Prosthetic Valvular Endocarditis

A 12-Year Review

By Laura Slaughter, M.D., James E. Morris, M.D.,
and Albert Starr, M.D.

SUMMARY

A retrospective examination was made of a total of 48 patients with infected prosthetic cardiac valves implanted in 1,236 patients during 1960-1972. Survival rate of the valvular infections was 40%. The purpose of the study was to determine the factors which aided or decreased patient survival and to develop a program of treatment with antimicrobial agents. Numerous antimicrobics and a variety of dosage schedules were used. Of 19 surviving patients, medical treatment alone was effective in 14, despite the continued presence of a valvular prosthesis. Reoperation was successful in five of nine patients. Lifetime chemoprophylactic or suppressive therapy was shown to be unnecessary to prevent relapse in 12 survivors. Prompt surgical replacement is indicated if antimicrobial therapy fails to eradicate infection of a prosthetic valve. A more systematic approach to antimicrobial therapy should improve survival of medically treated infections. Recommendations are made for prevention and treatment of prosthetic valvular endocarditis.

Additional Indexing Words:
Antibiotic therapy  Cardiac surgery  Infection

During the past decades as the use of artificial cardiac valves has become widespread, the problem of postoperative valvular infections has become prominent (table 1). Numerous articles have presented the difficulties of diagnosis and therapy.1-7 The outcome of such infections, whether treated medically or surgically, has generally been dismal.8-10 Other writers have emphasized the preventive value of prophylactic antimicrobial therapy at the time of surgery reporting a decrease in the incidence of prosthetic valvular endocarditis (PVE).11,12 Prosthetic infections, however, continue to occur. Accordingly, there may be a need for a systematic approach to the therapy of infected prosthetic cardiac valves. The purpose of this article is to review the experience since 1960 at three Portland hospitals. The details of the infections will be presented and recommendations made for the management of these serious infections.

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Methods

A total of 1,235 patients had valve replacements with Starr-Edwards prostheses from 1960 to 1972 in three Portland hospitals: University of Oregon Medical School Hospitals, St. Vincent Hospital, and the Veterans Administration Hospital. One additional patient in the series received a Cutter-Smeloff valve in another hospital. Postoperative valvular infections occurred in 48 patients (table 2) as evidenced by two or more positive blood cultures or valve cultures at open-heart surgery (nine patients) or autopsy (21 patients), and by clinical findings of fever, and at least two of the usual criteria for bacterial endocarditis, namely: a new, regurgitant murmur; splenomegaly or peripheral emboli (18 patients). Medical treatment of these infections was provided in one of the three Portland hospitals in 40 cases. The remaining eight patients were treated elsewhere. There were 34 males and 14 females. Their ages ranged from 15 to 69, averaging 44 years. The cardiac disease responsible for the initial valvular replacement was rheumatic valvulitis in 34 patients, calcific aortic stenosis in 11, and previous bacterial endocarditis in three patients. Nine of the 48 patients had second operations for valvular replacement as a consequence of their infection. Autopsies were performed on 21 patients. As a result of the initial five infections in this series,11 all subsequent patients have received prophylactic evaluation including dental and paranasal sinus roentgenograms, urine, and nasopharyngeal cultures with appropriate treatment, where indicated. In addition, chemoprophylaxis was undertaken. During the 12-year period (1960-1972), the antimicrobics used have varied but were usually directed against staphylococci. Currently,
Table 1
Summary of Valve Operations and Infections

<table>
<thead>
<tr>
<th>Year</th>
<th>Total pts (no.)</th>
<th>Early Infections (no.)</th>
<th>Late Infections (no.)</th>
<th>Total Infections (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960</td>
<td>4</td>
<td>0</td>
<td>0</td>
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<tr>
<td>1961</td>
<td>17</td>
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<td>131</td>
<td>1</td>
<td>0</td>
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<td>132</td>
<td>0</td>
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<td>1966</td>
<td>137</td>
<td>2</td>
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<td>3</td>
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<td>1967</td>
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<td>0</td>
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<td>7</td>
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<tr>
<td>1969</td>
<td>142</td>
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<td>5</td>
<td>11</td>
</tr>
<tr>
<td>1970</td>
<td>153</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>1971</td>
<td>158</td>
<td>3</td>
<td>5</td>
<td>8</td>
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<tr>
<td>Total</td>
<td>1236</td>
<td>23</td>
<td>25</td>
<td>48</td>
</tr>
</tbody>
</table>

*Numbers represent infections diagnosed in that year.

