
ANTIBIOTIC PROPHYLAXIS IN GASTROINTESTINAL ENDOSCOPY

SUMMARY

- Antibiotic prophylaxis is recommended for endoscopic procedures if the patient is at high risk of endocarditis and there is a high risk of bacteraemia as a consequence of the procedure. The high risk procedures are oesophageal dilatation, laser or argon beam ablation of a tumour and variceal injection. Antibiotic prophylaxis is also recommended if symptomatic bacteraemia is potentially life threatening as a consequence of immunosuppression or neutropenia. In most circumstances parenteral amoxicillin and gentamicin are recommended. Antibiotic prophylaxis should also be considered in moderate risk patients undergoing a high risk procedure. The addition of parenteral metronidazole is recommended in patients with neutropenia. Vancomycin or teicoplanin are recommended in patients allergic to penicillin.
- All patients having a percutaneous endoscopic gastrostomy should receive prophylactic antibiotics. IV antibiotics such as cefotaxime or co-amoxiclav are effective at reducing peristomal infection.
- Antibiotic prophylaxis is recommended for all patients undergoing ERCP with evidence of biliary stasis or pancreatic pseudocyst. Oral ciprofloxacin or parenteral gentamicin (or parenteral quinolone, cephalosporin or ureidopenicillin) are recommended for ERCP.

1. INTRODUCTION

Endocarditis or symptomatic bacteraemia following gastrointestinal endoscopy is infrequent but well recognised. There is little evidence to show whether antibiotic prophylaxis can reduce the incidence of either. Prophylactic antibiotics are widely used in patients regarded as susceptible to endocarditis and for procedures known to be associated with a high risk of bacteraemia, but there is considerable variation between gastroenterologists both in selection of patients and procedures warranting antibiotic prophylaxis.

Recommendations by the American Heart Association¹ and European Society of Gastrointestinal Endoscopy² reflect changes in practice since The British Society of Gastroenterology first published guidelines on the use of prophylactic antibiotics in gastrointestinal endoscopy in 1996. This document now supercedes the previous guidelines.

This updated report again addresses the various issues and problems of infection associated with gastrointestinal endoscopy. Particular emphasis is laid on the prevention of endocarditis and pancreatobiliary sepsis. Recommendations are made for the selection of suitable antibiotics in patients. These should be reviewed regularly in the light of new studies.

2. GENERAL CONSIDERATIONS

(i) Indications for antibiotics in gastrointestinal endoscopy

Perioperative antibiotics may be given immediately prior to gastrointestinal endoscopic procedures for several reasons. The most important are:

1. The attempted prevention of infective endocarditis.
2. The attempted prevention of symptomatic bacteraemia.
3. The prevention of colonisation of orthopaedic and other non-cardiac prosthetic implants.
4. The prevention of pancreatico-biliary sepsis following ERCP.
5. The prevention of wound infection following percutaneous procedures.

(ii) Problems with antibiotic usage

All antibiotics have side-effects. Though adverse reactions following one or two doses are rare, anaphylaxis or other serious side-effects have been reported following exposure to all antibiotics used in prophylaxis. Excessive or inappropriate use of antibiotics, particularly of broad spectrum agents including penicillins and cephalosporins, exerts selection pressure on bacteria in the hospital or clinic. Antibiotics, especially if given parenterally, cannot be administered without financial cost. Therefore their prophylactic use should be reserved for situations in which a clear clinical benefit can be demonstrated.

(iii) Infection following endoscopy

Rates of infection following gastrointestinal endoscopy are very low and cannot be calculated with any precision. Prospective studies to determine the value of antibiotic prophylaxis of endocarditis during gastrointestinal endoscopy have not been, and are unlikely to be carried out because of the need to recruit very large numbers of subjects. Thus, although recommendations for the use of perioperative antibiotics in endoscopy can be based on an understanding of the pathology of infective endocarditis, they are of necessity pragmatic.

