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DERMATOPHYTOSIS OF THE FEET

Gayle D. Masri-Fridling, MD

Tinea pedis is the most common fungal infection worldwide, affecting 30% to 70% of the population. It is a disease of civilized humans, having evolved in the late nineteenth and early twentieth centuries, that predominantly affects adults, with reportedly an equal male to female incidence.[14] Clinical practice, however, suggests a predominance of male patients.

The responsible agents are aerobic fungi that grow within the layers of the stratum corneum in the form of branching hyphae, and that lack the ability to penetrate through the keratinized layer into the viable epidermis and internal structures. The host response to the fungal antigens involves cell-mediated immunity, which becomes evident as the disease is resolving. The feet pose a favorable environment for dermatophyte proliferation owing to their lack of sebaceous glands that produce fungistatic lipids.[14] Fungi can be recovered on culture of 9% to 21% of clinically normal toewebs.[7] Resilient spores can survive long periods in unfavorable environments.[8]

Although dermatophytosis occurs primarily in the adult population, it has also been documented, though less frequently, in the pediatric population. The magnitude of the problem is shown by several large studies that revealed positive cultures in 2.9% to 8.2% of asymptomatic children and have found tinea pedis to account for approximately 50% of symptomatic cases (Fig. 1).[6,11] Similar studies in asymptomatic adults demonstrate positive cultures from 11% versus 31% (7.5%–61%) of symptomatic cases.[5]

PREDISPOSING FACTORS

Several factors can predispose patients to contract tinea pedis, including residence in warm climates with high humidity that cause sweating of the feet and thereby wash away protective surface lipids. Situations in which there are external sources of moisture in the environment are similar. For example, soldiers marching for long periods in cold and damp trenches have persistently wet feet, facilitating dermatophyte infection. In addition, the practice of sharing baths, showers, swimming pools, and even shoes facilitates the spread of infection. Rugs, linen, and clothing can act as fomites. Shoes themselves, through occlusion, are responsible for the development of tinea pedis because the disease does not occur in civilizations where shoes are not worn. Plastic shoes especially render the skin vulnerable because they are conducive to fungal growth and make infection of the skin more likely.

Patients with generalized immune deficiency, such as diabetics and those with HIV disease, are at increased risk for tinea pedis. It is the third most common cutaneous fungal infection in HIV.[2] One possible explanation for the high incidence in HIV is the lack of CD_4 lymphocytes to aid in cell-mediated immunity. Atopics can also develop chronic

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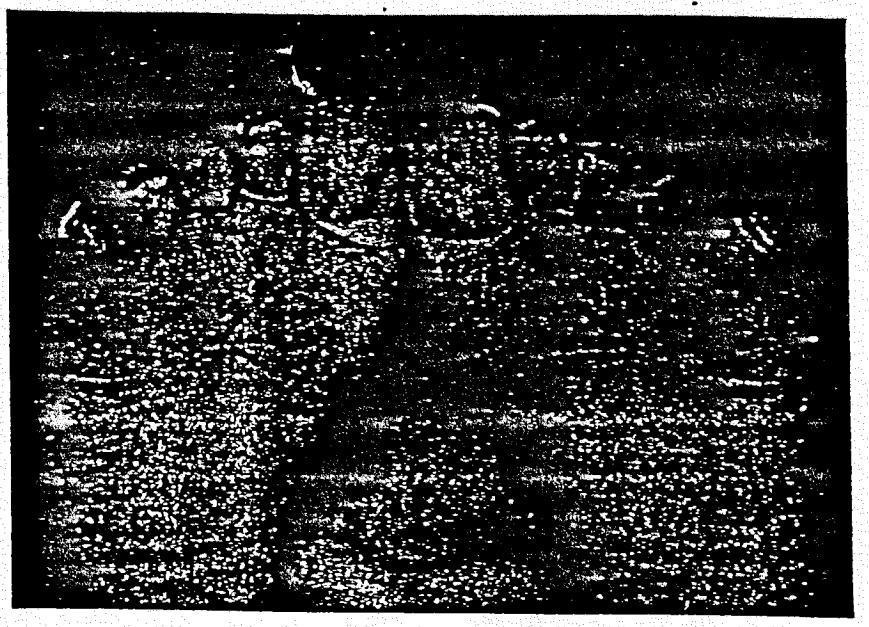

Figure 1. Tinea pedis in a child.

tinea pedis owing to a lack of cell-mediated immunity to specific dermatophytes, whereas the rest of their cell-mediated immunity remains intact. Furthermore, infections of the toenails or soles can behave as reservoirs harboring spores that can produce numerous recurrences.

