ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 1998, p. 1601–1604 Vol. 42, No. 7
0066-4804/98/$04.00+0

Antifungal Susceptibilities of *Paecilomyces* Species

C. AGUILAR,[1] I. PUJOL,[2] J. SALA,[3] AND J. GUARRO[1]*

Unitat de Microbiologia[1] and Unitat de Bioestadística,[3] Facultat de Medicina, Universitat Rovira i Virgili, and Laboratori de Microbiologia, Hospital Universitari de Sant Joan de Reus,[2] 43201 Reus, Tarragona, Spain

Received 18 August 1997/Returned for modification 25 February 1998/Accepted 13 April 1998

The MICs and minimum fungicidal concentrations (MFCs) of amphotericin B, miconazole, itraconazole, ketoconazole, fluconazole, and flucytosine for 52 isolates of *Paecilomyces* species were evaluated by the broth microdilution method, largely based on the recommendations of the National Committee for Clinical Laboratory Standards (document M27-A). The fungal isolates tested included 16 *P. variotii*, 11 *P. lilacinus*, 9 *P. marquandii*, 6 *P. fumosoroseus*, 4 *P. javanicus*, and 2 *P. viridis* isolates and 1 isolate of each of the following species: *P. carneus*, *P. farinosus*, *P. fulvus*, and *P. niveus*. The MFCs and the MICs at which 90% of isolates were inhibited (MIC_{90}s) for the six antifungal agents were remarkably high; the MIC_{50}s indicated that amphotericin B, miconazole, itraconazole, and ketoconazole had good activities, while fluconazole and flucytosine demonstrated poor efficacy. The ranges of the MICs were generally wider and lower than those of the MFCs. There were significant susceptibility differences among the species. All species with the exception of *P. variotii* were highly resistant to fluconazole and flucytosine; *P. variotii* was susceptible to flucytosine. Amphotericin B and the rest of the azoles showed good activity against *P. variotii*, while all the antifungal agents assayed showed low efficacy against *P. lilacinus*.

In recent years, opportunistic fungal infections have increased substantially, and the species of the genus *Paecilomyces* are emerging as the cause of a variety of infections in humans (4, 5, 14). *Paecilomyces* comprises numerous saprobic species, which are regularly isolated from soil and air and some of which are also rather common in food, paper, and other materials. *P. variotii*, a thermotolerant species often isolated from hay, is probably the most common. Apart from this species, five more species have been reported as producing opportunistic infections in humans (18). Nowadays, the number of reported cases of illness caused by the members of this genus has passed 60, ranging in severity from nail infections to fatal endocarditis. In approximately 90% of the patients some predisposing factor to infection was found: transplants, cardiac surgery, diabetes, trauma, prosthetic implants, leukemia, peritoneal dialysis, corticosteroid treatments, etc. The proper treatment for such infections is not yet well established; amphotericin B is the drug that has been mostly used for the treatment of *Paecilomyces* infections in humans and has been used alone or in combination with other drugs, although it has a failure rate of about 40%. There is very little information about the in vitro activities of antifungal agents against the *Paecilomyces* species. The widest-ranging study evaluated the susceptibilities of four strains of *P. lilacinus* to five antifungal drugs (13), while all the others tested the susceptibility of only one strain. Therefore, the main objective of this study was to evaluate the in vitro antifungal susceptibilities of a certain number of *Paecilomyces* sp. strains in order to obtain consistent data which could be used as a guide for in vivo treatments. The influence of incubation time on the MICs was also evaluated.

MATERIALS AND METHODS

Test organisms. The 52 *Paecilomyces* sp. isolates evaluated in this study included 16 *P. variotii*, 11 *P. lilacinus*, 9 *P. marquandii*, 6 *P. fumosoroseus*, 4 *P. javanicus*, and 2 *P. viridis* isolates and 1 isolate each of *P. carneus*, *P. farinosus*, *P. fulvus*, and *P. niveus*. *P. variotii* ATCC 36257 was included as the quality control and was tested whenever a set of isolates was tested.

