BILIARY SYSTEM AND GALLBLADDER

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Biliary atresia

- Presents as failure to thrive.
- Jaundice.
- Stools are characteristically are pale gray secondary to obstructed bile flow.

Extrahepatic biliary atresia

Rock hard liver.

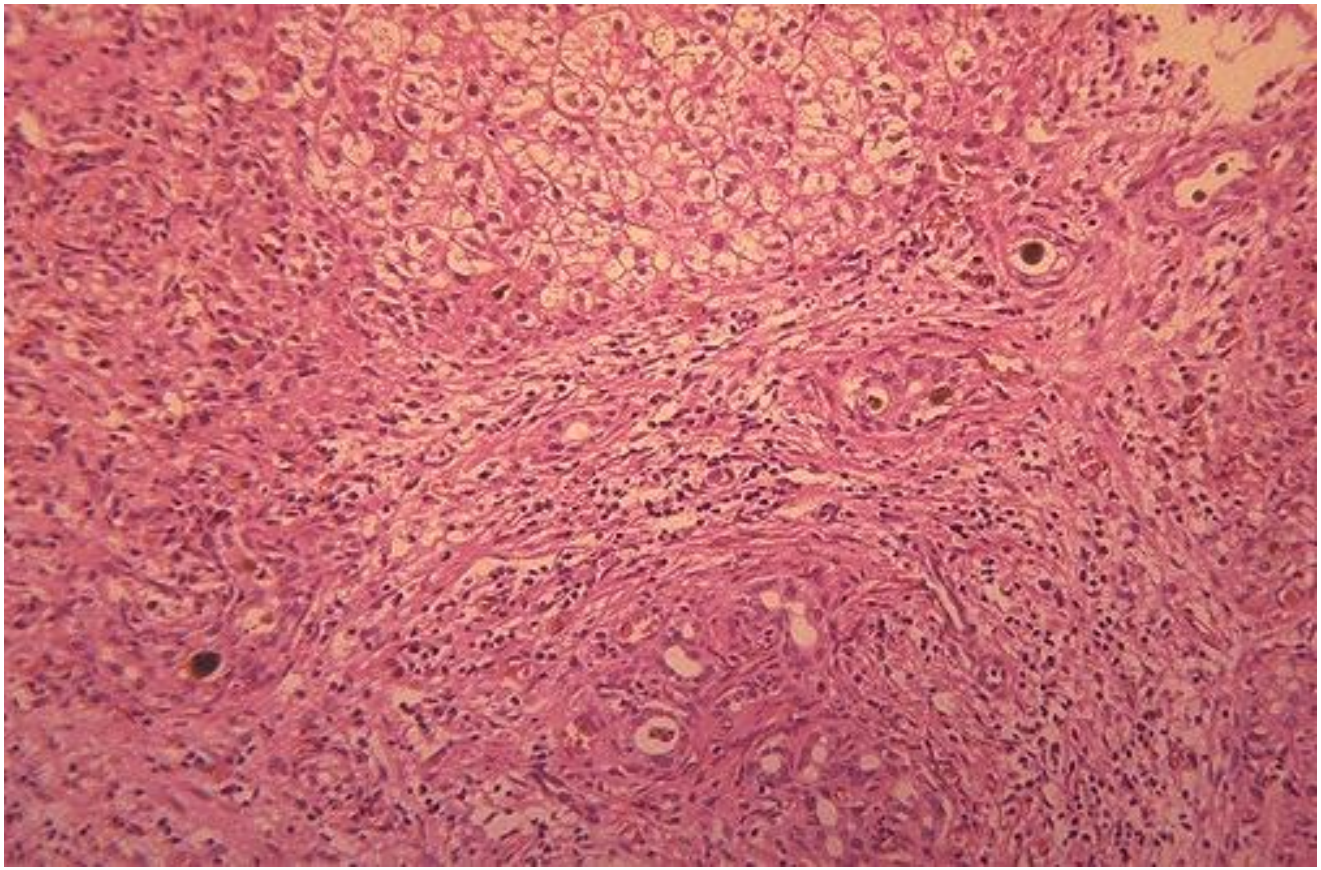
Green pigment is formalin converted bilirubin.

https://webpath.med.utah.edu/LIVEHTML/LIVER049.html
Accessed 12/10/2019

Biliary atresia

- Histopathology:
- Fibrosis of major ducts
- Periductular inflammation
- Portal tract edema
- Parenchymal cholestasis
- Type I is confined to the common duct;
- Type II is confined to hepatic bile ducts but with patent proximal branches.
- Liver failure and portal hypertension as sequelae.

Extrahepatic biliary atresia



Numerous brown-green bile plugs, bile duct proliferation (seen at lower center), and extensive fibrosis

https://webpath.med.utah.edu/LIVEHTML/LIVER050.html
Accessed 12/10/2019

Biliary atresia

- Unknown viral trigger.
- Rotavirus, Reovirus, CMV infection proposed but not demonstrated.
- Unknown environmental toxin based on animal studies.
- CFC1 gene mutation (determines laterality in embryo).
- Graft versus host disease.
- Coordination of T_{H1} activation genes.

Biliary atresia

- Abdominal ultrasound and hepatobiliary scintigraphy as initial diagnostic studies.
- Liver biopsy
- Cholangiogram as definitive study.
- Hepatoportoenterostomy followed by use of ursodeoxycholic acid (shifts biliary acids to hydrophilic forms) and supplementation with fat soluble vitamins, medium chain triglycerides, glucose polymers.
- Neomycin or trimethoprim-sulfisoxazole prophylaxis.
- Liver transplant if not surgically correctible.

