

Risk Factors for Colonization with Yeast Species in a Veterans Affairs Long-term Care Facility

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OBJECTIVES: To assess colonization and serious infection with yeasts and the risk factors that are associated with colonization by these organisms.

DESIGN: Monthly surveillance for colonization and infection over a period of 2 years.

SETTING: A long-term-care facility (LTCF) attached to an acute-care Veterans Affairs Medical Center.

PARTICIPANTS: The 543 men and 10 women in the facility.

MEASUREMENTS: Colonization and serious infection rates with yeasts. Analysis of risk factors associated with yeast colonization of residents.

RESULTS: Colonization rates were relatively stable during the 2-year period ($53 \pm 1.8\%$ patients colonized per month). *Candida albicans* was the most common colonizer, found in $35 \pm .9\%$ of patients colonized per month. The pharynx was the most commonly colonized site, with $41 \pm 1.4\%$ of patients per month with pharyngeal colonization. Eighty-four percent of patients remaining in the facility for 3 or more months were colonized by yeast at some time during their stay. Presence of neurogenic bladder, leg amputation, or a low serum albumin were independently associated with yeast colonization; neither diabetes mellitus nor functional status was a risk factor for colonization by yeasts. Only four serious yeast infections in four patients (esophagitis and three urinary tract infections) were found during the 2-year period; all infections occurred in patients who were colonized by yeasts previously.

CONCLUSION: In our LTCF, colonization of patients by yeasts occurred commonly in those residents remaining in the facility for 3 or more months. However, serious yeast infections occurred infrequently. It is likely that colonization of residents of LTCFs by yeasts may only become clinically important when the patient is transferred to an acute-care hospital where additional risk factors may allow the development of serious yeast infection. *J Am Geriatr Soc* 46:849-853, 1998.

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Candida spp have emerged as significant nosocomial pathogens in the acute-care hospital during the past decade; indeed, they are now the fourth leading cause of bloodstream infections and the sixth most common nosocomial pathogen in the United States.^{1,2} The epidemiology of *Candida* infections is still controversial. Infection is believed to result from invasion from the patient's own endogenous colonizing flora,³⁻⁷ although increasing reports of outbreaks of *Candida* infections support exogenous acquisition of *Candida* spp as important in some cases.⁸⁻¹² Thus, the clinical importance of *Candida* colonization at various body sites is debated. Reagen et al. showed that in 15 of 16 patients with various malignancies, the previous colonizing and bloodstream isolates of *Candida* species were identical.⁴ Other authors have shown a similar temporal relationship between colonization and subsequent candidemia with the same strain of *Candida*.³ In addition, a retrospective, case-control study of hospitalized patients showed that colonization was a risk factor for subsequent candidemia.⁵

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There are few data regarding the epidemiology of *Candida* colonization of residents of long-term care facilities (LTCF). Jackson et al. reported that 4% of all infections within the LTCF population were attributable to *Candida* spp, with an incidence of 0.28 per 1000 resident days.¹³ For other microbial pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci, trends seen in large acute-care hospitals are mirrored in LTCFs within a few years.^{14,15} Thus, yeast colonization of residents in a LTCF may predispose to infection. This report provides estimates of the rates and predominant *Candida* spp responsible for yeast colonization in residents of a LTCF associated with a Veterans Affairs hospital and identifies putative risk factors associated with yeast colonization in this population.

MATERIALS AND METHODS

Facility and Patients

Patients were residents of the Ann Arbor Veterans Affairs Nursing Home Unit, a 120-bed LTCF attached to a 300-bed acute-care Veterans hospital. Patients were admitted to the facility for long-term care, rehabilitation, or geriatric evaluation. From June 1, 1989, until May 31, 1991, all patients who were resident initially or admitted subsequently were

studied for colonization with various yeast-like organisms. Patients requiring intravenous therapy were excluded.

On admission to the study, the following information was recorded for all patients: age, sex, underlying chronic diseases, previous hospitalization, and nutritional status. Functional status was evaluated as follows: Group I patients were ambulatory, requiring minimal assistance in activities of daily living; Group II patients required minor assistance in activities of daily living and had intermittent bladder incontinence; Group III patients required assistance for almost all activities of daily living and had incontinence of bowel and/or bladder. Cultures of body sites were done at admission, and monthly thereafter. If the patient was transferred to the acute-care facility, additional cultures were performed when the patient returned to the LTCF.

