

## Clonal Dissemination of *Staphylococcus epidermidis* in an Oncology Ward<sup>∇</sup>

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**Coagulase-negative staphylococci (CoNS) are the main cause of catheter-related infections, especially among immunosuppressed and neutropenic patients, as well as a source of bacterial contamination in blood cultures. Using biochemical identification and pulsed-field gel electrophoresis (PFGE), we sought to identify possible clonal isolates of bacteremia in patients with central lines in an oncology ward (OW), with comparison to isolates that were recovered by venipuncture from an adult emergency room (ER). A total of 243 CoNS isolates were identified to species level from the OW (126) and ER (117), with *Staphylococcus epidermidis* isolates being the most common (OW, 79.4%; ER, 45.3%). PFGE demonstrated a predominant clone of *S. epidermidis* (major subtype A) which was 35.5 times more likely (odds ratio [OR] = 35.5; 95% confidence interval [CI] = 4.7 to 267.0;  $P < 0.00001$ ) to be present in the OW versus the ER. These (CoNS or major subtype A) isolates were more frequently resistant to gentamicin (OR = 2.83; 95% CI = 1.23 to 6.53;  $P = 0.016$ ) and less frequently resistant to trimethoprim-sulfamethoxazole (OR = 0.38; 95% CI = 0.18 to 0.80;  $P = 0.013$ ). Subset analysis of *S. epidermidis* isolates 2 years after the study period showed the persistence of the clone of major subtype A within the OW. This study demonstrates the presence of a predominant clone among central line isolates from an OW that is not present in CoNS venipuncture isolates from an ER.**

Coagulase-negative staphylococci (CoNS) are the main cause of catheter-related infections, especially among immunosuppressed and neutropenic patients (6, 43, 48, 50). Moreover, studies have used biochemical identification and genotypic analysis to illustrate clonal infections that occur in specific units. (2, 5, 6, 12, 17–19, 23, 24, 28–30, 33–35, 38, 43, 44, 48, 49, 51) Other studies have shown differences in the production of possible virulence factors such as lipase, esterase, elastase, and biofilm (polysaccharide intercellular adhesin [*ica* operon]) among strains seen in patients with catheter-related infections versus a nonseptic control groups (7, 11, 13, 29, 32, 43, 53). Production of biofilm may allow these isolates to preferentially colonize the catheter, catheter hub, and other indwelling medical devices while escaping the immune system and antibiotics. This may lead to an increased frequency of bacteremia, false-positive blood cultures, and catheter-related septicemia due to hub colonization (7, 9, 13, 15, 21, 32, 52, 53). Still, other studies suggest that gut translocation with its resultant bacteremia leads to a significant number of cases of CoNS septicemia, particularly in cancer patients (8, 9, 17, 33).

Blood culture contamination by CoNS is also a significant cause of positive blood cultures, leading to a problem in the determination of true bacteremia (9, 34, 36, 37, 52). As a result, there is a marked increase in the financial burden, with an estimated cost of \$5,000 to \$10,000 per false-positive blood culture due to more extensive laboratory testing, pharmacy costs, radiological procedures (echocardiograms), and unnecessary increased lengths of stay (4, 36, 37). Blood culture con-

tamination rates are considerably increased due to hub colonization if the blood is withdrawn from central venous lines as opposed to by venipuncture. (3, 16, 26, 40–42, 52) The purpose of the current retrospective case-control study was four fold. First, we desired to determine, over a period of 1 year, the rate of CoNS blood contamination and infection in a group of patients from a unit (adult oncology) with a high frequency of central lines and thus high contamination and infection rates. Second, we sought to identify to species level the study group CoNS isolates (those from central lines in the oncology ward [OW]) and isolates from a control group (samples obtained from peripheral venipuncture from the adult emergency room [ER]) and compare the colonization/infection rates between the two groups of patients by examination of the medical record and utilizing a clinical algorithm for classification of infection versus contamination (5). Third, genotyping (by pulsed-field gel electrophoresis [PFGE]) of selected isolates from each group was performed to determine if any clonal patterns existed within the study group and/or control group. Fourth, we wanted to determine if any of the possible clonal groups were associated with clinical findings indicative of infection, as proposed in a previously published algorithm (5).

