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Fungal Foot Infection

Introduction

Fungal foot infection is a very common infectious condition affecting the skin and nails frequently caused by dermatophytes. Clinically, dermatophytosis affects a significant number of patients, particularly older adults. Despite its prevalence and positive response to treatment, it continues to increase globally. The key to managing the condition is understanding its presentation, diagnosis and management. In this roundtable discussion, three experts answer questions about dermatophytes and their management.



Figure 1 Subtle dermatophyte infection of the feet across the soles

What are Dermatophytes and how do they live?

Ruth Ashbee: I'm sure most people have had experience in terms of fungi when they have either bread or cheese or fruit that goes furry and that nice green colour - that's fungi, and that's where a lot of people see it in an everyday setting.

That felty, fluffy appearance that you see is what's called a mycelium, and that is how fungi grow. Fungi have thread-like structures, and they will penetrate tissues. Now, dermatophytes, as a group are slightly unusual, because they produce enzymes, and those enzymes are able to break down keratin.



Figure 2 Dermatophytes are able to digest keratin as a food source

Keratin is what constitutes skin, hair and nail. Dermatophytes are unusual, because most fungi don't have that ability to digest keratin. They are quite varied as a group, but they all have that unifying feature to allow them to grow.

With these thread-like structures, and the keratinase they invade between the layers of keratin in the skin, or the hair, or the nail, and that's how they can cause disease.

How do we acquire them, how do they spread, and how do they reproduce?

Ruth Ashbee: Some dermatophytes are normally present in the environment and there are dermatophytes that specialize in living on animals. There are dermatophytes that specialize in living on humans, and there are some dermatophytes that live in the soil -they don't tend to cause disease, but we can get dermatophyte infections by contact with animals, like kittens or domestic animals. You can also get it from cattle.

How do they reproduce and spread?

Ruth Ashbee: The thread-like structures of the dermatophyte, can break up. So, if you think of a thread of cotton, and you cut it into pieces, and each of those pieces is able to transmit the infection. If you go to the swimming pool, or you go to a sports centre for example, and somebody else has got a dermatophyte infection and those bits of thread-like structure are on the floor in the swimming pool, you can tread on them and can they stick to the bottom of your foot then that potentially is the way that they will spread infection.

What about Spores?

Ruth Ashbee: The spores are the resistant part of the dermatophyte and all you need, in theory, is one spore to come in contact with skin or nail and it then grows into a new thread-like structure, and it can then initiate a new infection. The interesting thing is that if you have a piece of skin or nail which actually contains dermatophyte, the dermatophyte will remain viable in that material for up to 12 months. So, reinfection is a risk for all that time.

How does the infection thrive on the skin?

Ruth Ashbee: Carbon dioxide helps dermatophytes to form new mycelium and they also like warmth and a bit of moisture (see figure 3). So, if you think about it, certainly in the UK at this time of the year, most people have their feet in some fairly occlusive footwear, socks and shoes, and that's a lovely environment for the fungi to grow. A skin infection would probably take a few weeks to establish.

Ivan Bristow: There was some very good research that showed that the prevalence of fungal foot infection was related to the length of the winter. This was because longer winters meant more time in occlusive shoes. So, in countries with long winters prevalence was much higher. In Spain, the rates were about 8%, and in Russia, it was nearly 80%.

How far into the skin will the dermatophytes grow?

Kash Bhatti: Dermatophytes generally grow in the epidermis. It is possible to grow deeper, in the dermis, but this is a rare presentation in the UK. It may be seen in patients who are immunocompromised, in the elderly, or patients with diabetes or peripheral vascular disease, but on these shores, it is rare.

Ruth Ashbee: Yes, it's generally fairly superficial, so these fungi, when we grow them in the laboratory, they are grown at 27°C degrees, usually. Now, that is



Figure 3 Humidity and heat in shoes promote dermatophyte growth

a good deal cooler than core body temperature, so they will only penetrate quite superficially in the skin, because they very quickly become too hot.

And once the temperature starts to increase, then they just won't grow. You do very occasionally get things that go in a bit deeper, but usually that's in people who are immunocompromised, but generally they tend to stay relatively superficial.

