

Guidelines of the European Society of Gastrointestinal Endoscopy (E.S.G.E.) Antibiotic Prophylaxis for Gastrointestinal Endoscopy

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Bacteraemia occurring in a patient with a susceptible cardiac lesion may lead to infective endocarditis, a potentially fatal disease. Gastrointestinal endoscopy can infrequently give rise to transient bacteraemia but there is little evidence to suggest that endoscopic procedures have caused endocarditis. A number of prospective controlled trials have shown that antibiotic prophylaxis can reduce the incidence of bacteraemia but this does not prove that it will necessarily prevent infectious endocarditis. Indeed some reports have drawn attention to failure of antibiotic prophylaxis in preventing post-endoscopic endocarditis. Nevertheless endoscopic procedures with a higher than average risk of bacteraemia in a patient with a susceptible cardiac lesion may carry a significant danger, and in these it is prudent to use antibiotic prophylaxis.

Apart from cardiac infections there are a number of other infectious complications that may be attributable to gastrointestinal endoscopy procedures. These include pancreato-biliary sepsis following endoscopic retrograde cholangio-pancreatography (ERCP), infection of orthopaedic and other non-cardiac prostheses and wound infections secondary to percutaneous endoscopic gastrostomy (Table 1).

Table 1: Application of antibiotic prophylaxis in gastrointestinal endoscopy.

The prevention of:

- Infective endocarditis
- Symptomatic bacteraemia
- Colonisation of orthopaedic and other non-cardiac prostheses
- Pancreato-biliary sepsis following ERCP
- Wound infection after endoscopic percutaneous gastrostomy

There is no indication for the use of antibiotics in other circumstances, as it adds unnecessary costs and the potential for adverse events, such as allergic drug reactions, anaphylaxis and antibiotic related colitis.

There is need, therefore, to establish which are the high-risk endoscopic procedures, who are the patients in danger, which antibiotics are the most cost-effective in various procedures and what is their optimal regimen.

This report is based on review of the published data, including recommendations for antibiotic prophylaxis in infective endocarditis (1) and in gastrointestinal endoscopy (2,3) published by the working party of the British Society of Gastroenterology endoscopy committee, the American Society of Gastrointestinal Endoscopy (ASGE) and American Heart Association (AHA), and working group of the ESGE Guideline Committee.

Scientific Background

1. *The Risk of Infectious Complications Associated with Endoscopic Procedures*

A. The Rate of Bacteraemia

Transient bacteraemia is known to accompany normal daily activities such as brushing teeth where it can be as high as 25%. It also occurs after non-endoscopic medical procedures such as rectal examination and barium enema. Asymptomatic low titre bacteraemia following gastrointestinal endoscopy procedures is probably unimportant.

After *diagnostic upper gastrointestinal endoscopy* and *colonoscopy*, the bacteraemia rate is low, up to 4% (4,5). The risk of bacteraemia does not seem to increase with biopsy or polypectomy (5). Bacteria most often cultured after upper GI endoscopy are contaminants: coagulase negative staphylococci, *Bacillus* spp., *Propionibacterium* spp. and commensal organisms with rarely reported pathologic potential, e.g. *Serratia marcescens* or streptococci non haemolytic (4). In colonoscopy-related bacteraemia enterococci,

Escherichia coli and *Bacteroides* are the most common microorganisms (5).

Endoscopic ultrasonography is regarded as a safe technique but little data about possible infectious complications are available. Early reports of bacteraemia during this procedure vary between 0 and 9.8% (6,7).

Oesophageal dilatation and insertion of prostheses is a cause of significant bacteraemia reaching approximately 45%, though reports differ considerably (4). Zuccaro et al. found that the only factor clearly associated with bacteraemia was the initial stricture diameter (8). Although mouth commensals are found most often following oesophageal dilatation, oral decontamination with clindamycin palmitate was not an effective prophylaxis (9). Disinfection of bougie dilators did however reduce post-procedural bacteraemia (10,11).

There is no data concerning the risk of bacteraemia after balloon dilation. As this kind of dilator traverses the endoscope channel and has no contact with the oral cavity, the risk is probably small (12).

