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Spectrum of Fungal Keratitis at Wills Eye Hospital, Philadelphia, Pennsylvania

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Purpose. To report the spectrum of fungal keratitis at Wills Eye Hospital, Philadelphia. **Methods.** We reviewed the records of 24 cases of culture-positive fungal keratitis treated from January 1991 to March 1999 at Wills Eye Hospital. Risk factors, fungal identification, antifungal treatment, and outcomes were evaluated. **Results.** The study included 24 eyes (24 patients). Fourteen patients (58.3%) were female. The mean age was 59 years (range, 19–86 years). Predisposing factors included chronic ocular surface disease (41.7%), contact lens wear (29.2%), atopic disease (16.7%), topical steroid use (16.7%), and ocular trauma (8.3%). Early identification of fungal elements was achieved by staining of corneal scrapings in 18 cases (75%). Half of the cases (12 eyes) had corneal infections caused by yeast, and the other half by filamentous fungi. *Candida albicans* was the most commonly isolated organism (45.8%), followed by *Fusarium sp* (25%). Natamycin and amphotericin B were the topical antifungals most frequently used, while systemic treatment commonly used included fluconazole, ketoconazole, or itraconazole. Six patients (25%) had penetrating keratoplasty during the acute stage of infection. After a mean follow-up of nine months, 13 eyes (54.1%) had the best corrected visual acuity 20/100 or better. **Conclusions.** In contrast to other studies from the northern United States, we found *Fusarium sp* the most commonly isolated filamentous fungus. In our series, *C. albicans* was the most frequent cause of fungal keratitis, and a past history of ocular trauma was uncommon.

Key Words: *Candida albicans*—Contact lens—Corneal ulcer—Fungal ocular infection—Fusarium—Keratitis—Ocular mycosis—Penetrating keratoplasty.

The first case of fungal keratitis in the literature was reported by Leber in 1879.[1] Since then, despite numerous advances in the treatment of ocular infections, fungal keratitis is often a devastating event.[2–5] Once considered rare, the last four decades have shown an increase in the percentage of microbial keratitis caused by fungal infections.[6] Some of the factors that may be responsible for this increasing incidence of fungal keratitis include the development and widespread use of broad-spectrum antibiotics and steroids, the frequent and sometimes prolonged use of contact lenses, and the growing numbers of corneal surgeries performed, especially penetrating keratoplasty (PKP).[2–4,6–10] Heightened awareness of the problem among ophthalmologists, together with advances in the laboratory diagnostic techniques for fungal infections in ocular tissues, could also contribute to the increasing number of cases reported. Despite this, isolation of the infectious agent is sometimes elusive, with repeated corneal scrapings or biopsy being necessary to identify the organism.[2,3,6] Unfortunately, cases still remain where the fungus is positively identified only from the histopathology specimen of a PKP done when medical treatment failed to control the infection or when a perforation ensues.[11] Positive corneal cultures can still require several days or weeks for final identification. Sensitivity testing of the fungal isolates takes longer and is of questionable use.

More than 70 species of fungi have been reported as pathogenic to human cornea; the most frequently isolated pathogen varies with the geographical area studied.[2,5,6,10,12,13] Across the world, the single most commonly reported fungus isolated from mycotic keratitis is *Aspergillus sp.*[2] Fungal keratitis is reported more frequently from regions with a warm, humid climate and/or with an agricultural economy.[2–4,6,9,13–16] Yeast, especially *Candida sp*, predominate in temperate regions like the northern United States, while tropical isolates are most frequently filamentous fungi such as *Aspergillus sp* or *Fusarium sp.*[2–4,9,10,13,14] Filamentous organisms are associated with infections following trauma with vegetable-contaminated matter, whereas yeast infections typically occurs in eyes with preexisting ocular surface disease. To improve the management of cases of fungal keratitis, it is important for the ophthalmologist to be aware of the common fungal isolates within their region.

Reports analyzing the profile of keratomycoses in the northeastern United States are few and date back to studies done one or two decades ago.[9,10,13,17] This study reviewed a series of patients with culture-positive fungal keratitis at the Cornea Service, Wills Eye Hospital, Philadelphia (PA). We present the clinical characteristics, laboratory investigations, treatments, and outcomes of these patients.

