JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 2001, p. 274–278 Vol. 39, No. 1
0095-1137/01/$04.00+0 DOI: 10.1128/JCM.39.1.274–278.2001

Validity of Earlier Positivity of Central Venous Blood Cultures in Comparison with Peripheral Blood Cultures for Diagnosing Catheter-Related Bacteremia in Cancer Patients

VÉRONIQUE BUSSY MALGRANGE,[1]* MARIE CHRISTINE ESCANDE,[2] AND SERGE THEOBALD[3]

Laboratoire de Microbiologie Médicale[1] and Département d'Information Médicale,[3] Institut Jean Godinot, 51056 Rheims Cedex, and Laboratoire de Microbiologie Médicale, Institut Curie, 75231 Paris Cedex 05,[2] France

Received 3 April 2000/Returned for modification 1 September 2000/Accepted 31 October 2000

We carried out a prospective study in two French Comprehensive Cancer Centers (95 and 184 beds, respectively) to assess the validity of a test based on the earlier positivity of central venous blood cultures in comparison with peripheral blood cultures for predicting catheter-related bacteremia. The differences between the times to positivity for the 21 patients with clinical catheter-related bacteremia and the differences between the times to positivity for the nine patients with bacteremia due to another source were compared by the median test. The difference between the median values was significant ($P = 0.0003$). A receiver operating characteristic curve was constructed to determine the optimum threshold of the test, which appeared to be at the cutoff point of ≥+3 h, with 100% specificity and 81% sensitivity. The positive and negative predictive values obtained with this cutoff point confirmed the efficacy of the test for predicting the presence or absence of catheter-related bacteremia in cancer patients. The cutoff point was then used to post-classify the 68 episodes of bacteremia from an unknown source. The characteristics and clinical course of both the positive and negative post-classified episodes did not show that the test was clearly useful for a large number of clinical presentations. We therefore suggest restricting it to febrile neutropenic cancer patients for whom clinical signs of infection are slight or absent and when the test is positive.

Patients with cancer often need long-term intravascular devices (IVD), which can be externalized indwelling central venous catheters or subcutaneously implanted venous access systems. The use of IVD has improved the management of critically ill patients, but catheter-related bacteremia (CRB) is a frequent and potentially life-threatening complication (1, 8, 9, 12, 23). Several cancer centers have shown that CRB occurs in 10 to 20% of hospitalized patients with cancer (13, 16, 17). In cancer patients, it is preferable not to remove the IVD if the microorganism species allows it to be left in place, and several authors showed the efficacy of antibiotic treatment of port-associated bacteremia without IVD removal (26).

For several years, blood culture has benefited from the advantages of new semiautomatic methods. Time to positivity seems to correlate with the inoculum introduced into a bottle and can be accurately assessed by following indices of growth every 10 to 15 min (21, 28). Lastly, the authors of two recent interesting studies showed that earlier positivity of central venous blood cultures in comparison with peripheral blood cultures is highly predictive of CRB (4, 5).

We carried out the present prospective study at the Institut Jean Godinot (Rheims) and the Institut Curie (Paris), French Comprehensive Cancer Centers, with 95 and 184 beds, respectively. The first step was to assess the validity of the test for the diagnosis of CRB by comparing the times to positivity of blood cultures drawn simultaneously from a peripheral vein and from the central IVD. The second step was to show the test's usefulness for cancer patients with bacteremia from an unknown source.

MATERIALS AND METHODS

Preliminary study in vitro. To study the link between the microbial inoculum and the times to positivity of blood cultures, we performed several measurements with clinical isolates of the following four species of microorganisms (three strains each): *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, and *Candida albicans*. For the first three, bacteria were cultured at 37°C for 16 h in 10 ml of peptone water per colony (Sanofi Pasteur, Marnes la Coquette, France). *C. albicans* was cultured in 3 ml of glucose-buffered broth per colony (Sanofi Pasteur). Next, 10-fold serial dilutions were performed in 30 ml of saline. Aerobic bottles were then inoculated with 10 ml of each dilution and were placed in the automated blood culture system. The initial inoculum was counted on blood agar.

Diagnosis of CRB. The criteria of CRB diagnosis were derived from those described by Raad and Bodey (25) and were based on the clinical symptoms and/or results of a quantitative IVD tip culture, taking into account the presence of bacteremia or fungemia in all patients.

