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Article

Epidemiology of Yeast Colonization in the Intensive Care Unit

S.A. Hedderwick, M.J. Lyons, M. Liu, J.A. Vazquez, C.A. Kauffman

Abstract In order to investigate the epidemiology of colonization and possible transmission of yeasts among patients and healthcare workers in adult intensive care units (ICUs), 194 patients were followed for a mean of 9 ± 11 days and 63 healthcare workers were followed for a mean of 132 ± 52 days. Among the patients, 142 (73%) were colonized by yeast, with *Candida albicans* being the species most commonly recovered. Most patients (65%) were already colonized with yeast upon admission to the intensive care unit; only 17% became colonized after admission. Persistent colonization occurred in 51 (55%) of 92 patients who had more than three cultures performed; in 75% of them, colonization persisted with the same strain of *Candida albicans* or *Candida glabrata*. Bacterial infection in the month preceding entry into the ICU was the only risk factor significantly associated with yeast colonization. Among the healthcare workers, yeasts were isolated from 42 (67%). *Candida albicans* was most frequently recovered from the oropharynx (19% of occasions), and *Candida parapsilosis* was most frequently found on hands (8% of occasions). Persistent colonization of the oropharynx occurred in only six healthcare workers, and none had persistence of yeasts on hands. In this non-outbreak setting, 5 (4%) of 123 patient/healthcare worker interactions that were linked epidemiologically yielded the same strain of *Candida albicans*, providing evidence for possible cross-transmission. No similar link was found between healthcare worker-patient interactions and colonization with *Candida glabrata* or *Candida parapsilosis*.

Introduction

The incidence of serious *Candida* infections in critically ill patients in intensive care units (ICU) is increasing; currently, *Candida* species constitute the fourth most common nosocomial bloodstream isolate in the USA [1, 2]. The epidemiology of *Candida* infections is still controversial. It is generally believed that infection arises from invasion by the patient's own endogenous colonizing flora and that those strains of *Candida* that cause infection are the same as those previously found colonizing patients [3–5]. However, several reports of outbreaks of *Candida* infections support exogenous acquisition of the infecting yeast strains in some cases [6–13].

Several studies have documented that 60–70% of patients in ICUs are colonized with *Candida* spp. [14, 15]. Fewer studies, however, have assessed the prevalence of yeast colonization among healthcare workers in that same setting. Although one study found that 58% of ICU nurses carried yeasts of any type on their hands [16], others have noted low carriage rates for yeasts [13, 15].

The investigation of possible transmission of yeasts between patients and healthcare workers has been

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hampered by the lack of a reliable typing system to evaluate strain relatedness. Previous typing systems that relied on phenotypic or serologic differences were not sensitive enough. Recently, molecular typing systems for yeasts, including contour-clamped homogenous electric field (CHEF) electrophoresis and random amplified polymorphic DNA (RAPD) techniques, have facilitated the identification of strain types carried by individuals and have helped clarify the modes of transmission [17]. Using these techniques, we prospectively studied the patterns of yeast colonization and sought to determine whether yeast strains were being transmitted between healthcare workers and patients in the ICU setting.

Materials and Methods

Facility. The Ann Arbor Veterans Affairs Medical Center is a 200-bed acute-care veterans hospital with a long-term-care unit attached to the hospital. There are three ICU's: one seven-bed medical ICU with single rooms only, one seven-bed thoracic ICU with single rooms only, and one eight-bed surgical ICU with two single rooms and a six-bed open unit.

Study Participants. From 1 May 1995 through 31 October 1995, all patients who were expected to remain in one of the ICUs for at least 3 days were eligible for the study. If patients were readmitted to the ICU on a second occasion, they were not reenrolled into the study. During the same study period, healthcare workers caring for the patients in the ICUs were asked to participate; approximately 40 of them worked in the medical ICU only, and another 60 rotated through the thoracic ICU and the surgical ICU. All nurses worked 12-h shifts. Generally, each healthcare worker was assigned one or two patients according to the complexity of the patient's needs; occasionally, more than one healthcare worker cared for a single patient.

