Questions, Answers, and Critiques

1. The pathogenesis of cholesterol gallstone formation typically includes

A. bile containing excess triglycerides, cholesterol crystals, and hypermotility of the gallbladder
B. simultaneous release of cholecystokinin (CCK) and somatostatin
C. lack of endogenous prostaglandins and antinucleation factors coupled with relaxation of the sphincter of Oddi
D. bile supersaturated with cholesterol, stasis of bile within the gallbladder, and nucleation of cholesterol to form crystals
E. a period of rapid weight gain and calcium deficiency

The recommended response is D.

The three major mechanisms leading to gallstone formation are increased secretion of cholesterol into bile, decreased gallbladder motility, and formation of cholesterol crystals (Hyperlink to Cholesterol Gallstone Pathogenesis section). Patients with cholesterol gallstones characteristically have bile that is supersaturated with cholesterol as predicted from model solutions of cholesterol, bile acid, and phospholipids. Excess amounts of bile triglycerides have not been observed in gallstone formation. Altered gallbladder motility promotes gallstone formation by bile stasis. Gallbladder contractility is enhanced by cholecystokinin (CCK) release in response to the fat content of ingested food. The hormone somatostatin, however, has been shown to inhibit gallbladder contractility which aids in gallstone formation. Both the absence of antinucleation factors in bile and sphincter of Oddi relaxation contribute to the solubilization of cholesterol which prevents nidus formation. During rapid weight loss, bile lithogenicity is augmented by the decreased synthesis of bile acids and impaired gallbladder motility which increases the risk of gallstone formation. Calcium deficiency has not been implicated as a direct cause of gallstone formation.

2. Which of the following is true regarding gallbladder motility?
A. a gallbladder ejection fraction of less than 50% indicates dyskinesia
B. patients with gallbladder dysmotility commonly have histologic changes of chronic cholecystitis
C. contractile function is mediated by secretin
D. short-chain fatty acids are the most potent stimulators of intestinal CCK release
E. somatostatin release is associated with accelerated gallbladder emptying time

The recommended response is B.

Biliary dysmotility is usually associated with specific conditions such as gallstones or choledocholithiasis (Hyperlink to Gallbladder Dysmotility section). Biliary dyskinesia and sphincter of Oddi dysfunction are the two main categories of biliary motility disorders. Most patients present with unexplained chronic abdominal pain which has some features of biliary-type pain. The duration of pain, however, is often long-standing and may resemble luminal gastrointestinal disorders such as irritable bowel syndrome or functional dyspepsia.

Radionuclide scintigraphy (e.g. HIDA scan) enables the calculation of a gallbladder ejection fraction to objectively assess the severity of dysmotility. Biliary dyskinesia is defined as a gallbladder ejection fraction of less than 35% in the absence of cholelithiasis. Conflicting evidence exists regarding the effectiveness of cholecystectomy for the treatment of biliary dyskinesia. Relief of symptoms has been reported in 50-85% of cases. These patients have histologic changes of chronic cholecystitis in most cases.

Gallbladder contractility is regulated by a neurohumoral axis stimulated by the fat content of ingested
food, vagal nerve innervation, and release of CCK. Long-chain fatty acids are the most potent stimulus for the intestinal release of CCK which mediates postprandial gallbladder contraction and sphincter of Oddi relaxation. Somatostatin acts as a physiological inhibitor of gallbladder contraction.


3. Which one of the following is true about sphincter of Oddi dysfunction (SOD)?
A. abnormal serum liver biochemistries at the time of typical abdominal pain in the absence of gallstones or sludge is suspicious for type I and type II SOD
B. the preferred treatment for type I SOD includes beta-blockers
C. abnormal manometric findings correlate only with type I SOD
D. severe pancreatitis occurs after endoscopic sphincterotomy in 50% of patients with SOD
E. untreated symptomatic disease is associated with secondary biliary cirrhosis

The recommended response is A.

Sphincter of Oddi dysfunction (SOD) is a motility disorder associated with biliary-type pain, cholestasis, and pancreatitis (Hyperlink to Sphincter of Oddi Dysfunction section). The diagnosis of SOD requires strict exclusion of upper gastrointestinal tract diseases and functional disorders. Measuring serum hepatic and pancreatic biochemical parameters during an episode of biliary-type pain is most informative. ERCP is required to document normal biliary and pancreatic duct anatomy and for biliary manometry. Basal sphincter pressures exceeding 35-40 mm Hg are considered significant. The Milwaukee classification defines type I SOD (biliary-type pain and SGOT or alkaline phosphatase >2x the upper limit of normal on 2 or more occasions, delayed contrast drainage at ERCP, and a common bile duct diameter >12 mm); type II SOD (biliary type pain and 2 associated criteria), and type III SOD (biliary type pain alone). Medical therapy with calcium channel blockers has been successful in select cases of type II and type III SOD.
With type I or II SOD, endoscopic sphincterotomy relieves symptoms in >85% of cases, but lower success rates (55-60%) are seen with type III SOD. Severe pancreatitis from endoscopic sphincterotomy is observed in less than 10% of cases. No frequent association between SOD and secondary biliary cirrhosis has been observed.


4. Which one of the following is true regarding the epidemiology of cholesterol gallstone formation?

A. a decreased incidence of gallstones is associated with increasing age
B. the risk of gallstones is similar in normal and over-weight people
C. parenteral nutrition augments CCK release which promotes gallstone formation
D. ileal Crohn’s disease is a known cause of gallstone formation
E. pregnancy is not a period of high risk for formation of cholesterol gallstones

The recommended response is D.

Epidemiologic risk factors for cholesterol gallstones include gender, genetic predisposition, obesity, pregnancy, systemic conditions affecting cholesterol saturation in bile, and pharmacologic agents (Hyperlink to Risk Factors for Gallstones section). The incidence of gallstone formation is primarily influenced by gender and age. Between 5-20% of women ages 20 to 55 will develop gallstones. Beyond the age of 50, men and women are at similar risk of gallstones. Between 25-30% of men after the age of 50 have gallstones. The enhanced secretion of biliary cholesterol with increasing age appears to be the underlying mechanism. The absence of enteral food stimulation during total parenteral nutrition impairs CCK release and predisposes to gallstones in up to 45% of cases after 3 months of therapy. Systemic conditions associated with gallstone formation include diabetes mellitus and derangements in ileal
function such as Crohn’s disease. In women, the risk of developing gallstones is directly related to the number of pregnancies. As pregnancy progresses, bile becomes supersaturated with cholesterol because of high levels of estrogens, and gallbladder motility is impaired because of high levels of progestins. Thus, stasis of lithogenic bile within an enlarged, sluggish gallbladder occurs during late pregnancy, predisposing to sludge and gallstone formation.


5. A 28-year-old healthy man presents with a one-day history of fever, rigors, abdominal pain, and jaundice. He relocated to the United States from Taiwan 2 years ago. He had suffered several similar episodes prior to his move to the US. Physical examination is notable for a temperature of 100°F, scleral icterus, and right upper quadrant tenderness without peritoneal signs. Laboratory data are white blood cell count of 15,000/mm³, alkaline phosphatase of 350 IU/L, aspartate aminotransferase (AST) of 70 IU/L, and total bilirubin of 4.1 mg/dL. Which one of the following actions is most appropriate in the immediate management of this patient?
A. stool examination to exclude ova and parasites
B. cross-sectional imaging to exclude hepatic abscesses
C. percutaneous transhepatic cholangiography
D. intravenous fluid resuscitation and broad spectrum antibiotics
E. laparoscopic cholecystectomy

The recommended response is D.