Definite CRB was diagnosed when no detectable focus of infection except the catheter could be identified and one of the following criteria was present: (i) local purulence, increased warmth, and induration extending at least 2 cm from the IVD insertion site or (ii) a positive quantitative catheter tip culture according to Brun-Buisson et al. (7), with isolation of the same microorganism from the catheter and the bloodstream.

Likely CRB was diagnosed when no apparent source of sepsis could be identified except for the catheter or when a distal source of infection could be identified with a microorganism different from the one in the bloodstream and one of the following criteria was present: (i) bacteremia or fungemia with a common skin organism (coagulase-negative staphylococcus (CNS), *Staphylococcus aureus*, or *Candida* sp.) in a patient with clinical manifestations of sepsis (fever, chills, or hypotension) or (ii) fever, chills, or hypotension occurring at the time of catheter connection.

Patients were classified as having CRB when they had definite or likely CRB.

Patients were classified as having bacteremia due to another source when no clinical sign of infection was due to the catheter, when another focus of infection

* Corresponding author. Mailing address: Laboratoire de Microbiologie, Institut Jean Godinot, 1 rue du Général Koenig, BP 171, 51056 Rheims Cedex, France. Phone: 33 3 26 50 42 93. Fax: 33 3 26 50 42 94. E-mail: veronique.bussy@reims.fnclcc.fr.

could be identified, and when the same microorganism was isolated from another source of infection and the bloodstream.

Patients were classified as having bacteremia from an unknown source when the source of the bacteremia could not be determined.

Inclusion criteria for patients and episodes. All patients had cancer and were hospitalized for their cancer treatment or for palliative care. They all had a long-term IVD and one sign of fever, shown by a temperature of >38.5°C or <36°C once or >38°C twice within a 2- to 3-h interval (24). In some cases they exhibited other clinical signs, such as chills and/or hypotension. Some patients had neutropenia (<500 G/liter). We considered only one episode per patient. Patients were considered by clinicians to be cured when their temperature returned to normal within 24 h of IVD removal or within 72 h of a suitable antibiotic treatment when the IVD was left in place. When the course of the bacteremia could not be observed or when the patient had been transferred to another hospital or had been discharged and was at home, the episode could not be evaluated and the patient was considered lost to follow-up. For each episode, one or multiple simultaneous sets of blood cultures were tested. Each set consisted of a peripheral aerobic culture paired with a central aerobic culture and a peripheral anaerobic culture paired with a central anaerobic culture.

Blood culture techniques. The systems used were the BacT/Alert (Organon Teknika Corp., Durham, N.C.) and the BACTEC 9000 (Becton Dickinson Co., Sparks, Md.) (21, 28). With both systems, continued noninvasive monitoring of each bottle allows the detection of positive cultures with a computer-driven algorithm that monitors the initial, increased, and/or total level of CO_2 produced by microbial growth. The exact amount of blood inoculated into each bottle, which varied from 5 to 8 ml, was determined by weight. Each bottle was weighed before and after blood inoculation. Pre-sampling bottle weight was obtained by calculating the mean weight of 100 bottles from each batch (in the BACTEC system) or by asking the manufacturer (BacT/Alert; Organon Teknika) to specify the pre-sampling weight. The volume in each filled bottle was then calculated by subtracting the weight of the uninoculated bottle from the weight of the filled bottle. Weights were adjusted for caps and labels. When the weight of the inoculated blood in one bottle of a pair of aerobic or anaerobic blood cultures was more than three times that of the other, the pair was excluded. After inoculation, all bottles were incubated at 37°C for 6 days.

For each episode for which multiple sets of blood cultures were positive, we considered only the pair of the set containing the earliest positive aerobic or anaerobic culture.

The definitions proposed by the Centers for Disease Control and Prevention, Atlanta, Ga., were used for positive bloodstream cultures and contaminants (6, 15).

The time to positivity of each sample, and the difference between the time to positivity of peripheral aerobic and central aerobic blood cultures or of peripheral anaerobic and central anaerobic cultures (ΔTP), were calculated and expressed in hours and decimal fractions.

Positive samples were Gram stained, and microorganisms were cultured in the appropriate media for identification, using conventional methods. Susceptibility testing allowed us to compare samples of the same species.

