The use of antibiotic prophylaxis in patients predisposed to infective endocarditis (IE) who are undergoing oral surgery procedures is widely accepted. Because there have been no controlled clinical trials of antibiotic regimens for the prevention of endocarditis in humans, recommendations are based on the results of prophylaxis studies in animal models of endocarditis, in vitro susceptibility data of pathogens that cause endocarditis, procedure-related studies of bacteremia, and studies of the efficacy of antimicrobial prophylaxis for prevention of postsurgical bacteremia.

Minimizing the occurrence of postoperative bacteremia has been considered the most important factor in the prevention of IE, and the results of several clinical studies using conventional blood culture systems have demonstrated a marked reduction in bacteremia following dental extraction with the use of antibiotic prophylaxis. In recent studies using lysing and filtration of blood, prophylactic administration of penicillin V, amoxicillin, erythromycin, clindamycin, or cefaclor did not reduce the incidence or the magnitude of bacteremia after dental extraction, as compared to placebo.

The antimicrobial mechanism of protection for IE is apparently different from a mere killing in blood. The implications of this for prophylaxis for IE in humans is still not fully understood, but studies of animals suggest that the protective effect may be exerted by inhibiting bacterial growth on the vegetations, thus allowing host defense mechanisms to gradually eliminate the bacteria from the valves.

Microorganisms circulating in blood may settle on heart valves that are damaged or rendered defective by acquired or congenital disease and thereby cause IE. The disease remains prevalent, with approximately the same incidence as 40 years ago, and is associated with a mortality rate between 15% and 30%, despite advances in antimicrobial therapy and cardiovascular surgery.

Dental treatment has often been regarded as a major cause of the disease, mainly because of the high frequency of bacteremia after various oral invasive procedures and because of the high recovery rate of viridans streptococci in IE cases [1, 2]. The concept of antibiotic prophylaxis for IE in patients with underlying heart disease has been widely accepted, and guidelines and specific antibiotic regimens have been recommended by various national boards [3, 4]. For ethical as well as practical reasons, there has been no clinical documentation of the efficacy of antibiotics in preventing IE in humans, and therefore the guidelines are based mainly on data from experimental animal models, pharmacokinetic studies, bacterial susceptibility studies, clinical experience, and studies of procedure-related bacteremia and the efficacy of antimicrobial prophylaxis for bacteremia.

In animal studies, prophylactic administration of antibiotics has been attributed to effects such as rapid bacterial killing in blood, decreased bacterial adhesion to heart valves, and inhibition of bacterial growth on the heart valves, whereas studies in humans have mainly focused on the preventive effect on postsurgical bacteremia.

Results of clinical studies have indicated an immediate and marked reduction in bacteremia following dental extraction when prophylactic antibiotics were used, whereas other studies have questioned the efficacy of antibiotic prophylaxis for postextraction bacteremia.

Herein, we review the data published concerning bacteremia after oral surgical procedures and antibiotic prophylaxis.

Bacteremia of Oral Origin

Invasion of the bloodstream by bacteria may follow a wide variety of clinical procedures and manipulations, particularly those that involve infected sites or heavily colonized mucosal surfaces [5]. After the bacteria are mechanically translocated into tissues, they are transported via the lymphatic system to the vascular system and are then, under normal conditions, rapidly eliminated by the reticuloendothelial system. As early as 1945, Beeson and co-workers pointed out the significance of the macrophages in the spleen and liver for the clearance of bacteria from blood [6]. They showed that the bacterial colony counts in hepatic venous blood were 50% to 95% lower than
the colony counts observed in the arterial blood of patients with bacterial endocarditis.

Awareness of the relationship between IE and dental treatment dates back to 1909, when Horder noted the association between “Streptococcus viridans” in the oral cavity and IE in patients with heart disease [7]. Lewis and Grant, in 1923, postulated that healthy persons frequently have innocuous, transient bacteremia, but that defective heart valves may trap and retain organisms that cause IE [8].