CLINICAL FEATURES

There are three well-accepted clinical presentations of tinea pedis, based primarily on the offending organism, summarized in Table 1. The first type is intertriginous/interdigital, the chronic form. The fourth to fifth interspace is most commonly affected, followed by the third to fourth. The skin involved appears white and macerated with weepy red erosions beneath and can extend to both the toes and soles (Fig. 2). Hyperhidrosis is commonly found. Pruritus and a foul odor may be associated features. This compilation of findings is referred to as "dermatophytosis simplex," a term coined by Leyden and Kligman at the University of Pennsylvania. When this uncomplicated form is superinfected by bacteria, specifically lipophilic diphtheroids, that are able to gain entry through a defective stratum corneum previously acted on by dermatophytes, it is transformed into "dermatophytosis complex."[7]

The second or vesicobullous form is generally subacute and often occurs superimposed on a background of mild simple infection. With each relapse, there is thickening of the soles, secondary infection, itch, and maceration.[13] Vesicles or vesicopustules, in the pres-

Table 1. CLINICAL PRESENTATIONS OF TINEA PEDIS

Type	Agent	Presentation	Clinical Symptoms	Associated Features
Intertriginous, interdigital	*T. rubrum* *T. mentagrophytes* *E. floccosum*	Chronic	Hyperhidrosis, pruritus, odoriferous	Maceration, erosions, 4th to 5th toe web
Vesicobullous	*T. mentagrophytes*	Subacute on background of chronic mild infection	Secondary infection, itch	Vesicles and pustules ± fissures, extend out from web space
Moccasin	*T. rubrum* *E. floccosum*	Chronic	Onychomycosis possible	Branny scale over sole and sides of feet

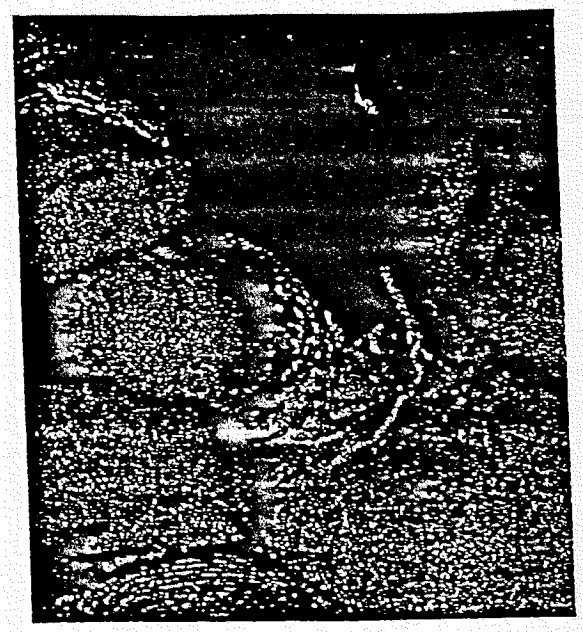

Figure 2. Intertriginous/interdigital tinea.

ence or absence of fissures, extend from the web space to the dorsum of the foot and soles, and especially the arches and lateral aspect of the feet (Fig. 3). The vesicular fluid is initially clear but can change in the presence of such complications as lymphangitis, lymphadenitis, or cellulitis.

The final presentation is the squamous or hyperkeratotic form, also referred to as the moccasin type. It presents as branny, furfuraceous scale, with silvery white flakes on a red thickened base distributed over the sole, heel, and sides of the feet, and tends to be chronic (Fig. 4). It can appear patchy and discrete or confluent and can affect the nails as well. Symptoms may or may not be apparent. The moccasin type of tinea pedis can be seen in patients with atopic dermatitis who also have a negative trichophyton test result to the fungus.

The chronic forms of tinea can also be manifested as "two foot one hand," involving the palm of one hand in addition to the soles of both feet (Fig. 5).