Statistical methods. To determine the optimal threshold of the test, a receiver operating characteristic (ROC) curve (19) was constructed with the ΔTP values obtained for the patients having CRB and the values obtained for the patients having bacteremia due to another source. The PROC LOGISTIC of the SAS Software (SAS Institute Inc., Cary, N.C.) was used. Differences between the ΔTP values obtained for patients having CRB and for those having bacteremia due to another source were calculated by the median test. Positive and negative predictive values were also calculated by taking into account the values for the prevalence of CRB shown in three U.S. cancer centers (13, 16, 17) and in one of our own hospitals.

RESULTS

Preliminary study. In the preliminary study in vitro, the trend curves obtained with the microorganisms tested confirmed the inverse linear relationship between the microbial inoculum and the time to positivity of the culture for each strain. However, the slopes of the curves of *E. coli*, *P. aeruginosa*, and *S. epidermidis* were similar, but the curve of *C. albicans* was not as steep.

Assessment of the validity of the test. This prospective study was carried out from 14 June 1995 to 17 December 1996. We counted 213 infectious episodes, 106 of which were excluded (3 for inappropriate weight of the inoculated blood in one of a paired bottles, 1 for different microorganisms in each paired bottle, and 102 for positivity of only one of the paired bottles, including 32 classified as contaminants). Of the remaining 107 episodes, 21 corresponded to patients having CRB, 9 corresponded to patients having bacteremia due to another source, and 77 corresponded to patients having bacteremia from an unknown source.

TABLE 1. Sensitivity and specificity of the 30 ΔTP values determined by a ROC curve

ΔTP (h)	Sensitivity (95% CI[a])	Specificity (95% CI)
−54.40	1.00 (0.762–0.999)	0.00
−41.00	0.95 (0.762–0.999)	0.00 (0.002–0.482)
−2.10	0.95 (0.696–0.988)	0.11 (0.002–0.482)
−1.60	0.90 (0.634–0.970)	0.11 (0.002–0.482)
−1.00[b]	0.86 (0.634–0.970)	0.14 (0.075–0.701)
−0.20[b]	0.86 (0.581–0.946)	0.38 (0.137–0.788)
0.00[c]	0.81 (0.581–0.946)	0.80 (0.518–0.997)
0.30	0.81 (0.581–0.946)	1.00
3.00[d]	0.80 (0.528–0.918)	1.00
4.00[b]	0.74 (0.430–0.854)	1.00
5.00	0.65 (0.384–0.819)	1.00
8.30	0.60 (0.340–0.782)	1.00
8.80	0.55 (0.298–0.743)	1.00
9.00[b]	0.47 (0.218–0.660)	1.00
13.00	0.40 (0.181–0.616)	1.00
14.00	0.35 (0.146–0.567)	1.00
15.00	0.30 (0.113–0.522)	1.00
17.00	0.25 (0.082–0.472)	1.00
24.00	0.20 (0.054–0.419)	1.00
26.00	0.15 (0.030–0.363)	1.00
26.70	0.10 (0.012–0.304)	1.00
35.00	0.05 (0.001–0.238)	1.00
60.40	0.00	1.00

[a] CI, confidence interval.
[b] Value was obtained with two experimental points.
[c] Value was obtained with four experimental points.
[d] Optimum threshold (100% specificity and optimal sensitivity).

Construction of the ROC curve showed that the ΔTP threshold with 100% specificity and 81% sensitivity was ≥+3 h (Table 1 and Fig. 1). The positive and negative predictive values were calculated, with a ΔTP of 3 h, taking into account the values for the prevalence of CRB shown in three U.S. cancer centers (13, 16, 17), ranging from 10.5 to 19.7%, and taking into account our own hospital prevalence data of 1.45%. Positive predictive values were 100% for each hospital, and negative predictive values ranged from 95.6 to 97.8% for the three U.S. cancer centers; the value was 99.7% for our own data.

The ΔTP values obtained for the 21 patients having CRB ranged from −54.4 to +60.4 h (median = +9 h), and the ΔTP values obtained for the 9 patients having bacteremia due to another source ranged from −41 to +0.3 h (median = 0 h). The difference between the median values was significant ($P = 0.0003$).