In 1935, Okell and Elliott noted streptococcal bacteremia following dental extraction in 61% of their 138 patients [9]. Two years later, in 1937, Burket and Burn painted the gingival crevices of 90 patients with pigmented Serratia marcescens before dental extraction [10]. After the procedure, the organism was recovered from 20% of the blood cultures, confirming that organisms in the oral cavity can gain entry to the blood circulation during dental manipulations. Taran’s report in 1944 showed that dental extraction with subsequent bacteremia could probably induce endocarditis [11]. In four children with rheumatic heart disease who had negative preoperative blood cultures, persistent streptococcal bacteremia was noted; all four died of subacute IE.

Viridans streptococci isolated from the blood of patients with endocarditis are generally thought to originate from the oral cavity, but absolute evidence for this assumption has been lacking. However, the relation has now been proved, according to a recent report by Fiehn and co-workers [12]. On the basis of conventional microbial methods and ribotyping, the viridans strains isolated from the blood and oral cavity were demonstrated to be identical in two patients with endocarditis.

Many investigators have assessed the incidence of transient bacteremia following various oral procedures (table 1).

Although viridans streptococci are the microorganisms most frequently isolated in these studies, considerable differences in frequency, type, and magnitude (colony counts per milliliter of blood) of postoperative bacteremia are reported. This is mainly the result of diversities in the type of surgical procedure (e.g., single vs. multiple dental extractions), time of blood sampling, volume of blood cultured, and the methods used to isolate and identify the microorganisms, which hinder interpretation and comparison of the results. The reports published before the 1960s may also underestimate the incidence of transient bacteremia, since no refined anaerobic culture technique was available. Recently, new methods for isolation of microorganisms from the bloodstream, combining anaerobic culture techniques and filtration of blood, have resulted in renewed interest in the field [16].

Heimdahl et al. [17] studied 100 patients with bacteremia after dental extraction, third-molar surgery, dental scaling, endodontic treatment, and bilateral tonsillectomy by means of lysis-filtration of blood samples with subsequent aerobic and anaerobic incubation. Samples were obtained before, during, and 10 minutes after treatment. Bacteremia was observed in 100% of patients after dental extraction, 55% after third-molar surgery, 70% after dental scaling, 20% after endodontic treatment, and 55% after bilateral tonsillectomy. Anaerobic microorganisms were isolated more frequently than aerobic microorganisms, and viridans group streptococci were the most commonly isolated bacteria. Ten minutes after treatment, the frequency as well as the magnitude of bacteremia showed pronounced reduction.

In another trial, Hall et al. [18] investigated the incidence of postextraction bacteremia after penicillin administration. Sixty healthy patients were randomized to receive placebo, penicillin V (2 g), or amoxicillin (3 g) 1 hour before dental extraction was performed. Blood samples for microbiological investigation were collected before, during, and 10 minutes after surgery and were processed by lysis-filtration under anaerobic conditions. There was no statistical difference between patients in the placebo group, the penicillin V group, and the amoxicillin group in terms of incidence or magnitude of bacteremia due to viridans streptococci or anaerobic bacteria during extraction or 10 minutes after the procedure. The overall incidence rates of bacteremia after dental extraction for the three groups were 95%, 90%, and 85%, respectively. For >90% of 126 strains of viridans streptococci tested, the MICs of penicillin V and ampicillin were ≤0.125 mg/L. The investigators concluded that the protective effect of prophylactically administered penicillins must be the result of interference with crucial steps in the development of endocarditis.

Erythromycin and clindamycin are currently recommended as antibiotic prophylaxis for IE in predisposed patients allergic to penicillin who are undergoing oral invasive procedures. Thirty-eight patients were randomized to receive either erythromycin (1 g) or clindamycin (0.6 g) orally 1.5 hours before dental extraction. Blood samples for microbiological investigation were collected before, during, and 10 minutes after surgery and were processed by lysis-filtration under anaerobic conditions [19]. The incidence of bacteremia due to viridans streptococci was 79% in the erythromycin group and 74% in the clindamycin group. No

