Predictive value of oral colonization by *Candida* yeasts for the onset of a nosocomial infection in elderly hospitalized patients

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The incidence of nosocomial yeast infections has increased markedly in recent decades, especially among the elderly. The present study was therefore initiated not only to determine the predictive value of oral colonization by yeasts for the onset of a nosocomial *Candida* infection in elderly hospitalized patients (> 65 years), but also to clarify the factors that promote infection and to establish a relationship between the intensity of oral carriage and the onset of yeast infection. During this prospective cohort study, 256 patients (156 women and 100 men with a mean age of 83 ± 8 years) were surveyed for yeast colonization or infection. Samples were collected every 4 days from day 0 to day 16 from four sites in the mouth, and intrinsic and extrinsic factors that might promote infection were recorded for each patient. Pulsed field gel electrophoresis was performed on *Candida albicans* isolates from all infected patients. Poor nutritional status was observed in 81 % of the patients and hyposalivation in 41 %. The colonization level was 67 % on day 0 (59 % *C. albicans*) and a heavy carriage of yeasts (> 50 c.f.u.) was observed for 51 % of the patients. The incidence of nosocomial colonization reached 6.9 % on day 4 (6.1 % on day 8 and 2.7 % on day 12), and that of nosocomial infection was 3.7 % on day 4 (6.8 % on day 8, 11.3 % on day 12 and 19.2 % on day 16). Of the 35 patients infected, 57 % were suffering from oral candidiasis. The principal risk factors for colonization were a dental prosthesis, poor oral hygiene and the use of antibiotics. The risk factors for infection, in addition to those already mentioned for colonization, were endocrine disease, poor nutritional status, prolonged hospitalization and high colony counts. Genotyping revealed person-to-person transmission in two patients. Thus, this study demonstrates a significant association between oral colonization and the onset of yeast infections in elderly hospitalized patients. Therefore, oral samples should be collected at admission and antifungal treatment should be administered in cases of colonization, especially in patients presenting a heavy carriage of yeasts. Genotyping of the strains confirmed the possibility of person-to-person transmission.

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INTRODUCTION

Candidiasis, which accounts for 66–80 % of fungal infections, is a superficial or deep-seated infection caused by opportunistic yeasts belonging to the genus *Candida* (Jarvis, 1995; Fridkin & Jarvis, 1996). Among all *Candida* species, *Candida albicans* is by far the most common in all clinical forms of candidiasis, representing 70–80 % of all yeast isolates (Taylor *et al.*, 1994; Jarvis, 1995; Wenzel, 1995). Since *Candida* is usually a commensal of the digestive tract, candidiasis mainly originates endogenously, but exogenous contamination may also occur, for example due to transmission

from patient to patient or from healthcare staff to patient (Fanello *et al.*, 2001). Many scientific investigations have dealt with nosocomial yeast infections, the frequency of which has increased steadily in recent decades from 6 % to more than 10 % (Beck-Sague & Jarvis, 1993). Moreover, community-acquired infections have also been described in hospitalized patients, where similar colonization levels of about 35 % have been reported in two studies, regardless of the hospital department (Aly *et al.*, 1991; Vazquez *et al.*, 1993).

Despite this extensive literature, little is known about candidiasis in the elderly. In our geriatric department, we

found that *Candida* yeasts were responsible for a third of nosocomial infections with an exclusively oral localization (Boussarie *et al.*, 1996). Further studies confirmed these data, showing colonization in 64 % of patients and a level of nosocomial contamination of 40 %, with oral infections predominating (Fanello *et al.*, 2001). Oral candidiasis is therefore a frequent disease in the elderly (Vazquez *et al.*, 1993; Odds, 1979; Fanello *et al.*, 2001) and may exacerbate an already precarious nutritional status in hospitalized patients (Fanello *et al.*, 2000).

However, whether these high levels reflect only colonization or whether they also predict the onset of a superficial or disseminated infection is still a matter of debate. The present study was therefore conducted in order to determine the predictive value of oral colonization by *Candida* yeasts for the onset of candidiasis in elderly hospitalized patients. Given the possibility of exogenous contamination and person-to-person transmission, it was necessary to check the genotype homology of the isolates recovered from the same patient, both during infection and before the onset of the infection. The secondary objectives were to determine the intrinsic or extrinsic promoting factors and to establish a relationship between the intensity of yeast carriage and the onset of infection.

