Bacteremia Following Prosthetic Valve Replacement

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The outcome of patients developing early bacteremia was investigated in 890 patients following cardiac valve replacement over a ten-year period. Thirty-two patients developed bacteremia during the hospital recovery period from valve replacement (3.6%). Sixty per cent of the organisms involved were gram-negative. Twenty-one of 23 patients had white blood counts greater than 14,000 at the time of positive blood culture. Nine patients died, seven of septic complications. Only two patients developed endocarditis. No patient with bacteremia diagnosed within ten days of surgery developed endocarditis, however two patients developed gram-negative sepsis in this period. The diagnosis and treatment of bacteremia requires continual vigilance if significant mortality and morbidity are to be averted.

THE MORTALITY of cardiac valve replacement continues to decrease due to improvements in patient selection, surgical technique, and methods of myocardial preservation. However, sepsis and its late complications remain one of the leading causes of mortality and morbidity following operation. Early postoperative bacteremia, if not successfully treated, sets the stage for progressive complications; the more significant being endocarditis or septic shock and progressive organ failure. A successful surgical outcome depends upon prevention of bacteremia or proper management if it occurs. The patient undergoing cardiac valve replacement has many sites from which nosocomial organisms may invade the blood stream. To assess the morbidity and mortality from early bacteremia and the results of therapy, all cases of bacteremia following cardiac valve replacement during the hospital convalescence period have been reviewed.

Methods

From January 1, 1971 through June 30, 1981, 930 patients underwent cardiac valve replacement at the Upstate Medical Center. There were 430 aortic valve replacements, 413 mitral valve replacements, six tricuspid valve replacements, 75 double valve replacements, and six triple valve replacements. Included in these numbers were 165 patients undergoing associated cardiac procedures such as coronary artery bypass grafting, tricuspid annuloplasty, and mitral commissurotomy. There were 516 males and 414 females with ages ranging from 22 months to 82 years. All patients were Class III or Class IV New York Heart Association functional classification. Forty patients died within three days of operation of causes other than infection. They are excluded from the study, leaving 890 patients at risk. A prophylactic antibiotic regimen was utilized in all patients. For the initial 36 months of the series, oxacillin and streptomycin were begun one hour prior to operation, and discontinued one week after operation. From 1974 to present, oxacillin has been the only drug utilized. In those patients with a penicillin allergy, lincocin was substituted. Valves utilized during this period included Starr-Edwards aortic model 1260, Beall mitral valve, Lillehei-Kaster aortic and mitral valve, and Hancock and Carpentier-Edwards bioprostheses. Prior to implantation, nonbioprosthetic valves were rinsed in a solution of 10,000 units of bacitracin.

The highest incidence of bacteremia over the nine-and one-half-year period was 9% in 1975 and the lowest was 1.5% in 1980 (Fig. 1). Concern over the high incidence in 1975 prompted a reassessment of the management of these patients. Attention was focused in areas that might represent bacteria access sites. Strict sterile precautions were adopted for insertion of indwelling monitoring lines. A dressing change with bacteriostatic ointment application at each insertion site was performed daily. Transducer flush bags were changed daily and transducers changed every other day. All monitoring lines and indwelling catheters were removed at the earliest appropriate opportunity.

After operation, a careful screening for bacteremia was performed in each patient. At least two blood cultures were obtained in all patients with fever. Chills,

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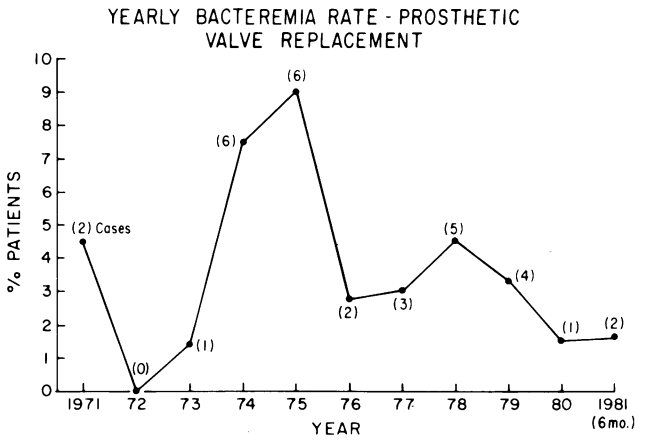

FIG. 1. The yearly incidence of bacteremias in patients undergoing prosthetic valve replacement.

