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Herpes simplex: Evolving concepts

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READER SERVICES

A U.S. epidemiologic survey of superficial fungal diseases

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Background: Large-scale studies performed outside the United States have demonstrated that most cases of onychomycosis and tinea pedis are caused by dermatophytes, primarily *Trichophyton rubrum*. However, other studies have suggested that yeasts and nondermatophytic molds may play a role, particularly in onychomycosis.
Objective: This study was undertaken to determine the epidemiology of superficial fungal infections in a U.S. population.
Methods: Fungal cultures were performed on patients with clinically suspected tinea cruris, tinea corporis, tinea capitis, tinea pedis, and onychomycosis.
Results: Dermatophytes were the most commonly isolated fungi in each type of superficial fungal disease studied. *T. rubrum* was the most commonly isolated dermatophyte species, although *Trichophyton tonsurans* was more common in tinea capitis and equally common in tinea corporis/tinea cruris. In tinea pedis and onychomycosis, dermatophytes appeared in approximately 95% and 82% of isolates, respectively. *Candida albicans* and nondermatophyte molds played only a minor role in onychomycosis; *C. albicans* was isolated in 7% of nail cultures and nondermatophytic molds were isolated in 11%.
Conclusion: These results are in general agreement with other major epidemiologic studies performed outside the United States. Dermatophyte fungi cause most superficial fungal infections.
(J Am Acad Dermatol 1996;35:539-42.)

Dermatophytes cause most superficial fungal infections, but some yeasts and nondermatophytic molds are also sometimes involved.[1] Onychomycosis and tinea pedis are two of the most common superficial fungal diseases. Recent discussion has focused on the importance of nondermatophytes in these diseases, particularly in onychomycosis.[2-4] However, data from studies in Canada[5] and the United Kingdom[6] indicate that nondermatophytes play a small role in these infections.

The purpose of this study was to determine the epidemiology of superficial fungal diseases including onychomycosis, tinea pedis, tinea cruris, tinea corporis, and tinea capitis in a U.S. population.

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METHODS

A total of 1222 specimens (no more than one from each patient) were analyzed between January and December 1994. These specimens of nail, skin, and hair came from clinics, private physicians, and clinical trial programs (initial isolate). In most instances, data were not available on patient demographics. Sixteen states were represented: Alabama, California, Colorado, Georgia, Illinois, Louisiana, Maryland, Michigan, Minnesota, New Jersey, North Carolina, Ohio, Oregon, Rhode Island, Virginia, and Wisconsin.

Specimens were submitted to the laboratory in (1) Sabouraud's dextrose agar with 0.04% cycloheximide, (2) dermatophyte test medium (DTM), or (3) a Derma-Pak (Microbiological Supply Co., Toddington, Bedfordshire, U.K.). Each specimen that arrived in a Derma-Pak was examined by Calcofluor (Sigma Chemical Co., St. Louis, Mo.) in 5% potassium hydroxide microscopy and was inoculated on Sabouraud's dextrose agar with and without 0.04% cycloheximide.

All cultures were incubated at 30° C and checked twice weekly; a minimum of 4 to 6 weeks was allotted to confirm any negative cultures.

Initial cultures that grew fungi suspected to be *Trichophyton* were inoculated on *Trichophyton* agars #1 and #4

Table I. Specimens with fungal growth

Suspected infection	Total specimens	Specimens with growth	%
Onychomycosis	736	370	50.3
Tinea pedis	129	38	36.5
Tinea cruris/tinea corporis	189	69	29.5
Tinea capitis	168	84	50.0
Total	1222	561	45.9

slants and on Christianson's urea agar slants. Baby mixed cereal agar[7] plates were used to induce conidia. These subcultures were examined after 1 week of incubation at 30° C. If test results were inconclusive, the hair perforation test was performed or rice grains were added to identify other dermatophyte species. Nondermatophytic molds were often identified by microscopic growth on potato dextrose agar and other media and by manipulation of the temperature and observation of their growth. Yeasts were grown in corn meal with Tween 80 agar, by means of the Dalmau technique. Growth on media containing cycloheximide and the presence of fermentation in carbohydrates (dextrose, maltose, sucrose, lactose, cellobiose, and trehalose) helped to identify yeasts. Occasionally, Christianson's urea, nitrate assimilation, or carbohydrate assimilation in the API 20C test (bioMerieux Vitek, Inc., Hazelwood, Mo.) was used to confirm identification.

