



# JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY

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## Cicatricial pemphigoid

Thomas E. Fleming, MD and Neil J. Korman, MD, PhD  
*Cleveland, Ohio*



## Monoclonal antibody treatment of psoriasis



## Late metastases of cutaneous melanoma



## Paraneoplastic pemphigus



## Prognostic indicators in venous ulcers



## Potassium iodide in dermatology



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or slides should, in general, be avoided.**

# A large-scale North American study of fungal isolates from nails: The frequency of onychomycosis, fungal distribution, and antifungal susceptibility patterns

M. A. Ghannoum, PhD,<sup>a</sup> R. A. Hajjeh, MD,<sup>b</sup> R. Scher, MD,<sup>c</sup> N. Konnikov, MD,<sup>d</sup> A. K. Gupta, MD,<sup>e</sup> R. Summerbell, PhD,<sup>f</sup> S. Sullivan, MD, PhD,<sup>g</sup> R. Daniel, MD,<sup>g</sup> P. Krusinski, MD,<sup>h</sup> P. Fleckman, MD,<sup>i</sup> P. Rich, MD,<sup>j</sup> R. Odom, MD,<sup>k</sup> R. Aly, MD,<sup>k</sup> D. Pariser, MD,<sup>l</sup> M. Zaiac, MD,<sup>m</sup> G. Rebell, MD,<sup>m</sup> J. Leshner, MD,<sup>n</sup> B. Gerlach, MD,<sup>o</sup> G. F. Ponce-de-Leon,<sup>b</sup> A. Ghannoum,<sup>a</sup> J. Warner, BA,<sup>a</sup> N. Isham, BA, M(ASCP),<sup>a</sup> and B. Elewski, MD<sup>a</sup>  
*Cleveland and Hudson, Ohio; Atlanta and Augusta, Georgia; New York, New York; Boston, Massachusetts; Toronto, Ontario, Canada; Jackson, Mississippi; Burlington, Vermont; Seattle, Washington; Portland, Oregon; San Francisco, California; Norfolk, Virginia; and Miami Beach, Florida*

**Background:** Onychomycosis, a fungal infection of the nail bed, is responsible for up to 50% of nail disorders. Although several surveys have been conducted in different parts of the world, there have been no multicenter epidemiologic surveys of onychomycosis in North America.

**Objective:** A 12-center study was undertaken to (1) determine the frequency of onychomycosis, (2) identify organisms recovered from the nails, and (3) determine the antifungal susceptibility of isolates.

**Methods:** A total of 1832 subjects participated in this study and completed a comprehensive questionnaire, and nail clippings were collected for potassium hydroxide examination and culturing.

**Results:** The frequency of onychomycosis, as defined by the presence of septate hyphae on direct microscopy and/or the recovery of a dermatophyte, was found to be 13.8%. In general, the dermatophyte isolates were susceptible to the antifungals tested.

**Conclusion:** Because of the limited number of large-scale studies, the baseline incidence is not firmly established. However, the higher frequency of onychomycosis in this study may confirm the suspected increase in incidence of disease in North America. (J Am Acad Dermatol 2000;43:641-8.)

Onychomycosis can be caused by dermatophytes, yeasts, or a select few nondermatophyte molds. Dermatophytes, particularly *Trichophyton rubrum* and *Trichophyton mentagrophytes*, are responsible for the majority of infections. Onychomycosis is the most common nail disorder in

adults, accounting for up to 50% of all nail diseases. Suggested predisposing factors include increasing age, immunosuppression, poor peripheral circulation, trauma, and tinea pedis. Although the incidence of onychomycosis in the United States has been arbitrarily estimated by Zaias<sup>1</sup> to be 15% to 20%

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in those persons 40 to 60 years of age, there have been no recent multicenter epidemiologic surveys in the United States. Previous studies from the United Kingdom,<sup>2</sup> Spain,<sup>3</sup> Finland,<sup>4</sup> and Canada<sup>5</sup> report the incidence of onychomycosis as 2.7%, 2.6%, 8.4%, and 6.85%, respectively. In a representative sample of 20,000 persons in the northeastern United States in the late 1970s, the US Health and Nutrition Examination Survey (NHANES I) found the overall prevalence of fungal nail infection to be 2.18%.<sup>6</sup> A 1997 cross-sectional survey conducted in a dermatology clinic waiting room in Cleveland, Ohio, found 8.7% of patients to have culture-confirmed dermatophyte onychomycosis.<sup>7</sup>

Because there are relatively few large multicenter studies, we sought to provide a benchmark on which trends in the incidence of onychomycosis may be determined. In this study, we performed a multicenter investigation to determine the frequency of onychomycosis, the range of fungal species isolated from nails, and the antifungal susceptibility patterns of the isolated organisms. Participants included 12 centers covering various regions (East, West, North, South, and Midwest) of the United States and one Canadian site.