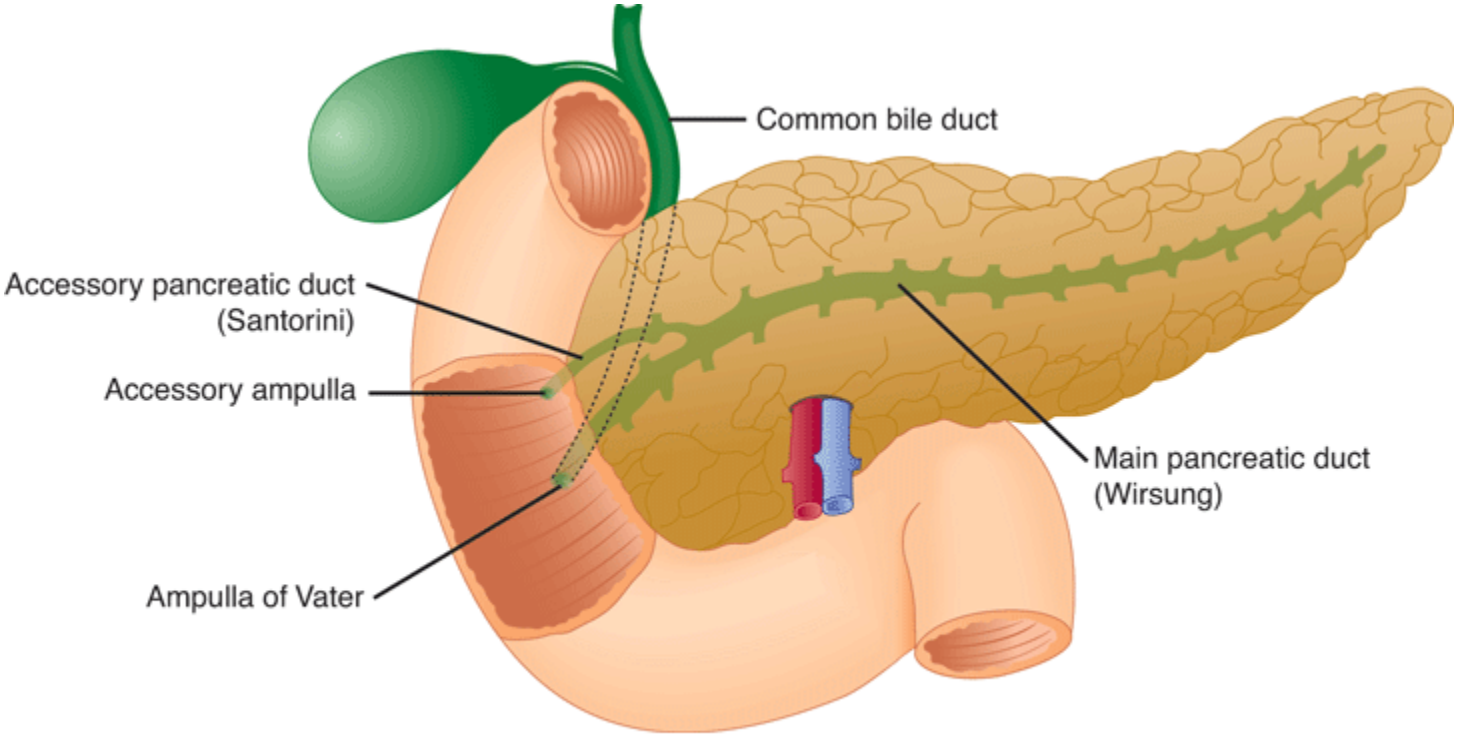
Fibropolycystic disease

- Manifest in late childhood as hepatosplenomegaly or portal hypertension in the absence of hepatic dysfunction
- Three types
- Associated with:
- Polycystic kidney disease in children (autosomal recessive)
- Polycystic kidney disease in adults (autosomal dominant)
- Increased risk of cholangiocarcinoma
- Resect involved lobe or liver transplant

Fibropolycystic disease

- Von Meyenburg complexes
- Small bile duct hamartomas
- Caroli syndrome
- Segmental dilatation of intrahepatic bile ducts
- Portal tract fibrosis
- Congenital hepatic fibrosis
- Portal tracts enlarged by broad bands of fibrous tissue forming septae (not cirrhosis)

Anatomic relationships



Source: McPhee SJ, Hammer GD: *Pathophysiology of Disease: An Introduction to Clinical Medicine, 6th Edition:* http://www.accessmedicine.com

Fig. 15-1 Accessed 02/01/2010

Gallbladder

- Extrahepatic bile ducts consist of left and right ducts that join to form a common hepatic duct close to its emergence from the liver.
- The common hepatic duct lies in front of the portal vein and to the right of the right hepatic artery.
- The common hepatic duct is joined at an acute angle by the cystic duct.
- The anatomy of the junction is highly variable.

Gallbladder

- The superior third of the common bile duct passes anterior to the portal vein and to the right of the right hepatic artery.
- The middle third curves behind the first portion of the duodenum and diverges from the portal vein and right hepatic artery.
- The lower third either curves behind the head of the pancreas or traverses it and enters the second part of the duodenum. There it is generally joined by the pancreatic duct.

Gallbladder

- 70% of common bile ducts and pancreatic ducts unite outside the duodenal wall and traverse the wall as a single duct, terminating in the ampulla of Vater, 10cm below the pylorus.
- 20% join within the wall and have either a short or no common duct, but empty into the duodenum through the same opening.
- 10% of patients have two distinct ducts and openings into the duodenum.