The most probable diagnosis is recurrent pyogenic cholangitis (RPC) (Hyperlink to Primary Intrahepatic
Stones section). This syndrome is characterized by recurrent attacks of cholangitis with bile duct dilatation and multiple pigmented stones. RPC is endemic to Southeast Asia with incidental cases in the Western Hemisphere among Asian immigrants. Stones are usually multiple in number and irregular in shape. The most common location for stones is the common bile duct, but they can also be found in the proximal intrahepatic ducts. Charcot’s triad (fever, right upper quadrant pain, and jaundice) is generally present. Biliary dilatation with or without stones is observed in 85% by ultrasonography and can exclude hepatic abscess formation.14

Up to 45% of subjects with RPC may have associated liver fluke infestation. However, routine stool examinations may not be indicated or of clinical value in diagnosis. CT provides no additional immediate advantage over abdominal ultrasonography. ERCP is the preferred method of biliary tree visualization and drainage. Most patients with RPC respond to intravenous fluids and empiric broad spectrum antibiotics. For the 15% of patients refractory to initial management, emergency surgical intervention is required. Operative treatment often includes common bile duct exploration and T-tube placement with or without cholecystectomy.


6. A major pathway for cholesterol excretion from the body is:
   A. conversion to bile acids in the liver
   B. conversion to fatty acids
   C. conversion to triglycerides
   D. metabolism to other sterols in the liver
   E. urinary excretion

   The recommended response is A.
A major pathway for cholesterol elimination from the body is synthesis of bile acids in the liver and excretion into bile (Hyperlink to Hepatic Cholesterol Metabolism section). Bile acids are synthesized from cholesterol by saturation of the sterol nucleus and addition of two or three hydroxyl groups. There are two pathways of bile acid biosynthesis: the classic and the alternate pathways. Cholesterol 7α-hydroxylase is the rate-limiting enzyme in the classic pathway. Its activity is regulated by the availability of cholesterol substrate, the hepatocellular bile acid concentration, the amount of enzyme (which decreases with age), and other metabolic and hormonal factors. In the alternate pathway, cholesterol is initially oxidated by the enzyme sterol 27-hydroxylase. While the alternate pathway leads primarily to the formation of chenodeoxycholic acid, both chenodeoxycholic acid and cholic acid are the end products of the classic pathway. Newly synthesized bile salts are actively secreted into the bile canaliculi. As the rate of bile salt secretion increases, a similar increase in cholesterol secretion occurs.

Cholesterol is also eliminated by direct secretion into bile. Cholesterol can also be converted into oxidized forms (oxysterols) within the liver, but this does not represent a major route of elimination. Cholesterol is not converted to fatty acids or triglycerides. Urinary excretion of cholesterol metabolites does not contribute significantly to its elimination.


7. After secretion into bile, the majority of primary bile acids are:

A. all excreted in the feces
B. absorbed in the small intestine and undergo enterohepatic circulation
C. normally deconjugated by bacteria in the small intestine
D. absorbed in the conjugated form in the colon to undergo enterohepatic circulation
E. used metabolically by bacteria in the colon
The recommended response is B.

Among healthy individuals, the enterohepatic circulation carries nutrient lipids and fat-soluble vitamins to the intestinal mucosa and transports cholesterol into bile, permitting its unchanged elimination from the body in feces. The enterohepatic circulation also transports bile acids from the liver to the small intestine and back to the liver after reabsorption on the terminal ileum (Hyperlink to Enterohepatic Circulation section). The circulating bile acid pool is primarily maintained by efficient ileal reabsorption (>95% per pool cycle). Under stable conditions, the rate of loss of bile acids is matched by an equivalent rate of hepatic synthesis. Unabsorbed bile acids pass into the colon where they are metabolized by bacteria to secondary bile acids including deoxycholic acid, ursodeoxycholic acid, and lithocholic acid. These deconjugated bile acids are absorbed inefficiently in the colon and undergo enterohepatic circulation for hepatic reprocessing and ultimate secretion into bile. Over half of the secondary bile acids in the colon are excreted in feces. The exposure of bile acids to anaerobic bacteria (primarily in the cecum) allows for hydroxyl substituent oxidation to facilitate deconjugation. There are reports that intestinal bile acid dehydroxylating bacteria employ bile acids as metabolic substrates, but this is not the main fate of primary bile acids.


8. Which of the following statements is true about HIV cholangiopathy?
A. an inverse association exists between CD4 T-cell count and the risk for HIV cholangiopathy
B. Diarrhea is rarely present
C. Bile duct abnormalities are found in the majority of patients with CMV and cholestatic liver disease
D. Isolated common bile duct strictures are common
E. 80% of affected patients have no identifiable opportunistic infection
The recommended response is A.

HIV-associated biliary tract disease resembles sclerosing cholangitis with papillary stenosis. CD4 T-cell counts less than 50/mm³ are associated with a risk for HIV cholangiopathy. Diarrhea is usually present related to small intestinal involvement with the characteristic pathogens. Approximately one-third of AIDS patients with CMV and cholestatic liver disease will have bile duct abnormalities. The most common presentation is epigastric and/or right upper quadrant abdominal pain and fever. Serum alkaline phosphatase is elevated in over 75% of cases with milder increases in serum transaminases. Normal biochemical parameters are found in 20% of patients. Ultrasonography or CT imaging can detect biliary duct dilatation in 77% of cases.

Cholangiography most commonly demonstrates papillary stenosis with intrahepatic sclerosing cholangitis. Other variations include sclerosing cholangitis without papillary stenosis, papillary stenosis alone, or long extrahepatic strictures. The presence of an isolated common bile duct stricture should raise the suspicion for primary lymphoma or pancreatic disease. Treatment is directed at biliary tree abnormalities as well as identified pathogens. For patients with papillary stenosis alone, endoscopic sphincterotomy has been associated symptomatic improvement. As many as 50% of affected patients will not have an identifiable opportunistic pathogen responsible for their cholangiopathy toward which treatment can be directed.


9. Which of the following is true about biliary sludge?
   A. Biliary sludge appears as high amplitude echoes with post-acoustic shadowing on ultrasonography
   B. Sludge is not a precursor to gallstones
   C. Sludge is composed of cholesterol dihydrate crystals
D. Sludge does not spontaneously resolve

E. Sludge can cause acute pancreatitis and other complications usually associated with gallstones

The recommended response is E.

Biliary sludge is defined as a mixture of particulate matter and bile that occurs when solutes in bile precipitate (Hyperlink to Clinical Course and Complications section). Cholesterol monohydrate crystals, calcium bilirubinate, and other calcium salts are the most common components. The clinical course of biliary sludge varies. Complete resolution, a waxing and waning course, and progression to gallstones are all possible outcomes. Biliary sludge may also cause complications including biliary colic, acute pancreatitis, and acute cholecystitis. Patients with cholesterol microlithiasis have biliary cholesterol supersaturation which is similar to patients with formed cholesterol gallstones. Clinical conditions and events associated with the formation of biliary sludge include rapid weight loss, pregnancy, ceftriaxone therapy, octreotide therapy, and bone marrow or solid organ transplantation. Sludge may be diagnosed by ultrasonography where the appearance of low-amplitude echoes without acoustic shadowing is characteristic. The use of bile microscopy may be required if a high clinical suspicion for biliary sludge exists with abnormal or indeterminate ultrasonographic exam. There are no proven methods for to prevent sludge formation, and patients should not be routinely monitored for the development of sludge. Asymptomatic patients with sludge can be managed expectantly. If patients with sludge develop symptoms or complications, cholecystectomy should be considered as the definitive therapy.6


10. A 60-year-old woman presents to the emergency room with fevers, chills, and right upper quadrant pain of 6 hours duration. Vital signs are noted for a temperature of 101.5°F, pulse of 110 and systemic blood pressure of 110/70. Physical exam is remarkable for jaundice, tenderness of the epigastrium and
right upper quadrant without signs of rebound tenderness. Serum laboratory data are noted for a WBC count of 12,800/mm³, alkaline phosphatase of 350 IU/L, aspartate aminotransferase of 120 IU/L and total bilirubin of 4.1 mg/dL. Serum amylase and lipase levels are within normal limits. Abdominal ultrasonography shows gallstones in the gallbladder, along with dilated intrahepatic and extrahepatic bile ducts.