METHODS

Study design. This was a prospective cohort study, which received the approval of the Ethical Committee of our University Hospital, conducted over a 16 month period (from November 2001 to February 2003) in 330 elderly patients hospitalized in an internal medicine ward orientated towards geriatrics.

All patients over the age of 65 years hospitalized during the study period, who were free of any clinical signs of fungal infection at admission and who agreed to the collection of samples, were included in this study.

The patients were informed about the methods for sample collection and signed an informed consent form. Oral samples were taken on day 0 and then every 4 days until day 12, after which they were collected once a week. In order to avoid swallowing dysfunctions due to oral rinses, samples were obtained by swabbing the anterior and exterior surfaces of the tongue, the gingivolingual groove and the palate. In addition, a fourth sample was acquired from the dental prosthesis of denture wearers. A heavy carriage of yeasts was defined by the detection of more than 50 c.f.u. from these samples, as described previously (Fanello *et al.*, 2001).

In the case of a clinical suspicion of candidiasis, additional samples were examined: swabbing of inguinal folds, urine (spontaneous specimen collected after local cleansing, sampling from urinary catheter if present or sterile minute specimen when required for medical reasons), stools (fresh stools or anal swabbing), bronchial aspirations and blood in the case of fever.

The criteria for exclusion were: patients aged less than 65 years, clinical signs of candidiasis at admission, patient refusal or the impossibility of systematic sampling.

The diagnosis of oral or urinary infection was based on the criteria proposed by Bodey (1993). A digestive candidiasis was suspected from

the presence of diarrhoea, the exclusive detection of yeasts in the microbiological examination of faeces samples and a cure resulting from antifungal treatment.

All patient characteristics considered as risk factors for *Candida* infection were recorded. Nutritional status was evaluated on the basis of anthropometric criteria, such as body mass index, triceps skin fold and brachial perimeter, and from biological data, i.e. serum albumin, serum pre-albumin and C-reactive protein (Fanello *et al.*, 2000). Physiological factors, such as the age of the patient, the presence of a dental prosthesis and its efficiency, maceration and salivary flow (assessed as satisfactory, poor or uncertain), as well as underlying diseases including diabetes, hypothyroidism, hypoparathyroidism, adrenal insufficiency and malignant disorders, were noted. Iatrogenic factors were also recorded: systemic antibiotic therapy, atropine therapy (responsible for oral dryness), psychotropic agents (neuroleptics) and, in particular, chlorpromazine, phenothiazine and imipramine, catheters and peripheral or central venous lines, urinary catheters, radiotherapy of the ear, nose and throat area and corticosteroid therapy.

Statistical analysis of the data. Univariate analysis was performed in the first instance using Pearson's χ^2 test and odds ratio (OR) for qualitative variables, Fisher's exact test when theoretical populations were less than five, Student's *t*-test for quantitative variables and the Mann-Whitney test if the distribution of variables did not follow a normal law or if the populations were less than 30.

Multivariate analysis was performed in the second instance. The logistic regression model was used as a variable to explain the presence of an oral *Candida* infection. Variables statistically significant at a 20 % threshold in the univariate analysis were introduced into the model to select predictive factors independent of *Candida* infection.

Considering a percentage of passage from colonization to infection of about 20 % (OR = 2) and a colonization level of 60 %, the recruitment of about 180 colonized patients was necessary and therefore 256 patients were included in this study, with an 80 % probability ($\alpha = 0.005$; bilateral test).

Biological study. Clinical samples were cultured on CHROMagar *Candida* agar plates (Becton Dickinson), which facilitate the detection of mixed populations of yeasts. For green colonies, which correspond to *C. albicans* or *Candida dubliniensis*, differentiation between these two species was performed using a Bichro-Dubli latex kit (Fumouze Laboratory). This latex co-agglutination card test, available for the direct identification of *C. dubliniensis* from colonies, is based on the agglutination of blastospores with coloured latex particles coated with a monoclonal antibody specific to the cell-surface antigen of *C. dubliniensis*. For colonies of another colour, biochemical identification was performed using ID32C strips (bioMérieux).