Table 2
Prevalence of Prosthetic Valvular Endocarditis

<table>
<thead>
<tr>
<th>Type of implant</th>
<th>Implants (no.)</th>
<th>Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic</td>
<td>585</td>
<td>22</td>
</tr>
<tr>
<td>Mitral</td>
<td>996</td>
<td>15</td>
</tr>
<tr>
<td>Multiple</td>
<td>255</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>1236</td>
<td>48</td>
</tr>
</tbody>
</table>

Table 3
Relationship of Mortality to Onset of Infection and Valve

<table>
<thead>
<tr>
<th>Type of implant</th>
<th>Early Mortality</th>
<th>Late Mortality</th>
<th>Total Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic</td>
<td>10/11*</td>
<td>5/11</td>
<td>15/22</td>
</tr>
<tr>
<td>Mitral</td>
<td>6/6</td>
<td>3/9</td>
<td>9/15</td>
</tr>
<tr>
<td>Multiple</td>
<td>4/6</td>
<td>1/5</td>
<td>5/11</td>
</tr>
</tbody>
</table>

*Ratio is the number of deaths to total number of cases.

Summary

Of the 48 patients with bacteriologic evidence of endocarditis, 19 survived the infection. Reference to Table 3 reveals mortality related to onset after valvular replacement. All percentages were calculated by patient rather than by valve. Eleven patients with multiple implants developed infections: six with aortic, mitral, and tricuspid; three with aortic and mitral; and two patients with mitral and tricuspid prostheses. Twenty-three early infections, those occurring within 2 months after surgery, had an overall mortality of 87% (20 of 23). Twenty-five infections occurred after 2 months with a 36% (nine of 25) mortality. The causes of death included valvular disruption, congestive heart failure, overwhelming sepsis, and multiple septic emboli, frequently with occlusion of the coronary arteries, usually a lethal occurrence. Thirty of the 48 patients with PVE (16 early and 14 late) were examined at autopsy or surgery. Only two in this group demonstrated an associated infection of a natural valve (one mitral and one tricuspid). Both had aortic impl-

plants for calcific aortic stenosis with no other valve abnormality reported. In one of these 30 patients was only a natural valve infected.

Staphylococcus aureus and epidermidis (formerly albus) accounted for 46% (22 of 48) of the total infections. Of these, 59% (13 of 22) occurred in the early and 41% (nine of 22) in the late postoperative period. Staphylococcus epidermidis was responsible for 62% (eight of 13) of the early staphylococcal infections with a mortality rate of 75% (six of eight), whereas S. aureus occurring in the remaining five was uniformly fatal. If we consider only those patients receiving prophylactic antimicrobics, omitting the initial five early infections (one from S. epidermidis and four from S. aureus), this reduced the early staphylococcal infections to eight, of which only one was attributable to S. aureus. Only one patient was receiving chemoprophylaxis (clindamycin) when endocarditis was diagnosed. The causative organism, S. epidermidis, was resistant to clindamycin. The prevalence of S. aureus has diminished to 13% (one of eight) from 38% (five of 13). In the late staphylococcal infections, S. aureus predominates, accounting for 56% (five of nine) with a 60% (three of five) mortality; S. epidermidis, isolated in the remaining four (44%), was fatal in only 25% of the cases. Together, staphylococci were responsible for 59% (13 of 22) of all the early infections and 50% (11 of 22) of the deaths in this group. Staphylococcal prevalence in late postoperative infections was 35% (nine of 26) with a mortality rate of 15% (four of 26).

