Hickman-Broviac Catheter-Related Infections in Children with Malignancies

SOTIRIS C. STAMOU, M.D.[1], HELEN C. MALTEZOU, M.D.[2], APOSTOLOS POURTSIDIS, M.D.[3], THEODORA PSALTOPOULOU, M.D.[1], CONSTANTINE SKONDRAS, M.D.[1], AND THEODORE AIVAZOGLOU, M.D.[4]

Abstract

Infectious complications are frequently encountered following Hickman-Broviac (H-B) catheter insertion. The medical records of 164 children with malignancies who underwent H-B catheter insertion from March 1, 1988 to December 31, 1997 were reviewed retrospectively. During a 35,697 catheter-day period, 77 catheter-related infections occurred, including 50 catheter-insertion-site infections and 27 bloodstream infections. The risk for the development of catheter-related infections was 2.15 per 1000 catheter-days (1.4 and 0.75 per 1000 catheter-days for catheter-insertion-site and bloodstream infections, respectively). In 17 (63%) of 27 episodes of bloodstream infections, antimicrobial treatment controlled the infection without catheter removal. A previous catheter-insertion-site infection caused by *Staphylococcus epidermidis* (p=0.01), the occurrence of mechanical catheter complications (p=0.007), and a normal coagulation status of the host (p=0.03) were significantly associated with the development of catheter-related bloodstream infections. H-B catheters remain important in pediatric oncology. Due to the significant morbidity associated with the development of catheter-related bloodstream infections, risk factors found to increase the incidence rate of such infections must be identified and properly managed. **Key Words:** Hickman-Broviac catheters, bloodstream infections, children, malignancies.

Introduction

CENTRAL VENOUS CATHETERS are widely used in children with malignancies. First described by Broviac (1) in 1973 and later modified by Hickman (2) in 1979, Hickman-Broviac (H-B) catheters constitute a useful tool for administration of chemotherapy, antimicrobial agents, blood products, hydration and total parenteral nutrition (3). Advantages over the usage of peripheral venous catheters include reduction of development of chemotherapy-induced dermatitis and improvement of the patient's quality of life, due to the avoidance of recurrent venipunctures (3). However, H-B catheter usage may be complicated by the development of bloodstream and catheter-insertion-site infections, and mechanical complications. The development of such infections in children with malignancies is a significant risk, due mainly to their deficient immune mechanisms (3). Therefore, identification of risk factors associated with the development of catheter-related infections in these patients is imperative. We present our 10-year experience on the use of H-B catheters in children with malignancies. In addition, the associated risk factors for the development of catheter-related infections and possible mechanisms accounting for such complications are discussed.

From the [1]Department of Pediatric Surgery and [2]Second Department of Pediatrics, University of Athens, Athens, Greece; [4]Department of Pediatric Surgery, Elena General Hospital, Athens, Greece, and [3]Department of Pediatric Oncology, Aglaia Kyriakou Children's Hospital, Athens, Greece.

Presented at the 3rd Symposium for the Control of Surgical Infections, Florence, Italy, April 14–16, 1999.

Address correspondence to Sotiris C. Stamou, M.D., 2950 Van Ness Street NW, Washington, DC 20008.

Patients and Methods

Patients

All children 14 years old or younger with a malignancy, who underwent H-B catheter insertion for therapeutic and/or supportive purposes at the Department of Oncology of the Aglaia

Kyriakou Children's Hospital from March 1, 1988 to December 31, 1997 were identified through a computerized database system. Patients who received more than one H-B catheter were excluded from the study. Patients were followed from the time of catheter insertion to the time of catheter removal (if any), or the most recent follow-up, whichever occurred first. The medical records of the patients were reviewed in detail and the following information was collected: age at the time of catheter insertion, sex, underlying disease, date of catheter insertion, vein of catheter insertion, usage of antimicrobial prophylaxis, date of catheter removal (if any), and reason for catheter removal. In cases where catheter-related infection developed, additional information was collected, including date of development of catheter-related infection, presence of fever, signs of inflammation at the catheter-insertion-site, neutropenia, coagulation status, microbiological reports, antimicrobial treatment, and outcome of the patient. The study was approved by the scientific committee of Aglaia Kyriakou Children's hospital.

