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# Validation of Catheter Semiquantitative Culture Technique for Nonstaphylococcal Organisms

DAVID P. DOOLEY,[1]* ALFREDO GARCIA,[1] J. WILLIAM KELLY,[1]† ROBERT N. LONGFIELD,[1]‡ AND LINDA HARRISON[2]

*Departments of Medicine[1] and Pathology,[2] Brooke Army Medical Center, Ft. Sam Houston, Texas 78234*

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**The catheter semiquantitative culture roll tip technique has been validated as a discriminator between non-catheter-related bacteremias and catheter-related bacteremias (CRBs) caused by *Staphylococcus* species. However, this technique has not been specifically validated when used for the evaluation of catheters infected with organisms other than staphylococci. We reviewed catheters that had been submitted for semiquantitative roll tip culture as well as hospital records to determine clinical correlates of infection. Local infection and CRB were defined by standard criteria. Catheter-related sepsis (CRS) was defined as fever, leukocytosis, or hypotension which resolved with catheter removal, without another source of infection. For 195 catheters from 93 patients, gram-negative rods and enterococci were present on 36, fungi were on 25, *Corynebacterium* species were on 5, *Bacillus* species were on 3, *Staphylococcus* species were on 79, and 41 demonstrated no growth. Of 21 episodes of CRB or CRS due to nonstaphylococcal organisms, only 1 (questionable) episode was due to a catheter with <15 CFU ($P < 0.05$). Eleven of these 21 episodes of CRB or CRS were due to gram-negative rods and enterococci, of which only the questionable episode was due to a catheter with <15 CFU. Nine of these 21 episodes of CRB or CRS were due to fungi, none of which were associated with a catheter with <15 CFU. The data for *Staphylococcus* species recapitulated published data (none of 21 CRB or CRS episodes were associated with catheters with <15 CFU) and validated this retrospective technique. The data presented in this study validate the use of the semiquantitative culture technique for the evaluation of catheter-related infections caused by organisms other than staphylococci.**

Intravascular catheters are an increasingly important cause of nosocomial infections. Catheter-related complications range from local exit site or tunnel infections to frank bacteremias and death (6). Catheters are responsible for 20 to 40% of nosocomial bacteremias (6, 10). Many patients with intravascular catheters have additional potential sources for infection, and historically it has been difficult to discern whether an individual catheter is responsible for an episode of bacteremia. Although some studies have suggested that formal quantitative cultures of organisms present on intravascular catheters correlate well with the presence or absence of catheter-related infection (2, 4, 9), the technique is generally considered too cumbersome for routine laboratory use.

Maki et al. (7) described a semiquantitative culture (SQC) (roll tip) technique in which an ~5-cm segment of the catheter tip is rolled on a sterile agar plate and the resulting colonies are counted. This technique permitted differentiation between contaminated catheters (<15 CFU per catheter tip) and infected catheters (≥15 CFU per catheter tip). Multiple studies (1–3, 5, 7, 11) have now indicated that catheter-related local infections were uncommon, and bacteremia almost never occurred, when catheters yielded <15 CFU on SQC. Conversely, all episodes of catheter-related bacteremias (CRBs) and most local infections were associated with catheters yielding ≥15 CFU on SQC.

Most isolates from the original SQC study (6) were *Staphylococcus* species (55 of 74 cultures). In that study and in all subsequent studies (1–3, 5, 11), insufficient data were presented to validate these observations for other organisms, such as gram-negative rods, enterococci, or fungi. Although catheter culture positivity with these other species is a common clinical problem, these organisms differ from staphylococci in their abilities to adhere to catheters (8), and it is uncertain whether the semiquantitative data available for staphylococci are applicable to them. In addition, unlike *Staphylococcus epidermidis*, gram-negative rods and fungi frequently gain entry to the bloodstream from sources other than vascular devices (12). Clinical decision making regarding the origin of bloodstream infections would be greatly aided if the SQC technique could be validated for these organisms.

We collected data on catheters submitted to the microbiology laboratory for SQC counts, selected for analysis those that had matched blood culture data, and then retrospectively reviewed clinical courses by chart review. The goal of this study was to determine whether the SQC roll tip technique could discriminate between catheter-related infections and non-catheter-related infections for nonstaphylococcal organisms such as gram-negative rods, enterococci, and fungi.

* Corresponding author. Phone: (210) 916-9554. Fax: (210) 916-9927.
† Present address: Greenville Hospital System, Greenville, SC 29605.
‡ Present address: Texas Center for Infectious Diseases, San Antonio, TX 78223.