Isolates from patients infected by *C. albicans* were compared with those obtained from the same patient before the onset of the infection. To do this, isolates were typed by pulsed field gel electrophoresis with the transverse alternating field electrophoresis technique, which has shown its validity and discriminatory power for various yeast species (Defontaine *et al.*, 1996).

RESULTS AND DISCUSSION

Study population

This study involved 256 patients over a period of 16 months. Of these, 195 patients were colonized, representing 97.5 % of the expected number of colonized patients. Twenty

dossiers could not be analysed because of the lack of some clinical samples.

The cohort comprised 100 men and 156 women. Of these, 99 % were admitted via the Emergency Room. Two-thirds came from their homes, whilst 31 % came from an institution. The body mass index was significantly lower among the women. The level of malnutrition or poor nutritional status, mainly due to exogenous undernourishment (85 %), was identical in the two sexes (about 80 %). All social and anthropometric data are summarized in Table 1.

The dominant pathologies encountered were cardiac, pneumonological and neurological diseases, which accounted for more than 60 % of diagnoses. Antibiotic therapy was being received by 35.2 % of patients (70 % amoxicillin alone or associated with clavulanic acid, and 20 % quinolones). Their medical histories revealed cancer (21.5 %) or diabetes (12 %), and 15 % of patients were being treated with psychotropic agents. Invasive procedures included peripheral lines (36 % of patients), central lines (2 %) and urinary catheters (5.5 %).

Frequency of oral colonization or infection by *Candida* yeasts

Because of the variable duration of hospitalization, second samples were obtained from 178 of the original 256 patients (69.5 %), third samples from 45 % of patients and fourth samples from 24 % of patients. A colonization level of 67 % was observed at admission and analysis of the subsequent samples revealed similar colonization levels of 71–72 %. Thus, the incidence of nosocomial colonization (newly colonized cases) reached 6.9 % for days 0–4, 6.14 % for days 4–8 and 2.7 % for days 8–12 (Fig. 1). The distribution of *Candida* isolates as a function of species is shown in Table 2. *Candida albicans*, which accounted for 59 % of all yeast

Fig. 1. Risk of oral colonization by yeast (open circles) and yeast infection (closed circles) according to the duration of hospitalization.

isolates, was by far the most common yeast isolated, whilst *C. dubliniensis* was recovered from only four patients.

During the study period, 35 patients presented with a nosocomial yeast infection. Twenty of these had an oral infection diagnosed from the following clinical signs: perleche (60 %), smooth glossal atrophy (30 %) and thrush (10 %). Two of them also presented an inguinal skin fold infection or pressure sores. Seventy-five per cent of the patients were treated orally with amphotericin B, whilst fluconazole was used for the other patients. There was no systemic complication. The time to the onset of the infection was 8 ± 5 days (Fig. 1).

Other infected patients (15) mainly presented an inguinal (six patients) or digestive (two patients) yeast infection. These patients were treated with fluconazole and a cure was achieved in 76.5 % of cases. Two deaths occurred in the cohort, due to a *Candida* lung infection and to *Candida* pyelonephritis. The time to the onset of the infection was 9 ± 5 days. The incidence level of nosocomial infection was 3.7 % for the first period, 6.8 % for the second period, 11.3 % for the third period and 19.2 % for the fourth period.

Of the 35 infected patients, 23 were infected by *C. albicans* (66 %) and no *C. dubliniensis* was recovered from these patients. Genotype analysis of these isolates revealed homologies between two patients, demonstrating person-to-person transmission. For all patients but one, the same genotype was found from clinical samples obtained during the infection and before the onset of the infection, thus attesting the endogenous origin of the infection.

Two previous studies carried out in our University Hospital revealed the importance of yeasts in nosocomial infections (Boussarie *et al.*, 1996; Fanello *et al.*, 2001). The level of nosocomial infections reached about 20 %, with an oral

Table 1. Anthropometric data

Percentages are expressed relative to the total number of patients examined.