Definitions

Fever was defined as a temperature of 38°C or more that was unrelated to the administration of blood products or other pyrogenic substances. Routine fever work-up included catheter-insertion-site cultures, blood cultures through the catheter, and peripheral blood cultures. Neutropenia was defined as an absolute neutrophil count of less than 500/μL. Abnormal coagulation status was defined as a prothrombin or partial prothrombin time of more than 3 times the values of healthy control blood donors and/or as an absolute platelet count of less than 50,000/μL. Bloodstream infection was defined as isolation of a pathogen from the blood at least once, except for coagulate-negative staphylococci for which at least two positive cultures in a 72-hour period were required. An infectious episode that developed within 30 days of an initial episode was counted as part of that episode. Definite catheter-related bloodstream infection was defined as presence of fever along with a positive blood culture obtained through the catheter in association with a negative blood culture obtained through a peripheral vein (3, 4). Probable catheter-related bloodstream infection was defined as fever along with a positive blood culture obtained through the catheter and a positive blood culture obtained peripherally with no other focus of infection (3, 4). Catheter-insertion-site infection was defined as signs of inflammation at the catheter-insertion-site (e.g., redness, edema, warmth, tenderness, discharge) and pathogen isolation from the catheter-insertion-site discharge with or without fever (3, 4). Mechanical catheter complications included catheter translocation, dislodgment, obstruction, and malfunction, as well as rupture of the catheter and hematoma at the site of catheter insertion.

Clinical Methods

The right atrial catheters used for venous access were Silastic subcutaneously tunneled H-B catheters (Bard Co., Salt Lake City, UT). All catheters were placed in the operating room by the same team of pediatric surgeons. Antimicrobial prophylaxis consisted of either cefotaxime 50 mg/kg or vancomycin 10 mg/kg, administered intravenously in a single dose within one hour prior to catheter insertion. In the postoperative period, the site of insertion was cleansed with povidone-iodine on a daily basis; following patient's discharge, cleansing was carried out every 72 hours. Following cleansing, povidone-iodine ointment and sterile dressing were applied locally. Catheter dressings (gauze or clear plastic dressings) were changed in hospitalized patients twice per week and in outpatients once per week. The catheter was flushed once daily with sterile heparinized saline (500 IU heparin in 3 mL of normal saline), and the injection cap was changed weekly. Routine surveillance cultures were not performed. Whenever patients had fever and/or neutropenia, catheter-insertion-site cultures, blood cultures through the catheter and peripheral blood cultures were attempted. Treatment of catheter-related infections consisted of a 10–14 day IV course of either vancomycin 10 mg/kg b.i.d. or ceftazidime 50 mg/kg t.i.d. administered through the catheter. Antimicrobial treatment was considered successful in cases of negative blood and catheter-insertion-site cultures, with no catheter removal required for infection control and treatment. A catheter was removed when fever persisted for 72 hours or more and/or positive blood cultures (either through the catheter or peripherally) were obtained beyond 72 hours of antimicrobial treatment based on susceptibility pathogen testing. Mechanical complications were managed by repair of the catheter, if damaged, movement of catheter position, relief of occlusion or replacement of the device, as appropriate.

Statistical Analysis

An intention-to-treat statistical analysis was used in this study. All statistical analyses were

two-tailed. Odds ratios were used as the measure of association, Z-scores were calculated (5), and corresponding p-values obtained. For bloodstream infections, the time to the event was used in a Kaplan-Meier survival analysis (6), the survival time being the infection-free interval. A univariate analysis searching for risk factors for bloodstream infections was conducted, including the following variables: age, sex, underlying disease, neutropenia, coagulation status, catheter-insertion-site infections, specific pathogens involved in catheter-insertion-site infections, and mechanical catheter complications. Multivariate analysis used stepwise forward logistic regression analysis with days of follow-up as a covariate, predictor factors as independent variables, with the probability of first infection as the dependent variable (7). In the multivariate logistic regression analysis, each patient was observed until the first episode of catheter-related infection. Categorical variables were studied using Fisher's exact test for proportions with appropriate degrees of freedom. In the analysis of quantitative variables, Student's unpaired t-test was used for variables with normal distributions and the Mann-Whitney U-test for variables with non-normal distributions. Values of $p \leq 0.5$ were considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows '95, version 7.5).