## METHODS

The study was performed from June 1997 to May 1998. All subjects attending primary care physician offices or persons accompanying them during their visits were approached and asked to participate in this survey. Excluded persons were those who refused examination and patients who presented for onychomycosis or tinea pedis. Nail clippings were taken from the most severely affected nail. When both fingernails and toenails were involved, samples were obtained from both sites. In cases in which no signs of onychomycosis were evident, nail clippings were taken from the big toenail. Subjects signed a consent form and completed an exhaustive questionnaire covering demographics, personal habits, and medical history. Information was not collected on persons who refused to participate.

All nail specimens were sent to the Mycology Reference Laboratory, Center for Medical Mycology, Cleveland, Ohio, for direct microscopic observation (with calcofluor in 10% potassium hydroxide) and culture (with the exception of the New York and Canadian specimens, whose laboratory results were provided to us). Furthermore, the Canadian site did not preserve the isolates and therefore susceptibility testing was not performed on these organisms. Primary isolation media included Mycosel agar (BBL, Cockeysville, Md) and potato dextrose agar with chloramphenicol and gentamicin. All cultures were

incubated at 30°C for up to 4 weeks. Dermatophyte isolates were identified by microscopic morphology, urea testing, and *Trichophyton* agars. All recovered yeasts were identified, using the germ tube test (for *Candida albicans*) and the API 20C identification system (bioMerieux Vitek, Hazelwood, Mo). Only those nondermatophyte molds, which in the past have been implicated in nail disease, were identified,<sup>8</sup> again using microscopic morphology. Thus molds considered as highly unlikely to be significant, such as *Alternaria*, *Curvularia*, and most *Aspergillus* and *Penicillium* spp, were not included in the analysis of data.

A case of onychomycosis was defined as a person with any one of the following: specimen positive for septate hyphae by microscopic examination and culture positive for a dermatophyte, specimen positive for septate hyphae by microscopic examination and negative for dermatophyte culture, or specimen negative by microscopy and positive for dermatophyte culture. The presence of septate hyphae and/or a dermatophyte was classified as a case of onychomycosis, regardless of the appearance of the nail. Because none of the cultures which grew *C albicans* were correlated with positive microscopic findings for yeast cells, it could not be ascertained whether the organism was a contaminant or was causing disease (eg, paronychia). Therefore these *C albicans* isolates were not included in the data for onychomycosis cases. Similarly, no attempt was made to implicate any nondermatophyte mold isolated from these subjects as a causative agent of onychomycosis because no results from serial cultures were available. Nondermatophytes are included here for the purpose of organism distribution in the nail and antifungal susceptibility pattern information only.

A microdilution broth assay, developed at the Center for Medical Mycology under the auspices of the National Committee for Clinical Laboratory Standards (NCCLS), was used to determine the pattern of antifungal susceptibility of all identified organisms.<sup>9</sup> Dermatophytes were grown on oatmeal agar (100 g Heinz baby oatmeal cereal, 15 g granulated agar, and 30 mg gentamicin per liter). Although approximately 15% of *T rubrum*<sup>10</sup> isolates make few conidia, we were able to produce excellent conidiation from all isolates in this study by growing them on the oatmeal agar. Conidia were harvested with a cotton-tipped applicator and transferred to sterile saline. The resulting suspension was counted with a hemocytometer and diluted in RPMI 1640 (with L-glutamine, without sodium bicarbonate and buffered with MOPS at pH 7.0, Bioorganic, Niagara Falls, NY) to the desired concentration. Nondermatophyte molds and yeasts were purified and harvest-

**Table I.** Selected characteristics of patients with onychomycosis in a multicenter onychomycosis survey (1997-1998, North America)