Study Design. Demographic and microbiologic data were obtained for each patient every 3 days while they were in the ICU and once more approximately 3 days following their discharge from the ICU. At entry and with each sampling, the following data were obtained: age, sex, underlying diseases, prior surgical procedures, parenteral nutrition, immunosuppressive therapy, recent history of bacterial or fungal infection, and antimicrobial treatment. Rectal and buccal mucosa were sampled for the presence of yeasts every 3 days. For healthcare workers, buccal mucosa and hands were sampled for the presence of yeasts every 3 days as their shift schedules permitted. Patient-healthcare worker interactions were studied as follows: culture data from each healthcare worker were matched with culture data from the individual patients they cared for on the day of the interaction, the prior sampling date, and the subsequent sampling date.

Definitions of Colonization. Colonization was defined as one or more cultures positive for yeasts from any site. For patients followed for at least three culture episodes, the following definitions were applied: persistent colonization was defined as a culture from at least one site being positive for yeast on every occasion that cultures were performed; probably persistent colonization was defined as a ratio of positive to total cultures performed of between 0.8 and 1; intermittent colonization was recorded when patients had more than one culture positive for yeast but were not persistently or probably persistently colonized; transient colonization was defined as only one culture positive for yeast.

Microbiologic Methods. Samples were obtained from the oropharynx and the rectum by use of sterile rayon applicator sticks, which were immediately streaked onto Sabouraud dextrose agar (Difco, USA) containing 50 μg/ml gentamicin sulfate (Sigma, USA) and 50 μg/ml vancomycin (Sigma).

Healthcare workers' hands were sampled using a modified broth-bag technique in which both hands were sequentially immersed in 50 ml sterile 0.9% saline in a sterile zip-lock bag and kneaded for 30 s. The hands were removed from the bag, and the saline remaining in the bag was passed through a 0.45 μm filter (Millipore, USA). The filter was carefully placed into 0.5 ml sterile Sabouraud broth and vortexed vigorously. A 0.1 ml aliquot of this fluid was spread with a sterile glass rod onto Sabouraud agar containing 50 μg/ml gentamicin sulfate and 50 μg/ml vancomycin. All plates were incubated at 35 °C for 72 h, and yeast-like colonies were isolated.

Germ-tube formation for identification of C*andida albicans* was assessed by incubating a small inoculum of organisms in 0.5 ml of fetal bovine serum at 35 °C for 2.5 h and then viewing the preparation under direct microscopy. Yeasts that were germ-tube negative were identified to species level by the API 20C System (Sherwood Medical Products, USA). All isolates were stored at –70 °C in Sabouraud broth and glycerol for further studies.

Typing of Yeast Strains. For CHEF typing, DNA was prepared in agarose plugs after yeast cells had been treated with zymolase and lysis with sarcosyl/pronase as described previously [18, 19]. For RAPD polymerase chain reaction (PCR) typing, DNA was extracted from zymolase-treated yeast cells, purified, and resuspended in Tris-EDTA buffer, as described previously [20].

CHEF electrophoresis was performed with agarose plugs containing whole yeast DNA after loading onto a horizontal electrophoresis gel. Chromosomal DNA from *Saccharomyces cerevisiae* (New England BioLabs, USA) was used as an internal standard. Chromosomal separation was achieved on CHEF DR-II (Bio-Rad, USA) equipment for *Candida albicans* and DR-III equipment for *Candida glabrata* and *Candida parapsilosis* using switch-time and voltage parameters appropriate for each species [18, 19, 21]. Gels were stained for 1 h in 1 μg/ml ethidium bromide and photographed with UV transillumination.

