MAJOR ARTICLE

# Epidemiology of Community-Onset Candidemia in Connecticut and Maryland

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***Background.*** Almost one-third of patients with bloodstream infections with *Candida* species (candidemia) have onset of disease that occurs outside of the hospital or ≤2 days after hospital admission (i.e., community-onset candidemia). We compared the characteristics of patients who developed candidemia by the timing of onset of infection.

***Methods.*** Incident episodes of candidemia were identified through active, population-based surveillance in Connecticut and in Baltimore and Baltimore County, Maryland, during 1 October 1998–30 September 2000. The molecular subtypes of a sample of 45 *Candida parapsilosis* isolates were evaluated using Southern blots hybridized with the complex probe Cp3-13.

***Results.*** Overall, 356 (31%) of the 1143 incident episodes of candidemia were classified as community-onset disease (occurring ≤2 days after hospital admission), and 132 (37%) were caused by *Candida albicans,* 89 (25%) were caused by *Candida glabrata,* 57 (16%) were caused by *C. parapsilosis,* and 53 (15%) were caused by *Candida tropicalis.* Community-onset disease was less likely to be associated with concurrent immunosuppressive therapy, recent surgery, or use of a central venous catheter, compared with inpatient disease. Among patients with community-onset disease, the median time from blood culture to initiation of antifungal treatment was 2.7 days, the 30-day case-fatality rate was 26%, and 262 patients (75%) had been hospitalized at least once in the previous 3 months. Although there were few differences between patients with very recent hospitalization (in the previous 1 month), less recent hospitalization (previous 1–3 months), and no documented past hospitalization, *C. parapsilosis* was more frequently associated with community-onset disease as hospitalization became more distant. *C. parapsilosis* strains tended to be unique to the patient, with little similarity found between strain types, on the basis of epidemiologic classification of patients.

***Conclusion.*** We report that community-onset candidemia is common and occurs in patients with extensive contact with the health care system. Disease caused by *C. parapsilosis* tends to involve unique strains.

Bloodstream infections with *Candida* species (candidemia) are an important cause of morbidity and mortality in hospitalized patients. In the United States, *Candida* species are ranked as the fourth-most common cause of hospital-acquired bloodstream infections [1], with an incidence of 8 infections per 10,000 hospital discharges (10 infections per 100,000 persons per year) [2]. In comparable European studies, the incidence is slightly lower, at 2–5 infections per 10,000 hospital discharges [3–5]. Candidemia is often a devastating disease with an attributable mortality of 20%–50%, and it is often associated with disseminated disease [6, 7], resulting in an estimated annual excess of 4256–5376 deaths due to candidemia in the United States [7]. Over the past decade, it is unclear whether the incidence of candidemia is increasing. Whereas a Swiss study documented a stable incidence over the past decade among all hospitalized patients [4], detailed data from a US study limited to intensive care unit patients demonstrated a 30% decrease in incidence [8]. However, the intensive care unit data unlikely represent all patients at risk for candidemia. Data from the US National Center for Health Statistics suggest that the number of patients discharged from the hospital with a diagnosis

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of sepsis caused by fungi has tripled over the past decade, with candidemia being the most likely cause of fungal sepsis in hospitalized patients [9].

One likely explanation for these findings is that advances in medical therapy have increased the number of patients susceptible to *Candida* blood stream infection; patients are surviving longer because of advances in management of critical illness, broad-spectrum antimicrobials are being used more frequently, and life-saving therapies are being applied outside of intensive care units. The established risk factors for candidemia, including prior colonization, use of central venous catheters and broad-spectrum antimicrobials, mucosal surface disruption (e.g., disruptions caused by cytotoxins, hypotension, and surgery), and neutropenia [10], are not limited to intensive care unit patients anymore. In fact, a US population–based study identified 28% of patients with candidemia as having had disease onset outside of the hospital or on the day of hospital admission (i.e., community-onset candidemia) [2].