Factor	All participants Total No. (%)	Onychomycosis cases No. (%)	Nononychomycosis cases No. (%)	Odds ratio	95% CI
Median age (y) (range)	41 (1-98)	57 (23-98)	40 (1-87)	4.10*	2.6-6.5†
Male	323 (41)	58 (58)	265 (38)	2.26	1.4-3.5†
Circulatory disease	104 (21)	24 (29)	80 (19)	1.72	0.97-3.0†
Athlete's foot	22 (5)	8 (10)	14 (3)	3.07	1.1-8.2†
Nail troubles	35 (7)	12 (15)	23 (6)	2.90	1.3-6.4†
Dystrophic nails	142 (8)	51 (20)	91 (6)	4.13	2.8-6.1†
Caucasian	608 (84)	77 (79)	531 (84)	0.68	0.39-1.2
African American	49 (7)	10 (10)	39 (6)	1.7	0.77-3.7
Hobbies					
Sports	234 (43)	23 (30)	211 (45)	0.52	0.30-0.9†
Painting/music	82 (15)	8 (10)	74 (16)	0.62	0.28-1.4
Gardening	85 (16)	12 (16)	73 (16)	1.00	0.49-2.0
Family members with nail disease or athlete's foot	351 (19)	39 (15)	312 (20)	0.74	0.51-1.1

Percentages represent the proportion of subjects with the specified characteristic out of all subjects who supplied pertinent information.

\*This odds ratio was obtained by comparing cases with noncases using 56 years as a cut-off point.

†Statistically significant factors ( $P \leq .05$ ).

ed from potato dextrose agar. Conidial suspensions were prepared and standardized as already described.

Microdilution plates were set up in accordance with the NCCLS M-27A reference method,<sup>11</sup> with the exception of inoculum preparation as described earlier. RPMI 1640 was used as a medium, 35°C and 4 days as incubation temperature and time, respectively, and 2 to 5 × 10<sup>3</sup> conidia/mL as an inoculum. The minimal inhibitory concentration (MIC) end point was defined as the concentration at which the organism was inhibited 80% as compared with the growth in the control well. Antifungal susceptibility was determined against fluconazole (Pfizer Pharmaceuticals, New York, NY), terbinafine (Novartis Pharmaceuticals, East Hanover, NJ), itraconazole (Janssen Research Foundation, Beerse, Belgium), and griseofulvin (Sigma Chemical Company, St Louis, Mo).

Statistical analysis was performed at the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia (CDC investigators were not involved in the design of this study or in the data collection). Univariate analysis was performed by means of Epi-Info version 6.03 and SAS 6.3 (SAS Institute, Cary, NC). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated with the statcalc option with Epi-Info. Chi-square tests were used to test for significant associations between defined variables. Values of  $P$  less than .05 were considered significant. The study was limited by the lack of information on basic demographics in many questionnaires, as well

**Table II.** Distribution of dermatophytes, nondermatophyte molds, and yeast species in the cultured nails

Organism	Total	Dermatophytes %	Total isolates %
<b>Dermatophytes</b>			
<i>T rubrum</i>	93	70.9	42.9
<i>T mentagrophytes</i>	35	26.7	16.1
<i>T tonsurans</i>	1	0.8	0.46
<i>M canis</i>	1	0.8	0.46
<i>E floccosum</i>	1	0.8	0.46
All dermatophytes	131		60.38
<b>Nondermatophytes</b>			
<i>Acremonium</i>	13	29.5	6.0
<i>Fusarium</i>	15	34.1	6.9
<i>Scopulariopsis</i>	9	20.5	4.1
<i>Scytalidium</i>	2	4.5	0.92
<i>A flavus</i>	1	2.3	0.46
<i>A fumigatus</i>	1	2.3	0.46
<i>A terreus</i>	1	2.3	0.46
<i>A versicolor</i>	2	4.5	0.92
All nondermatophytes	44		20.72
<b>Yeasts</b>			
<i>C albicans</i>	7	16.7	3.2
<i>C parapsilosis</i>	28	66.7	12.9
<i>C guilliermondii</i>	5	11.9	2.3
<i>C tropicalis</i>	1	2.4	0.46
<i>C lusitanae</i>	1	2.4	0.46
All yeasts	42		19.32