Parameter	Value
Total number of patients	256
Age (years)	82 ± 8
Weight (kg)	66 ± 16
Height (cm)	162 ± 9
Body mass index (height weight ⁻²)	25 ± 5
Well nourished (%)	18
Poor nutritional status (%)	68
Hyposalivation (<1 ml min ⁻¹) (%)	42
Dental prosthesis (%)	51
Oral hygiene: (%)	
Satisfactory	41
Poor	17
Uncertain	42

Table 2. Characteristics of oral colonization observed from the four samples

Characteristic	Day 0 (n = 256)	Day 4 (n = 178)	Day 8 (n = 115)	Day 12 (n = 62)
Colonization (%) ^{a*}	67	72	71	71
Nosocomial colonization (%) ^a	–	6·9	6·1	2·7
Heavy carriage of yeasts (%) ^b	51	51	49	45
Association of at least two yeast species: (%) ^b				
Palate	23	27·4	28	26
Tongue	26	27·7	27	28
Gums	27	28·4	29	37
Dental prosthesis	42	39·6	44	41
<i>Candida</i> species: (%) ^c				
<i>C. albicans</i>	59	54·5	52	53
<i>C. glabrata</i>	15	17·5	14·5	24
<i>C. tropicalis</i>	13·5	14	14·5	9
Others	12·5	14	19	14

*Results correspond to percentages of the total number of patients examined (a), positive patients (b) and yeasts isolated (c).

localization in 80 % of the cases, as also noticed in other studies (Eggimann *et al.*, 2003; Grimoud *et al.*, 2003; Lizioli *et al.*, 2003). Moreover, in agreement with other studies (Boccia *et al.*, 2002; Khan *et al.*, 2003; Vazquez *et al.*, 1993), we confirmed the possibility of person-to-person transmission of *C. albicans* and the high level (64 %) of oral colonization by yeasts at admission of the patients. Here, we have provided additional information, since we not only established a link between oral colonization and the onset of candidiasis, but also specified the risk factors for colonization and for infection.

During the present study, we found that colonization affected two-thirds of the patients, as previously reported in long-term geriatric care units (Grimoud *et al.*, 2003). As for the incidence of yeast infections, this exceeded that found in an intensive care unit (7·7 %) by Lupetti *et al.* (2002). However, this survey focused on deep-seated infections. More importantly, half of the colonized patients were heavy carriers (higher than 50 c.f.u.), thus confirming the previous findings of Akpan & Morgan (2002), and we found a

significant link between the intensity of carriage and the onset of yeast infections. The predominance of *C. albicans* was regular (54–60 %), as in most previous studies performed on hospitalized patients (Ellis *et al.*, 2000) or on healthcare workers (Bonassoli & Svidzinski, 2002).

Risk factors

Table 3 shows the different links observed in colonized patients. Nutritional status, salivation or underlying disease was not linked to colonization by yeasts. After logistic regression, three factors were still statistically linked to colonization: poor oral hygiene, the wearing of a dental prosthesis and the presence of a peripheral line, as previously reported (Shay *et al.*, 1997). However, although the presence of a peripheral line could not alone explain colonization, it is conceivable that patients requiring a line presented with an acute pathology at admission and required antibiotic therapy (a factor that disappeared after regression). Similarly, there was a significant link between colonization of the palate and the wearing of a dental prosthesis.

Table 3. Risk factors linked statistically to yeast colonization

CI, Confidence interval; ND, not determined; NS, not significant.

Risk factor	χ^2 test			Logistic regression	
	Significance	OR	95 % CI	Significance	OR adjusted
Dental prosthesis	0·008	1·2	1·0 < OR < 1·3	0·03	2
Peripheral line	0·015	1·2	1·0 < OR < 1·3	0·014	2·3
Antibiotic therapy	0·048	1·15	1·0 < OR < 1·3	NS	ND
Poor oral hygiene	0·0001	ND	ND	0·002	ND

Table 4. Risk factors linked statistically to the onset of a nosocomial yeast infection

See Table 3 for abbreviations.