<table>
<thead>
<tr>
<th>Oral procedure*</th>
<th>Incidence (%)</th>
<th>Range (%)</th>
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<tbody>
<tr>
<td>Dental extraction*</td>
<td>40</td>
<td>0–85</td>
</tr>
<tr>
<td>Dental scaling*</td>
<td>35</td>
<td>8–79</td>
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<tr>
<td>Periodontal surgery*</td>
<td>58</td>
<td>36–88</td>
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<tr>
<td>Endodontic treatment†</td>
<td>42</td>
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<td>0–51</td>
</tr>
<tr>
<td>Tonsillectomy*</td>
<td>34</td>
<td>28–38</td>
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</table>

NOTE. Data are from multiple studies* reviewed by Everett and Hirschmann [5] and Guntheroth [13], and from studies by Debelian et al. [14], Roberts et al. [2], and King et al. [15]. NA = not available.

Table 1. Incidence of bacteremia after various oral procedures.
statistically significant difference was noted in incidence or magnitude of bacteremia due to viridans streptococci or anaerobic bacteria between the two groups, at any sampling time. Ninety-six aerobic and 133 anaerobic strains recovered from the blood samples were tested for their susceptibility to erythromycin and clindamycin as well as to penicillin V and ampicillin. The antimicrobials were found to be highly active against the majority of bacteria except for some species of Enterococcus, Staphylococcus, and Veillonella. The investigators stated that protection from endocarditis by prophylaxis with erythromycin or clindamycin must be the result of elimination of bacteria at a later stage in the development of the disease, rather than by elimination of bacteria from blood during the short period of postoperative bacteremia.

In another study, Hall et al. [20] investigated the effects of prophylactic administration of cefaclor on bacteremia after dental extraction. Thirty-nine patients were randomly assigned to receive either 1 g cefaclor (19 patients) or placebo (20 patients) 1 hour before dental extraction. Blood samples for microbiological investigation were collected before, during, and 10 minutes after surgery, and were processed by lysis-filtration under anaerobic conditions. The incidence of bacteremia due to viridans streptococci was 79% in the cefaclor group and 50% in the placebo group during extraction. No difference in the incidence or magnitude of bacteremia was observed when the two patient groups were compared.

**Blood Culture Methods**

Detection of bacteria in blood is critically important, since invasion of the bloodstream represents one of the most important sequelae of infection. For efficient detection of the infecting microorganisms, blood culture procedures must be designed to overcome the generally low magnitude of bacteria circulating and to inhibit any antimicrobial properties or components in blood that might lower the recovery rate in the laboratory [21].

The simplest manual blood culture system consists of bottles filled with broth medium and with a partial vacuum in the headspace. After inoculation, the aerobic and anaerobic bottles are incubated, periodically examined for macroscopic evidence of growth, and then subcultured. The systems commonly incorporate a plastic paddle containing agar media.

Antibodies, complement, phagocytes, and antimicrobial agents are detrimental to the isolation of microorganisms from blood, and various measures to counteract these components have been proposed. With a 1:10 dilution of blood in broth to neutralize the serum bactericidal properties, any antimicrobial agent present in blood may also be diluted to noninhibitory concentrations.

Sodium polyanetholsulfonate (SPS) is usually added to blood culture media. In addition to its anticoagulant, antiphagocytic, anticomplementary, and antilysozymal activity, SPS inactivates aminoglycosides. Penicillinases may also be added to the medium for inactivation of penicillins.

The antimicrobial removal device is designed to remove antibiotics from blood before culture by means of antibiotic-adsorbent resins. These systems are reported to increase microbial recovery when compared with conventional blood culture techniques [22]. However, the exact mechanisms by which most of these products act are not known.

Another approach to neutralization of antimicrobial properties or components of blood is the lysis of blood cells. This aim of this technique is concentration of microorganisms by centrifugation or filtration, and subsequent culture on solid media that is free from antimicrobial substances. In the lysis-centrifugation technique, blood is inoculated into a tube with an anticoagulant and saponin (a lysing agent). After centrifugation, the supernatant is discarded and the sediment is removed from the tubes and inoculated onto agar media. The lysis-filtration system is founded on a similar principle, with the addition of a filtration procedure for sampling of the microorganisms. These two methods offer potential advantages such as removal of inhibitory agents present in blood, elimination of subculturing, and detection and faster identification of causative organisms; they make it possible to estimate the magnitude (number of colonies per milliliter of blood) of the bacteremia [23, 24]. The main disadvantage of these techniques is that they are labor-intensive, which may preclude routine use.

