

Antibiotic prophylaxis in digestive endoscopy: Guidelines from the French Society of Digestive Endoscopy



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ABSTRACT

Digestive endoscopy is a highly dynamic medical discipline, with the recent adoption of new endoscopic procedures. However, comprehensive guidelines on the role of antibiotic prophylaxis in these new procedures have been lacking for many years. The Guidelines Commission of the French Society of Digestive Endoscopy (SFED) convened in 2023 to establish guidelines on antibiotic prophylaxis in digestive endoscopy for all digestive endoscopic procedures, based on literature data up to September 1, 2023. This article summarizes these new guidelines and describes the literature review that fed into them.

Introduction

Antibiotic prophylaxis (AP) involves administration of one or more antibiotic molecules to prevent development of a specific infection under determined circumstances. It differs from curative antibiotic therapy, which is intended to treat an already established infection.

In digestive endoscopy, the objective of AP is to prevent local and/or general infectious complications following an endoscopic procedure. Although these types of complications

remain rare in endoscopy, the prevalence of bacteremia after certain endoscopic procedures can be high.

Transient bacteremia frequently occurs during our daily activities, at rates and frequencies higher than those associated with endoscopic procedures. For example, tooth brushing is associated with bacteremia rates between 20% and 68%, the simple physiological activity of chewing with rates between 7% and 51%, and the use of a toothpick with rates between 20% and 40% [1].

The bacterial infection risk secondary to an endoscopic procedure must also be balanced against the side effects of AP, including allergic reactions (of varying severity) and the potential induction of antibiotic resistance. Therefore, determining the risk situations in which AP is recommended for a limited number of patients is essential.

These types of situations depend on two factors, which must be independently analyzed in order to assess the indication: 1) patient-related infection risk (such as consideration of comorbidities: cardiovascular context, immunosuppression, peritoneal dialysis, and cirrhosis); and 2) procedure-related risk (consideration of bacterial infection risk induced by the examination).

Methods

The French Society of Digestive Endoscopy (SFED) and the French Society of Anesthesia and Intensive Care Medicine (SFAR) were responsible for developing these guidelines, and invited D.K. to be the Chair of the guidelines working group in November 2021. D.K. selected a working group from the SFED, including the listed authors, who were broadly representative in terms of their wide range of diagnostic and therapeutic gastroenterology procedure expertise and level of clinical experience and background and E.W. selected a working group from the SFAR. The first meeting of the working group was held in January 2022, where the overall aims of the project were defined and the methodology was agreed. Specific questions were developed using the Population, Intervention, Comparator, Outcome (PICO) format where possible, including 1) general principles; 2) therapeutic gastroenterology procedures; 3) diagnostic and therapeutic endoscopic ultrasound (EUS) procedures; and 4) retrograde cholangiopancreatography procedures.

The working group was organized into four sub-taskforces covering the above areas, with one group member nominated as the lead of each sub-group. Each area was the subject of a systematic literature review. A literature search of PubMed/MEDLINE, the Cochrane Library, and Embase was performed by the authors, focused on relevant randomized controlled trials (RCTs) and meta-analyses published up to June 2023. Retrospective analyses and case series were also included if the area concerned was not covered in prospective studies. Statements were drafted based on the evidence collected and evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework [2]. When a paucity of evidence was noted, the groups relied on expert opinion to develop statements.

Several task force meetings were held from January 2022 to November 2023, during which the statements were discussed and modified based on feedback from members, to improve their acceptability.

Each subgroup developed draft proposals that were discussed. After agreement on a final version, the manuscript was reviewed by all members of the guidelines committee. This final version was validated by the SFED and SFAR before submission to the journal *Endoscopy International Open* for publication. All authors agreed on the final revised manuscript.

Patient-related risk

Prevention of infective endocarditis

The European Society of Cardiology (ESC) has defined situations at risk for endocarditis that would require the use of AP [3]. These recommendations have been endorsed by the French Infectious Diseases Society (SPLIF), the French Society of Cardiology (SFC), and the French Society of Anesthesia and Intensive Care Medicine (SFAR).

AP is only recommended for patients with a cardiac condition who are at high risk for endocarditis. That includes patients with: prosthetic valves or prosthetic material used for valve repair, a history of infective endocarditis; unoperated cyanogenic congenital heart disease, residual leakage, or surgical shunt placement; congenital heart disease with prosthetic repair, placed surgically or percutaneously, up to 6 months after placement; and with residual leakage at the site of prosthetic material placement, placed surgically or percutaneously.

For these patients, the only interventions at risk of bacteremia that could lead to endocarditis are those involving dental manipulations of the gums or peri-apical region and perforation of the oral mucosa. For other procedures, including diagnostic endoscopies (esophagogastroduodenoscopy [EGD] and colonoscopy), AP is no longer indicated.