Study Design

The study of colonization with yeasts was part of a project that followed patients in a LTCF to assess colonization with several different organisms, including MRSA, high-level aminoglycoside-resistant enterococci, ceftriaxone- and aminoglycoside-resistant Gram-negative bacilli, and yeasts.^{14,16-18}

Definitions

Colonization was defined as one or more positive cultures for yeasts from any site. For patients followed for at least 3 months, the definitions applied were: persistent colonization was defined as having a culture positive for yeast in at least one site 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 believed to have occurred 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. Infections with yeast were defined using Centers for Disease Control and Prevention criteria.¹⁹

Microbiological Methods

Colonization for yeasts was assessed in the oropharynx, perineum, rectum, and wounds. Sampling was accomplished using sterile rayon applicator sticks, which were placed immediately in Stuart transport media, and, within 1 hour, were streaked onto Sabouraud dextrose agar (Difco Inc., Detroit, MI) containing 50 µg/mL gentamicin sulfate (Schering Inc., Summit, NJ) using a semiquantitative, four-quadrant method of streaking. Plates were incubated at room temperature for 72 hours, the amount of growth on the plates was quantified as 1+ to 4+, and colonies shown to be yeasts by direct microscopy were isolated.

Germ tube formation for identification of *Candida albicans* was assessed by incubating a small inoculum of organisms in 0.5 mL of fetal bovine serum at 35°C for 2 hours and then viewing the preparation under direct microscopy. Yeasts that were germ tube negative were speciated by the API Yeast 20C System (Sherwood Medical Products, Plainview, NY).

Statistical Methods

Data for risk factor analysis were analyzed with the use of SAS.²⁰ Categorical variables were analyzed by univariate analysis with the Chi-square or Fisher's exact test; continuous variables were analyzed with the Student's *t* test or

Mann-Whitney rank sum test. A *P* value of <.05 was considered significant on two-tailed testing. Multivariate analysis was done by stepwise logistic regression, and the limit for entering and removing variables was .05.

RESULTS

Five hundred fifty-three patients were entered into the study during the 2-year period and were followed for a mean of 4.3 ± 1.0 months. The mean age of the 543 men and 10 women was $64 \pm .5$ years.

Rate of Colonization with Yeasts

Colonization by yeasts at any site was relatively constant during the 2-year period. The mean monthly colonization rate was $53 \pm 1.8\%$. Regardless of site, the most common organism found to be colonizing patients was *C. albicans* ($35 \pm .9\%$) (Table 1). The pharynx and rectum were the most frequently colonized areas (Figure 1). Among colonized patients, yeasts were isolated simultaneously from one, two, three, or four sites in 63%, 27%, 9%, and 1% of occasions, respectively. Of those patients who were colonized with yeasts at any site, 78% had only one species present on each occasion, whereas 20% and 2% had two or three or more species isolated, respectively.

Acquisition and Persistence of Yeast Colonization

Of the 286 patients who had cultures performed on three or more occasions, 170 patients (59%) were colonized with yeast at entry to the study; 71 patients (25%) acquired yeast after their entry into the study (first culture negative but at least one subsequent culture positive for yeast); and yeasts were never isolated from 45 patients (16%) (Table 2). Yeast species were persistently or probably persistently isolated in 75 patients (26%), whereas 120 (42%) and 46 (16%) of patients had intermittent and transient yeast colonization, respectively. *C. albicans* and *C. glabrata* were the species most commonly isolated from all patients, regardless of their colonization status. Persistence was associated with pharyngeal more than with rectal colonization; 93% of persistently colonized patients had *Candida* in their pharynx, but only 64% of intermittently and transiently colonized patients had pharyngeal colonization.

Risk Factors for Colonization with Yeast Species

Evaluation of risk factors present on admission to the LTCF revealed that seven variables were associated with

Table 1. Yeast Colonization Rates per Month by Species

Yeast Species	Mean Percent \pm SEM, Patients Colonized/Month
<i>C. albicans</i>	35 \pm 0.9
<i>C. glabrata</i>	17 \pm 1.9
<i>C. parapsilosis</i>	4 \pm 0.1
<i>C. tropicalis</i>	2.5 \pm 0.6
<i>C. pseudotropicalis</i>	1.5 \pm 0.3
Other species*	6 \pm 0.4

* Includes *S. cerevisiae*, *T. beigeli*, *C. lusitanae*, *C. stellatoidea*, *C. guilliermondii*, *C. lambica*, *B. capitatum*, *C. lipolytica*, *R. rubra*, *Pr. wickerhamii*, *C. kefyri*, *R. glutinis*, *H. anomala*, *Pr. stagnora*.