Gallbladder

- Variant arterial blood supply in 50% of cases.
- Right hepatic artery from superior mesenteric artery in 20% of patients
- Two right hepatic arteries, one each from celiac and superior mesenteric arteries, in 5% of patients.
- The right hepatic artery may course anterior to the common duct and is vulnerable in surgical procedures if it runs parallel to the cystic duct or is in gallbladder mesentery.

Gallbladder

- The cystic artery arises from the right hepatic artery in 90% of patients.
- At times there are two cystic arteries, arising from right and left hepatic arteries or both from the right hepatic artery.
- The cystic artery is found within the hepatocystic triangle, the area bound by the cystic duct, common hepatic duct, and the liver margin (triangle of Calot).

Structural anomalies

- Choledochal cysts are congenital dilatations of the common bile duct.
- May be segmental or cylindrical
- Children younger than 10-years of age
- 20% symptomatic only as adults
- Females predominate 3-4:1
- Present with jaundice and biliary colic
- Predispose to stone formation, inflammation, obstruction

Normal gallbladder

- 50ml capacity
- 1L bile produced daily
- Concentrates bile 5-10x

Normal gallbladder

- The wall of the gallbladder has four layers:
- Mucosa and underlying lamina propria
- Lacks muscularis mucosae
- Folds are longitudinal and form the spiral valves of Hester at the gallbladder neck.
- Functionally equivalent to muscularis mucosae
- Lacks submucosa
- Smooth muscle layer
- Perimuscular connective tissue
- Serosa.

Gallbladder

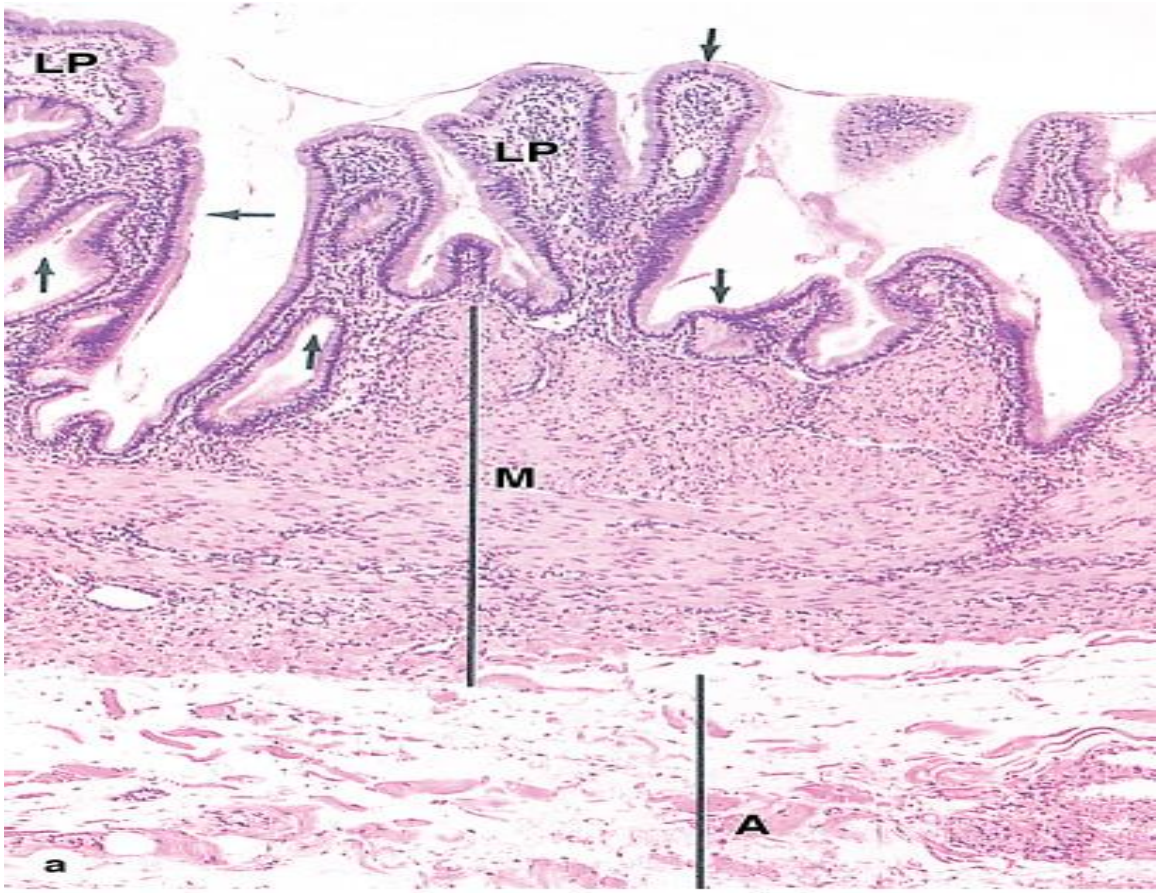


Fig. 16-21 Accessed 02/01/2010

Normal gallbladder

- Parasympathetic ganglion cells (T8-T9) in the wall cause expulsion of bile.
- Paraganglia are usually found adjacent to nerve fibers and ganglion cells in connective tissue.
- Ducts of Luschka are ducts buried within the gallbladder that communicate with intrahepatic biliary tree but rarely form accessory bile ducts.
- They are of surgical importance.

