Perioperative antibiotic prophylaxis and prosthetic valve endocarditis

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Summary
A study of twenty-five cases of prosthetic valve endocarditis suggests that the antibiotics used for perioperative prophylaxis may alter the type and antibiotic sensitivity of organisms which subsequently infect the artificial valves. Based on the results of this study, the authors have been able to modify their prophylactic regime to encompass these organisms and to predict the antibiotics most likely to be effective in the treatment of prosthetic valve endocarditis in their unit. No single prophylactic or therapeutic regime will be equally effective in all centres, but by examining the different types and sensitivities of bacteria which cause prosthetic valve endocarditis in a locality, antibiotic regimes can be chosen which best suit the local situation.

Introduction
Prosthetic valve endocarditis is a major hazard for patients with artificial cardiac valves. It occurs in approximately 4% of cases and has a high mortality, particularly during the early postoperative months. Perioperative antibiotic prophylaxis probably reduces the incidence of prosthetic valve endocarditis but, while eradicating some organisms, such therapy may encourage the overgrowth of other, insensitive, strains. If this is so, antibiotics used perioperatively may predetermine the types of organisms which subsequently infect the patients' valves. This hypothesis has not been tested because most centres have used a variety of prophylactic regimes (Dismukes et al., 1973; Hairston and Lee, 1970; Madison et al., 1975; Slaughter, Norris and Starr, 1973; Stein, Harken and Dexter, 1966) and this has obscured the long term effects of specific antibiotics. In this report, the characteristics of prosthetic valve endocarditis occurring in the relatively uniform context of only two related regimes of perioperative antibiotic prophylaxis are described and the implications discussed.

Details of antibiotic prophylaxis
The two regimes used were: (1) ampicillin and cloxacillin 500 mg four times daily of each for 10 days commencing 48 hr before operation; (2) cloxacillin 500 mg four times daily for 5 days beginning immediately after operation.

Details of patients studied, time of infection and outcome (Tables 1 and 2)
Prosthetic valve endocarditis occurred in twenty-five (3.4%) of 746 patients who underwent valve replacement during 1970-1975. Average age was 47.7 years. Nineteen were male (average age 49.1 years) and six were female (average age 40.8 years). Affected valves were aortic, seventeen cases; mitral, five cases; aortic plus mitral, three cases.

Thirteen (52%) patients died—eleven male and two female—average age 50.9 years.

The time interval between valve insertion and diagnosis of endocarditis varied from 1 to 57 months (average 15.1 months). The average time between operation and diagnosis of infective endocarditis in survivors was 19.8 months and in fatal cases was 11.3 months.

Six (25% of cases) presented within 2 months of surgery and of these, four died. A total of fifteen cases occurred within 1 year of surgery and ten of these died. Ten cases occurred more than 1 year after surgery, of whom only three died.

Bacteriology (Tables 2 and 3)
Table 2 records the organisms encountered and how they relate to the time between valve insertion and the development of infective endocarditis.

Table 3 relates antibiotic sensitivity to the time at which endocarditis occurred and to specific organisms. There were no significant differences between the two regimes of prophylaxis with respect to outcome, organisms cultured or antibiotic sensitivity.
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Table 1. Details of twenty-five patients with prosthetic valve endocarditis

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Average age (years)</th>
<th>Sex</th>
<th>Number of organisms affected</th>
<th>Prophylactic valve</th>
<th>Bacteriology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>M</td>
<td>F</td>
<td>A</td>
<td>A + M</td>
</tr>
<tr>
<td>All cases</td>
<td></td>
<td>19</td>
<td>6</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Non-fatal</td>
<td></td>
<td>8</td>
<td>4</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Fatal</td>
<td></td>
<td>11</td>
<td>2</td>
<td>9</td>
<td>3</td>
</tr>
</tbody>
</table>

A. aortic; M. mitral; Diphth., diphtheroid bacilli; Staph., Staphylococcus sp.; S.V., Streptococcus viridans; Cult. neg., culture negative.