(iv) Identification of at-risk patients

Units should ensure that there is a routine method (such as a check list) for drawing

the attention of the endoscopist to the patients to whom antibiotics should be given. The conditions which render the patient at high risk of developing endocarditis are listed later.

3. ENDOCARDITIS

(i) Background and literature survey

Over the last 30 years the number of patients with cardiac prosthetic implants has increased substantially. Over the same period millions of gastrointestinal endoscopic procedures have been carried out, mostly without antibiotic prophylaxis. It is therefore reassuring that there is no evidence of any increase in the incidence of endocarditis affecting prosthetic valves. In recent years there has been only a handful of published reports of endocarditis associated with endoscopic procedures³⁻¹¹ and it is not clear even in this small number of cases whether the association was always causal.

These population-based data and the paucity of anecdotal evidence linking gastrointestinal endoscopy to endocarditis suggest that widespread use of antibiotic prophylaxis in gastrointestinal endoscopy would have little effect on the incidence of endocarditis. Several other considerations all point to the same conclusion.

(ii) Experience of antibiotic prophylaxis

Firstly, only a small minority of patients with endocarditis affecting a known cardiac lesion develop the disease as a consequence of a medical or dental procedure¹². Secondly, there is only scant evidence that antibiotic administration during dental or surgical procedures reduces the risk of endocarditis¹²⁻¹⁴. Failures of antibiotic prophylaxis to prevent endocarditis are well recognised¹⁵ and include an example of failure of prophylaxis during a gastrointestinal endoscopic procedure⁹. Thirdly, many patients with

cardiac valvular lesions are unaware that they have such lesions. Thus ascertainment of at-risk patients will always be incomplete. Fourthly, several studies have shown that even if guidelines are established, many patients are given the wrong antibiotic or none at all.

(iii) Risk of endocarditis

The risk of endocarditis varies with the nature of the underlying cardiac condition. Both Safrany¹⁶ and Durack¹⁷, have summarised a number of authorities' opinions in ranking order of risk patients with various cardiac conditions (*Table 1*).

Table 1: Conditions associated with the risk of endocarditis or symptomatic bacteraemia

Higher risk

Prosthetic heart valve
Previous endocarditis
Surgically constructed systemic-pulmonary shunt or conduit Synthetic vascular graft less than 1 year old

Severe neutropenia
(neutrophils $<100 \times 10^9$ /litre)

Moderate, low or theoretical risk

Mitral valve prolapse with insufficiency
Rheumatic valvular or congenital cardiac lesion Hypertrophic cardiomyopathy
Ventriculo peritoneal shunt Heart transplant

Moderate neutropenia
(neutrophils $100-500/10^9$ /litre)

No increased risk

Mitral valve prolapse without insufficiency
Uncomplicated secundum atrial septal defect
Cardiac pacemaker
Coronary artery bypass graft Implanted defibrillator

All other patients

Table 2: Approximate incidence of bacteraemia in immunocompetent individuals following various procedures involving the gastrointestinal tract

Procedure	Incidence of bacteraemia (%) [*]
Rectal digital examination	4
Proctoscopy	5
Barium enema	11
Tooth brushing	25
Dental extraction	30-60
Colonoscopy	2-4
Diagnostic upper gastrointestinal endoscopy	4
Sigmoidoscopy	6-9
ERCP (no duct occlusion)	6
ERCP (duct occluded)	11
Oesophageal varices band ligation	6
sclerotherapy	10-50 ^{**}
Oesophageal dilatation/prosthesis	34-54
Oesophageal laser therapy	35

^{*} summary of published data
^{**} higher after emergency than elective management

The risk of endocarditis is also dependent on the incidence (*Table 2*) and intensity of bacteraemia associated with the endoscopic procedure and on the organism or organisms causing the bacteraemia. Bacteria vary greatly in their propensity to colonise damaged heart valves. Endocarditis is most commonly caused by streptococci and enterococci.