The most appropriate management is
A. immediate MRCP
B. Immediate cholecystectomy
C. Intravenous antibiotics alone
D. Intravenous antibiotics followed by endoscopic or percutaneous biliary ductal drainage
E. Immediate cholecystostomy

The recommended response is D.

This patient presents with the classic Charcot’s triad - fevers, right upper quadrant pain, and jaundice, which is observed in approximately 70% of patients with acute cholangitis (Hyperlink to Treatment of Gallstone Related Disorders section). Choledocholithiasis is seen in >80% of cases, with neoplasms and biliary strictures making up the remaining etiologies. Because of the risk of bacteremia and progressive infection, patients with cholangitis should be given supportive care and started on intravenous antibiotics against gram-negative aerobic enteric organisms, Enterococcus and anaerobic bacteria. Mild to moderate cases of acute cholangitis usually respond to antibiotic therapy within 48 to 72 hours. Definitive biliary decompression can then be performed on an elective basis. Approximately 20% of patients with acute cholangitis fail to respond to conservative treatment and require urgent biliary drainage, usually best accomplished by ERCP. Percutaneous transhepatic biliary drainage or surgical biliary decompression carry significantly higher morbidity and mortality. Emergency cholecystectomy is not indicated in acute cholangitis, but should be considered after the acute illness resolves. In most cases of acute cholangitis, abdominal CT is unlikely to provide additional diagnostic information and may delay institution of
antibiotic therapy and biliary drainage. Abdominal CT may be useful to exclude other causes of abdominal pain and fever.


11. Which one of the following is true about gallbladder polyps?
A. They are primarily found among patients with symptomatic cholelithiasis
B. The most common histologic type is inflammatory
C. The risk of malignant transformation approaches 50% at 15 years
D. Elective cholecystectomy is indicated when polyps >18 mm are detected
E. Polyps <10 mm in size require cholecystectomy in the presence of asymptomatic cholelithiasis

The recommended response is D.

Gallbladder polyps are often incidentally detected by ultrasonography when performed among asymptomatic patients for other reasons (Hyperlink to Gallbladder polyps section). Prevalence rates are estimated at 1-4% in the general population. The most common histologic type of polyps is cholesterol-based, followed by inflammatory and adenomatous types. Cholesterol polyps are usually less than 10 mm in diameter and are echogenic without acoustic shadowing. Endoscopic ultrasound (EUS) has high accuracy in distinguishing cholesterol polyps from other lesions of the gallbladder wall, including adenomyomatosis. Natural history studies suggest that a less than 10% risk for malignant transformation over 15 years is associated with gallbladder polyps. For most polyps <10 mm in diameter in the absence of symptomatic cholelithiasis, operative treatment is generally not indicated. Surveillance by abdominal ultrasonography at 3-to-6 month intervals to ensure polyp stability has been recommended. Otherwise, the treatment of choice for symptomatic cholelithiasis and polyps<10 mm in diameter is cholecystectomy.
Polyps between 10-18 mm in diameter independent of cholelithiasis have a small but appreciable risk for developing into carcinoma. Thus, cholecystectomy is recommended in patients who are acceptable operative candidates. A significant risk for carcinoma does appear to be associated with polyps>18 mm and requires cholecystectomy if possible.


12. A 65-year-old man presents with postprandial abdominal pain over the past month. The pain is located in the epigastrium, reaches a plateau of intensity after 15 minutes, and generally lasts up to 3 hours before slowly subsiding. Vomiting and disphoresis have occurred with these attacks. He is otherwise in good health. On physical examination, he is afebrile and non-tender on palpation in the right upper quadrant and epigastric regions. Laboratory tests show an alkaline phosphatase of 70 IU/L, total bilirubin 1.0 mg/dL, AST 40 IU/L, and ALT 35 IU/L. Ultrasound shows multiple stones in the gallbladder but no stones in the common bile duct or biliary dilation. Which one of the following management options is most appropriate?
A. Laparoscopic cholecystectomy with intraoperative cholangiography
B. Endoscopic ultrasound
C. Preoperative ERCP and sphincterotomy followed by laparoscopic cholecystectomy
D. Laparoscopic cholecystectomy and postoperative ERCP with sphincterotomy
E. ERCP with possible sphincterotomy and stone extraction.

The recommended response is A.

This patient presents with symptoms and signs suggestive of biliary colic (Hyperlink to Treatment of Gallstone Related Disorders section). Ultrasonographic findings in uncomplicated biliary colic include
cholelithiasis without pericholecystic fluid, and occasionally gallbladder wall thickening if a history of repeated episodes is elicited. Serum hepatic biochemistries are often normal during episodes of biliary colic. The treatment of choice for uncomplicated biliary colic is laparoscopic cholecystectomy. The universal use of preoperative ERCP to rule out common bile duct stones followed by laparoscopic cholecystectomy is not currently recommended based on improvements in techniques of intraoperative cholangiography and stone extraction. If choledocholithiasis is documented preoperatively, the choice of intraoperative or postoperative stone extraction depends on local expertise. Postoperative ERCP is indicated if common bile duct stones are diagnosed intraoperatively but not removed. If choledocholithiasis were clinically suspected pre-operatively (for example, if the alkaline phosphatase and bilirubin levels were elevated), then an endoscopic ultrasound exam, followed by an ERCP, or a preoperative ERCP alone, would be reasonable. Because there are no obvious contraindications as an operative candidate and because there is no clinical evidence of choledocholithiasis, this patient should undergo cholecystectomy with intraoperative cholangiography.

13. A 60-year-old woman presents with an 8 hour history of epigastric and right upper quadrant pain, low-grade fevers, and nausea and vomiting. On physical examination, her temperature is 101.4°F, pulse 110, blood pressure 110/65. Abdominal examination is remarkable for tenderness in the right upper quadrant, severe enough to cause an inspiratory pause. She is not jaundiced. Which one of the following radiologic findings is least likely?

A. Air in the gallbladder wall on plain abdominal radiographs
B. Dilated intra- and extrahepatic bile ducts with multiple small gallstones on ultrasound.
C. Thickened gallbladder wall with a pericholecystic fluid collection on ultrasonography
D. Visualization of the liver, common bile duct, and small bowel on hepatobiliary scintigraphy
E. Porcelain gallbladder.
The recommended response is E.