Furthermore, there are no reported cases of vascular graft infection related to gastrointestinal endoscopic procedures. Therefore, AP is not recommended before diagnostic gastrointestinal endoscopic procedures in a patient with non-valvular synthetic vascular materials, such as pacemakers, defibrillators, coronary or peripheral vascular stents, and inferior vena cava filters [3].

Comorbidity-related risk

Numerous factors may be considered to be potentially or definitely associated with the occurrence of a surgical site infection. As highlighted by the SFAR in its latest recommendations, the presence of such factors does not necessarily mandate systematic AP in situations where such treatment is not recommended [4].

Only studies providing significant evidence on administration of AP in the presence of a risk factor would be able to validate or negate the usefulness of AP in such a situation. To date, no such studies are available.

Thus, use of AP for any endoscopy with a risk of bacteremia (especially for polypectomy within 6 months following prosthetic surgery) was recommended by the American Association of Orthopedic Surgeons (AAOS) in the late 2010s for patients with orthopedic prostheses, following a few reported cases of pyogenic arthritis after endoscopy [5]. However, the American Society for Gastrointestinal Endoscopy (ASGE) did not endorse this indication in its 2015 guidelines, due to a lack of reliable data [6].

Nevertheless, it may be worth considering AP in certain specific situations, on a case-by-case basis and taking into account procedure-related risk. Some indications were discussed by the SFAR in its 2018 recommendations [4]. For patients with severe neutropenia (absolute neutrophil count < 0.5 G/L) or

advanced hematologic malignancy, there is an increased risk of bacteremia and septicemia after gastrointestinal endoscopy [7]. However, the benefit of AP in this specific population has not been studied. The same applies to patients who have undergone radiation therapy, immunocompromised patients with a normal neutrophil count (organ transplant recipients, HIV-positive individuals), patients who are undergoing chemotherapy or corticosteroid therapy, patients with uncontrolled diabetes, very elderly patients, and obese or malnourished patients. The decision to use AP in these situations should be made on a case-by-case basis. Furthermore, although these patients are at a higher risk of surgical site infection, they will have infections caused by the “target bacteria” of usual AP, and no modification of the proposed protocols seems justified in these patients.

Patients with end-stage renal failure undergoing peritoneal dialysis have higher rates of infection than those treated with hemodialysis. Since 2005, the International Society for Peritoneal Dialysis (ISPD) has suggested in its recommendations that AP be administered before lower endoscopy [8,9]. The ASGE adopted similar suggestions in its 2015 guidelines [10]. However, there are limited data, including no RCTs, to support these suggestions. A multicenter retrospective study showed that of 236 patients who underwent colonoscopy, nine (3.8%) developed peritonitis [11]. Polypectomy or mucosectomy rates were significantly higher in the peritonitis group vs. the non-peritonitis group (66.7% vs. 23.4%; $P = 0.009$). Moreover, among the 65 patients who received AP, none developed peritonitis and, conversely, none of the patients who developed peritonitis had received AP ($P = 0.067$). Thus, although the decision to use AP must also consider the associated risks, such as *Clostridium difficile* infections and development of multi-resistant organisms, the possibility of using AP should be systematically discussed. Lastly, a more recent retrospective study involving 1,316 endoscopic procedures in 570 peritoneal dialysis patients, reporting a peritonitis rate of 4.2% after colonoscopy, noted no reduction in risk of peritonitis with AP [12]. However, polypectomy was associated with an increased risk of post-colonoscopy peritonitis (odds ratio [OR] 6.5; 95% confidence interval [CI] 1.6–25.9) in this study.

Procedure-related risk

This non-exhaustive list aims to provide an overview of current knowledge regarding infectious risk and assessment of AP in specific conditions (► **Table 1**).

In cases of high risk of endocarditis, a confirmed infection and/or a high risk of bacteremia are required to consider AP.

Endoscopic procedures with a low risk of infection

EGD with or without biopsy

Although EGD with or without biopsy is associated with a bacteremia mean rate of 4.4%, bacteremia is generally of short duration (< 30 minutes) and not associated with infectious adverse events [13].

► **Table 1** Classification of bacterial infectious risk levels for endoscopic procedures.

Low-risk endoscopy	High-risk endoscopy
Diagnostic endoscopy with or without biopsy	Colonoscopy in a peritoneal dialysis patient, in combination with the aspiration of dialysate before the procedure
ERCP without suspected incomplete drainage	ERCP with suspected incomplete drainage
Diagnostic EUS-FNA/B (excluding mediastinal or pelvic cystic lesions, ascites, peritoneal nodules in ascites, pleural fluid)	PEG and jejunostomy
Endoscopic dilation	Endoscopy in peritoneal dialysis patients
Placement of digestive stent (excluding incomplete biliary drainage)	Endoscopic ultrasound with biliary-digestive or cysto-gastrostomy anastomosis
Esophagogastric and rectal radiofrequency	EUS-FNA/B of mediastinal or pelvic cystic lesions, ascites, peritoneal nodules in ascites, pleural fluid
Endoscopic mucosal resection or submucosal dissection	
ERCP, endoscopic retrograde cholangiopancreatography; EUS-FNA/B, endoscopic ultrasound-guided fine-needle aspiration or biopsy; PEG, percutaneous endoscopic gastrostomy.	