(iv) Endocarditis and bacteraemia

Previously healthy patients not known to have cardiac lesions and undergoing procedures known to be associated with a low bacteraemia rate have an extremely low risk of endocarditis and antibiotic prophylaxis is not justified. Patients with cardiac lesions associated with a high risk of endocarditis who undergo gastrointestinal

endoscopic procedures with a known high risk of bacteraemia run a higher risk of endocarditis and should be protected with perioperative antibiotics. In other situations the need for prophylaxis is even more uncertain and is likely to remain so. With the exception of the group of high risk patients undergoing high risk procedures we consider the case for giving prophylactic antibiotics prior to gastrointestinal endoscopic procedures to be weak. We give our recommendations in *Table 3*.

Individual endoscopists may consider antibiotics necessary for some additional patients and we accept that final judgments may be coloured by personal experience. Recommendations on the choice of antibiotics, doses and methods of administration are given in *Tables 3* and *4*.

Table 3: Recommendations for Antibiotic Prophylaxis in Gastrointestinal Endoscopy "Who to give antibiotics to"

Patient Risk Group	*	Antibiotic Prophylaxis
- higher risk of endocarditis	*	+ (regimen A1 or A2)#
- severe neutropenia (neutrophils <100x10 ⁹ /l)	*	+ (regimen C)#
- moderate or low risk of endocarditis	*	not necessary
- higher risk of endocarditis	*	+ (regimen A1 or A2)#
ERCP		
- bile stasis pancreatic pseudocyst previous cholangitis		+ (regimen B)#

NOTE:

+ = prophylaxis
- = no prophylaxis

* See Table 1
See Table 4

Table 4: Recommended antibiotics

A1. Patients not allergic to penicillin and who have not had penicillin more than once in the previous month.

Adults:

1 gram amoxicillin intramuscularly in 2.5ml 1% lignocaine hydrochloride *plus* 120mg gentamicin intramuscularly just before start of procedure (or 1 gram amoxicillin in 20ml water intravenously over 3-4 minutes *plus* 120mg gentamicin intravenously).

Then 500mg amoxicillin orally 6 hours later.

Children under 10 years: Amoxicillin 500mg intramuscularly in 2.5ml 1% lignocaine hydrochloride *plus* gentamicin 2mg/kg body weight intramuscularly (or 500mg amoxicillin in 10ml water intravenously over 3-4 minutes *plus* gentamicin 2mg/kg body weight intravenously).

Then one oral dose of amoxicillin 6 hours later. (Children 5-9 years, 250mg; children 0-4 years, 125mg.)

A2. Patients allergic to penicillin or who have had penicillin more than once in the previous month.

Adults:

Vancomycin 1 gram by slow intravenous infusion over 100 minutes followed by gentamicin 120mg intravenously at start of procedure or 15 minutes before the procedure.

OR teicoplanin 400mg intravenously followed by gentamicin 120mg intravenously at start of procedure or 15 minutes before the procedure.

Children under 10 years:

Vancomycin 20mg/kg by slow intravenous infusion followed by gentamicin 2mg/kg intravenously.

OR teicoplanin 6mg/kg intravenously followed by gentamicin 2mg/kg intravenously.

B. Biliary endoscopic procedures

Oral ciprofloxacin 750mg 60-90 minutes before procedure,

OR gentamicin 120mg intravenously just before the procedure,

OR a parenteral quinolone, cephalosporin or ureidopenicillin given intravenously just before the procedure.

C. Patients with severe neutropaenia (neutrophils <100x10⁹/litre)

Adults:

Add metronidazole 7.5mg/kg intravenously to any of the above regimes A1, A2 or B.

Children under 10 years:

Add metronidazole 7.5mg/kg intravenously to any of the above regimes A1, A2 or B.

D. Percutaneous endoscopic gastrostomy

IV Cefotaxime 2g given 30 minutes before the procedure

OR IV Co-amoxycylav 2.2g given 30 minutes before the procedure

4. BACTERAEMIA

(i) Evidence for bacteraemia in gastrointestinal endoscopy

The existence of bacteraemia during gastrointestinal endoscopy and some physiological processes has been well established in numerous series over twenty or more years (Table 2). Some published papers give misleadingly high rates because organisms which are probably often contaminants (coagulase negative staphylococci, *Propionibacterium* spp., *Bacillus* spp. and commensal organisms with little or no pathogenic potential) have been included. Other series, particularly some of the older studies, give misleadingly low rates because of deficiencies in culture techniques, especially those for anaerobic bacteria.