Duct of Luschka

A dilated Luschka's duct is lined by columnar biliary type epithelium and surrounded by concentric rings of collagen fibers. Smaller bile ducts and some chronic inflammatory cells are also present in the surrounding fibrous tissue. Luschka's ducts are most common in the perimuscular connective tissue adjacent to the liver. <u>This is not chronic inflammatory change.</u>

Fig. 10-22

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Bilirubin

- 750ml produced daily (250-400mg)
- Produced in phagocytic cell following breakdown of heme either from senescent cells or hemoproteins (99.5% as protoporphyrin-IXa).
- Heme oxidized intracellularly to biliverdin and reduced to bilirubin.
- Bilirubin is released from the cell and bound to albumin for transport.
- Carrier mediated transport at hepatocyte.
- Conjugated with one or two molecules of glucuronic acid by in the endoplasmic reticulum and excreted in the bile.

Bilirubin

- Liver produces bile salts from cholesterol.
- Bile salts metabolized further in small bowel by bacteria.
- 20% reabsorbed in ileum and colon and recycled.
- Only conjugated bilirubin excreted in urine (unconjugated is bound to albumin and cannot be filtered by the glomeruli).
- 5% lost in feces
- The body cannot degrade the sterol nucleus, thus only the 5% loss of bile accounts for the majority of cholesterol excreted per day.

Bile flow

- The most important ATP-dependent canalicular transport systems are:
- the bile salt export pump (Na^+/taurocholate cotransporter);
- the anionic conjugate export pump which mediates the canalicular excretion of various amphiphilic conjugates formed by phase II conjugation (e.g., bilirubin mono- and diglucuronides and drugs);
- the multidrug export pump for hydrophobic cationic compounds;
- and the phospholipid export pump.
- A "flippase“ is essential for maintaining the lipid asymmetry of the canalicular membrane.

Neurohormonal control of biliary secretion

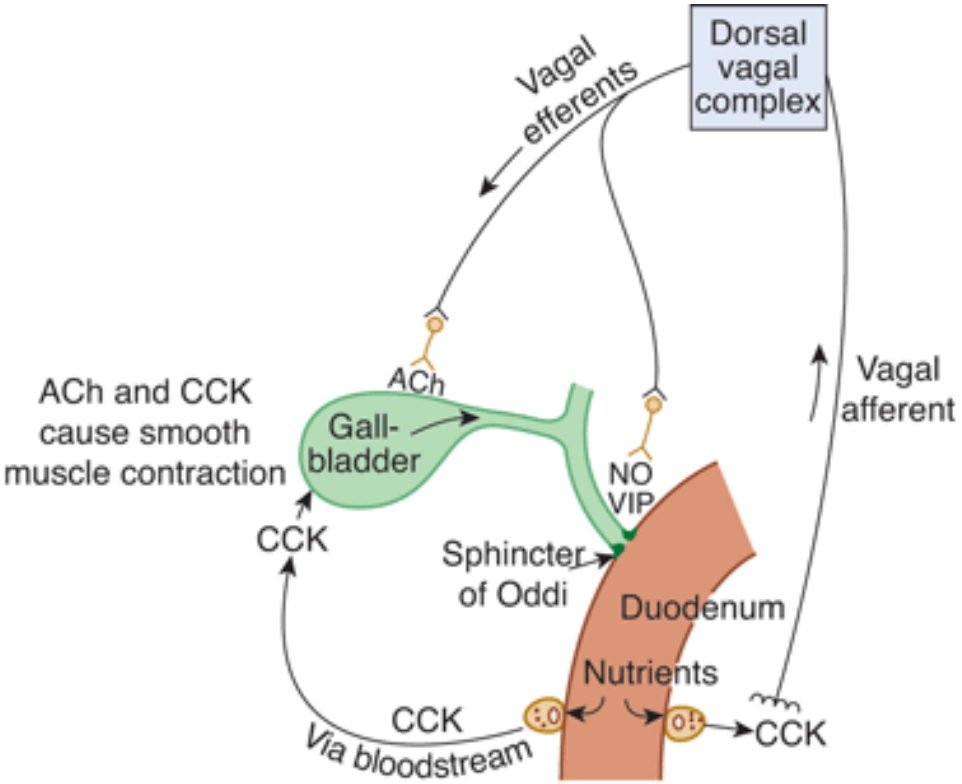


Fig. 29-9 Accessed 02/01/2010

Gallstones

- 67% women
- 5% less than 40 years old
- 75% of Native Americans, Asians have gallstones
- 80% are cholesterol with calcium
- Cholesterol stones occur exclusively in gallbladder
- Yellow
- 10% pigmented (brown to bloack stones, radiolucent)
- Reflecting deconjugation of biliary glucoronides in hemolysis