A simple blood culture technique that does not require the acquisition of expensive equipment is the pour-plate method. The blood is incorporated directly onto a nutrient agar and then incubated. This method has been evaluated for detection of low-grade polymicrobial bacteremia after dental extraction and found to be more effective than an automated BACTEC broth system (Becton Dickinson Microbiology Systems, Sparks, MD) for culturing small volumes (1 mL) of blood [25].

To make processing of blood cultures more efficient, several manufacturers have developed and marketed a number of automated blood culture systems, which mainly measure microbial growth in broth by CO₂ detection. Radiometric, as well as nonradiometric blood culture systems (BACTEC), have been used, while the commonest systems used in clinical practice today are the continuous-monitoring blood culture systems. Several systems are commercially available. Such systems monitor the bottles for evidence of microbial growth on a nearly continuous basis, which allows earlier detection.

**Antimicrobial Susceptibility Testing**

In vitro susceptibility tests are designed to guide clinicians in their choice of adequate therapeutic or prophylactic antibiotic regimens. Testing is recommended whenever the susceptibility of a pathogen is unpredictable or when an infection has not responded to therapy that otherwise appears appropriate. This test also provides valuable information for epidemiological studies of antibiotic resistance and is used to evaluate the efficacy of new antimicrobial agents.

*Minimum inhibitory concentration.* The determination of an agent’s ability to inhibit or suppress bacterial growth is
considered sufficient in most clinical situations. The lowest concentration of the antibiotic that completely inhibits growth of the microorganism is called the minimum inhibitory concentration (MIC).

**Breakpoint.** By the use of in vitro breakpoint antibiotic concentrations, the bacteria are classified into three categories of susceptibility to an antibiotic [26]. “Susceptible” implies that the infection is likely to respond to the normal dosage of the antibiotic recommended. “Intermediate” means that MICs for these isolates approach usually attainable blood and tissue levels and that response rates may be lower than those for susceptible isolates. Bacteria within the intermediate category may be affected in body sites where the drug is concentrated (e.g., β-lactams in urine) or when higher than normal dosage of a drug can be used. “Resistant” implies that the infection is unlikely to respond to that particular antibiotic.

However, because there is no general agreement on how to set the MIC breakpoints for the various categories of susceptibility, the limits established by different national and international boards may vary for a given drug. The values are established for each antibiotic by consensus decisions based on results of clinical trials, available data on pharmacokinetic properties such as serum concentration and tissue penetration, as well as microbiological considerations.

**Minimal bactericidal concentration.** In special clinical situations some authorities recommend susceptibility testing for bactericidal activity. This need has been proposed in bacterial endocarditis, meningitis, osteomyelitis, chronically infected implants, and for infections in immunocompromised patients [27]. The minimum concentration of a drug that causes at least a 99.9% reduction of the initial inoculum is known as the minimal bactericidal concentration (MBC).

The occurrence of a special type of resistance, antibiotic tolerance, may also, on rare occasions, necessitate bactericidal testing. This phenomenon has been linked to clinical failure in treatment of staphylococcal endocarditis [28]. In tolerant strains, bactericidal agents appear to have a normal inhibitory action but a reduced bactericidal activity. Many investigators include a MBC/MIC ratio of ≥32 as part of the definition of tolerance [29]. However, the reproducibility and clinical relevance of bactericidal testing have been questioned, since the test has many laboratory problems [30].

**Prevention of Endocarditis by Antibiotic Prophylaxis**

**Animal Studies**

Because clinical trials of antibiotic prophylaxis of endocarditis cannot be conducted in humans for ethical and statistical reasons, experimental animal models provide the only means for studying the effect of prophylaxis in subjects under controlled conditions.

