Surgical treatment of infective endocarditis with special reference to prosthetic valve endocarditis

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Abstract

Patients with native valve endocarditis treated surgically between 1968 and 1978 (n = 15) and all patients presenting with prosthetic valve endocarditis during this period (n = 21) were followed up for at least four years. Five of the patients with native valve endocarditis required urgent early surgical intervention, of whom two died. The remaining 10 underwent valve replacement after a course of antibiotic treatment: all survived, though one required further valve replacement. The 21 patients with prosthetic valve endocarditis suffered 25 attacks. Nine were cured by medical treatment alone; two died before surgical intervention was possible; 11 required valve replacement, of whom three died; and two required valve replacement after a course of antibiotic treatment. The incidence of early prosthetic valve endocarditis—that occurring within two months of operation—was 0-67%, but that of late prosthetic valve endocarditis could not be determined.

Medical treatment when started early should cure endocarditis in most patients, but vigilance should be maintained for the appearance of indications for surgery. When such indications exist surgery should not be delayed.

Introduction

The introduction of effective chemotherapy and development of valve replacement surgery have dramatically changed the outlook for patients with infective endocarditis. Since Wallace et al first reported successful excision and replacement of the valve in patients with active disease the role of surgery in the treatment of this condition has expanded steadily. Initial reluctance to insert a substitute prosthetic valve into an infected site diminished when emergency valve replacement proved life saving for patients with rapid haemodynamic deterioration, uncontrollable infection, or recurrent embolism, in whom the mortality with continued medical treatment approached 100%.1-4

Prosthetic valve endocarditis is a “new” disease that may occur early or late after valve replacement. Late infection develops as part of a continuing long term risk when bacteraemia from an active infection occurs. The infecting organisms are similar to those found in patients with native valve endocarditis.5 When infection appears within two months of operation it is usually attributable to contamination at the time of valve replacement, particularly after sternal wound infection, and an incidence of 10% in the early 1960s has been reduced to 1%, or less with the introduction of more effective antistaphylococcal prophylaxis.6 7

Perhaps more than any other condition the treatment of both primary and prosthetic valve endocarditis requires close cooperation between cardiologist, bacteriologist, and cardiac surgeon at an early stage of the disease. Surgical intervention, when required, must be carefully timed. Ten years ago Wise et al at this hospital advocated prompt replacement of the aortic valve for patients with severe acute aortic regurgitation despite active endocarditis.8 We describe the patients with infective endocarditis who have needed surgical treatment at this hospital since that time.

Patients and methods

The definition of infective endocarditis for the purpose of this study was an illness producing valvular dysfunction and incorporating characteristic clinical features that include fever, new cardiac murmurs, splenomegaly, or embolic manifestations. Positive blood cultures were obtained in 77% of attacks. Some patients at presentation had already received blind antibiotic treatment, and a few, in whom the diagnosis was initially made serologically, had infections caused by cell dependent organisms (Coxella or Chlamydia). Demonstration of typical vegetations by echocardiography, at surgery, or at necropsy was held as confirmation of infective endocarditis.

Twenty seven patients were operated on for endocarditis between 1968 and 1978 and were followed up for at least four years, 15 with native valve (primary) endocarditis and 12 out of 21 patients who presented with prosthetic valve endocarditis. Patients whose native valve endocarditis was successfully treated medically or for whom valve replacement was required at some time remote from the infection were not included. All patients with prosthetic valve endocarditis were included, though not all required surgical treatment.
When infective endocarditis was diagnosed clinically antibiotic treatment was started immediately after blood samples were taken for culture and before laboratory information was received. In the case of primary endocarditis treatment usually consisted of a combination of benzylpenicillin and gentamicin both given intravenously in high dosage. After the organism responsible had been isolated by blood culture bacterial efficiency was tested and the drugs altered appropriately.

Throughout the course of medical treatment patients were watched carefully for evidence of clinical deterioration, including embolism. Echocardiography was increasingly used to detect vegetations as the two dimensional technique is of great value in assessing their size and mobility and so the risk of embolisation. Aortography was used when indicated to show local tissue destruction, including paraavalvular abscess, though more recently two dimensional echocardiography has largely taken its place. Haemodynamic deterioration surgery was unhesitatingly undertaken in the active phase of the disease, particularly in cases of endocarditis caused by coagulase positive staphylococci.

