Bacteremia Associated With Tunneled, Cuffed Hemodialysis Catheters

Theodore F. Saad, MD

• **Bacteremia is a frequent complication associated with tunneled, cuffed, permanent catheters (PCs). The incidence, spectrum of infecting organisms, and optimal treatment for catheter–associated bacteremia (CAB) have not been clearly established. In this study, 101 chronic hemodialysis (HD) patients with PCs for blood access were prospectively monitored for infection during a 24-month period. Data recorded for each patient included the number of catheter-days, episodes of suspected bacteremia, blood culture results, method of treatment, complications, and outcomes. All patients with CAB were treated with a 21-day course of intravenous antibiotics. The PC was removed if the patient had uncontrolled sepsis or if other vascular access was ready for use. Once the infection was controlled, catheter salvage was attempted, either by exchanging for a new catheter over a guidewire or treating with antibiotics only, leaving the original PC in place. Catheter exchange was the recommended approach in our program, but this was decided in each case by the treating nephrologist. During this study, there were 15,581 catheter-days, with 86 episodes of CAB, or 5.5 episodes/1,000 catheter-days (95% confidence interval, 4.5 to 6.8/1,000 d). Forty-five infections (52.3%) were caused by gram-positive cocci only, including S*taphylococcus aureus*, coagulase-negative *Staphylococcus*, and *Enterococcus* species. Twenty-three infections (26.7%) were caused by gram-negative rods only, including a wide variety of enteric organisms. Eighteen infections (20.9%) were polymicrobial. Thirty-nine of 86 episodes (45.3%) included at least one gram-negative organism. Five PCs were removed because of severe uncontrolled sepsis, and eight PCs were removed because they were no longer required. Of the remaining 73 cases, attempted PC salvage was successful in 11 of 30 patients (36.7%) treated with antibiotics alone versus 35 of 43 patients (81.4%) who underwent PC exchange in addition to antibiotic therapy (*P* = 0.0005). The only important complication of CAB was endocarditis, occurring in 3 of 86 episodes (3.5%). We conclude that in our HD units, CAB is relatively common and frequently involves gram-negative bacteria. PC salvage is significantly improved when antibiotic treatment is combined with PC exchange over a guidewire.**

INDEX WORDS: Bacteremia; hemodialysis (HD); catheter.

SUBCUTANEOUSLY tunneled, cuffed, silicone, dual-lumen central venous catheters were introduced in 1984 and quickly gained acceptance for both temporary and permanent hemodialysis (HD) vascular access.[1] Whether used for long-term, temporary, or true permanent access, these devices are commonly referred to as permanent catheters (PCs). US Renal Data System data[2] show that in 1996, cuffed catheters were being used for access 60 days after the initiation of dialysis in 18.9% of HD patients. Catheter-associated bacteremia (CAB) is a serious complication of PC use and a common cause of catheter failure. Reported rates of CAB range widely. Several studies of patients using PCs for short-term vascular access have reported very low bacteremia rates: 0.15[3] and 0.21[4] episodes/1,000 catheter-days. Another study reported 0.7 episodes/1,000 catheter-days in patients with long-term PC access (median, 18.5 weeks).[5] A recent study of CAB[6] using rigorous methods for the diagnosis of bacteremia and determination of an appropriate denominator showed a much greater incidence of 3.9 episodes/1,000 catheter-days. This study also showed that gram-negative organisms were common, occurring in 31% of episodes, in contrast to most previous reports that showed predominantly gram-positive organisms,[7-9] particularly *Staphylococcus* species.

The optimal method of treatment for CAB is unknown. A long course of parenteral antibiotic therapy is commonly used. Options for management of the catheter itself include catheter removal, treatment with antibiotics while leaving the catheter in place (ABX), or combining antibiotics with catheter exchange over a guidewire (EXCH). Reported catheter salvage rates for CAB treated with ABX are poor,[5,6] ranging from 25% to 32%. Other reports of CAB have shown successful catheter salvage using an antibiotic catheter lock[10] or EXCH.[7,11,12]

Our own previous experience with PCs suggested a high incidence of bacteremia in our

From the Department of Medicine, Division of Nephrology, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Received May 27, 1998; accepted in revised form June 25, 1999.

Address reprint requests to Theodore F. Saad, MD, Nephrology Associates, PA, A94 Omega Dr, Newark, DE 19713. E-mail: tfsaad@aol.com

0272-6386/99/3406-0017$3.00/0

program, frequent gram-negative or polymicrobial infections, and poor catheter salvage when CAB was treated with ABX. Based on these observations, these data were collected to determine the incidence, bacteriology, and complications of CAB, as well as the outcomes of attempted catheter salvage. This was not designed as a prospective study to compare outcomes of different methods of catheter salvage. Based on the limited data available in 1995, our preferred approach to CAB was to treat with EXCH. However, in all cases of CAB, the method of treatment was determined exclusively by the nephrologist, based on clinical criteria. During the course of this prospective observational study, most patients with CAB underwent EXCH. Some patients were treated with ABX. Although these groups were inherently different, and it was not our original intent to compare methods of treatment for CAB, we used the opportunity created by these different treatment decisions to compare catheter salvage rates between the two techniques of attempted catheter salvage.