TABLE 1
Baseline Characteristics of Patients

	No. of patients (%) (n=164)
Age	
≤3 years	42 (26)
>3 years	122 (74)
Sex	
males	80 (49)
females	84 (51)
Underlying disease	
leukemia	107 (65)
solid tumors	57 (35)
Mechanical complications	
translocation	5 (3)
dislodgment	13 (8)
obstruction	7 (4)
malfunction	7 (4)
rupture	2 (1)
hematoma	8 (5)
Absolute neutrophil count	
$<100/mm^3$	15 (9)
$100-500/mm^3$	21 (13)
$>500/mm^3$	128 (78)
Coagulation status	
normal	135 (82)
abnormal	29 (18)

Results

During the study period, 185 children with H-B catheters were identified. Twenty-one patients were either excluded due to multiple H-B catheter insertions (18 patients) or lost to follow-up (3 patients). Therefore, the study population comprised 164 patients, of whom 84 were girls (51%) and 80 were boys (49%). Patients' median age was 5 years (range, 2 months to 14 years). Their characteristics are listed in Table 1. Inserted catheters included Broviac catheters in 133 (81%) patients and Hickman catheters in 31 (19%) patients. External and internal jugular veins were used in 130 (79%) patients and 34 (21%) patients, respectively. Catheters were inserted for a median of 235 days (range, 7–690 days). Overall, 35, 697 days of catheter usage were studied.

During the study period, 63 (38%) of the 164 children developed a total of 77 episodes of catheter-related infections, including 50 catheter-insertion-site infections and 27 bloodstream infections. The median number of catheter-related infections per patient infected was 1 (range, 1–2 catheter-related infections). In particular, 36 patients developed catheter-site infections only, 14 developed catheter-insertion-site infection followed by bloodstream infections, and 13 developed catheter bloodstream infections only. Twenty (40%) and 30 (60%) out of 50 catheter-insertion-site infections developed in the exit portion and tunnel, respectively. The number of probable episodes, and definite episodes, of catheter-related bloodstream infections were 17 (63%) and 10 (37%) episodes, respectively.

The risk for the development of catheter-related infections was 2.15 per 1000 catheter-days, and 1.4 and 0.75 per 1000 days for catheter-insertion-site and bloodstream infections, respectively. The median time interval from the time of catheter insertion to the onset of catheter-related infection was 30 days (range, 1–400 days). Catheter-insertion-site infections occurred at a median of 27.5 days (range, 1–400 days) following catheter insertion, while catheter-related bloodstream infections occurred at a median of 31 days (range, 5-390 days) following catheter insertion. Pathogens detected in catheter-related infections are summarized in Table 2. *Staphylococcus epidermidis* was the predominant isolate in patients with either catheter-insertion-site infections or catheter-related bloodstream infections, independent of age, catheter-insertion-vein, neutropenia, and coagulation status of the patient.

TABLE 2
Isolated Pathogens in Catheter-Related Infections

Pathogen	Catheter-insertion-site infections	Bloodstream infections
Staphylococcus epidermidis	30 (60)	15 (56)
Staphylococcus aureus	15 (30)	5 (18)
Escherichia coli	2 (4)	2 (7)
Pseudomonas aeruginosa	2 (4)	1 (4)
Klebsiella pneumoniae	0 (0)	2 (7)
Salmonella	0 (0)	1 (4)
Candida albicans	1 (2)	1 (4)