Indications for surgical intervention were: (i) increasing valvular regurgitation before, during, or after antibiotic treatment; (ii) systemic embolism; (iii) particularly if echo, echocardiography showed persisting large or mobile vegetations; (iv) removal of an infected leaking valve prosthesis during or after a full course of antibiotic treatment; (iv) a paravalvular abscess recognised by aortography or two dimensional echocardiography, or both, and often suspected by new conduction defects and continuing bacteremia; and (v) infection by antibiotic resistant organisms such as candida, or continuing evidence of infection despite apparently sensitive organisms.

After operation treatment was continued for as long as deemed necessary from the surgical findings, bacteriological studies, duration of preoperative treatment, and clinical state. For patients who had been operated on while in infection was still active the postoperative duration of treatment was usually six weeks.

### Results

#### SURGERY FOR PRIMARY INFECTIVE ENDOCARDITIS

Fifteen patients (nine men, six women) required valve replacement for primary infective endocarditis. Five patients gave a history of rheumatic fever, and in three there was a known congenital cardiac anomaly: in two this was a bicuspid aortic valve and in the third a ventricular septal defect. The remaining seven patients had no previous history of possible heart disease. Recent dental manipulation had been carried out without antibiotic prophylaxis in two patients. One had suffered meningitis with septicemia and the other was a narcotic addict. The remaining attacks were without a known source of infection.

The aortic valve was affected primarily in five attacks, the mitral valve in five, and the tricuspid valve in two. Both mitral and aortic valves were affected in three attacks. Of the eight patients with aortic valve infection, three had an aortic root abscess excavating the ventricular septum.

**Bacteriology**—The table shows the microorganisms responsible for infection. A variety of organisms were implicated, but most common were streptococci of the viridans group (this includes *Streptococcus mitis*, *Streptococcus salivarius*, and *Streptococcus sanguis*). Negative cultures were obtained in three patients.

**Results of treatment**—Early haemodynamic deterioration due to valve destruction and aortic or mitral regurgitation required surgical intervention during the active stage in five patients including the patient with a ventricular septal defect and aortic valve infection. This patient underwent aortic valve replacement with closure of the ventricular septal defect and recovered uneventfully. All five patients had evidence of systemic embolism with persisting infection and vegetations on the valve. Thus, as in most patients operated on at this stage, the indications for surgery were multiple. One patient died on the operating table and another from ventricular fibrillation on the second postoperative day. Ten patients underwent valve replacement after a full course of treatment, four because of persisting infection and six with damaged and regurgitant valves. Three of the patients with persistent bacteremia were found to have cavitation and an abscess in the aortic root. All patients in this group survived operation, though one man with an aortic root abscess developed a large para-prosthetic leak afterwards and required further valve replacement.

### PROSTHETIC VALVE ENDOCARDITIS

Twenty one patients (11 men, 10 women; age range 21-68) suffered 25 attacks of endocarditis on a valve prosthesis. Ten attacks occurred within two months of valve replacement and were classified as early prosthetic valve endocarditis; 15 attacks occurred late. Two attacks of *Staphylococcus aureus* infection preceded two early attacks of *Streptococcus viridans* infection, and one patient developed early *Staph aureus* infection on both mitral and aortic valve prostheses after insertion of a percutaneous transvenous pacing wire. Dental treatment preceded two late attacks of *Streptococcus viridans* prosthetic valve endocarditis. Two attacks of *Staphylococcus* prosthetic valve endocarditis followed acute cholecystitis and instrumentation of a urethral stricture respectively. Two attacks of late prosthetic valve endocarditis with klebsiella occurred in patients who had undergone valve replacement in the same operating theatre on consecutive days, and though late in presentation this evidence points to contamination in the operating theatre.

Infection occurred on an aortic prosthesis in 10 cases and a mitral prosthesis in five. Simultaneous infection on both mitral and aortic prostheses occurred in four patients with double valve replacements and on both mitral and tricuspid prostheses in two other patients. In four of the 14 infected aortic prostheses an aortic root abscess excavated the ventricular septum. Both Starr-Edwards and Bjork-Shiley prostheses had been used, but there were no differences in the incidence of infection between the two. One man with a Dacron graft replacement of both ascending thoracic and abdominal aorta and a bicuspic aortic valve developed salmonella endocarditis with aortic regurgitation. In this case the gall bladder probably harboured the infecting organism.