**Table III.** Percent distribution of dermatophytes, nondermatophyte molds, and yeast species from different regions of the United States and Canada

	Region				
	East	South	Midwest	West	North
<b>Dermatophytes</b>					
Total isolates	62	21	30	2	16
KOH positive	108	34	42	3	42
<i>T rubrum</i> (%)	79.0	66.6	73.3	—	50.0
<i>T mentagrophytes</i> (%)	19.4	33.3	26.7	100.0	37.5
<i>T tonsurans</i> (%)	1.6	—	—	—	—
<i>M canis</i> (%)	—	—	—	—	6.3
<i>E floccosum</i> (%)	—	—	—	—	6.3
<b>Nondermatophytes</b>					
Total isolates	17	3	11	1	12
<i>Acremonium</i> (%)	23.5	—	54.5	—	25.0
<i>Fusarium</i> (%)	23.5	33.3	45.5	100.0	33.3
<i>Scopulariopsis</i> (%)	23.5	66.6	—	—	25.0
<i>Scytalidium</i> (%)	11.8	—	—	—	—
<i>A flavus</i> (%)	5.9	—	—	—	—
<i>A fumigatus</i> (%)	5.9	—	—	—	—
<i>A terreus</i> (%)	5.9	—	—	—	—
<i>A versicolor</i> (%)	—	—	—	—	16.7
<b>Yeasts</b>					
Total isolates	18	4	12	1	7
<i>C albicans</i> (%)	16.7	25.0	16.7	—	14.3
<i>C parapsilosis</i> (%)	61.1	25.0	75.0	100.0	85.7
<i>C guilliermondii</i> (%)	11.1	50.0	8.3	—	—
<i>C tropicalis</i> (%)	5.6	—	—	—	—
<i>C lusitaniae</i> (%)	5.6	—	—	—	—

East, Maine, New York, Vermont, Virginia; South, Florida, Georgia, Mississippi; Midwest, Ohio; West, California; North, Oregon, Washington, Canada.

as lack of information on persons who refused to participate in this study. These limitations prevented the use of multivariate analysis.

## RESULTS

A total of 1832 persons agreed to participate in this survey, of whom 253 (13.8%) met the case definition for onychomycosis as described above. If positive microscopy is taken as the sole criterion, the frequency of onychomycosis would be 11.8% ( $n = 217$ ), whereas 7.2% ( $n = 131$ ) of the subjects were dermatophyte culture positive alone. The median age of all patients with onychomycosis was 57 years (range, 1-98 years), 58% were male, and 10% were African American. Univariate analysis identified several factors to be associated with increased risk of disease (Table I). These included some demographic factors such as age (those with onychomycosis were older than those without), sex (those with onychomycosis were more likely to be male), and clinical factors (the presence of diseases that affect the circulatory system, such as diabetes, vascular dis-

eases, and hypertension, was associated with increased risk of onychomycosis (OR = 2.0; 95% CI, 1.4-9.4), as well as having dystrophic nails (OR = 4.1; 95% CI, 2.8-6.1). Race, a family history of nail problems or athlete's foot, and participation in various sports or gardening activities were not associated with increased risk. In fact, participation in sports was associated with a decreased risk of having onychomycosis (Table I).

Of the organisms identified from all of the nail samples, dermatophytes were the most commonly isolated fungi (59%), followed by nondermatophyte molds and yeasts (representing approximately 20% each). Of the dermatophytes, *Trichophyton rubrum* was the most common isolate, followed by *T mentagrophytes*. *T tonsurans*, *Microsporium canis*, and *Epidermophyton floccosum* accounted for 0.8% of the dermatophytes each. *Acremonium*, *Fusarium*, and *Scopulariopsis* spp were the most common isolates among the nondermatophytes (representing 29.5%, 34.1% and 20% of nondermatophyte isolates, respectively). Small percentages (2.3%-4.5%) of