### MATERIALS AND METHODS

Institutional review board permission was obtained for all aspects of this study.

**Specimen selection.** The laboratory computer database was analyzed for CoNS blood isolates from both the adult OW and adult ER for a period of 1 year. Initial evaluation of the site of infection among the OW isolates demonstrated that most of them were drawn from central lines. In fact, most of the OW patients had central lines for chemotherapy, etc. (including a small number of patients who had a CoNS-positive blood culture that was designated as being from “peripheral”). Not all of these “peripheral” isolates were *Staphylococcus epidermidis* (which could be used in the epidemiologic comparison). After discussion with clinical staff, it was further determined that “peripheral” usually meant “peripheral line” and not “peripheral venipuncture.” Patients with OW venipuncture isolates usually also had a central line with the same sort of inherent risks for exposure to the clone (nurse to patient). Because of these factors, no significant

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number of true venipuncture isolates from the OW could be used for adequate epidemiological comparison with central line isolates from the OW.

A total of 243 isolates were evaluated. One hundred twenty-six were from the OW, and 117 were from the ER. Culture result records were obtained, and data were extracted for the study. Medical charts were examined, and relevant clinical information was obtained, such as hematology indices, immunosuppressive treatments and/or conditions, clinical diagnosis, vital signs at the time of culture, and the presence of any other focal signs/symptoms of infection. Specimens from the OW were included in the study if they were identified as being drawn from a central venous line. For the control group, isolates were included in the study if they were obtained from a peripheral venipuncture in the ER. In the control group, isolates were excluded from the study if they were from patients who had some form of central venous line or another type of implanted or indwelling device.

All *S. epidermidis* isolates (153) were examined further for clonality using PFGE, as this was the most frequent species isolated. For the analysis of the association between the largest clone of *S. epidermidis* (PFGE subtype A) with central line culture in the OW compared to peripheral venipuncture in the ER, duplicate clonal isolates were excluded (random exclusion of duplicate clonal isolates from the same patient). Non-*S. epidermidis* CoNS were also added to the analysis to more accurately represent the strength of the association of major subtype A compared to all CoNS.

**Isolate identification.** All CoNS isolates utilized in this study were obtained from frozen stocks at  $-70^{\circ}\text{C}$  and subcultured. These isolates were identified by the API Staph (bioMérieux, Inc., Durham, NC) commercial biochemical identification system according to the manufacturer's instructions.

**PFGE.** PFGE was performed on all isolates of *S. epidermidis* from both the OW and the ER as described previously (46). Briefly, chromosomal SmaI digests were prepared by incubating agarose plugs containing lysed, pure organism overnight at room temperature with a buffer containing the SmaI restriction enzyme. Plugs were loaded on an agarose gel and run for 18 h overnight equilibrated at  $14^{\circ}\text{C}$ , with a constant voltage of 6 V/cm and pulses ramped from 5.3 s to 34.9 s at an angle of 120 degrees. Gels were stained in 0.1% ethidium bromide and photographed. Along with the specimens, a DNA size ladder as well as the same *Staphylococcus* positive control were run on each gel. Each image was captured with the exact same camera and camera settings. The gel lanes were cut and pasted next to one another for comparison, using image software without modifying the image dimensions. These methods allowed definitive, consistent comparison between gels. The banding patterns of all isolates evaluated with PFGE were compared by visual inspection, and the isolates were grouped based on number of band differences from the dominant primary clone identified in the *S. epidermidis* isolates from the OW and the ER as suggested by Tenover et al. (47).

**Evaluation of infection status.** To evaluate associations between particular PFGE subtypes and central line use, we compared these types utilizing a standard for true infection that has been published previously (5), with a slight modification. The algorithm for deciding if an isolate from a patient was due to true infection is as follows.