The 7 hour duration of symptoms and low-grade fever are atypical for uncomplicated biliary colic. Pain lasting greater than 6 hours should raise suspicion for acute cholecystitis (Hyperlink to Treatment of Gallstone Related Disorders section). In addition, on physical examination, Murphy’s sign (an inspiratory pause during palpation of the right upper quadrant) was found. This patient most likely has acute calculous cholecystitis. On abdominal ultrasound, typical radiologic findings of acute cholecystitis include a thickened gallbladder wall and a pericholecystic fluid collection. Abdominal CT will also be abnormal with similar findings. Air in the gallbladder wall can be found in acute cholecystitis, but is relatively uncommon and indicates emphysematous cholecystitis. The finding of dilated intra- and extrahepatic bile ducts are more characteristic of extrahepatic biliary obstruction than of acute cholecystitis, but the clinical scenario depicted could also be due to choledocholithiasis. On hepatobiliary scintigraphy, the gallbladder is typically not visualized, despite visualization of the liver, common bile duct, and small intestine, in patients with acute cholecystitis. A porcelain gallbladder is associated with gallbladder cancer. While non-specific signs and symptoms that mimic those of benign biliary tract disease may occur in patients with gallbladder cancer, the acute presentation with fever as well as the statistical likelihood of cancer of this organ, makes this finding least likely.

14. The following are true statements regarding Alagille syndrome except:
A. The diagnosis is most often made in early adulthood.
B. Patients have characteristic facial features.
C. The syndrome is due to mutations in the JAG1 gene, which codes for a ligand for the Notch family of receptors that are important in fetal biliary ductal development.
D. The syndrome is characterized by a paucity of interlobular bile ducts.
E. Cirrhosis occurs rarely.

The recommended response is A.
Syndromic paucity of interlobular bile ducts is also called Alagille syndrome, and is an autosomal dominant disorder due to mutations in the JAG1 gene, which encodes the Jagged 1 ligand for the Notch family of receptors. The diagnosis is usually made in infancy. Intrahepatic cholestasis and biliary hypoplasia are characteristic, with patients developing pruritus and hepatomegaly. Extrahepatic manifestations include congenital heart defects, notched butterfly vertebrae, eye defects and a characteristic triangular face with a broad forehead and a pointed chin. Cirrhosis occurs rarely, and the cholestasis is mild. Orthotopic liver transplantation for severe symptomatic liver disease in the absence of cirrhosis has been advocated.


15. A 28-year-old woman presents with chronic, intermittent abdominal pain and symptoms of gastroesophageal reflux disease. Physical examination is unremarkable. Medical therapy with proton pump inhibitors fails to resolve the pain after 8 weeks. Abdominal ultrasound shows fusiform dilation of the common bile duct, without abnormalities of the cystic duct or intrahepatic ducts, and no evidence for cholelithiasis. CT confirms these findings. Which one of the following is true?

A. Hepatobiliary scintigraphy is useful for planning further therapy.
B. ERCP with sphincterotomy is the preferred treatment.
C. Pancreatitis is not a reported complication of this condition.
D. Surgical drainage without resection is the preferred method of treatment.
E. Malignancy in the biliary tree is a reported complication.

The recommended response is E.

The patient has a type I choledochal cyst as the cause of symptoms (Hyperlink to Biliary Cysts section).
Choledochal cysts are congenital abnormalities with a female predominance and varying incidence worldwide. Although cysts are anatomically quite variable, they have many features in common including intermittent abdominal pain and/or jaundice. Reported complications of choledochal cysts include recurrent cholangitis, pancreatitis, biliary cirrhosis, liver abscess, or cyst rupture. The most ominous complication, however, is malignancy (primarily adenocarcinoma).

Ultrasonography is the best diagnostic technique for identifying choledochal cysts. Hepatobiliary scintigraphy findings are nonspecific, and would not help in planning further treatment. CT and MRI are useful to confirm the diagnosis. Cholangiography by PTC or ERCP is useful in defining the anatomy of the cyst and planning surgical intervention, but there is no role for sphincterotomy. The preferred surgical management for type I or type IV cysts is cyst excision and reconstruction of the extrahepatic biliary tree. Type II cysts should be excised, while treatment for type III cysts varies depending on the anatomy. Treatment of intrahepatic cysts (type IVA or V) depends upon the extent of liver involvement. Long-term postoperative follow-up is recommended, since recurrent cholangitis, stone formation, strictures, and pancreatitis have been reported. Cyst excision lowers, but does not completely eliminate the risk of malignancy, since cancer may develop in other portions of the hepatobiliary tree.


16. A 45-year-old man with ulcerative colitis in clinical remission presents with progressive fatigue, pruritus and jaundice. On physical examination, there is scleral icterus and hepatomegaly without ascites. Laboratory values show an alkaline phosphatase of 850 IU/L, total bilirubin 5.5 mg/dL, AST 80 IU/L, ALT 95 IU/L. Ultrasound shows dilated intrahepatic ducts without choledocholithiasis. ERCP shows intrahepatic strictures with intervening saccular dilatations as well as a high-grade obstruction involving the mid-common bile duct consistent with primary sclerosing cholangitis (PSC). Endoscopic biliary stent
placement for biliary decompression is performed. Repeated ERCPs with endoscopic biopsies and
brushings reveal atypical cells suspicious for dysplasia but no definitive features of carcinoma are
identified. Which one of the following statements about this patient’s condition is true?
A. The simultaneous finding of PSC and cholangiocarcinoma at initial diagnosis is rare.
B. Serum CA19-9 and CEA levels will not provide additional aid in making the diagnosis.
C. Cirrhosis is not required for the development of cholangiocarcinoma in PSC
D. Serum antimitochondrial antibody (AMA) is positive in 90% of cases
E. Brush cytology will reveal the diagnosis of cholangiocarcinoma in 95% of affected patients

The recommended response is C.

Patients with primary sclerosing cholangitis (PSC) will develop cholangiocarcinoma at rates varying
between 5-20% in most reported series (Hyperlink to Primary Sclerosing Cholangitis and to
Cholangiocarcinoma sections). Conversely, 30-40% of patients will have cholangiocarcinoma at the time
PSC is diagnosed. While cholangiocarcinoma often develops as a late complication of long-standing
PSC, up to 20% of cholangiocarcinomas are found at the initial diagnosis of PSC. Risk factors for
developing cholangiocarcinoma in PSC may include coexistent colonic dysplasia from ulcerative colitis
and cigarette smoking\(^{19,20}\). Typical symptoms include right upper quadrant pain, pruritus, jaundice, and
unexplained weight loss. Cholangiocarcinoma is a leading cause of death in PSC (median survival from
diagnosis, 5 months). A number of investigations have suggested that elevated serum CA 19-9 and/or
CEA are predictive of cholangiocarcinoma among patients with PSC, with higher values being more
specific. Cirrhosis from PSC is not universally required for the development of cholangiocarcinoma.
Serum antimitochondrial antibody (AMA) is rarely positive in patients with PSC and has not been
recognized as a marker for cholangiocarcinoma development. ERCP is indicated for anatomic definition,
biopsy or brush cytology, and biliary decompression by stent placement for distal obstructing lesions.
Brush cytology alone in diagnosing cholangiocarcinoma is accurate in only 75% of cases.

17. A 68-year-old man in the ICU with major burns over 70% of his body is noted to have a rise in his WBC along with fever. He has been intubated and on TPN for 2 weeks. Abdominal examination is difficult due to his extensive dressings, and his level of sedation. Laboratories include: WBC 17,000/mm³ with a “left shift,” AST 60 IU/L, ALT 65 IU/L, total bilirubin 1.5 mg/dL, alkaline phosphatase 130 IU/L.

Imaging of the abdomen with ultrasound shows gallbladder wall thickening, pericholecystic fluid, with no evidence of gallstones or sludge. All of the following statements are true regarding this condition except:

A. In patients who are not candidates for cholecystectomy, placement of a cholecystostomy tube is often helpful
B. Plain abdominal films will show free air under the diaphragm
C. Mortality rates between 10-50% have been reported
D. A high index of suspicion is needed to diagnose this condition as signs and symptoms can be minimal
E. False-positive results from prolonged fasting limit the accuracy of hepatobiliary scintigraphy

The recommended response is B.