Therapeutic EGD procedures (endoscopic mucosal resection [EMR], endoscopic submucosal dissection [ESD] and peroral myotomy)

Use of AP after gastric ESD is controversial. A prospective study involving 103 patients who underwent gastric ESD without AP showed that incidence of bacteremia at 24 hours did not significantly differ between a group of patients with a procedure complicated by perforation ($N = 40$) and a group without perforation ($N = 63$) (2.5% vs. 3.2%; $P > 0.05$). No patient in this study developed septicemia. The authors concluded that, even in cases of perforation (treated endoscopically during the procedure), AP was not necessary [14].

Similarly, although a high incidence of bacteremia after esophageal endoscopic procedures has been reported, incidence of bacteremia associated with esophageal ESD remains unknown. A recent prospective study involving 101 patients who underwent esophageal ESD showed bacteremia in six patients (6%) immediately after ESD, and only one patient had a positive blood culture the next morning. None of these patients developed an infectious syndrome. Moreover, among the 10 patients who developed a post-ESD fever $\geq 38^\circ\text{C}$, none had a positive blood culture. Overall, none of the patients in this study required antibiotics after esophageal ESD [15]. The authors emphasized that post-ESD fever is not frequently associated with presence of bacteremia, making routine AP in patients undergoing esophageal ESD appear unnecessary.

Regarding endoscopic treatment of achalasia by per-oral endoscopic myotomy (POEM), a recent RCT involving 124 patients compared the efficacy of a single dose of AP with prolonged AP. The study compared a group receiving a prophylactic single dose of 2 g of intravenous (IV) cefazolin to a group receiving the same initial dose followed by 2 g of IV cefazolin three times a day, further followed by oral amoxicillin-clavulanic acid. No significant differences were found in terms of the occurrence of clinical signs, bacteremia, or infectious or inflammatory syndrome [16]. A case-control study of 226 patients showed no impact of AP on occurrence of post-POEM infectious complications, and even a higher risk of adverse events (AEs) ($P = 0.003$) [17].

Diagnostic colonoscopy

Colonoscopy-related bacteremia rates are low, even during certain procedures such as colonic stent insertion, where bacteremia is reported in only 6.3% of cases. The low rates seem to be linked to procedure duration, with the bacteremia remaining entirely asymptomatic, suggesting that AP is not necessary [18].

Therapeutic colonoscopy (EMR and ESD)

A recent meta-analysis, including three randomized trials and one retrospective study and involving 850 patients, assessed the utility of AP in patients undergoing endoscopic mucosal or submucosal resections (548/850 patients treated with antibiotics). The overall incidence rate of post-operative AEs was 2.4% in the treatment group vs. 19.9% in the control group. The analysis showed an 83% reduction in postoperative events in the antibiotic treatment group (relative risk [RR] 0.181; 95% CI 0.100–0.326; $P < 0.001$). The authors suggested that AP may be useful but highlighted the low level of evidence in their meta-analysis, ultimately concluding that additional large-sample, multicenter RCTs are needed, especially to evaluate the benefit of AP in specific subgroups such as patients undergoing extensive ESD [19].

A recent prospective, multicenter, randomized study involving 432 patients (216 in the AP group vs. 216 in the control group) in 21 centers in Japan evaluated the impact of AP in colorectal ESD. After the exclusion of 52 patients, 192 in the AP group and 188 in the control group were analyzed. A post-resection syndrome occurred in nine of 192 patients (4.7%) in the AP group vs. 14 of 188 patients (7.5%) in the control group, with an OR of 0.61 (95% CI 0.23–1.56; $P = 0.29$). The authors concluded that AP is not effective in reducing incidence of colitis syndrome in patients undergoing colorectal ESD [20].

It seems reasonable not to recommend routine AP for uncomplicated colorectal EMR procedures.

Due to the lack of consolidated data or well-conducted prospective multicenter studies, and given the widespread use of AP in many centers, the decision to use AP in colorectal ESD should be left to the discretion of the operator and anesthetist, in conjunction with the infectious disease specialists in the institution.

Device-assisted enteroscopy

There are no data on risk of bacteremia associated with device-assisted enteroscopy (double-balloon or spiral enteroscopy).

Diagnostic EUS

Frequency of bacteremia after diagnostic upper EUS is comparable to that of diagnostic upper endoscopy [21].

Prospective studies in patients undergoing endoscopic ultrasound fine-needle aspiration or biopsy (EUS-FNA/B) of solid lesions along the upper gastrointestinal tract indicate a low prevalence of bacteremia ranging from 4.0% to 5.8%, in most cases without clinical symptoms of infection [22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38].