(i) Those isolates that were from patients who had  $\geq 1$  additional CoNS-positive blood culture in a 5-day period were considered consistent with infection as the source.

(ii) Those isolates that were from patients who had no additional positive blood cultures in a 5-day period from the index blood culture were considered consistent with infection as the source if both of the following conditions applied: (a) a white blood cell [WBC] count of  $<2,000$  cells/ $\mu\text{l}$  or  $>14,000$  cells/ $\mu\text{l}$  and (b) either a temperature of  $<36^{\circ}\text{C}$  or  $>38.5^{\circ}\text{C}$  or a systolic blood pressure of  $<90$  mm Hg.

(iii) Those isolates that did not meet either criterion 1 or 2 were considered contaminants.

**Data analysis.** All data were entered into a database, and all statistical analyses were performed with SPSS version 10.0.1 for Windows (SPSS Inc., Chicago, IL) and GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego CA). *P* values were calculated by the two-tailed Fisher exact test unless otherwise specified. The independent-sample *t* test was utilized to evaluate the statistical significance of the comparisons of means. Differences between means were considered statistically significant if the *P* value was  $<0.05$ .

## RESULTS

Two-hundred forty-three isolates were included in the study (117 from the ER and 126 from the OW). Only one isolate out of all of those tested was repeatedly identified by the API

TABLE 1. Identification of CoNS isolates recovered from ER venipunctures and OW central lines

Species	No. (%) of isolates		
	OW	ER	Total
Unidentifiable	5 (4.0)	13 (11.1)	18 (7.4)
<i>S. epidermidis</i>	100 (79.4)	53 (45.3)	153 (63.0)
<i>S. haemolyticus</i>	10 (7.9)	3 (2.6)	13 (5.3)
<i>S. saprophyticus</i>	1 (0.8)	3 (2.6)	4 (1.6)
<i>S. hominis</i>	3 (2.4)	13 (11.1)	16 (6.6)
<i>S. lugdunensis</i>	5 (4.0)	8 (6.8)	13 (5.3)
<i>S. xylosum</i>	0 (0.0)	3 (2.6)	3 (1.2)
<i>S. capitis</i>	0 (0.0)	10 (8.5)	10 (4.1)
<i>S. cohnii</i>	0 (0.0)	2 (1.7)	2 (0.8)
<i>S. lentus</i>	0 (0.0)	1 (0.9)	1 (0.4)
<i>S. simulans</i>	0 (0.0)	1 (0.9)	1 (0.4)
<i>S. warneri</i>	0 (0.0)	3 (2.6)	3 (1.2)
<i>S. chromogenes</i>	0 (0.0)	1 (0.9)	1 (0.4)
<i>S. aureus</i>	0 (0.0)	1 (0.9)	1 (0.4)
<i>Micrococcus</i> sp.	2 (1.6)	2 (1.7)	4 (1.6)
Total	126 (100.0)	117 (100.0)	243 (100.0)

Staph ID system as *Staphylococcus aureus*. This isolate was also repeatedly Staphaurex negative and repeatedly tube coagulase negative at 2 h, 4 h, and 18 h. Table 1 shows the distribution of coagulase-negative organisms identified using the API Staph commercial system. The OW had a more narrow spectrum of species (total of 6) than the ER (total of 14). As expected, *S. epidermidis* was the predominant species out of all isolates identified (66.4% of 277 isolates). *S. epidermidis* was almost twice as frequent among central line isolates from the OW than among those venipuncture isolates identified from the ER (81.9% versus 45.3%;  $P < 0.00001$ ). *Staphylococcus haemolyticus* was three times more frequent among isolates from the OW than among those from the ER (7.9% versus 2.6%), but this was not statistically significant ( $P = 0.087$ ). Two isolates from each ward (four total) were identified as a *Micrococcus* sp.