This patient presents with a clinical picture consistent with acalculous cholecystitis (Hyperlink to Acute Acalculous Cholecystitis section). Ultrasonography or abdominal CT will show a thickened gallbladder with pericholecystic fluid but no stones. Additional findings may include sloughed mucosal membranes or air in the gallbladder wall. Sludge may be present with recent fasting. Plain abdominal radiographs will likely have only nonspecific findings; free air under the diaphragm indicates that another diagnosis is likely. Hepatobiliary scintigraphy will usually be abnormal with a nonvisualized gallbladder, but this test has its limitations due to the prolonged fasting state of these patients. The initiating event usually involves hypotension and ischemia, with bacterial infection occurring secondarily. Complications may develop more quickly in this disorder than in classic calculous cholecystitis, and up to 70% of patients
will have gangrene, empyema, or perforation of the gallbladder at the time of surgery. Mortality rates as high as 50% have been reported. Percutaneous cholecystostomy is a reasonable management option in these patients, who are often at high operative risk.


18. A 53-year-old man presents with his third episode of acute pancreatitis. He denies significant alcohol intake and is not using any medications. Laboratory values are normal except for elevations in serum amylase and white blood cell count. Gallbladder ultrasound shows no evidence of gallstones or biliary ductal dilation. Which one of the following is true?
A. Cholecystectomy will not prevent future episodes of pancreatitis.
B. Sludge is unlikely to be the cause of pancreatitis in this patient since it was not demonstrated on ultrasound.
C. He is likely to have a family history of severe hyperlipidemia.
D. The absence of gallstones on ultrasound rules out a biliary cause of pancreatitis.
E. Duodenal bile aspiration and microscopy may define an etiology for his pancreatitis.

The recommended response is E.

This patient presents with “idiopathic” pancreatitis, without demonstrable gallstones, significant alcohol intake, use of medications commonly associated with pancreatitis, hypercalcemia, or hyperlipidemia. Up to 70% of patients with “idiopathic” pancreatitis have biliary sludge as the etiology (Hyperlink to Diagnostic Studies for Gallstone Related Disorders section). Biliary sludge, a mixture of particulate matter in viscous bile, is also commonly called microlithiasis. Sludge may be missed in up to 50% with ultrasonography alone, and therefore the absence of gallstones does not rule out a biliary cause of pancreatitis. The gold standard for the diagnosis of biliary sludge or microlithiasis is duodenal bile
aspiration and microscopy. If sludge can be demonstrated, cholecystectomy will prevent future episodes of pancreatitis.


19. Which one of the following is true regarding laparoscopic cholecystectomy?
A. Post-surgery recovery times are shorter with open cholecystectomy than with laparoscopic cholecystectomy
B. Conversion to open cholecystectomy is required in 5% of cases.
C. Risks related to anesthesia are significantly lower with laparoscopic cholecystectomy than with open cholecystectomy.
D. If there is a bile duct leak after laparoscopic cholecystectomy, it may be managed expectantly.
E. If common bile duct stones are found during surgery, conversion to an open cholecystectomy will be required.

The recommended response is B.

Early in a surgeon’s experience, complication rates with laparoscopic cholecystectomy are higher than those with an open procedure (Hyperlink to Treatment of Gallstone Related Disorders and Optimal Management sections). As experience is gained, complication rates become fairly similar to open cholecystectomy. In general, recovery times are faster following laparoscopic cholecystectomy compared to the open route, which was an important factor in the rapid acceptance of this technique. Conversion to open cholecystectomy is required in about 5% of cases, and is often due to surrounding inflammation or difficulty in defining the biliary tract anatomy. Risks related to anesthesia with laparoscopic cholecystectomy may be somewhat higher than with the open procedure, due to the induction of pneumoperitoneum and placement of the patient in the Trendelenberg position, although respiratory risks
in general are lower with the laparoscopic route. Postoperative bile duct leaks usually come from the biliary duct radicals or the cystic duct stump. They usually require endoscopic stenting or surgical repair for management. Patients found to have common bile duct stones during surgery may undergo either laparoscopic stone extraction, if the surgeon has experience with this procedure, or postoperative ERCP with stone extraction. Conversion to open cholecystectomy for bile duct stones diagnosed intraoperatively is relatively rare.


20. A 45-year-old woman presents with intermittent episodes of right upper quadrant pain suggestive of biliary colic. Ultrasound demonstrates numerous small stones within the gallbladder. Laparoscopic cholecystectomy is performed for treatment. Histologic examination of the gallbladder reveals cholelithiasis and a 2 centimeter polypoid lesion histologically consistent with localized gallbladder carcinoma. Which one of the following statements is true?
A. Gallstones are found in up to 20% of patients with gallbladder carcinoma
B. The 5-year survival of patients with incidental gallbladder carcinoma at cholecystectomy is 5%
C. Adjuvant radiation therapy is indicated.
D. Most patients diagnosed with gallbladder carcinoma are symptomatic at presentation.
E. If the patient has locally advanced or metastatic disease, the 5-year survival is 30%.

The recommended response is D.

This patient has symptomatic gallstones and an incidentally found gallbladder carcinoma (Hyperlink to Gallbladder Carcinoma section). Gallstones are present in 80% of persons with gallbladder carcinoma, but no causal association has been established. Conversely, an estimated 1% of all patients undergoing cholecystectomy for cholecystitis are discovered to have carcinoma. Risk factors include ethnicity
(Alaskan or American Indian), a previous history of cholecystenteric fistula (15%) or porcelain
gallbladder (20-60%), Mirizzi’s syndrome and *Salmonella typhi* carriage.

Symptoms are often similar to benign gallbladder disease including epigastric/right upper quadrant pain,
nausea, and fever. Abdominal ultrasonography may be negative, demonstrate cholelithiasis, or reveal a
large polypoid lesion with abnormal gallbladder wall thickening. Cross-sectional imaging is required to
exclude local and metastatic spread of disease. Surgical resection offers the only substantial chance for
cure especially for incidentally discovered malignancies. In this setting, there is no indication for
adjuvant radiation or chemotherapy. Overall, the 5-year survival for resectable gallbladder carcinoma is
approximately 60%. The median survival rate for unresectable patients is approximately 5 months. The
use of either radiation therapy or chemotherapy in nonresectable cases of gallbladder carcinoma is also
associated with poor survival outcomes.

Bartlett DL, Fong Y, Fortner JG, et al. Long-term results after resection for gallbladder cancer:

21. A 45-year-old woman is referred for evaluation of chronic right upper quadrant pain that has been
present for 2 years. The pain is described as steady. It is localized to the RUQ, but can radiate to the
LUQ, and is not exacerbated or relieved by eating or defecation. The pain persisted after her
cholecystectomy one year ago. Laboratory values showed an AST=23, ALT=40, total bilirubin 1.0 and
alkaline phosphatase=78. A transabdominal ultrasound showed the common bile duct to be 7.5 mm in
diameter. The most likely cause of this patient’s pain is:

A. Retained common bile duct stone
B. Sphincter of Oddi dysfunction
C. Biliary microlithiasis
D. Papillary stenosis
E. Chronic functional abdominal pain

The recommended response is E.