After exclusion of false positives attributable to bacterial contamination, the rates of bacteraemia reported in association with particular endoscopic procedures will inevitably be underestimates, as no blood culture system is completely sensitive. One study of bacteraemia associated with upper gastrointestinal endoscopy in immunosuppressed patients (in whom intravascular destruction of bacteria is minimised) has been reported; a high rate of clinically significant bacteraemia was shown (9/47, 19%)¹⁸.

(ii) Importance of bacteraemia

The incidence of bacteraemia during endoscopy has been extensively studied but the incidence of *symptomatic* bacteraemia far less. In the great majority of cases, endoscopy-related bacteraemia is not associated with any recognisable symptoms. Asymptomatic bacteraemia is probably unimportant. It does not matter if, say, 20% of patients experience transient bacteraemia following gastrointestinal endoscopy, if none becomes ill. Is this of any greater significance than asymptomatic bacteraemia following tooth brushing?

There would seem to be little reason to attempt to reduce the rate of endoscopy associated asymptomatic bacteraemia unless there is some evidence of a later adverse effect. Such evidence is lacking.

One study has assessed prospectively (but in an open study design) the efficacy of antibiotic treatment in reducing bacteraemia rates during endoscopy. Alternate patients aged 60 and over undergoing gastroscopy were given antibiotics. Blood cultures were negative in all 130 patients receiving antibiotics but positive in 13/132 controls (9.8%, $p < 0.001$)¹⁹. However, the organisms isolated could all have been skin contaminants, and neither the antibiotic patients nor the controls experienced any symptoms likely to have been associated with bacteraemia.

At present recommendations reflect the higher incidence of bacteraemia associated with oesophageal dilatation,²⁰ variceal sclerotherapy²¹ laser therapy²² and presumably argon beam ablation.

(iii) Symptoms in bacteraemia

Pyrexia, hypotension and other symptoms of septicaemia can be mimicked by the injection into the bloodstream of bacterial cell wall components, particularly endotoxin from gram-negative bacteria. In patients without any added risk of endocarditis, perioperative antibiotic prophylaxis may serve no purpose other than to kill bacteria which would have been cleared by normal defence mechanisms.

(iv) Immunocompromised patients

Neutropenia¹⁸ appears to confer an increased risk of symptomatic bacteraemia after endoscopy, though the size of the increased risk is not clear. Patients with severe neutropenia ($< 100 \times 10^9$ /litre) should be offered antibiotic prophylaxis for gastrointestinal endoscopic procedures if these are known to be associated with a high risk of bacteraemia. Gram-negative aerobic (and less frequently anaerobic)

bacteria including *Escherichia coli* are the most likely pathogens in these conditions and the choice of prophylactic antibiotics should reflect the local sensitivities of organisms.

There are no data to establish whether patients with a normal neutrophil count but who are nevertheless immunocompromised eg. through drug treatment following organ transplantation, are at an increased risk of symptomatic bacteraemia following endoscopy. Until such time as data become available we do not recommend antibiotic prophylaxis routinely for this group. Routine antibiotic prophylaxis is not recommended in patients with HIV infection.

5. SPECIAL CONSIDERATIONS – ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

Bacteraemia is well recognised during ERCP²³⁻²⁵. Pancreato-biliary sepsis occurs after 0.4-0.8% of endoscopic biliary procedures²⁶. These episodes are important since the case fatality is 8-20%^{26,27}. Although early studies of antibiotic prophylaxis showed no overall benefit, this was probably because of the case mix of diagnostic and therapeutic procedures. Sepsis is rare after diagnostic ERCP.