**Results of treatment**—Nine patients, all with late prosthetic valve endocarditis, were cured by antibiotic treatment alone and required no further surgery. Three patients died without further surgery, the first with an obstructed Bjork mitral prosthesis, the second with a burst myotic aneurysm around an infected Starr-Edwards aortic valve prosthesis, and the last after late presentation with a large paraprosthetic leak, severe cardiac failure, and septicaemia. Eleven patients (four with early and seven with late prosthetic valve endocarditis) required urgent aortic valve replacement at an early stage for progressive valve deterioration and haemodynamic deterioration. Six of these patients recovered with the prosthesis intact. In two patients without severe haemodynamic deterioration bacteremia persisted despite appropriate antibiotic treatment and aortography showed them to have an aortic root abscess with a small paraprosthetic leak. In both cases the leaking aortic prosthesis was replaced and the patients recovered uneventfully with continued chemotherapy. Two survivors developed a paraprosthesis leak around the new valve, one of whom required a further valve replacement soon afterwards. Three patients died after surgery, one after cerebral embolism, the second with bronchopneumonia, and the third with renal failure.

**Bacteriology**—(table)—*Staphylococci* were most commonly implicated in both early and late prosthetic valve endocarditis, but the numbers were small. Most showed resistance to benzylpenicillin, and other antibiotics were used in their treatment but always in combination since many showed multiple resistance. *Staphylococcus* occurred more frequently than *Streptococcus* in patients with late endocarditis. *Streptococci* were responsible for one third of cases of late endocarditis in which a positive culture was obtained but were implicated only...
once in cases of early endocarditis. In five cases (three early, two late) negative cultures were obtained; the three patients with early endocarditis had received perioperative prophylaxis and the two with late endocarditis had been given blind antibiotic treatment.

Prosthetic valve endocarditis after valve replacement between 1968 and 1978—During the course of this study the prophylactic antibiotic regimen for patients undergoing cardiac surgery usually comprised penicillin, cloxacillin, and streptomycin given parenterally for five days beginning on the morning of operation. Altogether 1488 operations for valve replacement were carried out at this hospital during this period. Ten patients were known to have developed prosthetic valve endocarditis within two months of operation and three patients died. The incidence of early prosthetic valve endocarditis in this series was therefore 0·67%. The true incidence of late prosthetic valve endocarditis was difficult to establish and rigorous use of knowledge since several patients were treated without ever being readmitted to this hospital.

Discussion

Two major advances in treatment dramatically changed the prognosis of patients with infective endocarditis. The first was the introduction of effective chemotherapy and the second the recognition that surgical intervention during active endocarditis could save those patients who would otherwise die from the haemodynamic consequences of the disease. Indeed, the first successful surgical operation during active endocarditis was carried out by Tubbs, who ligated an infected ductus arteriosus and removed the infection before the days of penicillin. Infective endocarditis is curable, and the continuing overall mortality—estimated as up to 30%—may be wholly attributed to late diagnosis and poor management.

Previous reports have shown the efficacy of timely surgical intervention, but the need for surgery is itself a reflection on management and usually means that the onset of treatment had been delayed. Advanced destruction of a native valve or dehiscence of a prosthetic valve was the commonest reason for urgent surgical intervention, though most of our patients had multiple indications on referral. During this study eight other patients with native valve endocarditis were transferred when they were already moribund and died almost immediately after arrival before surgery could be contemplated. Sixteen patients, notably 11 with prosthetic valve endocarditis, required urgent valve replacement for valve failure that would otherwise have quickly led to a fatal outcome. Inevitably, operative morbidity and mortality in this group of patients is substantial.

Deterioration in valve function may be rapid at an early stage, particularly in Staphylococcus aureus infections and particularly also in the young with non-calcified, thin, bicuspid aortic valves. Antibiotic treatment should never await bacterial confirmation because valve destruction is most rapid during this phase of unchecked bacterial multiplication and because bacteriological confirmation may be absent in up to a third of cases. Most cases in which negative cultures are obtained are streptococcal, although some are caused by cell dependent organisms such as Coxiella and Chlamydia, in which case diagnosis depends on serological tests. Delay in the onset of treatment because of negative blood cultures undoubtedly swells the numbers requiring surgical intervention for haemodynamic reasons. Most of these infections are caused by penicillin sensitive organisms and may be effectively treated by a penicillin and gentamicin (or streptomycin) combination started speculatively on clinical grounds before bacteriological advice is received. Many but not all of these patients have already received blind chemotherapy before presentation.