Table 2. Infection organisms in prosthetic valve endocarditis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number encountered during first postoperative year</th>
<th>Number encountered &gt; 1 year postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheroids</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Staphylococcus sp.</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Streptococcus viridans</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Klebsiella sp.</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Culture negative</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

Eight cases (32% of total) were caused by diphtheroid bacilli; all occurred within 1 year of surgery. Only one was sensitive to penicillin and two to ampicillin. All were sensitive to erythromycin, fusidin, lincomycin and gentamicin. Six cases (25% of total) were caused by staphylococci (five coagulase negative, one coagulase positive) of which four occurred within 1 year of valve insertion. Three were sensitive to methicillin, erythromycin, fusidin and cephalosporins. All were sensitive to gentamicin.

The two cases due to Pseudomonas aeruginosa and the single case due to Klebsiella sp. occurred within 1 year of surgery and were resistant to the penicillins and to cephalosporins, erythromycin, fusidin and lincomycin, but were sensitive to gentamicin.

Thus, most organisms encountered within 1 year of surgery were resistant to all penicillins and the cephalosporins.

Two cases due to Streptococcus viridans occurred more than 1 year after surgery; one was sensitive to penicillin.

A single case due to meningococcus occurred 42 months after surgery and was sensitive to all antibiotics tested except lincomycin. Five cases of culture-negative endocarditis occurred all after the first postoperative year.

All organisms tested against gentamicin were sensitive to it and most were sensitive to erythromycin and fusidin. On a weight for weight basis, erythromycin and fusidin were usually the most active antibiotics; this was particularly so with respect to the diphtheroid bacilli.

Discussion

There is no objective evidence that the incidence of prosthetic valve endocarditis is reduced by antibiotic prophylaxis at the time of valve surgery; in fact Goodman et al. (1968) and Dismukes et al. (1973) implied that the antibiotics might, in some respects, be harmful. Nevertheless, most clinicians follow the recommendation of Geraci, Dale and McGoon (1963) and use some form of antibiotic prophylaxis. This action is justified by the results of several uncontrolled studies (Amoury, Bowman and Malm,

Table 3. *In vitro* antibiotic sensitivity of organisms from cases of prosthetic valve endocarditis

<table>
<thead>
<tr>
<th>Number of sensitive organisms cultured in first post-op. year</th>
<th>Number of sensitive organisms cultured &gt; 1 year post-op.</th>
<th>Sensitivity of specific organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td>1/14</td>
<td>1/8</td>
</tr>
<tr>
<td>Methicillin</td>
<td>2/6</td>
<td>3/5</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>2/10</td>
<td>3/8</td>
</tr>
<tr>
<td>Cephalosporin</td>
<td>5/13</td>
<td>4/5</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>11/14</td>
<td>3/5</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>9/12</td>
<td>3/5</td>
</tr>
<tr>
<td>Fusidin</td>
<td>9/12</td>
<td>3/5</td>
</tr>
<tr>
<td>Gentamicyn</td>
<td>13/13</td>
<td>3/3</td>
</tr>
</tbody>
</table>

Diphth., diphtheroid bacilli; Staph., staphylococci; S.V., Streptococcus viridans; Ps., Pseudomonas aeruginosa; Kl. sp., Klebsiella sp., Mening., meningococcus.
ever, this and the resistance to operation was of the cloxacillin for endocarditis (Jackson infections, of their early postoperative valve endocarditis caused by that organism in the high incidence of (1) Dismukes et al., 1973; Madison et al., 1975). It is clear, therefore, that recommendations to use specific antibiotics to treat prosthetic valve endocarditis (Stein et al., 1966; Gray, 1975) may be misleading and are not justified, for they fail to take these variable factors into account.

Thus, although the treatment of prosthetic valve endocarditis is primarily dependent on the antibiotic sensitivity of organisms cultured from individual patients, each centre should also plan its own treatment policy, based on the evaluation of past local experience with antibiotic prophylaxis and with in vitro sensitivity testing of organisms cultured from previous cases. This approach to treatment is particularly important when, as happens in approximately 33% of all cases, treatment has to be started "blind"—either because of the gravity of the patient's condition or because of persistently negative blood cultures. Furthermore, identification of the organisms which commonly 'break through' the prophylactic regime allows this cover to be altered so as to be effective against them. To this end, the effect of including erythromycin in their perioperative antibiotic prophylaxis is currently being studied by the authors.

References
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