The driving force for the emergence of community-onset candidemia is unknown, but it likely represents a shift in patient care from inside to outside the hospital, exposing patients to traditional risk factors for candidemia, such as total parenteral nutrition, use of central venous catheters, and treatment with broad-spectrum antibiotics [11]. The objective of this study was to determine whether these established risk factors are common among patients with community-onset candidemia and to ascertain whether there is a common strain of *Candida parapsilosis* associated with these episodes of candidemia.

## METHODS

***Definitions and surveillance.*** Cases of candidemia were identified through an active, population-based surveillance study that was conducted using the Centers for Disease Control and Prevention Emerging Infection Program in Connecticut (population of 3.3 million with 33 hospitals) and Baltimore and Baltimore County, Maryland (population of 1.4 million with 14 hospitals), during 1 October 1998–30 September 2000. Detailed methodology and surveillance results focusing on antifungal resistance have been published elsewhere [2]. An incident case was defined by the first isolation during the surveillance period of any *Candida* species from the blood of a resident of the surveillance area. A standardized screening form was collected from all patients. Only limited clinical information regarding exposures before hospitalization were collected during the second year of the study among patients with non–*Candida albicans* candidemia from the Baltimore site. The more-extensive data collection instrument, which was used for most patients, was used to gather information regarding demographic and clinical characteristics, underlying conditions, and outcomes. For patients who had >1 episode of candidemia, the second episode was also defined as being incident if it occurred at least 30 days after the previous episode. Outcome was defined as survival or death within 30 days after the incident episode of candidemia or hospital discharge (whichever came first). Patients who developed positive blood culture results either prior to or within the first 2 days after hospital admission were classified as having community-onset candidemia. Patients who developed positive blood culture results >2 days after hospital admission were classified as having inpatient candidemia. The number of days of hospitalization before onset of candidemia (patient-days) was calculated by using the difference between the date of hospital admission and the collection date of a blood culture with positive results. Recurrent candidemia was defined as a positive blood culture result obtained 30 days after the initial positive culture result.

Laboratory records of all hospitals in the surveillance areas were audited every 6–12 months to estimate completeness of reporting and to detect additional cases. Cases identified by means of auditing were included in the analysis. Detection of candidemia and species identification of isolates were performed using previously described methods [2].

***Molecular strain typing.*** Because infections with *C. parapsilosis* appeared to be inversely correlated with very recent or current hospitalization, we evaluated the genetic similarity among *C. parapsilosis* strains to determine whether the strains isolated from patients with community-onset candidemia were different from those isolated from patients with inpatient candidemia. Fifty *C. parapsilosis* isolates, including 32 (64%) from patients with incident episodes of inpatient candidemia and 18 (36%) from patients with incident episodes of community-onset candidemia, were selected for DNA strain subtyping from a total of 123 incident cases of *C. parapsilosis* candidemia. The criteria for selection included isolates from hospitals having the largest number of patients with candidemia and with equal representation from both the Baltimore and Connecticut areas. Molecular subtyping was done with Southern blots hybridized with the digoxigenin-labeled complex probe Cp3-13 [12]. Banding patterns were visualized by chemiluminescence detection (CDP-Star; Roche Molecular Diagnostics) and analyzed using Bionumerics software (Applied Maths; Sint-Martens-Latem). The number of bands observed ranged from 11 to 16. Similarity values ($s_{AB}$) were computed using the Dice coefficient. Dendrograms were displayed using an unweighted pair group analysis with arithmetic mean with a band tolerance of $\pm 1\%$. Isolates were considered to be moderately related if the $s_{AB}$ was $\geqslant 0.85$ and were considered to be highly related if the $s_{AB}$ was $\geqslant 0.95$. The 50 isolates selected for molecular subtyping were from 48 patients; 3 isolates (CAS99-0313, CAS99-0314, and CAS99-0315) were from the same inpatient and were collected during the same episode of candidemia. The *C. parapsilosis* strain B6194 served as an unrelated control.

