Opportunistic toenail onychomycosis. The fungal colonization of an available nail unit space by non-dermatophytes is produced by the trauma of the closed shoe by an asymmetric gait or other trauma. A plausible theory

N. Zaias,* S.X. Escovar, G. Rebell
Dermatology division, Greater Miami Skin and Laser, Mount Sinai Medical Center, Miami Beach, FL, USA
*Correspondence: N. Zaias. E-mail: nardozaias@aol.com

Abstract
Opportunistic onychomycosis is defined, when a non-dermatophyte mould is cultured from an abnormal nail unit in the absence of a dermatophyte. The presumption is that the mould has caused the abnormal clinical appearance of the nail unit, yet there are no data available to substantiate this claim. Reports have only identified the mould being recovered from the nail unit niche. A review of the published dermatologic literature describing toenail opportunistic onychomycosis by non-dermatophyte fungi has shown toenails with onycholysis, nail bed (NB) keratosis and nail plate surface abnormalities. The appearance of these clinical changes is indistinguishable from the diagnosis of the Asymmetric Gait Nail Unit Signs (AGNUS). AGNUS is produced by the friction of the closed shoe in patients with an asymmetric gait, resulting primarily from the ubiquitous uneven flat feet. Most commonly, species of Acremonium (Cephalosporium), Aspergillus, Fusarium, Scopulariopsis and rarely species of many different fungi genera are capable of surviving and reproducing in a keratinous environment and change the clinical appearance of the involved nail unit. AGNUS toenails predispose to the colonization by the non-dermatophyte opportunistic fungi but not by dermatophyte fungi.

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Introduction
A recent report1 clinically identified very prevalent toenail unit signs, dermatophyte free, resulting from the pressure to the toes and foot by the closed shoe, in subjects who had an asymmetric gait due to the ubiquitous uneven flat feet. Clinically one or more signs can be seen depending on which location of the toenail unit the pressure is focused by the closed shoe while walking. Initially, signs are seen unilaterally and when they are bilateral, one side is always more severe than the other. These signs are:

1 Nail Plate (NP) curved on one side due to pressure of shoe on the NP matrix while walking, Fig. 1 (lateral arrows inward).
2 Onycholysis and hyperkeratosis of distal toe skin, Fig. 1 (arrow up and down).
3 NB keratosis, similar to distal subungual onychomycosis (DSO), dermatophyte free, Fig. 2.
4 Changes of the surface of the NP, similar to white superficial onychomycosis (WSO), dermatophyte free, Fig. 3.

Onychomycosis is a general term that defines a physical relationship between the nail unit and a member of the order Mycota. Onychomycosis can exist when a fungus either initiates the invasion of the nail unit, as we see in the chronic dermatophytosis and scytalidium syndromes, where there is involvement of not only the nail units but also the skin of the soles and glabrous skin.

Opportunistic onychomycosis by non-dermatophyte fungi (moulds) with the exception of scytalidium
'The infected' nail unit is usually a solitary event, not accompanied by tinea pedis as seen in onychomycosis by dermatophytes2 and it does not follow an inheritance pattern, as do dermatophyte onychomycosis.3 The fungi recovered are all environmental and easily accessible to the human toenail niche from the shoe. These fungi include many families and genera, but only those that are capable to survive and repro-
duce in a keratinous environment can colonize the available nail unit niche.

Thus, it is a reasonable hypothesis to propose that opportunistic fungi colonize available spaces of the toenail unit. Why are toenail unit niches available? Mainly because of Asymmetric Gait Nail Unit Signs (AGNUS). The prevalence of AGNUS is greater than the clinician suspects. Of the available studies combined, over a thousand patients with a clinical impression of onychomycosis that were cultured for dermatophyte fungi, only 27–30% had dermatophyte fungi isolated.\(^5\)\(^-\)\(^7\) That could mean that AGNUS was responsible for the majority of the remaining 70–73% of abnormal toenails. In these nails a large variety of moulds were recovered. It is possible that a mould that can sustain itself in nail unit niche can alter the substrate and make the involved nail unit look more abnormal. Whenever there is toenail onycholysis, NB keratosis and NP surface abnormalities, there will be a possible colonization by environmental fungi.