Injection sclerotherapy of oesophageal varices is the second most important cause of bacteraemia associated with gastrointestinal endoscopy procedures (13–19). Cirrhotic patients have reduced levels of complement and impaired neutrophil function, making them prone to bacterial infections (13). Bacteraemia has been reported in up to 50% of patients undergoing endoscopic sclerotherapy, but it has also been detected in up to 13% prior to diagnostic endoscopy (4,14). The organisms usually found are oral flora, which also contaminate the endoscope and needle (13,15). The significant risk factors associated with bacteraemia were the length of the sclerotherapy needle (16), contamination of the water bottle (15) and the volume of sclerosant used. Emergency procedures seem to be associated with a higher incidence of bacteraemia (14). There is some data suggesting that the use of a 4 mm length needle (16) and a new needle catheter with covered tip may reduce the incidence (19).

Endoscopic band ligation of oesophageal varices is considered a safe technique with a low risk of bacteraemia (3–6%) (17,18). As this technique becomes more popular the danger of sclerotherapy may be eliminated (12).

Bacteraemia as a result of contamination of the injection needle catheter which passes through the suction channel of the endoscope is not likely to be eliminated altogether. The technique of *submucosal injection* is increasingly used for polypectomy or resection of flat mucosal lesions. There has been one report of *E. coli* bacteraemia following submucosal injection for polypectomy (20). As the suction channel contaminants are those of the digestive tract, contamination during submucosal injection cannot be avoided by using a disinfected endoscope, sterile needles and injection fluid. Bacteraemia may be reduced by using an aseptic

injection needle protected from contamination, for example by a covered tip (19,20).

Laser therapy may cause significant bacteraemia depending upon the nature of the procedure. In the upper gastrointestinal tract the rate of bacteraemia following laser therapy is 31–34% (21,22). The most common organisms are streptococci, corynebacteria and bacteroides. In the lower gastrointestinal tract the likelihood of bacteraemia is appreciably less – 19%. Bacteroides and *E. coli* are commonly found germs. Laser therapy is believed to mechanically irritate the tumor tissue or mucosa and the passage of the endoscope then promotes invasion by bacteria (21).

Percutaneous endoscopic gastrostomy (PEG) carries a risk of major complications, including a 1–3% mortality. The most common minor complication is peristomal infection, which occurs in 30–43% of patients (23–25). Two groups of bacteria are involved depending on the technique: oropharyngeal in the pull method and cutaneous in both the push and pull methods.

ERCP: Cholangitis and sepsis are the commonest cause of death following ERCP (26). The major risk factors are biliary obstruction, which increases the risk of bacteraemia to 11–16% (4,27,28), a history of previous cholangitis, pancreatic pseudocysts and the use of contaminated endoscopes or contrast media. The volume of injected contrast medium may play a role in damaging the duct epithelium, which may become susceptible to infection. There are two potential pathways for developing bacteraemia: infection of the pancreato-biliary system by instrumentation or dissemination of already existing organisms in an obstructed biliary tree. Organisms commonly cultured are: *Pseudomonas aeruginosa*, *Klebsiella* spp., *Escherichia coli*, enterococci, *Bacteroides*, coagulase negative staphylococci and *Serratia marcescens* (27–29).

B. The Risk of Infectious Complications

The majority of bacteraemias associated with gastrointestinal procedures are asymptomatic. As transient bacteraemia is unlikely to harm a normal individual. Antibiotic prophylaxis is unnecessary unless there is a susceptibility for endocarditis. There are only a few endoscopic procedures where the potential risk of infectious complications is significant (Table 2).

Table 2: Endoscopic procedures associated with higher risk of infectious complications.

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- Oesophageal stricture dilation
 - Endoscopic sclerotherapy for oesophageal varices
 - Laser therapy in the upper gastrointestinal tract
 - Endoscopic placement of percutaneous feeding tube
 - Endoscopic retrograde cholangiopancreatography for known biliary obstruction or pancreatic pseudocyst
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Sepsis is unlikely to follow *upper gastrointestinal endoscopy*. There are single case reports describing endocarditis as a complication of gastroscopy (30,31). The effect of immunosuppression is unclear. In one study a high incidence (19%) of clinically relevant bacteraemia was reported following upper gastrointestinal endoscopy (32), whereas in another report there were no such episodes (33).

Endocarditis attributable to *colonoscopy* is infrequently reported (34). Most septic complications were associated with reduced immunocompetence caused by hepatic cirrhosis, peritoneal dialysis or inflammatory bowel disease (35–37).

Zuccaro et al. showed that the 21% incidence of post-*dilatation* bacteraemia was entirely caused by *Streptococcus viridans*, which is a potential morbidity factor for bacterial endocarditis (8). Although the theoretical risk is high, the actual incidence of infectious complications is quite rare (10,11). Reported cases of bacterial endocarditis attributable to dilatation of oesophageal stricture concerned patients with mitral insufficiency (38) and mitral valve prolapse (39). These data support the use of antibiotic prophylaxis prior to endoscopic dilatation of oesophageal strictures in patients with valvular cardiac lesions.

