Y.-C. Huang, T.-Y. Lin, H.-S. Leu, H.-L. Peng, J.-H. Wu, H.-Y. Chang

Outbreak of *Candida parapsilosis* Fungemia in Neonatal Intensive Care Units: Clinical Implications and Genotyping Analysis

Summary: During a 5-month period, 17 infants hospitalized in neonatal intensive care units of a medical center and a branch hospital developed 18 episodes of *Candida parapsilosis* fungemia. The mean age at onset was 35 days. Prior to fungemia, all the infants had received hyperalimentation and antibiotics, and 15 infants had had central venous catheters. The presenting symptoms were variable but only vague in 40% of the episodes. Despite administration of antifungal agents, subsequent eradication of fungemia was achieved in only two-thirds of the episodes. None of the environmental samples was positive for *C. parapsilosis*, while 20% of hand-washing samples of staff working in both units yielded this microorganism. Four genotypes with two main types were identified from 14 outbreak strains and eight genotypes from 14 hand-washing strains, with one type predominant. The results suggest that *C. parapsilosis* fungemia increases the morbidity and mortality of neonates but does not cause acute lethal events. The outbreak was caused by two main genotypes, possibly via cross-infection by the hands of health care workers.

Introduction

Since invasive therapeutic and monitoring equipment has become a part of modern neonatal intensive care units (NICU), nosocomial fungal infections, particularly *Candida* species, have increased markedly and fungi have emerged as important nosocomial pathogens [1–3]. Most candidal infections in neonates arise sporadically from an endogenous source [4–6] and are associated with certain risk factors [1–4, 7] including prematurity, very low birth weight, prolonged hospitalization, indwelling central venous catheters, hyperalimentation, intravenous fat emulsion and broad-spectrum antibiotic usage. Exogenous acquisition via the hands of health care workers, contaminated infusates and biomaterials, and the inanimate environment is not infrequent and may even result in apparent occasional outbreaks [8–15]. Among fungal infections caused by *Candida* spp., *Candida albicans* is the most common pathogen and thus, most reports focus on this microorganism. Evidence indicates that non-*albicans Candida* species are becoming more frequent, but the description of clinical features was found infrequently.

Recently, we experienced an outbreak of *Candida parapsilosis* fungemia in 17 infants with 18 episodes in NICU. We present the clinical features and investigation with genotyping methods in this study.

Materials and Methods

Outbreak: Chang Gung Children's Hospital (CGCH), a 390-bed medical center, is a part of Chang Gung Memorial Hospital (CGMH) at Linko, which is a 3,443-bed tertiary care teaching hospital. Currently, there are 34 beds, distributed over two floors, with eight isolation beds in the NICU. In 1994, there were only 17 beds with four isolation beds on one floor. The Taipei branch hospital of CGMH is an outpatient-oriented hospital with pediatric and obstetric wards only. There were 15 beds in the pediatric NICU. The intern and resident doctors as well as respiratory therapists are rotated monthly between the center and branch hospitals. The patients can also be transported reciprocally.

Between August 1994 and January 1995, a cluster of ten infants (patients 1 to 10) hospitalized in the NICU at Linko center and seven infants (patients 11 to 17) hospitalized in the pediatric NICU at the Taipei branch developed 18 episodes of *C. parapsilosis* fungemia. In the preceding year, only one case of *C. parapsilosis* fungemia was noted at CGCH. Monthly episodes of *C. parapsilosis* fungemia in both NICU are shown in Figure 1. Yeast was recovered from blood cultures, drawn peripherally and performed by BACTEC system, at least twice with an interval of more than 24h and *C. parapsilosis* was identified by the standard clinical microbiological techniques in all but patients 9 and 17. They had positive blood cultures only once although pus culture from cellulitis also yielded *C. parapsilosis* in patient 17. Patient 12 developed fungemia in October 1994, which was eradicated after introduction of antifungal agents but recurred in January 1995. Patient 8 developed a persistent candidemia in October at Linko center and was transported to the Taipei branch in December.