**Table IV.** Comparison of the percent distribution of fungal isolates in the United States and Canada

Organism	United States %	Canada %
<b>Dermatophytes</b>	n = 124	n = 7
<i>T rubrum</i>	72.6	42.9
<i>T mentagrophytes</i>	25.8	42.9
<i>T tonsurans</i>	0.8	—
<i>M canis</i>	0.8	—
<i>E floccosum</i>	—	14.3
<b>Nondermatophytes</b>	n = 35	n = 9
<i>Acremonium</i>	34.3	11.1
<i>Fusarium</i>	34.3	33.3
<i>Scopulariopsis</i>	17.1	33.3
<i>Scytalidium</i>	5.7	—
<i>A flavus</i>	2.9	—
<i>A fumigatus</i>	2.9	—
<i>A terreus</i>	2.9	—
<i>A versicolor</i>	—	22.2
<b>Yeasts</b>	n = 41	n = 1
<i>C albicans</i>	17.1	—
<i>C parapsilosis</i>	65.9	100
<i>C guilliermondii</i>	12.2	—
<i>C tropicalis</i>	2.4	—
<i>C lusitaniae</i>	2.4	—

*Scytalidium*, *Aspergillus versicolor*, *A flavus*, *A fumigatus*, and *A terreus* were also cultured. Among yeast species, *Candida parapsilosis* represented 66.7%. *C albicans* was recovered from 16.7% of cultures. Lower numbers of *C guilliermondii*, *C tropicalis*, and *C lusitaniae* were also isolated (Table II).

In general, the same pattern of frequency of all organisms was observed when isolate distribution was queried by US regions, although there was a slight variation in distribution (Table III). Comparison of species distribution between the US and the Canadian sites revealed that although similar fungal species were isolated in the two countries, a difference in frequency patterns exists (Table IV).

Interpretive breakpoints for dermatophytic fungi have not yet been established, and the clinical relevance of MIC results remains uncertain.<sup>11</sup> However, all 4 antifungal drugs tested (terbinafine, fluconazole, itraconazole, and griseofulvin) appear effective against the tested dermatophyte isolates, although several *T mentagrophytes* isolates had elevated MICs to fluconazole. Overall, terbinafine (MIC<sub>50</sub> and MIC<sub>90</sub> of 0.001 µg/mL and 0.002 µg/mL, respectively) had a significantly greater activity than the other agents tested against the dermatophytes. For example, the mean MIC of terbinafine was 0.0012 as compared with a mean MIC of 0.104 for itraconazole (Table V).

**Table V.** In vitro susceptibilities of 117 dermatophyte isolates to fluconazole, itraconazole, terbinafine, and griseofulvin\*

Antifungal	MIC (µg/mL, range) <sup>†</sup>	MIC (µg/mL, mean)	MIC <sub>50</sub> (µg/mL) <sup>‡</sup>	MIC <sub>90</sub> (µg/mL) <sup>§</sup>
Fluconazole	0.125-32	2.77	1.0	4.0
Itraconazole	<0.06-1.0	0.104	0.06	0.125
Terbinafine	<0.001-0.004	0.0012	0.001	0.002
Griseofulvin	<0.125-2.0	0.44	0.25	0.5

\*Isolates include *T rubrum* (n = 82), *T mentagrophytes* (n = 33), *T tonsurans* (n = 1), and *M canis* (n = 1). No statistical differences in MIC ranges among species were noted.

<sup>†</sup>Inclusive MICs of all organisms tested.

<sup>‡</sup>Defined as the level at which 50% of all organisms were inhibited.

<sup>§</sup>Defined as the level at which 90% of all organisms were inhibited.

Terbinafine had higher in vitro antifungal activity compared with the other 3 agents against *Acremonium*, *Scopulariopsis*, and *Scytalidium* spp (Table VI). In contrast, itraconazole had lower MIC values than the other 3 drugs against *Aspergillus* and *C parapsilosis*. Finally, fluconazole was more active than the other agents against *C albicans* (Table VI). Of relevance for the antifungals evaluated, the mean MIC fell below the concentration found in skin or nails after the appropriate dosages (Table VII).<sup>12,13</sup>

## DISCUSSION

This survey found that onychomycosis occurred at a frequency of 13.8% in our centers in North America, as defined by positive potassium hydroxide or culture positive for dermatophytes, or both. The frequency was 11.8%, based on positive microscopy for septate hyphae alone, or 7.2% based on positive dermatophyte culture alone. Although the study designs differ, the frequency of onychomycosis in this study is higher than those previously reported in the United Kingdom (2.7%),<sup>2</sup> Spain (2.6%),<sup>3</sup> and in the NHANES I study of 1974 (2.18%).<sup>6</sup> This higher frequency rate may be due to the fact that, in the case of the UK and Spain surveys, data were collected by interview only, and some mycologic cases may have been overlooked. Our results may underscore the need for laboratory confirmation of onychomycosis cases in such surveys. However, our subjects were not selected randomly, and we may have overestimated the frequency of onychomycosis if persons with nail problems were more likely to participate. The incidence rates reported in the Finland (8.4%)<sup>4</sup> and Cleveland, Ohio (8.7%)<sup>7</sup> studies were based on positive dermatophyte culture alone and in general agree with the rate found in our study using culture as the criterion (7.2%). The observation that