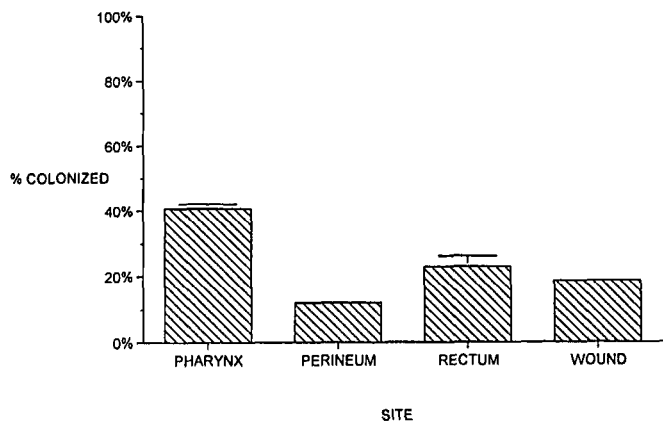


Figure 1. Monthly colonization rate (mean ± SEM) by yeasts in residents of a long-term care facility. Percentage of wound colonization is expressed as a proportion of residents with wounds that were cultured.

yeast colonization at any site (Table 3). However, using stepwise logistic regression, only three of these, namely the presence of a neurogenic bladder, leg amputation, or a low serum albumin concentration, were associated independently with yeast colonization (Table 4).

When only those patients with three or more cultures performed were considered, there were six variables associated with persistent or probably persistent colonization with yeasts (Table 5). Factors that remained independently associated with persistent/probably persistent yeast colonization were previous tuberculosis, depression, the presence of wounds, and an indwelling urinary catheter (Table 6). Previous antibiotic therapy, diabetes mellitus and functional status were not associated with either persistent/probable persistent colonization or with overall colonization.

Infections Caused by Yeasts

During the 2-year study period, four infections attributable to yeasts were identified in four different patients. Three of these were urinary tract infections (UTI), and one was *Candida* esophagitis diagnosed by endoscopy in a patient undergoing radiotherapy for an astrocytoma. Two of the three UTIs were caused by *C. albicans* in patients who were

Table 2. Acquisition and Persistence of Yeast Colonization in Patients Who Had Cultures Performed on Three or More Occasions (N = 286)

Colonization Status	Number (%) of Patients
Never colonized	45 (16)
Colonized	241 (84)
Transient colonization	46 (16)
Intermittent colonization	120 (42)
Probably persistent colonization	29 (10)
Persistent colonization	46 (16)
Colonized at entry to nursing home	170 (59)
Colonization acquired in nursing home	71 (25)

Table 3. Univariate Analysis of Factors Associated with Colonization by Yeasts (N = 553)

Factor	Percent of Patients		P Value
	Colonized	Not Colonized	
Underlying conditions			
Recurrent UTIs	15	9	.033
Neurogenic bladder	15	7	.015
Presence of wounds	38	27	.014
Leg amputation	13	6	.018
Dementia	21	13	.028
Devices			
Gastrostomy tube	4	1	.047
Nutritional parameters			
Serum albumin (mean ± S.D.)	3.7 ± 0.6	3.9 ± 0.6	.009

previously colonized by *C. albicans*. The third UTI was caused by a germ-tube negative yeast (not speciated further) in a patient previously colonized by *C. albicans* in the rectum and *C. tropicalis* in the oropharynx. The patient who subsequently developed esophagitis was colonized with *C. albicans* in the oropharynx and rectum. Thus, all yeast infections occurred in patients who were identified as previously colonized with yeasts.

DISCUSSION

The incidence of nosocomial yeast infections has increased dramatically during the past decade because of increased numbers of immunocompromised patients, the use of immunosuppressive drug regimens and broad-spectrum antibiotics, and the more aggressive use of life-support systems in the intensive care unit.⁵⁻⁷ Disseminated *Candida* infections are well documented in burn patients, low birth-weight infants, recipients of total parenteral nutrition, patients receiving hemodialysis, and those with intravascular catheters in place.^{4,5,8,12}

Surprisingly little is known regarding yeast colonization and infection in patients in LTCFs. Jackson et al. reported that 4% of all infections in LTCF residents followed for a 3-year period were attributable to *Candida* spp.¹³ These were all mucocutaneous infections, and no serious infections caused by yeasts were reported. Similarly, vaginal *Candida* infections were found in 7/186 (4%) of patients in a community LTCF.²¹ In another study assessing only oropharyngeal

Table 4. Factors Associated Independently with Colonization by Yeasts (N = 553)

Factor	Odds Ratio	95%	P Value
		Confidence Interval	
Neurogenic bladder	2.1	1.06-4.0	0.032
Leg amputation	3.0	1.37-6.48	0.006
Serum albumin	0.67	0.49-0.92	0.014

Table 5. Univariate Analysis of Factors Associated with Persistent/Probably Persistent Colonization by Yeasts of Patients with Three or More Cultures Performed (N = 286)

Factor	Percent of Patients		P Value
	Persistently/Probably Persistently Colonized	Not Persistently/Probably Persistently Colonized	
Underlying conditions			
Depression	32	19	.016
Prior tuberculosis	15	6	.019
Presence of wounds	53	34	.003
Devices			
Urinary catheter	5	1	.022
Prior intravenous catheter	4	0	.025
Nutritional parameters			
Serum albumin (mean \pm SD)	3.6 \pm 0.6	3.8 \pm 0.6	.012

