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Guidelines for the prevention of endocarditis: report of the Working Party of the British Society for Antimicrobial Chemotherapy

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These guidelines have been produced following a literature review of the requirement for prophylaxis to prevent bacterial endocarditis following dental and surgical interventions. Recommendations are made based on the quality of available evidence and the consequent risk of morbidity and mortality for 'at risk' patients.

Keywords: infection, bacterial endocarditis, dental and surgical interventions, prophylaxis, bacteraemia

Introduction

The Working Party reviewed the current guidelines on endocarditis prophylaxis produced by the American Heart Association,[1] European Cardiac Society[2] and British Cardiac Society,[3] together with published evidence (human and animal models)[4] linking a wide range of procedures with the risk of bacterial endocarditis in susceptible individuals. The changing spectrum of bacteria causing endocarditis (from streptococci to staphylococci) was also considered. The Working Party also acknowledged that some individuals may still develop endocarditis even if they receive 'appropriate' antibiotic prophylaxis.

Prevention of endocarditis does not solely concern antibiotic prophylaxis. The Working Party would like to emphasize the need for vigilance in patients at risk of endocarditis who are in receipt of medical care. For example, adequate treatment of infection that could cause bacteraemia or fungaemia, the prompt removal of colonized intravascular devices and effective management of conditions that can lead to chronic or repeated infections are essential in reducing the risk of subsequent endocarditis.

There are many anecdotal publications which suggest causal associations between various procedures and bacteraemia[5,6] and between procedures and endocarditis.[7–10] A case controlled study of 273 patients, however, found no link between endocarditis and dental treatment.[11,12] Evidence is accumulating that activities such as chewing or tooth brushing produce a bacteraemia of dental flora.[13,14] The emphasis for endocarditis causation has shifted from procedure-related bacteraemia to cumulative bacteraemia. This was extended in a theoretical study of cumulative bacteraemia over 1 year which postulated that 'everyday' bacteraemia is six million times greater than bacteraemia from a single extraction.[14] Any bacteraemia occurring during dental treatment therefore does not significantly increase the risk of endocarditis.[15] Indeed, a recent Cochrane review[16] concluded that there was no evidence to support the use of prophylactic penicillin to prevent endocarditis in invasive dental procedures.

In the rabbit model, antibiotic prophylaxis was shown to reduce the risk of the establishment of endocarditis on damaged valves following high bacterial challenge. The model is however not strictly comparable with the pathophysiology of spontaneous bacterial endocarditis in humans.[4]

The Working Party agreed that ideally a prospective double-blind trial to evaluate the risk/benefit of prophylactic antibiotics should be carried out, but this is unlikely to take place because of the numbers of patients required and while current guidelines recommend prophylaxis. Despite the lack of evidence of the benefit for prophylactic antibiotics to prevent endocarditis associated with dental procedures, the Working Party considered that many clinicians would be reluctant to accept the radical, but logical, step of withholding antibiotic prophylaxis for dental procedures. It was therefore agreed to compromise and recommend prophylaxis only for those patients in whom the risk of developing endocarditis is high and, if infected, would carry a particularly high mortality. This is in line with previous proposals.[17]

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Thus the indication for antibiotic prophylaxis for dental treatment should be restricted to patients who have a history of previous endocarditis, or who have had cardiac valve replacement surgery, or those with a surgically constructed systemic or pulmonary shunt or conduit.

Guidelines such as these have, in the past, received criticism for not being evidence based. While we appreciate that the gold standard for all clinical guidelines should ideally be based on good, prospective, randomized controlled trials, no such trials have ever been performed to assess the benefit of antibiotic regimens in the prevention of endocarditis. Consequently we have not attempted to classify the evidence for our recommendations, which remain consensus based. An extensive review of the literature—encompassing a number of different search methods and a range of criteria (e.g. endocarditis and staphylococci)—has been carried out, and publications used to support any changes we have made to the existing guidelines have been cited. Publications referring to *in vitro* or animal models have only been cited if appropriate clinical data are not available.

