Current practice in prevention of bacterial endocarditis

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A survey of Oxfordshire dentists showed that most practise prophylaxis of bacterial endocarditis, but that few follow currently recommended regimens. For example, prophylactic antibiotics are started one or more days before the procedure by 72 per cent of dentists, and two or more days before by 25 per cent. Eighty-seven per cent administer antibiotics for a total of four or more days. Penicillin is most often given, but tetracycline remains the commonest second choice. Only 12 per cent use intramuscular drugs as first choice, and procaine penicillin is seldom used. These practices are contrasted with current medical recommendations and discussed with reference to fresh experimental evidence on prevention of bacterial endocarditis.

Antibiotics are frequently given in order to prevent bacterial endocarditis when patients with valvular heart disease undergo operations which may result in bacteraemia. It follows that many doctors and dentists believe this practice to be effective. However, nothing to prove that antibiotics in fact prevent bacterial endocarditis in humans has so far been published (Hook and Kaye, 1962; Hilson, 1970), because though the risk of bacterial endocarditis after dental operations has not been defined precisely, it is certainly too small (Kelson and White, 1945) to permit a practicable controlled trial. Even in the field of cardiac surgery, where prophylactic antibiotics are almost always employed, conclusive proof is still lacking (Finland, 1972). Despite these uncertainties, recommendations abound that antimicrobials should be used to prevent endocarditis, and definite regimens have been proposed to 'cover' operations likely to cause bacteraemia (e.g. American Heart Association Committee, 1965, 1972). A review of current practice in this field was undertaken because some *in vivo* experimental evidence on these problems is now available. The survey reported below was conducted to determine whether well-known regimens, such as those proposed by the American Heart Association Committee, are actually being used. A survey of dental practice was chosen, because if bacterial endocarditis follows dental procedures in 25 per cent (Kelson and White, 1945) or even up to 40 per cent (Croxon, Altman, and O'Brien, 1971) of cases, dental patients comprise the largest identifiable group at risk.

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A letter and questionnaire were sent to 117 dentists listed in the 1973 telephone directory for Oxfordshire. An analysis of the 71 replies received is presented below. As some dentists did not answer every question, and some listed more than one form of penicillin as first choice, the answers do not total 71 in every case.

Results of survey

Question 1: Are antibiotics of proved value in the prevention of bacterial endocarditis?

Yes	69
No	2

Comment: As indicated above, the correct answer here is 'no'. The overwhelming 'yes' response emphasizes that current attitudes have come close to dogma despite lack of substantiating evidence. On the contrary, the scanty facts available suggest that antibiotics as presently employed may be ineffective. A few early cases of failed prophylaxis have been reported (Goerner, Geiger, and Blake, 1945; Thill and Meyer, 1947; Glaser *et al.*, 1948; Dormer, 1958). Though the doses of penicillin used in these cases might now be considered inadequate, a recent case in which bacterial endocarditis developed despite 'adequate' and repeated doses of penicillin has also been recorded (Durack and Littler, 1974). Further, risk of bacterial endocarditis in patients with damaged valves is neither reduced nor increased by long-term penicillin prophylaxis for rheumatic fever (Doyle *et al.*, 1967). Finally, recent experimental work has shown that even huge doses of penicillin may not prevent infection with penicillin-sensitive streptococci (Durack and Petersdorf, 1973).

Question 2: Do you ask about heart murmurs and rheumatic fever when a new patient presents?

<i>Always</i>	34
<i>Often</i>	15
<i>Sometimes</i>	16
<i>Never</i>	5

Comment: The majority of dentists are clearly aware of the dangers of dental work in susceptible patients (see Question 1) but not all take steps to identify all those patients.

Question 3: Do you use antibiotics to prevent bacterial endocarditis in patients with valvular heart disease?

<i>Yes</i>	65
<i>No</i>	5

Comment: A high proportion of dentists is currently employing antibiotics for prevention of bacterial endocarditis. This was to be expected from the overwhelmingly positive reply to Question 1. All but one of those five who answered 'no' here added that they expected the patient's general practitioner to manage prevention.

Question 4 (a): Please indicate the drugs you employ (first choice):

Penicillins (all forms)	60
Tetracycline	1
Clindamycin	1

Analysis of penicillin preparations named in answer to question 4 (a):

Penicillin V (250 mg 6 hourly)	58
Benzylpenicillin	16
Combined benzyl-, procaine, and benethamine penicillin	3
Procaine penicillin	1
Ampicillin	1
Propicillin	1

Question 4 (b): What drug do you employ if the patient is allergic to penicillin? (2nd and 3rd choices):

Tetracycline (250 mg 6 hourly)	33
Erythromycin (250 mg 6 hourly)	20
Cephalosporins	9
Clindamycin	1
Metronidazole	1

Comment: The predominance of penicillin is not surprising, because it has bactericidal activity against most relevant oral micro-organisms; it is therefore first choice of most authorities. Tetracycline was the most popular second-line drug chosen by dentists, probably because this drug was widely recommended as an alternative to penicillin in the past

(e.g. Hook and Kaye, 1962). Though its use is still occasionally advocated (Khairat, 1966) or listed as an alternative (Weinstein, 1970), there is an obvious theoretical objection to the use of bacteriostatic drugs for prevention of bacterial endocarditis in that micro-organisms inhibited from multiplication, but not killed, might still cause the disease when therapy was stopped. Perhaps for this reason, authoritative recommendations no longer list tetracycline (e.g. American Heart Association Committee, 1972; Garrod and O'Grady, 1973). A recent experimental study showed that tetracycline did not prevent streptococci in the blood from reaching heart valves. Though the drug checked their growth, bacteria remained viable on valves and multiplied promptly when treatment was withdrawn after as long as seven days of continuous therapy (Southwick and Durack, 1974).