Values in parentheses represent %

Antimicrobial treatment consisted of vancomycin in 60 (78%) of 77 episodes of catheter-related infections and cefotaxime in the remaining 17 (22%) patients. Of the 77 episodes of catheter-related infections, 63 (82%) responded promptly to antimicrobial treatment while catheter removal was required in 14 of them (18%). In particular, treatment was successful in 46 (92%) of the 50 episodes of catheter-insertion-site infections, while catheter removal was required in 4 (8%). Pathogens responsible for the catheter-insertion-site infections requiring catheter removal included *S. epidermidis* (n=2) and *Staphylococcus aureus* (n=2). Only two of the four patients needed catheter replacement and no recurrent infection was documented. Among the 27 episodes of bloodstream infections, treatment was successful in 17 (63%), as compared to 10 (37%) episodes, where removal was required. The following pathogens were detected in the catheters removed from patients with bloodstream infections: *S. epidermidis* (n=5, 50%), *S. aureus* (n=3, 30%), *Pseudomonas aeruginosa* (n=1, 10%), and *Candida albicans* (n=1, 10%). In total, catheters had to be removed in 9 (15%) out of 60 episodes treated with vancomycin and in 5 (29%) out of 17 episodes treated with cefotaxime (p=0.15).

Mechanical catheter complications occurred in 42 (26%) of the 164 patients. In 24 (57%) of the 42 patients with mechanical catheter complications, the catheter had to be removed, while flushing with heparin solution and repositioning of the catheter was required in 10 (24%) and 8 (19%) of them, respectively. In total, catheters were removed in 149 patients (91%) of the 164 patients, at a median of 235 days (range, 7–690 days) following catheter insertion. At the end of the study period, 15 catheters (9%) were still in place. Reasons for removing a catheter were: (1) the completion of chemotherapy in 96 out of 149 patients (64%); (2) mechanical complications in 24 out of 149 patients (16%); (3) death unrelated to catheter insertion in 19 out of 149 patients (13%); and (4) catheter-related infections in 10 out of 149 patients (7%). During the study period, no episode of death due to catheter-related infections occurred among the 164 patients studied. However, 2 out of 27 patients (7%) with bloodstream infection expired at 690 and 400 days following catheter insertion, of disseminated carcinomatosis and massive pulmonary embolism, respectively.

Risk Factors for Catheter-Related Bloodstream Infections

A univariate statistical analysis searching for risk factors for the development of catheter-related bloodstream infections in children with malignancies was conducted (Table 3). On logistic regression analysis, the following parameters emerged as statistically significant risk factors for the development of catheter-related bloodstream infections: a prior catheter-insertion-site infection with *S. epidermidis* (OR=3, 95% CI: 1.2–7.1, p=0.01), the occurrence of mechanical catheter complications (OR=4.1, 95% CI: 1.7–9.8, p=0.007) (Figure), and a normal coagulation status of the patient (OR=6.7, 95% CI: 1.6–51.8, p=0.03).

Discussion

H-B catheters are widely accepted as an effective means for vascular access over an

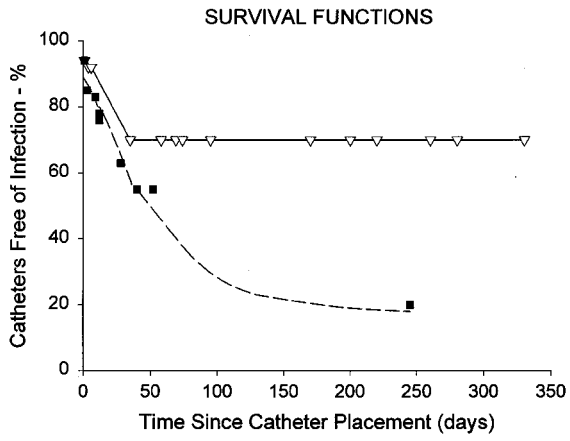

Figure. Kaplan-Meier survival curves of H-B catheters without mechanical catheter complications (open triangles and solid black line) and H-B catheters with mechanical complications (gray squares and dashed line). Survival curve indicates percentage of catheters that remain infection-free over time. A catheter is withdrawn from the analysis when infection first occurs in the catheter. Curves show statistically significant difference (p=0.03 by log-rank test).