The Working Party acknowledged that the change in guidance may result in patient or carer concern. Appendix 1 contains a patient information sheet, which may be helpful for dental professionals when they are explaining these changes.

There is no good epidemiological data on the impact of bacteraemia from non-dental procedures on the risk of developing endocarditis. The Working Party considered that these procedures carried risk on top of the background bacteraemia from daily activities by causing bacteraemia due to organisms such as staphylococci and enterococci. We therefore decided to expand the cardiac risk factors for these procedures and have recommended that antibiotic prophylaxis be offered to all patients at risk of endocarditis.

Where antibiotic prophylaxis is indicated, the Working Party is satisfied that a single oral dose will achieve adequate serum levels. There may be occasions where it is logistically easier to administer the antibiotic via the intravenous (iv) route, and so we have made recommendations for dosages for both routes.

1. Endocarditis prophylaxis for dental procedures

Good oral hygiene is probably the most important factor in reducing the risk of endocarditis in susceptible individuals, and access to high-quality dental care should be facilitated. Once a patient is found to have a cardiac anomaly putting him or her at a risk of endocarditis, the patient should be referred to have their dental hygiene optimized. Similarly, a patient who has received an intracardiac prosthesis (valve, conduit, aortic graft) should be referred for dental assessment. Interventions ideally should be performed at least 14 days prior to surgery to allow mucosal healing. Those patients who undergo urgent or emergency valve replacement should have a dental assessment performed as soon as practicable after surgery, and a risk assessment performed to determine the most appropriate plan for any remedial dental treatment. All elective dental procedures should ideally be delayed for at least 3 months post-surgery.

For high-risk patients (see Table 1) we recommend that prophylaxis be given for all dental procedures involving dento-gingival manipulation or endodontics. For antibiotic recommendations please see Table 2.

Table 1. Prophylaxis for dental procedures

High-risk cardiac factors requiring antibiotic prophylaxis
Previous infective endocarditis
Cardiac valve replacement surgery, i.e. mechanical or biological prosthetic valves
Surgically constructed systemic or pulmonary shunt or conduit
Dental procedures requiring antibiotic prophylaxis
All dental procedures involving dento-gingival manipulation

For those patients ≥10 years of age we recommend a single 3 g oral dose of amoxicillin (<5 years of age: 750 mg; ≥5 to <10 years of age: 1.5 g) to be given 1 h prior to the procedure, whether the procedure is performed using a general or a local anaesthetic. For iv administration we recommend a single dose of 1 g amoxicillin for patients ≥10 years of age (<5 years of age: 250 mg; ≥5 to <10 years of age: 500 mg), given just before the procedure or at induction of anaesthesia.

If the patient (≥10 years of age) has a documented penicillin allergy, a single dose of oral 600 mg clindamycin (<5 years of age: 150 mg; ≥5 to <10 years of age: 300 mg) should be given 1 h before the procedure. For iv administration we recommend a single dose of 300 mg clindamycin (given over at least 10 min) (<5 years of age: 75 mg; ≥5 to <10 years of age: 150 mg).

For those patients who are allergic to penicillin and cannot swallow capsules, oral azithromycin suspension (≥10 years: 500 mg; <5 years of age: 200 mg; ≥5 to <10 years of age: 300 mg) given 1 h before the procedure can be used as an alternative.

In addition, where practicable, a pre-operative mouthwash of chlorhexidine gluconate (0.2%) should be administered and held in the mouth for 1 min.

For patients requiring sequential dental procedures, these should ideally be performed at intervals of at least 14 days to allow healing of oral mucosal surfaces. If further dental procedures cannot be delayed, we suggest alternating amoxicillin and clindamycin. In this scenario if the patient has a penicillin allergy, we suggest that expert advice be sought.