In patients with obstructed bile ducts with features of previous sepsis, or pancreatic pseudocyst, data suggest a reduction in clinically significant sepsis when prophylactic antibiotics are used²⁸⁻³⁰. Organisms commonly recognised in clinically significant biliary sepsis are *Pseudomonas aeruginosa*, *Klebsiella spp.*, *Escherichia coli*, *enterococci*, *coagulase negative staphylococci* and *Bacteroides spp.* However the most important predictor of sepsis after therapeutic ERCP is incomplete bile duct drainage³¹.

Prophylactic administration of antibiotics is appropriate for patients likely to undergo a therapeutic procedure in the bile duct with prior or active features of

biliary sepsis or pancreatic pseudocyst. Other factors essential for the reduction of sepsis in the biliary tract during diagnostic or therapeutic ERCP are the optimal cleansing and disinfection of the endoscope, the use of sterile contrast medium and careful control of the volume of contrast used.

6. COLONISATION OF NON-CARDIAC PROSTHESES

It has been suggested that some late infections of orthopaedic, neurosurgical and other prostheses may be due to haematogenous spread of bacteria. If so, the incidence of such infections might be reduced by more widespread use of antibiotic prophylaxis in both dentistry and endoscopy. As bacteraemia occurs during activities as trivial and as frequent as tooth brushing, there appears to be little likely benefit from such treatment. Lifelong antibiotic prophylaxis for all patients with orthopaedic, neurosurgical and other implanted prosthetic materials would be more logical but adverse effects would almost certainly outweigh any potential benefit.

We are in agreement with the American Society of Colon and Rectal Surgeons in their view that the risk following colonic and rectal endoscopy is low for patients with orthopaedic prostheses, central nervous system vascular shunts, penile prostheses, intra ocular lenses, pacemakers and local tissue augmentation materials³². We do not recommend the use of prophylactic antibiotics in this setting.

7. WOUND INFECTIONS FOLLOWING PERCUTANEOUS ENDOSCOPIC GASTROTOMY (PEG)

Introduction

Previous guidelines published in 1996 indicated that this was an area where little

evidence existed in relation to 'best practice'. Since these original guidelines appeared a significant amount of new data has been published dealing with this particular issue. Many gastroenterologists have ignored this new data despite the appearance of more up to date guidelines³³.

Not all patients are at equal risk of developing peristomal infections and one study from the USA³³ showed little benefit from antibiotic prophylaxis, confirming an earlier study³⁴. However larger randomised, controlled trials do show benefit³⁵ and this may be particularly true for patients with malignant disease³⁶. This finding was also seen in another study recently reported from Germany³⁷ where a single dose of 1g ceftriaxone was more effective than placebo in preventing both peristomal infection (7.6% v 23.6% on day 4) and systemic infection (1.9% v 11.8%).

Another large randomised clinical trial³⁸ showed that although serious infections were rare (1.6%) antibiotic prophylaxis with 2g Cefotaxime significantly reduced overall wound scores compared to those not receiving an antibiotic.

(i) PEG in Malignancy

The evidence from randomised controlled trials is consistent and indicates that antibiotic prophylaxis is effective at reducing wound infection rates using a single dose of an appropriate antibiotic. Grade A evidence from a prospective, randomised, double blind, placebo controlled trial³³ showed that a single intravenous dose of 2.2g of co-amoxycylav reduced peristomal infection rate at one week from 65% to 20% and clinically important wound infection rates from 26% down to 2%.

Thus sufficient evidence exists to recommend that patients with malignant disease should have antibiotic prophylaxis (Grade A) whilst patients with non-malignant disease should also be given antibiotics to reduce wound infections and

post procedural pneumonia (Grade B). A second or third generation Cephalosporin or Co-amoxycylav given intravenously are both effective.

(ii) Cost Effectiveness of Antibiotic Prophylaxis for PEG

Although infection rates vary and appear higher for those patients with malignant disease a recent report would seem to indicate that it is cost effective to administer i.v. antibiotics to all patients undergoing endoscopic placement of a gastrostomy feeding tube³⁹.