PATIENTS AND METHODS

This study was designed as a retrospective review. Patients with fungal keratitis were identified by reviewing the microbiology laboratory records. The medical records of all patients treated at

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TABLE 1. *Clinical data of patients with fungal keratitis*

Age (y)	Sex	Onset of disease (season)	Risk factors	Previous ocular therapy	Fungus isolated
32	F	Su	Ocular allergy, chronic epithelial defect. BCL	Ciprofloxacin, trifluridine	*Candida albicans*
37	F	Su	Atopic eczema, systemic steroid	—	*Candida albicans*
28	F	A	Recurrent erosions	—	*Candida albicans*
78	M	Su	Chronic epithelial defect, diabetes mellitus	Cefazolin, FF tobramycin, ciprofloxacin, vancomycin, trifluiridine, fluorometholone	*Candida albicans*
44	M	A	—	Ciprofloxacin, trifluridine	*Candida albicans*
69	F	W	Atopic eczema	Tobramycin, ciprofloxacin	*Candida albicans*
86	F	Sp	PK, chronic epithelial defect, tarsorrhaphy, topical steroid	Ciprofloxacin	*Candida albicans*
42	F	Sp	Atopic eczema	Ofloxacin	*Candida albicans*
44	F	Sp	Dry eyes, floppy eyelids HIV + renal failure	Artificial tear, olopatadine, erythromycin	*Candida albicans*
68	M	A	PK/CE, chronic epithelial defect, topical steroid	Ofloxacin	*Candida albicans*
51	F	A	—	Ofloxacin, ciprofloxacin	*Candida albicans*
19	M	Su	—	Neomycin, polymyxin, ciprofloxacin, dexamethazone	*Cryptococcus neoformans*
65	F	Su	EW SCL (disposable)	Tobramycin, ciprofloxacin, trifluridine	*Fusarium sp.*
52	M	Su	EW SCL (disposable)	Cefazolin, FF tobramycin, trifluridine, PO acyclovir	*Fusarium sp.*
49	M	Sp	—	—	*Fusarium sp*
57	F	A	DW SCL (disposable) HSV keratitis	Tobramycin, ofloxacin, neomycin Trifluridine, acyclovir, propamidine I, PO ketoconazole, dexamethasone, fluorometholone	*Fusarium sp*
54	M	W	EW SCL (disposable)	Tobramycin, ofloxacin, dexamethasone	*Fusarium sp.*
48	F	W	DW RGPCL	Gentamicin, ciprofloxacin, trifluridine	*Fusarium sp.*
35	F	Sp	Vegetal trauma	Cefazolin, FF tobramycin, neomycin, dexamethasone	*Scedosporium apiospermum*
45	M	Su	DW SCL (disposable)	Erythromycin, ciprofloxain	*Scedosporium apiospermum*
64	M	Sp	Laceration with wire on farm	Tobramycin, IV cephalexin	*Aspergillus sp.*
70	M	Sp	PK/CE, chronic epithelial defect, tarsorrhaphy, topical steroid	Ofloxacin, ciprofloxacin, natamycin, PO fluconazole	*Penicillium sp*
54	F	A	HZO keratitis, topical steroid	Ofloxacin	*Alternaria sp*
76	F	A	HZO keratitis	Cefazolin, FF tobramycin	*Chrysonilia sp*

n, number; M, male; F, female; EW, extended wear; DW, daily wear; SCL, soft contact lens; BCL, bandage contact lens; RGPCL; rigid gas permeable contact lens; PK, penetrating keratoplasty; CE, cataract extraction; HZO, herpes zoster ophthalmicus; HSV, herpes simplex virus; HIV, human immune-deficiency virus; PO, oral; IV, intravenous; FF, fortified; sp, species; ARMD, age-related macular degeneration; LP, light perception; HM, hand movements; CF, counting fingers; Su, summer; Sp, Spring; A, autumn; W, winter.