Antifungal agents. The following six antifungal agents were used: amphotericin B (E. R. Squibb & Sons, Barcelona, Spain), flucytosine (Hoffmann-La Roche, Basel, Switzerland), fluconazole (Pfizer, Madrid, Spain), ketoconazole (Roig-Farma, Barcelona, Spain), miconazole (Roig-Farma, Barcelona, Spain), and itraconazole (Janssen Pharmaceutica, Beerse, Belgium). Fungizone and Diflucan, the commercial intravenous preparations of amphotericin B and fluconazole, respectively, were used as stock solutions. Antifungal solutions were prepared as described previously (34).

Broth microdilution method. Broth microdilution testing was performed in sterile, 96-well microplates with RPMI 1640 medium. The method that was followed has been described in a previous article (34). Aliquots of 100 μl of the drug dilutions were inoculated into the wells. The microplates were stored at −70°C until they were used. The isolates were maintained at 4°C as pure cultures on oatmeal agar (OMA) slants covered with mineral oil. For each experiment, the strains were subcultured onto the OMA slants at 30°C for 15 days, and the inoculum was prepared by scraping the surface of the sporulated fungi with a loop and directly suspending the fungal material in sterile distilled water. The organisms in the resulting suspension were manually counted with a hemacytometer, and the suspension was found to contain >95% conidia. The hemacytometer counts were verified by serial dilution on OMA plates. The conidia were diluted in sterile distilled water to produce a working suspension, which was 1×10^5 to 5×10^5 conidia per ml. The final test drug concentrations were 0.03 to 16 μg/ml for amphotericin B, miconazole, itraconazole, and ketoconazole, 0.125 to 64 μg/ml for fluconazole, and 0.25 to 128 μg/ml for flucytosine. The microplates were incubated without agitation at 25°C, and readings were made after 48 and 72 h.

The amphotericin B MICs were defined as the lowest drug concentration with which there was a complete absence of growth. The azole and flucytosine MICs were defined as the lowest drug concentrations that gave only a slight growth corresponding approximately to 25% of the growth control.

The minimum fungicidal concentrations (MFCs) were determined by plating 100 μl from each negative well and from the positive growth control well onto drug-free OMA, with subsequent incubation at 25°C for 48 h or until subcultures started to grow from the growth control well. The MFC was defined as the lowest concentration of drug from which subcultures were negative or which yielded fewer than two colonies, representing a killing factor of 99%.

Data analysis. The geometric mean MICs and MFCs were calculated for those species for which we tested at least four isolates (*P. variotii*, *P. lilacinus*, *P. marquandii*, *P. fumosoroseus*, and *P. javanicus*). The MICs and MFCs at which 50 and 90% of the strains are inhibited (MIC_{50}s and MIC_{90}s, respectively, and MFC_{50}s and MFC_{90}s, respectively) and the MIC and MFC ranges were calculated for all isolates tested. Off-scale MIC and MFC results were included in the analysis. The high off-scale MICs and MFCs (e.g., ≥16 μg/ml) were converted to the next highest concentrations (32 μg/ml). The low off-scale MICs and MFCs were left unchanged. When skips (uneven patterns) were present, the MIC endpoint was the highest drug concentration.

Because our MIC distribution values were far from being normal, we used nonparametric methods to compare the in vitro effect of each antifungal agent

* Corresponding author. Mailing address: Unitat de Microbiologia, Facultat de Medicina, Universitat Rovira i Virgili, Carrer Sant Llorenç, 21, 43201 Reus, Spain. Phone: 977-759359. Fax: 977-759322. E-mail: umb@astor.urv.es.