Slide cultures were performed when necessary. Molds growing in culture were routinely blotted with cellophane tape, and the material picked up by the tape was applied to a slide with Calcofluor in 5% potassium hydroxide. Dermatophyte conidia are produced more rapidly on media with less dextrose; therefore dermatophyte-like isolates were planted on cereal agar and incubation was continued for 1 week. The development of additional structures during that week indicated a dermatophyte. For nondermatophytic molds, slide cultures were prepared with potato dextrose agar, which encourages growth of conidia. When no conidia were seen, tap water, corn meal, Czapek solution agars (Difco Co., Detroit, Mich.), and/or cereal agars were used for these isolates.

All totals were tallied with the Paradox (Borland International, Inc., Scotts Valley, Calif.) program.

RESULTS

Of the 1222 specimens analyzed, 561 (45.9%) grew at least one fungal species (Table I). The pathogen recovery rate varied by disease, from 50.3% in clinically suspected onychomycosis to 29.5% in suspected tinea cruris/tinea corporis. Of the specimens that grew fungus, dermatophytes were predominant in each disease (Table II). Overall, *T. rubrum* was the most common dermatophyte. It was present most frequently in onychomycosis and tinea pedis, accounting for 76.2% and 78.9% of isolates, respectively. In tinea capitis, *T. tonsurans* was predominant, accounting for 88.1% of all isolates and 90.2% of dermatophyte isolates. In tinea cruris/tinea corporis, the combined frequency of isolation of *T. rubrum* and *T. tonsurans* was 40.6%.

C. albicans was isolated in each type of infection but was not considered clinically relevant except in patients with tinea cruris/tinea corporis.

DISCUSSION

This U.S. study confirms that the vast majority of superficial fungal infections are produced by dermatophytes. Dermatophytes caused 94.7% of cases of tinea pedis and were found in 81.9% of cases of onychomycosis. The epidemiology of onychomycosis and tinea pedis in the United States is similar to that reported in Canada[5] (90.7% and 97.1% dermatophytes, respectively) and in the United Kingdom[6] (80.6% dermatophytes in onychomycosis); dermatophytes are by far the most common fungi.

In the U.K. study, Clayton[6] found only 1% *Candida* species in the isolates of toenails but 58% in those of fingernails; however, the study included chronic paronychia as well as onychomycosis and had an unusually low rate of recovery (73% of fingernail isolates failed to grow). Of total samples in Clayton's study, only 16% grew *Candida.*

Yeasts have not been shown to be keratinolytic, and no mechanism for their primary invasion into nails has clearly been established. Yeasts may colonize glabrous skin, hair, and nails and may become pathogenic only in association with preexisting infection, trauma, loss of epidermal barrier function, or immunodeficiency.[6, 8, 9] For example, *Candida* can be recovered from the mouths of 30% of healthy adults,[10] but acute pseudomembranous candidiasis is rarely encountered in healthy adults and, when present, may be a harbinger of diabetes mellitus, AIDS, or other primary or secondary immunodeficiency. To assess the clinical significance of the recovery of *Candida*, clinical and pathologic correlation is important. We isolated *Candida* from 48% of tinea cruris/tinea corporis cultures. Without clinical correlation the significance is impossible to determine. Likewise, we cultured *C. albicans* in 2.3% of scalp isolates, but because *C. albicans* does not cause tinea capitis, we believe that all of the pathogens were dermatophytes. In tinea pedis, 5.3% of isolates