ETIOLOGY

Trichophyton rubrum is the most commonly isolated dermatophyte involved in tinea pedis, although any dermatophyte can be responsible. *T. rubrum* can give rise to all types of infection, except for the vesiculous type. Additional etiologic agents in order of decreasing frequency include *Trichophyton mentagrophytes* and *Epidermophyton floccosum*. One study yielded positive cultures for *T. rubrum* in 76%, *T. mentagrophytes* in 17%, and *E. floccosum* in 1%; *Candida* was responsible for 6% of infections.[12] Elewski has reported *Trichophyton tonsurans* as another possible pathogen given its presence in the epidemic number of cases of tinea capitis. Because each of these pathogenic dermatophytes is anthropophilic (*T. mentagrophytes* var *mentagrophytes* is zoophilic but var *interdigitale* is anthropophilic), they can be spread easily among people.

The moccasin form, though predominantly attributed to *T. rubrum*, can also be caused by *E. floccosum*. It is the most common tinea infection in the HIV-positive population, owing almost exclusively to *T. rubrum*.[2] The interdigital presentation can result from infection with any of the three common dermatophytes and can involve *Candida albicans* as well, whereas the vesicular type is typically induced by *T. mentagrophytes*. A virulent form manifesting itself with ulcers, pustules, and rapid extension is due to *Trichophyton mentagrophytes* var *mentagrophytes*.[14] As alluded to previously, infections can also be mixed and include *Candida* and bacteria, especially noted in the interdigital type.

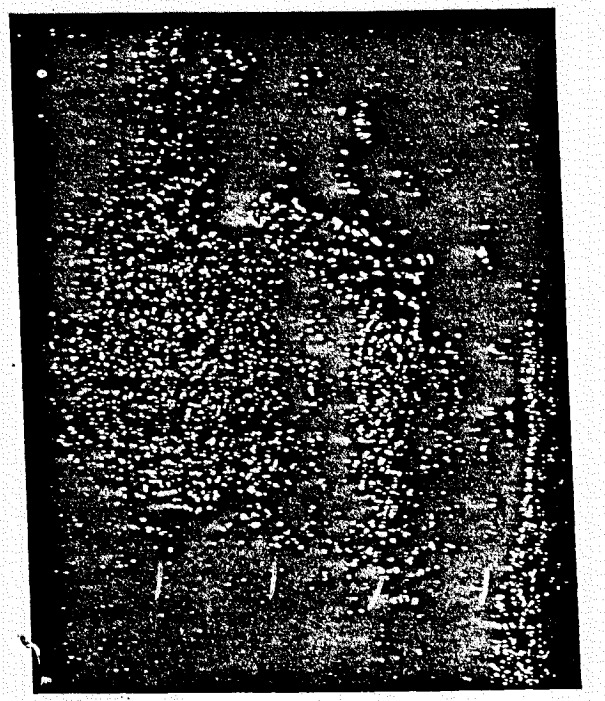

Figure 3. Vesicobullous form.

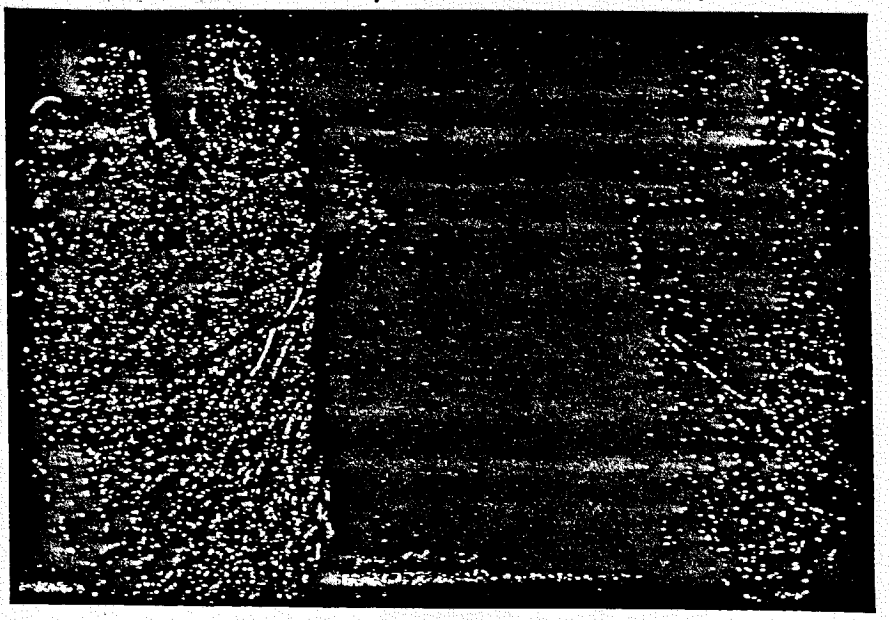

Figure 4. Moccasin type of tinea.