The next largest group of infections (35% or 17 of 48) was caused by Streptococcus sp.; 87% (14 of 16) of these occurred more than 2 months after valve implantation. Viridans group streptococci and Streptococcus fecalis, isolated in seven cases each, accounted for 54% (14 of 26) of all late infections but only 19% (five of 26) of the fatalities in this group. One unclassified streptococcus grew only in liquid media but could be subcultured in liquid or
Table 4

<table>
<thead>
<tr>
<th>Organism</th>
<th>Early (no.)</th>
<th>Late (no.)</th>
<th>Total (no.)</th>
<th>Infection</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis</td>
<td>8</td>
<td>4</td>
<td>12</td>
<td>25</td>
<td>58</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>21</td>
<td>80</td>
</tr>
<tr>
<td>Streptococcus sp., viridans group</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td>17</td>
<td>37</td>
</tr>
<tr>
<td>Streptococcus fecalis</td>
<td>1</td>
<td>7</td>
<td>8</td>
<td>17</td>
<td>25</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Unclassified streptococcus sp.</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Micrococcus sp.</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>100</td>
</tr>
</tbody>
</table>

solid media if yeast extract or filtrate of other bacterial cultures was added to the media (tables 4 and 5).

Fungal and aerobic gram-negative bacillary infections (three Candida sp., two Pseudomonas sp., one Achromobacter sp., one Serratia sp., and one Proteus mirabilis), although only 17% of the total (eight of 48) infections, represented 35% (eight of 23) of the early cases and were uniformly fatal. The Proteus mirabilis infection occurred late in a patient with obstructive uropathy caused by prostatic carcinoma.

In general, our bacteriologic findings (table 4) agree with the reports of others. An increased prevalence of staphylococci and gram-negative bacilli occurred in the early postoperative period whereas late infections were associated with a bacteriologic spectrum resembling that causing natural valvular infection.

Eighteen of the 48 infected patients, or 35%, were treated by other physicians prior to hospitalization on at least one occasion. All of these patients received some antimicrobial therapy prior to hospital admission, therapy that was uniformly ineffective. The interval between initial physician contact and hospitalization varied from 3 to 150 days, averaging 25 days. The mortality in this group was 56% (10 of 18).

During hospitalization, there was no standard regimen of antimicrobial therapy for endocarditis. For example, therapy of staphylococcal infections included a total of 10 antimicrobics given in various doses and by several methods of administration. Intermittent dosage schedules included both equal-time intervals and irregular intervals such as three or four times daily. The duration of therapy ranged from 14 to 72 days, averaging 38 days.

Serum bactericidal titers were carried out in 19 of the 48 cases of PVE. The titers were 1:8 or greater in 14 patients; however, the temporal relation of specimen sampling to antimicrobial dosage was recorded for only nine patients.

Nine of the 48 patients had operations as a consequence of valvular infection. The precipitating causes were uncontrolled infection in four patients (S. aureus in two, Streptococcus fecalis in two) and congestive heart failure, large arterial emboli, or the appearance of a diastolic murmur in five patients.

Of the 19 surviving patients, five had successful secondary operations and 14 had medical treatment alone (table 5). The duration of survival after hospital discharge ranged from 3 to 98 months, averaging 30 months. Streptococci accounted for 12 and staphylococci for seven prosthetic valvular infections among the 19 surviving patients. Five of the seven staphylococcal isolates were S. epidermidis.

Following medical or surgical therapy, the staff physicians of the three Portland hospitals recommended lifelong, suppressive, oral administration of antimicrobics. Consequently, at discharge 16 of the surviving patients from these hospitals were instructed to take antimicrobial agents active against streptococci or staphylococci. The remaining three survivors were discharged from other hospitals with no oral regimen of chemoprophylaxis.

Of the 16 surviving patients discharged taking oral antimicrobics, seven (four of whom had second operations) were instructed by their private physicians to stop the treatment after 1–27 months, averaging 14 months. The duration of survival after hospital discharge was 5–98 months, averaging 40 months. Of the five patients who received no suppressive therapy, the duration of survival was 12–84 months, averaging 44 months. The time without suppressive therapy for all 12 survivors was 3–81 months, averaging 41 months, compared with 20 months for the seven patients on continuous suppressive treatment.
Table 5