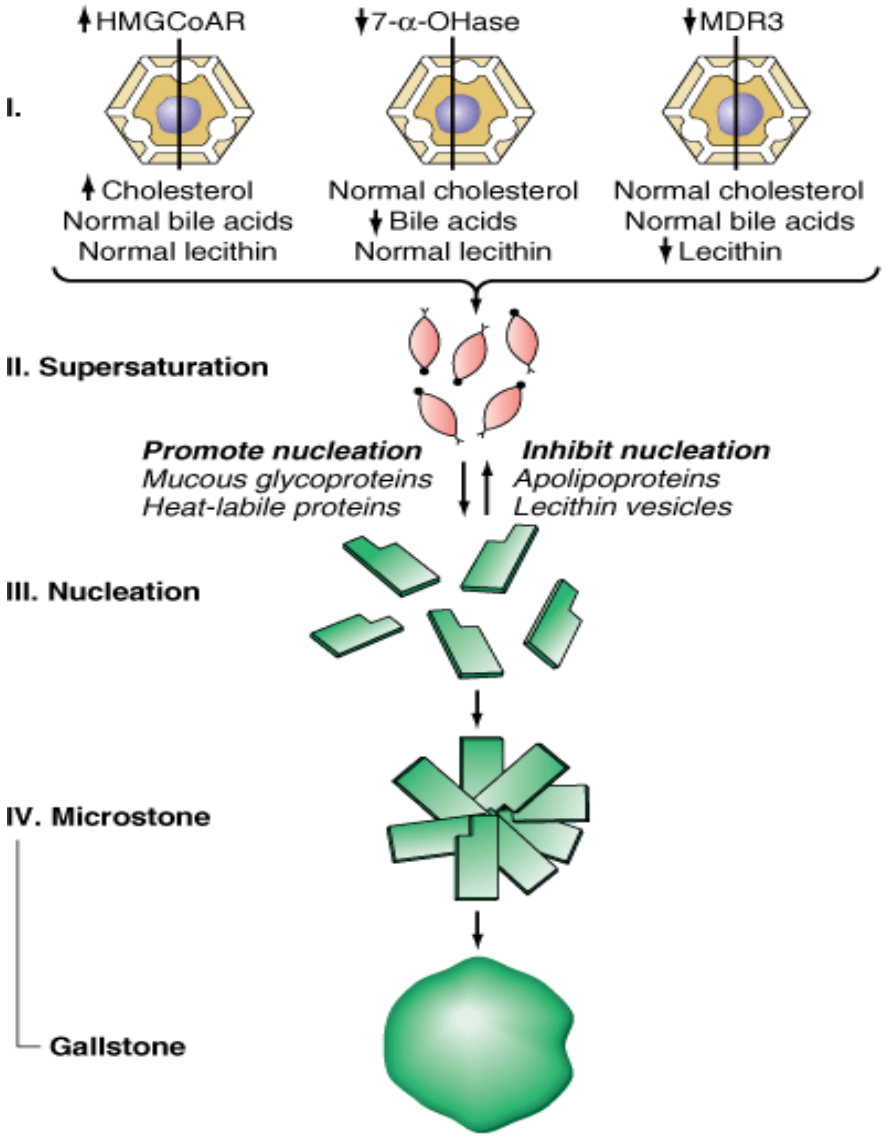
Table 18-13 Risk Factors for Gallstones

Cholesterol Stones
Demography: northern Europeans, North and South Americans, Native Americans, Mexican Americans
Advancing age
Female sex hormones
Female gender
Oral contraceptives
Pregnancy
Obesity and metabolic syndrome
Rapid weight reduction
Gallbladder stasis
Inborn disorders of bile acid metabolism
Hyperlipidemia syndromes
Pigment Stones
Demography: Asians more than Westerners, rural more than urban
Chronic hemolytic syndromes
Biliary infection
Gastrointestinal disorders: ileal disease (e.g., Crohn disease), ileal resection or bypass, cystic fibrosis with pancreatic insufficiency

Gallstones

- Associated with stones:
- Ascarasis
- Liver flukes
- Intestinal bypass
- Crohn’s disease
- Cystic Fibrosis
- Estrogen use
- Clofibrate
- Obesity
- Rapid weight loss
- Chenodeoxycholic acid, ursodeoxycholic acid promote stone dissolution <u>if cholesterol alone</u>.

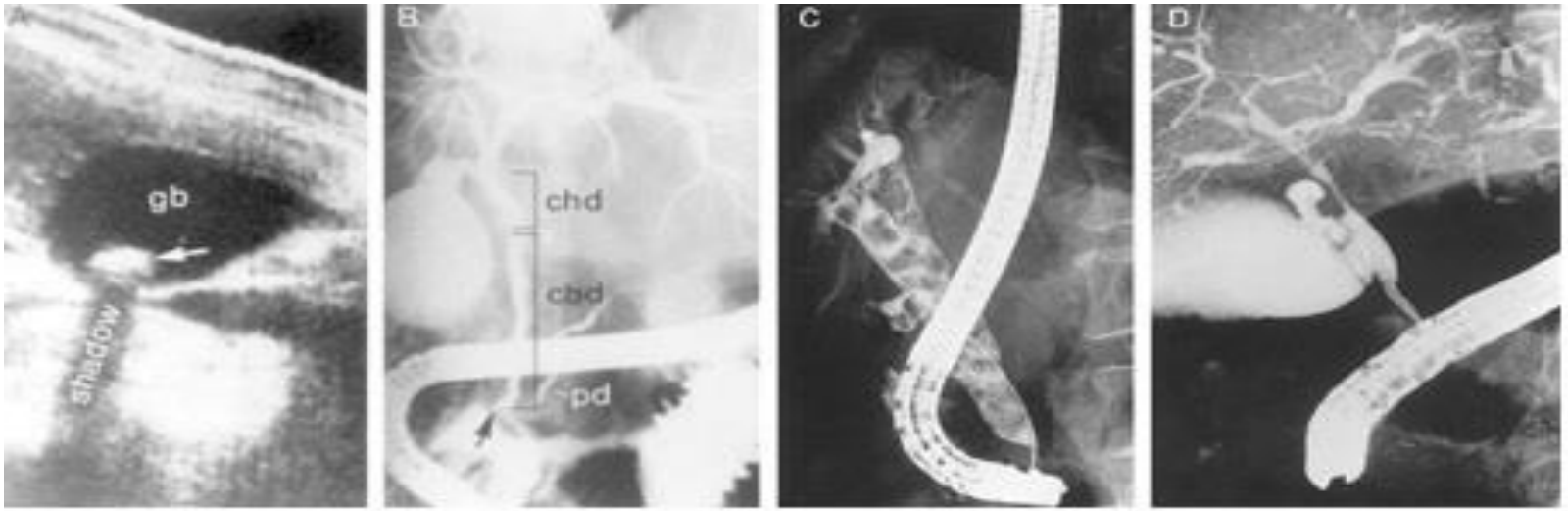
Gallstone formation



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Fig. 305-1 Accessed 02/01/2010