In both units, a central venous catheter (CAVA lines) was inserted peripherally and hyperalimentation and intralipid emulsion were administered in the first week of life in the case of very low birth weight infants (birth weight <1500 g) who could not tolerate milk feeding. Systemic oral decontamination with antifungal agents was not performed in this unit, nor was the fungal colonization study carried out. Sonographic evaluation of the brain

Received: 26 June 1998/Revision accepted: 7 December 1998

Y.-C. Huang, M. D., *T.-Y. Lin*, M. D., Div. of Infectious Diseases, Chang Gung Children's Hospital, 5 Fu-Hsin St., Kweishan; *H.-S. Leu*, M. D., Chang Gung Memorial Hospital, 5 Fu-Hsing St., Kweishan; *H.-L. Peng*, Ph. D., *J.-H. Wu*, Ph. D., *H.-Y. Chang*, Ph. D., Dept. of Microbiology and Immunology, School of Medicine, Chang Gung University, 259 Wien-Hwa 1st Rd., Kweishan, Taoyuan, Taiwan.

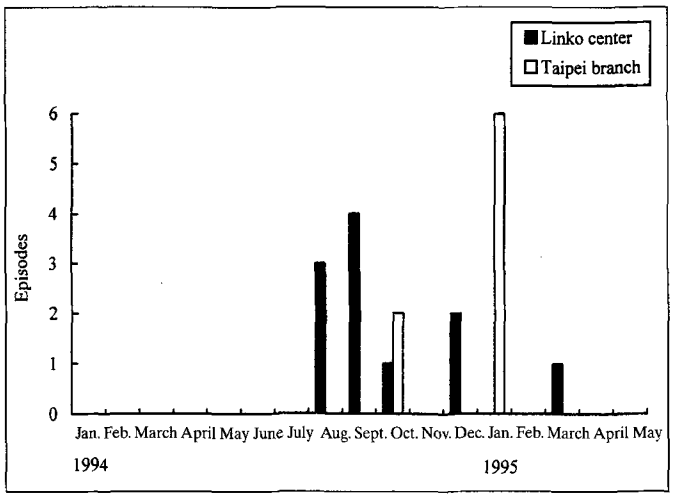

Figure 1: Monthly episodes of *Candida parapsilosis* fungemia in neonatal intensive care units of Linko center and Taipei branch of Chang Gung Children's Hospital during January, 1994 and June, 1995.

and urinary tract was recommended within 1 week of diagnosis; serial evaluations and other imaging studies were performed as clinically indicated.

Guidelines for management of fungemia included removal or replacement of indwelling vascular catheters and antifungal agents. Usually, amphotericin B was administered first (0.1 mg test dose advanced over 3 to 4 days to 1.0 mg/kg/day), then flucytosine (5-FC) was added (50–150 mg/kg/day); fluconazole (5–10 mg/kg/day) was used if the response was unsatisfactory.

Demographic data, clinical manifestations, laboratory data, management and outcomes of these infants were collected and are presented in Tables 1 and 2.

Fourteen isolates, recovered from 14 patient blood cultures, underwent antifungal susceptibility tests by broth microdilution method, according to the National Committee for Clinical Laboratory Standards [16].

Local Environment: For investigating the presence of *C. parapsilosis* in the local environment, 26 specimens from inanimate objects, including radiant warmers, incubators, washbasins and water faucets, were sampled using damp sterile swabs. The swabs were seeded onto the plates containing inhibitory mold agar with chloramphenicol and gentamicin, then incubated at 37°C for 1 week and examined for the presence of *C. parapsilosis*.