TABLE 1. Antifungal susceptibilities of 52 isolates of *Paecilomyces* spp. at 48 h of incubation

Antifungal agent	MIC (μg/ml)			MFC (μg/ml)		
	Range	50%	90%	Range	50%	90%
Amphotericin B	0.03–>16	1	>16	0.25–>16	>16	>16
Miconazole	0.03–>16	4	8	1–>16	>16	>16
Itraconazole	0.03–>16	2	>16	0.125–>16	>16	>16
Ketoconazole	0.03–>16	2	8	2–>16	>16	>16
Fluconazole	0.125–>64	>64	>64	16–>64	>64	>64
Flucytosine	0.25–>128	>128	>128	16–>128	>128	>128

with the three most common species of *Paecilomyces* (*P. variotii*, *P. lilacinus*, and *P. marquandii*). The rest of the species could not be analyzed because of the small number of strains of each species. The Kruskall-Wallis test was used to determine if the means for the analyzed species were significantly different. When they were, the Mann-Whitney U test was used to study which pairs of species were different. *P* values of <0.05 were considered statistically significant.

To compare the MICs obtained at 48 and 72 h, differences of no more than 1 dilution (one well) were used to calculate the percent agreement. The kappa test (12) was used to calculate the degree of agreement by SPSS (Statistical Package for Social Sciences, Inc., Chicago, Ill.). A kappa value (κ) greater than 0.75 was taken to represent excellent agreement, values below 0.40 were taken to represent poor agreement, and values between 0.40 and 0.75 were taken to represent fair to good agreement.

RESULTS

All the isolates of the *Paecilomyces* spp. tested with the exception of one strain of *P. niveus* produced clearly detectable growth in 48 h. The *P. niveus* isolate required 1 more day. Table 1 presents the MIC_{50}s, MIC_{90}s, MFC_{50}, and MFC_{90}s of the six antifungal agents for the 52 strains of *Paecilomyces* spp. tested. The MIC ranges were generally wider and lower than the MFC ranges. The MIC_{90}s, MFC_{50}s, and MFC_{90}s of the six antifungal agents were remarkably high. The MIC_{50}s indicated that amphotericin B, miconazole, itraconazole, and ketoconazole have high levels of activity, although, on the contrary, fluconazole and flucytosine demonstrated very poor efficacy.

The geometric mean MICs and MFCs of the antifungal agents for *P. variotii*, *P. lilacinus*, *P. marquandii*, *P. fumosoroseus*, and *P. javanicus* are presented in Table 2. In all cases the MFCs were considerably higher than the MICs. The MIC results showed significant differences in susceptibility among the species. All the species with the exception of *P. variotii* were highly resistant to fluconazole and flucytosine, *P. variotii* was susceptible to flucytosine. As far as the other antifungal agents are concerned, *P. variotii* was revealed to be the most susceptible species; the mean MICs of amphotericin B, miconazole, itraconazole, and ketoconazole for this species showed that they had high levels of activity. The MICs of amphotericin B, miconazole, and ketoconazole for *P. fumosoroseus* and *P. javanicus* were moderately low. Itraconazole showed efficacy against *P. javanicus* but not against *P. fumosoroseus*. All the antifungal agents assayed had poor activity against *P. lilacinus* and *P. marquandii*. The only significant difference between these two species was that *P. lilacinus* was much more resistant than *P. marquandii* to amphotericin B.

The degree of agreement between the MICs at 48 and 72 h for the six drugs is presented in Table 3. Excellent agreement was shown for flucytosine ($\kappa = 1$), ketoconazole ($\kappa = 0.86$), and fluconazole ($\kappa = 0.77$), good agreement was shown for miconazole ($\kappa = 0.75$), and poor agreement was shown for amphotericin B ($\kappa = 0.39$) and itraconazole ($\kappa = 0.29$).