Bacteraemia associated with *endoscopic sclerotherapy for oesophageal varices* is well recognised but again infectious complications are infrequent (13–18). Nevertheless, a number of septic complications such as septicemia (40), cerebral abscess, perinephric abscess and endocarditis (41) have been reported. Selby et al. (13) showed that intravenous cefotaxime significantly reduced the frequency of bacteraemia after endoscopic sclerotherapy. There were no clinical manifestations of bacteraemia in any patient and no infection of ascitic fluid. Antibiotic prophylaxis should be reserved for individuals with a higher risk of endocarditis. The efficacy of antibiotic prophylaxis is hard to prove particularly because there have been sporadic failures of antibiotic prophylaxis leading to endocarditis in some patients with valvular prostheses (41).

Infectious complications after *submucosal injection for polypectomy* are exceedingly rare (20). Postpolypectomy leucocytosis and fever associated with pain are usually caused by burning syndrome (particularly with hot biopsy forceps) or inflammatory response. Moreover the organisms grown on blood culture are not those typically responsible for infectious endocarditis. Therefore routine antibiotic prophylaxis is not indicated.

Bacteraemia following *laser therapy* of the upper gastrointestinal tract is common and septic complications, though uncommon, do occur (21,22). Moreover the organisms involved are those commonly associated with endocarditis. The risk therefore seems considerable and so antibiotic prophylaxis is recommended for the high-risk patients. As the risk of bacteraemia following laser therapy in the colon is lower, the need for antibiotic prophylaxis is less clear.

Despite the high incidence of minor complications following *percutaneous endoscopic gastrostomy* severe wound infection is very rare. In prospective randomised studies antibiotic prophylaxis with piperacillin/tazobactam (25), cefotaxime (24,25) and amoxycillin/clavulanic acid (23) have been shown to be effective in reducing the rate of early local infection. In another study, cefazolin was not successful (42). Although infectious complications, including peritonitis, requiring medical intervention do occur, they are, fortunately, sporadic. However as complication rates may be significantly reduced by antibiotic prophylaxis, it is recommended for all patients undergoing this procedure.

Biliary sepsis is one of the major complications of *ERCP*, and although it occurs in only 0.4–0.8% of cases (28), it is associated with an 8–20% mortality rate (43). The lack of adequate pancreatico-biliary drainage post ERCP, a previous history of cholangitis and injection of contrast into a pancreatic pseudocyst are major sepsis risk factors (27–29). It is recognised that the most important method of preventing cholangitis is to establish proper biliary drainage (44). Diagnostic procedures therefore should be avoided in those situations where therapeutic ones cannot follow. Antibiotic prophylaxis is recommended for patients who are likely to undergo therapeutic ERCP if there has been previous biliary sepsis, bile duct obstruction or pancreatic pseudocyst. There have been a few prospective randomised studies of prophylactic parenteral antibiotics in the prevention of cholangitis (28,45). The addition of gentamicin to the contrast medium did not offer protection (46).

2. Identification of High-Risk Patients

A. The Risk of Endocarditis

The risk of endocarditis depends largely on the nature of the cardiac condition. The identification of patients at high risk may be difficult in the emergency situation. Even in favourable conditions, many patients may be unaware of their cardiac lesion (47). Some cardiac lesions cannot be diagnosed on physical examination and require echocardiography. Even if patients have had a previous echocardiogram the result may not be known to them. Zuckerman et al. (48) estimated that these problems arise in about 15% of all patients, and according to the former guidelines of AHA 3% and of ASGE 1% of patients would have ultimately required antibiotic prophylaxis.

Cardiac and other clinical conditions have been divided into three groups according to their potential for the development of infective complications (Table 3) (2,49).

The risk of developing endocarditis is also dependent upon bacteraemia. Although bacteraemia is common following many invasive endoscopic procedures, only certain bacteria commonly cause endocarditis. Alpha-hemolytic streptococci and staphylococci are the most likely, comprising respectively 55% and 25% of cases associated with native valves and 30% and 45% of valvular prostheses infections. Al-

Table 3: Conditions associated with a risk of endocarditis or symptomatic bacteraemia.