Differentiating biliary pain from other types of abdominal pain is a key aspect of the history which determines the need for further diagnostic testing (Hyperlink to Diagnostic Studies section). As some of the diagnostic tests that can be offered, such as ERCP with sphincter of Oddi manometry, carry significant morbidity, obtaining a good history is critical to the management of these patients. This is particularly relevant for the situation where liver function tests are normal and transabdominal ultrasound shows extrahepatic bile ducts that are less than or equal to 10 mm in diameter (i.e. those patients that could potentially be classified as having type III Sphincter of Oddi dysfunction).\(^{15}\) Constant pain that is present 24 hours a day for a duration of several years is not consistent with a biliary source. It is not exacerbated by eating, relieved by defection or accompanied by diarrhea. Rather, biliary pain characteristically lasts from 30 minutes up to several hours, with pain-free intervals between attacks. In this patient, the pre-test probability of having any condition other than chronic functional abdominal pain is low. A retained common bile duct stone is less likely with her history and diagnostic test results; imaging studies such as with an MRCP or EUS can rule this out, but is not clearly indicated in this patient. Biliary microlithiasis is unlikely, given the patient’s history of a cholecystectomy, but can be ruled out by upper endoscopy with collection of duodenal bile for microscopic analysis for cholesterol crystals. Likewise, papillary stenosis is unlikely given the lack of dilation of the extrahepatic bile ducts on ultrasound.

A 41-year-old man with a history of ulcerative colitis and primary sclerosing cholangitis is found to have a total bilirubin of 8.9 mg/dl during a routine blood draw at his primary care provider’s office. His alkaline phosphatase is 238 mg/dl, but his AST and ALT are within normal limits. The patient has had several bouts of fever, chills and jaundice which required antibiotics approximately one year ago. He has noted recently that his weight has declined by 10 lbs. Currently, the patient denies any abdominal pain. On physical exam, the patient is afebrile, with normal vital signs, and he is alert. He has icteric sclerae. His abdomen is soft and nontender. A transabdominal ultrasound shows dilated intrahepatic bile ducts, but this appears unchanged from a previous ultrasound obtained 2 months prior. What is the most appropriate next step in establishing a diagnosis?

A. Check serum CEA
B. Order a contrast-enhanced, triple phase helical CT scan
C. Order an MRCP
D. Schedule an endoscopic ultrasound
E. Schedule an EGD

The recommended response is C.

In a patient with PSC, a high index of suspicion must be kept for the possibility of development of cholangiocarcinoma (Hyperlink to Cholangiocarcinoma section). The diagnosis of cholangiocarcinoma can be difficult because of the wide range of alternative diagnoses that can be present, including bile duct strictures due to PSC itself, choledocholithiasis, iatrogenic bile duct injuries, and other cancers such as gallbladder cancer and metastatic hilar nodal metastases. In this case, each of the options listed can be helpful in leading to the diagnosis of cholangiocarcinoma. However, the choice of test to order depends on the clinical scenario. CEA is a serum tumor marker that is more often associated with colorectal carcinoma. CA19-9 is a serum tumor marker that has an estimated sensitivity and specificity for predicting cholangiocarcinoma in patients with PSC that ranges from 38-89% and 50-98%, respectively. While a dynamic CT scan is a reasonable option, an MRCP has several potential advantages over CT.
Besides identifying intrahepatic mass lesions, MRCP can provide a detailed 3-D reconstruction of the biliary tree. These non-invasively acquired images are comparable to those obtained by invasive studies (ERCP or PTC). MRCP also has the advantage over ERCP that bile ducts can be visualized without introduction of potentially infected contrast into the biliary system. ERCP has the advantage of sampling ducts using brushings or pinch biopsy, and would be the procedure of choice if MRCP showed changes suggestive of cholangiocarcinoma that was accessible via this route. A more proximal lesion might require a percutaneous approach under ultrasound or CT guidance. EUS, which can provide more accurate imaging of associated lymphadenopathy, can also be used for sampling of tissue in a manner that avoids the risk of inducing cholangitis.


23. A 22-year-old woman presents to your clinic with a chief complaint of severe epigastric pain that occurred on two separate occasions separated by 3 weeks. On the first occasion, the pain came on gradually over 15 minutes and lasted 2 ½ hours, before subsiding slowly over the next hour. The patient recalled that this had occurred in mid-morning, when she was nursing her 1 month old infant. The second episode occurred on the evening preceding her clinic visit, and lasted 1 hour, and was less severe. You order serum biochemical studies including AST, ALT, total bilirubin, alkaline phosphatase, amylase and lipase; these are within normal limits. A transabdominal ultrasound shows a normal appearing gallbladder, without sludge or stones, and normal caliber intrahepatic and extrahepatic bile ducts. The most likely cause of the patient’s symptoms is:

A. Intermittent obstruction of the cystic duct with a gallstone.
B. Passage of biliary sludge causing acute pancreatitis.
C. Sphincter of Oddi dysfunction.
D. Gallbladder dysmotility
E. Biliary colic induced by microlithiasis.
The recommended response is E.

The patient’s symptoms are suggestive of biliary colic, as they present with discrete attacks of severe epigastric pain (Hyperlink to Clinical Course and Complications section). Each of the choices listed (with the exception of acute pancreatitis) classically presents with symptoms that are consistent with biliary colic. In this case, the attacks occurred when the patient was in the post-partum state. Pregnancy is known to induce conditions that are conducive to the formation of microlithiasis and gallstones in the gallbladder. This is due to several factors that favor cholesterol crystallization in bile, including cholesterol supersaturation of bile due to estrogen effects, and gallbladder hypomotility due to the effect of progestins. In a study of over 3,000 pregnant women, sludge or stones were found in ~10% of women by 4-6 weeks post partum. Regression of microlithiasis or stones was noted following pregnancy in a significant number of these women. In this case, sphincter of Oddi dysfunction and gallbladder dysmotility are possible, but are less likely than biliary colic induced by either microlithiasis or gallstones. Of the latter options, microlithiasis is more likely to regress in the time frame depicted, although passage of a gallstone is also a possibility. The lack of elevation of serum biochemical markers and the lack of biliary tract ductal dilation on ultrasound point to the former scenario as being more likely. The time course of her symptoms and the nature of her pain argue against acute pancreatitis as the etiology.


24. An 80-year-old woman presents with a complaint of diffuse epigastric pain that has been present off and on since the patient’s cholecystectomy done for gallstones 5 years prior. The pain can be exacerbated following meals, but this is not a consistent event. She underwent an EGD 3 months prior, which revealed chronic gastritis, with H. pylori organisms identified. She was subsequently treated with antibiotics and a proton-pump inhibitor, and H. pylori eradication was documented with a negative urease
breath test. Despite this, her symptoms have persisted. She has noted a gradual weight loss over 5 years of about 5 lbs, although she reports a good appetite. She also has hepatitis C virus infection. Her liver tests showed an ALT = 54 and an AST = 57 when last checked 3 months prior. Repeat labs show an AST = 39, ALT = 38, total bilirubin = 0.7, and alkaline phosphatase = 73. A CT scan of her abdomen is ordered, and this shows an absent gallbladder, and an 8 mm diameter common bile duct. A calcified lesion apparently located within the intrapancreatic portion of the common bile duct is noted. What is the most appropriate next step?

A. Schedule an ERCP
B. Schedule an EUS, with plans to proceed to an ERCP if choledocholithiasis is confirmed.
C. Schedule an MRCP
D. Reassure the patient
E. Repeat CT with contrast in 3 months.

The recommended response is B.