Figure 1 shows the PFGE band patterns for each of the major and minor subtypes observed among OW and ER *S. epidermidis* blood culture isolates. The predominant major subtype (A) had three minor subtypes (A1, A2, and A3), which corresponded to zero to three, four, and five to seven band differences, respectively, from the predominant A1 minor subtype band pattern seen in lane 2. Table 2 defines the distribution of the *S. epidermidis* subtypes exhibited in Fig. 1 between the OW and ER and contains all clonal isolates (including duplicates from the same patient). Eight different subtypes were seen in both the OW (A1, A2, A3, B, C, D, E, and F) and the ER (A1, B, G, H, I, J, K, and L). The two locations had in common two subtypes (A1 and B). Only 40% of OW *S. epidermidis* isolates were nonclonal, compared to 52.8% of ER *S. epidermidis* isolates. The most common *S. epidermidis* subtype was A1, at 21.6% of all isolates, and it comprised 32.0% and 1.9% of the OW and ER *S. epidermidis* isolates, respectively. The second most common major subtype (B) was present in equal proportions in the OW and ER. Six isolates in the ER exhibited a G major subtype, which was not present in the OW isolates.

The association of *S. epidermidis* PFGE major subtype A

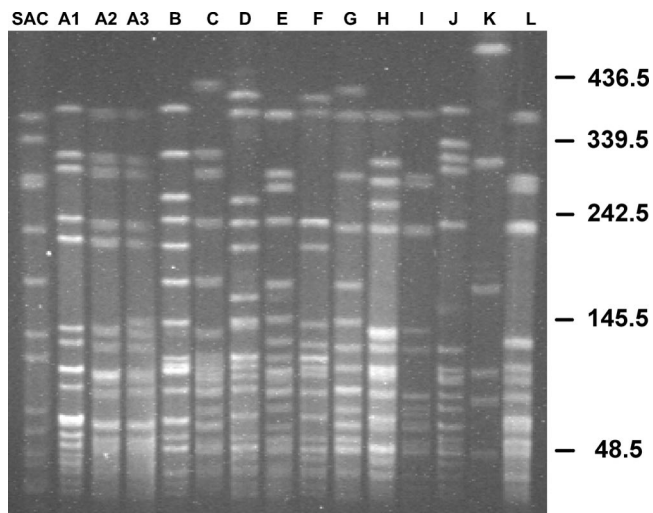


FIG. 1. *S. epidermidis* PFGE gel demonstrating all major and minor subtypes present among OW and ER blood culture isolates. SAC, *Staphylococcus aureus* control. DNA fragment size is measured in kilobases on the right. The A1 minor subtype showed a one- to three-band difference compared to the predominant A major subtype pattern. A2 showed a four-band difference from the predominant A major subtype pattern. A2 showed a five- to seven-band difference from the predominant A major subtype pattern.

with central line culture from the OW compared to peripheral venipunctures from the ER is demonstrated in Table 3. Duplicate clones from the same patient were excluded from the analysis to ensure that there was no artificial inflation of the strength of the association of the major subtype A and central line use among OW patients. Non-A includes those PFGE subtypes that were other than type A as well as those isolates that were *Staphylococcus* spp. other than *S. epidermidis*. Thus, all non-A samples were not clonally related to major subtype A. The total number of isolates included in the analysis was 221. This included 131 isolates from the data in Table 2 (153 minus 22 duplicates) and 90 non-*S. epidermidis* CoNS isolates.

A total of 24.1% of OW isolates were the major subtype A versus non-subtype A, compared to 0.9% of ER isolates (odds ratio [OR] for major subtype A detected in OW = 35.5; 95% confidence interval [CI] = 4.7 to 267.0;  $P < 0.00001$ ). Of the major subtype A, minor subtypes A1 and A3 had statistically significant associations with isolation from the OW central lines. Subtype A1 had an OR of 22.4 (95% CI = 2.9 to 171.0;  $P = 0.000014$ ) for isolation from the OW central lines as opposed to the ER venipunctures. Subtype A3 was seen in 4.6% (95% CI = 2.0 to 10.4) of OW isolates, compared to 0% of ER isolates ( $P = 0.027$  for difference). Among all other subtypes, no statistically significant association was found ( $P > 0.115$ ) for those patients who did or did not have a central line.