Polymerase Chain Reaction Assay. PCRs were performed in a Robocycler 40 Thermocycler (Stratagene, USA) using a 10 bp primer (CX-5) [20]. The sequence of CX-5 is 5′-ACACTGCTTC-3′. Briefly, the program utilized was as follows: 5 cycles of 94 °C × 30 s, 25 °C × 2 min, 72 °C × 2 min; 45 cycles of 94 °C × 30 s, 31 °C × 2 min, 72 °C × 2 min, and 1 cycle of 72 °C × 10 min. Typical reactions in 25 μl, overlaid with mineral oil, were in 25 mM Tris-HCl, pH 8.4, 50 mM KCl, 1.5 mM $MgCl_2$, 100 μl dNTPs, 50 pmoles primer, and 2.5 U *Taq* DNA polymerase (Bethesda Research Laboratories, USA). Template DNAs were genomic DNA (< 100 ng). PCR reaction products were analyzed by ethidium bromide agarose gel electrophoresis (2% agarose). Positive and negative controls were run simultaneously. All PCR studies were carried out in duplicate to ensure stability and reproducibility of the results.

Strain differentiation by CHEF was performed by visual delineation of the banding pattern existing between 225 and 1900 kb. For each isolate, the number of bands and their position relative to the *Saccharomyces cerevisiae* standard bands were recorded. A strain was considered unique if it had a different number of bands and/or a different position of the bands relative to other previously described banding patterns in our library of CHEF patterns [18, 19]. For PCR assays, visual elucidation of the patterns were recorded; polaroids of gels and autoradiograms were scanned with a Logitech Scanner for printing at 300 dpi. On occasion, exposures of lanes that were over- or underloaded were enhanced by the scanning software so that originally visible fragments were not lost in reproduction.

Statistical Analysis. Data are expressed as mean ± standard deviation. Data for risk factor analysis were analyzed using Statistical Analysis System 6.12 (SAS Institute, USA). Categorical variables were analyzed with the chi-square or Fisher's exact test; continuous variables were analyzed with the Student's *t* test. Multivariate analysis was done by stepwise logistic regression in which the limit for entering and removing variables was 0.1.

Results

Colonization of Patients with Yeasts. A total of 194 patients (191 men and 3 women) were included in the study; 48 patients were admitted to the medical ICU, 52 to the surgical ICU, and 94 to the thoracic ICU. Patients were followed for a mean of 9 ± 11 days (range 4–103 days); the mean length of ICU stay was 11 ± 12 days (9.5 ± 7 days in the thoracic ICU; 11 ± 7.7 days in the medical ICU; and 13.9 ± 21 days in the surgical ICU). The mean age of the study population was 64.1 ± 10.5 years (range 27–83 years).

Patients were sampled for yeast colonization a mean of 3.3 ± 3.1 times (range 2–30). Overall, 142 (73%) patients were positive for yeast on at least one occasion, including 133 (69%) patients with yeast isolated from the oropharynx and 91 (47%) patients with yeast isolated from the rectum. In the medical ICU, 38 (79%) patients were colonized with yeasts; in the surgical ICU, 38 (73%) patients were colonized; and in the thoracic ICU, 66 (70%) patients were colonized.

Of the 632 occasions on which samples were taken, yeasts were recovered from either the oropharynx or the rectum on 430 (68%). On 343 (80%) of these occasions, only one species was present, while on 77 (18%) and 10 (2%) occasions, two or more than three species were isolated, respectively. The most common colonizing species isolated from both the oropharynx and the rectum of patients was *Candida albicans* (Table 1). *Candida glabrata* was found as frequently as *Candida albicans* in the rectum but was less common in the oropharynx. When separated by individual ICUs, *Candida albicans* accounted for 48.1% and 58.1% of all isolates in the medical and thoracic ICUs, respectively (Figure 1). However, in the surgical ICU, only 40.5% of isolates were *Candida albicans*; *Candida glabrata* was more common (49.2% of isolates). No other major differences were noted in the types of colonizing yeast species among the three units.