During the 1970s, Durack and co-workers [31–33] utilized the rabbit model to test the efficacy of various antibiotic regimens against IE caused by streptococci. In these experiments, a catheter passed across the aortic or tricuspid valve produced sterile vegetations that served as a locus for bacterial adhesion and growth after intravenous injection of 10⁶ cfu of viridans streptococci. Under these conditions, different prophylactic antibiotics were given for various periods. The results indicated that cell-wall active antibiotics were needed for successful prophylaxis. Vancomycin and combinations of β-lactams and aminoglycosides in a single dose were uniformly effective, whereas administration of penicillin alone required both an early high serum level and a prolonged effective antimicrobial action (>9 h) to be successful. In contrast, bacteriostatic antibiotics such as tetracycline, erythromycin, and clindamycin were ineffective in the experimental model, even when given in multiple doses.

These observations strongly suggested that prophylaxis was mediated via bacterial killing and influenced the American Heart Association (AHA) recommendations in 1977 for the prophylaxis of IE [34]. At that time, the basic approach was to use initial parenteral administration of antibiotics with subsequent oral doses for 48 hours. However, the extrapolation of data from the studies in rabbits to humans was criticized because of the high bacterial inoculum used, which was thought to be irrelevant in the human situation [35].

During the 1980s, Glauser and colleagues refined the rabbit endocarditis model for use in rats and used a lower bacterial inoculum that produced endocarditis in 90% of the animals (ID₉₀). They reported that under these conditions the efficacy of the prophylactic antibiotics was highly dependent on the size of the inoculum injected. A single dose of vancomycin or amoxicillin prevented endocarditis when ID₉₀ was used, but failed with larger inoculum sizes [36, 37]. In the latter condition, endocarditis could be prevented only by prolonged levels of antibiotics, such as are achievable after additional doses [38].

Further studies indicated that the bactericidal activity, as previously suggested, was not the main mechanism of action of antibiotics in IE prophylaxis. Even if strains tolerant to bactericidal antibiotics, or bacteriostatic antibiotics, were used excellent protection for IE was achieved, provided that the inoculum size was in the range of ID₉₀ [37, 39, 40]. The results raised the question that inhibition of bacterial adherence to the vegetations might be the main mechanism of action of antibiotic prophylaxis. Several in vitro experiments supported the theory, since bacteria treated with antibiotics showed a decreased ability to adhere to platelet-fibrin surfaces [41, 42], whereas further experimental animal studies questioned the theory. Moreillon et al. [43] showed that the protective effect of amoxicillin given before bacterial challenge was lost, if amoxicillin was inactivated by penicillinase injected at the end of bacteremia, when adhesion of bacteria was completed. In a study by Berney and Francioli [44], amoxicillin given 30 or 120 minutes after bacterial challenge was as effective as the antibiotic given before challenge in preventing Streptococcus.
sanguis and Enterococcus faecalis endocarditis in rats, but failed when the administration was delayed for up to 240 minutes.

The results show that successful antibiotic prophylaxis for endocarditis may be achieved in the absence of bacterial killing of circulating bacteria and interference with bacterial adhesion, and suggest that antibiotics may act by inhibiting bacterial growth on the vegetations, allowing other defense mechanisms to gradually eliminate these bacteria from the valves [43, 44].

From Animal to Human Studies

Experimental studies have an important influence on the development of the regimens recommended as prophylaxis for endocarditis, although arguments have been raised against the clinical relevance of findings in animals. The disadvantages of these models include the nonhuman nature of the model, the large inoculum used to ensure endocarditis in untreated animals, and the foreign body (an intracardiac catheter) left in place during the experiment, while there is usually no intravascular foreign body present in humans.

However, a placebo-controlled study in humans on the efficacy of antibiotic prophylaxis is not likely to become available for ethical and practical reasons. A powerful enough prospective study would probably require ≥6,000 patients, all with well-defined cardiac disease [45]. Further, the relationship between the magnitude of bacteremia and the risk of developing endocarditis is unknown in humans, and the presence of an intracardiac catheter is thought to mimic the clinical situation of patients with prosthetic heart valves or other intravascular foreign bodies. Thus, experimental animal models provide a stringent test of an antibiotic regimen to prevent IE and may increase the margin of safety when applied to humans [35].