## MATERIALS AND METHODS

**Catheter culture technique.** The catheter culture protocol was similar to that previously reported (7). Following removal of the catheter from the insertion site under aseptic conditions, the distal (~5-cm) tip of the catheter was cut and placed in a sterile container for transport to the microbiology laboratory. By an aseptic technique, the catheter tip was rolled several times on a blood agar plate and then was immersed in sterile tryptic soy broth. The inoculated agar plate and the broth tube were cultured at 37°C for 72 h. Colonies were enumerated on the agar plates and identified by standard techniques, and the results were entered into the laboratory information system. Most heavily infected catheters demonstrated confluent growth; the SQC for these were recorded as too numerous to count. During the period of this study, it was unusual for the microbiology technicians to enumerate colony counts of >100, and it is probable that many

catheters with counts in the 100- to 200-CFU range were reported as CFU too numerous to count.

**Microbiologic and clinical data collection.** Microbiologic data were obtained with the laboratory information system. Data were recorded for all catheters which had grown any isolate on SQC between January 1992 and July 1994. The data included the type of catheter submitted, the date of submission, identification of the organism(s) recovered, the number of CFU, matched blood culture data, and available culture data from other sites (sputum, urine, and soft tissue, etc.). Only those catheters for which blood culture data were available within 48 h before and 24 h after catheter removal were included in the study.

Inpatient charts were reviewed to examine the clinical courses of patients from whom the catheters were removed. Chart review data included the number of days the catheter was in place, evidence for local infection in physicians' or nurses' notes (see "Definitions" below), and whether the catheter had been changed over a guide wire. (If no mention of local infection was noted, it was then assumed that none was clinically suspected.) If a catheter had been exchanged over a J wire, the duration of catheterization was considered to be the time between the date the catheter was inserted over the wire to the date the catheter was removed.

Physicians' notes, temperature records, and laboratory flow sheets were reviewed for evidence of CRB or catheter-related sepsis (CRS) (see "Definitions" below), as well as for evidence for other potential sources of bacteremia or sepsis. A causal relationship between a catheter and bloodstream infection was not accepted if there was another identifiable source (e.g., candidemia in the setting of identical catheter and urine culture positivity was not accepted as coming from a catheter source).

Catheters from which two or more different isolates were identified but which were associated with neither a local nor a systemic infection were accepted and counted as one catheter for each isolate. If a CRB was associated with a catheter from which multiple organisms grew, the responsible organism(s) was assumed to be that present on blood culture and the catheter was counted only for the blood isolate(s). If a catheter-related local infection was from a catheter with multiple organisms, the catheter was excluded entirely because it was impossible to determine which was the causative organism.

**Statistical analysis.** Categorical data were analyzed with Fisher's exact test (two tailed). Differences were considered significant at $P < 0.05$.

**Definitions. (i) Local infection.** Local infection was defined as the presence of at least one of the following three criteria: erythema, induration, or exudate at the catheter exit site, as documented in the physicians' or nurses' notes.

**(ii) CRB or catheter-related fungemia.** CRB or catheter-related fungemia was defined as bacteremia or fungemia with no other source evident except the catheter. Identical isolates on the catheter and from blood cultures drawn within 48 h before and 24 h after catheter removal were required.

**(iii) CRS.** CRS was defined as the presence of clinical sepsis (two or more of the following: fever of ≥100.5°F [ca. 38.06°C], leukocyte count of ≥12,000/mm$^3$, or systolic blood pressure of <90 mm Hg), documentation of a catheter isolate (irrespective of quantitative count), and negative blood cultures obtained within 48 h before and 24 h after catheter removal. No other source of sepsis could be demonstrated, and the sepsis syndrome resolves following catheter removal.

## RESULTS

**Catheter data collected.** A total of 121 charts were reviewed for this study. Of these, 28 were excluded because they lacked matching blood culture data ($n = 14$), the catheters were nonintravenous ($n = 3$), the catheters were extracted at autopsy ($n = 3$), or chart data were inadequate ($n = 8$). A total of 93 charts were ultimately accepted for study. From these, data from a total of 173 catheters were recorded. Types of catheters included triple lumen ($n = 70$), introducer sheath ($n = 26$), Swan-Ganz ($n = 24$), arterial ($n = 18$), unspecified central ($n = 14$), Quinton ($n = 5$), Hickman ($n = 3$), implantable ($n = 2$), Broviac ($n = 1$), and peripheral ($n = 1$); for 6 other catheters, location and type were unspecified. Both implantable devices (Port-A-Cath; Pharmacia Deltec, St. Paul, Minn.) were cultured at the distal ~5-cm catheter tip, per protocol, rather than at the reservoir. For three catheters, determinations could not be reliably made regarding appropriate microbiologic associations: one catheter causing a local infection was infected with both too-numerous-to-count *Klebsiella* species and coagulase-negative staphylococci, and two catheters with multiple organisms were associated with CRS. As the specific identification of the organisms responsible for these complications was impossible, the catheters were excluded from further analysis, leaving 170 for the raw analysis.