8. ANTIBIOTIC RECOMMENDATIONS (SEE TABLES 3 & 4)

(i) Ampicillin and amoxycillin

Gram-positive bacteria, especially streptococci and enterococci, cause most infective endocarditis. Because of the possibility of enterococcal bacteraemia, more likely after instrumentation of the lower gastrointestinal tract, ampicillin or amoxycillin are preferred to penicillin for prophylaxis. All three are effective in killing most oral streptococci.

(ii) Aminoglycosides

The use of an aminoglycoside such as gentamicin increases the bactericidal power of ampicillin or amoxycillin against streptococci and enterococci. The use of one or two doses only of gentamicin confers negligible risk of nephro- or ototoxicity.

Gentamicin is also active against most aerobic coliforms (and most *Pseudomonas* spp.) and is suitable for use in neutropenia, where metronidazole should be added to the perioperative antibiotic regime to provide cover against anaerobic organisms.

(iii) Ciprofloxacin

Ciprofloxacin has generally high activity against gram-negative bacteria but is much less active against many gram-positive

species, including enterococci. It is therefore not suitable for prevention of endocarditis but is widely used for the prevention of gram-negative sepsis after ERCP. Oral ciprofloxacin is considerably cheaper than the intravenous preparation and gives good blood levels.

(iv) Other agents

Glycopeptides such as vancomycin or teicoplanin, with a very broad spectrum of activity against gram-positive bacteria, have a role when the patient has been exposed in the recent past to penicillin, ampicillin or amoxicillin, and in patients who are allergic to penicillins.

The incidence of enterococcal infections is increasing rapidly in some countries at present, often associated with heavy use of cephalosporins. Cephalosporins have very poor activity against enterococci and are therefore inappropriate for endocarditis prophylaxis. Because of their otherwise broad spectrum of activity and the fact that they penetrate relatively freely into the bowel contents, heavy use of cephalosporins has been associated with outbreaks of *Clostridium difficile* enterocolitis.

Ureidopenicillins, eg piperacillin are also broad spectrum agents but with little activity against most strains of staphylococci. Like cephalosporins, they may provoke *Clostridium difficile* enterocolitis.

Most streptococci of bowel origin remain sensitive to traditionally used antibiotics. However, though still rare in the UK, vancomycin resistant enterococci (VRE) are being encountered with increasing frequency in some hospitals and units. Antibiotic resistance trends in the UK must be kept under review.

(v) Patients on antibiotics

Patients who have been receiving continuous antibiotic prophylaxis for the prevention of recurrent symptomatic bacteraemia following biliary stenting, may have acquired a resistant bacterial

flora and should be given a different antibiotic to cover endoscopic procedures.

9. CONCLUSIONS

We recommend antibiotic prophylaxis for:

- all patients with higher risk cardiac lesions
- neutropaenic patients
- patients likely to undergo therapeutic manoeuvres in the bile duct or with prior or active cholangitis or pancreatic pseudocyst
- Endoscopic placement of PEG feeding tubes

ACKNOWLEDGMENTS

Dr Katherine Taubert of the American Heart Association, Dallas, USA very kindly made available to us a copy of the draft report on antibiotic prophylaxis in gastrointestinal endoscopy of the American Society of Gastroenterology and the American Heart Association. Dr Norman Simmons (Chairman) and members of the British Society for Antimicrobial Chemotherapy Endocarditis Working Party and Dr David Durack commented helpfully on earlier drafts of this report, as did a number of endoscopists and microbiologists.

AUTHORSHIP

This guideline was prepared by members of the British Society of Gastroenterology, with valuable assistance from Dr K. Cartwright, Consultant Microbiologist, Gloucestershire Royal Hospital and Dr C. Oakley, Consultant Cardiologist, Royal Postgraduate Medical School, and approved by Council.

Revised from the original guidelines in January 2001 (Prof. M. G. Bramble MD FRCP). Comments or suggestions for use in subsequent editions should be sent to: The Clinical Services and Standards Committee, British Society of

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