TABLE 3
Univariate Analysis for Risk Factors for Catheter-Related Bloodstream Infections

	Bloodstream Infections N (%)	Catheter-days	Infection rate /1000 catheter-days	OR	CI	p
Age						
≤3 years	6 (22)	8327	0.7	1.2	0.4–3.3	0.8
>3 years	21 (78)	27370	0.7	1.00		
Sex						
females	12 (44)	19057	0.6	0.9	0.6–1.5	0.5
males	15 (56)	16640	0.9	1.00		
Mechanical complications						
yes	14 (52)	7561	1.8	4.1	1.7–9.8	0.001
no	13 (48)	28136	0.4	1.00		
Coagulation status						
normal	26 (96)	29559	0.9	6.7	1.6–51.8	0.02
abnormal	1 (4)	6138	0.2	1.00		
Catheter colonization						
yes	14 (52)	11099	1.3	2.9	1.2–6.9	0.01
no	13 (48)	24598	0.5	1.00		
Neutropenia						
yes	6 (22)	7936	0.7	0.9	0.4–2.1	0.5
no	21 (78)	27761	0.7	1.00		
Disease						
leukemia	19 (70)	22754	0.8	1.3	0.5–3.2	0.6
solid tumors	8 (30)	12943	0.6	1.00		

* Comparisons were performed with Fisher's exact test, OR=odds ratio; CI=95% confidence intervals.

extended time period in children with malignancies. However, their wide usage has been associated with the subsequent development of infectious and mechanical complications (8–12). Previous reports have documented an infectious complication rate of 0.1–0.7 per 1000 catheter-days (12–20). The present study demonstrates that H-B catheters constitute a safe therapeutic intervention in children with malignancies. The rates of catheter-insertion-site infections (1.4 per 1000 catheter-days) and catheter-related bloodstream infections (0.75 per 1000 catheter-days) were low and comparable to those previously reported (2, 11, 14, 17).

Mechanical complications of H-B catheters have been well recognized as potentially associated with the development of bloodstream infections (20–22). The present study showed that mechanical complications are associated with a 4-fold increased risk for bloodstream infections as well as for catheter-insertion-site infections. The underlying cause for such an association might be inflammation following local trauma which predisposes bacterial colonization and growth at the site.

The development of a prior catheter-insertion-site infection was associated with a 3-fold increased risk for subsequently developing a bloodstream infection, especially when the colonizing organism was a coagulase-negative staphylococcus. Biofilm, the thrombin sleeve around the catheter, produced by the inflammatory reaction of the organism, is the main site of staphylococcal colonization (3). Coagulase-negative staphylococci adhere to fibronectin and not to fibrin of the biofilm (3, 23–29). The ability of this pathogen to colonize catheters is due to its prevalence on the skin and its capacity to adhere to and degrade catheter material, as well as to produce a self-protective glycocalyx substance or extracellular slime (3, 23–29). Microbial organisms such as slime-producing coagulase-negative staphylococci enhance their adherence by producing this glycocalyx material, which constitutes the microbial substance of the biofilm. Following the formation of the biofilm around the catheter, the embedded organisms are highly protected from antimicrobial agents, neutrophils and macrophages (23–25). Consequently, colonizing organisms can easily pass to the bloodstream and cause bacteremia. There is conflicting evidence regarding the value of antimicrobial prophylaxis administered prior to H-B catheter insertions (11, 30, 31). All patients in the present study had received prophylactic agents intravenously prior to catheter insertion.

In the present study, patients with normal coagulation status had a 7-fold higher risk for developing a bloodstream infection, as compared with patients with abnormal coagulation status. A possible explanation for this finding might be that the reduced formation of the fibrin and fibronectin

layer of the biofilm in patients with abnormal coagulation status prevents bacterial adherence on the catheter material (27–29). Furthermore, catheter clotting was more probable in patients with normal coagulation status, predisposing them to catheter-related bloodstream infections.