2. Endocarditis prophylaxis for non-dental procedures

Increases in understanding of the pathogenesis of endocarditis suggest that prophylaxis for dental procedures is not required. The same cannot be applied to bacteraemia-inducing, non-dental procedures undertaken in patients who are at the risk of developing endocarditis. Indeed it is likely that the pathogenesis of endocarditis differs between the oral streptococci and other pathogens, such as enterococci, and until more information becomes available, the Working Party has taken a cautious approach to prophylaxis for non-dental procedures.

The risk of endocarditis associated with various procedures can be inferred by two, equally unsatisfactory, sources:

(i) the chance of a procedure causing a bacteraemia and thus seeding an ‘at risk’ cardiac lesion and

Table 2. Antibiotic prophylaxis for dental procedures

Population	Age			Timing of dose before procedure
	>10 years	≥5 to <10 years	<5 years	
General	amoxicillin 3 g po	amoxicillin 1.5 g po	amoxicillin 750 mg	1 h
Allergic to penicillin	clindamycin 600 mg po	clindamycin 300 mg po	clindamycin 150 mg po	1 h
Allergic to penicillin and unable to swallow capsules	azithromycin 500 mg po	azithromycin 300 mg po	azithromycin 200 mg po	1 h
Intravenous regimen expedient	amoxicillin 1 g iv	amoxicillin 500 mg iv	amoxicillin 250 mg iv	just before the procedure or at induction of anaesthesia
Intravenous regimen expedient and allergic to penicillin	clindamycin 300mg iv[a]	clindamycin 150 mg iv[a]	clindamycin 75 mg iv[a]	just before the procedure or at induction of anaesthesia

[a]Given over at least 10 min.
Where a course of treatment involves several visits, the antibiotic regimen should alternate between amoxicillin and clindamycin.
Pre-operative mouth rinse with chlorhexidine gluconate 0.2% (10 mL for 1 min).

Table 3. Gastrointestinal procedures associated with bacteraemia and endocarditis and prophylaxis recommendation

Procedures	Anecdotally associated with endocarditis?	% Bacteraemia	Requires IE prophylaxis?	Comment
Oesophageal varices–sclerotherapy	yes[21,22]	10–50[23,24]	yes	
Oesophageal stricture dilatation	yes[25]	21–54[23,26–29]	yes	
Oesophageal varices–Banding	no	6[23]	no*	
Oesophageal laser therapy	no	35[23]	yes	significant risk of bacteraemia but no reported endocarditis cases
Endoscopy–upper	yes[30–33]	4[23]	no*	
Sigmoidoscopy/colonoscopy	yes[34–37]	0–9[23,26,38]	no*	
ERCP	no[39]	6–11[23]	yes	standard perioperative prophylaxis may need modification
Percutaneous endoscopic gastrostomy	no	0[40]	no*	
Echocardiography–transoesophageal	yes[41]	1–13[42,43]	no*	some isolates obtained post TOE may have been skin contaminants.[42] In one study patients who received peri-procedure antibiotics were included.[30] Use of prophylaxis for TOE varies widely between centres[44]
Barium enema	no	5–11[23,26]	no*	
Proctoscopy	no	5[23]	no	
Hepatic/biliary operations	NK	NK	yes	standard perioperative prophylaxis may need modification
Liver biopsy–percutaneous	no	3–13[26]	no*	
Gall stones–lithotripsy	no	22[45]	yes	
Surgical operations involving intestinal mucosa	yes[46,47]	NK	yes	standard perioperative prophylaxis may need modification

ERCP, endoscopic retrograde cholangiopancreatography; NK, not known.
*Prophylaxis recommended only for high-risk patients as in dental recommendations.

(ii) whether such a procedure has been anecdotally linked to cases of endocarditis.