METHODS

Patients, Setting, and Data Collection

Data were collected prospectively on all chronic HD patients in the University Health System using a tunneled, cuffed venous catheter for dialysis access from November 1995 through October 1997. Hospitalized patients with end-stage renal disease (ESRD) with PC access who were not enrolled as University Health System chronic HD patients were excluded. Demographic information, including age, sex, race, cause and duration of ESRD, diagnosis of diabetes mellitus, and indication for PC access, was collected at the time of PC placement. All study patients were prospectively monitored for the total number of days the PC was in place from the date of insertion to the date of catheter removal or exchange, patient transfer, or death. Unassisted catheter survival was defined as the number of days from initial catheter placement to the first catheter intervention (removal or exchange for any purpose). Assisted catheter survival was defined as the total duration of catheter use through the original venipuncture, including catheters replaced over a guidewire because of malfunction, exit-site infection, or bacteremia. HD was performed in two facilities: a university hospital–based unit and an affiliated free-standing chronic outpatient unit. In both units, PCs were accessed only by experienced dialysis nurses using masks, nonsterile latex gloves, and a thorough povidone-iodine disinfection of the catheter ports before removing caps or disconnecting blood lines.

CAB Diagnosis and Treatment

Every patient with a PC who had fever, chills, or other symptoms suggesting systemic infection (eg, nausea, vomiting, malaise, or back pain) was considered to have possible bacteremia. Physical examination was performed, and other potential sources of infection were noted, including the catheter exit site or tunnel, peripheral venous catheter site, arteriovenous graft, skin ulcer, or wound. Further studies, including chest radiograph and urinalysis, were performed as indicated for specific signs or symptoms. Patients presenting with severe symptoms, including hypotension, high fever, rigors, mental status changes, or vomiting, did not have HD initiated. Those who developed severe symptoms during HD had their treatment interrupted or discontinued. If the patient was clinically stable with mild symptoms, HD was initiated or continued as prescribed. All patients with suspected bacteremia had blood cultures drawn, either directly through the catheter ports or from the ‘‘arterial’’ dialysis tubing port. Usually, at least two sets of aerobic and anaerobic cultures were obtained, although in a few cases, only one set was obtained. Peripheral blood cultures through separate venipuncture sites were not routinely performed. All patients were treated with intravenous antibiotics pending culture diagnosis. Initial coverage in most cases consisted of vancomycin combined with either gentamicin or ceftazidime. Some patients with only mild signs and symptoms of infection or a history of allergy to vancomycin received only a cephalosporin initially.

All episodes confirmed by positive blood cultures were diagnosed as CAB regardless of other possible sources and were included on this study. Antibiotics were adjusted based on culture and sensitivity results and continued for 21 days unless other indications warranted a longer course. If initial culture results were negative, the patient was not diagnosed with CAB and antibiotics were discontinued. Management of

the PC was determined by the treating nephrologist. In cases with severe or uncontrolled clinical sepsis, the PC was usually removed without an attempt to salvage the catheter. The PC was also removed if other permanent dialysis access was ready for use. If the PC was not removed and the patient responded well to antibiotics over 24 to 48 hours, catheter salvage was attempted, either with ABX or EXCH. EXCH was preferred and strongly encouraged but not required by unit policy or study protocol. Treatment was not determined by randomization, and there was no attempt to create equal treatment groups. Informed consent was not required or obtained for treatment. It was expected that the two treatment groups would be different because of the clinical factors leading to selection of ABX or EXCH.

CAB Outcomes

Patients were monitored by regular nursing assessments at each dialysis session and weekly physician visits. In most cases, follow-up blood cultures were drawn 7 to 14 days after the completion of antibiotic therapy. CAB was considered cured by clinical criteria if the patient remained afebrile and free of infectious symptoms for 30 days after completion of antibiotic therapy. Clinical cure confirmed by negative follow-up blood culture was classified as a culture-proven cure. A patient with a positive blood culture for the same bacterial species within 30 days after completion of therapy was considered a treatment failure. Treatment outcome was considered indeterminate if the patient died of causes unrelated to infection, was transferred or lost to follow-up, or responded well to therapy but, before completion of treatment or follow-up, the PC was removed for other reasons (eg, matured graft or fistula). Patients were monitored for complications, including death, endocarditis, abscess, and antibiotic allergy or toxicity.

Exit-site infection was diagnosed clinically based on pain, erythema, or purulent drainage at the exit site. Cultures of suspected infected exit sites were not uniformly obtained, and patients received either oral or parenteral antibiotics. Evidence of infection in the soft tissues or tunnel proximal to the cuff was diagnosed as tunnel infection and obligated PC removal.

Catheter Placement and Exchange Techniques

Most PCs were placed and exchanged in the inpatient dialysis unit by the author and nephrology fellows under his direct supervision. A few procedures were performed by the nephrologists in the intensive care units, the surgeons in the operating room, or the radiologists in their interventional suite. The right internal jugular vein was preferred, but if this site was unsuitable, the left internal jugular, subclavian, or femoral vein was used. Ultrasound was used for vein localization or venipuncture guidance for all new insertions after July 1996. Fluoroscopy was not used for insertion or exchange. A chest radiograph was performed after each procedure to confirm acceptable catheter course and tip position. One gram of cefazolin or cefotaxime was administered intravenously at the time of catheter placement or exchange as prophylaxis, unless the patient was allergic to cephalosporins or was already receiving antibiotics. Povidone-iodine ointment was applied to the exit site immediately after placement and with each dressing change for the first several weeks of use.