This patient has symptoms that are difficult to characterize, and are not entirely characteristic for biliary colic. Nevertheless, biliary colic is finally a clinical diagnosis, so that the entire clinical context must be evaluated carefully to determine what is the best means of proceeding. The findings on the CT scan bring up the possibility of choledocholithiasis (Hyperlink to Diagnostic Studies section). Choledocholithiasis is a condition that should prompt further evaluation leading to removal of stones within the common bile duct, as such stones are at risk for causing cholangitis, even in the situation where the patient is asymptomatic or the symptoms are not characteristically of biliary origin. Imaging of the biliary system can be accomplished by several means, each of which carries risks and benefits. While ERCP would be the most comprehensive approach, as it would afford the means to provide therapy to remove common bile duct stones, in this patient, the possibility of a calcific lesion originating from the head of the pancreas extrinsic to the common bile duct also needs to be considered as CT scan is not the most
accurate modality for imaging the common bile duct. Furthermore, the risks of ERCP need to be considered in this elderly patient. Alternatives include MRCP and EUS. While MRCP could be performed in this patient, the most appropriate approach would be to schedule the EUS with an ERCP to follow if the EUS confirms choledocholithiasis.\textsuperscript{11,12} Reassuring the patient, or waiting and repeating the CT scan in 3 months are not recommended.


25. A 65-year-old man presents with an ultrasound report that states that a 5 mm polyp is present in his gallbladder. The patient is asymptomatic from a GI perspective, and he specifically denies abdominal pain, weight loss, or jaundice. The ultrasound was obtained because his primary care provider was concerned about a pulsatile mass on his abdominal exam, which turned out to be an aortic abdominal aneurysm measuring 5 cm in diameter. You recommend a cholecystectomy. The patient undergoes surgery, but one week following the operation the surgeon calls to say that the pathology report indicates that the gallbladder was normal, with no polyp found. The patient then makes an appointment to discuss why he underwent an unnecessary operation. What is the most effective management strategy?

A. Consult with an official from the Risk Management department at your institution or your malpractice insurance company.
B. Reiterate the justifications for proceeding with surgery to the patient.
C. Ask for a second opinion from another pathologist.
D. Review the ultrasound with a radiologist.
E. Order an MRCP.
The recommended response is A.

False positive findings of polypoid lesions on transabdominal ultrasound imaging has been noted to occur at a rate ranging from 6 to 43% (Hyperlink to Gallbladder Polyps section). Therefore, occasionally a patient will undergo cholecystectomy for suspected polypoid lesions of the gallbladder for which no lesions are found in the resected specimen. This may occur because of mucosal folds, sludge, or small stones impacted in the gallbladder wall. Polyps and stones may also be dislodged when the organ is palpated or handled laparoscopically during the operation. Due to these possibilities, patients should be informed before the operation of finding a gallbladder without a polyp, or of finding stones instead of a polyp. This information should be included in the informed consent discussion prior to the operation. In this case, an additional confounding factor is that polyps less than 1 cm in size that are found incidentally in an asymptomatic patient are unlikely to be malignant. Therefore, the rationale for pursuing a cholecystectomy is less defensible than if the polyp size on the initial ultrasound were greater than 1 cm. The literature suggests that polyps greater than 18 mm are at greatest risk for malignancy. The best strategy would be to share this information with the patient and admit that the rationale for recommending cholecystectomy was not as strong as if the polyp had been larger. It would also be prudent to consult with an official from the Risk Management department at your institution or your malpractice insurance company in case the patient decides to pursue litigation. At this juncture, review of the initial ultrasound, a review of the pathology report, or an MRCP are not likely to affect subsequent events.


26. A 50-year-old man presents with progressive jaundice, pruritus, and weight loss for 3 months. Laboratory investigations show direct hyperbilirubinemia and high alkaline phosphatase. CT scan shows dilated intrahepatic bile ducts. The findings from ERCP and EUS are shown in Figures 16A and 16B. Which of the following techniques is most likely to demonstrate the diagnosis of this condition?

A. Bile cytology
B. Brushing cytology
C. Endobiliary forceps biopsy
D. Endoluminal FNA
E. EUS-guided FNA

The recommended response is E.

The radiographic figure from ERCP shows a complex common hepatic duct stricture at the confluence with proximal extension into both the right and left intrahepatic ducts. The endosonographic evaluation shows a 2.4 cm lesion surrounding the common hepatic duct. These findings are consistent with Bismuth-Corlette type IV cholangiocarcinoma.

Cholangiocarcinoma remains a very challenging neoplasm to diagnose preoperatively. Although, the radiographic appearance of bile ductal strictures, in particular contour abnormalities, shape, and borders of the stenosis are helpful, these criteria cannot reliably differentiate benign from malignant lesions. Several diagnostic modalities for cytologic diagnosis have been evaluated.
Cytology from bile duct aspiration and brushings across the dominant stricture at the time of ERCP represent the conventional methods currently used, with reported diagnostic sensitivities of only 6-32% and 15-69%, respectively. Endobiliary forceps biopsy of the stricture has been reported to enhance the sensitivity to 43-88%. Triple-tissue sampling at ERCP combining brush cytology, endobiliary forceps biopsy, and endoluminal FNA has the highest reported sensitivity of 77%.

The role of EUS with FNA for the diagnosis of cholangiocarcinoma has been investigated recently. With its high-resolution imaging, EUS can clearly visualize and follow the bile duct. EUS-guided FNA is a well-established method of tissue diagnosis for lesions in the pancreas and for masses near the bowel wall. Using similar approaches, EUS-guided FNA has also been demonstrated to have an extremely high accuracy in 2 prospective studies of 44 and 28 patients with a sensitivity of 89% and 86%, and an accuracy of 91% and 88%, respectively. Thus, EUS-guided FNA appears to be the most accurate modality for diagnosis of cholangiocarcinoma, especially in patients with a high clinical suspicion. However, these studies were performed in non-primary sclerosing cholangitis patients. Therefore, the role of EUS in identifying cholangiocarcinoma in primary sclerosing cholangitis remains unclear and requires further investigations.


Case 22: Post-cholecystectomy bile duct stricture

27. A 44-year-old woman presents with persistently abnormal liver chemistries and a low-grade fever. She underwent laparoscopic cholecystectomy for symptomatic cholelithiasis 6 months ago. A cholangiogram is shown in Figure 17. Which of the following is the most appropriate management?

A. ERCP with balloon dilation of bile duct  
B. ERCP with balloon dilation followed by placement of plastic biliary endoprosthesis  
C. ERCP with placement of self-expandable metallic biliary endoprosthesis  
D. ERCP with placement of iridium implants for brachytherapy  
E. Surgical exploration and bile duct decompression

The recommended response is B.

A cholangiogram from ERCP shows the classic appearance of benign biliary stricture with proximal biliary ductal dilation. The most common cause of benign biliary stricture is iatrogenic
bile duct trauma during cholecystectomy. With the widespread use of the laparoscopic approach, the rate of iatrogenic bile duct injuries has increased significantly with the reported incidence of 0.16-2.35%. Despite worldwide expertise in the procedure, reports from the United States have demonstrated no decline in the annual incidence with time. A number of risk factors have been well described, including severe inflammation, bleeding, anatomical variations, and lack of surgical experience. The less frequent causes of benign biliary stricture include external trauma, intra-arterial chemotherapy, primary sclerosing cholangitis, liver transplantation, congenital stenosis, or external compression from chronic pancreatitis, hilar lymphadenopathy, or pancreatic pseudocyst. Patients often present with signs, symptoms, and biochemical evidence of biliary obstruction. Superimposed infection or cholangitis can also develop. Unlike a bile duct transection or complete occlusion, which is usually detected intraoperatively or immediately during the postoperative period, bile duct trauma that progresses to stricture formation often takes months to years to become clinically apparent. These consequences cause significant morbidity and mortality, and also have a significant economic impact.