**Table VI.** In vitro susceptibilities of 15 nondermatophyte mold isolates and 13 yeast isolates to fluconazole, itraconazole, terbinafine, and griseofulvin

Organism	No. of isolates	Antifungal	MIC (range)*	MIC (mean)
<i>Acremonium</i>	5	Fluconazole	>64	>64
		Itraconazole	1.0-4.0	2.2
		Terbinafine	0.06-0.125	0.099
		Griseofulvin	16-32	19.2
<i>Aspergillus</i>	2	Fluconazole	>64	>64
		Itraconazole	0.25-0.5	0.375
		Terbinafine	0.06-1.0	0.53
		Griseofulvin	>64	>64
<i>Fusarium</i>	4	Fluconazole	>64	>64
		Itraconazole	4.0-8.0	6.0
		Terbinafine	0.5->16	>16
		Griseofulvin	64	64
<i>Scopulariopsis</i>	2	Fluconazole	>64	>64
		Itraconazole	4.0	4.0
		Terbinafine	0.5-1.0	0.75
		Griseofulvin	64	64
<i>Scytalidium</i>	2	Fluconazole	16	16
		Itraconazole	1.0-4.0	2.5
		Terbinafine	<0.03-0.06	0.038
		Griseofulvin	1.0-4.0	2.5
<i>C albicans</i>	7	Fluconazole	0.25-0.5	0.39
		Itraconazole	0.06	0.06
		Terbinafine	>16	>16
		Griseofulvin	64->64	64
<i>C parapsilosis</i>	5	Fluconazole	0.25-1.0	0.45
		Itraconazole	<0.06-0.125	0.08
		Terbinafine	0.03->16	3.33
		Griseofulvin	64->64	>64
<i>C lusitanae</i>	1	Fluconazole	0.25	—
		Itraconazole	0.06	—
		Terbinafine	0.125	—
		Griseofulvin	>64	—

\*Inclusive MICs of all organisms tested.

**Table VII.** Antifungal drug concentration in skin and nails\*

Antifungal agent	Levels in skin (µg/mL)	Levels in nails (µg/mL)
Griseofulvin	16.4	14.6 <sup>†</sup>
Itraconazole	N/A	0.93
Terbinafine	2.5	0.39
Fluconazole	23.4	11.7

Adapted from Epstein WL, Shah VP, Riegelman S. Griseofulvin levels in stratum corneum. Arch Dermatol 1972;106:344-8; from Faergemann J, Zehender H, Millerioux L. Levels of terbinafine in plasma, stratum corneum, dermis-epidermis (without stratum corneum), sebum, hair and nails during and after 250 mg terbinafine orally once daily for 7 and 14 days. Clin Exp Dermatol 1994;19:121-6.

N/A, Data not available.

\*Drug levels are dependent on the duration of treatment, dosages, and host factors.

<sup>†</sup>Indicates level in the sole.

our study shows a higher frequency than the NHANES I study, which was conducted in the 1970s, may confirm the previously suspected increase in onychomycosis in the United States.

In our study, significant factors predisposing to onychomycosis were found to include age, sex, a history of circulatory disease, athlete's foot, and dystrophic nails. The subject's age was a strong risk factor, which agrees with the results from each of the studies from the United Kingdom,<sup>2</sup> Spain,<sup>3</sup> Finland,<sup>4</sup> Canada,<sup>5</sup> and the United States.<sup>7</sup> Roberts<sup>2</sup> suggests that the higher incidence of onychomycosis in patients older than 55 years may be due to the greater tendency of younger patients to seek treatment at an earlier stage. It may also reflect the comparative importance placed on cosmetic issues by patients in different age groups.