DISCUSSION

This is the most extensive study on the antifungal susceptibilities of *Paecilomyces* spp. performed up to now. We used a broth microdilution method because in general its results agreed with the ones obtained by the broth macrodilution method recommended by the National Committee for Clinical Laboratory Standards (document M27-A) (29), as has been repeatedly demonstrated with clinical yeasts (3, 8, 9, 36) and filamentous fungi (10, 33). In a previous comparative study performed with six strains of *Paecilomyces* spp., there were no significant differences in the MICs obtained by both techniques (unpublished data). For these reasons and because it is more practical and economical than the broth macrodilution method, we chose the microdilution method. Moreover, most clinical microbiology laboratories are more familiar with the broth microdilution techniques used for antibacterial agents.

Only 18 of the 58 published cases of *Paecilomyces* sp. infections in humans reported data on the in vitro antifungal susceptibilities of the isolates. The broth dilution method was the method that was most often used, followed by the disk diffusion method. In only one case was a semisolid agar dilution method used (13). The in vitro test results were compared with the outcomes of therapy for 13 patients. For nine patients (70%) the susceptibilities of the strains in vitro and the efficacy of the treatment in vivo were found to agree, while for four patients (30%) they were found not to agree.

Our data seem to confirm, with some exceptions, the general

TABLE 2. Susceptibilities of five species of *Paecilomyces* to six antifungal agents at 48 h of incubation

Species	No. of strains	Amphotericin B		Miconazole		Itraconazole		Ketoconazole		Fluconazole		Flucytosine	
		MIC (μg/ml)	MFC (μg/ml)	MIC (μg/ml)	MFC (μg/ml)	MIC (μg/ml)	MFC (μg/ml)	MIC (μg/ml)	MFC (μg/ml)	MIC (μg/ml)	MFC (μg/ml)	MIC (μg/ml)	MFC (μg/ml)
P. variotii	16	0.08[a]	13.96	1.04[a]	24.83	0.07[a]	6.47	0.47[a]	14.55	24.75[a]	111.68	0.30[a]	198.15
P. lilacinus	11	10.29[b]	31.04	6.02	32.06	7.51	31.99	3.52	23.33	116.46	127.93	255.96	255.96
P. marquandii	9	1.41	8.01	5.03	23.49	5.88	31.99	3.17	14.79	123.16	127.94	255.96	255.96
P. fumosoroseus	6	0.63	10.09	1.99	21.37	6.35	23.98	4.00	25.35	50.79	128.23	255.96	255.96
P. javanicus	4	0.84	2.37	2.37	15.99	1.66	15.99	2.37	26.91	45.26	90.57	255.96	255.96

[a] Significantly different from those for *P. lilacinus* and *P. marquandii* ($P < 0.05$).
[b] Significantly different from that for *P. marquandii* ($P < 0.05$).

TABLE 3. Comparison of the MICs obtained at 48 and 72 h for 52 strains of *Paecilomyces* species

Differences in drug dilution	No. (%) of strains					
	Amphotericin B (κ = 0.39)	Miconazole (κ = 0.75)	Itraconazole (κ = 0.29)	Ketoconazole (κ = 0.86)	Fluconazole (κ = 0.77)	Flucytosine (κ = 1)
0	26 (45.6)	25 (43.8)	34 (59.6)	26 (45.6)	44 (77.1)	57 (100)
1	13 (22.8)	25 (43.8)	6 (10.5)	27 (47.3)	9 (15.7)	
2	13 (22.8)	5 (8.7)	4 (7.0)	3 (5.2)	1 (1.7)	
3	5 (8.7)	2 (3.5)	1 (1.7)	1 (1.7)	1 (1.7)	
4			9 (15.7)		1 (1.7)	
5			3 (5.2)			
10					1 (1.7)	