Insertions were performed using a conventional percutaneous technique.[13] The PC exchange technique varied depending on the anatomy and presence of local infection. If the catheter cuff was less than 2 cm from the exit site, the exit site was anesthetized and incised, and the cuff dissected free. In cases in which the cuff was too far to reach from the exit site, an incision was made directly over the cuff, and it was dissected free at this point. If exit-site infection was evident, a small incision was made over the proximal part of the tunnel so the catheter could be retrieved remote from the infected area. In all cases, once the cuff was free, the PC was retracted several centimeters, clamped, and then severed proximal to the cuff. Frequently a stitch was placed through the catheter to ensure that the distal segment could not be lost up the tunnel. The external portion was discarded, the field was resterilized, and all operators changed to new sterile gloves. A guidewire was then placed through the venous port of the severed catheter into the right atrium. In most cases, if the old exit site was clean, the new PC was placed over the guidewire directly through the same exit site. When required, a new exit site was incised and the new catheter was tunneled from this point to

an incision over the proximal portion of the tunnel. The new PC was then inserted over the guidewire. All incisions were closed with nylon suture.

Data Analysis

An approximate confidence interval for CAB rate was estimated assuming an exponential model for the time from catheter placement to the development of bacteremia. Differences between treatment groups were analyzed using the chi-squared or *t*-test. Outcomes were compared using multiple logistic regression analysis (StatView; SAS Institute, Cary, NC, 1998).

RESULTS

Patients and Incidence

During the 24-month study period, 101 eligible patients were dialyzed using 310 double-lumen, tunneled, cuffed catheters. Average patient age was 50.6 years. Causes of ESRD included diabetes mellitus (56.7%), hypertension (6.2%), glomerulonephritis (13%), systemic lupus erythematosus (5.2%), human immunodeficiency virus (1.0%), unknown (9.3%), autosomal dominant polycystic kidney disease (2.0%), obstruction (3.1%), and other (3.0%). There were 15,581 catheter-days. The mean unassisted and assisted catheter survival was 50 and 104 days, respectively. Most PCs were used as a bridge to arteriovenous vascular or peritoneal access in patients with new ESRD or in established patients with access failure. Catheters used included Soft-Cell (Vas-cath, Ontario, Canada), Circle-C (Neostar, Atlanta, GA), and PermCath (Quinton, Seattle, WA). The author and nephrology fellows placed 294 of these catheters, 4 were placed by the surgeons, and 12 by the radiologists.

Eighty-six new episodes of CAB occurred in 52 patients during the study period. Thirty-two patients had one episode of CAB, and 20 patients had two or more episodes (Table 1). The incidence of CAB was 5.5 episodes/1,000 catheter-days (4.5 to 6.8/1,000 d). Data were also analyzed by censoring patients after their first episode of CAB. The 52 first episodes of CAB occurred over 10,938 catheter-days, resulting in an incidence of 4.75 episodes/1,000 catheter-days. The median number of days from PC insertion to bacteremia was 74 days (range, 6 to 353 days). Twenty exit-site infections (1.25/1,000 catheter-days) and two tunnel infections were diagnosed.

Table 1. Number of Episodes of CAB per Patient

No. of Episodes	Patients
None	49
1	32
2	12
3	3
4	4
5	1
Total	101

Microbiology

A single species of gram-positive coccus was responsible for 45 of 86 episodes (52.3%) of CAB. A single species of gram-negative rod was isolated in 23 of 86 episodes (26.7%). The remaining infections were associated with more than one organism (Table 2). Gram-positive organisms were present in 67.4%, and gram-negative organisms in 45.3% of all episodes. The organisms isolated from all episodes of CAB are shown in Table 3.

Treatment and Outcome

Immediate PC removal because of severe sepsis was required in five cases (5.8%) of CAB. In eight cases (9.3%), the PC was removed without attempted salvage because other dialysis access was mature. The remaining 73 patients had PC salvage attempted. Thirty patients were treated with ABX, and 43 patients with EXCH. Patient characteristics in these two groups were similar (Table 4). The EXCH group had a higher fraction of patients requiring hospitalization than the ABX group, but this difference did not achieve significance. Outcomes in these groups are shown in

Table 2. Types of Infecting Organisms

Type of Organism	No. of Infections	%
GPC only	45	52.3
GNR only	23	26.7
Polymicrobial:		
GPC + GNR	11	12.8
GNR	5	5.8
GPC	2	2.3
Total	86	100

Abbreviations: GPC, gram-positive cocci; GNR, gram-negative rods.