A pragmatic combination of these observational data forms the basis of our current recommendations. A risk of bacteraemia does not necessarily equate to a risk of endocarditis and the significance of both magnitude and duration of bacteraemia is unknown. For common, or particularly 'high-risk' procedures, the chance of bacteraemia, whether the procedure has been associated with endocarditis, and recommendations for prophylaxis are shown in Tables 3–6. Procedures involving non-infected skin incision but no mucosal breach, for example, cardiac catheterization or cosmetic piercing of nipple or pinna, do not require prophylaxis but

adequate skin disinfection should be carried out prior to the procedure. Other specific procedures have not been included where the evidence for risk of infective endocarditis (IE) is limited; advice of a microbiologist should be sought and a risk assessment undertaken. It is currently recommended that all patients at a risk of endocarditis, as described in Appendix 2, should receive prophylaxis as outlined in these tables except where stated otherwise.

Table 4. Genitourinary procedures associated with bacteraemia and endocarditis and prophylaxis recommendation

Procedure	Anecdotally associated with endocarditis?	% Bacteraemia	Requires IE prophylaxis?	Comment
Cystoscopy	NK	0–26[26,48,49]	yes	standard perioperative prophylaxis may need modification Risk of bacteraemia increases with presence of bacteriuria. If possible, treat bacteriuria before the procedure
Urethral catheterization	yes[50]	0–17[26,48]	no[a]	
Urethral dilatation	yes[46]	18–33[26,48]	yes	standard perioperative prophylaxis may need modification
Transurethral prostatic resection	yes[51,52]	70–76[53,54]	yes	standard perioperative prophylaxis may need modification
Transrectal prostatic biopsy	yes[55]	12–46[26,48]	yes	standard perioperative prophylaxis may need modification
Vasectomy	yes[56–58]	NK	no	cases developing after vasectomy have been reported in patients without known cardiac defects[58]
Lithotripsy of renal stones	yes[59,60]	8[61]	no[a]	
Circumcision	yes[62]	NK	no	
Cosmetic piercing involving urethral mucosa	no	NK	no	

[a]Risk of bacteraemia increases with presence of bacteriuria. Treatment is recommended pre-procedure.
NK, not known.

Table 5. Gynaecological and obstetric procedures associated with bacteraemia and endocarditis and prophylaxis recommendation

Procedures	Anecdotally associated with endocarditis?	% Bacteraemia	Prophylaxis required?	Comment
Uterine dilatation and curettage	no	5[63]	no	prophylaxis not required unless there is clinical evidence of uterine infection
Vaginal hysterectomy	no	NK	yes	standard prophylaxis may need altering
Therapeutic abortion	yes[64,65]	NK	no[a]	reported cases have often occurred in patients without known cardiac defects, therefore prophylaxis would not have been given.[64,65] IE is very rare after termination of pregnancy[66]
Insertion/removal of intrauterine device	yes[67]	0[49]	no[a]	
Sterilization procedures	no	NK	no	
Smears	yes[68]	0	no	
Caesarean section	NK	11[69]	yes	standard perioperative prophylaxis may need modification
Vaginal delivery	yes[70–72]	1–5[49,71]	no[a]	the overall incidence of infective endocarditis after childbirth is low (0.03–0.14 per 1000 deliveries[66]), an underlying cardiac defect has been identified in 31% of cases[72]

NK, not known.
[a]Prophylaxis required if infection suspected or in prolonged rupture of membranes.

Table 6. Respiratory tract procedures associated with bacteraemia and endocarditis and prophylaxis recommendation

Procedures	Anecdotally associated with endocarditis?	% Bacteraemia	Prophylaxis required?	Comment
Tonsillectomy/adenoidectomy	yes[49]	33–38[49]	yes	standard perioperative prophylaxis may need modification the same prophylactic regimens for dental procedures can be used
Surgical procedures on upper respiratory tract	no	NK	yes	routine perioperative prophylaxis may be sufficient; otherwise, the same prophylactic regimens for dental procedures can be used
Rigid bronchoscopy	no	15[49]	no	no associated cases have been described
Flexible bronchoscopy ± biopsy	yes[73]	<1–6.5[74]	no	
Nasal packing and nasal intubation	yes[75]	NK	yes	a potential risk of staphylococcal bacteraemia. See Table 7
Endotracheal intubation	no	NK	no	
Tympanostomy tube insertion	no	NK	no	
Cosmetic piercing of tongue or involving oral mucosa[a]	yes[76]	NK	yes	same recommendations as for dental procedures

NK, not known.
[a]The Working Party advises that these procedures should be discouraged in patients who are at risk for endocarditis.