(*continued*)

the Cornea Service, Wills Eye Hospital, between January 1991 and March 1999, with a diagnosis of culture proven fungal keratitis, were reviewed. Patients in whom the diagnosis of fungal keratitis was based on the observation of fungal elements from specimens of corneal scrapings or histopathology specimens from corneal biopsy or PKP—without supporting evidence of fungal isolation in culture—were excluded from this study (n = 10). The Cornea Service protocol for laboratory diagnosis of corneal ulcers was identical in all patients in this series. On presentation, corneal specimens from scrapings were submitted for staining with Gram, Giemsa, and/or calcofluor white and cultures on blood agar, chocolate agar, Sabouraud's dextrose agar, and thioglycolate broth. Patients with negative cultures from initial specimens who had a progression of corneal infection underwent repeat cultures and/or biopsies, sometimes with the addition of Lowenstein-Jensen media for acid fast organisms. All of the corneal specimens were submitted to the Wills Eye Hospital microbiology laboratory. The Sabouraud's agar was kept at ambient temperature and the other media were incubated at 37°C. The fungal cultures were followed for four weeks before a negative result was declared and the plates were discarded, which is in contrast to bacterial cultures where the final results are reported after five days.

Natamycin was the standard topical treatment for fungal keratitis, especially infections caused by filamentous organisms. Topical amphotericin 0.15% was used for the treatment of Candida infections. Both drugs may be used when Candida is suspected on the basis of the smears but is not yet confirmed by cultures. Systemic antifungal drugs were used when infection was deep in the cornea, unresponsive to topical antifungal treatment, or extension into the anterior chamber was suspected.

Medical records of the patients in this series were reviewed for the following features: age, sex, month of onset of infection, predisposing risk factors for the development of keratomycosis, results of microbiology examinations, medications used topically and systemically before or after the onset of fungal keratitis, duration of hospitalization, surgery performed, and follow-up of patients until the most recent evaluation at the Cornea Service.

RESULTS

The study included 24 eyes (24 patients) (Table 1). Of these, 10 patients were men (41.7%) and 14, women (58.3%). Age of patients ranged 19–86 years (mean, 59 years). With regard to the time of onset of infection, we noted a similar distribution of cases

TABLE 1. *Continued*

Topical antifungal therapy	Systemic antifungal therapy	Surgical therapy (indication)	Follow-up (mo)	Outcome
Amphotericin	—	—	6	20/50
Natamycin, amphotericin	Ketoconazole	—	53	20/60
Natamycin, amphotericin	—	—	9	20/25
Amphotericin, fluconazole	Fluconazole	PK (perforated)	3	HM, graft failure, cataract
Amphotericin, fluconazole	Fluconazole	—	5	20/20
Amphotericin	—	—	18	20/30
Amphotericin	—	—	36	20/200, graft clear, ARMD
Amphotericin	Fluconazole	—	4	HM, scar, cataract
Amphotericin	Itraconazole	—	4	20/100, scar
Amphotericin	Fluconazole	—	5	20/200, irregular astigmatism
Amphotericin	Fluconazole	PK (imminent perforation)	3	20/50, graft clear
Natamycin	—	—	3	20/20
Natamycin, amphotericin	—	—	2	20/20
Natamycin, fluconazole	Fluconazole	PK (no response to therapy)	11	HM, graft failure, cataract
Natamycin	Itraconazole	—	7	20/70, scar
Natamycin, ketoconazole	Ketoconazole, itraconazole	PK (perforated) Tarsorrhaphy (epithelial defect)	4	HM, graft failure
Natamycin	Ketoconazole	—	3	20/25
Natamycin	Ketoconazole	—	3	20/200, scar
Natamycin	—	—	2	20/25
Natamycin	Fluconazole	—	9	20/25
Natamycin, clotrimazol, amphotericin	Amphotericin IV	PK + CE (perforated)	6	HM, graft failure
Natamycin	Itraconazole	PK (scar)	10	CF, epithelial defect
Natamycin	Ketoconazole	—	5	LP, scar
Natamycin	Itraconazole	PK (perforated)	8	LP, scar

through spring, summer, and autumn (seven patients each), with fewer cases presenting in winter (three patients).

Predisposing risk factors for fungal keratitis were noted in 20 patients (83.3%) (Table 2). Eleven patients had a single risk factor, and nine patients had two or more risk factors. Ten patients (41.7%) had chronic ocular surface diseases; six of these had yeast infections, and the remaining four had filamentous fungal keratitis. This group included eyes with chronic herpes simplex keratitis, neurotrophic keratitis secondary to herpes zoster ophthalmicus, atopic conjunctivitis, recurrent erosions, dry eyes, and surface disorders following recent PKP.