Table 6. Factors Associated Independently with Persistent/Probably Persistent Colonization by Yeasts of Patients with Three or More Cultures Performed (N = 286)

Factor	Odds Ratio	95% Confidence Interval	P Value
Tuberculosis	4	1.61-9.75	.003
Depression	2.4	1.23-4.50	.01
Presence of wounds	2.7	1.54-4.91	<.001
Urinary catheter	17.3	1.68-178.6	.017

candidiasis, 38% of denture-wearing residents of a LTCF had chronic atrophic candidiasis.²²

Few yeast infections occurred during the 2-year period of the study. One drawback of our study was that it was not designed to detect mucocutaneous yeast infections so that vaginitis and oral candidiasis probably occurred but were not documented. However, all serious infections, such as bacteremia, esophagitis, and urinary tract infection, were documented and were found to be uncommon. Only four such infections occurred, and all four occurred in previously colonized patients. Three of these four infections were urinary tract infections.

Our study did not assess funguria per se, and presumably this was higher than actual *Candida* urinary tract infection. Overall, however, the number of urinary tract infections appeared lower than that noted by others.²³ This could be related to the low proportion of women in our study and the infrequent use of chronic indwelling catheters. Both of these factors seem to carry an increased risk of fungal urinary tract infections.²³⁻²⁵ In a previous study, we noted that *Candida* species were the third most common colonizing organism in patients who underwent intermittent urethral catheterization, but fungal urinary tract infection was not found in that population.²⁶ Thus, our predominantly male population and our policy of rarely using chronic indwelling catheters may have contributed to the low rate of urinary tract infections.

The pathogenesis of yeast infection is believed to be caused by invasion by the patient's own colonizing flora.³⁻⁷ In acute-care hospitals, previous colonization of patients by

yeasts has been shown to be associated with candidemia, and a temporal trend between yeast colonization and subsequent serious *Candida* infection has been demonstrated.³⁻⁵ No such association has been shown in LTCF residents, but the low number of serious *Candida* infections that occur within LTCF may make such an association difficult to demonstrate.

Yeast colonization has been studied in various patient populations, including those with HIV infection, diabetes mellitus, adults and neonates in the intensive care setting, and patients in acute-care hospitals.²⁷⁻³² Such studies have shown that colonization with *Candida* spp varies little with age.^{28,33} Oral *Candida* colonization in the absence of clinical disease was found to occur in 59% of healthy community-dwelling individuals aged 60 years or older, and yeasts were found in saliva and urine in 49% and 11%, respectively, of asymptomatic patients over 45 years.^{28,33} These rates did not vary significantly between age groups. Similarly, the overall rate of colonization with yeasts in the patients that we studied was 53%. *C. albicans* and *C. glabrata* were the yeasts isolated most commonly, in accordance with studies of other patient populations.^{28,34,35}

Patients who remained in the facility for 3 or more months were more likely to be colonized with yeasts (84% of patients were colonized); 59% of these patients were colonized before they entered the LTCF, and 25% acquired yeast while they were there. Colonization was mostly intermittent (42%), but more persistent colonization with yeasts occurred in 26% of patients. Only 16% of patients remained free of yeast colonization during their stay.

Risk factors that were associated with yeast colonization by logistic regression analysis included the presence of a neurogenic bladder, leg amputation, and a low serum albumin. Surprisingly, previous antibiotic therapy, poor functional status, and diabetes mellitus were not associated with yeast colonization. Others have noted no significant differences in the yeast colonization rates found in diabetic compared with non-diabetic patients.^{21,22,28} Neither salivary nor urinary yeast colonization differed significantly between patients with or without diabetes unless glycosuria was present,²⁸ and a higher yeast carriage rate was seen in patients with poorly controlled diabetes in comparison with those patients with good diabetic control.²⁹ In older women, vaginitis was increased significantly in those with insulin-

dependent diabetes mellitus when compared with either healthy patients or diabetics not requiring insulin.²¹ It may be that our study did not demonstrate a difference in yeast carriage between diabetic and non-diabetic patients because glucose intolerance was less marked than that noted in previous studies.

In summary, yeast colonization was common among patients in the LTCF, with 84% of those patients who remained in the facility for 3 or more months colonized at some time during their stay. It is likely that colonization with yeasts is a prerequisite for infection, but the presence of other factors is probably also necessary for infection to develop. Colonization with yeasts in residents of a LTCF may not become clinically important until the patient is transferred to an acute-care hospital, where additional risk factors such as broad-spectrum antibiotic therapy and intravenous catheterization culminate in the development of serious yeast infection. In those LTCFs that have upgraded their services, e.g., those administering intravenous drugs and caring for patients receiving hemodialysis and those with chronic intravenous ports and catheters, serious *Candida* infections, including candidemia, may become a significant problem.

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