Clinical Presentations & Complications

What sort of problems do dermatophytes cause for patients?

Kash Bhatti: As Ruth alluded to, dermatophytes are pathogenic organisms and do lead to some problem or the other. They feast on keratin; keratin is found in the stratum corneum of the skin, hair and nails, and dermatophytes therefore tend to cause skin, hair and nail infections.

Dermatophytes do not tend to elicit much of an inflammatory response. As a result, some people can have rashes for years and years, the infection escaping detection. An example is tinea pedis (fungal infection) of the soles of the feet. Dermatophytes can infect any area of skin: infections of the face are called tinea faciei, on the body tinea corporis (commonly known as ringworm), tinea cruris in the groins (jock itch in men), tinea pedis of the feet – either in the web spaces (interdigital tinea) or on the soles of the feet (moccasin-type tinea pedis). Tinea imbricata is a particular type of tinea corporis caused by a particular dermatophyte species. Nail infection is called onychomycosis, and scalp and hair infection is tinea capitis. A kerion is a particular significant inflammatory response to tinea capitis. By far, the commonest dermatophyte infection I come across is moccasin-type tinea pedis, which is often mistaken for dry skin.

Ivan Bristow: As long as there's keratin, as a food source, there's always a risk. On the foot, if you look at the data, the largest study, the Achilles study surveyed over 80,000 feet. And the prevalence of dermatomycosis on the skin of the feet was 36%.

A third of the European population are carrying it, and if you get into the over-60s age group, then you're talking almost half of the patients. Walking into a podiatry clinic, or walking into a surgery, or the dermatology clinic, are bringing dermatophytes with them on their feet. The data for fungal nail infection suggests between 8% and 10% in the UK.

Ruth Ashbee: In fingernails, it's much less common, but there is an association to certain occupations, so if you have your hands in water that can soften your nails and the skin on your fingers, that can

predispose to dermatophyte infection. If people get onychomycosis in the fingernails, they tend to be more inclined to get treatment.

Why is it quite often the index finger?

Ruth Ashbee: I suspect it's the scratching finger, and therefore, dermatophytes will travel.....

There was a wonderful study that was published many years ago in the Korean Journal of Medical Mycology, and they looked at if people had tinea pedis, and then looked at other sites on the body and found that there was a significant proportion of people who also had infection at other sites, demonstrating its infectious nature even within an individual.

Ivan Bristow: We know that there's a high level of undiagnosed tinea, but a Japanese study showed that only if it itched did people actively seek treatment, meaning a lot of tinea that didn't itch went untreated.

One of the big problems in dermatology and podiatry is the subtlety of fungal foot infection. So often patients come in with one dry foot and one normal foot and you say to the patient, have you ever looked at your foot?

They say, what do you mean? I've never noticed that before. Why is that foot dry and that one's alright? That's because it's not really dry - it's athlete's foot. You do get bilateral cases, but many are unilateral and often passed off as dry skin. Dry heel fissures are often associated with tinea pedis too.

Why is it, do you think, that dermatophytes are very good at hiding under the radar, as it were? Is it just because they're so superficial?

Ruth Ashbee: The sort of presentation is often quite subtle, people just think it's dry skin, and so they can't be bothered to moisturise. They don't realize that it's not just dry skin.

In terms of in the lab, you could always tell when the weather started to get better, and people wanted to get the sandals out, because the numbers of samples we got kind of increased exponentially, because everyone suddenly looked at their feet and thought, "Hmm, maybe I'd better do something about that". I think it is a classic case of out of sight, out of mind with them, and as you say, if they don't itch....

So, how does tinea pedis in the skin turn into nail infection?

Kash Bhatti: Dermatophytes, by virtue of being close to the nail, can spread by contact (e.g. from contact in shoes, or spread by socks laden with fungus spreading over the nails, to the nails. When the circumstances are optimal, e.g. a traumatized nail, or wet after



Figure 4 Fungal nail infection under the nail

swimming, or vulnerable in some way, and the dermatophytes have access to keratin, then they seize the opportunity to invade and the infect the nail unit.

