Antibiotic prophylaxis in gastrointestinal endoscopy

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1. INTRODUCTION

Bacteraemia is common following some forms of gastrointestinal endoscopic therapy, such as dilatation or injection sclerotherapy, and can occur with diagnostic endoscopy alone. Fortunately complications resulting from dissemination of endogenous bacteria are uncommon, and infective endocarditis is an extremely rare complication. Furthermore, for most diagnostic and therapeutic procedures there is scant evidence that antibiotic prophylaxis can reduce the incidence of infective complications.

The area that has attracted the most controversy in recent years has been the use of antibiotics to prevent infective endocarditis. The recommendations by the American Heart Association (AHA)[1] have traditionally guided the advice of the national bodies representing endoscopic practice,[2 3] including the British Society of Gastroenterology (BSG).[4] The traditional guidance has been that patients at high risk of endocarditis, such as those with a prosthetic (ie, tissue or mechanical) valve and/or a past history of endocarditis should receive antibiotics for all endoscopic procedures. More recently the European Society of Cardiology recommended antibiotic prophylaxis to cover therapeutic endoscopy in patients with acquired valvular heart disease,[5] and the British Cardiovascular Society went even further, advising antibiotic prophylaxis for patients at moderate risk of endocarditis undergoing any endoscopic procedure.[6]

The Endoscopy Committee of the BSG recognised the need for consensus on this issue, and convened a Working Party in the spring of 2006. The membership, comprised doctors with a special interest in gastroenterology, gastroenterologists, cardiologists and microbiologists. The gastroenterologists and microbiologists from this Working Party also took the opportunity to review the evidence underpinning the use of antibiotic prophylaxis in other areas of endoscopic practice, in particular endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous endoscopic gastrostomy (PEG). In view of new guidance from the AHA, and from the National Institute for Health and Clinical Excellence (NICE), the Working Party reconvened in 2008 to reconsider, in particular, the issue of prophylaxis against infective endocarditis.

2. REMIT

2.1 Aim

These guidelines aim to help clinicians in deciding which patients undergoing gastrointestinal endoscopy should receive antibiotic prophylaxis.

2.2 Development

The BSG first published guidelines on the use of prophylactic antibiotics in 1996, and these were revised by Professor Mike Bramble in 2001.[4] The 2006 BSG Working Party was chaired by Dr Robin Teague, and, in addition to members of the Endoscopy Committee, incorporated representation from the BCS and the British Society for Antimicrobial Chemotherapy (BSAC). The latter professional society was simultaneously in the process of reviewing its guidelines on antibiotic prophylaxis.[7] Dr Miles Allison researched the current literature using PubMed and UltraMED software (the latter includes Medline), prepared the briefing documentation and, after the Working Party met, set about revising the previous version of the guidelines and preparing the first draft of the current guidelines.

Further changes have been made in the light of new guidelines from the AHA,[8] the American Society for Gastrointestinal Endoscopy (ASGE),[9] a clinical guideline from NICE[10 11] and in response to comments from members of BSG Council and Endoscopy Committees, and six international referees who undertook peer review of the 2007 submission. A final conference comprising the six authors of this guideline took place in June 2008.

The guidelines conform to the North of England Evidence based Guidelines Development Project. The grading of each recommendation is dependent on the category of evidence supporting it. Recommendations based on the level of evidence are presented and graded as:

- A: requires at least one randomised controlled trial of good quality addressing the topic of the recommendation (evidence categories Ia and Ib);
- B: requires the availability of clinical studies without randomisation on the topic of the recommendation (evidence categories IIa, IIb and III);
- C: requires evidence from expert committee reports or opinions or clinical experience of respected authorities in the absence of directly applicable clinical studies of good quality (evidence category IV).

2.3 Scheduled review

The content and evidence base for these guidelines should be reviewed within 5 years of publication.

3. EXECUTIVE SUMMARY

3.1 Antibiotic prophylaxis is no longer recommended for the prevention of infective endocarditis in patients with cardiac risk factors who undergo

diagnostic or therapeutic endoscopy. *Evidence Grade III, Recommendation Grade B*.

3.2 The possibility of infective endocarditis should be considered in patients with known cardiac risk factors who develop symptoms and signs of infection during the weeks following an endoscopic procedure. Such patients should undergo prompt investigation and appropriate treatment. *Evidence Grade IV, Recommendation Grade C*.

3.3 Patients with ongoing cholangitis (or other infections for which therapeutic endoscopy is indicated as part of their management plan) should already have been established on appropriate antimicrobial therapy. *Evidence Grade Ia, Recommendation Grade A*.

3.4 Additional single-dose ERCP prophylaxis is not normally recommended for those already established on antimicrobial treatment for cholangitis. *Evidence Grade IV, Recommendation Grade C*.

3.5 Routine prophylaxis for ERCP is no longer considered appropriate, but, if it proves impossible to achieve adequate biliary decompression, a full antibiotic course is indicated while arrangements are being made to achieve this goal by repeat ERCP or some other means. *Evidence Grade III, Recommendation Grade B*.

3.6 There are specific circumstances where antibiotic prophylaxis should be given routinely to cover ERCP. These include

- patients with biliary disorders, such as primary sclerosing cholangitis or hilar cholangiocarcinoma, in whom it can be anticipated that complete biliary drainage will be difficult or impossible to achieve during one procedure,
- patients with a history of liver transplantation,
- patients with pancreatic pseudocyst,
- patients with severe neutropenia ($<0.5\times10^9$/l) and/or advanced haematological malignancy.

Evidence Grade III, Recommendation Grade B.

3.7 When prophylaxis for ERCP is given, oral ciprofloxacin or intravenous gentamicin is recommended. *Evidence Grade IIa, Recommendation Grade B*.

3.8 The recommended antibiotic regimen for ERCP prophylaxis and/or persisting biliary obstruction following attempted decompression at ERCP may need to be altered locally in the light of epidemiological patterns in isolates of microorganisms resistant to these agents. *Evidence Grade IV, Recommendation Grade C.*

3.9 Patients having a percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ) should normally receive a single dose of intravenous co-amoxiclav during the hour before the procedure. Cefuroxime is an alternative, but should be avoided where possible in regions with a high incidence of *Clostridium difficile* infection, or infections due to extended-spectrum β-lactamase-producing organisms. *Evidence Grade Ia, Recommendation Grade A*.