Early surgical intervention is imperative when haemodynamic impairment occurs and may be needed in its absence for embolisation, particularly if echocardiography shows large vegetation or a paravalvular abscess is seen on angiography. Replacement of an infected leaking valve or prosthesis not only re-establishes competence and haemodynamic stability but also helps to cure the disease by removing the bulk of infected tissue. This reduces the risk of embolisation and formation of mycotic aneurysm and prevents local spread into vital or inaccessible myocardial tissue. Abscesses are particularly likely to form when there is neglected infection on a calcified valve that is not readily made regurgitant. Infection may extend along the mitral annulus or from the aortic valve out into the pericardium. Aortic root abscesses may erode the conduction system, so development of fascicular block may produce a diagnostic clue. Of these seven patients, second degree atrioventricular block, though four did not. If treatment is delayed a mycotic aneurysm of the aortic root may burst with fatal consequences. Aortography is invaluable in the earlier recognition of aortic root abscess that requires surgery even in the absence of severe aortic valvular destruction. We, and others, recommend the use of two dimensional echocardiography at an early stage for detection of vegetations and aortic root abscess, particularly in prolonged endocarditis in which negative cultures are obtained, when the diagnosis may still be in doubt.

Tissue softened by chronic infection provides a poor setting for valve replacement as shown by patients who survived emergency operation for endocarditis but subsequently developed a paraprosthetic leak and required further surgery.

Patients who undergo valve replacement after completing antibiotic treatment subsequently have few problems, but this apparent safety of surgery after prolonged chemotherapy must not be used as an argument for achieving bacteriological cure before surgery in patients who are deteriorating haemodynamically. Firstly, any further deterioration in circulatory or renal function may cause death before operation or prejudice a second operation. Secondly, the risk of embolism is high; and, thirdly, in many cases bacteriological cure is impossible to achieve without surgery. Stinson et al found 29%, of valve specimens to contain microorganisms despite many weeks of antibiotic treatment.

Prosthetic valve endocarditis remains an important problem due to the large volume of cardiac surgery undertaken. Early prosthetic valve endocarditis from preoperative contamination is now rare, but late prosthetic valve endocarditis is an continuing long term risk when bacteriaerna from any cause occurs. Dissects et al reported 1671 valve replacements with 38 cases of prosthetic valve endocarditis, 19 early (1·1% of the total) with 13 deaths and 19 late with eight deaths. Slaughter et al reported 1235 cases of Starr-Edwards valve replacement with 48 cases of prosthetic valve endocarditis, 23 early (1·9%) with 20 deaths and 25 late with nine deaths. Wilson reported 4586 valve replacements with 45 cases of prosthetic valve endocarditis, 16 early (0·35%) with 14 deaths and 29 late with eleven deaths. We have reported here 1488 valve replacements with 10 known early cases (0·67%). An accurate assessment, especially of late disease, is unrealistic, however, since it is difficult to discover how many patients were treated successfully outside this hospital or who died without treatment.

Some authors have suggested that heterographs preserved in glutaraldehyde may be more resistant to infection or to certain of its complications than mechanical prosthetic valves. Rossier et al reviewed 2184 patients who underwent prosthetic valve replacement and compared 837 patients with heterograft valves with 1347 patients with mechanical valves. There was no difference in the incidence of prosthetic valve endocarditis in either group, but analysis showed that heterograft endocarditis was more easily cured by medical treatment than mechanical valve endocarditis. There was no difference between the two valves in the distribution or type of infecting organisms. The considerable mortality of patients with early prosthetic valve endocarditis is evident from these figures, and over the past 10 years the management of these patients has changed.