Survivors of Prosthetic Valvular Endocarditis

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Valve</th>
<th>Onset of infection</th>
<th>Bacterium</th>
<th>Length of parenteral therapy (days)</th>
<th>Date of diagnosis (mo-yr)</th>
<th>Suppressive antimicrobial*</th>
<th>Length of suppression (mos)</th>
<th>Date suppression stopped (mo-yr)</th>
<th>Second operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>L</td>
<td>Str. viridans</td>
<td>21</td>
<td>12-65</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>L</td>
<td>Staph. aureus</td>
<td>90</td>
<td>12-65</td>
<td>Oxacillin</td>
<td>9</td>
<td>12-66</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>A</td>
<td>E</td>
<td>Staph. epidermidis</td>
<td>18</td>
<td>12-71</td>
<td>Cloxacillin</td>
<td>Pr</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>A</td>
<td>L</td>
<td>Str. fecalis</td>
<td>72</td>
<td>10-71</td>
<td>Ampicillin</td>
<td>Pr</td>
<td>—</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>A</td>
<td>L</td>
<td>Str. sp.</td>
<td>60</td>
<td>10-71</td>
<td>Ampicillin</td>
<td>Pr</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>A</td>
<td>L</td>
<td>Staph. aureus</td>
<td>14</td>
<td>11-70</td>
<td>Ampicillin</td>
<td>11</td>
<td>10-71</td>
<td>—</td>
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<tr>
<td>7</td>
<td>A</td>
<td>L</td>
<td>Str. viridans</td>
<td>21</td>
<td>7-72</td>
<td>Cloxacillin</td>
<td>12</td>
<td>10-71</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>L</td>
<td>Str. fecalis</td>
<td>20</td>
<td>10-70</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>L</td>
<td>Str. fecalis</td>
<td>38</td>
<td>7-70</td>
<td>Ampicillin</td>
<td>Pr</td>
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<td>—</td>
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<tr>
<td>10</td>
<td>M</td>
<td>L</td>
<td>Str. fecalis</td>
<td>34</td>
<td>3-70</td>
<td>Ampicillin</td>
<td>27</td>
<td>7-72</td>
<td>Yes</td>
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<tr>
<td>11</td>
<td>M</td>
<td>L</td>
<td>Str. viridans</td>
<td>60</td>
<td>12-71</td>
<td>Ampicillin</td>
<td>Pr</td>
<td>—</td>
<td>—</td>
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<tr>
<td>12</td>
<td>M</td>
<td>L</td>
<td>Staph. epidermidis</td>
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<td>1-64</td>
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<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>13</td>
<td>M</td>
<td>L</td>
<td>Staph. epidermidis</td>
<td>34</td>
<td>1-72</td>
<td>Cephalothin</td>
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<td>4-72</td>
<td>Yes</td>
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<td>14</td>
<td>AM</td>
<td>L</td>
<td>Str. fecalis</td>
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<td>11-68</td>
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<td>AM</td>
<td>L</td>
<td>Str. fecalis</td>
<td>38</td>
<td>9-69</td>
<td>Penicillin V</td>
<td>13</td>
<td>12-71</td>
<td>Yes</td>
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<tr>
<td>16</td>
<td>TAM</td>
<td>L</td>
<td>Str. viridans</td>
<td>42</td>
<td>7-71</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>17</td>
<td>TAM</td>
<td>E</td>
<td>Staph. epidermidis</td>
<td>45</td>
<td>1-71</td>
<td>Clindamycin</td>
<td>Pr</td>
<td>—</td>
<td>—</td>
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<tr>
<td>18</td>
<td>TAM</td>
<td>E</td>
<td>Staph. epidermidis</td>
<td>23</td>
<td>6-69</td>
<td>Lincomycin</td>
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<td>3-72</td>
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<td>Str. viridans</td>
<td>40</td>
<td>6-69</td>
<td>Erythromycin</td>
<td>Pr</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*Where not stated none given. Does not include rheumatic fever prophylaxis.
†Pr indicates patient is still being treated as of August 1972.

Abbreviations: A = aortic valve; A = aortic cutter-Smeloff valve; M = mitral valve; T = tricuspid valve; E = early infection (<2 mos); L = late infection (>2 mos).
**Discussion**

Advances in medical and surgical technology have resulted in an expanding number of both prosthetic valve recipients and physicians involved in their care. With increased longevity and the use of prophylactic antimicrobics at the time of surgery in these patients, the majority of infections occur in the late postoperative period. The enhanced susceptibility to and the difficulty of eradicating infection in the presence of a foreign body make for a grim prognosis in this now quite common clinical dilemma.