Personnel: In December, the hands of all 75 staff working in the NICU at Linko center, including 13 doctors (intern, resident and attending doctors), 36 nurses and 26 respiratory therapists, were sampled without prior preparation by immersing and rinsing their hands in a plastic bag containing 100 ml of sterile saline when they were caring for the infants. The same procedure was followed for all 26 staff working in the pediatric NICU at the Taipei branch in January. Washings were centrifuged, seeded onto inhibitory mold agar with chloramphenicol and gentamicin plates, and after incubation at 37°C for 1 week examined for the presence of *C. parapsilosis*.

Genotyping Analysis of Candida parapsilosis Isolates: Fourteen stocked *C. parapsilosis* isolates (outbreak strains) from 14 patient blood cultures, four control isolates from blood cultures of patients admitted at other units in the preceding year, and all isolates recovered from the environmental survey and handwashings of personnel were collected and analyzed by two genotyping methods. All isolates were genotyped as described by *White* et al. with polymerase chain reaction (PCR) amplification and direct sequencing of the rRNA gene [17]. The nucleotide sequence of the purified DNA fragment containing the ITS region was determined using the Sequitherm kit (Epicentre Technologies, USA). Homology analysis of the nucleotide sequences obtained was performed using the BLAST network service of the National Center for Biotechnology Information. With electrophoretic karyotyping using contour-clamped homogenous electric field gel electrophoresis, all isolates were genotyped as described by *Scheartz* et al. [18]. Pulse field gel electrophoresis was performed on a CHEF Mapper (Bio-Rad, USA) using an auto-algorithm program. All isolates were analyzed in two or more runs. Isolates were judged to have different DNA subtypes if their electrophoretic karyotyping profile differed by one or more bands.

Results

Clinical Data

With the exception of case 8, the other 16 infants were premature (gestational age, 26 to 33 weeks; mean, 29.2 ± 2.0 weeks), and had a low birth weight (780 to 1,842 g; mean, 1,249 ± 259 g). Patient 8, a male term infant with a birth weight of 3,566 g, was a case of intestinal malrotation with midgut volvulus and resultant short bowel syndrome due to massive resection of necrotic bowels. Seven infants were male and ten female. Excluding the second episode of patient 12, the mean age at onset of *C. parapsilosis* fungemia was 35 days, ranging from 16 to 76 days. Prior to the onset of fungemia, 15 infants had had central venous catheters (CVC) for a mean of 22.7 days, and 13 of them had CVC in place at the time fungemia developed. All 17 infants had received hyperalimentation and antibiotics for a mean of 27.7 days and 19.5 days, respectively, before fungemia developed. The detailed demographic data are shown in Table 1.

The clinical manifestations were variable. Three episodes were identified unexpectedly, as a result of the septic workup for pneumonia or cellulitis. The presenting symptoms of another four episodes were only vague, with not-doing-well (decreased activity and/or decreased response to stimulation) in three infants and feeding intolerance (gastric residual milk) in one. The relatively common manifestations included not-doing-well in ten (56%) episodes, respiratory symptoms in 11 (61%) episodes and gastrointestinal symptoms in seven (39%) episodes. The laboratory data were also nonspecific. Thrombocytopenia (67%) and leukopenia (56%) detected within 3 days of onset of fungemia were the common features. The detailed clinical manifestations and laboratory data are shown in Table 2. Central venous catheter tip culture for *C. parapsilosis* was positive in seven (54%) of 13 infants who underwent CVC tip cultures. Two patients had a positive culture for *C. parapsilosis* from sites other than the bloodstream (urinary tract and wound sites). In the case of patient 11, *C. parapsilosis* fungemia developed 8 days

Infection 27 (1999) No. 2 © MMV Medien & Medizin VerlagsGmbH München 1999

Table 1: Demographic data and outcomes of 17 infants with *Candida parapsilosis* fungemia.