EUS-FNA/B of a solid rectal and peri-rectal lesion also appears to be associated with a low risk of bacteremia without clinical consequence and infection, estimated at 1% to 2% in studies [32, 39, 40]. In a large prospective study, there was no statistically significant difference in bacteremia between patients who received AP and those who did not [21]. Thus, current recommendations do not advocate for AP before EUS-FNA/B of solid lesions along the upper and lower gastrointestinal tract [21, 41].

EUS fine-needle aspiration (EUS-FNA) of pancreatic cystic lesions (CLs) is considered a relatively safe technique, with a reportedly low infection risk of 0.44% in a recent meta-analysis [42]. The AE rate is similar when using a 19-gauge needle (5.84% [95% CI 0.88%–13.64%]) or a 22-gauge needle (2.38% [95% CI 1.38%–3.63%]), and does not seem to be influenced by the number of passes within the pancreatic CL: 2.17% with a single pass (95% CI 1.21%–3.40%) vs. 3.45% with multiple passes (95% CI 1.41%–6.33%) [42].

To reduce the risk of infection after pancreatic CL EUS-FNA, and despite the lack of any prospective randomized controlled studies, current recommendations suggest complete aspiration of the pancreatic CL (in only one pass, where possible), using large-caliber suction needles (22 or 19 gauge), and administering AP (usually with fluoroquinolones or beta-lactams) [21, 41, 43]. However, this approach is mainly based on historical clinical practice with a low level of scientific evidence. Routine AP has several drawbacks, such as increased procedure cost and risk of drug resistance [44, 45], and can be associated with potentially severe allergic reactions and secondary infections, with rates ranging from 1.4% to 3.4% in studies [42, 46, 47]. Moreover, treatment regimens involving parenteral antibiotic administration before endoscopic procedures or oral treatments after the procedure increase the complexity of the procedure, leading to non-adherence to treatment.

Another important point to underscore is lack of homogeneity in the definition of pancreatic CL infection in the literature [48, 49, 50] and in current recommendations [21, 41, 43].

In recent years, several studies have questioned the systematic use of AP for pancreatic CL EUS-FNA and queried its effectiveness. In the retrospective comparative trial by Guarner-Argente et al., no protective effect of AP on incidence of infectious complications after pancreatic CL EUS-FNA/B was observed, and the incidence of complications remained very low (1.1% in the AP group vs. 0.6% in the non-AP group) [46].

Recently, a Spanish multicenter randomized trial compared use of AP with ciprofloxacin vs. placebo in 205 patients undergoing pancreatic CL EUS-FNA [49]. The infection rate was very low (0.44%), with no significant difference between the two groups in terms of infection (RR 0.87%; 95% CI -0.84%-2.59%), fever (2 patients in each group: 1.78% vs. 1.76%; $P = 1.00$), or other AEs [49].

In the propensity score-matched retrospective study by Facciorusso et al., there was no significant difference in the rate of infectious complications in patients undergoing pancreatic CL EUS-FNA between the groups with (1.4%) and without (2.2%) AP ($P = 0.65$) [47]. A recent meta-analysis including six studies (1 randomized and 5 retrospective) and 1,706 patients (of whom 1,038 received AP, mostly with fluorquinolones) showed no difference between the two groups in terms of infection: 0.77% (8/1,038 cases) in the AP group vs. 1.8% (12/668) in the control group (RR 0.65; 95% CI 0.24–1.78; $P = 0.40$), or in terms of other complications [51].

Very few studies have evaluated the infection risk associated with “through-the-needle” techniques, such as confocal endomicroscopy and intra-cystic biopsy with the Moray micro-forceps. In the meta-analysis by Facciorusso et al., including 10 studies and 536 patients, only three cases (0.6%) of infection occurred after EUS-FNA coupled with exploration of pancreatic CL with the confocal endomicroscopy probe; however, systematic AP had been administered in six studies [52].

In a recent propensity score-matched multicenter retrospective study involving 147 patients with pancreatic CL, Facciorusso et al. evaluated the rate of infectious complications associated with EUS-FNA coupled with intra-cystic biopsy with the Moray micro-forceps in two patient groups, without (49) and with (98) AP [48]. Only one case of infection occurred in each group (2% without AP and 1% with AP) ($P = 0.48$) [48]. In a retrospective study involving 506 patients with pancreatic CL (intraductal papillary mucinous neoplasm [IPMN] 45%; serous cystadenoma 18.8%; and mucinous cystadenoma 12.8%) undergoing intra-cystic biopsy with the micro-forceps, the rate of infectious complications was 2%, half of which were severe [34]. In multivariate analysis, age (RR 1.32, 1.09–2.14; $P = 0.05$), the number of passes (RR 2.17, 1.32–4.34 to RR 3.16, 2.03–6.34 with an increase in the number of passes), complete cyst aspiration (RR 0.56, 0.31–0.95; $P = 0.02$), and diagnosis of pancreatic (IPMN) (RR 4.16, 2.27–7.69; $P < 0.001$) were defined as independent predictive factors of complications [53].