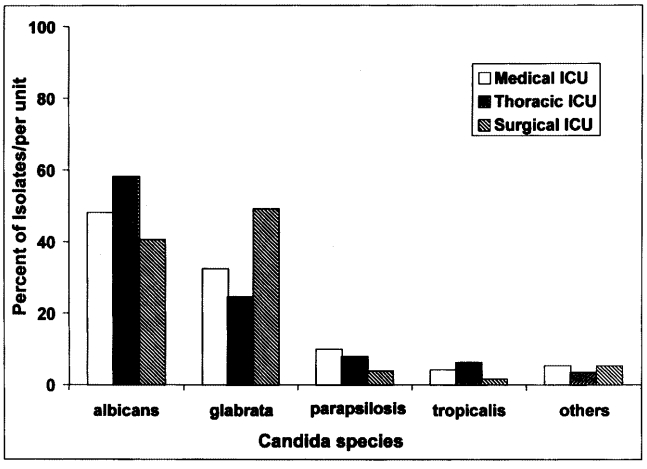

Figure 1 *Candida* species isolated from patients on 632 occasions according to type of intensive care unit (ICU)

Acquisition and Persistence of Yeast Colonization in Patients. There were 92 patients on whom cultures were performed on more than three occasions. Of these 92 patients, 76 (82.6%) were colonized with yeasts. In

Table 1 Yeast species isolated from patients ($n = 632$ occasions) and healthcare workers ($n = 524$ occasions)

Yeast sp. isolated	No. (%) of positive samples			
	Rectum	Oropharynx	Hands	Oropharynx
Patients				
C. albicans	94 (14.8)	230 (36.4)		
C. glabrata	102 (16.1)	126 (19.9)		
C. parapsilosis	34 (5.4)	11 (1.7)		
C. tropicalis	7 (1.1)	18 (2.8)		
C. kefyr	1 (0.2)	9 (1.4)		
Other[a]	7 (1.1)	10 (1.6)		
No yeasts isolated	410 (64.9)	255 (40.3)		
Healthcare workers				
C. albicans			25 (4.8)	102 (19.4)
C. glabrata			20 (3.8)	10 (1.9)
C. parapsilosis			44 (8.4)	1 (0.2)
C. tropicalis			1 (0.2)	0
C. kefyr			0	2 (0.4)
Other[a]			13 (2.5)	0
No yeasts isolated			440 (84.0)	413 (78.8)

[a] *C. lusitaniae*, *Saccharomyces cerevisiae*, *C. lipolytica*, *Trichosporon beigelii*, *Hansenula* and *Rhodotorula* sp.

Table 2 Acquisition and persistence of yeast colonization in patients and healthcare workers who had cultures performed on three or more occasions

Colonization status	No. (%) of persons	
	Patients ($n=92$)	Healthcare workers ($n=58$)
Persistent colonization	47 (51.1)	6 (10.3)
Probably persistent colonization	4 (4.3)	3 (5.2)
Intermittent colonization	21 (22.8)	23 (39.7)
Transient colonization	4 (4.3)	7 (12.1)
Total colonized	76 (82.5)	39 (67.3)

60 (65.2%) of them, yeasts were isolated at entry into the study; in 16 (17.4%), yeasts were acquired subsequent to their admission to the ICU; and in another 16 (17.4%), yeast colonization did not occur at any time during the study.

Yeasts were persistently and probably persistently isolated from 51 (55.4%) of the 92 total patients, while 21 (22.8%) and 4 (4.3%) patients had only intermittent or transient yeast colonization, respectively (Table 2). On 90 occasions, these 51 patients were simultaneously colonized with the same species of yeast in the rectum and the oropharynx. Strain delineation of 39 randomly selected pairs of *Candida albicans* and *Candida glabrata* recovered on these 90 occasions revealed that the strains from the rectum and the oropharynx were similar in 27 (69.2%) of 39 pairs tested.

Candida albicans was most often associated with persistent or probably persistent colonization. Fifty-three percent of patients colonized with *Candida albicans* had persistent or probably persistent colonization, whereas only 25.5% and 11.1% of patients colonized with *Candida glabrata* or *Candida parapsilosis*, respectively, had persistent or probably persistent colonization. Strain delineation was performed on isolates recovered from 40 patients who had persistent or probably persistent colonization with *Candida albicans* (29 patients) or *Candida glabrata* (11 patients). Twenty-two (75.9%) of the 29 patients colonized with *Candida albicans* and 8 (73.7%) of 11 patients colonized with *Candida glabrata* were found to be persistently colonized with the same strain throughout their ICU stay.