The increased vulnerability of an intravascular prosthesis to infection has been well documented. Consequently, chemoprophylaxis at the time of the initial surgery and during subsequent procedures that might be accompanied by transient bacteremias is commonly supported. Drug selection for chemoprophylaxis during valve replacement should be determined by the bacterial susceptibility patterns prevalent at the hospital of operation. For example, currently at the University of Oregon Medical School Hospitals disc-diffusion testing of 176 isolates of S. epidermidis yielded susceptibility frequencies of 67% to nafcillin and methicillin, 24% to penicillin G, and 97% to cephalothin. Apparently, cephalothin would be the agent of choice for prevention of infection by S. epidermidis in these hospitals.

With diagnostic or therapeutic procedures, selection varies with the procedure and is directed against the resident flora that might be implicated in bacteremia. Generally, antimicrobial therapy is begun 1 hour before and continued for 2 days after the procedure (table 6). Because of the presence of resistant resident bacterial flora, it has been suggested that elective procedures should not be performed during the course of treatment for infective endocarditis.

Criteria for the diagnosis of PVE have been suggested by several authors. It should be emphasized that fever alone is inadequate as a basis for diagnosis. Recently, Sande and his associates proposed three criteria for separating intracardiac from extracardiac sources of bacteremia in patients with prosthetic valves: (1) an incubation period less than 25 postoperative days; (2) the isolation of gram-negative bacilli or microorganisms resistant to the prophylactic agents; or (3) detection of an extracardiac source for bacteremia. As Weinstein has pointed out, such criteria, while helpful, are not absolute and the possibility of secondary colonization of the prosthesis must be considered.

The success enjoyed by the 14 patients who received a single course of therapy with antimicrobics supports the view that systematic medical therapy of PVE can be highly successful. However, certain principles deserve emphasis. Because host defenses are ineffective, potentially bactericidal agents which will penetrate vegetations should be used. Intermittent intravenous administration at regular time intervals are preferred by some authors. Injection sites should be changed every 48–72 hours. Aside from the obvious mechanical difficulties of maintaining and regulating flow, continuous infusion therapy may result in imprecise dosage because of drug deterioration and adsorption to container surfaces. Table 7 outlines antimicrobial therapy for the common causes of PVE.

Because PVE is so often lethal and because of the great value of the penicillins in treatment, a history of penicillin allergy should not deter the physician from use of these agents. Williams and his associates have urged a program of increasing penicillin dosage, reserving cephalosporin drugs or

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Suspected bacterium</th>
<th>Antimicrobics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental</td>
<td>Streptococcus sp., viridans group</td>
<td>Procaine penicillin G 600,000 u i.m. 1 hr before the procedure and daily for 2 more days. Alternatives include penicillin V 400,000 u q 6 hrs orally, erythromycin 250 mg or clindamycin 150 mg q 6 hrs orally for 3 days.</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Streptococcus fecalis</td>
<td>Procaine penicillin G 1.2 million u q 8 hrs i.m. and streptomycin, 0.5 g q 12 hrs i.m. Begin therapy 1 hr before the procedure and continue for 72 hrs.</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>Staphylococcus aureus or epidermidis</td>
<td>Cephalaxin 250 mg orally 1 hr before and q 6 hrs for 72 hrs.</td>
</tr>
</tbody>
</table>
vancomycin for patients with severe or uncontrollable hypersensitivity reactions.23

Therapy should be guided by both laboratory and clinical evaluation. Once susceptibility has been determined, preferably by tube-dilution assay, a regimen of therapy selected, the serum bactericidal titer (SBT) should be determined on the third day after initiation of therapy using serum collected ½ hour before a dose, the predicted low point of blood concentration.25 A minimal bactericidal titer of 1:8 has been selected.23, 26 This titer was adopted as the critical level when penicillin G was virtually the sole agent for therapy; validation with other antimicrobics is necessary.

The need for prophylactic or suppressive antimicrobial therapy after medical or surgical treatment of PVE is controversial. It is, moreover, both expensive and inconvenient. In the case of fungal or gram-negative bacillary infections, appropriate antiinfective drugs may be nearly impossible to prescribe over a prolonged period. Whether or not such therapy can truly suppress a persisting infection over a long period without the reappearance of clinical endocarditis remains to be proven. Because 12 of 19 patients survived for an average of 2 years without antimicrobics, we believe that lifelong chemoprophylaxis is not always necessary following treatment of nonstaphylococcal PVE. Limited, extended therapy following staphylococcal infections is recommended because of potential intracellular persistence and abscess formation. For such patients, we arbitrarily recommended oral suppressive therapy for 6–12 months with cloxacillin, 0.25 g every 6 hours or, in patients with hypersensitivity to penicillins, clindamycin 0.15 g every 8 hours, or cephalaxin 0.25 g every 6 hours.