Increased risk of infection after mediastinal CL EUS-FNA, supported by numerous case series, is why this procedure is generally contraindicated. AP has not been prospectively studied for this indication [54], but AP is currently recommended by some authors, given the morbidity associated with the occurrence of potential mediastinitis [21, 55, 56, 57, 58, 59, 60, 61].

Incidence of infectious complications associated with pelvic CL EUS-FNA has not been evaluated [62]. Puncture of vestigial cysts in the retrorectal space is generally contraindicated, because it is usually insufficient for diagnosis and can cause infection in the case of a meningocele and tumor dissemination in the case of carcinoma [63]. As a rare situation, only a few case series on diagnosis of pelvic CL by EUS-FNA [64, 65, 66, 67, 68]

have been reported, with the occurrence of infectious complications in some cases [66].

Moreover, no infectious complication was recorded in the 20 patients (4%) who underwent pelvic CL EUS-FNA in the study by Levy et al.; however, systematic AP had been administered in 75% of cases [40]. Rzuq et al. reported no infectious complications following puncture of five pelvic CLs after ciprofloxacin-based AP, starting on the day of sampling for a total of 3 days [69]. Two cases of infection (7%), one occurring despite AP, were described by Mohamadnejad et al. [70].

Risk of infection following EUS-FNA/B of ascites or peritoneal nodules in ascites and pleural fluid, despite AP, has been reported in two studies involving a total of 85 patients, estimated at 4% (1/25) and 3% (2/60), respectively [71, 72]. Three other studies reported no complications in 47 patients who did not receive AP [73, 74, 75].

Currently, there is no consensus on the optimal type of AP that should be administered for diagnostic or therapeutic EUS-FNA/B [21, 41, 43].

The reported data show the diversity of AP used in studies, which significantly limits evaluation of the effectiveness of these different types of AP in reducing incidence of infection following EUS procedures.

There is also no consensus on the duration of AP, with some authors administering the treatment only during the procedure, while others continue after the procedure, for a duration ranging from 2 to 5 days in studies. However, no study has evaluated the benefit of continuing AP for a short duration after the procedure. Therefore, there is currently no scientific evidence to recommend short-duration antibiotic treatment after per-procedure AP.

Therapeutic EUS

Currently, there are no data indicating that AP is beneficial in preventing infectious complications after therapeutic EUS. Until data become available, a single dose of IV antibiotics during a transmural therapeutic procedure is recommended, analogous to protocols in surgery and interventional radiology [76]. Longer administration periods may be necessary in the presence of ascites, in immunocompromised patients, or in patients for whom adequate biliary drainage has not been achieved [76].

Isolated cases of retroperitoneal abscesses following EUS-guided celiac plexus neurolysis have been reported [77, 78, 79, 80, 81].

High-risk endoscopic procedures

Percutaneous endoscopic gastrostomy

Percutaneous endoscopic gastrostomy is recognized as a procedure with a high-risk of infection, which occurs in 4.3% to 16% of cases, with pathogens primarily originating in the oropharyngeal area. Seven randomized studies with placebo control have been published. A meta-analysis of these trials shows a significant reduction in relative and absolute infection risks when AP is used, by 73% and 17.5%, respectively [82]. The benefit of AP is demonstrated regardless of patient type. The antibiotics administered in these studies were cephalosporins or amoxicillin-clavulanic acid.

Esophageal variceal sclerosis (EVS)

Risk of bacteremia after EVS ranges from 4% to 56%, with an average of 20% [83]. Two controlled studies using cefuroxime or cefotaxime have shown a significant decrease in the rate of bacteremia, but the reduction in the rate of clinical infection is not clearly evident [84]. However, AP is recommended for all patients (especially frail patients who are often neutropenic and immunocompromised). Esophageal variceal ligation (EVL) is associated with a lower rate of bacteremia, ranging from 1% to 25%, with an average of 9%.

EVL during hemorrhagic and non-hemorrhagic episodes

During a hemorrhagic episode in a patient with cirrhosis, AP leads to a reduction in the infection rate and an improvement in survival [85,86,87]. A short-duration regimen appears to be sufficient, as shown in a recent randomized study comparing 3 days vs. 7 days of ceftriaxone at 1 g/day in terms of re-bleeding and survival [88].