Patient no.	Sex	Gestational age (weeks)	Birth weight (g)	Date of onset of infection	Age at onset (days)	CAVA days before onset	Antibiotics days before onset	TPN days before onset	Concomitant bacterial infection	Eradication of fungemia	Survival
1	M	28	982	8/3	39	31	28	36	+	–	–
2	F	30	1,460	8/8	31	16	14	21	–	–	–
3	F	27	1,000	8/29	31	25	15	28	–	+	+
4	F	30	1,450	9/1	34	15	32	29	–	+	+
5	F	28	1,036	9/7	24	19	12	21	+	–	–
6	M	31	1,842	9/8	76	16	20	22	+	+	–
7	F	26	934	9/9	37	28	15	30	+	–	–
8	M	38	3,566	10/3	28	–	22	20	+	–	–
9	M	27	880	12/8	67	39	31	64	+	+	+
10	F	27	780	12/11	40	30	38	34	+	+	+
11	M	29	976	10/13	59	46	53	57	+	–	–
12	M	33	1,294	10/25	35	25	22	31	+	+	+
				1/12	114	48	75	110	+	+	
13	F	29	1,300	1/5	20	16	6	17	+	+	+
14	F	27	1,206	1/9	16	12	7	12	–	+	+
15	M	31	1,800	1/17	16	–	8	13	–	+	+
16	F	33	1,374	1/18	21	20	17	18	–	+	+
17	F	33	1,680	1/21	24	5	9	18	+	+	+

CAVA = type of central venous catheter; TPN = total parenteral nutrition.

later although amphotericin B had been administered for asymptomatic candiduria before fungemia.

Among 13 infants with CVC in place at the time fungemia developed, CVC were removed and inserted from a new site. All 17 infants received antifungal agents and fungemia was subsequently eradicated in 11 infants with 12 episodes (66.7%). Amphotericin B was given to each patient initially and fungemia was eradicated later in seven infants with eight episodes (47%). Flucytosin was added in six patients and clearing of the fungemia was achieved in two. Fluconazole was used instead in six infants (accumulated amphotericin B dosage < 20 mg/kg in three patients) and fungemia was cleared subsequently in two infants, both of whom had low accumulated amphotericin B dosages. Six infants had persistent fungemia despite administration of antifungal agents and died later, 28 to 163 days after the onset of fungemia (mean, 66 days), as a result of other neonatal problems. The detailed clinical outcome is shown in Table 1. Autopsy was performed in case 5, who died 79 days after the onset of fungemia, and showed systemic candidiasis of the heart, lung, liver, spleen, kidney, thyroid, bone marrow and brain. Also, systemic bacteremia of bacilli (ascites culture yielded *Klebsiella pneumoniae*) colonizing the lung, liver, gastrointestinal tracts, bone marrow and brain was noted.

The antifungal susceptibility tests showed that most strains were sensitive to amphotericin B, 5-FC and fluconazole. The amphotericin B minimal inhibitory concentrations (MIC) were 1 μg/ml in all but one strain, where the MIC was 2 μg/ml. The MIC of 5-FC ranged from 0.13 to 0.25 μg/ml in all but one strain with a MIC of 2 μg/ml. All 14 isolates with fluconazole with a MIC ranging from 0.5 to 2 μg/ml were identified.

Investigation

None of the 26 specimens sampled from the environment was *C. parapsilosis* positive. Of the 75 samples collected from the hand-washings of personnel working in the NICU at Linko center, 18 (24%) samples (including one sample from a doctor, eight from respiratory therapists and nine from nurses) were *C. parapsilosis* positive. From the hand-washings of personnel in the pediatric NICU at the Taipei branch, two of 26 (8%) samples were *C. parapsilosis* positive.

By PCR-based direct sequencing of rRNA gene, only two genotypes were identified and all isolates but two from the hand-washings of personnel were of the same type. On the other hand, genotypic analysis with PFGE revealed that the DNA-fragment profiles of the isolates were distinct and nine types could be identified. Of the 14

Table 2: Clinical manifestations and laboratory data of 17 neonates with 18 episodes of *Candida parapsilosis* fungemia.