Prompt valve replacement is indicated when medical therapy fails. In our series, five of nine patients survived secondary operations and four of these had positive bacterial cultures at surgery. Others have reported similar satisfactory results from secondary operations.27–29 Medical failure is indicated by uncontrolled infection, large or multiple emboli, refractory congestive heart failure, and valvular disruption. These complications rarely occur singly and progressive cardiac

Table 7

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antibiotic therapy*</th>
<th>Alternate antibiotic therapy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus sp., viridans group (susceptible to 0.3 meg/ml of penicillin G)</td>
<td>Crystalline penicillin G one million u q 4 hrs i.v. or procaine penicillin G 1.2 million u q 6 hrs i.m. for 4 weeks</td>
<td>Cephalothin 1 g q 4 hrs i.v. or vancomycin 0.5 g q 6 hrs i.v. for 4 weeks</td>
</tr>
<tr>
<td>Streptococcus sp. enterococcal or viridans group (susceptible to more than 0.3 meg/ml of penicillin G)</td>
<td>Crystalline penicillin G 20 million u i.v. daily and streptomycin 0.5 g q 12 hrs i.m. for 6 weeks</td>
<td>Ampicillin 2 g q 4 hrs i.v. and gentamicin 5 mg per kg body weight daily or vancomycin 0.5 g q 6 hrs i.v. for 6 weeks</td>
</tr>
<tr>
<td>Staphylococcus aureus or epidermidis (susceptible to 0.6 meg/ml)</td>
<td>Crystalline penicillin G 20 million u i.v. daily for 6 weeks†</td>
<td>Cephalothin 2 g q 3 or 4 hrs or vancomycin 1 g q 6 hrs i.v. for 6 weeks†</td>
</tr>
<tr>
<td>Staphylococcus aureus or epidermidis (susceptible to more than 0.6 meg/ml of penicillin G)</td>
<td>Nafcillin or oxacillin 2–3 g q 3 or 4 hrs i.v. for 6 weeks†</td>
<td>None</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td>Therapy is guided by antibiotic susceptibility tests. Bactericidal antibiotics such as kanamycin, ampicillin, carbencillin, gentamicin, cephalothin or streptomycin are preferable</td>
<td>None</td>
</tr>
<tr>
<td>Negative blood cultures</td>
<td>Cephalothin 2 g q 6 hrs i.v., crystalline penicillin 20 million u daily i.v., and streptomycin 0.5 g q 12 hrs for 6 weeks</td>
<td>None</td>
</tr>
</tbody>
</table>

*If normal renal function.
†See Discussion section for suppressive therapy.
deterioration may ensue rapidly. Once medical failure has become apparent, hesitation only increases operative mortality and morbidity.

In summary, during the years 1960–1972, the total number of PVE cases has increased. Coincident with the use of preoperative antimicrobial chemoprophylaxis, the number of early postoperative PVE cases has decreased. As causative organisms of these early infections, the prevalence of S. epidermidis increased while S. aureus has decreased. Further, the in vitro resistance of S. epidermidis to the semisynthetic penicillins has increased to the current 33%. Overall mortality in 48 cases of PVE was 60%; it was highest in patients with early postoperative infections, single valves, gram-negative bacilli, S. aureus, and Candida species. Endocarditis in the presence of prosthetic valves in the cases in our series confirmed at open-heart surgery or autopsy always involved the prostheses and, occasionally, also included a natural valve. Medical therapy proved effective in eradicating PVE in 30%. When medical treatment failed, prompt surgical intervention was rewarding. The use of prophylactic or suppressive antimicrobial drugs after treatment of active PVE was not necessary in all patients. No relapses have occurred in 12 patients not receiving lifelong antimicrobial agents. The role of suppressive antimicrobics in the successful management of patients with nonstaphylococcal PVE and the factors influencing their selection for such therapy remain to be determined. When the diagnosis of PVE is established, the use of a systematic program of therapy is essential to improve existing survival rate. Despite the reported successes of second operations, the need for repeated valvular replacement will hopefully thereby be decreased.

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