Risk factor	χ^2 test			Logistic regression	
	Significance	OR	95 % CI	Significance	OR adjusted
Deficient pre-albumin	0.006	3.6	1.3 < OR < 9.8	NS	ND
Deficient albumin	0.006	2.8	1.3 < OR < 6.2	NS	ND
Underlying endocrine disease	0.027	2.4	1.2 < OR < 5.2	0.03	11.1
Antibiotic therapy	0.011	2.2	1.2 < OR < 4.1	NS	ND
Prolonged hospitalization	0.008	2.1	1.3 < OR < 3.5	NS	ND
Underlying lung disease	0.004	1.8	1.1 < OR < 3.1	NS	ND
Heavy carriage of yeasts	0.0001	1.6	1.4 < OR < 2	0.004	9.44
Colonization	0.0004	1.4	1.3 < OR < 1.5	NS	ND
Poor oral hygiene	0.014	ND	ND	NS	ND
Poor nutritional status	0.014	ND	ND	NS	ND

Among the main variables statistically linked to the onset of nosocomial yeast infection (Table 4), only two factors remained statistically linked to nosocomial yeast infections after logistic regression: the existence of endocrine disease and a heavy carriage of yeasts. As for diabetes, this factor appeared at the limit of significance retained.

In patients harbouring at least two yeast species, the main risk factors were, after logistic regression, the presence of a dental prosthesis and a heavy carriage of yeasts. In addition, the risk factors statistically linked to a heavy carriage of yeasts are shown in Table 5. After logistic regression, these were found to be the use of psychotropic agents and a hospitalization time longer than 3 weeks.

In conclusion, the results of the present study confirmed the high prevalence of oral colonization by yeasts in patients hospitalized for an acute pathology in an internal medicine ward. The levels of nosocomial yeast infections rose steadily during hospitalization. A link was established between colonization and fungal infection, as well as with the intensity of carriage. In addition, this study enabled the definition of an elderly population at high risk of colonization and of subsequent nosocomial yeast infection. This population is

made up of elderly patients hospitalized for a community-acquired infection and receiving probabilistic antibiotic therapy. They also often wear dental prostheses. Faced with these elements, swabbing of the mouth should be performed to detect any yeast colonization. If the results are positive, and particularly in the case of a heavy oral carriage of yeasts (> 50 c.f.u.), such elderly patients could benefit from antifungal therapy. Some therapeutic regimens have been proposed, depending on the identified yeast (Shay *et al.*, 1997) and on the endogenous or exogenous origin of colonization (Pfaller, 1996). A clinical study showed that prophylactic treatment with fluconazole reduced the risk of nosocomial infection by 55 % in a surgical intensive care unit (Pelz *et al.*, 2001). However, the risks and benefits of prophylactic treatment in elderly patients remain to be determined and the possibility of the development of resistance to antifungal agents among yeasts in the genus *Candida* needs to be considered.

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REFERENCES

- Akpan, A. & Morgan, R. (2002). Oral candidiasis. *Postgrad Med J* **78**, 455–459.
- Aly, F. Z., Blackwell, C. C., MacKenzie, D. A., Weir, D. M., Elton, R. A., Cumming, C. G., Sofaer, J. A. & Clarke, B. F. (1991). Chronic atrophic oral candidiasis among patients with diabetes mellitus – role of secretor status. *Epidemiol Infect* **106**, 355–363.
- Beck-Sague, C. & Jarvis, W. R. (1993). Secular trends in the epidemiological fungal infections in the United States, 1980–1990. National Nosocomial Infections Surveillance System. *J Infect Dis* **167**, 1247–1251.
- Boccia, S., Posteraro, B., La Sorda, M., Vento, G., Matassa, P. G., Tempera, A., Petrucci, S. & Fadda, G. (2002). Genotypic analysis by 27A DNA fingerprinting of *Candida albicans* strains isolated during

Table 5. Risk factors linked statistically to a heavy carriage of yeasts

See Table 3 for abbreviations.

Risk factor	Significance	OR	95 % CI
Multiple colonization	0.0001	6.6	2.2 < OR < 19.6
Inflammatory syndrome	0.001	3.61	1.6 < OR < 7.9
Underlying lung disease	0.003	3.37	1.4 < OR < 7.8
Antibiotic therapy	0.001	3.0	1.5 < OR < 5.9
Psychotropic drugs	0.015	2.7	1.2 < OR < 6.3
Poor oral hygiene	0.018	ND	ND
Poor nutritional status	0.021	ND	ND

an outbreak in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 23, 281–284.

Bodey, J. P. (editor) (1993). *Candidiasis: Pathogenesis, Diagnosis and Treatment*. New York: Raven Press.