In this study, male subjects were twice as likely to have onychomycosis as female subjects. Sais,

Juggla, and Peyri<sup>3</sup> found the exact opposite to be true, suggesting that trauma from wearing women's fashionable shoes might account for the difference. In contrast, Heikkila and Stuff<sup>4</sup> found 3 times as many men were infected as women, which they attributed to the suggestion that "men exercise more." Roberts<sup>2</sup> found the incidence rate to be the same between the sexes, although these authors also cited Haneke<sup>14</sup> in implicating mechanical damage to the nails from athletic shoes. Because of the recent fitness trends among both sexes, resulting in the development of high-tech athletic footwear, the above arguments may no longer be as important. In this regard, our study also found that hobbies such as sports and exercise were associated with a decreased risk of onychomycosis, possibly reflecting generally healthier persons. However, when we looked at sports stratified by sex, this association persisted among women, but was no longer observed among men. The previously noted difference between the incidence of onychomycosis in men and women may also reflect the degree to which subjects are bothered by cosmetic appearances and thus seek treatment.

Other significant factors predisposing to onychomycosis were found to include a history of circulatory disease, athlete's foot, and dystrophic nails (greater than 3 and 4 times more likely to have onychomycosis if a person has athlete's foot or dystrophic nails, respectively). These would all agree with the previous findings of Haneke,<sup>14</sup> who suggested that slower nail growth due to poor circulation may be responsible, and of Alteras and Cojocar, <sup>15</sup> who report that about 20% of those with tinea pedis also have nail involvement.

On the other hand, race and family history of nail disease or athlete's foot, as opposed to athlete's feet in individual patients, were shown to be insignificant in our survey. Unlike the possible role of race in determining the degree of inflammatory response to *T tonsurans* scalp infections,<sup>16</sup> no racial differences were detected in this study. This could be due to the low percentage (6.7%) of African Americans who participated in this study. In addition, we did not demonstrate any familial correlation, possibly because of the few family units involved and the fact that we did not specifically target this question.

Our study confirms that *T rubrum* is the most common dermatophyte species isolated from the nails, followed by *T mentagrophytes*. In agreement with other reports (Ellis<sup>8</sup> and Williams<sup>17</sup>), several nondermatophyte species were isolated from study participants. *Fusarium* was the most common nondermatophyte mold isolated in our study, followed by *Acremonium* and *Scopulariopsis*. Other non-

dermatophyte isolates included *Scytalidium*, *A flavus*, *A fumigatus*, *A terreus*, and *A versicolor*. In agreement with Summerbell,<sup>18</sup> the lack of successive repeat follow-up cultures meant that the origin of these nondermatophyte isolates could not be determined, and most, if not all, of these organisms are likely to have been contaminants. In our study, these nondermatophyte isolates are reported for organism distribution and antifungal susceptibility pattern information only.

Consistent with previous published findings, the most prevalent yeast isolate from our study was *C parapsilosis* (66.7% of all yeast species). In a study of hospital personnel, Strausbaugh et al<sup>19</sup> reported that 81% of nonnursing participants and 75% of nurses carried yeasts on their hands. Of these isolates, 29% from nonnursing personnel and 31% from nurses were identified as *C parapsilosis*. Because *C parapsilosis* is part of the normal skin flora, it is unlikely to be important as a causative agent in onychomycosis. The significance of the isolation of *C albicans* from these subjects also could not be determined because none of the nail specimens that grew *C albicans* showed yeast cells by microscopy.

As far as we could determine, this is the first study to measure the susceptibility of dermatophytes to clinically used agents. The lack of susceptibility studies is not unexpected because there is no standard for susceptibility testing of dermatophytes. Efforts to develop such a standard method are under way. We recently optimized the conditions for determining the antifungal susceptibility of dermatophytes,<sup>9</sup> and these conditions were used to determine the MIC values of 4 antifungals, terbinafine, fluconazole, itraconazole, and griseofulvin against all fungal isolates. Generally, the dermatophyte isolates were susceptible to these agents, although several *T mentagrophytes* strains had elevated MICs to fluconazole. Overall, terbinafine was the most potent antifungal against the dermatophytes. There was a wide range in the MICs of the nondermatophyte molds and yeasts, with itraconazole and terbinafine showing greater activity against the filamentous molds and fluconazole higher antifungal activity against the yeasts.

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