An aggressive surgical approach is usually advocated, especially when the more virulent staphylococci, Gram negative organisms, and fungi are involved. Replacement of an infected prosthesis is now undertaken at the first definitive sign of valve dehiscence shown by a new aortic diastolic murmur and even more urgently if there is motion on fluoroscopy. One third of our patients with
late prosthetic valve endocarditis were satisfactorily treated with antibiotics alone, and the success of medical treatment in this group might be as high as that in patients with native valve endocarditis despite the foreign body mass. Since infection occurs at the interface of the tissue annulus and rigid prosthesis, disruption of sutures in early prosthetic valve endocarditis may occur even with organisms of low virulence, but in late prosthetic valve endocarditis with tissue ingrowth a new leak means en- trenched infection. These factors, with the added proviso that the patients may have only limited haemodynamic reserve from the pre-existing valvular heart disease, dictate that indications for operation should be more aggressive than those in primary endocarditis, which should be cured by early medical treatment before haemodynamic deterioration occurs.

Three of the most serious complications of prosthetic valve endocarditis—namely paraprosthetic leak with severe left ventricular failure, obstruction of a tilting disc prosthesis, and burst myotic aneurysm—were responsible for the deaths of those patients who died without further operation. As in other series, a large proportion of patients with prosthetic valve endocarditis required operation during the active stage of the disease compared with patients with primary endocarditis. Early prosthetic valve endocarditis in particular has a high prevalence of staphylococcal infection, and the organisms may well be sensitive to the antibiotics used in prophylaxis. This possibility must not be ruled out when treatment is considered. Our experience caused us to change the prophylactic regimen, and antibiotics are no longer started early but the first dose is given intravenously by the anaesthetist immediately before the skin incision.

Fungal infection with Candida albicans accounted for one late case of prosthetic valve endocarditis in this series and may present early or pursue an indolent course with delayed recognition for a year or more. Primary aetiological factors for this type of endocarditis are prolonged antibiotic treatment, general debility, and the use of steroids. Late bacterial infections presumably arise after transient bacteraemia, particularly after procedures such as urinary tract manipulation or dental treatment. Awareness of the prosthetic valve should make adequate antibiotic prophylaxis much easier in this group, and endocarditis should be suspected early if there is unexplained fever or malaise. It is vital to remember that constitutional signs such as anaemia, weight loss, clubbing, or splenomegaly take weeks to develop, by which time medical care may no longer be possible because of dehiscence of the prosthetic valve ring. An important contributory cause of late diagnosis has been expectation of a change in prosthetic valve sounds, a naive concept since no change in prosthetic valve function occurs until there is either dehiscence or interposition of a large vegetation between the moving parts, both of which are late events.

Conclusion—Cardiac surgery has been responsible both for a dramatic improvement in the outlook of patients with infective endocarditis and for a new disease—namely, prosthetic valve endocarditis. When indications exist surgery for endocarditis should not be delayed because by this means can haemo- dynamic correction be achieved, the bulk of the infected material removed, and embolism of persisting vegetations prevented. Medical treatment if started early should cure most patients, but continuous vigilance should be maintained for the appearance of indications for surgery.

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References


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GILBERT’S WATER—“Take of Scabious, Burnet, Dragons, Bawn, Angelica, Pimpernel, with purple flowers, Tormentil, roots and all, of each two handfuls, let all of them, being rightly gathered and prepared, be steeped in four gallons of Canary Wine, still off three gallons in an alembick, to which add three ounces of each of the cordial flowers, Clove-gilliflowers six ounces, Saffron half an ounce, Turmeric two ounces, Galanga, Basil seeds, of each one dram, Citron pills one ounce, the seed of Citrons and Carduus, Cloves of each ounce, Harr’s-horn four ounces, steep them twenty four hours and then distil them in Balney Maries: to the distilled water add Pears prepared, an ounce or a half, red Coral, Crabs eyes, white Amber, of each two drams, Crabs claws, six drams, Bezoar, Ambergreece, of each two scruples, steep them six weeks in the sun, in a vessel well stopped, often shaking it, then filter it (you may keep the seeds) for Spermidation or for preventing twelve ounces of Sugar candy, with six ounces of red Rose-water, and four ounces of spirit of Cinnamon with it.”

I suppose this was invented for a cordial to strengthen the heart, to relieve languishing nature. It is exceeding dear. I forbear the dose, they that have money enough to make it themselves, cannot want time to study both the virtues and dose; I would have gentlemen to be studious. (Nicholas Culpeper (1616-54) The Complete Herbal, 1850.)