Table 3. Organisms Isolated From 86 Episodes of CAB

Organism	No. of Episodes	Frequency (%)*
Coagulase-negative staphylococci	34	39.5
Methicillin-sensitive *Staphylococcus aureus*	15	17.4
Methicilin-resistant *S aureus*	4	4.7
Enterococcus sp	17	19.8
Vancomycin-resistant *Enterococcus*	0	0.0
Streptococcus sp	2	2.3
Other GPC	4	4.7
Escherichia sp	11	12.8
Acinetobacter sp	9	10.5
Pseudomonas sp	11	12.8
Enterobacter sp	14	16.3
Klebsiella sp	10	11.6
Citrobacter sp	3	3.5
Stenostrophomonas sp	3	3.5
Serratia sp	1	1.2
Diptheroids and GPR	4	4.7
Fungal	0	0.0
Total	142	

Abbreviation: GPC, gram-positive cocci; GPR, gram-positive rods.

*Number of isolates per number of CAB.

Table 5. Five patients in the ABX group and two patients in the EXCH group had indeterminate outcomes because of transfer, death, or removal of PC for reasons unrelated to infection. The remaining 66 patients with CAB with attempted catheter salvage were followed up to a definitive outcome. Thirty-five of 43 patients (81.4%) treated with EXCH had successful catheter salvage versus only 11 of the 30 patients (36.7%) treated with ABX ($P = 0.0005$). Of the 14 patients in whom ABX failed, eight catheters were removed and 6 patients underwent a second course of treatment combined with catheter exchange. Five of these patients experienced successful catheter salvage, and one outcome was indeterminate because of elective removal of PC. If these six exchanges after ABX failure were included for analysis with the EXCH group, the successful salvage for EXCH would be 40 of 49 (81.6%).

Table 4. Treatment Group Characteristics

	ABX	EXCH	*P*
Age (y)	52.2 ± 9.8 (25.3-71.6)	52.0 ± 10.9 (20.6-83.3)	>0.5
Diabetes	19/30 (63.3)	25/43 (58.1)	>0.5
Hospitalization	11/30 (36.7)	24/43 (55.8)	0.17
PC use, permanent	14/30 (46.7)	15/43 (34.9)	>0.5
Days PC in use*	68 (9-200)	75 (6-353)	>0.5
Duration of ESRD (y)	1.63 ± 0.43 (0.06-9.51)	1.15 ± 0.35 (0.02-8.69)	0.13

NOTE. Values expressed as mean ± SD (range) or number (percent) unless otherwise noted.

*Median (range).

Table 5. Outcomes of Attempted PC Salvage

Outcome	ABX	EXCH
Indeterminate	5 (16.7)	2 (4.7)
Total cured*	11 (36.7)	35 (81.4)
Cured by culture criteria	4	22
Cured by clinical criteria	7	13
Failed	14 (46.7)	6 (13.9)
Total	30	43

NOTE. Values expressed as number (percent).

*$P = 0.0005$ EXCH versus ABX.

Multiple logistic regression analysis showed no differences in outcome of all cases based on age as a continuous variable ($P = 0.089$) or age older than 55 years ($P = 0.74$). There was no difference based on diagnosis of diabetes mellitus ($P = 0.76$), duration of PC use ($P = 0.16$), gram-negative infection ($P = 0.58$), or treatment as an inpatient ($P = 0.71$). Polymicrobial infection was associated with more treatment failures ($P = 0.03$; Table 6). There were no differences in outcome based on the species of infecting organism. Outcome data were also analyzed for episodes of first CAB only. Forty-one patients were

Table 6. Outcome by Infection Type

Treatment	Outcome	GPC	GNR	Poly
ABX	Cure	8	3	0
	Fail	4	4	6
	Poly *v* GPC, $P = 0.01$; others NS			
EXCH	Cure	15	13	7
	Fail	3	0	3
	All comparisons NS			
Total	Cure	24	16	7
	Fail	7	4	9
	Poly *v* GPC and GNR, $P < 0.05$			

NOTE. Indeterminate outcomes were censored.

Abbreviations: GPC, gram-positive cocci; GNR, gram-negative rods; Poly, polymicrobial; NS, not significant.

followed up to a definitive outcome. Twenty of 22 patients (91%) treated by EXCH experienced cure versus 9 of 19 patients (47%) treated with ABX alone ($P = 0.0004$). Multiple logistic regression analysis of outcomes from first episodes of CAB produced similar results, with no significant differences between groups based on a variable other than treatment. Catheter salvage was attempted in 12 episodes of CAB caused by *Staphylococcus aureus*. Outcome was indeterminate in one case. Successful catheter salvage was achieved in four of six patients with *S aureus* bacteremia treated with ABX and four of six patients treated with EXCH.

Three episodes of CAB were complicated by subacute bacterial endocarditis (3.5%). One patient had a characteristic mitral valve vegetation seen by transesophageal echocardiogram several months after successful treatment for coagulase-negative *Staphylococcus* bacteremia. Two had prolonged *S aureus* (one methicillin resistant, the other sensitive) bacteremia with mitral valve vegetation on echocardiogram and required immediate PC removal. One of these patients had severe preexisting mitral regurgitation and ultimately required elective mitral valve replacement. Two patients died while receiving treatment for CAB. One died of complications of severe pulmonary hypertension, and the other had dialysis withdrawn because of chronic failure to thrive. Neither patient had clinical sepsis or positive blood cultures at the time of death, and death was not directly attributed to CAB. No cases of epidural abscess, septic arthritis, osteomyelitis, or other metastatic infections were detected during this study.