Gallbladder images



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

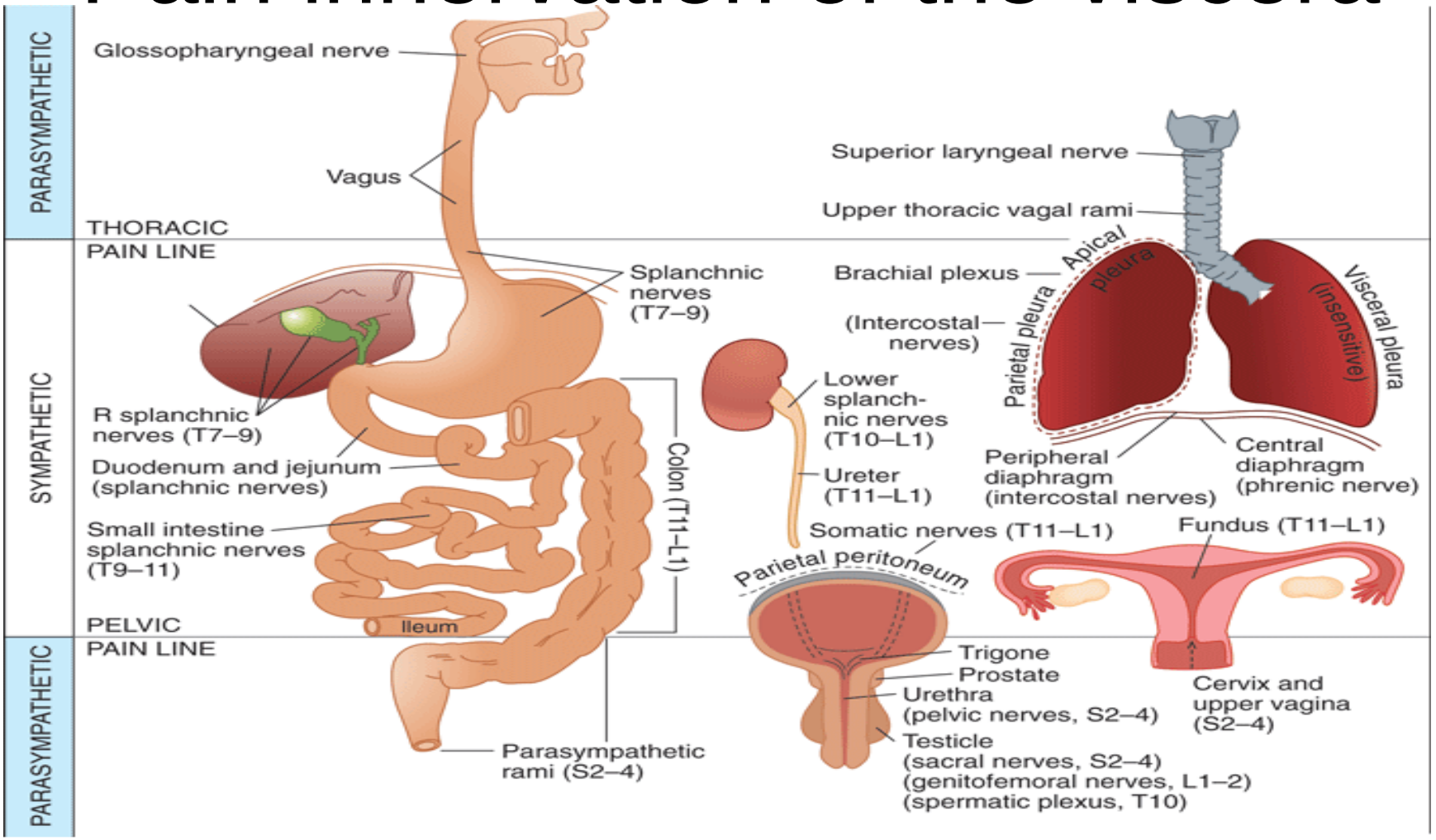
Fig. 305-2 Accessed 02/01/2010

A. Distended gallbladder containing a single large stone (*arrow*) which casts an acoustic shadow on ultrasound. *B.* ERCP showing normal biliary tract anatomy. The arrow points to the ampulla of Vater.
C. Choledocholithiasis. The biliary tract is dilated and contains multiple radiolucent calculi. *D. S*clerosing cholangitis. The common bile duct shows areas that are structured and narrowed.

Figure 18-62 Cholesterol gallstones. The wall of the gallbladder is thickened and fibrotic due to chronic cholecystitis.

Figure 18-63 Pigment gallstones. Several faceted black gallstones are present in this otherwise unremarkable gallbladder from a patient with a mechanical mitral valve prosthesis, leading to chronic intravascular hemolysis.