Infections that closely resemble those caused by the dermatophytes can be caused by nondermatophyte saprophytic molds found in soil, air, water, and on fomites. They are referred to as dermatomycoses because they mimic dermatophyte infections. These agents rarely affect skin and hair and are most likely contracted by direct transmission.[4] *Scytalidium dimidiatum* (formerly *Hendersonula torloidea*) and *Scytalidium hyalinum* can result in both tinea pedis and onychomycosis. Interdigital and moccasin type infections occur, as can "two foot one hand" tinea.[4, 12] These saprophytic molds can also coexist with the dermatophytes and both can be pathogenic. *S. dimidiatum* is endemic in

Figure 5. Two foot, one hand tinea.

the western and southeastern United States, California, Washington, Canada, South America, the Caribbean, Africa, India, and the Far East.[4] *S. hyalinum* has not yet been cultured from the environment but may be endemic in the southeastern United States given the case reports from patients originating in those areas. *Scopulariopsis, Fusarium,* and *Aspergillus* are additional fungal species that are able to produce infections that mimic classic tinea pedis.

Organisms that can be cultured from normal toe webs include such microflora as *Micrococcae* (staph), aerobic coryneforms, and a few gram-negative bacteria. The interspaces can also be colonized by dermatophytes and yeasts such as *Candida.* Once the stratum corneum barrier is disrupted by dermatophytes, producing maceration and inflammation, bacteria are able to proliferate.[7]

Other pathogenic dermatophytes include *Trichophyton violaceum* in the Near East, eastern Europe, the countries of the former Soviet Union, north Africa, and Latin America and much more rarely *Microsporum persicolor, Microsporum canis,* and *Trichophyton megninii.*

PATHOGENESIS

The dermatophyte functioning as the inciting agent in these infections is responsible for the destruction of the normal barrier role of the stratum corneum. The host response to proliferation of the fungus is to increase growth of the basal cell layer of the epidermis, resulting in scaling and thickening of the skin.[13] Under appropriate environmental circumstances such as occlusion and humidity, local conditions favor overgrowth of opportunistic bacteria at the expense of the dermatophyte. Initially large colony diphtheroids proliferate but increasing severity leads to a dominance of gram-negative organisms. Without the initial invasion of the dermatophyte, gram-negative bacteria grow minimally. These changes are manifested as progression from an uncomplicated superficial fungal infection to a much more aggressive picture with erosions and maceration of the web spaces.[5] Bacterial organisms isolated include *Staphylococcus aureus,* gram-negative bacteria such as *Pseudomonas* and *Proteus, Corynebacterium minutissimum, Corynebacterium jeikeium, Brevibacterium epidermidis,* and *Micrococcus sedentarius.*[7,8]

With progression of symptomatology and infection, it becomes more and more difficult to isolate the offending dermatophyte source on culture. A study performed in 1978 by Leyden and Kligman revealed that in dermatophytosis simplex cultures were positive for dermatophyte in 84.6% for *T. rubrum* and *T. mentagrophytes.* Moderate dermatophytosis complex showed dermatophytes present in 56%, decreasing further to a low 36% in severe dermatophytosis complex. At the same time, cultures for *Proteus* and other gram-negative bacteria increased respectively from 12% to 35% and 18% to 65%. The incidence of *Staphylococcus aureus* increased as well from 8% to 11%.[9]

The dermatophytes produce penicillin and streptomycin-like antibiotics that then select for growth of more resistant bacteria. The bacteria in turn elaborate proteolytic enzymes, which increase tissue destruction.[8] One possible explanation for the elimination of fungi as disease progresses is the production of sulfur compounds that possess antifungal properties, for example, methanethiol, ethanethiol, and dimethyl sulfide by *Micrococcus sedentarius* and *Brevibacterium epidermidis.*[8]