Current recommendations usually list either erythromycin or cephalosporins as second choice to the penicillins. Erythromycin has the advantage of being an orally administered drug which may be bactericidal under suitable conditions. Cephaloridine has suitable bactericidal activity against oral streptococci *in vitro* and has been recommended as an alternative to penicillin on these grounds (Tozer, Boutflower, and Gillespie, 1966). However, in limited experiments *in vivo*, both erythromycin and cephaloridine were ineffective under conditions in which vancomycin, or penicillin plus streptomycin, successfully prevented streptococcal endocarditis (Durack and Petersdorf, 1973). The rabbit model used in these experiments sets an extreme test for any drug, in that a relatively large intravenous inoculum of streptococci is given to animals carrying an intracardiac catheter. Therefore, one should not conclude from this work that erythromycin or cephaloridine cannot prevent bacterial endocarditis after dental procedures, but one might conclude that vancomycin or penicillin plus streptomycin are more likely to do so.

Analysis of the different preparations of penicillin used by the dentists shows that procaine penicillin is rarely chosen, despite the fact that it is the mainstay of most recommended regimens. Convenience of prescribing and other factors appear to be more important in deciding choice of drug than published advice.

Only 12 per cent of dentists listed parenteral therapy as first choice, probably because they prefer to prescribe tablets rather than give injections. Another reason may be that injectable antibiotics kept in surgeries must be provided by the dentist, whereas prescriptions for tablets involve him in less trouble and expense. Unfortunately, oral therapy is dogged by the familiar objections of irregular

absorption and relatively low serum levels of antimicrobial activity. One 250 mg tablet of penicillin V might not provide effective serum bactericidal activity in a patient who had recently taken a heavy meal, or spent a long time in his dentist's waiting room. Another major problem with oral antibiotics was summed up by a dentist who wrote after his answer to this question: 'One anxiety is the number of patients who we know do not take the tablets given to them.'

There is no doubt that effective oral therapy would be convenient for the dentist and painless for the patient. For these reasons, further experiments are being carried out in rabbits in an attempt to define reliable oral regimens (Pelletier, Durack, and Petersdorf, 1975). Unfortunately, while drug regimens may be reliable, many patients are not. When it is realized that most dentists are presently prescribing a five-day course of tablets to prevent endocarditis (see below), the advantages of a single injection given just before the operation become clear.

Question 5: How long before the procedure does the patient receive the antibiotic?

3 or 4 days	6
2 days	11
1 day	31
12 hours or less	18
After the procedure	1

Comment: A surprising number of dentists (25%) give antibiotics two or more days before operation. It is now over 10 years since Garrod and Waterworth (1962) showed that administration of penicillin for two or more days before dental operations could be dangerous because of selection of penicillin-resistant oral flora. There is no other direct evidence to indicate the optimum time and duration of therapy. However, in rabbits one dose of an effective drug 30 minutes before bacteraemia prevented endocarditis (Durack and Petersdorf, 1973).

Question 6: Please indicate duration (of therapy)

1 day	0
2 or 3 days	9
4 or 5 days	45
More than 5 days	7

Comment: Since most authors suggest that antibiotics be given for two days, it is remarkable that 87 per cent of dentists treat patients for four or more days. Their rationale must be that longer-term therapy would be safer, but as there is no proof that any prophylactic regimen is effective, this reasoning is doubtful. Moreover, few patients

would complete a five-day course of tablets when they felt perfectly well. Experimental evidence discussed above suggests that one-dose parenteral prophylaxis should be adequate if the right agents were chosen. Therefore, it seems likely that four or five-day regimens are merely wasteful.

Almost half the dentists indicated that they would seek the advice of the patient's general practitioner, either for every patient at risk or, more often, for special cases such as penicillin allergy. This presents doctors with a valuable opportunity to discuss and perhaps influence current practice in this field.

Conclusions

While remembering that final proof is lacking, and may always be lacking, the following points may be regarded as fairly well established.

- 1) The experimental evidence available indicates that bacterial endocarditis can be prevented by antibiotics, but only if the best drug or combination of drugs is used.
- 2) Even under experimental conditions apparently adverse to the success of prophylaxis, one dose is sufficient to prevent endocarditis if the best drug or combination is used (Durack and Petersdorf, 1973). The five-day oral regimens most often used by the dentists who responded to this questionnaire are probably unnecessary and wasteful.
- 3) Clinical and experimental evidence now available strongly suggests that penicillin alone is not the best choice for prophylaxis (Durack and Littler, 1974; Durack and Petersdorf, 1973). This is probably because penicillin kills oral streptococci relatively slowly, and leaves a proportion of survivors (Wolfe and Johnson, 1974). The addition of an aminoglycoside enhances the rate and completeness of bacterial killing; this combination was highly effective in prevention of bacterial endocarditis in animals. Vancomycin alone was equally effective.
- 4) Bacteriostatic drugs are ineffective in this situation and should never be used (Southwick and Durack, 1974).

With these considerations in mind, the following recommendations for prevention of bacterial endocarditis are offered:

Dental manipulations

Benzylpenicillin 2,000,000 units plus procaine penicillin 600,000 units plus streptomycin 1.0 g i.m. 30 minutes before the procedure.

Alternative

Vancomycin 1.0 g i.v. 5 minutes before the procedure.

Urethral, gynaecological, and other abdominal procedures

Ampicillin 1.0 g plus gentamicin 80 mg i.m. 30 minutes before the procedure, both repeated 8 and 16 hours later.

Alternative

Cephazolin 1 g plus gentamicin 80 mg i.m. 30 minutes before the procedure, both repeated 8 and 16 hours later.

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