As per the latest European recommendations on portal hypertension (Baveno VII), AP is an integral part of treatment for patients with cirrhosis who are experiencing upper gastrointestinal bleeding. AP should be initiated as soon as the patient is admitted, without waiting for diagnostic and therapeutic EGD. Risks of bacterial infection and mortality are very low in patients with Child-Pugh class A cirrhosis, but there are a lack of prospective studies to show that AP should not be administered to this patient subgroup. Individual patient risk characteristics and local antibiotic sensitivity patterns should be considered when choosing the antibiotic. As a first-line approach, 1 g of IV ceftriaxone every 24 hours should be considered for patients with advanced cirrhosis (strong recommendation, high level of evidence), especially for hospitalized patients due to the high prevalence of quinolone resistance and for patients treated with quinolones for prophylaxis [89].

On the other hand, there are no data in the literature to recommend systematic AP for EVL outside hemorrhagic episodes.

Endoscopic retrograde cholangiopancreatography

In a large consecutive prospective study involving 2,769 patients, post-ERCP cholangitis was reported in 0.87% of cases [90]. In a recent retrospective study involving 4,324 patients, independently identified risk factors for post-ERCP cholangitis in unselected patients were hilum obstruction, age ≥ 60 years, and a history of ERCP, whereas complete extraction of bile duct stones was protective [91]. Incomplete biliary drainage (cannulation failure, persistence of stones, unstented intrahepatic or extrahepatic stenosis, and suboptimal clearance at the end of the procedure according to operator judgment) is recognized as the primary risk factor for cholangitis [92,93].

Primary sclerosing cholangitis (PSC) and hilum obstruction, both of which expose the patient to incomplete biliary drainage, are also associated with risk of post-ERCP cholangitis, although no controlled studies are available [92,93,94]. Ultimately, whereas AP reduces the risk of bacteremia, as demonstrated in the most recent meta-analysis of 10 randomized trials, it is not associated with a reduction in risk of cholangitis, septicemia, pancreatitis, or death, thereby limiting its utility

[95]. In a large retrospective study involving 4,214 ERCPs, cholangioscopy appears to increase the risk of cholangitis, likely due to the need for bile irrigation (1.0% vs. 0.2%; OR 4.98; 95% CI [1.06–19.67]) [96]. A recent study suggested that bacteremia was specifically linked to cholangioscopy in 13.9% of patients (10/72), based on serial blood samples [97]. Another prospective study, which reported bacteremia and cholangitis rates of 8.8% and 7%, respectively, without AP, found that bacteremia was significantly associated with biopsy procedures and the presence of strictures [98].

ERCP with placement of a self-expandable metal biliary stent exposes the patient to risk of acute cholecystitis due to obstruction of the cystic duct, with an incidence rate ranging from 1.9% to 12% [99]. According to two meta-analyses, the fact that the stent is covered or uncovered does not seem to have any impact on the incidence rate [100,101]. Cases of cholecystitis after metal stent placement are mainly described in patients with malignant biliary obstruction, likely due to filling of the gallbladder with non-sterile bile and/or contrast agent during opacification. Gallbladder opacification during ERCP should be avoided to prevent exacerbating this risk.

In its latest 2020 recommendations, the European Society of Gastrointestinal Endoscopy (ESGE) advises against systematic use of AP before ERCP (strong recommendation, moderate level of evidence). However, AP before ERCP should be considered in the case of pre-interventional doubt about the ability to complete biliary drainage, in severely immunocompromised patients, and during cholangioscopy (weak recommendation, moderate level of evidence). The ESGE also suggests evaluating patients with post-ERCP cholangitis by abdominal ultrasound or computed tomography (CT) and, in the absence of improvement with conservative treatment, considering a repeat ERCP. In the case of a repeat ERCP, it recommends sampling bile for bacteriological examination (weak recommendation, low level of evidence) [102]. While the benefit of AP has not been studied in the case of placement of a self-expandable metal biliary stent in a gallbladder in situ, AP may still be indicated, as highlighted in the recommendations of the American Society for Gastrointestinal Endoscopy (ASGE) [103].

Currently, there are no data indicating that AP is beneficial in preventing infectious complications after pancreatoscopy. Until data become available, the decision for AP administration should be considered by endoscopist and anesthesiologist, accordingly with the institutional protocol.

Bariatric procedures (endoscopic sleeve procedure)

Currently, there are no data indicating that AP is beneficial in preventing infectious complications after endoscopic sleeve procedure. Until data become available, the decision for AP administration should be considered by endoscopist and anesthesiologist, accordingly with the institutional protocol.

► **Table 2** Antibiotic prophylaxis in digestive endoscopy (expert opinion).