3.10 Patients already receiving broad-spectrum antibiotics do not require additional prophylaxis for PEG. *Evidence Grade III, Recommendation Grade B*.

3.11 The choice of antibiotic for patients with a history of clear-cut penicillin allergy (such as anaphylaxis or angioedema) who require PEG has not been established, but teicoplanin is a logical alternative. *Evidence Grade IV, Recommendation Grade C*.

3.12 Patients with suspected variceal bleeding (or patients with decompensated liver disease who develop acute gastrointestinal bleeding) should have already been established on intravenous antibiotics before undergoing endoscopy. *Evidence Grade Ia, Recommendation Grade A*.

3.13 Antibiotic prophylaxis is indicated for the fine needle aspiration of cystic lesions in or adjacent to the pancreas, and for endoscopic transgastric or transenteric drainage of pancreatic pseudocysts. *Evidence grade IIa, Recommendation Grade B*.

3.14 Antibiotic prophylaxis is recommenended for patients with severe neutropenia ($<0.5\times10^9$/l) and/or profound immunocompromise (eg, advanced haematological malignancy) who undergo procedures that are known to be associated with a high risk of bacteraemia (table 1). *Evidence Grade IV, Recommendation Grade C*.

3.15 Recent positive culture results should be taken into account when deciding on antibiotic prophylaxis regimens, and microbiological advice sought if required. *Evidence Grade IV, Recommendation Grade C*.

3.16 Given that endocarditis prophylaxis will no longer be routinely given, professional bodies and specialist societies should work towards establishing national prospective registries of patients with endocarditis to enable analysis of the temporal relationship to any preceding endoscopic procedure. Likewise cholangitis complicating ERCP may become more common now that prophylaxis for patients with biliary obstruction will no longer be routine, and consideration should be given to establishing national registries of post-ERCP cholangitis.

4. GENERAL CONSIDERATIONS

4.1 Rationale for prophylaxis against endocarditis

The hypothesis underpinning the practice of prophylaxis against infective endocarditis is: (1) endocarditis usually follows bacteraemia; (2) certain interventional procedures cause bacteraemia with organisms that can cause endocarditis; (3) such bacteria are usually sensitive to antibiotics; (4) antibiotics should thus be given to patients with predisposing heart disease before procedures that may cause bacteraemia.

Table 1 Approximate incidence of bacteraemia in immunocompetent individuals undergoing gastrointestinal endoscopy

Bacteraemia	BSG review (%)[4]	Nelson *et al* (%)[12]
Rectal digital examination	4	
Rigid proctosigmoidoscopy	5–9	7.6
Barium enema	11	
Tooth brushing	25	
Dental extraction	30–60	
Colonoscopy	2–4	4.4
Diagnostic OGD ± biopsy	4	4.1
Flexible sigmoidoscopy		0.5
ERCP (no duct occlusion)	6	6.4
ERCP (duct occluded)	11	18
Variceal band ligation	6	8.8
Sclerotherapy	10–50	14.6
Oesophageal dilatation/prosthesis	34–54	
Oesophageal laser therapy	35	
EUS + FNA	0–6[13–16]	0

Figures for barium enema and dental manipulation are given for comparison.
BSG, British Society of Gastroenterology; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; FNA, fine needle aspiration; OGD, oesophagogastroduodenoscopy.

4.2 Arguments in favour of prophylaxis against endocarditis and other consequences of bacteraemia

The hypothesis is that antimicrobial prophylaxis before endoscopy can reduce the risks of:

- Infective endocarditis
- Symptomatic bacteraemia
- Colonisation of vascular grafts and endovascular stents, orthopaedic and other non-cardiac vascular implants.

4.3 Arguments against prophylaxis against endocarditis

The potential benefits of antibiotic prophylaxis should be weighed up against:

- The questionable clinical significance of bacteraemia arising from an endoscopic procedure, given that bacteraemia is an everyday event associated with toothbrushing, for example
- The potential contribution to the selection of resistant bacteria, such as MRSA (methicillin-resistant *Staphylococcus aureus*)
- The knowledge that antibiotics may fail to prevent infective endocarditis or other infective complications
- The small risk of adverse events, including anaphylaxis and *C difficile* infection
- The practical difficulties and costs of antibiotic administration, especially in patients who are allergic to penicillin.

4.4 Endocarditis risk following endoscopy

Prospective studies to determine the value of antibiotic prophylaxis against endocarditis during gastrointestinal endoscopy are not available. Such research is unlikely to be done because endocarditis complicating endoscopy is extremely rare, so prospective studies would need to recruit very large numbers of subjects over several years.

5. BACTERAEMIA

5.1 Evidence for bacteraemia in gastrointestinal endoscopy

The existence of bacteraemia during upper and lower gastrointestinal endoscopy has been well established in numerous series (summarised in table 1). These studies were reviewed in the previous edition of these guidelines[4] and more recently by Nelson.[12] Some published papers overestimate the rates of potentially significant bacteraemia because microorganisms which are frequent contaminants (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.

One study of upper gastrointestinal endoscopy in immunosuppressed patients (in whom intravascular destruction of bacteria is minimised) reported a high rate of clinically significant bacteraemia (9/47, 19%) in bone marrow transplant recipients receiving corticosteroids.[13]

Bacteraemia during ERCP is considered to result mainly from contrast injection and manipulation around endogenous bacteria in bile and/or pancreatic tissue of patients with pre-existing pathology such as biliary obstruction or pancreatic pseudocyst. Bacteraemia during ERCP is infrequent among patients without evidence of biliary or pancreatic ductal obstruction.[12]

More recent attention has been given to the potential risk of bacteraemia during the diagnostic and therapeutic interventions that are undertaken under endoscopic ultrasound (EUS) guidance. Fine needle aspiration (FNA) and ultrasound-guided biopsy appear to carry a low risk of bacteraemia,[14–17] even though EUS-guided aspiration of pancreatic and peripancreatic cystic lesions can lead to infective complications (see Section 11).