DISCUSSION

This study confirms that bacteremia is a frequent occurrence in our chronic HD patients with long-term, tunneled, cuffed, venous catheter access. Our rate of 5.5 episodes/1,000 catheter-days (or 4.75 first episodes/1,000 catheter-days) is similar to the rate of 3.9 episodes/1,000 catheter-days reported by Marr et al,[6] but all these rates are considerably greater than those reported in most previous studies of long-term, tunneled, cuffed catheters. Moss et al[5] reported 0.70 episodes/1,000 catheter-days in patients with median catheter duration of use of 18.5 weeks. Dryden et al[14] reported 0.5 episodes of septicemia/1,000 catheter-days. They attributed this low rate in part to the strict aseptic technique practiced by nursing staff. However, they reported a relatively high rate of exit-site infections (4.5/1,000 catheter-days). Their catheter access method was similar to ours, except they used sterile gloves and a second povidone-iodine disinfection of the catheter ports after removal of the caps.

It is not clear what factors are responsible for our relatively high rate of CAB. Inadequate skin disinfection or poor placement technique could account for bacteremia or exit-site infections soon after the procedure but would be unlikely to cause infections long after catheter placement. There was only a single episode of bacteremia that occurred within 1 week of catheter insertion. That we see relatively few tunnel or exit-site infections also suggests that placement factors are not the principal causes of bacteremia.

The source of bacteria and route for bacterial entry to the bloodstream in CAB are not clear. In our program, bacteremia is rarely associated with exit-site infection, and most episodes occur many weeks after PC insertion, when fibroblast growth into the catheter cuff should be well established, providing an effective barrier to bacterial migration up the catheter tunnel. In a few cases, we identified another likely source of infection, including infected vascular graft, skin ulcers, or surgical wounds. Other sources may include bowel, urine, skin, or gingiva. Alternatively, patients with indwelling venous catheters may be susceptible to episodes of transient bacteremia occurring with such normal activities as brushing teeth. We did not diagnose bacteremia in association with dental or surgical procedures, for which prophylactic antibiotics were uniformly administered. It is most likely that bacteria gain entry to the bloodstream through the PC ports during catheter access despite rigorous nursing adherence to access protocol. There are few impediments to optimal nursing practice in the HD units participating in this study. These are nonprofit facilities with staff (nurse or patient care technician) to patient ratios of 1:3 or 1:4 and no significant care limitations based on time, cost, or supplies. There is continuous scrutiny of all PC infections by both nursing and medical directors, and regular nursing training sessions are held. Although continued improvement is essen-

tial, we believe our relatively high rate of CAB is not associated with excellent nursing practice.

A number of measures have been studied for the prevention of catheter-associated infections. Povidone-iodine ointment applied to the insertion site[15] and catheters impregnated with antibiotics[16] or antiseptics[17] have been shown to reduce bacteremia associated with the use of temporary venous catheters but have not been studied for tunneled, cuffed catheters. A preliminary report using a gentamicin and sodium citrate solution for packing long-term, tunneled, cuffed catheters resulted in a very low rate of bacteremia,[18] and this approach warrants further clinical study.

We diagnosed CAB based on blood cultures drawn directly from the PC port or from the dialysis blood tubing coming from the PC. Most other studies have not described their criteria for diagnosis of CAB in detail. Marr et al[6] required peripheral blood culture confirmation for the diagnosis of CAB. They did not report how many patients with suspected infection and positive catheter-derived cultures were excluded based on negative peripheral culture results. Blood specimens drawn from indwelling arterial or venous catheters in the intensive care unit have been shown to have a high rate of positive culture results, with organisms deemed contaminants compared with blood drawn by direct venipuncture.[19] This has not been shown for tunneled, cuffed dialysis catheters. It is possible that contamination of the catheter port or poor culture technique could result in false-positive culture results from the catheter, resulting in overdiagnosis of CAB. This would be of greater concern if we were performing surveillance cultures in asymptomatic patients with no clinical suspicion of infection. However, for patients with a PC presenting with distinct signs and symptoms of systemic infection, the clinical suspicion for CAB must be high, and false-positive catheter-derived culture results are less likely. Furthermore, cultures were commonly drawn from the extracorporeal circuit during dialysis, blurring the distinction between catheter-drawn and peripheral cultures. Ours is also a practical and commonly used approach in a busy dialysis unit, obviating the requirement for a separate venipuncture, which may be technically difficult or poorly accepted by many dialysis patients and nursing staff. It is possible that our reliance on catheter-derived cultures resulted in more diagnoses of CAB and contributed to the greater infection rate than that reported by Marr et al.[6] Nevertheless, in the setting of suspected clinical sepsis, positive cultures drawn through the catheter should be interpreted as pathological and treated, irrespective of peripheral culture results.

A method for establishing the catheter as the source of infection has been proposed, using differential quantitative cultures from the catheter and peripheral blood.[20] This method has not been studied for PCs and may not be routinely available in many clinical microbiology laboratories. Although positive catheter-tip cultures are commonly used as evidence for infection of temporary venous catheters, the same evidence does not exist for PCs, and we did not routinely culture catheter tips when PCs were exchanged or removed. In most cases, the patient had already received several days of antibiotic therapy, and the blood culture results were diagnostic. Furthermore, the catheter tip was usually withdrawn through a nonsterile exit site, raising the possibility of false-positive tip culture results. For these reasons, in the setting of suspected CAB, we elected to make the diagnosis based primarily on catheter-derived cultures.