The mean time until colonization was 6 ± 1.6 days for the 16 patients who became colonized after admission to the ICU. The organism first acquired was *Candida glabrata* in six patients, *Candida albicans* in five, *Candida parapsilosis* in two, and mixtures of *Candida glabrata* with other yeasts in three patients. Once acquired, *Candida glabrata* persisted in five of nine patients, while *Candida albicans* persisted in only two of eight patients.

Risk Factors for Colonization of Patients with Yeasts. Evaluation of risk factors present on admission to the ICU revealed that only bacterial infections within the previous month were associated with yeast colonization at either site ($P=0.002$) (Table 3). Renal failure was more common in colonized patients, but differences were not statistically different. Multivariate analysis confirmed that the only factor significantly associated with fungal colonization was prior bacterial infection (relative risk = 4.2 [1.6–10.6], $P=0.002$).

Fungemia Episodes. One patient developed fungemia on two occasions during the 6-month study period. This patient, whose length of stay in the surgical ICU was 103 days, had *Candida glabrata* fungemia followed 3 months later by *Candida albicans* fungemia. He had probably persistent colonization with *Candida glabrata* in both the oropharynx and the rectum throughout the study period, but *Candida albicans* was never isolated from either site prior to the fungemic episodes.

Table 3 Factors associated with colonization of 194 ICU patients by yeasts

Characteristic	No. (%) of patients		Relative risk (95% CI)	*P* value
	Colonized ($n=142$)	Not colonized ($n=52$)		
Age (mean ± SD)	64.5 ± 10.9	63.4 ± 9.3		0.54
Prior intravenous antibiotics[a]	136 (95.8)	47 (90.4)	1.8 (0.8–3.9)	0.15
Prior surgical procedure[b]	105 (73.9)	44 (84.6)	0.6 (0.3–1.1)	0.12
Diabetes mellitus	53 (37.3)	15 (28.8)	1.3 (0.8–2.2)	0.27
Cancer	30 (21.1)	14 (26.9)	0.8 (0.4–1.3)	0.39
Alcoholism	24 (16.9)	9 (17.3)	1.0 (0.5–1.8)	0.95
Neutropenia	1 (0.7)	0	1.1 (0.1–12.7)	0.55
Renal failure	9 (6.3)	0	5.6 (0.4–84.9)	0.06
Corticosteroid therapy[b]	8 (5.6)	2 (3.8)	1.4 (0.4–4.5)	0.62
Parenteral nutrition[a]	13 (9.2)	2 (3.8)	2.1 (0.6–6.8)	0.22
Bacterial infection[a]	37 (26.1)	3 (5.8)	4.2 (1.7–10.6)	0.002

[a] Within preceding month
[b] Within preceding 3 months

Colonization of Healthcare Workers with Yeasts. A total of 63 healthcare workers (54 women and 9 men) were followed for a mean of 132 ± 52 days and were sampled for yeast colonization on 8.3 ± 4.5 occasions (range 1–22). Among them, 42 (66.7%) were positive for yeast on at least one occasion; 27 (42.9%) had oropharyngeal colonization and 30 (47.6%) had hand colonization.

Yeasts were isolated from either the oropharynx or the hands of healthcare workers on 166 (31.7%) of the 524 total occasions that samples were taken. On 135 (81.3%) of these occasions, only one species was present, whereas on 26 (15.7%) and 5 (3%) occasions, two or more than three species were isolated, respectively. Overall, 16% of hand samples and 21% of oropharyngeal samples yielded yeasts. *Candida albicans* was the species most commonly isolated from the oropharynx of healthcare workers (19.4%), whereas *Candida parapsilosis* was the species most frequently isolated from hands (8.4%) (Table 1). *Candida glabrata* was infrequently isolated from either site in healthcare workers.