Table II. Fungi isolated

	No. of isolates		% Total growth		% Dermatophytes
Onychomycosis					
Dermatophytes					
T. rubrum	282		76.2		93.1
T. mentagrophytes	12		3.2		4.0
T. tonsurans	7		1.9		2.3
Epidermophyton floccosum	1		0.3		0.3
Microsporum gypseum	1		0.3		0.3
Subtotal		303		81.9	100.0
C. albicans		26		7.0	
Nondermatophyte molds*					
Scopulariopsis brevicaulis	13		3.5		
Acremonium species	11		2.9		
Aspergillus versicolor	8		2.2		
Fusarium solani	4		1.1		
Aspergillus terreus	3		0.8		
Aspergillus flavus	1		0.3		
Scytalidium dimidiatum	1		0.3		
Subtotal		41		11.1	
Total		370		100.0	
Tinea capitis					
Dermatophytes					
T. tonsurans	74		88.1		90.2
T. rubrum	3		3.6		3.7
M. canis	3		3.6		3.7
T. mentagrophytes	1		1.2		1.2
M. gypseum	1		1.2		1.2
Subtotal		82		97.7	100.0
C. albicans		2		2.3	
Total		84		100.0	
Tinea cruris/tinea corporis					
Dermatophytes					
T. rubrum	14		20.3		38.9
T. tonsurans	14		20.3		38.9
M. canis	5		7.2		13.9
T. mentagrophytes	2		2.9		5.5
T. verrucosum	1		1.4		2.8
Subtotal		36		52.1	100.0
C. albicans		33		47.9	
Total		69		100.0	
Tinea pedis					
Dermatophytes					
T. rubrum	30		78.9		83.3
T. mentagrophytes	6		15.8		16.7
Subtotal		36		94.7	100.0
C. albicans		2		5.3	
Total		38		100.0	

*We cannot determine whether these are pathogens because we have no potassium hydroxide results.

grew *Candida*, but we cannot tell whether they were pathogenic because we lack the clinical data.

Nondermatophytic molds may be recovered as "contaminants" from glabrous skin, hair, and nails. Stringent criteria must be met before a yeast or nondermatophytic mold grown from a specimen is accepted as a causative agent. English[11] has proposed that a nondermatophytic mold must grow from at least 5 of 20 inocula, with no dermatophyte growth, to be considered clinically significant. Summerbell,

Kane, and Krajden[5] added the presence in direct microscopy of atypical hyphae and/or conidia to the list of criteria.

The relations between dermatophytes and nondermatophytes in onychomycosis may be similar to the situation in interdigital tinea pedis in which dermatophytosis simplex can progress to dermatophytosis complex.[12, 13] According to Leyden, dermatophyte infection of the toe-webs may create a hospitable environment for bacteria that normally would not colonize the area. These bacteria can overgrow and mask the underlying dermatophyte infection. Similarly, dermatophyte infection of the nail may create conditions favorable to both bacteria and saprophytic molds, which on culture often overgrow dermatophytes, impeding their isolation. Therefore a saprophytic mold growing from a patient with a clinical impression of onychomycosis may not be the original pathogen, but may represent valid growth. Laboratory isolation of the dermatophyte may have been impeded by the saprophyte in the same way isolation of dermatophytes can be impeded by bacteria in the dermatophytosis complex syndrome.[12, 13] This phenomenon in the nail could be called "onychomycosis complex." Fungal culture results need to be interpreted closely in correlation with the clinical situation. The clinician should be alert for this when the potassium hydroxide reveals septate hyphae and only saprophytes were recovered in the laboratory.

The majority of cultures received in our study were already planted on media plates; therefore no direct microscopy was done; this hampered analysis of the significance of the recovered nondermatophytic molds (Table II).

The most likely reason that more than half the cultures failed to grow is that there was no fungus. Fungi cause only 50% of nail disorders,[14] and other skin conditions can mimic cutaneous fungal infections. Other factors that may account for the low recovery rate are antimycotic use by the patient, variable methods of culture collection, and bacterial or saprophytic overgrowth. In Clayton's study[6] of onychomycosis, 66% of samples from toenails and 73% of samples from fingernails had no growth, which is somewhat less than our recovery rate.

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