As previously discussed, the same *S. epidermidis* subtype was seen in an individual patient on multiple blood cultures ( $n = 46$ ). Patient 15 had seven blood culture isolates with the same exact minor subtype of A1, which was the most frequent occurrence among all patients. These seven isolates were obtained on four different days, three of which were 2 to 4 months apart. Thirty-nine of the total of 46 repeat positives (84.8%) were isolated from the OW. Out of all repeat positives, the

major subtype A showed the largest number of repeat positives (24/46; 52.2%) Within the major subtype A, minor subtype A1 was the most frequent at 20 (43.5%), followed by minor subtypes A2 (4.3%) and A3 (4.3%). Another group of patients had repeat positive subtypes, and each of these subtypes was unique to one of these patients (not clonally related to more than one patient and thus not defined by a letter designation). This was the second largest group of repeat positive cultures from the same patient, with a total of 11 of 46 (23.9%) repeat positives.

Using a previously published algorithm for diagnosis of a true clinical infection, *S. epidermidis* major subtype A was evaluated for the possibility that it might be responsible for true infection as opposed to colonization and transient bacteremia among isolates from both the OW and ER (5). In the combined OW and ER patients with clonal isolates, there was no association between major subtype A and infection as defined by the algorithm (OR = 1.41; 95% CI = 0.58 to 3.42;  $P = 0.504$ ;  $n = 85$ ). Interestingly, major subtype G showed a statistically significant negative association with infection versus lack of infection (OR = 0.10; 95% CI = 0.01 to 0.88;  $P = 0.023$ ) as defined by the algorithm. There were no other statistically significant associations between infection as assessed by the algorithm and the particular subtypes.

Table 4 shows the values among major subtype A (or a subtype other than A) for different laboratory and physical exam findings that are indicative of infection. Mean systolic blood pressure, mean diastolic blood pressure, and total WBC count were all lower in patients from whom major subtype A was isolated, compared to those with subtypes ( $P = 0.013$ ,  $P = 0.022$ , and  $P = 0.002$ , respectively). Temperature was higher ( $P = 0.001$ ) and there was a trend for higher respiratory rates ( $P = 0.072$ ) among patients from whom major subtype A was isolated, compared to other subtypes.

TABLE 2. *S. epidermidis* PFGE type distribution of the adult OW central line isolates and the adult ER isolates

PFGE major (minor) subtype <sup>a</sup>	No. (%) of isolates <sup>b</sup>		
	OW	ER	Total
A (1)	32 (32.0)	1 (1.9)	33 (21.6)
A (2)	4 (4.0)	0 (0.0)	4 (2.6)
A (3)	6 (6.0)	0 (0.0)	6 (3.9)
B	7 (7.0)	4 (7.5)	11 (7.2)
C	2 (2.0)	0 (0.0)	2 (1.3)
D	3 (3.0)	0 (0.0)	3 (2.0)
E	3 (3.0)	0 (0.0)	3 (2.0)
F	3 (3.0)	0 (0.0)	3 (2.0)
G	0 (0.0)	6 (11.3)	6 (3.9)
H	0 (0.0)	3 (5.7)	3 (2.0)
I	0 (0.0)	2 (3.8)	2 (1.3)
J	0 (0.0)	4 (7.5)	4 (2.6)
K	0 (0.0)	3 (5.7)	3 (2.0)
L	0 (0.0)	2 (3.8)	2 (1.3)
Nonclonal	40 (40.0)	28 (52.8)	68 (44.4)
Total	100 (100.0)	53 (100.0)	153 (100.0)

<sup>a</sup> The A1 subtype showed a one- to three-band difference from the predominant A major subtype pattern. A2 showed a four-band difference from the predominant A major subtype pattern. A2 showed a five- to seven-band difference from the predominant A major subtype pattern.

<sup>b</sup> Includes duplicate clones from the same patient isolated on different days.