5.2 Clinical importance of bacteraemia

Recent evidence confirms that everyday activities such as chewing or tooth brushing produce a bacteraemia of dental flora.[18 19] The incidence of bacteraemia during endoscopy has been extensively studied, but the incidence of symptomatic bacteraemia is less well understood. In the great majority of cases, endoscopy-related bacteraemia is not associated with any recognisable symptoms or infection-related complications. Thus, in most instances, there would seem to be little reason to attempt to reduce the rate of endoscopy-associated asymptomatic bacteraemia in the absence of delayed clinical sequelae.

The most serious potential sequelae of bacteraemia include infective endocarditis, meningitis, cerebral abscess, and infected ascites (bacterial peritonitis) in patients with cirrhosis.[12] These complications, whilst rare, are more likely to follow procedures associated with the highest risk of bacteraemia, such as oesophageal dilatation or injection sclerotherapy of varices.

5.3 Prevention of bacteraemia

One study has assessed prospectively (but in an open study design) the efficacy of antibiotic treatment in reducing bacteraemia rates during endoscopy.[20] Alternate patients aged 60 years 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%, $p<0.001$). However, the microorganisms isolated could all have been skin contaminants, and neither the patients who received antibiotics nor the controls experienced any symptoms likely to have been associated with bacteraemia.

6. INFECTIVE ENDOCARDITIS

6.1 Background and literature survey

Over recent decades the numbers of gastrointestinal endoscopic procedures which have been carried out worldwide has risen exponentially. It is therefore reassuring that there is no evidence of any concomitant increase in the incidence of endocarditis. Published reports of endocarditis associated with endoscopic procedures have occurred less than once per year (table 2) and it is not clear even in this small number of cases whether the association was always causal. No published case of endocarditis complicating ERCP was identified. On the other hand, not all cases of infective endocarditis following endoscopy are reported, and the association may not always be recognised.

A UK collaborative survey of 582 patients with infective endocarditis identified three patients in whom there was a history of recent gastroscopy.[21] The significance of these findings has been questioned because there was no control group. The other case reports linking infective endocarditis to recent endoscopic procedures[22–43] are summarised in table 2. Some important points arise from these cases:

- There is marked variation in the time interval between endoscopy and onset of symptoms, and thus uncertainty as to whether endocarditis had been caused by the procedure or an unrelated incidental bacteraemia.
- There is an example of failure of antibiotic prophylaxis.[25]
- There are examples of patients with no prior history of cardiac disease.[24 30 39 42]
- Other clinical factors, including the underlying condition for which endoscopy was indicated, may have influenced the endocarditis risk.[27 31]

Table 2 Case reports of infective endocarditis occurring within weeks after endoscopic procedures

Type of endoscopy	Author and reference	Year	Organism	Patient details
Oesophageal bougienage	Yin[22]	1983	*Streptococcus viridans*	Known mitral regurgitation
	Niv[23]	1985	*Streptococcus viridans*	Known MV prolapse
	Breuer[24]	1998	*Streptococcus capitis*	No known prior valve disease
Variceal sclerotherapy	Baskin[25]	1989	*Streptococcus viridans*	Prosthetic valve (failure of prophylaxis)
	Wong[26]	1997	*Streptococcus salivarius*	Native valve
Diagnostic OGD ± biopsy	Rumfeld[27]	1980	*Streptococcus* spp.	MV stenosis (patient also had RIH repair)
	Logan[28]	1988	*Streptococcus sanguis*	Known MV prolapse
	Pritchard[29]	1991	*Cardiobacterium* spp.	Prosthetic aortic valve replacement
	Pentimone[30]	1991	*Streptococcus sanguis*	Young man; no known cardiac disease
	Montalko[31]	2002	*Streptococcus oralis*	MV prolapse (symptoms pre-dated OGD in patient on steroids)
	Cho[32]	2004	*Streptococcus intermedius*	Valvular heart disease
	Yu-Hsien[33]	2008	*Acinetobacter* spp.	Prosthetic valve
Lower GI	Rodriguez[34]	1984	*Enterococcus* spp.	Rheumatic mixed valve disease following flexible sigmoidoscopy
	Rigilano[35]	1984	*Enterococcus* spp.	MV prolapse, rigid sigmoidoscopy
	Greco[36]	1986	*Enterococcus* spp.	Polypectomy
	Watanakunakorn[37]	1988	*Enterococcus* spp.	Known aortic stenosis, following polypectomy
	Norfleet[38]	1991	*Streptococcus sanguis*	Aortic regurgitation: flexible sigmoidoscopy for polyp follow-up
	Millaire[39]	1991	*Enterococcus* spp.	Polypectomy. No known prior valvulopathy
	Giusti de Marle[40]	2000	*Enterococcus* spp.	Mixed AVD, colonoscopy
	Heiro[41]	2000	*Eikenella* spp.	Prosthetic valve
	Avlami[42]	2001	*Lactobacillus* spp.	No known prior valvulopathy
	Malani[43]	2006	*Cardiobacterium* spp.	Two cases of prosthetic valve endocarditis following colonoscopy

AVD, aortic valve disease; GI, gastrointestinal; MV, mitral valve; OGD, oesophagogastroduodenoscopy; RIH, right inguinal hernia.

6.2 Does antibiotic prophylaxis prevent endocarditis?

There is only limited evidence that antibiotic administration during dental or surgical procedures reduces the risk of endocarditis.[44] Failures of endocarditis prophylaxis are well recognised.[25 45] In the rabbit model, antibiotic prophylaxis has been shown to reduce the risk of infection in damaged valves following high bacterial challenge.[46] A retrospective case–control study of patients at risk suggested that antibiotic prophylaxis might be effective in preventing endocarditis in dental practice,[47] but a recent Cochrane review came out against the routine use of prophylactic penicillin for invasive dental procedures.[48]

6.3 Factors predisposing to endocarditis

Cardiovascular risk factors for endocarditis have been discussed in detail elsewhere.[5 6 8] The risk of endocarditis is probably influenced by the frequency of bacteraemia (table 1) and may be affected by the intensity of any bacteraemia associated with an endoscopic procedure. Microbial characteristics such as adhesion factors are likely to be relevant, and bacteria appear to vary greatly in their propensity to infect damaged heart valves.