trend that has been discussed in the literature about the in vitro susceptibilities of *Paecilomyces* spp. The two most common *Paecilomyces* species causing infections in humans, *P. variotii* and *P. lilacinus*, show very clear differences in their in vitro susceptibilities to the currently used antifungal agents. Of the six drugs tested, only fluconazole showed poor activity against *P. variotii*, and *P. variotii* was the only species susceptible to flucytosine. Only a few clinical isolated of *P. variotii* have been tested by various investigators (5, 7, 15, 22, 23, 27, 31, 35, 37, 38). More than one strain was tested in only two cases: three strains were tested by Marzek et al. (22) and two strains were tested by Chan et al. (5). The techniques used were variable but showed that isolates were susceptible to both flucytosine and itraconazole whenever they were tested. Only one strain was defined as being resistant to amphotericin B (27). Miconazole was tested with eight isolates, and four of the strains were resistant (5, 22). Ketoconazole was assayed with nine isolates, and two were observed to be resistant (27, 31). Fluconazole was tested with seven isolates and six of them were resistant (5, 7, 22).

There is less information about the antifungal susceptibility of the other common species, *P. lilacinus*. In our study, ketoconazole was the only antifungal agent that had moderate activity against this species. Seven strains were previously tested by different investigators (4, 13, 26, 30, 43). One group of investigators tested three strains (13), and the rest tested only one strain each. They reported resistance to amphotericin B, flucytosine, and fluconazole and susceptibility to ketoconazole, miconazole, and clotrimazole; one of the three strains tested was resistant to itraconazole. The results of clinical treatments with amphotericin B have been contradictory. The drug was not effective in three patients (1, 19, 30) and gave good results in five patients (11, 21, 25, 39, 41). Jade et al. (19) described one case of cellulitis caused by *P. lilacinus* that could not be cured with amphotericin B but which was resolved when flucytosine was added to the therapy. A potential synergism or additivism between these drugs (32) may explain the result.

Apart from the species mentioned above, only one strain of *P. marquandii* has been tested in vitro, and it was resistant to amphotericin B and flucytosine and was susceptible to miconazole (16).

There were no previous data about the in vitro susceptibility of *P. javanicus*, even though this species has been responsible for two cases of endocarditis (2, 17). Our study included four strains of *P. javanicus*, for which the MICs of amphotericin B, miconazole, itraconazole, and ketoconazole were low. However, the two patients with endocarditis died, despite treatment with amphotericin B.

Endocarditis is among the most severe infections caused by *Paecilomyces* spp., and the mortality rate among patients with *Paecilomyces* endocarditis is high. In total seven cases of endocarditis have been reported, five of which (15, 20, 23, 40, 42) were caused by *P. variotii* and two of which (2, 17) were caused by *P. javanicus*. All seven patients died, and they had all been treated with amphotericin B.

Peritonitis is another relatively common infection caused by *Paecilomyces* spp., and *P. variotii* complicated continuous ambulatory peritoneal dialysis in nine patients. Four patients received amphotericin B intravenously (6, 22, 28), and the rest were treated only with oral antifungal drugs (5, 7, 22). Surprisingly, one patient was cured after being treated only with fluconazole (7), despite the in vitro resistance of his isolate. All patients were cured, but the peritoneal catheter had to be removed before the fungus was eradicated.

Miconazole was efficient in vitro and was successfully used on two occasions, one of which was for a patient with cellulitis caused by *P. marquandii* (16) and the other was for a patient with keratitis caused by *P. lilacinus* (13). Nowadays, this drug is hardly used because of its known side effects.

Itraconazole has been used very little against *Paecilomyces* spp. infections, but on the basis of its good in vitro response against *P. variotii* and *P. javanicus*, it may be worthy of use in patients with severe cases of infection, such as endocarditis, when other drugs have failed.

Only rarely have the MFCs of antifungal drugs for filamentous fungi been determined, and this could be a more predictive parameter (24). It is probable that the MFCs would have shown a higher degree of correlation than the MICs for the isolates mentioned above.