There's a paper that you know that has looked at the time course.

Ivan Bristow: I suspect that most tinea is acquired in teenage years after puberty, and then people pick it up. Researchers refer to the "plantar reservoir" as the source of the infection. He suggested that it can take decades. Quite literally, it can remain there for ages, without any symptoms and then gradually and insidiously spread to other areas.

Usually, the first indication to a patient's they've got any tinea is when their nail changes colour. They'll come in and say, why has my nail changed colour? And you look at the soles of their feet, and you can see it's subtly dry and you know it's what it is - it's tinea. But the first clue the patient gets is when the nail changes colour, and that's usually by the time they're middle aged. Earlier if the nail has been damaged.

Interestingly, the pattern of nail infection tells us about the cause. which nails are affected? It is trauma so it's the first, it's the fifth, and the fourth, or long second, but it's always the third, which is the most protected because tucked out the way from the shoes, from the edge of the shoes.

What does fungal skin infection lead to? What do you see most?

Ivan Bristow: Local secondary bacterial infections do occur and can be problematic particularly for patients who are immunocompromised as minor skin infection can lead to further problems (see figure 5).

Kash Bhatti: Most people are only aware of a rash or something wrong due to the cosmetic appearances.

Some people have symptoms, such as itch, or scaling, but in my setting, most tinea comes to my attention either due fungal nail disease, or recurrent cellulitis. Fungal nail disease in toes is often embarrassing, for the patient, and they seek advice on how to treat it. For recurrent cellulitis, there is usually a portal by which bacteria access the skin: often, it is from fungal skin disease, or fungal nail disease, where the affected skin allows bacterial invasion.

Cellulitis is a big infection. It causes a large inflammatory response, resulting in damage to lymphatics. This makes the skin more vulnerable to infection, which, once infected, sets up a vicious cycle to damage more lymphatics, and so on and so forth. The skin suffers from inadequate 'drainage', becomes eczematous, erythematous, the deeper tissues become fibrotic and the leg feels woody. Besides skin care, compression for any concomitant swelling or venous insufficiency, dermatophyte nail and skin diseases should be treated to prevent recurrence.

So, clinically, how would you diagnose fungal foot and nail infection?

Kash Bhatti: Dermatology is a visual specialty and there are some visual clues to help with diagnosis. Clinical suspicion should be supported, where possible, with mycology.

Tinea pedis (moccasin-type) is recognized by excessive scaling of the soles of the feet: white scale, sometimes adherent and difficult to scratch off, in the furrows of the skin. There is usually a minimal inflammatory response and so often a red rash is not seen. Differentials can be dry skin, particularly congenitally dry skin (ichthyosis), dermatitis and psoriasis, but usually, there are other clues to support those diagnoses. Dermoscopy can be invaluable in diagnosing dermatitis and psoriasis.



Figure 5 Secondary infection of tinea with Pseudomonas



Figure 6 Interdigital infection with T. rubrum

Interdigital tinea can be recognized by maceration and malodour in the web spaces; a secondary bacterial infection may be present. Some interdigital disease is caused by candida, particularly in patients with diabetes or peripheral vascular disease.

Fungal nail disease is recognized by thickened nail plates, discoloured or multicoloured nails (yellows, greens, browns; dark brown and black sometimes!) and greasy debris and hyperkeratosis under the nail plate (subungual hyperkeratosis). Again, dermoscopy can be invaluable in making a diagnosis of suspected onychomycosis, but mycology to confirm is the gold standard.

For nail disease, psoriatic nail disease is an important differential, but, when I see patients with nail disease, my differentials are onychomycosis, onychomycosis, onychomycosis, then something else. It really is the commonest toenail dermatosis, and a close second in fingernails, after traumatic nail disease from nail cosmetics.

In the lab, how can it help diagnosing fungal infection?

Ruth Ashbee: There are two things usually that we would do with any sample that we receive. The first thing to do is to look at it down the microscope (figure 7). And to do that, we would use potassium hydroxide, and that digests away the skin or the nail material. The stain that's mostly used is something called Calcofluor White that binds to the chitin in the fungal cell wall to make it fluoresce.