Despite the previously reported increased bloodstream infection rate among patients younger than three years of age, the present study did not confirm these results (9). A possible explanation might be the small number of such patients in the present study. Moreover, in the present study, febrile patients with H-B catheters were found to be at significant risk for systemic bacterial infections, regardless of their absolute neutrophil count. However, Hiemenz et al. reported that the insertion of central venous catheters was associated with a 10-fold increased rate of bloodstream infection rate among patients with normal absolute neutrophil counts as compared to neutropenic patients (32). Indeed, the failure to reveal an association between neutropenia and bloodstream infections supports the view that H-B catheter insertion independently enhances the incidence of bacteremia.

In the present study, no significant association was documented between specific pathogens and the risk of treatment failure after bloodstream infections. In previous studies, catheter-related bloodstream infection with *S. aureus* was associated with a higher risk of treatment failures and therefore for subsequent need for catheter removal (8, 33).

Factors that were significantly associated, in the present study, with the development of catheter-related bloodstream infections included a prior catheter-insertion-site infection with *S. epidermidis*, the occurrence of mechanical catheter complications, and a normal coagulation status of the patient. It is suggested that in children with malignancies, who develop an H-B catheter-insertion-site infection, empiric antistaphylococcal treatment should be prescribed in association with avoidance of catheter manipulations. An interesting finding of the present study was that in the majority of cases with catheter-related bloodstream infections, catheter removal was not required in order to control infection. Antimicrobial treatment was highly effective and no child died of catheter-related infection.

Limitations of our study were the exclusion of patients with multiple H-B catheter insertions, which may bias toward a more favorable outcome of patients selected. Future prospective studies might be needed to investigate risk factors for catheter-related bloodstream infection in this subset of patients. Additionally, the retrospective methodology could not, with certainty, establish direct causal relationships.

In conclusion, H-B catheters remain a safe and effective tool in the management of pediatric malignancies. This finding implies the need to recognize and properly manage risk factors for bloodstream infections in children with malignancies, in whom H-B catheters have been inserted.

References

1. Broviac JW, Cole JJ, Scribner BH. A silicone right atrial catheter for prolonged parenteral alimentation. Surg Gynecol Obstet 1973; 136:604–606.
2. Hickman RO, Buckner CD, Clift RA, et al. A modified right atrial catheter for access to the venous system in marrow transplant recipients. Surg Gynecol Obstet 1979; 148:871–875.
3. Raad II, Bodey GP. Infectious complications of indwelling vascular catheters. Clin Infect Dis 1992; 15:197–210.
4. Pearson ML. The Hospital Infection Control Practices Advisory Committee: Guideline for prevention of intravascular device-related infections. Infect Control Hosp Epidemiol 1996; 17:438–473.
5. Rothman KJ. Modern epidemiology. Boston (MA): Little Brown; 1986. pp. 177–236.
6. Elandt-Johnson RC, Johnson NL. Survival models and data analysis. New York: Wiley; 1980. pp. 150–180.
7. Abbott RD. Logistic regression in survival analysis. Am J Epidemiol 1985; 121:465–471.
8. Wurzel CL, Halom K, Feldman JG, Rubin LG. Infection rates of Broviac-Hickman catheters and implantable venous devices. Am J Dis Child 1988; 142:536–540.
9. Johnson PR, Decker MD, Edwards KM, et al. Frequency of Broviac catheter infections in pediatric oncology patients. J Infect Dis 1986; 154:570–578.
10. Smith RC, Hartemink RJ, Duggan D. Prolonged multipurpose venous access in burned patients: Three years experience with Hickman right atrial catheters. J Trauma 1985; 25:634–638.
11. Press OW, Ramsey PG, Larson EB, et al. Hickman catheter infections in patients with malignancies. Medicine 1984; 63:189–200.
12. Raucher HS, Hyatt AC, Barzilai A, et al. Quantitative blood cultures in the evaluation of septicemia in children with Broviac catheters. J Pediatr 1984; 104:29–33.
13. Thomas JH, MacArthur RI, Pierce GE, Hermreck AS. Hickman-Broviac catheters. Indications and results. Am J Surg 1980; 140:791–796.
14. Fuchs PC, Gustafson ME, King JT, Goodall PT. Assessment of catheter-associated infection risk with the Hickman right atrial catheter. Infect Control 1984; 5:226–230.
15. Pessa ME, Howard RJ. Complications of Hickman-Broviac catheters. Surg Gynecol Obstet 1985; 161:257–260.
16. Cairo MS, Spooner S, Sowden L, et al. Long-term use of indwelling multipurpose Silastic catheters in pediatric cancer patients treated with aggressive chemotherapy. J Clin Oncol 1986; 4:784–788.
17. Reed WP, Newman KA, DeJongh C, et al. Prolonged venous access for chemotherapy by means of the Hickman catheter. Cancer 1983; 52:185–192.
18. Shapiro ED, Wald ER, Nelson KA, Spiegelman KN. Broviac catheter-related bacteremia in oncology patients. Am J Dis Child 1982; 136:679–681.