***Analysis of data.*** For select patient characteristics, cases of

community-onset candidemia were compared with cases of inpatient candidemia. For analysis between groups of community-onset candidemia, 3 groups of community-onset candidemia were defined on the basis of previous hospitalization, as follows: patients with very recent hospitalization (i.e., 1–30 days before date of candidemia), less recent hospitalization (31–90 days before candidemia), and no past hospitalization (no documented hospital stay in the 90 days before candidemia). Patients were cross-referenced for hospitalizations within the surveillance areas but not for hospitalizations in hospitals outside of the surveillance areas. The $\chi^2$ and Fisher's exact tests were used to assess differences between groups using the very recent hospitalization group as the baseline group.

## RESULTS

***Clinical description.*** During the 2 years of surveillance, 356 (31%) of the 1143 cases of candidemia were classified as community-onset candidemia. Although the time of onset of candidemia was considered to have occurred outside of the hospital (i.e., ⩽2 days after hospital admission), 325 cases (91%) were identified on the day of hospital admission, and only 31 cases (9%) were identified on day 2 of hospitalization. Demographic and clinical characteristics, as well as the distribution of the various underlying patient comorbidities and outcomes, are summarized by species in table 1. All patients with community-onset disease were hospitalized for their candidemia, and the median duration of hospitalization was 9 days (range, 1–108 days). At the time that blood culture was performed, patients were located throughout the hospital, as follows: 141 patients (40%) were located in an outpatient, observational, urgent care, or emergency department setting; 130 (37%) were located in medicine wards; 53 (15%) were located in intensive care units; 20 (6%) were located in surgical wards; and 12 (3%) were located in pediatric service units. The median time from when blood culture was performed to the initiation of antifungal treatment was 2.7 days. The crude in-hospital case-fatality rate at 30 days was 26%, which varied slightly by infecting species of *Candida* (*C. albicans,* 31%; *Candida glabrata,* 27%; *C. parapsilosis,* 14%; *Candida tropicalis,* 28%; *Candida krusei,* 0%).

***Established risk factors for candidemia.*** Among conditions known to be associated with candidemia, having had surgery in the previous 3 months (29%) and receiving immunosuppressive therapies (28%) were the most common, followed by malignancies (21%), neutropenia (10%), and HIV infection (8%). Central venous catheters were being used in 197 patients (55%). The additional data regarding prehospitalization exposures were evaluated for patients comprising 220 of the community-onset cases; 70 patients (32%) were transferred from a nursing home in the previous 30 days; 158 patients (72%) received systemic (either oral or parenteral) antibacterial agents; and 52 patients (24%) had received parenteral nutrition.

***Comparisons by status of hospitalization exposures.*** We compared patient characteristics of the 356 patients with community-onset candidemia with those of the 787 patients with inpatient candidemia (table 2). Patients with community-onset candidemia were significantly less likely to have a central venous catheter in place at the time of infection (55% vs. 83%; $P <$ .01), to have had recent surgery (29% vs. 57%; $P <$ .01), to be receiving immunosuppressive therapies (28% vs. 48%; $P <$ .01), or to have died within 30 days of infection (26% vs. 40%; $P <$ .01), compared with patients with inpatient candidemia.

Most community-onset candidemia patients (262 [75%]) had been hospitalized at least once in the previous 3 months, as follows: 158 patients (45%) had very recent hospitalizations; 104 patients (30%) had less recent hospitalizations; and 90 patients (25%) had no documented hospitalization (table 1). Comparisons between these different groups of patients with community-onset candidemia identified only a few differences, suggesting that these groups of patients are similar. Compared with patients in the referent group (the very recent hospitalization group), patients with no past hospitalization in the preceding 90 days were less likely to be receiving immunosuppressive therapy, to have an underlying malignancy, to have had recent surgery, or to have receipt of antibacterial agents (table 3). For patients with a less recent hospitalization, there were no statistically significant differences in recent exposures of catheter types (table 3).