Pain innervation of the viscera



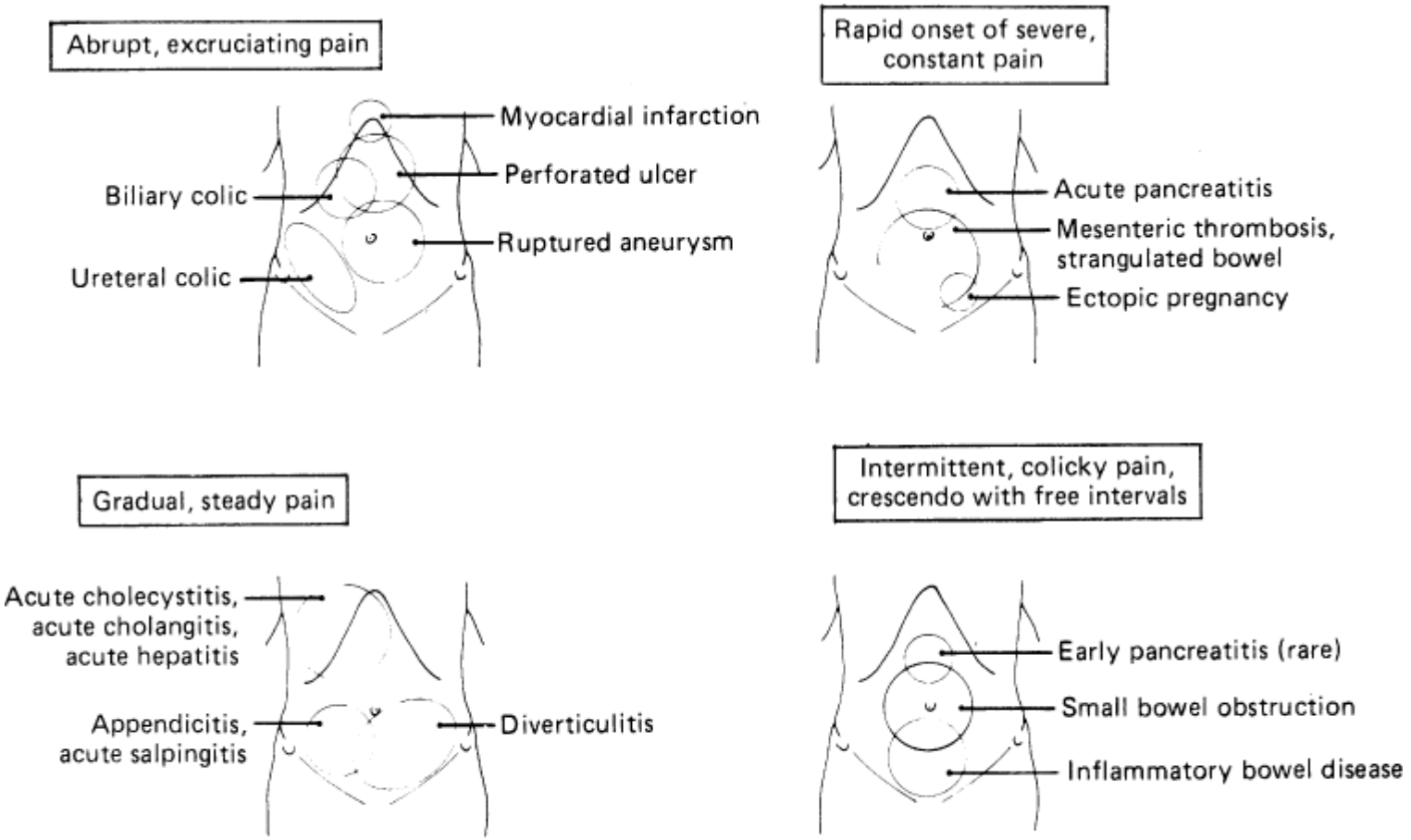
Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

(After White JC. Reproduced with permission from Ruch TC: In *Physiology and Biophysics,* 19th ed. Ruch TC, Patton HD (editors). Saunders, 1965.) Fig. 10-2 Accessed 07/01/2010

Chapman's reflex points

- Smooth, firm, discretely palpable nodules 2-3mm in diameter located within deep fascia or on the periosteum of a bone.
- May represent viscerosomatic reflexes (empirical evidence only)
- T5 adjacent to right and at base of transverse process is associated with somatic dysfunction of the gallbladder

Abdominal pain



Reproduced, with permission, from Way LW [ed]: *Current Surgical Diagnosis & Treatment*, 9th ed. Lange, 1991.)
Fig. 13-2 Accessed 07/01/2010

Cholecystitis

- Severe, constant right upper quadrant pain with waves of cramps are usually associated with gallstone lodged in neck or cystic duct.
- Pain begins up to 4 hours following meal.
- May be precipitated by fatty meal.
- Associated with nausea and vomiting.
- History may disclose episodes of pain with long pain free intervals.
- (Biliary colic recurs in 50% of symptomatic patients.)

Cholecystitis

- 10-20% have stones within the common bile duct.
- Will have abnormal liver function tests.
- May be bacteremic.
- Right upper quadrant pain, nausea and vomiting are often seen but are not specific for cholecystitis.
- RUQ tenderness may be absent in elderly patients.
- An episode of pain longer than 4 hours, fever, or marked right upper quadrant tenderness suggest cholecystitis.
- A positive Murphy sign is associated with a positive likelihood ratio (LR+) of 2.8 for cholecystitis.