Nineteen catheters were subsequently counted twice (10 catheters with two isolates and no associated infection; 3 catheters with two isolates and bacteremia from both; 6 catheters with one isolate but demonstrating both local and bacteremic infections), and 3 catheters were subsequently counted three times (each with three isolates and no associated infection). Therefore, the data from an apparent 195 catheters were entered for the analysis of quantitative counts and related infections.

TABLE 1. Catheter microbiologic data

| Type of organism | No. of catheters |
|---|---|
| *Staphylococcus* spp. | 79 |
| Gram-negative rods or enterococci | 36 |
| *Pseudomonas aeruginosa* | 9 |
| *Klebsiella pneumoniae* | 3 |
| *Acinetobacter calcoaceticus* | 3 |
| *Serratia marcescens* | 4 |
| *Enterobacter aerogenes* or *Enterobacter cloacae* | 3 |
| *Escherichia coli* | 3 |
| *Proteus mirabilis* | 2 |
| Enterococci | 9 |
| Fungi | 25 |
| *Candida albicans* | 13 |
| *Candida tropicalis* | 3 |
| *Torulopsis* (*Candida*) *Glabrata* | 3 |
| *Streptomyces* spp. | 3 |
| *Candida parapsilosis* | 2 |
| *Saccharomyces cerevisiae* | 1 |
| *Corynebacterium* spp. | 5 |
| *Bacillus* spp. | 3 |
| No growth | 41 |
| Total counted | 189 |

**Microbiologic data.** The species identification of catheter isolates is presented in Table 1. *Staphylococcus aureus* (9 catheters) and *S. epidermidis* (70 catheters) were present on 79 catheters. Gram-negative rods and *Enterococcus* species, present on 36 catheters, were analyzed together in this study because of their similar sources and patterns of infections (12). Catheters demonstrating no microbial growth were not retrievable from the laboratory information system, and the 41 sterile catheters included in the study were identified by their coincident appearance in inpatient records during the clinical data collection.

**Catheter SQC results and associated infection.** The organism-specific distribution of SQC results, with associated local infections or CRB or CRS, is depicted in Fig. 1. The bimodal distribution of SQC data, evident in this study and previous studies (7), for *Staphylococcus* isolates was recapitulated for gram-negative rod–enterococcal and fungal organisms. With one exception, no local infections or CRB or CRS occurred in association with catheters demonstrating growth of <15 CFU by SQC. The single exception occurred when a Hickman catheter, clearly associated with a tunnel infection and bacteremia with *Pseudomonas aeruginosa*, grew this isolate only from the broth culture of the catheter tip. We suspect that the distal 5 cm of the catheter (the intravascular segment) was cultured in this case, as per protocol, and the infected long intracutaneous segment was discarded by the laboratory. Clinical syndromes (all bloodstream infections) first appeared for catheters infected with staphylococci at 23 CFU, for catheters infected with gram-negative rods and enterococci at 39 CFU (excepting the single Hickman catheter on which *P. aeruginosa* grew from broth only), and for catheters infected with fungi at 50 CFU.

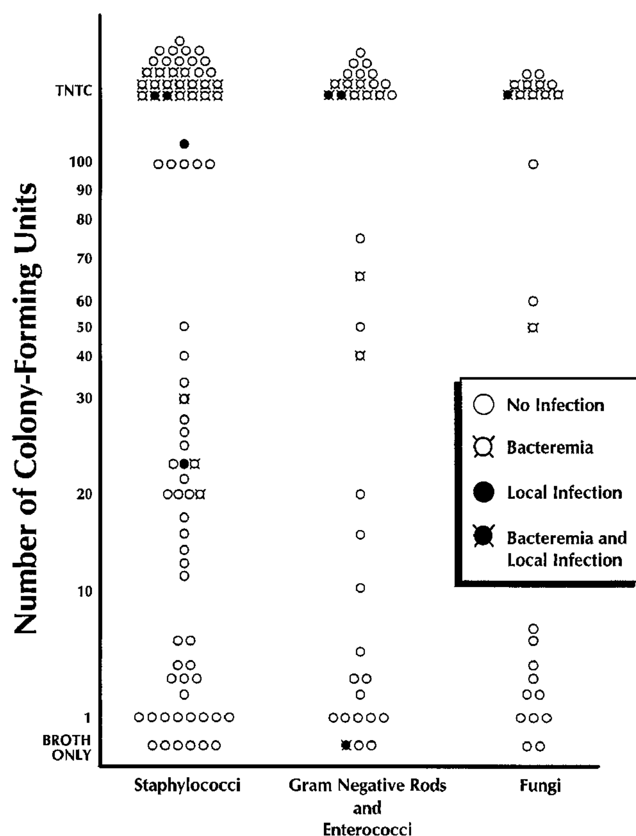


FIG. 1. Organism-specific distribution of SQC results. The presence or absence of an infectious syndrome is depicted. TNTC, too numerous to count.