***Species distributions.*** *C. albicans* was the most common species isolated (37%), followed by *C. glabrata* (25%), *C. parapsilosis* (16%), and *C. tropicalis* (15%) (table 1). Compared with patients with inpatient candidemia, community-onset candidemia was significantly less often caused by *C. albicans*. The increase in the relative proportion of non-*albicans* species of *Candida* associated with community-onset disease, compared with inpatient disease, was mostly attributed to increases in the prevalence of *C. parapsilosis* and *C. tropicalis* (table 2). The association between *C. parapsilosis* disease and outpatient status was further evident after evaluating the different categories of community-onset disease; patients in either the less recent or no hospitalization groups were significantly less likely to be infected with *C. albicans* and more likely to be infected with *C. parapsilosis* than patients with very recent hospitalization (table 3).

***Molecular strain subtyping of* C. parapsilosis *isolates.*** A dendrogram depicting genetic relatedness based on Cp3-13 banding patterns is shown in figure 1. Five isolates did not bind well to the Cp3-13 probe [12], thus they were presumed to be members of *Candida orthopsilosis* or *Candida metapsilosis,* which hybridize weakly or not at all to the Cp3-13 probe sequence [13]; of these, 3 isolates were from inpatients.

**Table 1. Selected demographic and clinical characteristics and outcomes of patients with community-onset candidemia.**

| Characteristic | Total ($n$ = 356) | Connecticut ($n$ = 127) | Baltimore and Baltimore County ($n$ = 229) |
|---|---|---|---|
| Male sex | 185 (52)[a] | 68 (54) | 117 (63) |
| Race | | | |
| White | 170 (48) | 95 (75) | 75 (33) |
| Black | 165 (46) | 20 (16) | 145 (63) |
| Age, years | | | |
| <18 | 21 (6) | 4 (3) | 17 (8) |
| 18–24 | 6 (2) | 0 (0) | 6 (3) |
| 25–44 | 71 (20) | 27 (21) | 44 (20) |
| 45–64 | 107 (30) | 33 (26) | 74 (33) |
| >64 | 147 (42) | 63 (50) | 84 (37) |
| Previous hospitalization | | | |
| Very recent (≤30 days before candidemia) | 158 (45) | 49 (39) | 109 (48) |
| Less recent (31–90 days before candidemia) | 104 (30) | 31 (25) | 73 (32) |
| None (either >90 days before candidemia or none documented) | 90 (25) | 45 (36) | 45 (20) |
| *Candida* species | | | |
| *Candida albicans* | 132 (37) | 47 (37) | 85 (37) |
| *Candida glabrata* | 88 (25) | 24 (19) | 64 (28) |
| *Candida parapsilosis* | 56 (16) | 26 (21) | 30 (13) |
| *Candida tropicalis* | 54 (15) | 22 (18) | 32 (14) |
| *Candida krusei* | 13 (4) | 1 (1) | 12 (5) |
| Recurrent candidemia | 26 (7) | 3 (2) | 23 (10) |
| Death during hospitalization | 92 (26) | 33 (26) | 59 (26) |
| Comorbid condition | | | |
| HIV infection | 29 (8) | 6 (5) | 23 (10) |
| Malignancy | 73 (21) | 35 (28) | 38 (17) |
| Neutropenia | 37 (10) | 30 (24) | 7 (3) |
| Diabetes mellitus | 107 (30) | 37 (29) | 70 (31) |
| Immunosuppressive treatment | 98 (28) | 43 (34) | 55 (24) |
| Cardiovascular disease | 216 (61) | 85 (67) | 131 (57) |
| Pulmonary disease | 180 (51) | 75 (59) | 105 (46) |
| Recent surgery (≤3 months before candidemia) | 102 (29) | 36 (28) | 66 (29) |
| Abdominal | 50 (14) | 21 (17) | 29 (13) |
| Cardiothoracic | 8 (2) | 5 (4) | 3 (1) |
| Genitourinary | 7 (2) | 4 (3) | 3 (1) |
| Central catheter in place at time of candidemia | 197 (55) | 56 (44) | 141 (62) |

**NOTE.** Positive results of blood culture were obtained either prior to or within 2 days after hospital admission. Data are no. (%) of patients.