COMPLICATIONS

Gram-negative toe web infections are at the extreme end of the spectrum of dermatophytosis complex. The clinical presentation is one of white macerated interspaces with painful erosions. These lesions are exudative and odoriferous and can be inflammatory to the point of disability. In these patients cultures are most likely to reveal *Pseudomonas* or *Proteus* (Fig. 6). Antibacterial agents are able to halt progression to symptomatic disease via inhibition of large colony diphtheroid growth.[9]

The ID reaction (autoeczematization) is a vesicular, eczematous, or anhidrotic eruption on the fingers, palms, and toes. Tense pruritic vesicles containing clear or cloudy fluid, which may or may not be tender, develop after a flare of tinea pedis.[10] The reaction is due to allergic sensitization from hematogenous spread of fungi or fungal antigens from the primary focus. By definition, fungi can be demonstrated at the primary focus on the feet and not in the secondary focus or ID. Although the ID usually occurs on the fingers and hands, it can be seen on the legs and feet as well.

Figure 6. *Pseudomonas* (gram negative) toe-web infection.

Another possible complication is secondary infection by saprophytic molds, which in this case are not primary pathogens.

DIAGNOSIS

Direct microscopy is performed with 10% to 20% potassium hydroxide from the scaly advancing border of the lesion. It should be lightly heated prior to viewing to enhance penetration of the potassium hydroxide (KOH). Best viewing conditions occur with the microscope at a low light intensity and the condenser down. Ten or 40 power can be used, looking for septate branching hyphae. In the case of vesicular lesions, the top of the vesicle should be sliced off and placed on the glass slide for testing. The KOH preparation has a sensitivity of 77% and a specificity of 62% according to one study on 333 specimens.[12] A negative result does not rule out the diagnosis, and a positive result, although suggestive, does not completely prove the diagnosis either. It will not distinguish dermatophytes from nondermatophytes (such as pathogenic saprophytic molds) and *Candida*. Chlorozol black E is specific for chitin in fungal cell walls and stains hyphae blue-black. This stain contains DMSO (dimethyl sulfoxide) and therefore will not require heating.

A culture should follow the potassium hydroxide examination even if it is positive. A KOH preparation of the saprophytic molds (*Scytalidium dimidiatum* and *hyalinum*) demonstrates atypical long septate branching hyphae and mycelia with walls of varying thickness and can be confused with typical dermatophytes.[1]

Standard cultures are performed on Sabouraud dextrose agar, which is the standard for judging colony color and morphology. Lactophenol cotton blue tease preparations are used to study morphology after growth of the organism on culture. Saprophytic molds can also be grown on this medium. If chloramphenicol and cycloheximide are added to the media for the inhibition of bacteria and molds, respectively, Mycosel agar is produced. The disadvantage of this medium is that growth of pathogenic nondermatophytes and molds would be inhibited.

Pathogenic molds should be suspected in the case of failure of the usual antifungal treatments and failure of growth on standard cultures in the presence of a positive KOH preparation.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes other common entities that can produce scaling, vesicles, or pustules on the feet such as contact dermatitis, candidiasis, erythrasma, and dyshidrosis. Other disorders to consider include pustular psoriasis, acrodermatitis continua, pustular bacterids, pyodermas, and secondary syphilis.

The hands should be examined for conditions such as "two foot one hand" tinea, nail pits or onycholysis for a diagnosis of psoriasis, or keratotic copper colored papules on the palms for syphilis. A thorough history should be obtained of exacerbating factors, hyperhidrosis, or family members with similar symptoms. The distribution of the eruption may be suggestive of a diagnosis such as contact dermatitis, with a history of worsening with certain shoes, socks, or medications. Additional studies, for example, Wood's lamp, can be used to diagnose *Corynebacterium minutissimum* by its distinctive coral red fluorescence and *Pseudomonas*, which fluoresces green. *Candida albicans* can exhibit a Swiss cheese-like punched out appearance to the web space.[5]

TREATMENT

General guidelines for the management of tinea pedis begin with maintaining a dry local

environment and avoiding occlusive footwear to the extent possible. Socks should be 100% cotton and changed frequently to prevent dampness. Shoes should be alternated so that they may air dry over 2 to 3 days. Antifungal powder can be used in shoes daily and shower sandals worn at health clubs and other communal bathing facilities or swimming pools.