leukocytosis, or other signs of sepsis also required blood cultures. All blood cultures were placed in tryptic soy broth and handled for both aerobes and anaerobes. Urine, sputum, and wound cultures, if appropriate, were also obtained. With persistence of fever and no localization of its source, antibiotics were discontinued and further blood cultures obtained. White blood counts were measured at the time of the fever spike in the majority of the patients. Bacteremia was diagnosed with the appearance of at least two positive blood cultures or a single positive culture and obvious signs of sepsis. With a proven bacteremia, appropriate antibiotics were chosen by antimicrobial susceptibility tests and verified by bactericidal tube dilution methods. Treatment was carried out for a minimum of two weeks.

Results

Of the 890 patients at risk, 32 developed a postoperative bacteremia for an incidence of 3.6%. The source of the bacteremia was found in 22 patients (68.8%). Sources included lungs (sputum) two; urinary tract nine; wound eight, pleural space one, central venous catheter tip one, infected cephalic vein one. Organisms involved included *Escherichia coli* seven, *Staphylococcus epidermidis* eight, Staphylococcus coagulase positive one, Enterobacter species five, *Serratia marascens* three, *Candida albicans* two, *Proteus mirabilis* one, Enterococcus one, *Streptococcus viridans* one, and *Pseudomonas aeruginosa* three. Gram-negative organisms accounted for 60% of the infections.

The bacteremia was successfully treated in 25 patients (78.1%). Nine patients died (28.1%), two from nonseptic causes (Table 1). Five patients succumbed to generalized sepsis, two dying within one week of surgery from gram-negative shock (*E. coli*), and three dying at 14, 20, and 40 days, respectively, of progressive organ dysfunction due to left ventricular failure, generalized sepsis, and renal failure. Organisms involved in these later deaths were Candida species, Enterobacter species, and *Pseudomonas aeruginosa*, respectively.

Endocarditis accounted for two deaths. Both died over one month following valve replacement, one during an attempt to replace an infected valve, and the other of irreversible sepsis and generalized organ failure before valve replacement could be performed. Organisms included Candida species and *Pseudomonas aeruginosa*. The risk of endocarditis in the entire series was 0.22%, but in those with bacteremia 6.3%, a twenty-five-fold increase.

Both patients with fungemias had had multiple different antibiotics given for other infections in the postoperative period. These infections were in wound, urinary tract, and lung in both patients.

Two patients died of nonseptic causes following cure of their septicemia, one of cerebral dysfunction, and the other of a severe upper gastrointestinal bleed. Seven patients who died had a known source for their septicemia, two patients had no known source (Table 1).

The high bacteremia incidence of 9% in 1975 decreased to 1.8% by 1981. Introduction of new methods of catheter and transducer care appear to have aided this decrease.

White blood counts at the time of initial bacteremia were obtained in only 23 patients. Twenty-one of these had a white count greater than 14,000 at the time of positive blood culture. The white counts ranged from 9.7 to 32.5 thousand/cu/mm. All leukocytoses revealed a leftward shift.

Of those patients (15) developing bacteremia within the first two weeks of surgery, there were no cases of endocarditis. The first positive culture occurred at 16 and 35 days, respectively, in each case of endocarditis. The source of infection in each case was the urinary tract.

Discussion

Bacteremia following prosthetic valve replacement remains a threat and, if unsuccessfully managed, results in significant mortality and morbidity including septic shock, generalized sepsis, localized infection, and endocarditis. There are few reports that speak to the risk of bacteremia following cardiac valve replacement. Lockey reported an incidence of 2.7% in 1640 patients undergoing open heart surgery, but the number of prosthetic valves in this series is not mentioned. Twenty per cent of these patients developed endocarditis.[1] Goldman reported an incidence of 4% in 200 patients undergoing prosthetic valve replacement with no cases of endocarditis in the first two months.[2]

TABLE 1. *Deaths in Patients Developing Bacteremia While in Hospital Recovering from Prosthetic Valve Replacement*