[a] Sex was only known for 345 patients.

Subtyping results of the remaining 45 *C. parapsilosis* isolates from 43 patients, including 27 isolates associated with inpatient candidemia and 18 isolates associated with community-onset candidemia, showed marked heterogeneity of subtyping patterns overall (figure 1). Results also indicated that 3 serial isolates from the same inpatient (CAS99-0313, CAS99-0314, and CAS99-0315) were indistinguishable (figure 1). Five *C. parapsilosis* strain types, all from Baltimore-area hospitals, were at least moderately related ($s_{AB}$, ≥0.85); 2 were from patients with inpatient candidemia, and 3 were from patients with community-onset candidemia (group 1 in figure 1). Another cluster of 5 moderately-related strain types ($s_{AB}$, ≥0.90) included 4 isolates from Connecticut and 1 from Baltimore; all were from patients with inpatient candidemia (group 2 in figure 1). Finally, there were 2 pairs of highly related strain types ($s_{AB}$, ≥0.95). The first pair, CAS99-0204 and CAS99-0287, was obtained from inpatients seen at the same hospital (CT011) in 1999. The second pair, CAS99-0431 and CAS99-0489, originated from

**Table 2. Selected clinical variables for 1143 patients with candidemia, by type of onset.**

| Characteristic | Type of onset | | Relative risk (95% CI)[b] | *P* |
|---|---|---|---|---|
| | Inpatient (*n* = 787) | Community[a] (*n* = 356) | | |
| Infecting *Candida* species | | | | |
| *Candida albicans* | 384 (49) | 132 (37) | 0.76 (0.65–0.89) | <.01 |
| *Candida glabrata* | 186 (24) | 89 (25) | 1.05 (0.85–1.32) | .61 |
| *Candida parapsilosis* | 96 (12) | 57 (16) | 1.31 (0.97–1.78) | .08 |
| *Candida tropicalis* | 88 (11) | 53 (15) | 1.33 (0.97–1.83) | .08 |
| *Candida krusei* | 5 (0.6) | 18 (5) | 7.96 (2.97–21.2) | <.01 |
| 30-Day mortality | 317 (40) | 92 (25) | 0.641 (0.53–0.78) | <.01 |
| Comorbid condition | | | | |
| HIV infection | 56 (7) | 29 (8) | 1.14 (0.74–1.76) | .53 |
| Malignancy | 193 (24) | 73 (21) | 0.84 (0.67–1.06) | .13 |
| Neutropenia | 83 (10) | 37 (10) | 0.99 (0.68–1.42) | .93 |
| Diabetes mellitus | 215 (27) | 107 (30) | 1.10 (0.91–1.34) | .34 |
| Immunosuppressive therapy | 375 (48) | 98 (28) | 0.58 (0.48–0.69) | <.01 |
| Surgery in 3 months prior to candidemia | 446 (58) | 102 (29) | 0.51 (0.42–0.60) | <.01 |
| Central venous catheter in place at time of candidemia | 655 (83) | 197 (55) | 0.66 (0.60–0.73) | <.01 |

**NOTE.** Data are no. (%) of patients, unless otherwise indicated.

[a] Patients who had positive blood culture results ⩽2 days after hospital admission were classified as having community-onset candidemia.

[b] Relative risk of community-onset disease, compared with inpatient-onset disease.

patients with community-onset and inpatient candidemia, respectively; both were from the Baltimore area (figure 1). Strains showing significant similarity were rerun in adjacent lanes on the same gel, with similar results.

## DISCUSSION

To our knowledge, this report provides the first population-based description of community-onset candidemia in the United States. Community-onset candidemia was frequent, accounting for 31% ($n = 356$) of all episodes of candidemia reported through this surveillance; 28% ($n = 325$) of episodes occurred prior to or on the first day of hospitalization, an increase from a previous study that found that only 20% of episodes of candidemia occurred prior to the first day of hospitalization [14]. However, patients with community-onset candidemia often have established risk factors for candidemia, including use of central venous catheters and receipt of systemic antimicrobials and immunosuppressive agents. In addition, most patients had documented hospitalizations in the previous 90 days, suggesting that most, if not all, of these episodes of candidemia were related to contact with the heath care system.