High risk:

- Prosthetic heart valve
- Previous endocarditis
- Surgically constructed systemic-pulmonary shunt or conduit
- Synthetic vascular graft less than 1 year old
- Severe neutropenia (neutrophils < 1 G/l)

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 1–5 G/l)

No increased risk:

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

though rare, *Streptococcus viridans* is the commonest cause of endocarditis following oesophageal “high-risk” therapeutic procedures. Other gastrointestinal procedures are even less likely to cause bacteraemia with a dangerous organism. Antibiotic prophylaxis for bacterial endocarditis should be specifically directed against these organisms.

It should be stressed that endocarditis hardly ever develops as a consequence of an endoscopic procedure. Moreover most cases of endocarditis are not attributable to any invasive procedures and in any event antibiotic prophylaxis is not always successful (41, 50).

B. Other Patient-Related Risk Factors

Infection of a synthetic vascular graft has a serious and potentially fatal consequence. Complete endothelialisation of the graft does not occur for a period of one year and bacter-

aemia is potentially dangerous (51). Antibiotic prophylaxis is therefore recommended over this period.

There is little data concerning the possibility of infection of orthopaedic, neurosurgical and other prostheses following gastrointestinal endoscopy. Existing evidence is insufficient to recommend antibiotic prophylaxis.

There is little data to estimate the impact of immunosuppression on the incidence of infectious complications after endoscopic procedures. Therefore antibiotic prophylaxis for transplant recipients or patients with HIV infection cannot be recommended. Nevertheless neutropenia appears to increase the risk of post-endoscopic symptomatic bacteremia with *Escherichia coli* as the most common pathogen (32). This should be taken into account when providing antibiotic prophylaxis in these patients.

Recommendations*I. Recommendation of Antibiotic Prophylaxis According to the Procedure (Table 4)*

- I. For the “high-risk” upper and lower gastrointestinal tract endoscopic procedures (excluding retrograde cholangiopancreatography)
 - a) antibiotic prophylaxis is recommended for “high-risk” patients.
 - b) there is no data to support the necessity of prophylaxis in patients with moderate risk factors. The endoscopist may individually consider potential benefits.
 - c) no prophylaxis is recommended for patients with low or average risk for endocarditis.
- II. Other endoscopic procedures without increased risk of infectious complications:
 - a) there are insufficient data to recommend antibiotic prophylaxis for the “high-risk” patients. Every case may be considered separately.

Procedure	Patients risk group	Antibiotic prophylaxis
high risk procedures: oesophageal dilation variceal sclerotherapy laser therapy in upper GI	<ul style="list-style-type: none"> - high risk patients - severe neutropenia - moderate risk patients - low or average risk patients 	regimen A or B regimen A or B plus C not necessary regimen A or B may be considered not recommended
low risk procedures	<ul style="list-style-type: none"> - high risk patients - moderate or low risk patients 	not necessary regimen A or B may be considered not recommended
ERCP	<ul style="list-style-type: none"> - all patients with: <ul style="list-style-type: none"> - biliary occlusion - pancreatic pseudocyst - previous cholangitis or - therapeutic ERCP 	regimen C
PEG	<ul style="list-style-type: none"> - all patients 	regimen D

Table 4: Recommendations of the antibiotic prophylaxis according to the procedure.

- b) no prophylaxis is recommended for patients with moderate, low or average risk for endocarditis.

III. For "high-risk" ERCP

- a) Antibiotic prophylaxis is recommended for all patients with biliary obstruction or a pancreatic pseudocyst or previous cholangitis.
b) ESGE recommends antibiotic prophylaxis for all therapeutic ERCP.

IV. For endoscopic placement of percutaneous feeding tube

Antibiotic prophylaxis is recommended for all patients undergoing the procedure.

2. Recommendation of Antibiotic Regimens (Table 5)

Table 5: Recommended antibiotic regimens.

A. Patients not allergic to penicillin

Adults:

1 g amoxicillin intramuscularly in 2.5 ml 1 % lignocaine hydrochloride plus 120 mg gentamicin intramuscularly just before start of the procedure, followed by 500 mg amoxicillin orally 6 hours later

Children under 10 years:

500 mg amoxicillin intramuscularly in 2.5 ml 1 % lignocaine hydrochloride plus 2 mg/kg body weight gentamicin intramuscularly, followed by 250 mg (children 5–9 years) or 125 mg (children 0–4 years) amoxicillin orally 6 hours later

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

Adults:

1 g vancomycin in slow intravenous infusion over 100 minutes followed by 120 mg gentamicin intravenously 15 minutes before the procedure or 400 mg teicoplanin intravenously followed by 120 mg gentamicin 15 minutes before the procedure