6.4 Factors predisposing to a poor outcome with endocarditis treatment

The recently published guidelines of the AHA[8] identify a group of cardiac risk factors that predispose to a poor outcome following the development of endocarditis. These include patients with a history of valve replacement in whom eradication of infection may be especially difficult. Whilst the AHA guidelines do recommend prophylaxis for certain dental procedures in such patients, the NICE review of the evidence did not agree with the AHA assessment.[10] There is also evidence to challenge the assumption that endocarditis caused by enterococci (which accounts for a large proportion of endocarditis cases linked to colonoscopy—see table 2) has a worse prognosis in patients with prosthetic valves in comparison with native valves.[49 50]

6.5 The NICE guidelines

While advising against endocarditis prophylaxis in general, NICE argued that "if a person at risk of infective endocarditis is receiving antimicrobial therapy because they are undergoing a gastrointestinal or genitourinary procedure at a site where there is a suspected infection, the person should receive an antibiotic that covers organisms that cause infective endocarditis".[9] Many patients with cardiac pathology, however, are unaware that they have any abnormality, and even those with documented acquired valvular disease may not carry an antibiotic card or be aware of the findings from previous echocardiography. Thus the ascertainment of at-risk patients will always be incomplete. Furthermore, it may be difficult to rule out the possibility of low grade infection in patients with biliary obstruction and/or pancreatic pseudocyst. The BSG Working Party agrees with the view that patients who present with cholangitis (or other infection for which therapeutic endoscopy is indicated), who have a history of valve replacement or other known cardiac risk factor, should receive antibiotics which are active against enterococci (such as amoxicillin) until the results of cultures are known.

6.6 Recommendations on endocarditis prophylaxis during endoscopy

Antibiotic prophylaxis is no longer recommended for the prevention of infective endocarditis in patients with cardiac risk factors who undergo diagnostic or therapeutic endoscopy. *Evidence Grade III, Recommendation Grade B.*

This conclusion is based on three main considerations:

- The rarity of infective endocarditis as a complication of endoscopy, and the absence of an exponential increased incidence to parallel the growth of endoscopy
- The failure in many case reports to demonstrate a causal relationship between infective endocarditis and a preceding endoscopic procedure
- The risks associated with antibiotic administration, namely allergy, antibiotic resistance and *C difficile* infection.

6.7 Potential consequences of withholding prophylaxis

Until recently it has been standard practice to give prophylaxis against endocarditis to patients with a history of valve replacement and/or previous endocarditis. The possibility that some such patients may thus have been prevented from developing endocarditis cannot be ruled out. It is therefore possible that the coming years will witness a rise in the incidence of postprocedure endocarditis. Thus it is important for healthcare professionals to be alert to this possibility in patients who develop symptoms and/or signs of infection (box 1) during the weeks following endoscopy.

The possibility of infective endocarditis should be considered in patients who develop symptoms and signs of infection during the weeks following an endoscopic procedure. Such patients should undergo prompt investigation and appropriate treatment. *Evidence Grade IV, Recommendation Grade C*.

A group of patients who may turn out to be the most difficult to advise are those who have become accustomed to receiving antibiotic prophylaxis to cover procedures over many years and are thus known not to be allergic to the previously recommended antibiotic regimens. For such individuals the NICE guidance[9] states "Treatment and care should take into account patients' needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals." It is expected that the majority of such individuals will accept the changes in guidance, which have arisen with international consensus. It is recognised that some patients will still choose to receive prophylaxis.

Box 1 Clinical features of infective endocarditis[6]

Systemic features: intermittent pyrexia, sweats, chills, rigors, anorexia, weight loss, arthralgia and fatigue. Systemic symptoms may be acute or insidious in onset.

Cardiac manifestations: new or worsening cardiac murmurs—typically due to valvular regurgitation; or the development of cardiac failure.

Extracardiac manifestations: embolic as well as vasculitic phenomena. All major vessels may be the recipient of infected emboli from valve vegetations. Renal, splenic and neurological complications may be particularly serious.

7. ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

7.1 Bacteraemia during ERCP

Bacteraemia is well recognised during ERCP.[51–54] Pancreaticobiliary infection occurs after 0.4–0.8% of endoscopic biliary procedures. These episodes must always be taken seriously because fatality has been reported in 8–20% of such cases.[55]

7.2 The evidence

It was initially believed that the failure of early studies of antibiotic prophylaxis to show benefit was because the case mix included both diagnostic and therapeutic procedures. Infection is rare after diagnostic ERCP in the absence of stones or pancreatic or biliary obstruction. In patients with obstructed bile ducts with features of previous infection, or pancreatic pseudocyst, the available data suggest a reduction in clinically significant infective complications when prophylactic antibiotics are used.[53 56 57] On closer scrutiny of these papers, however, the examples of procedure-related cholangitis were almost all in patients for whom adequate biliary drainage had not been achieved during ERCP. The contention that relief of biliary obstruction is more important than antibiotic prophylaxis is reinforced by the finding that the chief predictor of infective complications after therapeutic ERCP is incomplete bile duct drainage.[58]

Although not all authorities are in agreement,[59–62] the case has been made for prophylactic administration of antibiotics for patients likely to undergo a therapeutic procedure in the context of ongoing biliary obstruction and/or infection and/or pancreatic pseudocyst.[63 64] There is also a suggestion that antibiotic prophylaxis is cost-effective in these circumstances.[63] This begs the question as to what constitutes "biliary obstruction"; potential scenarios include the following: (1) patients presenting with bacterial cholangitis should already be established on antibiotics at the time of ERCP; (2) patients with jaundice secondary to obstructing common duct stones or strictures in the absence of cholangitis may not necessarily require antibiotics provided that the obstruction can be properly relieved at ERCP[59]; (3) non-jaundiced patients with common duct stones may not need antibiotic cover provided that the stones can be removed or drainage can be secured by means of stenting (with or without biliary sphincterotomy). These arguments have led Subhani and colleagues to propose that antibiotics can be administered immediately after ERCP if it has not been possible to decompress the biliary tree.[61] Whilst this pragmatic approach has not been tested in clinical practice, the Working Party agreed this to be a logical way forward given the risk-benefit analysis for prophylactic antibiotic administration, and it is also in keeping with American opinion.[9 65]

Other factors that are important in reducing the risk of infection include (1) optimal decontamination of the endoscope; (2) the employment of single-use accessories down the working channel of the duodenoscope; and (3) the use of sterile contrast medium and careful control of the volume of contrast used. Some experts advocate that the endoscopist should aspirate bile from the biliary tree in order to attenuate the rise in intrabiliary pressure following contrast injection. Some authorities add antibiotics to the contrast media prior to injection. Neither of these two strategies can be recommended however, because there is no evidence that either reduces the risk of bacteraemia or cholangitis.