For chronic or recurrent infections patients may be treated with long-term topical antifungal agents on an every other day or twice weekly basis. Mild keratolytic agents such as Whitfield's ointment can be substituted for noninflammatory asymptomatic infections. Antibacterial soaps can be recommended in cases of interdigital maceration due to mixed bacterial and fungal infection. Finally, Burow's compresses or vinegar soaks can aid in bullous disease or hyperhidrosis with maceration to dry out toe webs and decrease the bacterial load.

The palms and soles present a unique treatment problem because of the thick horny layer of skin without sebum excretion and minimal sweating. Topical imidazoles such as clotrimazole, isoconazole, econazole, and ketoconazole inhibit ergosterol biosynthesis, which is necessary for fungal cell membranes. A lack of ergosterol results in a defective and permeable cell membrane. These agents are fungistatic only and can be used for chronic infections and to treat mild pruritus or erythema. The allylamines such as naftifine and terbinafine inhibit fungal squalene epoxidase and are fungicidal.

Severe infection requires more than topical antifungal agents. An oral antibiotic may be used with the topical antifungal agent for recurrent interdigital infection with bacterial involvement, especially *Staphylococcus* or *Pseudomonas* superinfection. A more acute presentation of tinea, extensive chronic disease, or even one that appears resistant to topical agents possibly through an inability to penetrate the thick stratum corneum will require systemic antifungal therapy. The mainstay of therapy had been griseofulvin for extensive dermatophyte infection. It does not have activity against nondermatophytes. Griseofulvin acts on the cell nucleus, an uncommon site. Problems, however, have developed with emerging antifungal resistance both to this and to ketoconazole, which had been the second choice owing to reported idiosyncratic hepatotoxicity. Other potential reported side effects include nausea, vomiting, abdominal pain, headache, gynecomastia, and impotence. These will reportedly resolve with discontinuation of the medicine.

Newer oral imidazoles show promise, including itraconazole and fluconazole, and the new oral allylamine terbinafine. Fixed treatment schedules for these medications are being reported. Itraconazole has certain advantages, such as a broad spectrum covering *Candida*, dermatophyte, and some molds, and is 10-fold more active than ketoconazole owing to its increased affinity for fungal cytochrome P_{450}. It also demonstrates an affinity for keratinized tissues, resulting in much higher skin levels than sebum. Side effects, reported in up to 7% include pruritus, rash, dizziness, sleepiness, nausea and vomiting, abdominal pain, and headache. Reported treatment schedules have included 100 mg/d for 2 to 4 weeks, 400 mg/d for 7 days, and 200 mg/d for 1 week per month for 3 to 4 months.[15]

Oral terbinafine is also a potentially useful agent because of its primary fungicidal effects. It has been used at doses of 250 mg/d for 2 weeks and symptoms continue to improve off the medication.[16] Side effects are reported in approximately 10% and include gastrointestinal upset, urticaria, pruritus, loss of taste, and elevated liver functions. Both agents appear to produce results superior to ketoconazole, but oral terbinafine is still in clinical trials in the United States at the time of this writing.

SUMMARY

Tinea pedis is the most common fungal infection. Positive culture results can be obtained from both symptomatic and asymptomatic toe webs. Although infection is much more likely in adults, it can occur in prepubertal children as well. Predisposition to the development of tinea pedis occurs with generalized immunodeficiency and in atopic dermatitis. Cell-mediated immunity is necessary to mount a response to the dermatophytes.

Most cases are caused by *T. rubrum* but can also occur with *T. mentagrophytes* and *E. floccosum*. Three general presentations are noted: interdigital, moccasin, and vesicobullous. Bacterial superinfection can occur once the stratum corneum barrier is disrupted. Complications such as gram-negative toe web infections and ID reactions can occur.

Diagnosis should be made through a KOH

preparation followed by culture. Treatment is based on the severity of symptoms. General guidelines for foot care should be followed in all cases, and topical antifungal agents can be applied to chronic forms. More widespread or inflammatory cases may require the addition of an oral antifungal and antibiotic.

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