Study of microorganism distribution showed that cutaneous microorganisms occurred only among the 21 CRB patients. They comprised *S. aureus* in nine episodes, coagulase-negative staphylococci in seven episodes, and *Candida* sp. in two episodes, which constituted 81.8% (18 out of 22) of all microorganisms. The other microorganisms were environmental (*P. aeruginosa*, *Acinetobacter* sp., and *Bacillus* sp.) except for one (*Klebsiella* sp.). Fourteen patients with CRB had their IVD

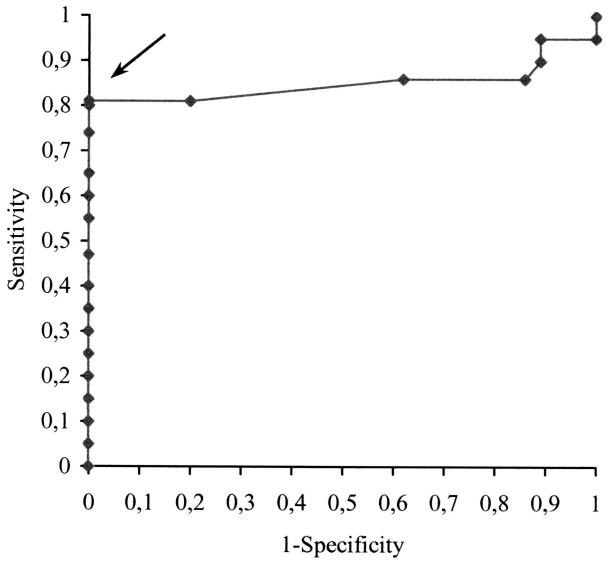

FIG. 1. ROC curve constructed from the experimental differences between times to positivity of peripheral and central blood cultures. Arrow, threshold obtained with 100% specificity and 81% sensitivity (≥+3 h).

removed, received appropriate antibiotic treatment, and were cured. Five patients were cured out of the seven having CRB who did not have IVD removed. Death, which occurred for the two uncured patients, was not related to CRB but was caused by myocardial infarction in one case and concerned a patient on palliative care in the other.

Among the nine patients having bacteremia due to another source, we counted 10 microorganisms, none of which was cutaneous. These microorganisms were *Enterobacteriaceae* species in six cases, *Streptococcus* sp. in two cases, and *Streptococcus pneumoniae* in one case. One case involved two *Enterobacteriaceae* species in the same blood sample. None of these nine patients had IVD removed, and seven were cured. Death was caused by pneumococcal pneumonia in one patient, and the other patient who died was on palliative care.

Episodes with bacteremia from an unknown source. The ΔTP cutoff point of ≥+3 h was used to post-classify the 77 episodes of bacteremia from an unknown source. Forty-four episodes with a ΔTP of ≥+3.0 h (range, +128.2 to +3.0) were classified as positive, and 33 episodes with a ΔTP of <+3.0 h (range, +2.8 to −17.0) were classified as negative. Nine patients were lost to follow-up because they left the hospital before their clinical course could be observed. These nine patients who were not included in the study corresponded to five positive and four negative post-classified episodes. This left a total of 68 episodes that were followed up (39 positive and 29 negative). The positive episodes included many more cutaneous microorganisms than the negative episodes (27 out of 41 [66%] versus 11 out of 32 [34%]; $P = 0.0075$).

The characteristics and course of the 39 positive post-classified bacteremia episodes from an unknown source were studied. Ten patients showed clinical IVD infection. Eight of them had IVD removed and were cured. The remaining two patients whose IVD was left in place were not cured within 72 h, but their clinical presentation accounted for the nonremoval. Thus, one of these patients, who had *S. aureus* bacteremia, also had a cutaneous infection due to the same *S. aureus* strain. This patient was cured within 14 days of the beginning of a suitable antibiotic treatment. The other patient, who had *E. coli* bacteremia, was on palliative care. No clinical IVD infection occurred in the last 29 positive post-classified bacteremia cases from an unknown source. The IVD was removed from two of them who were cured within ≤24 h, and the IVD was left in place in 27 of them. Fifteen, among whom were six non-neutropenic patients without any other infection, of the 27 were cured within ≤72 h of a suitable antibiotic treatment and never relapsed. We paid special attention to the positive post-classified episode caused by an *Enterobacter* sp., which affected one patient with no neutropenia or other infection. Careful study of the later clinical course of this patient showed that he did not relapse, even though the IVD was not removed. Six patients died. Four deaths were due to an infection other than CRB, and two concerned patients who were on palliative care. The remaining six patients were cured within >72 h but three of them had an infection other than CRB. Of the other three comprised patients without neutropenia or any other infection, one of them was on palliative care and the two others were cured within 96 and 120 h, respectively, without relapse.