	No. of episodes (%) (n = 18)
Not-doing-well	10 (56)
Respiratory symptoms	11 (61)
Apnea	7 (39)
Cyanosis	6 (33)
Respiratory distress	2 (11)
Hypoxemia	2 (11)
Gastrointestinal symptoms	7 (39)
Abdominal distention	6 (33)
Feeding intolerance	5 (28)
Bradycardia	6 (33)
Fever	3 (17)
Hypothermia	2 (11)
Tachycardia	2 (11)
Elevated CRP (> 10 mg/l)	12/15 (80)
Highly elevated (> 40 mg/l)	7/15 (47)
Thrombocytopenia (> 10^5/cmm)	12 (67)
Leukopenia (< 5,000/cmm)	10 (56)
Leukocytosis (> 15,000/cmm)	1 (6)

CRP = C-reactive protein.

outbreak strains, there were four genotypes. The strains from patients 6, 9, 11, 12, 16 and 17 were of the same genotype and were classified as type A. The genotypes of the strains from patients 2, 5, 7, 8 and 14 were also identical, and were defined as type B. Two isolates from patients 4 and 10 were of a common source and were defined as type C. Type D was a unique strain from patient 1.

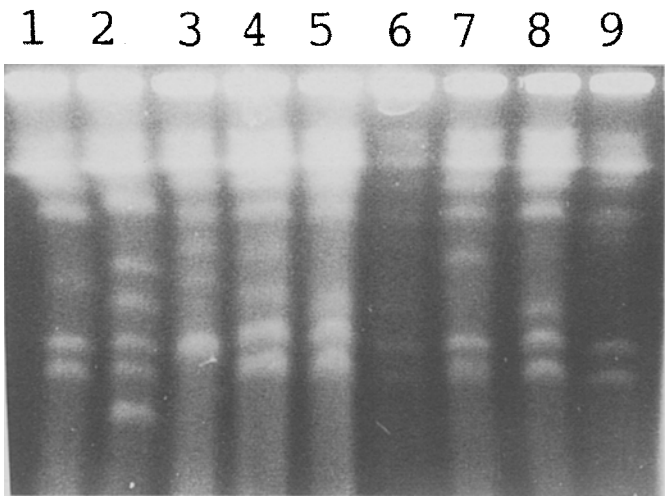

Figure 2: CHEF electrophoresis of genomic DNA from separate *Candida parapsilosis* isolates. Different genotypes were noted. Lanes 1–4 were from hand-washing strains and identified as type D, E, F, G. Lanes 5, 6 and 8 were of common source (type B) and from patients 5, 10 and 14. Lanes 7 and 9, from patients 12 and 4, were identified as type A and C.

Among the 14 strains from hand-washings, eight separate types could be identified. The genotype of six strains was type A, while two strains belonged to type C. The other six strains were unique and classified as types D, E, F, G, H and I. For the four control strains, the DNA-fragment profiles of three strains were type A, while the other one was type D. The genotyping results are shown in Figure 2.

Discussion

C. parapsilosis, an important fungal colonization species in very low birth weight infants, has become a leading pathogen among non-*albicans* candidal species causing bloodstream infections in NICU [19–21]. Fungal outbreaks caused by *C. parapsilosis* have been reported in the literature [8, 12–14]. Evidence suggests that the growth and adherence of *C. parapsilosis* is enhanced in high glucose and certain hyperalimentation solutions [21]. Also, infection with *C. parapsilosis* often occurs in association with indwelling CVC. Since both indwelling CVC and hyperalimentation solution are almost essential in the case of very low birth weight infants, it is no wonder that *C. parapsilosis* infection has recently increased markedly. We can even predict that *C. parapsilosis* infection will continue to increase in the near future in NICU. Most cases in this series did have CVC in place at the time fungemia developed, and were receiving hyperalimentation solution and lipid emulsion.