TABLE 3. Association of *S. epidermidis* PFGE major subtype A with central line culture from the OW compared to peripheral venipunctures from the ER

Subtype <sup>a</sup>	No. (%) of isolates <sup>b</sup>			OR (95% CI); <i>P</i>
	OW	ER	Total	
Non-A	82 (75.9)	112 (99.1)	194 (87.8)	35.5 (4.7–267.0); <0.00001
A	26 (24.1)	1 (0.9)	27 (12.2)	
Total	108 (100.0)	113 (100.0)	221 (100.0)	

<sup>a</sup> Duplicate clones from the same patient have been excluded from the analysis.

<sup>b</sup> Non-A includes those PFGE subtypes that were other than major type A as well as those isolates that were *Staphylococcus* spp. other than *S. epidermidis*. Thus, all non-A samples were not clonally related to major subtype A.

Antibiotic susceptibility data for the central line isolates were available for vancomycin, penicillin, levofloxacin, clindamycin, minocycline, cefazolin, rifampin, methicillin, erythromycin, amoxicillin/clavulinate, gentamicin, and trimethoprim-sulfamethoxazole. Central line isolates that were major subtype A were more likely to be resistant versus sensitive/intermediate to gentamicin than central line isolates that were not major subtype A (OR = 2.83; 95% CI = 1.23 to 6.53; *P* = 0.016). These same central line isolates (major subtype A) were less likely to be resistant to trimethoprim-sulfamethoxazole (OR = 0.38; 95% CI = 0.18 to 0.80; *P* = 0.013). All central line isolates were sensitive to vancomycin and resistant to penicillin and minocycline. No other association of antibiotic susceptibility was observed when comparing central line isolates of major subtype A versus non-major subtype A. Antibiotic resistance was not associated with algorithm infection status (data not shown).

Sixty-nine percent of clonal OW central line isolates were cultured from patients with leukemia, and all of the OW patients with clonal isolates had some type of lymphoproliferative disorder. Acute myelogenous leukemia was the most common disorder in the OW (45.2%). A total of 57.1% of the ER

venipuncture clonal isolates were cultured from patients with a neurological disorder who had impaired motor function.

Subset analysis of *S. epidermidis* isolates obtained 2 years after the initial study period demonstrated by PFGE that the major subtype A (minor subtype A1) continued to circulate within the OW central line isolates (data not shown).

## DISCUSSION

Many of the previously mentioned studies in the literature have utilized controls from patients similar to, or the same group of patients as, those under study. We chose the adult ER so as to exclude those patients who would have possibly had an indwelling catheter or other medical device that might have been obtained at our hospital. This choice of a control group would also give a good comparison of the ecological diversity of CoNS in the community compared to the selective population of OW patients. From the data, we demonstrate that *S. epidermidis* is the predominant organism isolated from CoNS-positive blood cultures from ER venipunctures and OW central lines and that there is a more narrow spectrum of different species seen among OW line isolates than among ER veni-

TABLE 4. Univariate analysis of values for clinical indicators of infection among the different subtypes

Clinical parameter (unit)	Subtype	<i>n</i>	Mean ± SEM	<i>P</i> value for difference <sup>a</sup>
Temp (°C)	A	50	38.5 ± 0.1	0.001
	Non-A	43	37.7 ± 0.2	
Systolic blood pressure (mm Hg)	A	50	122.6 ± 2.8	0.013
	Non-A	43	134.2 ± 3.5	
Diastolic blood pressure (mm Hg)	A	50	69.0 ± 2.3	0.022
	Non-A	43	76.0 ± 2.0	
Heart rate (beats/min)	A	50	104.0 ± 2.9	0.460
	Non-A	43	101.1 ± 2.6	
Respiratory rate (breaths/min)	A	50	21.5 ± 0.8	0.072
	Non-A	43	19.7 ± 0.5	
Total WBC (cells/μl)	A	50	2,791 ± 613	0.002
	Non-A	43	6,858 ± 1,088	
Absolute neutrophil count (cells/μl)	A	41	3,098 ± 915	0.220
	Non-A	24	4,910 ± 982	

<sup>a</sup> By *t* test for independent samples.