The characteristics and course of the 29 negative post-classified bacteremia cases from an unknown source were also studied. Four of the six patients with clinical IVD infection had IVD removed and were cured. Of these, one non-neutropenic patient had bacteremia caused by both coagulase-negative staphylococci and *S. pneumoniae* and also had another infection by a microorganism different from the one in the bloodstream. The three other patients had neither neutropenia nor any other infection and were cured within 24 h. In these three patients, bacteremia was caused by pathogenic microorganisms (an *Enterobacter* sp. in one case and *S. aureus* in two cases). The two other patients with clinical IVD infection who did not have IVD removed were cured after more than 72 h, but both had an infection other than CRB and one had neutropenia.

In this group of 29 negative post-classified bacteremia cases from an unknown source, 2 of the 23 patients without clinical IVD infection had no neutropenia or any other infection and did not have IVD removed but were not cured within ≤72 h. However, one of them, who had *Listeria* sp., was cured within 96 h and did not relapse, but the other, who had CNS infection, was on palliative care.

DISCUSSION

Despite the valid guidelines issued for good practice in central venous catheterization (14, 22), CRB still occurs and is a serious infectious problem, particularly among cancer patients who need long-term catheterization (1, 13, 16, 17). For these patients, unnecessary removal of an IVD must be avoided. Until now, no easy cheap laboratory test has been available to help clinicians diagnose CRB and decide whether to remove the catheter.

The first part of this prospective study assessed the validity of the use of ΔTP as an indicator of CRB. This validity was easily obtained with the new automated blood culture systems and with the ΔTP values obtained for patients with CRB or patients with bacteremia due to another source. The results

obtained are in agreement with the definitions chosen for the study (25) and confirm the correct classification of the episodes. The ΔTP cutoff point of ≥+3 h was close to the one of ≥+2 h found by others in similar studies (4, 5). The laboratory test by which ΔTP is obtained is easy to carry out, and its results seem to be very helpful to clinicians for the diagnosis of CRB, with 100% specificity and high sensitivity (81%). The positive and negative predictive values obtained with this ΔTP cutoff point of ≥+3 h confirmed the efficacy of the test for predicting the presence or absence of CRB in cancer patients.

In the second part of this study, the usefulness of the ΔTP cutoff point of ≥+3 h based on the clinical course of the 68 post-classified episodes of bacteremia from an unknown source was more difficult to evaluate. The characteristics and course of the infections which occurred for the 39 positive and 29 negative post-classified episodes showed that in many cases, the test was no better than appreciation of the clinical and microbiological presentation.

There were many more cutaneous microorganisms among the positive post-classified episodes than among the negative ones (66% versus 34%), and the difference was significant ($P = 0.0075$). The 10 patients with a positive test (ΔTP ≥+3 h) and clinical IVD infection exhibited characteristics and a clinical course which corresponded to the criteria used to define a CRB. In these cases, the test seemed of little benefit.

The study of the usefulness of the test may have been easiest for the patients with no clinical catheter-related infection and no neutropenia or any other infection and whose IVD was not removed. But in these cases, the test did not appear to yield better results than clinical observation. It is noteworthy that even without IVD removal, a large proportion of the positive post-classified episodes without clinical IVD infection were cured after suitable antibiotic treatment based on both the clinical symptoms and the microbiological data.

CRB is known to be frequently caused by CNS, a microorganism known for its low pathogenicity and its high probability of cure without IVD removal (3) but is less often described when caused by pathogenic microorganisms (26). Therefore, it seems extremely difficult to draw any conclusions about episodes affecting patients with neutropenia and/or another infection. It is noteworthy that the positive post-classified episode caused by an *Enterobacter* sp., which affected one patient with no neutropenia or other infection, was cured within ≤24 h and that the patient did not relapse, even though the IVD was not removed.

Clinical results did not agree with those of the test for negative post-classified episodes showing IVD infection. Study of the clinical course of negative post-classified episodes without clinical IVD infection involved many difficulties. Firstly, for patients whose IVD was removed and who had either an infection other than CRB or neutropenia, the return to a normal temperature could have been due either to antibiotic treatment for the other infection or to the end of their neutropenia. Secondly, for patients whose IVD was not removed, the time to cure of the fever was due to their clinical status, especially when they were neutropenic, whether or not they had an infection other than CRB.