The choice of antibiotic depends on the clinical context. Common causative microorganisms in ascending cholangitis are *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella* spp.,

Table 3 Summary of prophylactic antibiotic regimens recommended for gastrointestinal endoscopy

Scenario for prophylaxis	Rationale	Antibiotics	Dose/route
1. Patients with valvular heart disease, valve replacement, and/or surgically constructed systemic–pulmonary shunt or conduit, or vascular graft	Prevention of infective endocarditis or conduit/graft infection	Not indicated	
2. ERCP for the following patient groups:			
a. ongoing cholangitis or sepsis elsewhere	Prevention of procedure-related bacteraemia	Be guided by recent culture results. Patients should already have been established on antibiotics	May need advice from clinical microbiologist
b. biliary obstruction and/or common bile duct stones and/or straightforward stent change	Prevention of cholangitis	Not indicated unless biliary decompression not achieved. A full course of antibiotics becomes indicated if adequate biliary decompression is not achieved during the procedure	
c. ERCP when complete biliary drainage unlikely to be achieved (eg, sclerosing cholangitis and/or hilar cholangiocarcinoma) (special considerations may apply in cover for a repeat ERCP: see Section 7.2.4]	Prevention of cholangitis	Ciprofloxacin	750 mg orally 60–90 min before procedure (but not recommended in children)
		OR	
		Gentamicin	1.5 mg/kg intravenously. over 2–3 min
d. communicating pancreatic cyst or pseudocyst	Reducing risk of introducing infection into cavity	As above	As above
e. biliary complications following liver transplant	Prevention of cholangitis	As (c) PLUS amoxicillin	1 g intravenously single dose
		OR	
		Vancomycin	20 mg/kg intravenously infused over at least 1 h
3. Endoscopic ultrasound intervention for the following patient groups:			
a. fine needle aspiration solid lesions	Prevention of local infection	Not indicated	
b. fine needle aspiration of cystic lesions in or near pancreas, or drainage of cystic cavity	Prevention of cyst infection	Co-amoxiclav	1.2 g intravenously single dose
		OR	
		Ciprofloxacin	750 mg one oral dose
4. Percutaneous endoscopic gastrostomy (PEG)	Prevention of peristomal infection	Co-amoxiclav	1.2 g intravenous injection or infusion just before procedure
		OR	
	Possibly reduction in risk of other infections such as aspiration pneumonia	Cefuroxime	750 mg intravenous injection or infusion just before procedure
		Teicoplanin can be used if past anaphylaxis or angioedema with penicillin/cephalosporin	400 mg intravenously for adults
5. Variceal bleeding (not strictly prophylaxis)	Prevention of infections such as bacterial peritonitis	Piperacillin/tazobactam	4.5 g intravenously three times daily
		OR	
		Third-generation cephalosporin	eg, cefotaxime 2 g three times daily
		Seek advice of local microbiologist or regional liver unit in patients who are allergic to penicillin	
6. Profound immunocompromise (eg, neutropenia $<0.5\times10^9$/l or advanced haematological malignancy	Prevention of procedure-related bacteraemia	Only indicated in procedures with high risk of bacteraemia (eg, sclerotherapy, dilatation, ERCP with obstructed system)	Discuss with haematologist and/or clinical microbiologist

ERCP, endoscopic retrograde cholangiopancreatography.

enterococci, coagulase-negative staphylococci and *Bacteroides* spp., but many infections are polymicrobial.[61]

Our recommendations are summarised in Section 7.3 and in table 3. There are several scenarios to consider.

7.2.1 Patients with cardiovascular risk factors for endocarditis

Given that enterococci are commonly present in the bile of patients with biliary obstruction, and that enterococci cause endocarditis and have been linked to endocarditis complicating colonoscopy, it would be expected that antienterococcals might have a role in the prevention of endocarditis following ERCP. Whilst enterococci are commonly found in infected bile, their isolation in blood cultures from corresponding patients is uncommon.[61 66] Moreover, the Working Party was unable to identify reports of infective endocarditis complicating ERCP. There is therefore no reason to recommend antibiotic prophylaxis for patients undergoing ERCP where the sole aim is the prevention of endocarditis.

7.2.2 Patients with ongoing pancreatic or biliary sepsis

These patients will normally already be receiving appropriate antibiotics. Those with a history of valve replacement or known cardiac risk factors for endocarditis should be receiving antibiotics that will cover enterococci, such as amoxicillin, pending the results of culture studies. Additional single-dose prophylaxis is not routinely recommended (except in some patients with a history of prior biliary manipulations—see Section 7.2.4 below).

7.2.3 Patients with first ERCP for biliary obstruction with no clinical evidence of infection

In these circumstances it is reasonable for the endoscopist to elect not to give preprocedure antibiotics provided that their

administration is ensured as soon as possible postprocedure in the event that adequate decompression of the biliary tree has not been achieved. The course of antibiotics should continue whilst arrangements are being made to relieve biliary obstruction as soon as possible (either by repeat ERCP or by some other means) and should last at least until this end point has been achieved.