19. Darbyshire PJ, Weightman NC, Speller DCE. Problems associated with indwelling central venous catheters. Arch Dis Child 1985; 60:129–134.
20. Snydman DR, Murray SA, Kornfeld SJ, et al. Total parenteral nutrition-related infections: Prospective epidemiologic study using semiquantitative methods. Am J Med 1982; 73:695–699.
21. Hampton AA, Sheretz RJ. Vascular-access infections in hospitalized patients. Surg Clin North Am 1988; 68:57–71.
22. Schuman ES, Winters V, Gross GF, Hayes JF. Management of Hickman catheter sepsis. Am J Surg 1985; 149:627–628.
23. Davenport DS, Massanari RM, Pfaller MA, et al. Usefulness of a test for slime production as a marker for clinically significant infections with coagulase-negative staphylococci. J Infect Dis 1986; 153:332–339.
24. Sheth NK, Franson TR, Sohnle PG. Influence of bacterial adherence to intravascular catheters on in vitro antibiotic susceptibility. Lancet 1985; 2:1266–1268.
25. Farber BF, Kaplan MH, Clogstron AG. *Staphylococcus epidermidis* extracted slime inhibits the antimicrobial action of glucopeptide antibiotics. J Infect Dis 1990; 161:37–40.
26. Ray S, Stacey R, Imrie M, Filshie J. A review of 560 Hickman catheter insertions. Anaesthesia 1996; 51:981–985.
27. Herrmann M, Vaudaux PE, Pitter D, et al. Fibronectin, fibrinogen and laminin act as mediators of adherence of clinical staphylococcal isolates to foreign material. J Infect Dis 1988; 158:693–701.
28. Christensen GD, Simpson WA, Younger JJ, et al. Adherence of coagulase-negative staphylococci to plastic tissue culture plates: A quantitative model for the adherence of staphylococci to medical devices. J Clin Microbiol 1985; 22:996–1003.
29. Christensen GD, Simpson WA, Bisno AL, Beachey EH. Adherence of slime-producing strains of *Staphylococcus epidermidis* to smooth surfaces. Infect Immun 1982; 37:318–324.
30. Al-Sibai MB, Harder EJ, Faskin RW, et al. The value of prophylactic antibiotics during the insertion of long-term indwelling Silastic right atrial catheters in cancer patients. Cancer 1987; 60:1891–1895.
31. Lim SH, Smith MP, Machin SJ, Goldstone AH. Teicoplanin and prophylaxis of Hickman catheter insertions. Eur J Surg Suppl 1992; 567:39–42.
32. Hiemenz J, Skelton J, Pizzo PA. Perspective on the management of catheter-related infections in cancer patients. Pediatr Infect Dis 1986; 5:6–11.
33. Van Hoff J, Berg AT, Seashore JH. The effect of right atrial catheters on infectious complications of chemotherapy in children. J Clin Oncol 1990; 8:1255–1262.