Analysis of the results for the 68 undetermined episodes shows the slight usefulness of the time-to-positivity test when the clinical presentation is obvious. For cancer patients, the clinical symptoms, the presence or absence of a clinical IVD infection, and the microorganism species causing the bacteremia appear to provide sufficient information in most cases. Despite the high specificity and sensitivity of this attractive test, we therefore suggest limiting its use to febrile neutropenic cancer patients, especially when it is positive, and when clinical signs of IVD infection are slight or absent. In this way, the test could provide additional information for clinicians who hesitate to remove a very effective IVD, especially when the bacteremia is caused by a pathogenic microorganism.

ACKNOWLEDGMENTS

We are grateful to F. Cuzon, A. Crevoisier, J. Elart, V. Fournier-Boutault, S. Lecuru, and C. Mestrude for technical assistance.

REFERENCES

1. **Astagneau, P., S. Maugat, T. Tran-Minh, M. C. Douard, P. Longuet, C. Maslo, R. Patte, A. Macrez, and G. Brücker.** 1999. Long-term central venous catheter infection in HIV-infected and cancer patients: a multicenter cohort study. Infect. Control Hosp. Epidemiol. **20:**494–498.
2. **Atela, I., P. Coll, J. Rello, E. Quintana, J. Barrio, F. March, F. Sanchez, P. Barraquer, J. Ballus, A. Cotura, and G. Prats.** 1997. Serial surveillance cultures of skin and catheter hub specimens from critically ill patients with central venous catheters: molecular epidemiology of infection and implications for clinical management and research. J. Clin. Microbiol. **35:**1784–1790.
3. **Blanc Vincent, M. P., T. Lesimple, J. Béal, M. C. Escande, C. Lion, V. Bussy, P. Biron, B. Pottecher, F. Crokaert, J. M. Senet, C. Fuhrmann, J. Raveneau, and M. Viot.** 1999. Standards, options et recommandations pour la prévention, le diagnostic et le traitement des infections liées aux voies veineuses en cancérologie, p. 63–128. *In* Fédération nationale des Centres de lutte contre le cancer standards, options et recommandations, infection et cancer. John Libbey Eurotext, Paris, France.
4. **Blot, F., E. Schmidt, G. Nitenberg, C. Tancrede, B. Leclercq, A. Laplanche, and A. Andremont.** 1998. Earlier positivity of central-venous- versus peripheral-blood cultures is highly predictive of catheter-related sepsis. J. Clin. Microbiol. **36:**105–109.
5. **Blot, F., G. Nitenberg, E. Chachaty, B. Raynard, N. Germann, S. Antoun, A. Laplanche, C. Brun-Buisson, and C. Tancrede.** 1999. Diagnosis of catheter-related bacteremia: a prospective comparison of time to positivity of hub-blood versus peripheral-blood cultures. Lancet **354:**1071–1077.
6. **Bone, R. C., R. A. Balk, F. B. Cerra, R. P. Dellinger, A. M. Fein, W. A. Knaus, R. M. Schein, and W. J. Sibbald.** 1992. Definitions for sepsis and organ failure and guidelines for the uses of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest **101:**1644–1655.
7. **Brun-Buisson, C., F. Abrouk, P. Legrand, Y. Huet, S. Larabi, and M. Rapin.** 1987. Diagnosis of central venous catheter-related sepsis. Arch. Intern. Med. **147:**873–877.
8. **Brun-Buisson, C., F. Doyon, J. Carlet, P. Dellamonica, F. Gouin, A. Lepoutre, J. C. Mercier, G. Offenstadt, and B. Régnier.** 1995. Incidence, risk factors, and outcome of severe sepsis and septic shock in adults. A multicenter prospective study in intensive care units. JAMA **274:**968–974.
9. **Brun-Buisson, C., F. Doyon, and J. Carlet.** 1996. Bacteremia and severe sepsis in adults: a multicenter prospective survey in ICUs and wards of 24 hospitals. Am. J. Respir. Crit. Care Med. **154:**617–624.
10. **Capdevila, J. A., A. M. Planes, M. Palomar, I. Gasser, B. Almirante, A. Pahissa, E. Crespo, and J. M. Martinez-Vazquez.** 1992. Value of differential quantitative blood cultures in the diagnosis of catheter related sepsis. Eur. J. Clin. Microbiol. **11:**403–407.
11. **Capdevila, J. A.** 1997. Current methods for the diagnosis of catheter-related bacteremia. Rev. Med. Microbiol. **8:**189–195.
12. **Coullioud, D., P. Van der Auwera, M. Viot, and C. Lasset.** 1993. Prospective multicentric study of the etiology of 1051 bacteremic episodes in 782 cancer patients. Supportive Care Cancer **1:**34–46.
13. **Eastridge, B. J., and A. T. Lefor.** 1995. Complications of indwelling venous access devices in cancer patients. J. Clin. Oncol. **13:**233–238.
14. **Elliott, T. S. J., M. H. Faroqui, R. F. Armstrong, and G. C. Hanson.** 1994. Guidelines for good practice in central venous catheterization. J. Hosp. Infect. **28:**163–176.
15. **Gardner, J., W. R. Jarvis, T. G. Emori, T. C. Horan, and J. M. Hugues.** 1988. CDC definitions for nosocomial infections. Am. J. Infect. Control **16:**128–140.
16. **Groeger, J. S., A. B. Lucas, H. T. Thaler, H. Friedlander-Klar, A. E. Brown, T. E. Kiehn, and D. Armstrong.** 1993. Infectious morbidity associated with long term use of venous access devices in patients with cancer. Ann. Intern. Med. **119:**1168–1174.