Then we also would put the other parts onto two different agar plates to grow the dermatophyte. We'll grow them, put them in an incubator, and just attempt

to grow it, and as I say, it's usually 27°C degrees for between 2-4 weeks. But what you do get is that you will sometimes see fungal material under the microscope, but it doesn't grow - we call a fail to grow - not surprisingly. And perhaps somewhere around about 10-15% of samples, that will happen, so that you can see it under the microscope, but you never grow anything.

There are other tests that some labs will use, so you can use molecular tests. With those you're trying to find the genetic material of the fungus. That can be beneficial in that even if the fungus isn't able to grow, you can still detect its genetic material and identify it. There are some commercially available tests.

What's your choice when you're, investigating your patients with fungal nails and fungal skin infection.

Kash Bhatti: Most patients coming to see me arrive with negative mycology. Usually, it is the patients themselves who have been asked to obtain their own samples, and generally, patients will clip their nails and send samples that are just too distal; the fungus has long left the distal part of the nail plate is marching up to the nail matrix - that is what should be sampled! I always repeat clippings, and go as proximal as I can, to catch the fungus. I also complement mycology with histopathology.

Histopathology is tough. Softening nails, staining, and making slides is an arduous task, so I thank my Histopathology colleagues for helping me. It is so helpful - seeing fungi interspersed amongst the layers of the nail plate can clinch the diagnosis, even when mycology is negative. The downside is that histopathology can take 6-8 weeks for a result, and it does not tell you what name and species of the fungus it is.

Ivan Bristow: Also there is the 5-minute fungus test, which is a test strip with an antibody field specific to fungal proteins. Published in several journals it shows a high sensitivity and so it is very useful to detect if dermatophytes are present.

Occasionally, you may get a non-dermatophyte mould. What is it, and how common is it from a laboratory perspective, and what are the implications?

Ruth Ashbee: Okay, so the non-dermatophytes tend to be things like Scopulariopsis, Fusarium, Acremonium, you can get a range of different fungi. So, these usually are not able to cause the disease on their own. They don't produce keratinases, so they can't digest the nail. They usually move into damaged nails or more commonly they can get in secondary to a dermatophyte infection. The dermatophyte is there in