The choice of antibiotics has been debated and reviewed in depth,[61–63] and the role of specific antibiotics is discussed in Section 13. Most authorities recommend either oral ciprofloxacin taken 90 min before the procedure, or intravenous gentamicin at the time of sedation. Both ciprofloxacin and gentamicin have gaps in the cover they provide. Both have generally good activity against Gram-negative aerobic bacteria but are much less active against many Gram-positive species, including enterococci. Increasing ciprofloxacin resistance among coliforms (Enterobacteriaceae) has also been reported.[67] Therefore, the choice between ciprofloxacin and gentamicin may be influenced by the local epidemiology in microbial resistance.

Oral ciprofloxacin is less expensive than the intravenous formulation and results in satisfactory blood concentrations. Although gentamicin does not penetrate into bile very well, and has limited activity against enterococci, it probably has broader Gram-negative activity than ciprofloxacin. Therefore, the combination of amoxicillin and continued treatment with the antibiotic chosen for prophylaxis should be considered in a patient who becomes febrile postprocedure.

7.2.4 Patients with a history of prior biliary manipulations

Bile within the biliary tree is normally sterile. ERCP with sphincterotomy and/or stenting disrupts the normal ampullary barrier to the gut, and is associated with long-term bacterobilia.[68 69] It is therefore logical to infer that patients needing repeat biliary intervention at ERCP are at increased risk of bacteraemia and cholangitis. In a large prospective series cholangitis complicating ERCP was more likely to occur in patients with a history of prior ERCP (with sphincterotomy and/or stenting).[65] Patients who have been receiving continuous antibiotic prophylaxis for the prevention of recurrent symptomatic bacteraemia following biliary stenting may have acquired resistant bacterial flora, and should be given a different antibiotic to cover further biliary endoscopic procedures (such as stent changes) unless it is anticipated that complete biliary drainage is achievable by means of repeat ERCP. Because of the lack of an evidence base, we believe that the decision as to whether to use prophylactic antibiotics in patients undergoing repeat ERCP rests with the endoscopist, the local clinical microbiologist and the clinical team caring for the patient. When ERCP is performed in patients who have previously received full treatment courses of one antibiotic, consideration should be given to the use of an alternative antibiotic (or combination of antibiotics) to cover the procedure. For example, if a patient has been exposed to prolonged and/or frequent ciprofloxacin, a combination of amoxicillin and gentamicin, or monotherapy with a wider spectrum penicillin such as piperacillin with tazobactam, could be given.

7.2.5 Other settings in which prophylaxis for ERCP should be given

Thes include (1) patients undergoing biliary intervention post liver transplant[70]; (2) patients with known Caroli's disease or primary sclerosing cholangitis, not only because bacterial cholangitis is common following biliary manipulation[71] but also because complete relief of biliary obstruction is unlikely to be achieved at ERCP; (3) patients with Bismuth type III or type IV cholangiocarcinoma, for whom it may likewise be difficult or impossible to secure drainage of all liver segments; (4) patients with pancreatic pseudocysts; (5) patients with severe neutropenia ($<0.5\times10^9$/l) and/or advanced haematological malignancy.

7.3 Recommendations for prophylaxis before ERCP

Patients with ongoing cholangitis (or other infections for which therapeutic endoscopy is indicated as part of their management plan) should already have been established on appropriate antimicrobial therapy. ***Evidence Grade Ia, Recommendation Grade A.***

Additional single-dose ERCP prophylaxis is not normally recommended for those already established on antimicrobial treatment for cholangitis. ***Evidence Grade IV, Recommendation Grade C.***

Routine prophylaxis for ERCP is not necessary, but, if it proves impossible to achieve adequate biliary decompression, a full antibiotic course is indicated while arrangements are being made to achieve this goal by repeat ERCP or some other means. ***Evidence Grade III, Recommendation Grade C.***

There are specific circumstances where antibiotic prophylaxis should be given routinely to cover ERCP. These include:

- **patients with biliary disorders, such as primary sclerosing cholangitis or hilar cholangiocarcinoma in whom it can be anticipated that complete biliary drainage will be difficult or impossible to achieve during one procedure;**
- **patients with a history of liver transplantation;**
- **patients with pancreatic pseudocyst;**
- **patients with severe neutropenia ($<0.5\times10^9$/l) and/or advanced haematological malignancy.**

Evidence Grade III, Recommendation Grade B.

When prophylaxis for ERCP is given, oral ciprofloxacin or intravenous gentamicin is recommended. ***Evidence Grade IIa, Recommendation Grade B.***

The recommended antibiotic regimen for ERCP prophylaxis and/or persisting biliary obstruction following attempted decompression at ERCP may need to be altered locally in the light of epidemiological patterns in isolates of microorganisms resistant to these agents. ***Evidence Grade IV, Recommendation Grade C.***

8. COLONISATION OF VASCULAR GRAFTS AND OTHER IMPLANTED MATERIAL

8.1 Background

It has been suggested that some delayed infections of orthopaedic, neurosurgical and other prostheses may be due to haematogenous spread of bacteria following endoscopy or surgery. 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,[18 19] there appears to be minimal 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.

8.2 Recommendations

We are in agreement with the American Society of Colon and Rectal Surgeons[72] and the ASGE[9] that the risk following colonic and rectal endoscopy is low for patients with orthopaedic prostheses, central nervous system vascular shunts, penile prostheses, intraocular lenses, pacemakers and local tissue augmentation materials. We do not recommend the use of prophylactic antibiotics for any form of endoscopy in these settings.

Expert opinion has suggested that patients who have undergone vascular grafting and/or endovascular stenting within the preceding 3 months should be treated in the same manner as patients at moderate endocarditis risk. Given that endocarditis prophylaxis is no longer recommended, there is no logic to recommending prior antibiotics in such patients.

9. PERCUTANEOUS ENDOSCOPIC GASTROSTOMY

9.1 Clinical trials

Early evaluations of single-dose intravenous cephalosporins failed to demonstrate efficacy in the prevention of peristomal infections.[73 74] The last 20 years have witnessed a wealth of controlled trials in this area. The evidence from these is consistent and indicates that antibiotic prophylaxis is effective at reducing wound infection rates using a single dose of an appropriate antibiotic.[75–82] Two meta-analyses have concluded in favour of antibiotic prophylaxis, suggesting a number needed to treat of between 5.7 and 10 to prevent one peristomal infection.[83 84] Co-amoxiclav or a second- or third-generation cephalosporin given intravenously are both effective, and there is also some evidence that antibiotic prophylaxis is cost-effective.[85] Single doses of cephalosporins have been shown to predispose to *C difficile* infection.[86 87] Therefore, co-amoxiclav is preferred to cephalosporins in units where *C difficile* infection is common.