Of the 58 (92.1%) healthcare workers who had samples taken on more than three occasions, 6 (10.3%) were persistently colonized with yeasts and 3 (5.2%) were probably persistently colonized; 23 (39.7%) and 7 (12.1%) had intermittent and transient colonization, respectively (Table 2). Persistent colonization was documented in the oropharynx only, not on the hands, of healthcare workers. Persistent or probably persistent colonization by one yeast species occurred in only three healthcare workers, while six had more than one *Candida* species isolated over time. Only two healthcare workers were persistently colonized by the same species simultaneously in the oropharynx and on the hands.

Although there were no healthcare workers whose hands were persistently colonized by yeast, three had probably persistent colonization and two others had multiple positive cultures from hands, but by strict definition they were judged to be intermittent carriers. Four of these five healthcare workers carried multiple different yeast species on their hands over time and three had multiple species isolated on most sampling occasions. Strain delineation showed that one strain persisted over time in two of four healthcare workers colonized with *Candida albicans*, one of three healthcare workers colonized with *Candida glabrata*, and one of three healthcare workers colonized with *Candida parapsilosis*. The one healthcare worker who had *Candida parapsilosis* only isolated on each sampling occasion had four different strain types isolated. There were 11 healthcare workers in whom *Candida albicans* was frequently isolated from the oropharynx over time; in contrast to the results noted with hand carriage, 9 of these 11 healthcare workers had the same strain of *Candida albicans* isolated from the oropharynx over time.

Transfer of Yeasts Between Healthcare Workers and Patients. In order to investigate the possibility of yeasts being transferred between healthcare workers and patients, we studied each interaction ($n = 123$) between a healthcare worker and a patient in which the healthcare worker had yeasts isolated and the patient had cultures obtained at, right before, or right after the time of the interaction. For 56 of these 123 patient-healthcare worker interactions, the same species of yeast was isolated (35 *Candida albicans*, 12 *Candida parapsilosis*, and 9 *Candida glabrata*). For those 21 interactions in which *Candida glabrata* or *Candida parapsilosis* were found in both healthcare workers and patients, the strains obtained from healthcare workers were not similar to those obtained from patients.

CHEF typing showed that for 13 of the 35 interactions yielding *Candida albicans*, the same strain was isolated from both the healthcare worker and the patient. RAPD analysis differentiated 8 of these 13 as different strains, with 5 strains being similar by both techniques (Figure 2). Thus, for 5 (4.1%) of 123 interactions, evidence for possible transmission was obtained. None of these interactions was between a healthcare worker and any of the 16 patients who entered the ICU without prior *Candida* colonization. Thus, no direct evidence was obtained to link initial acquisition of yeasts upon entry into the ICU with transmission from a healthcare worker. In fact, for these five interactions, the patient was found to carry the strain before the healthcare worker in three instances, and in two other instances, both the healthcare worker and the patient were found to carry the same strain for the first time on the same day.

Discussion

Over the past decade nosocomial infection with *Candida* species has emerged as a major problem for patients in acute-care hospitals. The recent trend of an increase in the incidence of nosocomial candidemia is especially worrisome, with a fivefold increase having been noted among hospitals participating in the National Nosocomial Infections Surveillance system in the USA [1], a 2.3-fold increase recorded in the Netherlands [22], and a 27-fold increase noted in Taiwan [23]. The greatest risk for fungemia appears to be in the ICU with certain units (e.g., burn/trauma and neonatal units) showing the highest rates [1, 24].

In the present study, colonization of ICU patients with *Candida* spp. was common, occurring at least once in 73% of patients, a figure not dissimilar to that found in prior studies [5, 14, 25]. Most patients who entered the ICU were already colonized by their own *Candida*