Interestingly, many patients with CAB presented to dialysis with few or no symptoms but then developed fever, rigors, nausea, or severe manifestations of systemic sepsis during the HD session. This suggests that bacteria or pyrogens were sequestered in or around the PC and then released into the bloodstream after blood flow was established. Many of our patients with CAB were using high-flux reprocessed kidneys, and CAB presenting in this way may be indistinguishable from a sterile pyrogen reaction related to inadequate disinfection or poor water quality. However, most of the CAB presenting after the initiation of dialysis occurred well into the treatment (30 to 90 minutes) in contrast to sterile pyrogen reactions that would typically occur earlier. During this study, there were no sterile pyrogenic reactions diagnosed in a patient without a PC and no positive test results for pyrogens in the water treatment or reuse systems.

The wide variety of both gram-positive and gram-negative infections seen in this study contrasts with other series that have reported a

predominance of gram-positive organisms but is similar to the spectrum of organisms reported by Marr et al.[6] It is not clear if this represents a true change in microbiology of CAB, and if so, why this change should have occurred. The implications for choice of initial treatment for suspected CAB are significant. Guidelines published by the National Kidney Foundation Dialysis Outcomes Quality Initiative recommend initial coverage for CAB with antibiotics effective against *Staphylococcus* and *Streptococcus* organisms[21] but do not include a recommendation for treatment to include gram-negative rods or *Enterococcus* organisms. Because of our high incidence of gram-negative infections, including *Pseudomonas* species, initial antibiotic coverage for our patients includes an agent effective against these organisms. Also, because of our relatively high incidence of *Enterococcus*, we have frequently used vancomycin (usually with gentamicin) for initial empiric coverage of severe infections. With the increasing incidence of vancomycin-resistant *Enterococcus*,[22,23] there is considerable pressure to minimize its use, and this approach may no longer be appropriate. It is possible that initial coverage using a single agent with a narrower spectrum, such as cefazolin, may be acceptable pending culture identification,[24] especially for patients presenting with less severe sepsis. Because the bacteriology of CAB in different HD programs may vary, it is important for each unit to closely monitor its bacterial isolates to determine the optimal initial coverage for CAB.

This study was not designed to compare different methods of attempted catheter salvage. The selection of treatment with ABX versus EXCH was neither random nor systematic. The nephrologist responsible for the patient made this treatment decision based on the circumstances of each case. Some patients were reluctant or frankly refused catheter exchange. In some cases, exchange was delayed because of scheduling or compliance problems, with the subsequent decision to attempt treatment with ABX. It is not known how the culture results may have affected decisions regarding catheter management, but there was no difference in the microbiology between the ABX and EXCH groups. Age, diagnosis of diabetes, duration of ESRD, and percentage of PCs intended for permanent access were the same in both treatment groups. Hospitalization was considered an indicator of infection severity, recognizing that the decision to admit was based on a variety of clinical factors related to severity. Other more objective signs of infection, such as fever, leukocytosis, or blood pressure, were not believed to be consistent enough to use as reliable markers for infection severity. For example, a severe infection might present with either a very high or very low white blood cell count. Hospitalization rates for CAB appeared greater in the EXCH group, suggesting that patients in this group may have been sicker; however, this difference did not reach statistical significance. It is possible that clinically less severe infections were treated with ABX and more severe or complicated infections were treated with EXCH. If so, this selection bias would further support the advantage of EXCH over ABX for treatment of CAB. A randomized trial comparing these two treatment modalities would be required to answer this question with certainty. However, with mounting evidence showing poor results of ABX treatment, such a study may not be justifiable. EXCH should be considered the treatment of choice for catheter salvage in CAB.

We did not require negative blood culture results to confirm clinical resolution of infection in all cases. Patients who remained afebrile and asymptomatic for 30 days after completion of antibiotic therapy were unlikely to have silent bacteremia. In those patients who had follow-up blood cultures, there were no positive results that failed to correlate with clinical signs of infection. If a follow-up period as long as 60 days was used to define cure, the results were not significantly different from those at 30 days, except that more outcomes were indeterminate because of catheter removal for reasons other than infection (data not shown).

It is possible that early detection and aggressive early antibiotic treatment are partly responsible for our high catheter salvage and low complication rates. Every episode of suspected bacteremia for which blood cultures were drawn was treated immediately with antibiotics, leaving no patient untreated pending culture results. This is especially important when CAB is treated on an outpatient basis and blood cultures turn positive on the day after HD. If appropriately treated with long-acting antibiotics after dialysis, outpa-

tients can usually wait until after their next dialysis session to be redosed and only be brought back early if they have persistent symptoms of infection or if culture results are positive for organisms unlikely to be covered by the initial antibiotics.