Many patients who claim to be allergic to penicillin will have previously received a cephalosporin without incident, and cefuroxime can be used in this setting. Cefuroxime can be given safely to most patients who have a history of penicillin allergy,[88] but should be avoided in people who have a clear history of anaphylaxis or angioedema with penicillin and/or cephalosporins. In such circumstances an infusion of teicoplanin (400 mg in adults) will cover most staphylococci, streptococci and enterococci.

9.2 Uncertainties and MRSA issues

Three areas of uncertainty remain on this topic. First, many patients undergoing PEG are already receiving courses of broad-spectrum antibiotics, and there is some evidence that wound infections are less common in this group.[73 75 81] Such patients may not need further prophylaxis, and the use of additional antibiotics could predispose to MRSA colonisation. Secondly, the most common end point in clinical trials of antibiotic prophylaxis is the development of peristomal wound infections, many of which are of doubtful clinical importance. Notwithstanding this caveat, there is some evidence that a single-dose intravenous antibiotic may help in preventing more serious infections such as aspiration pneumonia.[76 79 81] Thirdly, a significant proportion of peristomal infections are MRSA related, particularly in patients with nasopharyngeal colonisation.[89 90]

It has recently been suggested that MRSA decolonisation using oral and nasally delivered preparations might reduce the risk of MRSA-related peristomal infection in such patients.[91] Two small non-randomised studies point to a potential role for prophylaxis with vancomycin in patients with MRSA colonisation undergoing PEG.[92 93] Further studies are needed before definitive recommendations can be made.

It is considered that the passage of the PEG tube via the oropharynx during deployment is one of the determinants of infection risk. A recently described deployment system (PEG gastropexy) enables deployment of a balloon-tipped PEG catheter directly into the stomach under endoscopic vision. One randomised controlled study has suggested that the infection risk is very low using this method and concluded that prophylactic antibiotics are not required.[94]

9.3 Percutaneous endoscopic jejunostomy

There are no trials to address the role of antibiotic prophylaxis for patients undergoing direct PEJ. Given that the risk of complications is higher than that for PEG,[95] it is logical to recommend antibiotic prophylaxis as for PEG.

9.4 Recommendations

Patients having a PEG or PEJ should normally receive a single dose of intravenous co-amoxiclav during the hour before the procedure. Cefuroxime is an alternative, but should be avoided where possible in regions with a high incidence of *C difficile* infection or infections due to extended-spectrum β-lactamase-producing organisms. *Evidence Grade Ia, Recommendation Grade A*.

Patients already receiving broad-spectrum antibiotics do not require additional prophylaxis for PEG. *Evidence Grade III, Recommendation Grade B*.

The choice of antibiotic for patients with a history of serious penicillin allergy who require PEG has not been established, but teicoplanin is a logical alternative. *Evidence Grade IV, Recommendation Grade C*.

10. ANTIBIOTICS IN VARICEAL BLEEDING

Bacterial infections occur within 48 h of admission in about 20% of patients with cirrhosis with upper gastrointestinal bleeding.[96] Variceal sclerotherapy in the emergency setting commonly causes bacteraemia.[97] Prognosis in terms of rebleeding, failure to control bleeding and in-hospital outcome is worsened in patients with associated bacterial infection.[98 99] In a meta-analysis of five controlled trials of antibiotic prophylaxis in patients with variceal bleeding, antibiotic use was associated with significantly improved short-term survival.[100] A Cochrane review also suggests that patients with cirrhosis and upper gastrointestinal bleeding should receive antibiotic prophylaxis.[101] There is even evidence to suggest that antibiotic prophylaxis might be associated with a reduced risk of variceal rebleeding.[102 103]

Patients with suspected variceal bleeding should already have been commenced on antibiotics before endoscopy. There is limited evidence to suggest superiority of any particular regimen in this setting.[104] Intravenous ceftriaxone has been shown to reduce infection risk more effectively than oral norfloxacin in one study.[105] The choice of antibiotic in this setting should be discussed with the hospital's microbiology department, and should take account of both the regional liver unit practice and the local microbial epidemiology and resistance patterns.

Patients with suspected variceal bleeding (or patients with decompensated liver disease who develop acute gastrointestinal bleeding) should have already been established on

intravenous antibiotics before undergoing endoscopy. *Evidence Grade Ia, Recommendation Grade A*.

11. ENDOSCOPIC ULTRASOUND

Although bacteraemia following EUS with FNA is uncommon,[14–17] complications can occur following aspiration of pancreatic cystic lesions.[106–110] It is therefore recommended that prophylaxis is given to patients undergoing EUS-guided therapeutic endoscopy where there is a possibility of pre-existing infection within the cyst or cavity being treated. EUS-guided FNA does not normally require antibiotic prophylaxis.[111]

Antibiotic prophylaxis is indicated for the fine needle aspiration of cystic lesions in or adjacent to the pancreas, and for endoscopic transgastric or transenteric drainage of pancreatic pseudocysts. *Evidence grade IIa, Recommendation Grade B*.

12. NEUTROPENIC AND IMMUNOCOMPROMISED PATIENTS

Neutropenia predisposes to sepsis after endoscopy,[13] though the magnitude of the increased risk is not clear. Patients with severe neutropenia ($<0.5\times10^9$/l) who are febrile should have already been established on empirical antibiotic therapy according to local haematology protocols. Afebrile patients with a neutrophil count below 0.5×10^9/l should be offered antibiotic prophylaxis for those gastrointestinal endoscopic procedures which are known to be associated with a high risk of bacteraemia such as variceal sclerotherapy, oesophageal dilatation/laser therapy and ERCP with biliary obstruction (table 1). Gram-negative aerobic (and less frequently anaerobic) bacteria including *E 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, organ recipients) are at an increased risk of infective complications 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.