Bonassoli, L. A. & Svidzinski, T. I. (2002). Influence of the hospital environment on yeast colonization in nursing students. *Med Mycol* 40, 311–313.

Boussarie, M., Fanello, S., Foucault, J. P., Roquelaure, Y. & Morel Cardinal, S. (1996). Nosocomial and community infections incidence survey among elderly patients. *Santé Publique* 2, 105–116 (in French).

Defontaine, A., Coarer, M. & Bouchara, J.-P. (1996). Contribution of various techniques of molecular analysis to strain identification of *Candida glabrata*. *Microb Ecol Health Dis* 9, 27–33.

Eggimann, P., Garbino, J. & Pittet, D. (2003). Epidemiology of *Candida* species infections in critically ill non-immunosuppressed patients. *Lancet Infect Dis* 3, 685–702.

Ellis, M., Richardson, M. & de Pauw, B. (2000). Epidemiology. *Hosp Med* 61, 605–609.

Fanello, S., Foucault, S., Delbos, V. & Jousset, N. (2000). Assessment of nutritional state of elderly patients in hospital. *Santé Publique* 12, 83–90 (in French).

Fanello, S., Bouchara, J.-P., Jousset, N., Delbos, V. & LeFlohic, A.-M. (2001). Nosocomial *Candida albicans* acquisition in a geriatric unit: epidemiology and evidence for person-to-person transmission. *J Hosp Infect* 47, 46–52.

Fridkin, S. K. & Jarvis, W. R. (1996). Epidemiology of nosocomial fungal infections. *Clin Microbiol Rev* 9, 499–511.

Grimoud, A. M., Marty, N., Bocquet, H., Andrieu, S., Lodter, J. P. & Chabanon, G. (2003). Colonization of the oral cavity by *Candida* species: risk factors in long-term geriatric care. *J Oral Sci* 45, 51–55.

Jarvis, W. R. (1995). Epidemiology of nosocomial fungal infections, with emphasis on *Candida* species. *Clin Infect Dis* 20, 1526–1530.

Khan, Z. U., Chandy, R. & Metwali, K. F. (2003). *Candida albicans* strain carriage in patients and nursing staff of an intensive care unit: a study of morphotypes and resistotypes. *Mycoses* 46, 479–486.

Lizioli, A., Privitera, G., Allia, E. & 7 other authors (2003). Prevalence of nosocomial infections in Italy: result from the Lombardy survey in 2000. *J Hosp Infect* 54, 141–148.

Lupetti, A., Tavanti, A., Davini, P., Ghelardi, E., Corsini, V., Merusi, I., Boldrini, A., Campa, M. & Senesi, S. (2002). Horizontal transmission of *Candida parapsilosis* candidemia in a neonatal intensive care unit. *J Clin Microbiol* 40, 2363–2369.

Odds, F. C. (1979). *Candida and Candidosis*. Leicester: Leicester University Press.

Pelz, R. K., Hendrix, C. W., Swoboda, S. M., Diener-West, M., Merz, W. G., Hammond, J. & Lipsett, P. A. (2001). Double-blind placebo-controlled trial of fluconazole to prevent candidal infections in critically ill surgical patients. *Ann Surg* 233, 542–548.

Pfaller, M. A. (1996). Nosocomial candidiasis: emerging species, reservoirs, and modes of transmission. *Clin Infect Dis* 22 (Suppl. 2), S89–S94.

Shay, K., Truhlar, M. R. & Renner, R. P. (1997). Oropharyngeal candidosis in the older patient. *J Am Geriatr Soc* 45, 863–870.

Taylor, G. D., Buchanan-Chell, M., Kirkland, T., McKenzie, M. & Wiens, R. (1994). Trends and sources of nosocomial fungaemia. *Mycoses* 37, 187–190.

Vazquez, J. A., Sanchez, V., Dmuchowski, C., Dembry, L. M., Sobel, J. D. & Zervos, M. J. (1993). Nosocomial acquisition of *Candida albicans*: an epidemiologic study. *J Infect Dis* 168, 195–201.

Wenzel, R. P. (1995). Nosocomial candidemia: risk factors and attributable mortality. *Clin Infect Dis* 20, 1531–1534.