Relatively few catheters were removed early because of overwhelming sepsis. We attempted catheter salvage in many patients who presented with quite severe clinical sepsis as long as they responded well to initial therapy. Most patients were afebrile and asymptomatic within 24 to 48 hours. If the response to antibiotics was not prompt and complete, the catheter was removed. Catheter exchange was not performed in the setting of persistent clinical sepsis, fever, or suspected ongoing bacteremia. Unless urgent dialysis was indicated, patients presenting with signs or symptoms of severe sepsis (hypotension, temperature $>$103°F, rigors, or vomiting) did not have HD initiated until they were cultured, treated, and stabilized. There are no known data showing the risk of dialysis under these circumstances. However, it has been our observation that some patients with CAB develop much worse manifestations of sepsis during the dialysis session. It is possible that avoiding dialysis through an infected PC while there are signs of uncontrolled sepsis may reduce the severity or duration of bacteremia and minimize the risk for metastatic infections.

The most common important complication attributed to CAB was endocarditis. Endocarditis was suspected in the setting of CAB when there was failure to respond rapidly to initial antibiotic therapy or when there was persistent bacteremia and fever after removal of the PC. All patients with suspected endocarditis had an echocardiogram performed. The presence of valvular vegetation was not required for diagnosis, but the three patients diagnosed with endocarditis had characteristic lesions. The sensitivity and specificity of echocardiography for diagnosis of endocarditis are not established for chronic HD patients with CAB. With the increased use of transesophageal echocardiography, it is likely that the sensitivity will be improved, but at the price of lower specificity, leading to the overdiagnosis of endocarditis. The diagnosis of endocarditis complicating CAB should be made primarily on clinical grounds.

We diagnosed no other metastatic infections attributable to CAB. Epidural abscesses have been reported in this population[25] but were not diagnosed in patients during this study. Severe low-back pain was a common presenting symptom of sepsis but usually resolved quickly with effective treatment. One patient with recent CAB developed low-back pain and underwent a computed tomographic scan, showing no evidence of epidural abscess or vertebral osteomyelitis. Her pain resolved spontaneously without medical treatment. The patient with coagulase-negative *Staphylococcus* endocarditis developed severe thigh muscle pain during the course of treatment. Magnetic resonance imaging was characteristic of sterile diabetic myonecrosis with hemorrhage, confirmed by surgical biopsy, drainage, and negative culture. Marr et al[6] reported that 22% of the patients with CAB developed complications, including 10% with endocarditis. The reasons for our comparatively low rates are unclear. It is unlikely that osteomyelitis, septic arthritis, or other important infections were overlooked in our study. More liberal use of echocardiography could explain their greater rate of endocarditis, either because of the detection of more true cases or possibly because of false-positive diagnoses in a group of patients likely to have preexisting valvular lesions. Because we reserved echocardiography for those patients who failed to clear CAB promptly, it is unknown how many valvular lesions we may have missed.

Aminoglycoside ototoxicity was clinically suspected in two patients who developed vertigo while receiving gentamicin for treatment of CAB. Neurodiagnostic study was confirmatory in one case and equivocal in the other. Both patients received doses adjusted for ESRD and had appropriate drug levels. In both cases, symptoms slowly improved over several weeks after discontinuation of gentamicin. Although mild and self-limited in these patients, ototoxicity may be devastating and permanent.[26] When aminoglycosides are used to treat CAB, patients should be informed of the risk for ototoxicity and monitored closely for signs of vestibular dysfunction or hearing loss.

There were no deaths directly attributable to CAB. The two patients who died while receiving antibiotic therapy had responded well to antibiotic treatment and had no evidence for ongoing

infection at the time of death. One was chronically debilitated and died after withdrawal of dialysis. The other had severe pulmonary hypertension, and death was attributed to intractable right-sided heart failure, hypoxia, and hypotension without bacteremia (although sepsis could not be absolutely excluded as a contributing cause).

This study confirms that in our patients, bacteremia is a frequent complication of PC access, and a wide variety of organisms, including gram-negative rods, may be responsible for these infections. Despite the high frequency of bacteremia, few serious complications occur, with the notable exception of endocarditis. This study also confirms previous reports showing poor catheter salvage rates when CAB is treated with ABX alone. EXCH is safe, easily performed by a nephrologist without fluoroscopy, and may significantly improve the chance for successful catheter salvage.

In the 12 months after the reported study period, we have had 27 episodes of CAB over 7,174 catheter-days, for a rate of 3.8 episodes/1,000 catheter-days. There has been no intentional change in our catheter access protocol or other medical or nursing policies. It is possible that continuous attention to this issue has resulted in improved practices. Most patients who had recurrent infections during the study period are no longer receiving HD through venous catheters. There were only two patients with multiple infections during the 12 months after the study period.