Patient	Age	Sex	Procedure	Organism	Source	Treatment	Outcome
M.W.	63	M	Aortic valve replacement; graft to right coronary artery	*Pseudomonas aeruginosa*	Urine—Epididymitis	Ticarcillin Tobramycin	Endocarditis
I.F.	60	F	Aortic valve replacement; graft to right coronary artery	Candida	Urine	Died before therapy begun	Endocarditis
H.N.	68	M	Mitral valve replacement; grafts to left anterior descending & circumflex arteries	*Pseudomonas aeruginosa*	Unknown	Unknown	Generalized sepsis—renal failure
S.B.	68	M	Aortic and mitral valve replacement; graft to right coronary artery	Enterobacter	Urine	Gentamycin Cefazolin	Generalized sepsis—renal failure
J.J.	69	F	Mitral valve replacement	Candida	Unknown	Amphotericin B	Septicemia, renal failure
M.W.	60	F	Aortic and mitral valve replacement	*E. coli*	Urine	Lincocin	Septic shock
C.J.	69	F	Aortic valve replacement	*E. coli*	Sputum	Cefazolin Gentamycin	Septic shock
C.C.	63	M	Aortic valve replacement	*Pseudomonas aeruginosa*	Urine—Epididymitis	Gentamycin Ticarcillin Tobramycin Kefzol	Gastric hemorrhage
L.S.	61	F	Mitral valve replacement	*E. coli*	Urine	Cefazolin	Cerebral infarction

The patient undergoing and recovering from open heart surgery has many potential contamination sites. Chronic infections such as in the mouth, sinuses, ears, lungs, and skin can secondarily cause significant postoperative infection if not carefully searched for and treated prior to operation. Elective operations should be cancelled if there is evidence of acute infection and not rescheduled until it has been successfully treated. At the time of operation, atmospheric exposure of the pericardial contents and the prosthesis may be the original source of contamination. Hornick cultured six different intraoperative sites in 66 patients undergoing all types of cardiac surgery. The majority of patients had at least one positive culture with the repaired area of the heart and the prosthesis being the most common sites.[3] The oxygenator and tubing associated with the heart/lung machine also represent another potential contamination site. Blakemore found positive cultures from this area in 75% of patients, with the coronary suction line being the worst offender.[4] Ankeney cultured five intraoperative sites during 383 open heart procedures and also found the coronary suction line to be the most common site of positive culture.[5]

These patients require numerous sophisticated monitoring systems, most of which require invasion of the cardiovascular system. Arterial and venous indwelling catheters are a continual source of bacterial invasion. Kluge routinely cultured indwelling arterial and venous catheter tips at the time of removal and found that 30% of the venous lines and 75% of arterial catheters yielded pathogenic bacteria on culture.[6] Bacteremia secondary to contaminated pressure transducers has been well documented.[7,8] Indwelling urinary catheters are a major source of contamination.[9] Twenty-five per cent of the bacteremias reported in this article emanated from the urinary tract. Kluge found pathogenic organisms in 41% of urinary catheter tips following removal.[6] The modern inhalation equipment surrounding the cardiac surgery patient is also a potential source of infection.[10] Other sources of postoperative bacteremia may include rigid tube endoscopy, barium enema and hemo- or peritoneal dialysis.[11-13]

The bacteriology of postcardiac surgery bacteremias remains varied. Most infections are presumably secondary to resistant organisms not sensitive to the prophylactic antibiotics. Due to the virulence of hospital-acquired staphylococcal infections, most antibiotic regimens concentrate on antistaphylococcal drugs. Currently, there appears to be a decreasing incidence of staphylococcal coagulase positive bacteremias compared with the earlier period of open heart surgery. In recent years, many causative organisms appear to emanate from patients' normal flora, organisms thought to be of extremely low virulence. Foremost among these are staph-

ylococcal epidermidis and diphtheroids.[3,6,14,15] No longer can a positive blood culture of these organisms be viewed as a simple contaminant but must be treated with great respect and repeated cultures performed to rule out bacteremia.[16] At times, even though a contaminant is suspected, antimicrobial therapy may be appropriate. Gram-negative organisms continue to be a cause of bacteremia and predominate in some series.[1] Fungal infections remain a constant threat in the seriously ill patient who has required multiple antibiotics for acquired infection in the postoperative period. Fungemias associated with the overgrowth of such organisms are associated with an extremely high mortality.[17] The authors' own series appears to bear out current trends. Staphylococcal epidermidis accounted for nearly one third of the bacteremias. Only one patient exhibited a staphylococcal coagulase positive septicemia. Eighteen patients revealed gram-negative organisms. Two patients exhibited a yeast septicemia, both of whom succumbed. With over one half of the infections coming from gram-negative organisms, it is necessary to speculate whether a specific gram-negative antibiotic should have been utilized to prevent these infections, particularly in view of the high mortality associated with gram-negative infections in this series. However, risk of fungal overgrowth with multiple antibiotics must be considered.