Seven patients (29.2%) were using a contact lens in the affected eye at the onset of keratitis. Five patients were using disposable hydrophilic contact lenses; three of these patients used the lens on a extended wear basis (cases 13, 14, and 17) and two patients used the lens on a daily wear basis (cases 16 and 20). One patient was wearing a rigid gas permeable contact lens on a daily wear basis (case 18). One patient was using an extended wear bandage contact lens for recurrent epithelial defects secondary to atopic eye disease (case 1). Two patients (cases 14 and 18) revealed contact lens hygiene regimens that were considered inadequate. The patient wearing a bandage contact lens developed candida keratitis. All of the other contact lens wearers developed filamentous fungal infections.

Topical corticosteroid use in the affected eye at the onset of fungal keratitis was noted in four patients (16.7%). Three patients were using corticosteroid as prophylaxis against rejection following PKP (cases 7, 10, and 22), and one patient was on topical corticosteroid for chronic recurrent herpetic stromal disease (case 23). Another patient was on oral corticosteroids for the treatment of atopic eczema (case 2).

Four patients had a history of atopic diseases; three of these had atopic eczema (case 2, 6, and 8) and one patient had atopic conjunctivitis (case 1). Systemic conditions with possible immunosuppressive effects included diabetes mellitus (case 4) and HIV infection (case 9). *Candida albicans* was the fungus isolated in all of the above cases.

Ocular trauma immediately preceding the infection was noted in only two cases (8.3%). One patient had trauma from a plant (case 19) and the other patient sustained a corneal laceration from a metallic wire in a farm setting (case 21). Both patients with a history of trauma developed infections caused by filamentous fungi. One patient gave a history of cleaning compost using a pressurized air nozzle prior to the onset of infection (case 5), and another patient retrospectively related cleaning bird cages (case 20), but both did not recollect any ocular injury related to these activities.

Most patients were misdiagnosed prior to referral to the Cornea Service. A majority of patients (87.5%) were already using topical and/or systemic treatment prior to presentation. Of these, 21 patients used topical antibiotics (87.5%); 7, topical antiviral medications (29.2%); and 5, topical corticosteroid medications (20.8%).

TABLE 2. *Risk factors for fungal keratitis*

Risk factors	Yeast n	Yeast %	Filamentous n	Filamentous %	Total n	Total %
Chronic ocular surface disease	6	25.0	4	16.7	10	41.7
Contact lens wear	1	4.2	6	25.0	7	29.2
EW SCL—disposable	0	—	3	12.5	3	12.5
DW SCL—disposable	0	—	2	8.3	2	8.3
DW RGPCL	0	—	1	4.2	1	4.2
Bandage CL	1	4.2	0	—	1	4.2
Chronic use of steroids	3	12.5	2	8.3	5	20.8
Topical	2	8.3	2	8.3	4	16.7
Systemic	1	4.2	0	—	1	4.2
Systemic disease	5	20.8	0	—	5	20.8
Atopic eczema	3	12.5	0	—	3	12.5
Diabetes mellitus	1	4.2	0	—	1	4.2
Renal failure, HIV +	1	4.2	0	—	1	4.2
Trauma	0	—	2	8.3	2	8.3

n, number; EW, extended wear; DW, daily wear; SCL, soft contact lens; RGPCL, rigid gas-permeable contact lens.

One patient (case 16) was treated with topical antibiotics, topical and systemic antivirals, topical corticosteroids, and topical and systemic antiprotozoals. Among the patients treated with topical antibiotics, 16 used fluoroquinolones and 5 had a combination of a fortified cephalosporin and an aminoglycoside. One patient (case 21) was treated with systemic antibiotic for suspected endophthalmitis. In addition to the patient with suspected Acanthamoeba keratitis, one patient (case 22) was treated with systemic antifungals.

Corneal scrapings stained with Gram, Giemsa, and/or calcofluor white showed fungal elements in 18 patients (75%). Individual sensitivities for detection of fungi for Gram, Giemsa, and calcofluor white were 65%, 80%, and 75%, respectively. The most common fungi isolated were *C. albicans* in 11 eyes (45.8%), and *Fusarium sp* in 6 eyes (25%). Other fungi isolated are shown in Table 3.