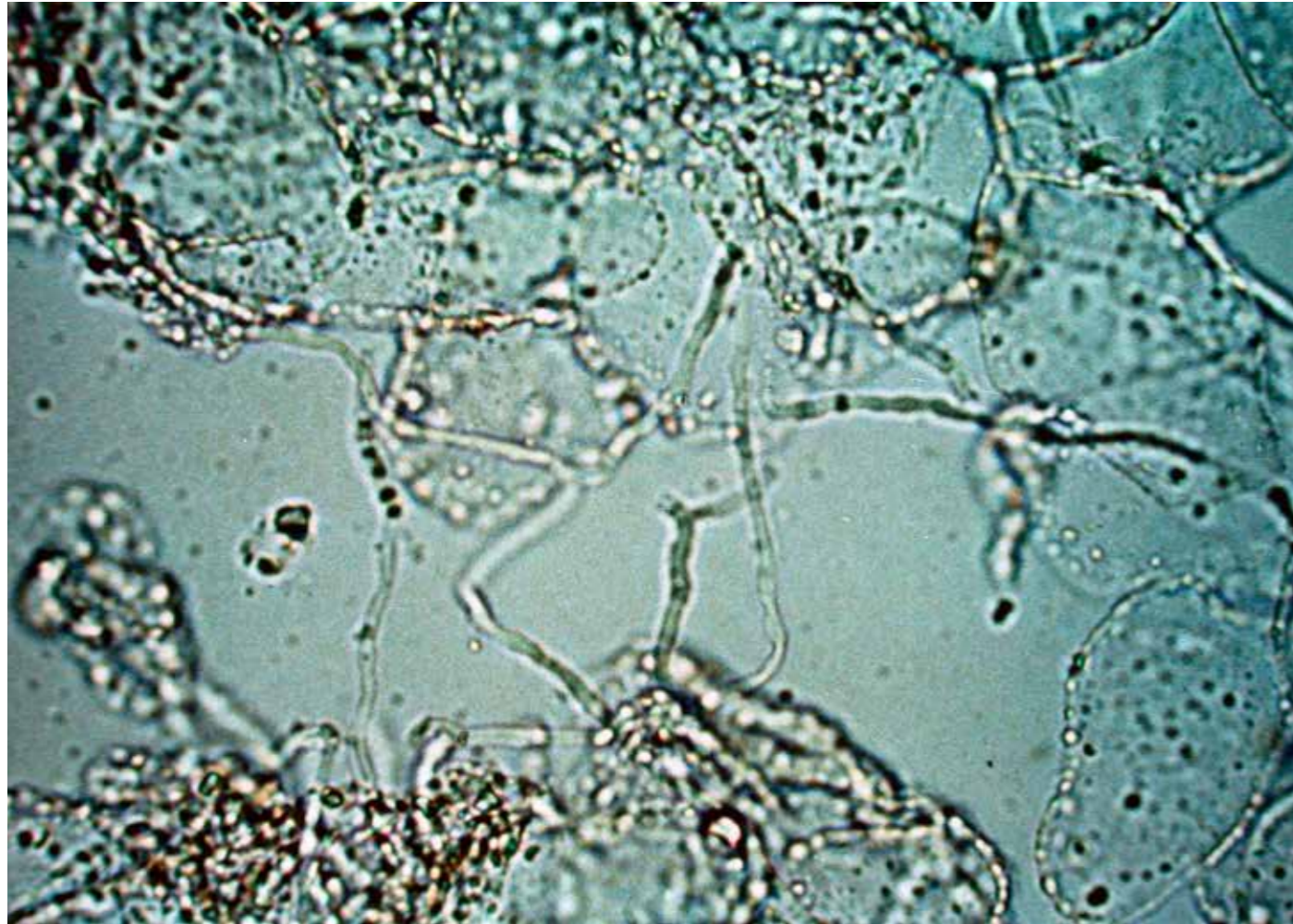


Figure 7 Microscopy showing fungal elements

the first place, damages the nail, and these things can get in.

If you do get a co-infection with a dermatophyte and a non-dermatophyte, non-dermatophyte moulds tend to grow faster than the dermatophyte, so often you will only recover something like Scopulariopsis, and the assumption is that they have kind of competed out the dermatophyte, which is there as well.

And clinically, non-dermatophyte moulds? What does that mean to you and your patients?

Kash Bhatti: For the most part, non-dermatophyte moulds do not hold much clinical value in the patients I see. Perhaps these are commensals, or a chance finding, but practically, they are call for me to repeat clippings and search again. Of course, in the setting of immune compromise or diabetes or peripheral vascular disease, there may be meaning, but generally, in the majority, I see them as innocent bystanders.

Managing Fungal Foot Infection

Ivan Bristow: Let's start with tinea pedis. I think we

could all agree that if it's a dermatophyte that most dermatophytes generally respond to all of their typical over-the-counter drugs like terbinafine, clotrimazole and miconazole.

Kash Bhatti: I advocate terbinafine: it is fungicidal for dermatophytes, rather than the fungistatic -azoles. Terbinafine cures quicker than -azoles. I particularly like terbinafine solution ('Lamisil once') which is a convenient, single use, version of terbinafine, that can give prolonged benefit rather than daily treatment with cream.

Ivan Bristow: and it's good as a preventative.

Can we expect any new antifungals?

Ruth Ashbee: There's a number of new antifungals that are coming. They're going to be tested out for the systemic diseases, but some may make into topical use as well.

What about treating the nails?

Kash Bhatti: There are two considerations when treating nails: treat the source of infection and treat the nail infection.



Figure 8 Late fungal nail infection with nail plate collapse

Using an oral antifungal such as terbinafine should treat current tinea pedis. After treatment, prevention of recurrence is important with ongoing skin care. For nails, specifically, I use a combination of reducing the fungal load ('debulking') by removing as much disease nail as I can and uncovering any dermatophytoma. I use topical agents – terbinafine cream or solution to exposed nail bed, and amorolfine lacquer to any remaining nail plate. Oral terbinafine is the mainstay of my oral armamentarium.