Antibiotic prophylaxis is recommenended for patients with severe neutropenia ($<0.5\times10^9$/l) and/or profound immunocompromise (eg, advanced haematological malignancy) who undergo procedures that are known to be associated with a high risk of bacteraemia (table 1). *Evidence Grade IV, Recommendation Grade C*.

13. ANTIBIOTICS USED IN PROPHYLAXIS

Recent positive culture results should be taken into account when deciding on antibiotic prophylaxis regimens and microbiological advice sought if required. *Evidence Grade IV, Recommendation Grade C*.

13.1 Ampicillin and amoxicillin

Gram-positive bacteria, especially streptococci and enterococci, cause most infective endocarditis. Because of the possible sequelae from enterococcal bacteraemia, particularly after instrumentation of the lower gastrointestinal tract, ampicillin or amoxicillin are preferred to penicillin in prophylaxis. All three are effective in killing most oral streptococci.

13.2 Aminoglycosides

The use of an aminoglycoside such as gentamicin increases the bactericidal power of ampicillin or amoxicillin against streptococci and enterococci. Although the use of one or two doses only of gentamicin confers negligible risk of nephrotoxicity or ototoxicity, care must be taken in patients with a history of pre-existing renal impairment and/or a history of gentamicin nephrotoxicity. Gentamicin is also active against most aerobic coliforms (and most *Pseudomonas* spp.) and is also suitable for use in neutropaenic patients.

13.3 Quinolones

Ciprofloxacin has good antimicrobial activity against aerobic 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.[112–115] Oral ciprofloxacin is considerably cheaper than the intravenous preparation and results in adequate blood concentrations.

13.4 Glycopeptides

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. These agents may also have an occasional role in prophylaxis against MRSA infection. However, though still uncommon in the UK, vancomycin-resistant enterococci (VRE) are being encountered with increasing frequency in some hospitals. Teicoplanin is recommended in preference to vancomycin for two reasons; first it is simpler and quicker to administer, and secondly more sustained blood levels occur following a single dose.[116]

13.5 Other β-lactam agents

The incidence of enterococcal infections is increasing rapidly in some countries at present, and is often associated with heavy use of cephalosporins. Cephalosporins have no activity against enterococci. As they have an overall broad spectrum of activity (particularly against coliforms) and are present in bowel contents, extensive use of cephalosporins has been associated with outbreaks of *C difficile* infection. Single doses of cephalosporins and other antibiotics used in prophylaxis have been implicated in the development of *C difficile* infection.[86 87] Ureidopenicillins, for example piperacillin, are also broad-spectrum agents but with limited activity against most strains of staphylococci. Like cephalosporins, they may provoke *C difficile* infection, but the risks may be less.

14. CONCLUSIONS AND SUGGESTED TOPICS FOR FURTHER RESEARCH

14.1 Infective endocarditis is an illness that can be associated with devastating and life-threatening complications. In order to understand better whether a true risk of postprocedure endocarditis exists, professional bodies and specialist societies should cooperate in working towards national prospective registries of patients with endocarditis that would allow investigation of the temporal relationship to any preceding endoscopic procedure.

14.2 Percutaneous endoscopic gastrostomy: there is good evidence favouring antibiotic prophylaxis in the prevention of PEG-associated wound infection, but there is uncertainty regarding its value in the prevention of more serious infections such as peritonitis or aspiration pneumonia. MRSA, and its importance in such wound infections, is worthy of further study. The reports that the risk may be reduced by local

measures, such as nasal decolonisation and/or glycopeptide prophylaxis, require confirmation.

14.3 ERCP: the recommendation of selective administration of prophylactic antibiotics to patients with biliary obstruction (according to the criteria set out in Sections 7.2.4 and 7.2.5), with immediate antibiotic commencement in patients for whom suboptimal drainage is achieved, deserves prospective evaluation. Cholangitis complicating ERCP may become more common now that prophylaxis for patients with biliary obstruction will no longer be routine, and consideration should be given to establishing national registries of post-ERCP cholangitis.

Furthermore, there should be better understanding of the frequency with which quinolone-resistant Gram-negative bacteria complicate therapeutic ERCP. Ciprofloxacin resistance is becoming increasingly common, and for patients undergoing ERCP would be expected to be more of a problem in those with a history of prior biliary manipulations, such as sphincterotomy and/or stent insertion for stones, primary sclerosing cholangitis or malignant disease. There is a need to perform multicentre studies of cholangitis and bacteraemia following repeat ERCP in patients with a history of prior therapeutic ERCP.

It is the practice of some endoscopists to prescribe antibiotics after endoscopic sphincterotomy for patients with a gallbladder containing stones, for fear of introducing cholecystitis before cholecystectomy. This common clinical scenario is ripe for a prospective controlled trial.

14.4 Immunocompromised patients. Antibiotic prophylaxis for therapeutic endoscopic procedures associated with a high risk of bacteraemia is recommended for patients with severe neutropaenia ($<0.5\times10^9$/l) and/or advanced haematological malignancy. It remains unclear whether other patients receiving immunosuppressive agents are at increased risk of infective complications following therapeutic endoscopy, and prophylaxis is not recommended. It is likely that a large multicentre collaboration would be required in order to address this topic.

15. AUDIT

In clinical practice it is difficult to audit prophylaxis against infective endocarditis. A possible approach is to review the case notes on all patients diagnosed with infective endocarditis in a hospital over the course of 1 year, specifically focusing on any endoscopic procedures that had taken place during the 2 months before diagnosis.

It is also recommended that Endoscopy Users Groups perform spot checks to ensure that their units have ready access to stocks of the antibiotics discussed in table 3.

Audits of outcomes following PEG should include a review of prophylactic antibiotics used. Units could also review their local surveillance, prophylaxis and monitoring of patients with known MRSA colonisation undergoing PEG.

Units undertaking ERCP should audit postprocedure cholangitis, focusing on (1) comments in the endoscopist's report regarding success in biliary decompression; (2) subsequent trends in liver biochemistry; and (3) the use of prophylactic and postprocedure antibiotics.

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