In an attempt to assess clinically the efficacy of antibiotic prophylaxis, a few case-control studies have been published. Imperiale and Horwitz [46] reported a protective efficacy of prophylaxis of 91%, but their study had methodologic limitations, since the case group consisted of only eight patients whose native valve IE occurred within 12 weeks of a dental procedure. Furthermore, information about the prophylactic regimen used was defined in part by the patient’s recall. Van der Meer et al. [47] reported a 49% protective efficacy for native valve endocarditis occurring within 30 days of a medical or dental procedure for which prophylaxis was indicated. Likewise, in the previously mentioned report, the group that was eligible for examination was small. Only 25 (12.7%) of 197 patients developed endocarditis within the period of 30 days and five of these 25 patients did receive antibiotic prophylaxis. However, the results indicate that clinical procedures play only a minor role in the cause of endocarditis and that prophylaxis may prevent endocarditis in only a small group of patients with native valve endocarditis. Total compliance with prophylaxis might, theoretically, have prevented endocarditis in 6% of all IE cases in this study.

Another study demonstrating the protective effect of antibiotic regimens was done by Horstkotte et al. [48]. Six cases of prosthetic valve endocarditis were retrospectively recorded following 390 invasive procedures performed without prophylaxis, as compared to none among 287 procedures performed with antibiotic prophylaxis.

The use of antibiotics, however, does not guarantee the prevention of endocarditis, since many case reports on apparent failures have been published. In an analysis of 52 cases of endocarditis prophylaxis failure, 92% occurred after a dental procedure and 75% were caused by viridans streptococci [49]. The failures were not due to antibiotic resistance, because data on antibiotic susceptibility indicated that two thirds of the causative bacteria were susceptible to the antibiotics used for prophylaxis.

Since studies on the efficacy of antibiotic prophylaxis of IE in humans is controversial, clinical studies have focused on the prevention of bacteremia by administration of antimicrobial agents before treatment. One approach has been to attack the bacteria by application of topical antiseptics before they enter the circulatory system. Studies have shown a benefit from chlorhexidine and povidone iodine, when used as a mouth rinse or an irrigant in the gingival sulcus before dental extraction [50, 51], while other studies have failed to alter significantly the nature and incidence of bacteremia [52, 53]. Despite these conflicting results, antiseptic mouth rinsing before oral invasive procedures is recommended by the American Heart Association [4] and the British Society for Antimicrobial Chemotherapy (BSAC) [54]. Another approach, and one most extensively studied, is the efficacy of systemic administration of antibiotics on postsurgical bacteremia.

Since the reports of early studies published during the 1940s, it has been well established that bacteremia is not completely eliminated by antibiotic prophylaxis [55]. Yet, several studies have demonstrated that prophylaxis reduces the frequency and magnitude of bacteremia and thus, theoretically, lowers the risk for development of IE [25, 56–61]. Shanson et al. [62] reported a reduction in bacteremia following dental extractions, from 70% in controls to 25% and 20% in those who had received 2 g of amoxicillin or 2 g of penicillin V, respectively. The incidence of bacteremia due to streptococci was also reduced, from 40% in the control group to 5% and 12% in each prophylaxis group, respectively. Roberts et al. [63] confirmed the efficacy of amoxicillin prophylaxis in their reporting of a decrease in postextraction bacteremia from 38% in the control group to 2% in the treated group.

IV administration of vancomycin and teicoplanin has also been shown to be highly effective in reducing the prevalence of dental streptococcal bacteremia [64, 65].

Concerning bacteriostatic drugs, prophylactic erythromycin is reported to reduce the prevalence of postextraction streptococcal bacteremia from 43% in controls to 15% [66], and clindamycin is reported to be more effective than erythromycin [67].
However, few clinical studies have questioned the preventive effect of antibiotic prophylaxis on postextraction bacteremia [64, 65, 68, 69]. Sefton et al. [70] reported no difference in postextraction bacteremia when cases of prophylaxis with erythromycin and josamycin were compared to a placebo group.