Most studies also indicate that the virulence of *C. parapsilosis* is limited compared with that of *C. albicans* and *C. tropicalis* and thus, the mortality caused by *C. parapsilosis* is lower than that caused by other candidal species. The presenting symptoms in this series were variable, ranging from minor cases of not-doing-well or feeding intolerance to serious incidents of respiratory deterioration requiring intubation, whereas about 40% of the patients had only vague symptoms or were identified by chance. The manifestations, if present, were also nonspecific and could not be differentiated from other fungal or bacterial bloodstream infections. Moreover, suppurative complications and cultures from sites other than the bloodstream were seen infrequently in this series. Mortality associated with *C. parapsilosis* fungemia was 35% in the study, which is consistent with previous reports [8, 20], but no immediate death (within 7 days of the onset of fungemia) was noted. Case 5, with persistent fungemia, died from other neonatal complications, but systemic candidiasis could be identified at autopsy. It is likely that *C. parapsilosis* fungemia increases mortality and morbidity of the very low birth weight infants but does not appear to cause acute lethal events.

Although all 17 infants received therapy with antifungal agents and all 14 isolates undergoing antifungal susceptibility tests were susceptible to these agents, eradication of fungemia was achieved in only two-thirds of 18 episodes in this series. These data again suggest that host factors

potentially can have more influence on the clinical outcome than intrinsic drug susceptibility [22, 23]. However, case 11 developed *C. parapsilosis* fungemia when receiving amphotericin B for funguria for 8 days. Amphotericin B intolerance had been reported as a characteristic of *C. parapsilosis* not shared by other *Candida* species [23]. Amphotericin B intolerance, as a result, should be considered in our isolates.

Outbreaks of candidemia in the NICU are infrequently, though increasingly, reported [8–15]. An outbreak of fungemia occurring in the NICU of both a medical center and a branch hospital simultaneously, as in this report, is quite rare. As the resident and intern doctors as well as respiratory therapists are rotated between the medical center and the branch hospital and the patients can be transported reciprocally, spread of the microorganism cannot be prevented if the rotating staff were the carriers or the patients were infected or colonized. The outbreak presented here occurred under these circumstances. Thus, we suggest that rotation of staff or transportation of infected patients between institutes should be strictly limited or even avoided if there is an outbreak of any microorganism in one institute.

Although the investigation of this outbreak identified nine separate genotypes, only four types could be identified from the outbreak strains, and apparently two main types could be identified in this outbreak. These two genotypes of *C. parapsilosis* were isolated from six and five patients, respectively. Co-occurrence of two or more genotypes of *Candida* species encountered in an outbreak of candidemia have been reported [15], although they are rare, and that was the case in this outbreak. No reservoir was identified from environmental objects, while the hand-carriage rate of *C. parapsilosis* in personnel was not low in either unit and a predominant genotype (type A) could be identified from both the outbreak and the hand-washing strains. Cross-infection via the hands of personnel might play a role in this outbreak. Actually, after strict hand-washing with an alcoholic chlorhexidine handrub was requested before and after contact with patients, the outbreak was brought under control temporarily. *C. parapsilosis* carriage on the hands of personnel working in the ICU is not uncommon [24, 25] and this carriage was reported to be implicated in an outbreak of *C. parapsilosis* fungemia recently [26].

In summary, infants with *C. parapsilosis* fungemia usually had certain risk factors. The presenting symptoms were usually vague and nonspecific. Mortality associated with *C. parapsilosis* fungemia was about one-third, but acute lethal events seemed unlikely. The results of this investigation suggested that an outbreak of *C. parapsilosis* fungemia caused by two main genotypes occurred in the NICU of the medical center and the branch hospital, possibly due to cross-infection by hand carriage of the personnel. The need for strict hand-washing with appropriate disinfectants before and after contact with patients cannot be overemphasized.