**Methods**

The dermatologic literature relating to 'Opportunistic onychomycosis' from 1960 to 2012 was reviewed. The clinical pictures of the affected toenail units included in the reports were analysed looking for AGNUS clinical signs such as onycholysis, NB keratosis, half of an omega-shaped NP, NP surface damage and hyperkeratosis of the affected skin of the distal toes.

**Results**

AGNUS is the most common toenail unit damage. It is dermatophyte free but can coexist with any other affliction of toenails for independent reasons. Typical AGNUS images, Figs 1–3, demonstrate the toenail unit niches available from AGNUS. The figures presented in all reviewed articles on opportunistic fungi show characteristic AGNUS features, see Figs 4–14.

Fungi reports and their confirmation are summarized in Table 1.\(^8\)\(^-\)\(^24\) All the clinical images of the halluces are identical to what is described as AGNUS.

**Discussion**

We propose the theory that opportunistic environmental fungi of many genera can colonize toenail niches that exist because of an asymmetric gait and the closed shoe (AGNUS), as long as
they can survive and utilize keratinous material. AGNUS clinical signs have not been recognized before 2012 when the AGNUS publication appeared. It is very plausible that earlier descriptions of clinical classifications of dermatophyte onychomycosis were in fact aided by AGNUS-derived nail unit lesions. It is possible that the authors description of WSO\textsuperscript{23} could have been the colonization of a trachonychia damage on the surface of the NP.
commonly seen in AGNUS and that *Trichophyton interdigitale* (*mentagrophytes*) also found in the interdigital spaces, set up household there to clinically appear as WSO.

In another experiment by a group of Spanish dermatologists\(^2_6\) attempted to prove Koch’s postulates, inoculated cultures of dermatophyte on the surface of scarified normal toenail plates and occluded them. Lesions of WSO were seen after 1 month but as soon as the occlusion was removed all lesions disappeared. No lesions of DSO were seen. Could it be that the artifactual scarification of the surface of the NP needs to be continuous, as seen in the shoe damage produced by AGNUS?

Other descriptions and new classifications merit discussion here. Recently described dermatophytoma, Fig. 12,\(^2_7\) is a fungus ball of *Fusarium* in an onycholytic area of the NB produced by AGNUS in a patient who for independent reasons also had *T. rubrum* DSO.

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Another example of a mixed diagnosis is shown in Fig. 13. A patient who had dermatophyte DSO coexisting with AGNUS and finally the onycholytic space inhabited by *Pseudomonas*, which tinted the nail space green.

Other diseases have been described to cause toenail abnormalities, as shown in Fig. 14, who clinically had AGNUS and developed paraneoplastic vascular disease in that toe.

**The treatment of opportunistic onychomycosis**

Treatment of onychomycosis caused by non-dermatophyte moulds (NDM) is still not well standardized and several authors underline the fact that NDM onychomycosis frequently does not respond to systemic antifungals. The use of topicals with the NP avulsion is commonly described but without reproducible results.

In an interesting *in vitro* study, Vander-Straten and colleagues* found that most opportunistic fungi had a very high minimal inhibitory concentration (MIC) to 5-fluorocytosine and fluconazole. The best results were produced with amphotericin B and itraconazole was a little better than ketoconazole.

In the reported studies, the treatment time with systemic antifungals appeared to be very short to accomplish complete cure when compared with the growth rate of the hallux NP and the length of the infected nail plate.

In summary, we theorize it is impossible for opportunistic fungi to infect a normal toenail unit without a previous alteration of the nail unit anatomy, as for example onycholysis, NB keratosis and superficial NP damage, as seen classically in the majority of AGNUS cases and trauma.

**References**