Recommendations for Prevention of Endocarditis

Recommendations for prophylaxis of IE have been established in most countries for >30 years and have been updated regularly according to new scientific information. The key principles of prophylaxis include identification of patients at cardiac risk, identification of risk procedures, the use of bactericidal drugs and to reach serum concentrations that exceed the MIC of the bacteria most likely to cause endocarditis, during treatment and following the “critical period” of about 9 hours [4].

Cardiac Considerations

Consequently, most national boards classify the cardiac conditions into specific groups, according to their degree of risk. Because the classifications are based on consensus decisions, there may be slight variations between different national guidelines [4, 71, 72].

High-risk conditions commonly include prosthetic valves, cyanotic congenital heart disease, and previous IE. Moderate-risk lesions primarily include valvular dysfunction with regurgitation, congenital heart disease that does not cause cyanosis, and hypertrophic obstructive cardiomyopathy.

Most guidelines also define cardiac diseases as generally believed to entail negligible risk (no greater risk than in the general population) and, consequently, no antibiotic prophylaxis is recommended. This group includes patients with cardiac pacemakers, coronary artery bypass grafting, intraatrial communication, mitral valve prolapse without regurgitation, and corrected left-to-right shunts.

Procedures Entailing Risk

Most guidelines include all dental procedures known to induce gingival or mucosal bleeding [72]. The AHA [4] lists dental procedures for which prophylaxis is recommended or not recommended.

Antibiotic Considerations

Earlier regimen recommendations by the AHA [34] included parenteral administration of antibiotics and also subsequent oral administration every 6 hours for eight doses. This guideline was criticized, since most dental procedures in susceptible patients take place outside hospitals in situations where injections are hardly feasible, and Brooks [73] found a compliance rate for oral prophylaxis of <15% among dentists. There was obviously a need for a simplified oral regimen.

The BSAC published its first recommendations in 1982 [74], and since then subsequent revisions advocate a simple regimen of a large dose of oral amoxicillin (3 g), which is considered appropriate for most clinical conditions. The serum concentrations after the 3 g oral dose were shown to be well above the MBCs for viridans streptococci for at least 10 hours [62, 75], and the compliance rate with this simplified regimen proved to be high (77%) [76].

For patients who are allergic to penicillin, a two-dose regimen of erythromycin was proposed in the 1982 and 1986 recommendations [74, 77]. The 1993 revisions [3] propose a single oral dose of clindamycin, thereby reflecting the Swiss [78] and the Scandinavian [79] recommendations. This international trend is not surprising given that erythromycin has been ascribed negative characteristics, such as production of considerable individual variations in serum concentrations [80], nausea and abdominal discomfort [81, 82], and selection of resistant oral streptococci [83].

In the most recent guidelines by the AHA [4], a single-dose regimen of 2 g of amoxicillin is recommended for the first time. The change from the previously recommended regimen, 3 g 1 hour before a procedure and then 1.5 g 6 hours after the initial dose [84], was explained by referring to the prolonged serum levels above the MIC of most oral streptococci [85] and the prolonged serum inhibitory activity (6–14 hours) induced by amoxicillin against such strains [86]. Clindamycin has also replaced erythromycin for penicillin-allergic patients, but other alternatives such as cephalaxin, cefadroxil, azithromycin, and clarithromycin are now also suggested [4].

In an attempt to reach a European consensus on antibiotic prophylaxis for IE, the International Society for Chemotherapy has recently issued its recommendations [72]. The standard regimen is amoxicillin, 3 g orally, whereas patients who are allergic to penicillin should be given 300–600 mg of clindamycin orally. A maximal regimen is proposed in special cases, as in patients at high cardiac risk, patients undergoing multiple procedures, and patients undergoing general anesthesia. For this group, amoxicillin (ampicillin) 2 g iv plus gentamicin 1.5 mg/kg iv is recommended, whereas vancomycin 1 g iv plus gentamicin 1.5 mg/kg iv is proposed for penicillin-allergic patients.

Apart from the use of antimicrobial prophylaxis, most committees emphasize the need for regular dental examinations for the maintenance of optimum oral health to reduce potential sources of bacterial seeding in patients who are susceptible to IE.

References

CID 1999;29 (July)  Antibiotic Prophylaxis and Bacteremia