Endoscopic procedure	Administration modalities (products, initial dose, dosage and duration)
Low-risk endoscopy	No AP
ERCP with suspected incomplete drainage* EUS-FNA/B of ascites, peritoneal nodules in ascites or pleural fluid EUS with biliary-digestive anastomosis Cystogastrostomy	Administration of ceftioxin (2 g, slow IV, single dose) In the case of allergy, administration of gentamicin 6–7 mg/kg/day combined with metronidazole (1000 mg, slow IV, single dose) To be completed ideally 60 minutes before and no later than the start of the intervention
PEG	Administration of cefazolin (2 g, slow IV, single dose)
Peritoneal dialysis	Administration of AP 30 minutes before the procedure, including ampicillin (1 g) and a single dose of aminoglycoside In addition, complete drainage of all peritoneal dialysate before the endoscopic procedure should be performed according to the recommendations of the ISPD

*Criteria for incomplete biliary drainage = cannulation failure, persistence of stones, unstented intra- or extrahepatic stenosis, and suboptimal clearance at the end of the procedure according to operator judgment.

AP, antibiotic prophylaxis; ERCP, endoscopic retrograde cholangiopancreatography; EUS-FNA/B, endoscopic ultrasound fine-needle aspiration or biopsy; PEG, percutaneous endoscopic gastrostomy; IV, intravenous; ISPD, International Society for Peritoneal Dialysis.

Prescription modalities for AP

Organizational modalities

As emphasized by the SFAR in its 2018 recommendations [104], the selected protocols must be written, co-signed by anesthesiologists-intensivists and operators, and validated by the Infection Control Committee (CLIN) and, depending on the internal organization, by the Drug and Sterile Medical Devices Committee or the Anti-infective Agents Committee.

These protocols should be available and may be displayed in pre-anesthetic consultation rooms, operating rooms, post-intervention surveillance rooms, and care units.

The endoscopist and anesthesiologist-intensivist must jointly determine, based on the type of planned intervention, the level of bacterial infection risk, and the patient's history (allergies, infections, etc.), the necessity for using AP.

It is up to each team to decide which physician is responsible for prescribing AP.

AP protocols must be updated regularly, taking into account new scientific data, developments in interventional techniques, and bacterial resistance profiles.

Furthermore, it is recommended to administer AP with a cephalosporin (or its alternatives in the case of allergy, excluding vancomycin) as early as 60 minutes before and no later than the start of the interventional procedure, to reduce the incidence of surgical site infection. If vancomycin is used for AP, experts suggest starting IV administration over 60 minutes in non-obese patients as early as 60 minutes and no later than 30 minutes before the start of the interventional procedure, to reduce incidence of surgical site infection. There should be a gap of 5 to 10 minutes between injection of the anesthetic induction products and the AP, in order to be able to determine – in the case of an allergic reaction – the contribution of each in the occurrence of the complication. The operator must ensure that AP has been properly prescribed, especially by checking the “checklist”.

The spectrum of action of the antibiotic should include the bacteria most frequently involved in the infection of the interventional site. In digestive endoscopy, the antibiotic agent should thus be active against *Escherichia coli* and other Enterobacteriaceae, methicillin-sensitive *Staphylococcus aureus*, and, in certain circumstances, anaerobic bacteria. It is necessary to check for any allergic history before administration.

Administration schemes

The commonly accepted protocol is 2 g of IV ceftioxin as early as 60 minutes before and no later than the start of the interventional procedure. In the case of penicillin allergy, a 30-minute infusion of gentamicin at a dose of 6 to 7 mg/kg/day of adjusted weight combined with IV metronidazole at a dose of 1000 mg could be an alternative.

However, concerning ERCP, because clinical scenarios such as failed cannulation or remnant stones cannot be anticipated prior to the procedure, to decrease risk of cholangitis, AP is initiated during or immediately at the end of the procedure in cases where prevention before the ERCP was not initially required.

The protocols below, taking into account certain specific situations to adapt AP to specific bacterial infection risks, reiterate, for clarity, the proposals made by the SFAR in its 2018 recommendations, drawn up jointly with the SPLIF and updated in 2023 in collaboration with the recommendations committee of the French Society of Digestive Endoscopy (SFED). Given the low level of evidence for some indications, administration schemes have been retained by assimilation and expert opinion, and will need to be updated in light of evolving knowledge (► **Table 2**).

SFED recommendations

Diagnostic endoscopy with or without biopsy: No AP (strong recommendation, low level of evidence).

ERCP: No systematic AP (strong recommendation, moderate level of evidence).

ERCP with suspected incomplete biliary drainage*, or in immunocompromised patients, or in the case of cholangioscopy: Administration of cefoxitin (2 g, slow IV). In the case of allergy, administration of gentamicin (6–7 mg/kg/day) combined with metronidazole (1 g, single-dose infusion), to be completed ideally as early as 60 minutes before and no later than the start of the interventional procedure (weak recommendation, moderate level of evidence).

Because clinical scenarios such as failed cannulation or remnant stones cannot always be anticipated prior to the procedure, to decrease risk of cholangitis, AP is initiated during or immediately at the end of the procedure in cases where prevention before the ERCP was not initially required (weak recommendation, moderate level of evidence).

* *Criteria for incomplete biliary drainage:* cannulation failure, persistence of stones or microlithiasis especially at the end of lithotripsy, unstented intrahepatic or extrahepatic stenosis, and suboptimal clearance at the end of the procedure according to operator judgment.