puncture isolates. There is also a predominant clone of *S. epidermidis* that is circulating in our OW among patients who have central lines. Antibiotic usage in this unit has likely influenced the ecology and selected organisms with resistance to antibiotics, in particular, penicillins, minocycline, and gentamicin, which has been documented in other studies (1, 21, 22, 24, 27). Although we did not evaluate for the presence of biofilm production in these clonal isolates, evidence from other studies suggests that this helps establish and select organisms that are more resistant and invasive and evade the immune system (7, 21, 32). Our data appear to suggest that a predominant clone was consistently and frequently isolated from patients with central lines and that this clone (A) was isolated multiple times from the same patients (Table 4). This suggests a propensity of this isolate to colonize central lines, which is likely to involve extensive biofilm production.

We believe that a significant cause of the proliferation of clone A in our OW was patient-to-patient transfer by medical staff. In neonatal typing studies, clusters of CoNS have been shown to be distributed among both neonates and hospital staff, while CoNS isolates associated with sepsis may be more homogeneous (10, 24, 25, 35). In operating room environments and radiological suites, extensive shedding of CoNS into the air by medical staff is seen, even with contact barrier precautions and masks (31, 45). Frequent utilization of central lines for blood tests and intravenous administration of drugs promotes frequent distribution of the biofilm-producing clones that are more resistant and likely to produce central line infections. Further evidence that supports our hypothesis that patient-to-patient transfer of these organisms is occurring in our OW was the fact that the minor A1 subtype of the major subtype A was still present in central line isolates 2 years after the initial data were collected.

Another contributor to the clonal spread of sepsis-related *S. epidermidis* in our OW may have been colonization and gut mucosal translocation of these organisms. Several studies have implicated this pathogenic mechanism (1, 8, 9, 14, 17, 20, 39), especially in cancer patients. All of our OW patients with clonal isolates had some type of lymphoproliferative disorder (69% had leukemia). Many of these patients had recent transplants, gastrointestinal graft-versus-host disease, low WBC counts (clone A mean WBC = 2,791 cells/ $\mu$ l [Table 4]), and some form of chemotherapy which would make them particularly susceptible to mucosal translocation of colonizing *S. epidermidis* organisms. Another possibility is that mucosal translocation seeds the bloodstream with biofilm-producing isolates that then adhere to and colonize catheters, further promoting the spread of these organisms.

As previously defined, we utilized an algorithm of infection status to further characterize the possibility of clonal organisms causing catheter-related infections (5). There was no statistically significant increase in infections among those patients with major subtype A versus non-major subtype A, indicating that major subtype A isolates do not cause more infection than non-major subtype A isolates. In Table 4, the means of several clinical indicators were marginally but statistically significantly different between major subtype A and non-major subtype A isolates. These values were minimally from the cutoffs that have been shown in the literature to be predictive of infection.(5) When these univariate indicators were incorporated

into the algorithm, these effects did not predict infection. An explanation for the lower WBC count (not low enough to define infection) might be that this allows preferential colonization of a catheter by the clone, while being an indicator not of "infection" but of mere colonization.

The fact that major subtype A was not associated with our definition of infection suggests that these isolates may have been contaminants from extensively colonized central lines instead of true line infections or mucosally translocated organisms causing sepsis. Further, these major subtype A isolates may be no more pathogenic than non-major subtype A isolates, and this could be a possible explanation for the lack of an association with infection status. It is important to also note that the fact that many of the central line OW patients had leukemias/lymphoproliferative disorders may affect our definition of sepsis, because these patients do not always express every physical sign and symptom of infection.

In summary, we found a clonal group (group A) of isolates that was responsible for a significant number of positive blood cultures among OW patients, and only one major subtype group A isolate was present in the comparison group (ER patients). Central line usage for blood draws and administration of medications appears play a significant role in colonization, blood culture contamination, and bacteremia among OW patients. Blood cultures from only venipuncture sites should be the standard procedure for evaluating sepsis and clinically relevant bacteremia in cancer patients.

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