Children under 10 years:

20 mg/kg vancomycin by slow intravenous infusion followed by 2 mg/kg gentamicin intravenously or 6 mg/kg teicoplanin intravenously followed by 2 mg/kg gentamicin intravenously

C. Prior to biliary procedures

750 mg ciprofloxacin orally 60–90 minutes before the procedure or 120 mg gentamicin intravenously just before the procedure or a parenteral quinolon, cephalosporin or ureidopenicillin just before the procedure

D. Prior to percutaneous endoscopic gastrostomy

2 g cefotaxime (or equivalent) parenterally 30 minutes before the procedure or 4 g piperacillin/0.5 g tazobactam parenterally or 1 g amoxicillin/clavulanic acid intravenously

E. Patients with severe neutropenia

Adults:

Add 7.5 mg/kg metronidazole intravenously to any of the above regimens

Children:

Add 7.5 mg/kg metronidazole intravenously to any of the above regimens

3. Characteristics of Recommended Antibiotics

A. Amoxicillin

Amoxicillin is believed to prevent endocarditis commonly caused by streptococci and enterococci. Its application may be limited by hypersensitivity reactions in some patients.

Moreover according to Lorenz et al. (52) amoxicillin plus clavulanic acid showed 87.3% sensitivity for most frequently isolated germs from biliary ducts. Therefore it seems to be suitable antibiotic also in the prophylaxis of cholangitis after ERCP.

B. Gentamicin

Gentamicin added to amoxicillin enhances its power against drug-resistant germs such as gram-negative *Pseudomonas*, *Proteus*, *Serratia* and gram-positive *Staphylococci*. Although parenteral aminoglycosides have been associated with significant nephrotoxicity and ototoxicity a single dose of gentamicin is safe.

C. Ciprofloxacin

Bacterial strains that are susceptible to ciprofloxacin include gram-negative organisms, therefore it can be recommended for the prevention of infective complications following ERCP. As it is less effective against gram-positive bacteria it is not suitable for the prevention of endocarditis.

D. Vancomycin or teicoplanin

Glycopeptides are adapted for prophylaxis of endocarditis in patients who are allergic to penicillins or were given penicillin during last month.

E. Ureidopenicillins

Piperacillin used with tazobactam is effective in the prevention of post-ERCP cholangitis. A disadvantage of piperacillin is that it may provoke pseudomembranous colitis.

F. Cephalosporins

Cephalosporins have poor activity against enterococci and therefore are not suitable for endocarditis prophylaxis. Nevertheless they are widely used for the prevention of sepsis after ERCP. Niederau et al. (28) showed that a single dose of 2 g cefotaxime given 15 minutes prior to procedure prevented post-ERCP cholangitis or sepsis.

G. Metronidazole

Metronidazole is added to the prophylaxis regimen in all neutropenic patients as it provides cover against anaerobic organisms.

4. Other Considerations

As all of the proposed regimens may occasionally fail to prevent infectious complications after various endoscopic procedures the use of other more efficient antibiotics must be considered. *In vitro* testing of different antibiotics showed that imipenem has the greatest sensitivity (98.4%) against germs isolated from the bile and pancreatic fluid (52). Imipenem has also proved effective in the prophylaxis of sepsis in acute necrotizing pancreatitis (53). Nevertheless although imipenem may be recommended for the treatment it is at present too expensive to be recommended for prophylaxis.

5. Summary

There are two situations when antibiotic prophylaxis is recommended. The first is associated with procedures known to be followed by high rates of bacteraemia, involving organisms prone to cause endocarditis. These include oesophageal dilatation, variceal sclerotherapy and laser therapy in the upper gastrointestinal tract. As bacteraemia following these procedures is usually harmless in average risk patients antibiotic prophylaxis is recommended only for a patient with a lesion susceptible to endocarditis or one who is at increased risk of symptomatic bacteraemia due to neutropenia or immunosuppression. In most cases parenteral amoxicillin and gentamicin is recommended plus metronidazole for neutropenic patients. Vancomycin or teicoplanin replace amoxicillin in a case of allergy.

The second situation concerns procedures with a high incidence of local infection or which may lead to serious sepsis. These include therapeutic retrograde cholangiopancreatography and percutaneous endoscopic gastrostomy where antibiotic prophylaxis is recommended even in average risk patients. Several antibiotics are recommended including oral ciprofloxacin or parenteral gentamicin or quinolone for ERCP and amoxicillin for PEG or cephalosporin or ureidopenicillin for both.

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