References

1. **Butler, K. M., Baker, C. J.:** *Candida*: an increasingly important pathogen in the nursery. Pediatr. Clin. North Am. 35 (1988) 543–563.
2. **Baley, J. E.:** Neonatal candidiasis: the current challenge. Clin. Perinatol. 18 (1991) 263–280.
3. **Ng, P. C.:** Systemic fungal infections in neonates. Arch. Dis. Child. 71 (1994) F130–135.
4. **Baley, J. E., Kliegman, R. M., Fanaroff, A. A.:** Disseminated fungal infections in very low-birth-weight infants: clinical manifestations and epidemiology. Pediatrics 73 (1984) 144–152.
5. **Rowen, J. L., Rench, M. A., Kozinatz, C. A., Adams, J. M., Baker, C. J.:** Endotracheal colonization with *Candida* enhances risk of systemic candidiasis in very low birth weight neonates. J. Pediatr. 124 (1994) 789–794.
6. **Johnson, D. E., Thompson, T. R., Green, T. P., Ferrieri, P.:** Systemic candidiasis in very-low-birth-weight infants (<1,500 grams). Pediatrics 73 (1984) 138–143.
7. **Weese-Mayer, D. E., Fondriest, D. W., Brouillette, R. T., Shulman, S. T.:** Risk factors associated with candidemia in the neonatal intensive care unit: a case-control study. Pediatr. Infect. Dis. J. 6 (1987) 190–196.
8. **Saxen, H., Virtanen, M., Carlson, P., Hoppu, K., Pohjavuori, M., Vaara, M., Vuopio-Varkila, J., Peltola, H.:** Neonatal *Candida parapsilosis* outbreak with a high case fatality rate. Pediatr. Infect. Dis. J. 14 (1995) 776–781.
9. **Betremieux, P., Chevrier, S., Quindos, G., Sullivan, D., Polonelli, L., Guiguen, C.:** Use of DNA fingerprinting and biotyping methods to study a *Candida albicans* outbreak in a neonatal intensive care unit. Pediatr. Infect. Dis. J. 13 (1994) 899–905.
10. **Burnie, J. P., Odds, F. C., Lee, W., Webster, C., Williams, J. D.:** Outbreak of systemic *Candida albicans* in intensive care unit caused by cross infection. BMJ 290 (1985) 746–748.
11. **Hunter, P. R., Harrison, G. A. J., Fraser, C. A. M.:** Cross infection and diversity of *Candida albicans* strains carriage in patients and nursing staff in an intensive care unit. J. Med. Vet. Mycol. 28 (1990) 317–325.
12. **Plouffe, J. F., Brown, D. G., Silva, J. Jr., Eck, T., Stricof, R. L., Fekety, R. Jr.:** Nosocomial outbreak of *Candida parapsilosis* fungemia related to intravenous infusions. Arch. Intern. Med. 137 (1977) 1686–1689.
13. **Weem, J. J. Jr., Chamberland, M. E., Ward, J., Willy, M., Padhye, A. A., Solomon, S. L.:** *Candida parapsilosis* fungemia associated with parenteral nutrition and contaminated blood pressure transducers. J. Clin. Microbiol. 25 (1987) 1029–1032.
14. **McCray, E., Rampell, N., Solomon, S. L., Bond, W. W., Martone, W. H., O'Day, D.:** Outbreak of *Candida parapsilosis* endophthalmitis after cataract extraction and intraocular lens implantation. J. Clin. Microbiol. 24 (1986) 625–628.
15. **Sheretz, R. J., Gledhill, K. S., Hampton, K. D., Pfaller, M. A., Givner, L. B., Abramson, J. S., Dillard, R. G.:** Outbreak of *Candida* bloodstream infections associated with retrograde medication administration in a neonatal intensive care unit. J. Pediatr. 120 (1992) 455–461.
16. **National Committee for Clinical Laboratory Standards:** Reference method for broth dilution antifungal susceptibility testing of yeasts: approved standard. NCCLS document M27-A. NCCLS, Pennsylvania, 1997.
17. **White, T. J., Bruns, T., Lee, S., Taylor, J.:** Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. In: *Innis, M. A., Gelfand, D. H., Sninsky, J. J., White, T. J.* (eds.): PCR protocols: a guide to methods and applications. Academic Press, San Diego, CA 1990, pp. 315–322.
18. **Schwartz, D. C., Cantor, C. R.:** Separation of yeast chromosome-sized DNAs by pulse field gradient gel electrophoresis. Cell 37 (1984) 67–75.
19. **Stamos, J. K., Rowley, A. H.:** Candidemia in a pediatric population. Clin. Infect. Dis. 20 (1995) 571–575.
20. **Faix, R. G.:** Invasive neonatal candidiasis: comparison of *albicans* and *parapsilosis* infection. Pediatr. Infect. Dis. J. 11 (1992) 88–93.