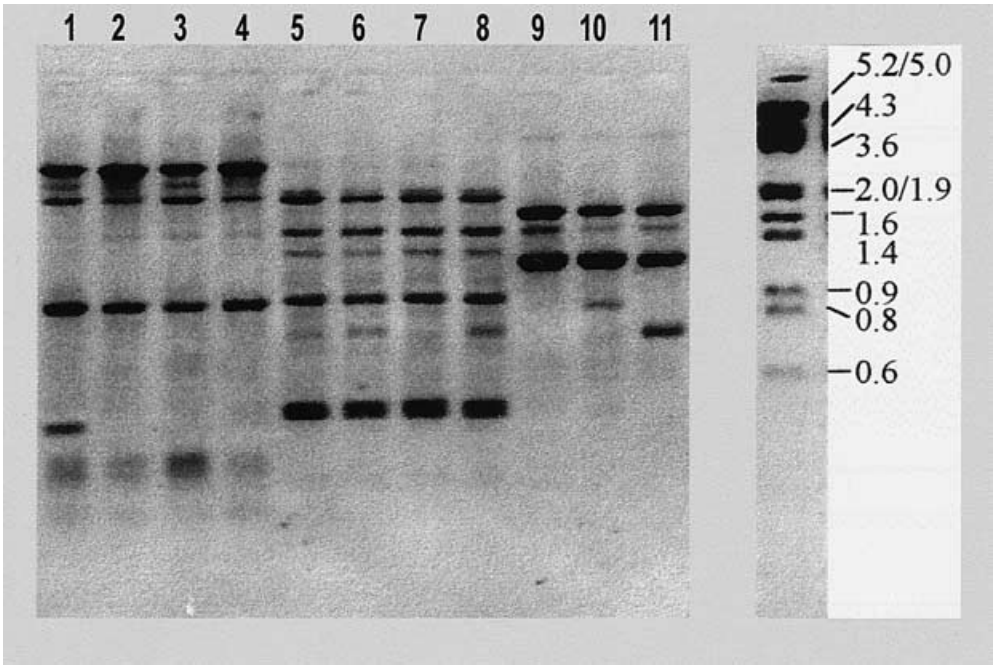

Figure 2 RAPD fingerprinting of *Candida albicans* isolates recovered from healthcare worker-patient interactions. *Lanes 1* and *2* represent isolates from a healthcare worker and a patient who did not share a similar strain. *Lanes 3* and *4* are isolates from a healthcare worker-patient interaction in which the strains appeared similar. *Lanes 5* through *8* contain isolates from 2 healthcare workers (*lanes 5* and *8*), each of whom shared a similar strain with a patient for whom they cared (*lanes 6* and *7*, respectively). *Lanes 9* and *10* are patient isolates recovered during interactions with the healthcare worker represented in *lane 11*; no similarities are noted. The lane on the far right contains the size standards (in Kb) that were generated by *Eco*R1-*Hind*III digestion of bacteriophage lambda

strain, mostly *Candida albicans*. Colonization with this same strain persisted in the majority of patients, verifying results of a prior study [5].

Most factors typically associated with an increased risk of developing candidemia [1, 26, 27] did not appear to contribute to *Candida* colonization. Multivariate analysis revealed that bacterial infection within the previous month was the only factor associated with an increased risk of yeast colonization. We did not find, as others have, an association between prior antibiotic therapy and yeast colonization [15, 28]. However, the extensive use of antibiotics in this population, often without a documented bacterial infection, could be responsible for this lack of relationship to colonization.

Current understanding of the epidemiology of acquisition and infection with *Candida* species in the ICU setting is incomplete. Several investigators have studied the unique situation afforded by the neonatal ICU, in which initial acquisition of yeasts by a *Candida*-naive patient can be assessed [29–31]. Reef et al. [30] found that all neonates were free of yeast colonization at the time of birth, while others have shown that colonization was present at first sampling in a small percentage of neonates [31]. Those neonates who did become colonized with *Candida* spp., especially *Candida parapsilosis*, appeared to acquire yeasts most often from the ICU setting and less often from their mothers [29–31]. However, none of these studies on neonates assessed the carriage of yeasts by healthcare workers and the role which carriage might play in transmission to neonates.

