

The Application of Photodynamic Therapy for the Treatment of Onychomycosis

Presented by Genesis Health Light Corp®

Onychomycosis

Onychomycosis is a fungal infection of the toenails or fingernails. Onychomycosis causes fingernails or toenails to thicken, discolor, disfigure, and split. At first, onychomycosis appears to be only a cosmetic concern. Without treatment, however, the toenails can become so thick that they press against the inside of the shoes, causing pressure, irritation, and pain. Fingernail infection may cause psychological, social, or employment-related problems.

Half of all nail disorders are caused by Onychomycosis, and it is the most common nail disease in adults. Toenails are much more likely to be infected than fingernails. The incidence of Onychomycosis has been increasing and is related to diabetes, a suppressed immune system, and increasing age. Adults, especially the elderly, are more likely to have Onychomycosis than children.

Onychomycosis Symptoms and Signs

- Onychomycosis usually does not cause any symptoms unless the nail becomes so thick that it causes pain when wearing shoes. People with Onychomycosis usually go to the doctor for cosmetic reasons, not because of physical pain or problems related to onychomycosis.
- As the nail thickens, onychomycosis may interfere with standing, walking, and exercising.
- Paresthesia (a sensation of pricking, tingling, or creeping on the skin having no objective cause and usually associated with injury or irritation of a nerve), pain, discomfort, and loss of agility (dexterity) may occur. Loss of self-esteem, embarrassment, and social problems can also develop.
- Severe cases of *Candida* infections can disfigure the fingertips and nails.



Photo of onychomycosis on the hallux; SOURCE: CDC/Dr. Edwin P. Ewing, Jr.

Symptoms or signs (appearances) of onychomycosis based on subtype

Onychomycosis is divided into subtypes that can be identified based on where the infection appears to be located relative to the structure of the nail.

- In distal lateral subungual onychomycosis (DLSO), the nail plate is thick with a cloudy appearance (opaque), the nail bed underneath the nail thickens and hardens (nail bed hyperkeratosis), and the nail separates from the bed underneath (onycholysis). The nail can be discolored in appearance which can range from white to brown. The edge of the nail becomes severely eroded.
- In endonyx onychomycosis (EO), the nail plate has a milky white discoloration, but unlike DLSO, the nail does not separate from the bed (no onycholysis). The area under the nail (subungual area) does not thicken or harden (no hyperkeratosis).
- White superficial onychomycosis (WSO) is usually confined to the toenails. Small white speckled or powdery-looking patches appear on the surface of the nail plate. The nail becomes rough and crumbles easily.
- In proximal subungual onychomycosis (PSO), an area of white spotting, streaking, or discoloration (leukonychia) develops near the nail fold and may extend to deeper layers of the nail. The nail plate becomes white near the cuticle and remains normal at the end.
- In total dystrophic onychomycosis, the nail is thickened, opaque, and yellow-brown. The entire nail plate and matrix are affected.
- Yeast infection (*Candida albicans*), while affecting the nail, can appear with additional signs. Candidal infection can occur in the toenails and the fingernails but may also infect the tissue that surrounds the nail. The nail fold becomes inflamed (erythematous), or the nail plate separates from its bed (onycholysis). The nail bed thickens and hardens (nail bed hyperkeratosis), and inflammation of the nail fold is observed in chronic mucocutaneous disease (disease of mucous membrane and regular skin). The affected fingers or toes start to look rounded on the ends, like drumsticks, and, sometimes, the entire thickness of the nail becomes infected.

Causes of Onychomycosis

Onychomycosis is caused by three main classes of organisms: dermatophytes (fungi that infect hair, skin, and nails and feed on nail tissue), yeasts, and nondermatophyte molds. All three classes cause the very similar early and chronic symptoms or appearances, so the visual appearance of the infection may not reveal which class is responsible for the infection. Dermatophytes (including *Epidermophyton*, *Microsporum* and *Trichophyton* species) are, by far, the most common causes of onychomycosis worldwide. Yeasts cause 8% of cases and nondermatophyte molds cause 2% of onychomycosis cases.

- The dermatophyte *Trichophyton rubrum* is the most common fungus causing distal lateral subungual onychomycosis (DLSO) and proximal subungual onychomycosis (PSO).
- The dermatophyte *Trichophyton mentagrophytes* commonly causes white superficial onychomycosis (WSO), and more rarely, WSO can be caused by species of nondermatophyte molds.
- The yeast *Candida albicans* is the most common cause of chronic mucocutaneous candidiasis (disease of mucous membrane and regular skin) of the nail.

Risk Factors for Onychomycosis

- Risk factors for onychomycosis include family history, advancing age, poor health, trauma, living in a warm climate, participation in fitness activities, immunosuppression (can occur from HIV or certain drugs), bathing in communal showers (ex. within fitness centres), and wearing shoes that cover the toes completely and do not allow for airflow.