21. **Weems, J. J. Jr.:** *Candida parapsilosis*: epidemiology, pathogenicity, clinical manifestations, and antimicrobial susceptibility. Clin. Infect. Dis. 14 (1992) 756–766.
22. **Ghannoum, M. A., Rex, J. H., Galgiani, J. N.:** Susceptibility testing of fungi: current status of correlation of *in vitro* data with clinical outcome. J. Clin. Microbiol. 34 (1996) 489–495.
23. **Seidenfeld, S. M., Cooper, B. H., Smith, J. W., Luby, J. P., Mackowiak, P. A.:** Amphotericin B tolerance: a characteristic of *Candida parapsilosis* not shared by other *Candida* species. J. Infect. Dis. 147 (1983) 116–119.
24. **Strausbaugh, L. J., Swell, D. L., Ward, T. T., Pfaller, M. A., Heitzman, T., Tjoelker, P.:** High frequency of yeast carriage on hands of hospital personnel. J. Clin. Microbiol. 32 (1994) 2299–2300.
25. **Huang, Y.-C., Lin, T.-Y., Leu, H.-S., Wu, J.-L., Wu, J.-H.:** Yeast carriage on hands of hospital personnel working in intensive care units. J. Hosp. Infect. 39 (1998) 47–51.
26. **Levin, A. S., Costa, S. F., Mussi, N. S., Basso, M., Sinto, S. I., Machado, C., Geiger, D. C., Villares, M. C. B., Schreiber, A. Z., Barone, A. A., Branchini, M. L. M.:** *Candida parapsilosis* fungemia associated with implantable and semi-implantable central venous catheters and the hands of healthcare workers. Diagn. Microbiol. Infect. Dis. 30 (1998) 243–249.

Book Review

B. Greenwood, K. de Cock (eds.)
Prediction, Detection and Management of Tomorrow's Epidemics
220 pages, several figures and tables
John Wiley & Sons, Chichester-New York-Weinheim-Brisbane-Singapore-Toronto 1998
Price: GBP 45

The past two decades have witnessed the emergence of several new microbial agents, as well as an increasing resistance to drugs. The influence of global changes upon patterns of infectious diseases is now recognized as an important factor. Foodborne infections may be of increasing significance in the next century. Living in a global village facilitates the spread of infectious diseases. The lesson learned from the AIDS pandemic is that other biological agents may emerge and result in a global infectious disaster.
In 17 chapters, the editors and several other renown experts in the field provide a wealth of information on several points regarding emerging and reemerging infections. Among the causative agents, the history and future significance of Ebola virus infection, bovine spongiform encephalitis and Creutzfeld-Jakob disease are also presented. An excellent chapter deals with the contributing factors causing the global spread of dengue fever. In another chapter, an economic analysis of infections with *Escherichia coli* O157:H7 is presented, indicating the difficulty in the assessment of total costs associated with food-borne pathogens.
Other chapters cover global alert and infectious disease control. The importance of public health agencies is emphasized as well as international collaboration of centers dealing with infectious diseases.
This book may be recommended for all readers with an interest in infectious diseases, and for those who want to gain an insight into the contributing factors of various new infections. It serves as a concise summary and should be especially useful for public health officials.

T. F. Schwarz
Würzburg

Infection 27 (1999) No. 2 © MMV Medien & Medizin VerlagsGmbH München 1999