Incubation time had little or no effect on the MICs of fluconazole, flucytosine, ketoconazole, and miconazole. In contrast, amphotericin B and itraconazole MICs showed considerable differences when the two incubation times were compared. They were higher at 72 h. This behavior has also been shown for amphotericin B with other filamentous fungi (34). The low degree of stability of amphotericin B during incubation may account for this difference, but in the case of itraconazole, it is more difficult to explain.

ACKNOWLEDGMENTS

This work was supported by a grant from the Fundació Ciència i Salut of Spain.

We thank L. Ajello (Emory University School of Medicine, Atlanta, Ga.) for critical comments.

REFERENCES

1. **Agrawal, P. K., B. Lal, W. Seema, O. P. Srivastava, and S. C. Misra.** 1979. Orbital paecilomycosis due to *Paecilomyces lilacinus* (Thom) Samson. Sabouraudia **17:**363–370.
2. **Allevato, P. A., J. M. Ohorodnik, E. Mezger, and J. F. Eisses.** 1984. *Paecilomyces javanicus* endocarditis of native and prosthetic aortic valve. Am. J. Clin. Pathol. **82:**247–252.
3. **Barchiesi, F., A. L. Colombo, D. A. McGough, and M. G. Rinaldi.** 1994.

Comparative study of broth macrodilution and microdilution techniques for in vitro antifungal susceptibility testing of yeasts by using the National Committee for Clinical Laboratory Standards' proposed standard. J. Clin. Microbiol. **32:**2494–2500.
4. **Castro, L. G. M., A. Salebian, and M. N. Sotto.** 1990. Hyalohyphomycosis by *Paecilomyces lilacinus* in a renal transplant patient and a review of human *Paecilomyces* species infections. J. Med. Vet. Mycol. **28:**15–26.
5. **Chan, T. H., A. Koehler, and P. Kam Tao Li.** 1996. *Paecilomyces variotii* peritonitis in patients on continuous ambulatory peritoneal dialysis. Am. J. Kidney Dis. **27:**138–142.
6. **Crompton, C. H., J. W. Balfe, R. C. Summerbell, and M. M. Silver.** 1991. Peritonitis with *Paecilomyces* complicating peritoneal dialysis. Pediatr. Infect. Dis. J. **10:**867–871.
7. **Eisinger, R. P., and M. P. Weinstein.** 1991. A bold mould? *Paecilomyces variotii* peritonitis during continuous ambulatory peritoneal dialysis. Am. J. Kidney Dis. **5:**606–608.
8. **Espinel-Ingroff, A., T. M. Kerkering, P. R. Goldson, and S. Shadomy.** 1991. Comparison study of broth macrodilution and microdilution antifungal susceptibility tests. J. Clin. Microbiol. **29:**1089–1094.
9. **Espinel-Ingroff, A., C. W. Kish, T. M. Kerkering, R. A. Fromtling, K. Bartizal, J. N. Galgiani, K. Villareal, M. A. Pfaller, T. Gerarden, M. G. Rinaldi, and A. Fothergill.** 1992. Collaborative comparison of broth macrodilution and microdilution antifungal susceptibility tests. J. Clin. Microbiol. **30:**3138–3145.
10. **Espinel-Ingroff, A., K. Dawson, M. Pfaller, E. Anaissie, B. Breslin, D. Dixon, A. Fothergill, V. Paetznick, J. Peter, M. Rinaldi, and T. Walsh.** 1995. Comparative and collaborative evaluation of standardization of antifungal susceptibility testing for filamentous fungi. Antimicrob. Agents Chemother. **39:**314–319.
11. **Fenech, F. F., and C. P. Mallia.** 1972. Pleural effusion caused by *Penicillium lilacinum*. Br. J. Dis. Chest **66:**284–290.