Nineteen patients were hospitalized during the course of their treatment. Stay in the hospital ranged 3–21 days, with a mean of 9 days.

Natamycin and amphotericin B were the most common topical antifungals used in the treatment of patients in this series (Table 4). Sixteen patients were treated with a single topical antifungal, seven received a combination of two antifungals, and one patient was on triple topical antifungal therapy. The mean duration of topical therapy was 70 days (range, 18–150 days). Seventeen patients (70.8%) also received oral antifungal medications. Duration of the treatment ranged 21–153 days, with a mean of 61 days (Table 5). One patient was also treated with intravenous amphotericin B, following positive culture of fungus from aqueous humor paracentesis, which was done for suspected anterior chamber infection (case 21).

TABLE 3. *Fungal isolates*

Fungus	n	%
Yeast		
Candida albicans	11	45.8
Cryptococcus neoformans	1	4.2
Total	12	50.0
Filamentous		
Fusarium sp	6	25.0
Scedosporium apiospermum	2	8.3
Alternaria sp	1	4.2
Aspergillus sp	1	4.2
Chrysonilia sp	1	4.2
Penicillium sp	1	4.2
Total	12	50.0

n, number.

TABLE 4. *Topical antifungal therapy*

Drugs	n	%
Yeast		
Amphotericin B	7	29.2
Amphotericin B + natamycin	2	8.3
Amphotericin B + fluconazole	2	8.3
Natamycin	1	4.2
Filamentous		
Natamycin	8	33.3
Natamycin + ketoconazole	1	4.2
Natamycin + fluconazole	1	4.2
Natamycin + amphotericin B	1	4.2
Natamycin + amphotericin B + clotrimazole	1	4.2
Total	24	100

n, number.

PKP was performed in six eyes (25%) during the acute stage of infection. Indications for keratoplasty included corneal perforation (cases 4, 16, 21, and 24), imminent perforation (case 11), and failure of medical management with progression of infection (case 14). Only one of the grafts performed during the acute stage remained clear in the postoperative period. One PKP patient (case 22) had a repeat corneal graft performed for visual rehabilitation. In this patient, surgery was done two months after presentation with the ulcer, once the infection was eradicated and the eye was quiet.

After a mean follow-up of nine months (range, 2–53 months), 13 eyes (54.1%) had a best corrected visual acuity (BCVA) better or equal to 20/100 (Table 6). One third of the eyes had a BCVA equal or better than 20/40 and another third had a BCVA of counting fingers or less at the final follow-up. Of the patients with acuity less than 20/100, two were from causes unrelated to fungal keratitis (macular degeneration [case 7]) and irregular astigmatism from a previous PKP (case 10). Of six eyes that required PKP during the acute disease, one resulted in a final BCVA of 20/50 (case 11) and the remainder were 20/200 or less.

DISCUSSION

We review the spectrum of fungal keratitis presenting to a tertiary cornea referral center in the northeastern United States over

TABLE 5. *Systemic antifungal therapy*

Drugs	n	%
Yeast		
Fluconazole	5	20.8
Ketoconazole	1	4.2
Itraconazole	1	4.2
None	5	20.8
Filamentous		
Ketoconazole	3	12.5
Itraconazole	3	12.5
Fluconazole	2	8.3
Amphotericin B (IV)	1	4.2
Ketoconazole, followed by itraconazole	1	4.2
None	2	8.3
Total	24	100.0

n, number.

TABLE 6. *Final BCVA following medical or surgical treatment*

	Medical		Surgical	
BCVA	n	%	n	%
20/20–20/40	8	33.3	0	—
20/50–20/100	4	16.7	1	4.2
20/200–20/400	3	12.5	0	—
CF–LP	3	12.5	5	20.8
Total	18	75.0	6	25.0

n, number; BCVA, best corrected visual acuity; CF, counting fingers; LP, light perception.

a period of eight years. *C. albicans* was the most frequent fungus isolated, followed by *Fusarium sp*. An overwhelming majority of patients had predisposing factors, either local or systemic, that favored the development of keratitis. Chronic ocular surface disease was the most common underlying risk factor. One fourth of patients required PKP for complications in the acute stage of the infection. After a mean follow-up of nine months, 54% of eyes regained vision 20/100 or better.