17. **Keung, Y. K., K. Watkins, S. C. Chen, S. Groshen, H. Silberman, and D. Douer.** 1994. Comparative study of infectious complications of different types of chronic central venous access devices. Cancer **73:**2832–2837.
18. **Maki, D. G., C. E. Weise, and H. W. Sarafin.** 1977. A semiquantitative culture method for identifying intravenous-catheter-related infection. N. Engl. J. Med. **296:**1305–1309.
19. **Metz, C. E.** 1978. Basic principles of ROC analysis. Semin. Nucl. Med. **4:** 283–298.
20. **Mosca, R., S. Curtas, F. Forbes, and M. M. Meguid.** 1987. The benefits of isolator cultures in the management of suspected catheter sepsis. Surgery **102:**718–723.
21. **Nolte, F. S., J. M. Williams, R. C. Jerris, J. A. Morello, C. D. Leitch, S. Matushek, L. D. Schwabe, F. Dorigan, and F. E. Kocka.** 1993. Multicenter clinical evaluation of a continuous monitoring blood culture system using fluorescent-sensor technology (BACTEC 9240). J. Clin. Microbiol. **31:**552–557.
22. **Pearson, M. L., and the Hospital Infection Control Practices Advisory Committee.** 1996. Guidelines for prevention of intra-vascular-device-related infections. Infect. Control Hosp. Epidemiol. **17:**438–473.
23. **Pittet, D., D. Tarara, and R. P. Wenzel.** 1994. Nosocomial bacteremia in critically ill patients. JAMA **271:**1598–1601.
24. **Pizzo, P. A.** 1989. Evaluation of fever in the patient with cancer. Eur. J. Cancer Clin. Oncol. **25:**S9–S16.
25. **Raad, I. I., and G. P. Bodey.** 1992. Infectious complications of indwelling vascular catheters. Clin. Infect. Dis. **15:**197–210.
26. **Rubin, L. G., S. Shih, A. Shende, G. Karayalcin, and P. Lanzkowsky.** 1999. Cure of implantable venous port-associated bloodstream infections in pediatric hematology-oncology patients without catheter removal. Clin. Infect. Dis. **29:**102–105.
27. **Siegman-Igra, Y., A. M. Anglim, D. E. Shapiro, K. A. Adal, B. A. Strain, and B. M. Farr.** 1997. Diagnosis of vascular catheter-related bacteremia: a meta-analysis. J. Clin. Microbiol. **35:**928–936.
28. **Thorpe, T. C., M. L. Wilson, J. E. Turner, J. L. Diguiseppi, M. Willert, S. Mirrett, and L. B. Reller.** 1990. BacT/Alert: an automated colorimetric microbial detection system. J. Clin. Microbiol. **28:**1608–1612.