And if they can't take terbinafine orally, is there a second choice?

Kash Bhatti: Alternatives are the -azoles itraconazole or fluconazole. I do find though that terbinafine tends to cause less problems than itraconazole. I find itraconazole causing drug rashes, or nausea and vomiting, in some of my patients, young or old. Terbinafine for the most is very well tolerated.

Many patients are worried by oral terbinafine damaging the liver. Is this justified?

Kash Bhatti: There is a massive, prevailing, overestimation of the risks of terbinafine. Conversely, itraconazole has a much better 'rep'. In each consultation I take to explain the safety of terbinafine, and other antifungals. There are risks, no medicine is without risks, but I frame benefits and risks, back up with numbers to things into perspective.

Ivan Bristow: Statistically, terbinafine, there is a very small chance of liver damage, but it's no higher than any other drugs that work on that enzyme pathway in the liver, is it?

Kash Bhatti: If one drills down the numbers, flucloxacillin is 5 times likelier to cause hepatotoxicity than terbinafine!

Ruth Ashbee: Itraconazole, again, is a significant inhibitor of the cytochrome pathway and can cause liver problems. Interestingly, itraconazole breaks down into around 30 metabolites risking more problems and interactions than terbinafine. Terbinafine is a cleaner drug to use than itraconazole.

Kash Bhatti: I do think people get lulled into a false sense of security with pulsed itraconazole. They do not realize that itraconazole has more idiosyncratic risks than terbinafine, pulsed or not.

Reinfection and relapse

How significant is reinfection? And how do you prevent it?

Ruth Ashbee: I think it's highly likely that it will. If you have shoes and socks that are not properly disinfected, if you have it in the home environment. To a certain extent, there's a question around, is it reinfection, or is it just that you've never eradicated it in the first place? And also, if you're a keen sports person, or you like saunas and gyms you're going to carry on being exposed to fungal elements.

What is your key message for patients who say, "How do I stop it coming back?"

Kash Bhatti: Meticulous care, as much as one can do. Lamisil once® as a topical to treat skin; never wearing shoes two days in a row, not recycling socks without washing, and decontaminating shoe wear. Look at the environment! If other household members have signs of infection, they may spread fungus via carpets and using shoe wear etc. Reinfection is common. There is emerging evidence of genetic susceptibilities and



A range of treatments are available from Canonbury Healthcare

onychomycosis running in families, no pun intended. Fortunately, recurrent infection can be treated.

Ivan Bristow: I think if you keep the skin clear, then the risk of reinfection of the nail is quite low, dermatophytes don't often just jump into a nail. They're usually on the skin first. So good skin care with regular antifungals can help. Also cleaning footwear and insoles. There is a good information sheet available on my website here which can be given to patients: <https://www.foot.expert/post/preventdermatophyte>

How do you clear the socks and shoes of infection?

Ivan Bristow: I don't think there's a 100% way to wash a sock, is there, to remove all the dermatophytes?

Ruth Ashbee: I don't think there is. I mean, dermatophytes and fungi are very stubborn.

Ivan Bristow: One of the things that podiatrists are using is hypochlorous solution. There aren't many bugs of any type, virus, fungi, or bacteria, that can survive hypochlorous exposure. Spraying it in shoes is effective.

Summary

Dermatophytes are resilient fungi which are highly adapted to living on the epidermis. The foot, owing to several factors, offers an excellent environment for their survival. Although the infection may be subtle, it will insidiously spread to the nails and other areas of the skin. Its subtlety requires careful assessment and diagnosis to ensure the correct treatment is offered. Nail infection in particular owing to the longer treatment time and potential side effects, requires proper diagnosis and management according to the patient's needs.

Currently, a range of options are available including oral, topical or a combination of which have shown effectiveness in managing the condition. A key aspect of the disease is managing the patient after a cure is achieved. Relapse and reinfection rates are notoriously high. Therefore, patients should be informed of the high likelihood of the infection recurring in the future. Regular application of topical antifungals / antimicrobials to the skin and footwear should be encouraged.

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