulsion vehicle for the treatment of brittle nails: a randomized controlled pilot study. J Drugs Dermatol. 2014;13(10):1232–9.
96. Sparavigna A, Setaro M, Genet M, Frisenda L. Equisetum arvense in a new transungual technology improves nail structure and appearance. J Plast Dermatol. 2006;2(1):31–8.
97. Sparavigna A, Caserini M, Tenconi B, De I. Effects of a novel nail lacquer based on hydroxypropyl-chitosan (HPCH) in subjects with fingernail onychoschizia. J Dermatol Clin Res. 2014;2(2):1013.
98. Petrosian S, Meehan S, Lasky S, Saitta P. A case of median nail dystrophy treated with poly urea-urethane solution. JAOCD. 2003;75(3):39.