REFERENCES

1. Dunn J, Nylander W, Richie R: Central venous dialysis access: Experience with a double-lumen, silicone rubber catheter. Surgery 102:784-789, 1987

2. US Renal Data System 1997 Annual Report. IV. The USRDS Dialysis Morbidity and Mortality Study: Wave 2. Am J Kidney Dis 30:S67-S85, 1997 (suppl 1)

3. Moss AH, McLaughlin MM, Lempert KD, Holley JL: Use of a silicone catheter with a Dacron cuff for dialysis short-term vascular access. Am J Kidney Dis 12:492-498, 1988

4. Schwab SJ, Buller GL, McCann RL, Bollinger RR, Stickel DL: Prospective evaluation of a Dacron-cuffed hemodialysis catheter for prolonged use. Am J Kidney Dis 11:166-169, 1988

5. Moss AH, Vasilakis C, Holley JL, Foulks CJ, Pillai K, McDowell DE: Use of a silicone dual-lumen catheter with a Dacron cuff as a long-term vascular access for hemodialysis patients. Am J Kidney Dis 16:211-215, 1990

6. Marr KA, Sexton DJ, Conlon PJ, Corey GR, Schwab SJ, Kirkland KB: Catheter-related bacteremia and outcome of attempted catheter salvage in patients undergoing hemodialysis. Ann Intern Med 127:275-280, 1997

7. Shaffer D: Catheter-related sepsis complicating long-term, tunnelled central venous dialysis catheters: Management by guidewire exchange. Am J Kidney Dis 25:593-596, 1995

8. Shusterman NH, Kloss K, Mullen JL: Successful use of double-lumen, silicone rubber catheters for permanent hemodialysis access. Kidney Int 35:887-890, 1989

9. Shaffer D, Madras PN, Williams ME, D'Elia JA, Kaldany A, Monaco AP: Use of Dacron cuffed silicone catheters as long-term hemodialysis access. ASAIO J 38:55-58, 1992

10. Capdevila JA, Separra A, Planes AM, Ramirez-Arellano M, Pahissa A, Piera L, Martinez-Vasquez JM: Successful treatment of hemodialysis catheter-related sepsis without catheter removal. Nephrol Dial Transplant 8:231-234, 1993

11. Robinson D, Suhocki P, Schwab SJ: Treatment of infected tunneled venous access hemodialysis catheters with guidewire exchange. Kidney Int 53:1792-1794, 1998

12. Beathard G: Management of bacteremia associated with tunneled-cuffed hemodialysis catheters. J Am Soc Nephrol 10:1045-1049, 1999

13. Swartz RD, Messana JM, Boyer CJ, Lunde NM, Weitzel WF, Hartman TL: Successful use of cuffed central venous hemodialysis catheters inserted percutaneously. J Am Soc Nephrol 4:1719-1725, 1994

14. Dryden MS, Samson A, Ludlam HA, Wing AJ, Phillips I: Infective complications associated with the use of Quinton 'Permcath' for long-term central vascular access in hemodialysis. J Hosp Infect 19:257-262, 1991

15. Levin A, Mason AG, Jindal KK, Fong IW, Goldstein MB: Prevention of hemodialysis subclavian vein catheter infections by topical povidone-iodine. Kidney Int 40:934-938, 1991

16. Raad I, Darouchie R, Dupuis J, Abi-Said D, Gabrielli A, Hachem R, Wall M, Harris R, Jones J, Buzaid A, Robertson C, Shenaq S, Curling P, Burke T: Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections. Ann Intern Med 127:267-274, 1997

17. Maki DG, Stolz SM, Wheeler S, Mermel LA: Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. Ann Intern Med 127:257-266, 1997

18. Sodermann K, Lubrich-Birker I, Berger O, Baumert J, Feldmer B, von Hodenberg E: Gentamicin/sodium-citrate mixture as antibiotic-lock technique for salvage and prevention of catheter-related infections. A four-year trial. J Am Soc Nephrol 8:173A, 1997 (abstr)

19. Bryant JK, Strand CL: Reliability of blood cultures collected from intravascular catheter versus venipuncture. Am J Clin Pathol 88:113-116, 1987

20. Capdevila JA, Planes AM, Palomar M, Gasser I, Almirante B, Pahissa A, Crespo E, Martinez-Vasquez JM: Value of differential quantitative blood cultures in the diagnosis of catheter-related sepsis. Eur J Clin Microbiol Infect Dis 11:403-407, 1992

21. National Kidney Foundation: NKF-DOQI clinical practice guidelines on vascular access and anemia of chronic renal failure. Am J Kidney Dis 30:S173-S178, 1997 (suppl 3)

22. Brady JP, Snyder JW, Hasbargen JA: Vancomycin-resistant *Enterococcus* in end-stage renal disease. Am J Kidney Dis 32:415-418, 1998

23. Roghmann MC, Fink JC, Polish L, Maker T, Brewrink J, Morris JG Jr, Light PD: Colonization with vancomycin-resistant enterococci in chronic hemodialysis patients. Am J Kidney Dis 32:254-257, 1998

24. Fogel MA, Nussbaum PB, Feintzeig ID, Hunt WA, Gavin JP, Kim RC: Cefazolin in chronic hemodialysis patients: A safe, effective alternative to vancomycin. Am J Kidney Dis 32:401-409, 1998

25. Kovalik EC, Raymond JR, Albers FJ, Berkoben M, Butterly DW, Montella B, Conlon PJ: A clustering of epidural abscesses in chronic hemodialysis patients: Risks of salvaging access catheters in cases of infection. J Am Soc Nephrol 7:2264-2267, 1996

26. Schacht J: Biochemical basis of aminoglycoside ototoxicity. Otolaryngol Clin North Am 26:845-856, 1993