On the basis of this data, it seems that the emergence of candidemia in the community may, in part, be caused by the movement of established risk factors into the community, such as home-based intravenous antimicrobial therapy, parenteral nutrition, and chemotherapy [11, 15]. These types of home-based therapies have been implicated in at least 1 outbreak of candidemia in the community [16]. However, apart from outbreaks of infection, it is not clear whether any 1 established risk factor can explain the community-onset disease phenomena. We compared documented exposures and underlying conditions in an attempt to describe groups of patients with community-onset candidemia who were least likely to have established risk factors for candidemia, patients with no documented past hospitalization. We found that, overall, patients without any past hospitalization, as well as patients with a less recent hospitalization (31–90 days candidemia), were similar to patients with very recent hospitalization (⩽30 days before candidemia).

Furthermore, few epidemiologic features of patients with candidemia could be used to distinguish patients with inpatient disease from patients with community-onset disease; however, 3 established risk factors were found with decreasing frequency among the different groups of patients with candidemia who were studied. Patients with inpatient candidemia more often had underlying malignancy, were exposed to immunosuppressive therapy, had recent surgery, and had recent use of antibacterial agents, with a decreasing proportion of patients being those with community-onset candidemia who had these exposures, moving from categories of very recent hospitalization, less recent hospitalization, and no hospitalization in the previous 90 days.

One difference apparent between these groups of patients with community-onset candidemia was the increasing relative frequency of *C. parapsilosis* as the infecting species as hospi-

**Table 3. Selected clinical variables for 352 patients with community-onset candidemia with data available regarding timing of previous hospitalizations, by category of past hospitalization.**

| Characteristic, % of patients | Very recent hospitalization ($n$ = 158) | Less recent hospitalization ($n$ = 104) | $P$[a] | No past hospitalization ($n$ = 90) | $P$[a] |
|---|---|---|---|---|---|
| Infecting *Candida* species | | | | | |
| *Candida albicans* | 41 | 28 | .03 | 39 | .80 |
| *Candida glabrata* | 28 | 27 | .84 | 21 | .26 |
| *Candida parapsilosis* | 8 | 20 | <.01 | 23 | <.01 |
| *Candida tropicalis* | 17 | 16 | .85 | 10 | .13 |
| Comorbid condition | | | | | |
| HIV infection | 7 | 9 | .69 | 13 | .12 |
| Malignancy | 28 | 22 | .28 | 14 | .01 |
| Neutropenia | 10 | 15 | .21 | 11 | .86 |
| Diabetes mellitus | 31 | 38 | .24 | 24 | .27 |
| Insulin dependence | 63 | 59 | .70 | 76 | .55 |
| Inflammatory bowel disease | 2 | 2 | 1.00 | 2 | 1.00 |
| Liver disease | 19 | 7 | .87 | 7 | .87 |
| Autoimmune disease | 11 | 7 | .56 | 7 | .56 |
| Chronic renal failure | 35 | 39 | .74 | 8 | .55 |
| Chronic renal failure requiring dialysis | 12 | 8 | .56 | 14 | .75 |
| Immunosuppressive therapy | 34 | 37 | .59 | 21 | .05 |
| Cardiovascular disease | 66 | 65 | .84 | 60 | .38 |
| Pulmonary disease | 56 | 52 | .50 | 49 | .34 |
| Surgery in 3 months prior to candidemia | 36 | 39 | .66 | 17 | .002 |
| Central venous catheter | | | | | |
| Central catheter at time of candidemia | 60 | 65 | .22 | 37 | .09 |
| Temporary central venous catheter | 46 | 28 | .09 | 33 | .3 |
| Peripherally inserted central catheter | 20 | 7 | .13 | 0 | .03 |
| Permanent central venous catheter | 33 | 53 | .07 | 30 | .8 |
| Implanted catheter | 22 | 39 | .10 | 41 | .09 |
| Hemodialysis catheter | 14 | 14 | 1.0 | 25 | .33 |
| Systemic antifungals in 30 days before candidemia | 8 | 12 | .76 | 2 | .81 |
| Systemic antibiotics in 1 month before candidemia | 87 | 77 | .07 | 58 | .0001 |
| Hyperalimentation in the past 3 months | 32 | 32 | .99 | 16 | .62 |
| Death | 32 | 18 | .12 | 23 | .13 |