The majority of patients were treated prior to presentation at the Cornea Service. Topical antibiotics were used in 87.5% of patients, 29.2% were initially treated with antivirals, and 20.8% of patients were treated with topical steroids. Other authors have also reported the frequent administration of topical corticosteroids in patients with acute keratitis before the diagnosis of fungal infection was made.[9,10,14,18]

It is interesting to note that in 75% of our cases, the identification of fungal elements was made on initial stain of corneal scrapings with Gram, Giemsa, and/or calcofluor white. This is consistent with other reported sensitivity rates for detection of fungi on initial stains.[2,13–15,18,19] Given this high diagnostic yield from a test that is relatively inexpensive, simple, and widely available in microbiology laboratories, it would seem prudent to perform corneal scrapings on atypical corneal ulcers with a history of possible fungal infection. Possible fungal infection remains a major indication for culture and sensitivities of corneal scrapings. We may then be able to avoid the inadvertent use of corticosteroids and the prolonged and ineffective use of antibiotics and antivirals, to reduce the incidence of iatrogenic corneal toxicity, and to prevent progression of disease due to delay in the treatment of choice. Topical steroids should be avoided in ulcers of unknown etiology due to the possibility of fungal infection.

C. albicans was the most frequently isolated pathogen in our series of patients. This is similar to the findings of other authors who have studied fungal keratitis in temperate climates. Kelly et al.,[13] reporting on 25 cases of keratomycosis over a five-year period (1983–1988) in New England, noted that *Candida sp* was the fungus most frequently isolated (12 eyes, 48%). They also isolated *Aspergillus sp* (five eyes, 20%), *Penicillium sp* (three eyes, 12%) and *Fusarium sp* (two eyes, 8%). Doughman et al.,[10] at the University of Minnesota, reviewed a series of 19 cases of fungal keratitis over a ten-year period (1971–1981). Their population came from a strong agricultural area in the north central United States. *C. albicans* and *Aspergillus sp* were the most commonly isolated fungi, with each accounting for 31.6% of cases. *Fusarium sp* accounted for 15% of isolates. A report in 1975 from Wisconsin[9] found *C. albicans* in three of six patients with culture-positive fungal keratitis. Griffiths et al.,[12] from Moorfields Eye Hospital, England presented 31 cases of culture positive fungal keratitis from 1975–1990. The most commonly isolated fungus was *C. albicans* (48.4%) followed by *Aspergillus sp* (19.3%) and *Fusarium sp* (12.9%).

Our study differs from those cited above in that *Fusarium sp* was the most commonly isolated filamentous fungus in this series (one fourth of all cases) not *Aspergillus sp*, as was previously noted. Similar findings of *Fusarium sp* as the leading filamentous fungal pathogen have been described in the United States, but from the warmer climate of California. In that study, Thygeson and Okumoto[8] reviewed 42 cases of culture-positive fungal keratitis. They found the highest number of cases with *C. albicans* (16 eyes, 38%), followed by *Fusarium sp* (9 eyes, 21.4%). It will be interesting to conduct further studies in other centers of the northern United States to determine if our finding of a predominance of *Fusarium sp* among filamentous fungal isolates is duplicated.

Fungal keratitis from yeast infections commonly occurs in host corneas with compromised immune defenses. This may result from the use of topical steroids, antibiotics, antivirals, epithelial defects, contact lens wear, previous corneal surgery, or atopic disease, among other causes.[6,8,13–15] In our series of 24 patients, 20 had predisposing risk factors. The leading cause was chronic ocular surface diseases. It is noteworthy, however, that although a majority of patients with ocular surface disease had yeast keratitis (6/10, 60%), filamentous infections were also common (4/10, 40%). A subgroup analysis of patients with *C. albicans* infections (11 eyes) showed that six patients (54.5%) had underlying chronic ocular surface disease, and three other patients (27.2%) had atopic disease. This finding has been previously noted in other studies. Ross and Laibson[17] presented two cases of *C. albicans* keratitis, one on post radiation keratopathy and the other on topical corticosteroids after PKP. Doughman et al.[10] found four patients with chronic epithelial defects who developed *C. albicans* keratitis in a series of six patients with culture-positive fungal keratitis. In a New England study,[13] of the 11 eyes that developed fungal keratitis after PKP, 9 were from *Candida sp*. In our series, *C. albicans* was isolated from two of the three patients who developed fungal keratitis after PKP. Of 11 patients with *C. albicans* infections, 2 were on topical steroid therapy to the eye at the time of onset of infection.