Although the risk of early endocarditis following prosthetic valve replacement remains low, a high mortality is associated with its appearance. A proven early bacteremia breeds much anxiety as the stage appears set for endocarditis. However, there is evidence that an early postoperative bacteremia is secondary to extracardiac infection without valvular involvement. Sande reported on a series of patients with acquired bacteremias following prosthetic valve replacement. In those with early bacteremia (mean 12 days), endocarditis did not develop, but in late bacteremias (mean 60 days), there was a 100% incidence of valvular involvement, presumably due to the valve being the infection source.[18] Magilligan, reporting on infection following implantation of porcine bioprostheses, found six cases of early postoperative bacteremia (less than two weeks) with no early mortality or endocarditis. One of these patients developed endocarditis at 21 months from the same organism as found earlier.[19] In this series, none of the early bacteremias (<10 days) developed endocarditis and 80% had a known extracardiac source of infection. The endocarditis cases, although few, had their first episode of bacteremia more than two weeks following operation. Although the risk of endocarditis developing from an early bacteremia is low, it must be emphasized that early bacteremias from extracardiac sources are not benign, and endocarditis, though unusual, may still be the end result.

In spite of the lack of prospective studies attesting to the worth of prophylactic antibiotics, it would contradict current practice to perform prosthetic valve replacement without their presence. Many antibiotic regimens are currently available. It appears reasonable to include an effective antistaphylococcal agent. Early cardiotomy series not utilizing prophylactic antistaphylococcal agents revealed an incidence of staphylococcal infection as high as 10%.[20] There has been a decrease in staphylococcal endocarditis over the past several years due to the use of these agents. The drugs most commonly utilized to this end are the penicillinase resistant penicillins and cephalosporins. A recent study comparing these two drugs revealed no endocarditis in 432 patients receiving cephalothin and 11 episodes in 129 patients receiving methicillin.[21]

There has been no properly defined duration and schedule for prophylactic antibiotics. A prospective double blind study involving cephalothin given for two and six days, respectively, in cardiac valve patients revealed no difference.[2] Administration for too lengthy a time may promote overgrowth of resistant organisms and should be discouraged. Antibiotics should be present during the time of greatest risk, *i.e.*, operation, presence of indwelling catheters for monitoring, and intravenous therapy. There are no current studies that examine the use of antibiotics specifically designed to decrease the incidence of gram-negative infection in cardiac patients. Newsom suggests such a trial would be meaningless due to the fact that a large number of cases of endocarditis in the control group would be required for validity.[22] The actual worth of the prophylactic regime continues to lie in the low incidence of early endocarditis. These results which reveal a preponderantly high incidence of gram-negative bacteremias suggest a trial of an antimicrobial with a high degree of activity against these organisms.

Careful attention must be paid to postoperative fever. Although bacteremia is the cause in a low percentage of cases, early diagnosis is crucial. Attempts at diagnosis and subsequent management should be as aggressive as the surgery itself. With persistent fever and leukocytosis, multiple blood cultures are necessary. All indwelling intravenous and arterial lines must be assiduously protected. Strict aseptic precautions on insertion and daily application of bacterostatic ointments at the insertion site are required. The catheters must be firmly anchored, as undue motion at the insertion site encourages bacterial entrance. Sterility of transducers must be assured and flush bags changed daily. Removal of indwelling lines at the earliest safe opportunity is mandatory. All catheter tips are routinely cultured. Indwelling urinary catheters should be handled in a similar fashion, including early removal, urine culture, and culture of the

catheter tip. This type of management appears to have helped decrease the incidence of bacteremia over the past several years.

With a diagnosed bacteremia, appropriate antibiotics should be begun immediately. Proper bactericidal levels of the antimicrobial must be attained and killing levels measured. Therapy should be continued for a minimum of 14 days. With an established extracardiac infection, proper therapeutic measures should be taken to prevent bacteremia. Recognition of intramediastinal or thoracic purulence requires immediate drainage. At the conclusion of therapy, repeat blood cultures should be performed to assure adequacy of treatment.

The risk of bacteremia in the immediate postoperative period has progressively diminished in the past several years. The vast majority of bacteremias are from extracardiac sources and can be appropriately treated with antibiotics if discovered. A high index of suspicion for bacteremia must be maintained and appropriate diagnostic measures taken in all patients undergoing prosthetic valve replacement.

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