Treatment Options *

Medications

In the past, medicines used to treat onychomycosis (OM) were not very effective. OM is difficult to treat because nails grow slowly and receive very little blood supply. However, recent advances in treatment options, including oral (taken by mouth) and topical (applied on the skin or nail surface) medications, have been manufactured. Newer oral medicines have improved treatment of onychomycosis. However, the rate of recurrence is high, even with newer medicines. Treatment has certain risks, and recurrence is possible.

- Topical antifungals are medicines applied to the skin and nail area that kill fungi and some other pathogens.
 - These topical agents should only be used if less than half the nail is involved or if the person with onychomycosis cannot take the oral medicines. Medicines include amorolfine (approved for use outside of the United States), ciclopirox olamine (Penlac, which is applied like nail polish), sodium pyrithione, bifonazole/urea (available outside of the United States), propylene glycol-urea-lactic acid, imidazoles such as ketoconazole (Nizoral Cream), and allylamines such as terbinafine (Lamisil Cream).
 - Topical treatments are limited because they cannot penetrate the nail deeply enough, so they are generally unable to cure onychomycosis. Topical medicines may be useful as additional therapy in combination with oral medicines. This results in treatment medicine concentrations that come from two directions, topically and from within the body via oral medication.

- Newer oral medicines are available. These antifungal medicines are more effective because they go through the body to penetrate the nail plate within days of starting therapy.
 - Newer oral antifungal drugs terbinafine (Lamisil Tablets) and itraconazole (Sporanox Capsules) have replaced older therapies, such as griseofulvin, in the treatment of onychomycosis. They offer shorter treatment periods (oral antifungal medications usually are administered over a three-month period), higher cure rates, and fewer side effects. These medications are fairly safe, with few contraindications, but they should not be taken by patients with liver disease or heart failure. Before prescribing one of these medications, doctors often order a blood test to make sure the liver is functioning properly. Common side effects include nausea and stomach pain.
 - Fluconazole (Diflucan) is not approved by the American Food and Drug Administration (FDA) for treatment of onychomycosis, but it may be used by some clinicians as an alternative to itraconazole and terbinafine.
- To decrease the side effects and duration of oral therapy, topical and surgical treatments (see below) may be combined with oral antifungal management.

Surgery

Surgical approaches to onychomycosis treatment include surgically or chemically removing the nail (nail avulsion or matrixectomy).

- Thick nails may be chemically removed by using a urea compound. This technique should usually be deferred to a surgeon, podiatrist/chiropractist or dermatologist.
- Surgically removing the nail plate (fingernail or toenail) is not effective treatment of onychomycosis without additional therapy. This procedure should be considered an adjunctive treatment combined with oral medical therapy.
- A combination of oral, topical, and surgical therapy may increase the effectiveness of treatment and reduce the cost of ongoing treatments.

Laser Treatment

One of the newest treatments to kill pathogens infecting the nails is laser therapy. The laser beam can penetrate the nail tissue and disrupt fungal (and other) pathogens enough to kill them. Some patients may experience some mild discomfort during the procedure. Reports suggest that laser therapy is about as effective as medical therapy. Some patients may require more than one treatment. This treatment can be very expensive and the cure rate is poor.

Alternative Treatments

There are many claims made that home remedies can be used to treat a fungal nail infection. Products such as Listerine, VapoRub, beer soaks, peroxide, and others are purported to be effective. Unfortunately, there is little or no data to support these claims. Some of the commercially available products do not promote their use for nail infections, although some individuals may use them for alternative treatments. These should be avoided.

*Source WebMD review 06/2014

Photodynamic Therapy for Onychomycosis

Definition

Photodynamic therapy (PDT) can be defined as a “method of disinfecting or sterilizing a hard or soft tissue site by topically applying a photosensitizing compound to the site, and then irradiating this with light at a wavelength that is absorbed by the photosensitizing compound, so as to destroy microbes at the site”. The concept of killing human cells or microbial cells via photosensitive agents is well established in medicine and the application of this to the treatment of malignancies has proven successful in certain types of tumors. The application of PDT in dentistry and medicine are wide and include the destruction of bacterial, fungal and viral pathogens in a range of clinical settings.

Method of Action

Certain molecules known as photosensitizers generate cytotoxic species, particularly singlet oxygen, when irradiated with light of an appropriate wavelength. On absorbing a photon, the photosensitizer molecule is promoted to a higher energy state, which then transfers its energy to an oxygen molecule, resulting in the generation of singlet oxygen. This phenomenon can be used to kill fungi and bacteria in a process called “lethal photosensitization” in which the reactive oxygen singlet damages bacterial and fungal membranes and DNA. Singlet oxygen has a very short lifetime and must be generated in close proximity to cells to produce the cytotoxic effects.