Fusarium sp and *Aspergillus sp* predominate in isolates from fungal keratitis in subtropical and tropical climates.[6,14,16,18,20–22] These reports also show a predominance of cases associated with ocular trauma (33–78% of cases), generally from organic material. In a study from Minnesota,[10] with a colder climate than Philadelphia, 69.2% of filamentous fungal infections were related to ocular trauma during farming activities. However, in our series, of a total of 12 cases of filamentous fungal keratitis, only 2 patients (16.7%) gave a definite history of trauma related to the infection, although perhaps minor trauma was a factor in others patients. We did find a high percentage of these cases (50%) related to contact lens use. Five of six patients with *Fusarium sp* keratitis were using contact lenses. This association of fungal keratitis with contact lens use has been previously reported.[3,6,11,13,23] Wilhelmus et al.[24] reported that filamentous fungal infections were more commonly associated with cosmetic contact lenses and aphakic contact lenses, while yeast infections predominate in eyes with bandage contact lenses. Only one of our patents was using a bandage contact lens, and the infection in this case was caused by *C. albicans*. All six of our patients using cosmetic contact lenses had infections with filamen-

tous fungi. Variable efficacy of contact lens disinfection systems against filamentous organisms may be a factor in these infections.[25]

This retrospective study covered an eight-year period. As a result, there are varying therapeutic approaches seen among cases. In this series, candida keratitis was typically treated with topical amphotericin B and oral fluconazole. Filamentous fungal infection in our patients was largely treated with topical natamycin and systemic ketoconazole or itraconazole. Recently we have used oral fluconazole for Candida and filamentous fungal infections. While individual reports vary between geographic regions, the approach we have used for the medical management of fungal keratitis is consistent with published reports.[6,10,13,18]

Six (25%) of our patients required PKP during the acute stage of infection. Indications for grafting included frank perforation, threatened perforation, or failure of medical management with progressive infection. We found no common factor that may have predisposed these patients to corneal perforation. It is likely that we could not identify predisposing factors for perforations due to the small number of cases studied (n = 5). Previous studies report rates of 26–35% of cases requiring grafting in the acute stage; our figure of 25% is at the lower end of this range.[6,9,10,13,18] Others studies support our experience that patients with fungal keratitis require therapeutic PKP more frequently than those with bacterial ulcers.[14,26] Problems of drug penetration are thought to contribute to the decreased efficacy of medical therapy of fungal keratitis. Use of oral antifungals is helpful in achieving deeper therapeutic drug levels.[2–4,10]

Despite the availability of effective antifungal agents, fungal keratitis continues to have a poor visual prognosis. Only 13 eyes (54%) in our series had a final best-corrected visual acuity 20/100 or better. However, some patients (eight eyes) had potentially treatable causes of reduced vision, including graft failure, cataract, irregular astigmatism, and scarring; and one patient had reduced visual acuity due to age-related macular degeneration unrelated to fungal infection (Table 1). The guarded visual prognosis is also confirmed by previous reports. Percentages of patients with residual visual acuity 20/100 or better have been 33%, 50%, and 71% as reported by Doughman et al.,[10] Kelly et al.,[13] and Chin et al.,[9] respectively. In the present study, of seven eyes that presented with initial visual acuity of 20/100 or better, six retained it. On the other hand, among the 17 eyes with initial visual acuity 20/200 or less only 7 (41.2%) had final BCVA 20/100 or better.

We have presented an overview of our experiences with fungal keratitis in the past few years. Fungal infections were caused by yeast (mostly *C. albicans*) or filamentous (mostly *Fusarium sp*) organisms with equal frequency. Pre-existent eye disease and contact lens use were more common than trauma in association with fungal keratitis in our series. Corneal smears and cultures are required for diagnosis and appropriate therapy of ulcers caused by fungal infections. Despite accurate diagnosis and appropriate treatment, 25% of our patients failed medical therapy and required therapeutic PKP, often with reduced final visual acuity.

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