

Adapted from SABISTON, Textbook of Surgery

Bile in the gallbladder or bile ducts is normally sterile, in the absence of gallstones or any other biliary tract disease. In the presence of gallstones or biliary obstruction the prevalence of bactibilia increases.

The presence of positive bile cultures is influenced by several factors including the severity or type of biliary disease and the patient's age.

- The percentage of positive gallbladder bile cultures among patients with symptomatic gallstones and chronic cholecystitis ranges from **11% to 30%**.
- The prevalence of positive gallbladder bile cultures is higher in patients with acute cholecystitis than chronic cholecystitis (**46% vs. 22%**)
- The prevalence of positive gallbladder bile cultures increases further in the presence of common bile duct stones.
- **58%** of patients with gallstones and common bile duct stones but without cholangitis had positive gallbladder and common duct bile cultures
- **94%** of patients with gallstones, common bile duct stones, and cholangitis had positive bile cultures.
- **All patients** with common bile duct stones after cholecystectomy had bactibilia.
- Positive bile cultures were significantly more common in elderly (>60 years) patients with symptomatic gallstones than in younger patients (**45% vs. 16%**).
- Patients with cholangitis due to malignant biliary obstruction are also more likely to have a positive bile culture than patients with a benign cause of biliary obstruction (stones, stricture, sclerosing cholangitis).

Gram-negative aerobes are the organisms most frequently isolated from bile in patients with symptomatic gallstones, acute cholecystitis, or cholangitis.

- Escherichia coli and Klebsiella species are the most common gram-negative bacteria isolated.
- However, the more resistant organisms Pseudomonas and Enterobacter are being seen with increased frequency, particularly in patients with malignant biliary obstruction, who may have been treated with antibiotics previously for a biliary tract infection (see table below).
 - Other common isolates include
 - the gram-positive aerobes,
 - Enterococcus,
 - Streptococcus viridans.
 - Anaerobes, such as Bacteroides species and Clostridium, continue to play a small but significant role in biliary infections.
 - The prevalence of anaerobic bacteria is 10% to 13% in patients with acute cholecystitis or cholangitis.
 - Candida species are also being increasingly recognized as a significant biliary pathogen particularly in critically ill patients.

The majority of patients with symptomatic cholelithiasis, acute cholecystitis, or common bile duct stones in the absence of cholangitis have a single organism isolated in bile cultures.

Polymicrobial infections are more common in patients with cholangitis.

In analyzing response to therapy, the isolation of *Candida*, panresistant bacteria, and more than two bacteria are associated with treatment failures.

Organisms Isolated from Bile of Patients with Either a Benign or Malignant Etiology of Cholangitis

Organisms	Benign Cause (%) (n =42)	Malignant Cause (%) (n =54)
GRAM NEGATIVE		
<i>Klebsiella</i> species	31	72*
<i>Escherichia coli</i>	43	35
<i>Enterobacter</i> species	17	48*
<i>Pseudomonas</i> species	12	33 [†]
<i>Citrobacter</i> species	17	24
<i>Proteus</i> species	12	13
GRAM POSITIVE		
<i>Enterococcus</i>	36	33
<i>Streptococcus</i> species	24	48 [†]
Anaerobes		
<i>Bacteroides</i> species	17	13
<i>Clostridium</i> species	2	7
FUNGI		
<i>Candida</i> species	5	28*
OTHERS	19	9
At least one organism isolated	64	96 [†]

The source of bacteria in patients with biliary tract infections is controversial. The majority of evidence favors an **ascending route via the duodenum** as the main source of biliary bacteria.

- The bacterial flora in the small intestine is similar to that detected in the biliary tract.
- In the majority of patients gallbladder and common bile duct cultures yield a similar result.
- Furthermore, the prevalence of bactibilia is highest in the elderly in whom biliary motility and clearance have decreased.

Antibiotic Selection

Antibiotics should be used prophylactically in most patients undergoing elective biliary tract surgery or other biliary tract manipulations such as endoscopic or percutaneous cholangiography.

- The risk of postoperative infectious complications corresponds to the presence of bactibilia, which occurs in 11% to 30% of patients with gallstones, but is difficult to determine preoperatively.
- In low-risk patients undergoing elective laparoscopic cholecystectomy for chronic cholecystitis, the incidence of wound infections is low (1%)
 - several prospective randomized trials have not demonstrated any benefit to prophylactic antibiotics.
- In high-risk patients (elderly, recent acute cholecystitis, high risk of conversion to open cholecystectomy) undergoing elective laparoscopic cholecystectomy for chronic cholecystitis a single dose of the first-generation cephalosporin, cefazolin, provides good coverage against the gram-negative aerobes commonly isolated from bile and skin flora.

Recommended Antibiotics for Use in Biliary Tract Surgery

ANTIBIOTIC PROPHYLAXIS

Open Cholecystectomy

- Cefazolin (1-2 g single dose)

Laparoscopic Cholecystectomy

- **Low risk**
 - None
- **High-risk***
 - Cefazolin (1-2 g single dose)

Other Open Biliary Tract Operations

- Piperacillin/tazobactam, ampicillin/sulbactam, ticarcillin/ clavulanate
- Ciprofloxacin + metronidazole
- Cefoperazone, cefotetan, cefotaxime, ceftriaxone

ERCP-Low Risk

- None

ERCP-High Risk†/Percutaneous Biliary Drainage

- Piperacillin/tazobactam, ampicillin/sulbactam, ticarcillin/clavulanate
- Ciprofloxacin + metronidazole
- Cefoperazone, cefotetan, cefotaxime, ceftriaxone

THERAPEUTIC ANTIBIOTICS

- **Acute Cholecystitis**
 - Cefotetan, cefoxitin, ceftizoxime
 - Ciprofloxacin + metronidazole
- **Acute Cholangitis**
 - Piperacillin/tazobactam, ampicillin/sulbactam, ticarcillin/ clavulanate
 - Ciprofloxacin + metronidazole
 - Imipenem/cilastatin, meropenem
 - Cefepime

Therapeutic antibiotics are used in patients with acute cholecystitis and acute cholangitis.

- In both diseases gram-negative aerobes play a major role and are well covered by
 - the second- or third-generation cephalosporins,
 - aminoglycosides,
 - Ureidopenicillins
 - Ureidopenicillins, such as piperacillin, offer the advantage of gram-positive coverage, including the enterococci and of anaerobic coverage.
 - When combined with a β -lactamase inhibitor such as tazobactam, piperacillin offers extended and improved coverage against organisms with acquired resistance.
 - carbapenems,
 - fluoroquinolones.
 - Most fluoroquinolones such as ciprofloxacin do not cover the anaerobes and should be used in combination with an agent with anaerobic coverage (i.e., metronidazole).
- Pseudomonas has been recovered with increased frequency in patients with cholangitis, particularly with chronic indwelling stents, and should be covered in severely ill patients.
 - Both mezlocillin and piperacillin have performed as well as combination therapy including an aminoglycoside in prospective, randomized trials in patients with cholangitis