Pancreatostomy: The decision for AP administration should be considered by endoscopist and anesthesiologist, accordingly with the institutional protocol (weak recommendation, no evidence).

PEG: Administration of cefazoline (2 g, slow IV). In the case of allergy, administration of vancomycin (20 mg/kg IBW, slow IV) (strong recommendation, high level of evidence).

If vancomycin is used for AP, experts suggest starting IV administration over 60 minutes in non-obese patients as early as 60 minutes and no later than 30 minutes before the surgical incision or the start of the interventional procedure, in order to reduce incidence of surgical site infection (expert opinion).

Sclerotherapy of esophageal varices: No systematic AP, because sclerotherapy of esophageal varices outside an hemorrhagic episode is no longer indicated (strong recommendation, low level of evidence).

LVO during a hemorrhagic episode: IV administration of ceftriaxone (1–2 g/24 hours) for patients with advanced cirrhosis (1b; A), hospitalized patients due to the high prevalence of quinolone resistance, and patients treated with quinolone prophylaxis, or administration of fluoroquinolone for other patients (oral norfloxacin, 400 mg twice daily for 7 days) (strong recommendation, high level of evidence).

LVO outside a hemorrhagic episode: No systematic AP (strong recommendation, high level of evidence).

Peritoneal dialysis: Administration 30 minutes before antibiotic therapy with ampicillin (1 g) and a single dose of aminoglycoside. Moreover, complete drainage of all peritoneal dialysate before the endoscopic procedure should be performed according to recommendations of the International Society for Peritoneal Dialysis (ISPD) [9] (strong recommendation, low level of evidence).

EUS-FNA/B of solid lesions, along the gastrointestinal and biliary-pancreatic tract or lymph nodes: No systematic AP (strong recommendation, low level of evidence).

EUS-FNA of pancreatic cystic lesions, including “through the needle” techniques (confocal endomicroscopy, biopsies with the Moray micro-forceps): No solid scientific evidence to suggest systematic AP. The decision is left to the discretion of the practitioner and should be discussed based on risk factors associated with the endoscopic procedure (intra-cystic bleeding, incomplete aspiration of the cystic lesion after puncture) and/or patient (immunosuppression, neutropenia, and/or high risk of infective endocarditis) (weak recommendation, low level of evidence).

EUS-FNA of mediastinal or peri-rectal cyst: Due to a high risk of morbidity, these procedures should be avoided (strong recommendation, low level of evidence).

EUS-FNA/B of ascites or peritoneal nodules in ascites and pleural fluid: Systematic AP (weak recommendation, low level of evidence).

EUS with cystogastrostomy/cystoduodenostomy; biliary-digestive or wirsungogastro-gastric anastomosis, cholecystostomy, gastrojejunal anastomosis, endoscopic ultrasound directed transgastric ERCP, tissue destruction by EUS-guided radiofrequency, EUS-guided celiac plexus neurolysis, drainage of pelvic collections: Systematic AP (weak recommendation, low level of evidence).

Endoscopic dilation: No AP (strong recommendation, low level of evidence).

Placement of biliary-digestive stents (excluding incomplete biliary drainage, PSC, or tumor obstruction with the gallbladder in situ): No AP (strong recommendation, low level of evidence).

Esophagogastric and rectal radiofrequency: No AP (strong recommendation, low level of evidence).

EMR (esophagogastric or colorectal): No AP (strong recommendation, low level of evidence). In the case of therapeutic breach, non-prophylactic antibiotic therapy should be discussed, on a case-by-case basis and according to the circumstances (weak recommendation, low level of evidence).

Submucosal dissection (esophago-gastric or colorectal):

The decision for AP administration should be considered by endoscopist and anesthesiologist, accordingly with the institutional protocol. In the case of therapeutic breach, non-prophylactic antibiotic therapy should be initiated (weak recommendation, moderate level of evidence).

Endoscopic sleeve procedure: The decision for AP administration should be considered by endoscopist and anesthesiologist, accordingly with the institutional protocol (weak recommendation, no evidence).

Conflict of Interest

Competing interests in relation to the guidelines: None declared. Other competing interests: David Karsenti, MD: Consultant for Olympus, Covidien and Norgine; support for attending meetings from Alfigma, Cook and Fujifilm. Rodica Gincul, MD: Consultant for Olympus; honoraria for lectures from Olympus; support for attending meetings from Celtrion, AbbVie. Arthur Belle, MD: Consultant for Boston Scientific; support for attending meeting from Mayoli. Geoffrey Vanbiervliet, MD-PhD: Consultant for Boston Scientific and Ambu; honoraria for lectures, presentations and speeches from Pentax, Fujifilm, Tillots, and Norgine. Olivier Gronier, MD: Support for attending meetings from Dr Falk.

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