**NOTE.** The number of patients for whom exposure status was known differs by exposure. The number of patients evaluated in each comparison differed by the exposure of interest, because data were not available for all exposures for all patients; however, to simplify the table, denominators are not shown. Very recent hospitalization is defined as hospitalization 1–30 days before the index date, less recent hospitalization is defined as hospitalization 31–90 days before the index date, and no past hospitalization is defined as no documented hospital stay in the 90 days before the index date.

[a] Comparison by the $\chi^2$ test using the very recent hospitalization group as baseline.

talization exposures became more distant. We tested the hypothesis that the emergence of community-onset candidemia may, in part, be explained by unique characteristics of the infecting *C. parapsilosis* strains associated with infection in the community. However, the molecular subtyping results of *C. parapsilosis* isolates did not support this hypothesis. Although there were 5 examples of ⩾2 patients sharing moderately to highly related isolates, there were no clear trends toward increased genetic relatedness among isolates from patients with inpatient versus community-onset candidemia. Furthermore, any similarities among strains were predicated more by hospital or geographic location than by epidemiologic status as inpatient or community-onset candidemia. For example, 1 cluster of strain types included 5 isolates from patients with inpatient and community-onset disease, who were treated and residing in the Baltimore area. In another example, genetically related isolates from patients treated at the same hospital were observed. Related strain types from the same hospital among inpatients treated during the same time period (1998–1999) raises the possibility that such strains may be acquired in a hospital. Although this analysis does not include sufficient numbers of strains to test this hypothesis, a recent report describing genetic relatedness among *C. parapsilosis* bloodstream isolates collected over a 12-year period in a Finnish hospital were found to be