12. **Fleiss, J. L.** 1981. Statistical methods for rates and proportions, p. 212–236. John Wiley & Sons, Inc., New York, N.Y.
13. **Gordon, M. A., and S. W. Norton.** 1985. Corneal transplant infection by *Paecilomyces lilacinus*. Sabouraudia: J. Med. Vet. Mycol. **23:**295–301.
14. **Gucalp, R., P. Carlisle, P. Gialanella, S. Mitsudo, J. McKitrick, and J. Dutcher.** 1996. *Paecilomyces* sinusitis in an immunocompromised adult patient: case report and review. J. Infect. Dis. **164:**944–948.
15. **Haldane, E. V., J. L. MacDonald, W. Gittens, K. Yuce, and C. E. Van Rooyen.** 1974. Prosthetic valvular endocarditis due to the fungus *Paecilomyces*. Can. Med. Assoc. J. **111:**963–968.
16. **Harris, L. F., B. M. Dan, L. B. Lefkowitz, and R. H. Alford.** 1979. *Paecilomyces* cellulitis in a renal transplant patient: successful treatment with intravenous miconazole. South. Med. J. **72:**897–898.
17. **Ho, K. L., P. A. Allevato, P. King, and J. L. Chason.** 1986. Cerebral *Paecilomyces javanicus* infection. An ultra-structural infection. Acta Neuropathol. (Berlin) **72:**134–141.
18. **Hoog, G. S., and J. Guarro.** 1995. Atlas of clinical fungi. Centraalbureau voor Schimmelcultures, Baarn, The Netherlands.
19. **Jade, C. K. B., M. F. Lyons, and J. W. Gnann.** 1986. *Paecilomyces lilacinus* cellulitis in an immunocompromised patient. Arch. Dermatol. **122:**1169–1170.
20. **Kalish, S. B., R. Goldschmidt, C. Li, R. Knop, F. V. Cook, G. Wilner, and T. A. Viktor.** 1982. Infective endocarditis caused by *Paecilomyces variotii*. Am. J. Clin. Pathol. **78:**249–252.
21. **Malbran, E., E. J. Albesi, H. Daro, and R. C. Zapater.** 1973. Endoftalmitis por *Penicillium lilacinum*. Arch. Oftalmol. Buenos Aires. **48:**253–258.
22. **Marzec, A., L. G. Heron, R. C. Pritchard, R. H. Butcher, H. R. Powell, A. P. S. Disney, and F. A. Tosolini.** 1993. *Paecilomyces variotii* in peritoneal dialysate. J. Clin. Microbiol. **31:**2392–2395.
23. **McClellan, J. R., J. D. Hamilton, J. A. Alexander, W. G. Wolfe, and J. B. Reed.** 1976. *Paecilomyces variotii* endocarditis on a prosthetic aortic valve. J. Thorac. Cardiovasc. Surg. **71:**472–475.
24. **Melcher, G. P., D. A. McGough, A. W. Fothergill, C. Norris, and M. G. Rinaldi.** 1993. Disseminated hyalohyphomycosis caused by a novel human pathogen, *Fusarium napiforme*. J. Clin. Microbiol. **31:**1461–1467.
25. **Minogue, M. J., T. C. Frances, P. Quartermass, M. B. Kappagoda, R. Bradbury, R. S. Walls, and P. I. Motum.** 1984. Successful treatment of fungal keratitis caused by *Paecilomyces lilacinus*. Am. J. Ophthalmol. **98:**626–627.
26. **Mori, T., M. Matsumura, T. Ebe, M. Takahashi, T. Kohara, M. Inagaki, H. Isonuma, S. Horie, I. Hibiya, T. Hamamoto, K. Watanabe, H. Ikemoto, T. Yokoyama, Y. Yokoyama, H. Kinumaki, and M. Ichinoe.** 1991. Clinical study of treatment of fungal infections with itraconazole. Jpn. J. Med. Mycol. **32:**279–290.
27. **Naidu, J., and S. M. Singh.** 1992. Hyalohyphomycosis caused by *Paecilomyces variotii*: a case report, animal pathogenicity and "in vitro" susceptibility. Antonie Leeuwenhoek **62:**225–230.