Photosensitizers

The photosensitizer specifically for toe fungus is Methylene Blue (MB). MB is a common stain used in medicine and is well known within the literature to have antiseptic properties. It causes no damage to normal healthy human cells. The concentration used for PDT is 0.01% w/v in aqueous solution. The optimal wavelength of light for stimulation of MB is 670nm.

Protocol

Debride affected nail as much as possible. Apply 1 drop of 0.01% w/v Methylene Blue to the debrided nail and allow solution to absorb for 30 seconds. Irradiate the area with a CS1000 Genesis Health Light on High setting for 3 minutes, treating up to a maximum of 2 nails at a time to allow for maximum light absorption. Provide patient with after-care products for sanitization of shoes, socks and bedding, such as Biotext textile disinfectant spray and detergent, as well as over-the-counter (OTC) antifungal skin and nail creams/solutions. Repeat process in 3 weeks. In due course, the affected area will stain less blue as an indication of the decreased presence of fungus. Full effect can be achieved in up to 3-4 treatment cycles maximum.

Efficacy

Light treatment alone has been found to have a 5% kill rate in the literature. Methylene Blue has an individual kill rate of 17%. Combined, the kill rate is 97%*.

Genesis Health Light

The Genesis Health Light is a full spectrum light that provides light energy at the widest spectrum in the marketplace today. Therefore, it is particularly effective in treating a wide range of tissue types including muscle, tendon, ligament, bone and blood vessels. The complete spectrum of wavelengths produced by Genesis is shown below in *Fig. 1* and the power output at 670nm is 49 mW/cm², which allows it to stimulate Methylene Blue into a cytotoxic state.

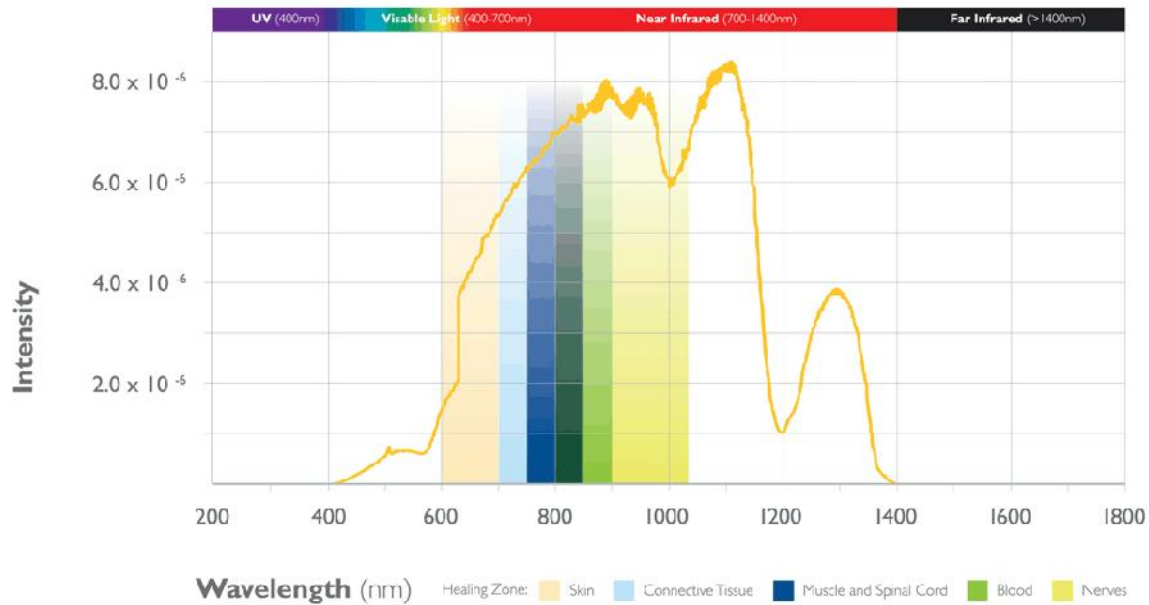


Figure 1: Full spectrum of Wavelengths (nm) and intensity outputs (mW/cm²) emitted by CS1000 Genesis Health Light.

*Source: McMaster University Physics Dept. 2010

The Clinical Application

Toe fungus affects about 10% of the adult population. Treatments so far have had poor results and often were expensive for both the clinician and the patient. The use of PDT in medicine and dentistry is well documented and this technique is very effective, completely safe and very cost effective. The application of PDT using methylene Blue and Genesis Health Light in a clinical setting is both efficient and has a very high success rate for the patient.