Surgical treatment of benign biliary stricture remains challenging even for surgeons who specialized in hepatobiliary surgery. In addition, it is associated with significant morbidity, mortality, and recurrence rates, necessitating repeat operation in 10-35% of patients. Therefore, a trial of endoscopic treatment by placement of endoprosthesis is appropriate, especially in mild case. In addition, initial nonoperative management does not preclude subsequent surgery. The initial choice between operative and nonoperative treatment also depends on local expertise. The endoscopic approach is a preferred method over percutaneous transhepatic therapy because of greater patient comfort and reduced complications related to leakage or hemorrhage. In the
patients with partial gastrectomy and Billroth II gastroenteric anastomosis, the ampulla can still be reached in the vast majority of patients and though occasionally challenging ERCP is still the method of choice.

Balloon dilation alone of the bile duct is sometimes effective for treatment of benign biliary stricture after cholecystectomy but usually requires multiple sessions and would not be an acceptable alternative in this patient who has coexisting cholangitis. The adequate biliary drainage must be established by the placement of biliary endoprosthesis. Several studies with long-term follow-up have been reported. Prolonged placement of biliary endoprosthesis, typically in conjunction with balloon dilation, appears to be the safest and most effective endoscopic treatment with 70-88% of the patients symptom-free without biochemical evidence of persistent obstruction. The site of stricture is also an important factor in predicting response to endoscopic treatment. Hilar lesions are the most challenging to treat endoscopically. The optimal duration of endoprosthesis placement is unknown and varies depending on the severity of stricture, cause, and individual patient. The goal is to dilate the stricture to have a diameter similar to the surrounding bile duct.

Use of metallic endoprosthesis has been reported to provide longer periods of patency compared to plastic endoprosthesis for malignant biliary stricture. However, it may be less effective for benign biliary stricture because of more frequent recurrence of stricture at the margins of endoprosthesis. In addition, subsequent surgical treatment is very difficult and occasionally impossible when metallic endoprosthesis has been placed. Brachytherapy with iridium implants can be considered for malignant lesion, but not indicated for benign stricture.


28. A 40-year-old woman with a past medical history significant for diabetes mellitus presents to emergency room with abdominal pain, fever, and jaundice. Laboratory studies show serum total bilirubin level of 4.3 mg/dL, serum alkaline phosphatase level of 334 U/L, serum AST level of 90 U/L, and serum ALT level of 60 U/L. Transabdominal ultrasonography shows cholelithiasis and mildly dilated intrahepatic bile ducts. ERCP findings are as shown in Figure 18. Which of the following is the most appropriate management?

A. Sphincterotomy and removal of the impacted stones  
B. Brush cytology and placement of metallic biliary endoprosthesis  
C. Insertion of a nasobiliary drain or temporary plastic biliary endoprosthesis followed by operative management  
D. Endoscopic balloon dilation  
E. Oral administration of ursodeoxycholic acid
The recommended response is C.

The radiographic figure shows an extrinsic compression of common bile duct, consistent with Mirizzi’s syndrome. This condition is a relative rare complication of long standing gallstone disease in which a stone becomes impacted in the neck of the gallbladder or the cystic duct and extrinsically compresses the common bile duct with resulting jaundice and bile duct obstruction (type I) or erodes into the common bile duct leading to the formation of a cholecystocholedochal fistula (type II). It is reported in approximately 0.05-1.1% of patients undergoing cholecystectomy. The typical clinical presentation is obstructive jaundice with or without associated cholangitis or cholecystitis. Preoperative ERCP is useful to confirm the diagnosis and determine whether a fistula is present in order to avoid common bile duct injury and operative complication. Surgical dissection of the cystic duct can be difficult and the bile duct may be inadvertently ligated if it is mistaken for the dilated cystic duct. Conventional treatment is generally an open cholecystectomy, although endoscopic stent placement and laparoscopic cholecystectomy have been utilized successfully.

In this patient who has Mirizzi’s syndrome with clinical cholangitis, the most appropriate treatment is an insertion of nasobiliary drain or temporary plastic biliary endoprosthesis to relieve obstruction, followed by definitive surgical management. Occasionally, the appearance of cholangiography at ERCP may resemble a malignant obstruction. Endoscopic attempts at stone removal usually fail because of inability to access or capture the impacted cystic duct stone with a basket or balloon catheter. A variety of endoscopic techniques have been described as alternatives for patients who are at high risk for surgery, including long-term palliative biliary
decompression by placement of plastic biliary endoprosthesis if possible, disimpaction of the stone by mechanical, contact (electrohydraulic), and extracorporeal lithotripsy, and chemical dissolution therapy. Temporary placement of percutaneous cholecystostomy may be considered for patients with cholecystitis to prevent the progression to acute suppurative cholecystitis and septicemia.


29. A 35-year-old woman who underwent laparoscopic cholecystectomy for symptomatic cholelithiasis one week ago presents with jaundice and right upper quadrant abdominal pain. A retrograde cholangiogram is shown in Figure 19. Which of the following is the most appropriate treatment?

A. Balloon dilation of the papilla
B. Placement of plastic biliary endoprosthesis
C. Surgical bile duct repair
D. Placement of metallic biliary endoprosthesis

E. Percutaneous transhepatic drain placement

The recommended response is B.

The retrograde cholangiogram shows a bile leak with extravasation of contrast into the subhepatic space. The most appropriate treatment of this condition is placement of plastic biliary endoprosthesis. Postoperative bile leaks are a well-documented complication of cholecystectomy. With the widespread acceptance of laparoscopic cholecystectomy as the treatment of choice for symptomatic cholelithiasis, the incidence of significant postoperative bile leaks has risen from 0.2-0.5% during the era of open cholecystectomy to approximately 1.1%. The most common origin of bile leaks is cystic duct stump or an accessory cystohepatic duct connecting the gallbladder to the right hepatic duct (duct of Luschka). Most bile leaks are unrecognized at the time of surgery, with a mean delay in making diagnosis of 4-10 days. A high index of suspicion is required and the diagnosis should be suspected in patients with persistent abdominal pain, fever, abnormal liver chemistries, and leukocytosis. Occasionally, symptoms may be atypical, including nonspecific pain in the right shoulder, shortness of breath, and nausea.

ERCP has become the preferred diagnostic and therapeutic modality for clinically significant bile leaks, obviating the need for repeat operation. The goal of endoscopic treatment is to minimize the pressure gradient across the sphincter of Oddi, thereby promoting preferential flow of bile into the duodenum and allowing the leak to heal. This can be successfully achieved by a variety of methods, including biliary sphincterotomy, placement of plastic biliary endoprosthesis (with or without sphincterotomy), or nasobiliary tube drain. Treatment success has ranged from 85% to
100% in most series, with extremely low complication rates. Balloon dilation of the papilla is an alternative treatment, but it is likely to provide only transient reduction in papillary pressure. Therefore, it is unlikely to be effective. Placement of metallic biliary endoprosthesis, percutaneous transhepatic drain, and surgical bile duct repair are alternative options that would likely result in the closure of the leak, but are unnecessarily invasive or permanent. Thus, they should not be considered as the initial treatment.


Figures

Biliary Tract Figure 16A
Biliary Tract Figure 16B
Biliary Tract Figure 17
Biliary Tract Figure 18
Biliary Tract Figure 19