28. **Nankivell, B. J., D. Pacey, and D. L. Gordon.** 1991. Peritoneal eosinophilia associated with *Paecilomyces variotii* infection in continuous ambulatory peritoneal dialysis. Am. J. Kidney Dis. **5:**603–605.
29. **National Committee for Clinical Laboratory Standards.** 1997. Reference method for broth dilution antifungal susceptibility testing of yeasts. Approved standard. NCCLS document M27-A. National Committee for Clinical Laboratory Standards, Wayne, Pa.
30. **O'Day, D. M.** 1977. Fungal endophthalmitis caused by *Paecilomyces lilacinus* after intraocular lens implantation. Am. J. Ophthalmol. **83:**130–131.
31. **Otcenasek, M., Z. Jirousek, Z. Nozicka, and K. Mencl.** 1984. Paecilomycosis of the maxillary sinus. Mykosen **27:**219–226.
32. **Polak, A., and M. Zaug.** 1990. Amorolfine, p. 505–521. *In* J. F. Ryley (ed.), Book of experimental pharmacology. Chemotherapy of fungal diseases. Springer Verlag, Berlin, Germany.
33. **Pujol, I., J. Guarro, C. Llop, L. Soler, and J. Fernández-Ballart.** 1996. Comparison study of broth macrodilution and microdilution antifungal susceptibility tests for the filamentous fungi. Antimicrob. Agents Chemother. **40:**2106–2110.
34. **Pujol, I., J. Guarro, J. Gené, and J. Sala.** 1997. In-vitro antifungal susceptibility of clinical and environmental *Fusarium* spp. strains. J. Antimicrob. Chemother. **39:**163–167.
35. **Rodrigues, M. M., and D. MacLeod.** 1975. Exogenous fungal endophthalmitis caused by *Paecilomyces*. Am. J. Ophthalmol. **79:**687–690.
36. **Sewell, D. L., M. A. Pfaller, and A. L. Barry.** 1994. Comparison of broth macrodilution, broth microdilution, and E test antifungal susceptibility tests for fluconazole. J. Clin. Microbiol. **32:**2099–2102.
37. **Sherwood, J. A., and A. S. Dansky.** 1983. *Paecilomyces* pyelonephritis complicating nephrolithiasis and review of paecilomyces infections. J. Urol. **130:**526–528.
38. **Shing, M. M. K., M. Ip, C. K. Li, K. W. Chik, and P. M. P. Yuen.** 1996. *Paecilomyces variotii* fungemia in a bone marrow transplant patient. Bone Marrow Transplant. **17:**281–283.
39. **Silliman, C. C., D. W. Lawellin, J. A. Lohr, B. M. Rodgers, and L. G. Donowitz.** 1992. *Paecilomyces lilacinus* infection in a child with chronic granulomatous disease. J. Infect. **24:**191–195.
40. **Silver, M. D., P. G. Tuffnel, and W. G. Bigelow.** 1971. Endocarditis caused by *Paecilomyces variotii* affecting an aortic valve allograft. J. Thorac. Cardiovasc. Surg. **61:**278–281.
41. **Tan, T. Q., A. K. Ogden, J. Tilliman, G. J. Demmier, and M. G. Rinaldi.** 1992. *Paecilomyces lilacinus* cathether-related fungemia in an immunocompromised pediatric patient. J. Clin. Microbiol. **30:**2479–2483.
42. **Uys, C. J., P. A. Don, V. Schrine, and C. N. Barnard.** 1963. Endocarditis following cardiac surgery due to the fungus *Paecilomyces*. S. Afr. Med. J. **37:**1276–1280.
43. **Westenfeld, F., W. Kemper Alston, and W. C. Winn.** 1996. Complicated soft tissue infection with prepatellar bursitis caused by *Paecilomyces lilacinus* in an immunocompetent host: case report and review. J. Clin. Microbiol. **34:**1559–1562.