Table 7. Recommended prophylactic antibiotic regimens for genitourinary, gastrointestinal, respiratory or obstetric/gynaecological procedures in patients at risk of endocarditis

Antibiotics	Dose/route	Comment
Ampicillin/ amoxicillin	a single iv dose of 1 g amoxicillin (<5 years of age: 250 mg; ≥5 <10 years of age: 500 mg) given just before the procedure or at induction of anaesthesia	given just before the procedure or at induction of anaesthesia
+ gentamicin	1.5 mg/kg iv	
If allergic to penicillin		
Teicoplanin	400 mg iv children <14 years 6 mg/kg	given just before the procedure or at induction of anaesthesia
+ gentamicin	1.5 mg/kg iv	

Enterococci, streptococci and staphylococci are the prominent causes of endocarditis associated with non-dental procedures in most settings. Comparison of different antimicrobial regimens requires animal models, the value of which has been reviewed.[18] It is noteworthy that amoxicillin may retain prophylactic activity even against resistant 'viridans' streptococci.[19]

The recommended combination of a penicillin or glycopeptide and gentamicin includes cover for both enterococci and staphylococci. Gentamicin alone has good efficacy in protecting against *Staphylococcus epidermidis*.[20] Recommended prophylactic regimens are shown in Tables 7 and 8.

Table 8. Recommended prophylactic antibiotic regimens for nasal packing and nasal intubation

Antibiotic	Dose/route	Comment
Flucloxacillin children <4 years	1 g iv 50 mg/kg	given at induction of anaesthesia or just prior to procedure
If allergic to penicillin		
Clindamycin children <5 years children ≥5 <10 years children ≥10 <16 years	600 mg iv 75 mg 150 mg 300 mg	

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All the authors declare that during the preparation of this document they were not in the employment of, not receiving funding from, any pharmaceutical firm or other organization that may have resulted in a conflict of interest.

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Appendix 1

British Society for Antimicrobial Chemotherapy (BSAC)

Prevention of Infective Endocarditis Guidelines Information for Patients and Parents February 2006. A BSAC group of experts has spent a lot of time carefully looking at whether dental treatment procedures are a possible cause of infective endocarditis (IE) [sometimes called bacterial endocarditis (BE)], which is infection of the heart valve.

After a very detailed analysis of all the available evidence they have concluded that there is no evidence that dental treatment procedures increase the risk of these infections.

Therefore it is recommended that the current practice of giving patients antibiotics before dental treatment be stopped for all patients with cardiac abnormalities, except for those who have a history of healed IE, prosthetic heart valves and surgically constructed conduits.

The main reasons for this are the lack of any supporting evidence that dental treatment leads to IE and the increasing worry that administration of antibiotics may lead to other serious complications such as anaphylaxis (severe allergy) or antibiotic resistance.

The advice from the BSAC is that patients should concentrate on achieving and keeping a high standard of oral and dental health, as this does reduce the risk of endocarditis. Help for this will be provided by your Dental Professional.

British Society for Antimicrobial Chemotherapy, 2 February 2006.

Appendix 2

Cardiac conditions for which antibiotic prophylaxis is indicated for non-dental procedures

(1) History of previous endocarditis
(2) Prosthetic cardiac valves

(3) Surgically constructed shunt/conduit
(4) Complex congenital heart disease (except secundum atrial septal defects)
(5) Complex LV outflow abnormalities, including aortic stenosis and bicuspid aortic valves.
(6) Acquired valvulopathy*
(7) Mitral valve prolapse*

*With echocardiographic documentation of substantial leaflet pathology and regurgitation.