In adults, most of whom enter an ICU already colonized with yeasts, the epidemiology of *Candida* acquisition differs from that found for neonates. Presumably, exogenous strains have to compete with those endogenous *Candida* strains already present. One source of exogenous yeast acquisition could be the hands of healthcare workers. Although 48% of healthcare workers in this study had yeasts on their hands, none had persistent carriage and only five had frequent carriage at this site. Other investigators have found the rate of carriage of *Candida* on healthcare workers' hands to vary from 0 to 58% [13, 15, 16, 25, 28, 32–34]. Of the five healthcare workers whose hands were frequently colonized with *Candida* in our study, only one was colonized with a single species (*Candida parapsilosis*) over time, and this person had different strains of that species on each occasion. All of the healthcare workers with frequent colonization had either multiple species isolated at each sampling or had multiple strains of the same species isolated over time. Thus, it appears that hand carriage of *Candida* by healthcare workers is usually short-lived. One recent study that assessed persistence of carriage during an ICU shift found that nurses initially had *Candida parapsilosis* on their hands and acquired *Candida albicans* only after patient care activities [33].

The most common species isolated from the hands of healthcare workers was *Candida parapsilosis*, a finding consistent with that noted by several investigators [13, 16] but different from that noted by others [25]. In spite of the common presence of *Candida parapsilosis* on healthcare workers' hands and data showing that persistence on hands may be longer for *Candida parap-*

silosis than other species [35], *Candida parapsilosis* was uncommonly noted in our patients, rarely persisted when it did occur, and no link between healthcare worker carriage and patient acquisition could be found.

Although transmission of *Candida parapsilosis* in non-outbreak settings has been postulated [36], proof of transmission has been lacking. Future studies assessing transmission of *Candida parapsilosis* might be most fruitfully performed in two settings: (i) neonatal ICUs, in which the rates of colonization and serious infection with *Candida parapsilosis* appear to be much higher than those noted in adult ICUs [37–39]; and (ii) outbreak settings, in which contamination of central intravenous catheters or other devices may be related to the carriage of yeasts on the hands of healthcare workers [6, 29].

In our study, *Candida glabrata* was found to be most common in the surgical ICU. This finding is similar to that noted in a large multicenter study of colonization and infection in ICUs, in which *Candida glabrata* was more common among patients in a surgical ICU than among those in neonatal or cardiothoracic ICUs [39]. Among those patients who were not colonized with yeasts on admission to the ICU, acquisition of *Candida glabrata* was more common than acquisition of *Candida albicans*. However, healthcare workers were infrequently colonized with *Candida glabrata* on their hands, and no evidence of transmission of *Candida glabrata* from a healthcare worker to a patient was found. Thus, possible mechanisms of acquisition of *Candida glabrata* have not been specifically elucidated by this study. Prior studies in a medical ICU noted environmental contamination by *Candida glabrata* [28]. It is possible that more frequent sampling of healthcare workers' hands in our study could have revealed transient contamination of hands with this species. It should be noted that fluconazole, restricted to use by the Infectious Disease Section of our hospital, was dispensed infrequently in the ICUs.

In the absence of an outbreak, the possibility of yeasts being transmitted between healthcare workers and patients remains controversial. Hunter et al. [25], using insensitive strain typing techniques, found little to support cross-transmission. Using a more sensitive restriction enzyme analysis method, Vazquez et al. [15, 28] found possible cross-transmission of both *Candida albicans* and *Candida glabrata* in a medical ICU and a bone marrow transplant unit. However, a link between colonization of healthcare workers' hands and transmission was not made in those studies, possibly because sensitive hand sampling techniques were not performed over time.

Our study, which utilized multiple samplings over time, was conducted in a non-outbreak setting to assess whether usual healthcare worker-patient interactions might play a role in the transmission of yeasts. On only 5 (4.1%) of 123 occasions were both the healthcare worker and the patient for whom care was provided found to carry the same strain of yeast. This finding, obtained using two different typing methods [40], supports prior studies showing possible cross-transmission of yeast strains from healthcare workers to patients [11, 15, 28, 36], but it does not prove that cross-transmission occurred. Further studies focusing on daily healthcare worker-patient interactions, taking into account such factors as hand washing, glove use, and use of invasive devices, should help define further the role that healthcare worker-patient interactions play in the transmission of yeasts.

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