When these SQC results were tabulated in relation to associated infections (Table 2, using the cutoff of ≥15 CFU per infected catheter), the absence of infection (especially bacteremia) associated with noninfected catheters was significant ($P < 0.05$). When the incidence of CRB or CRS was related to the duration of catheterization (data not shown), the incidence for nonstaphylococcal isolates increased by a proportionate measure, and over a similar period, compared with that seen with staphylococci both in this study and previously (6).

Noncatheter sources of febrile syndromes, identified during chart review in 89 patients, were common and easily defined (data not shown). In 41 instances, the catheter was discontinued routinely, without any signs or symptoms of infection; in another 40 instances, the catheter was clinically associated with an infectious syndrome.

## DISCUSSION

This study provides evidence that the catheter SQC technique can effectively differentiate CRBs from non-CRBs caused by organisms other than staphylococci, particularly gram-negative rods, enterococci, and fungi. Our data were generated under standard hospital and laboratory operating conditions. Therefore, although the data were not strictly controlled by this retrospective technique, we feel that they are generally applicable to the conditions currently found in most inpatient settings.

Catheter infections caused by the organisms analyzed in this study—chiefly gram-negative rods, yeasts of the genus *Candida*, and enterococci—have appeared infrequently in previous investigations of this issue, and the sparse data presented have always been lumped together under "all" catheter infections. These organisms, however, differ from staphylococci in that they either do not uniformly adhere to catheters or colonize catheters by different routes (8). Nevertheless, when an arbitrary—but historically useful (7)—cutoff of 15 CFU per catheter was used to define catheter infection, the rates of catheter-associated local or systemic infections did not differ in this study between staphylococci and nonstaphylococcal isolates.

Catheters infected with two or more microbial species were encountered commonly in this series. As these catheters have been excluded from consideration in previous series, there is a paucity of data addressing the significance of multiple catheter isolates. This study addressed this problem by counting each catheter with multiple isolates as one catheter for each isolate, followed by the usual correlations with clinical syndromes. Multiple isolates, when present at <15 CFU per catheter, were never associated with a local or systemic infection; in contrast, multiple isolates causing systemic infection were always associated with >15 CFU of the respective isolate on the catheter. These results indicate that the SQC technique can be reliably applied to the evaluation of catheters infected with more than one microbial species and for the first time suggest an appropriate approach to this common clinical problem.

Particular strengths and weaknesses stem from the retrospective nature of this study. As noted, no attempt was made to control data collection over the study period: catheter removal, processing, and subsequent identification and enumeration of organisms were performed by a standard protocol similar to that used, we believe, in most hospitals. These data would therefore include that generated in most practices, i.e., information adulterated with occasional breaks in technique (e.g., nonsterile line removal) or contamination (e.g., dropping catheters). As such, the data are particularly representative of most working environments. The validity of the retrospective technique is supported by our staphylococcal bacteremia data, which recapitulate data demonstrated in prospective, controlled studies.

An obvious weakness of the retrospective technique is the lack of data addressing local infections at the sites of catheter insertion. By our protocol, a site was not considered infected unless a relevant feature (erythema, purulence, or induration) was specifically described in either the physicians' or nurses' notes. Of 170 catheters, only 9 were so described; of the remaining 161 catheters considered not infected, only 96 were specifically described (within 24 h) as lacking signs of infection. The remaining 65 catheters, unable to be specifically identified as infected, were arbitrarily defined as uninfected for this study. Subtle signs of infection were almost certainly not recorded for many of these catheters, and therefore this study's sensitivity for evaluating local site infection suffers. We cannot, therefore, draw conclusions regarding quantitative counts of

TABLE 2. Results of SQC for catheters infected with all nonstaphylococcal isolates

| SQC result[a] | No. of catheters | | |
|---|---|---|---|
| | Total | Associated with: | |
| | | Local infection | CRB or CRS |
| Negative | 27 | 1 | 1 |
| Positive | 46 | 3 | 20[b] |

[a] Negative, <15 colonies on primary plate or broth only (sterile catheters excluded); positive, ≥15 colonies on primary plate.
[b] $P < 0.0001$.

catheter-associated nonstaphylococcal organisms in relation to local site infection.

In contrast, retrieval of data from inpatient charts in order to classify a bloodstream infection as catheter related or non-catheter related generally presented little difficulty. Alternate etiologies for febrile syndromes were almost always easily identifiable. These data are consistent with those previously reported, suggesting that bacteremia caused by nonstaphylococcal organisms is generally associated with identifiable, non-catheter-related foci of infections (12). Our data specifically suggest that, in the setting of a catheter tip colonized with <15 CFU of a nonstaphylococcal organism, the catheter must not be assumed to have been the source of a bacteremia and that a search for an alternative focus of infection must be assiduously pursued.

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