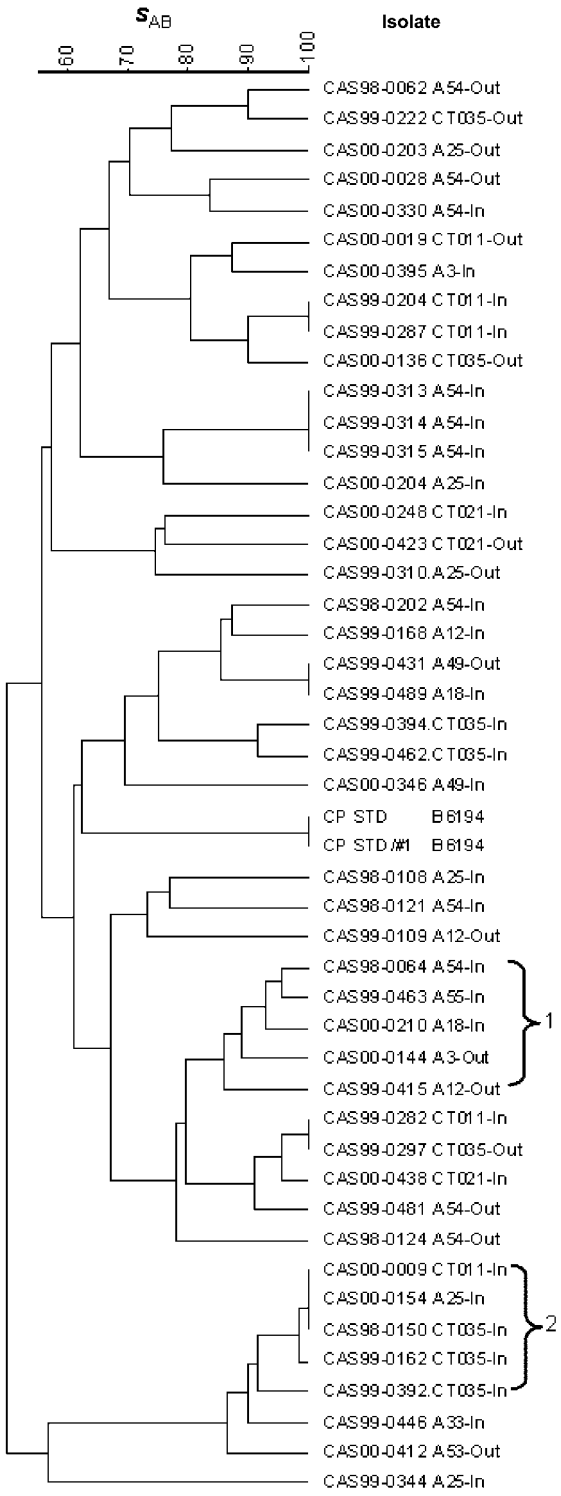


**Figure 1.** Dendrogram showing similarity among 45 *Candida parapsilosis* bloodstream isolates from Baltimore- and Connecticut-area hospitals (each similarity value [$s_{AB}$] represents the percent similarity). Baltimore-area hospitals are denoted by the prefix *A* and Connecticut hospitals by *CT*. *C. parapsilosis* bloodstream isolates are denoted by the year of collection and the culture number. In, inpatient candidemia; Out, community-onset candidemia; CP-STD, standard tester strain *C. parapsilosis* B-6194.

clonal or close variants of the same persistent strain by Cp 3-13 subtyping [17].

The epidemiologic findings of less frequent immunosuppression, use of systemic antimicrobials, or recent surgery among patients with community-onset candidemia, taken together with the more-frequent association with *C. parapsilosis,* strains of which overall tend to be unique to the individual patient, suggest that the pathogenesis of community-onset disease is more likely to involve skin colonization with *Candida* species rather than gastrointestinal tract colonization followed by translocation and subsequent infection. It is the latter type of colonization that drives the pathogenesis among inpatients [10]. *C. parapsilosis* is often the most frequently identified skin colonizer among patients and health care workers and is often more likely to be associated with central venous catheter–related infections than are other types of candidemia [2, 3, 10]. Further study to confirm these findings may help to focus prevention efforts among outpatients towards improvement in skin hygiene and disinfection and catheter care, rather than in eradication of gastrointestinal colonization, as is the focus of prevention efforts among inpatients [18, 19].

This study was limited by several factors. Although the surveillance was population based and excluded nonresidents of the surveillance area who had received care at a participating institution within the surveillance area, it did not seek out residents of the surveillance area who may have received care at an institution outside of the surveillance area. Because of the observational nature of this study, there were missing data; this was particularly true in the descriptions of the type of central venous catheter used by patients. However, every attempt was made, including data audits, to ensure that record abstractions were as complete as possible. Furthermore, the dates and documentation of recent hospitalizations were limited to hospital medical records from facilities within the surveillance area, resulting in some misclassification of patients with past hospitalizations into the category of patients with no past hospitalization, if these records were absent.

As an increasing number of patients with more-complex medical issues receive treatment as outpatients, community-onset candidemia can be expected to become a more common occurrence. Health care professionals must recognize that *Candida* is no longer a pathogen acquired by inpatients only and that it must be kept in the differential diagnosis of patients from the community who are hospitalized with clinical evidence of sepsis. This is especially true for patients with multiple medical problems requiring a high level of outpatient care that might include the presence of central catheters, hyperalimentation, or treatment with systemic antibiotics. Our data suggest some delay in the initiation of antifungal therapy, where the median time to institution of antifungal therapy was 2.7 days. A high index of suspicion and earlier implementation of an-

tifungal therapy in cases of community-onset candidemia may reduce morbidity and mortality among patients presenting with these infections.

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