Cholecystitis

- Ultrasound can identify stones, wall thickening, and distinguish between obstructive and non-obstructive lesions. Positive likelihood ratio (LR+) 30; LR- 0.1.
- BUT, a dilated common bile duct is only occasionally seen on transabdominal ultrasound in patients with common duct stones.
- If stones not found on transabdominal ultrasound, endoscopic ultrasound will likely be diagnostic.

Pathological change in cholecystitis

- Normal gallbladder mucosa lined by columnar epithelium.
- Fibromuscular layer and subserosal fat are covered by peritoneum.
- Fibrin deposition on the surface of gallbladder in acute inflammation.
- Chronic inflammation leads to fibrosis in subepithelial and subserosal tissues.
- Crypts are buried.

Pathologic change in cholecystitis

- In calculous cholecystitis, an obstructing stone is usually present in the neck of the gallbladder or the cystic duct.
- The gallbladder lumen may contain one or more stones and is filled with a cloudy or turbid bile that may contain large amounts of fibrin, pus, and hemorrhage.
- If filled with purulent material, empyema
- Clostridium and coliform organisms may produce gas and dissect the wall, emphysematous
- If necrotic, gangrenous

Chronic cholecystitis

- Proliferation of hypertrophic nerve bundles in the muscular and perimuscular connective tissue.
- This change may simulate a plexiform neurofibroma.
- Rokitansky- Aschoff sinuses, or crypts, are epithelial invaginations that may penetrate the muscle layer and reach the perimuscular connective tissue.
- Analogous to the diverticula that develop in other hollow viscera, such as the colon or urinary bladder.
- Hallmark of chronic inflammation.

Chronic cholecystitis

- A strawberry gallbladder is characterized by small yellow flakes on mucosal surface. Lipid laden macrophages are bound in submucosal tissues.
- This is cholesterolosis.

Cholecystitis

- Acalculous cholecystitis
- Motility disorder of the gallbladder or sphincter of Oddi.
- Detected with cholecystokinin enhanced cholecystography.
- Thought to be related to ischemia of the cystic artery (an end artery.)

Cholecystitis

- Minimal survival difference between surgical removal of gallbladder and medical therapy with hydration and antibiotics.
- Laparoscopic surgery preferred mode of gallbladder removal because of lesser morbidity.
- ERCP for removal of biliary tree stone (choledocholithiasis) or emergency decompression.

Endoscopic retrograde choleopancreatography

- ERCP is primarily indicated in patients with severe disease who are suspected of having biliary obstruction.
- May permit sphincterotomy to remove impacted stones.
- Complications include precipitating an acute episode of pancreatitis as well as infection and hemorrhage.
- Mortality reduction in early use.

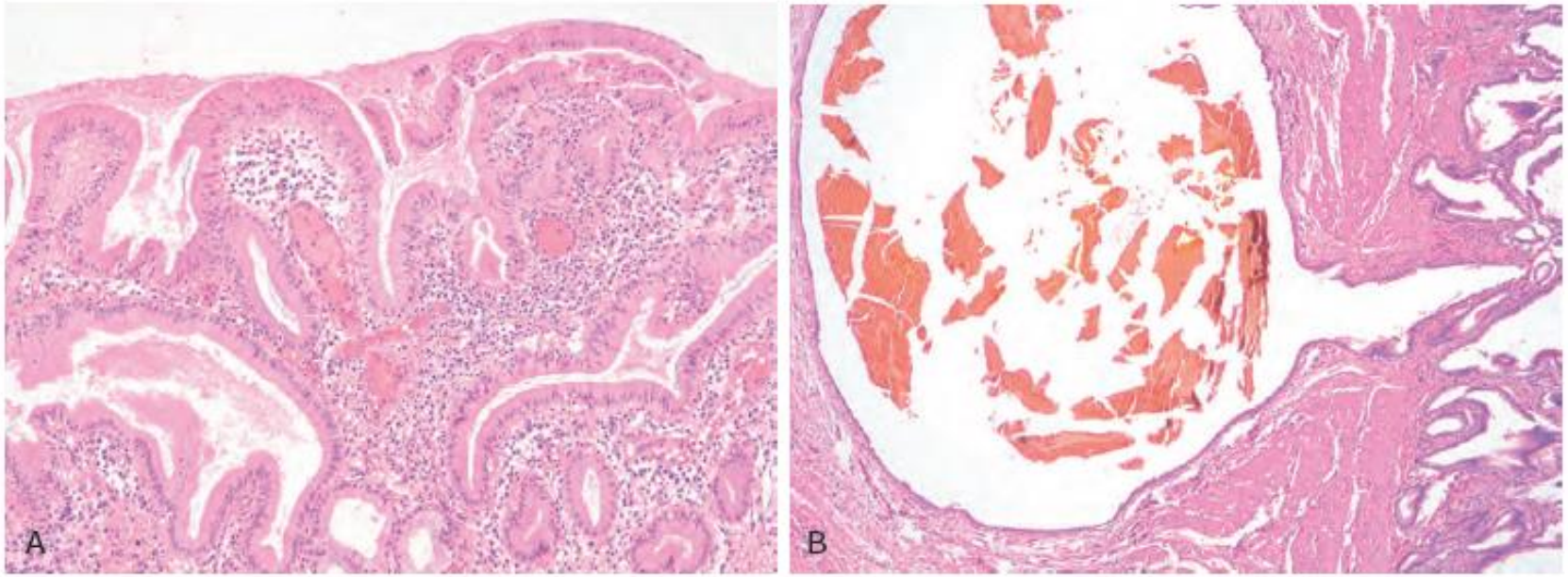
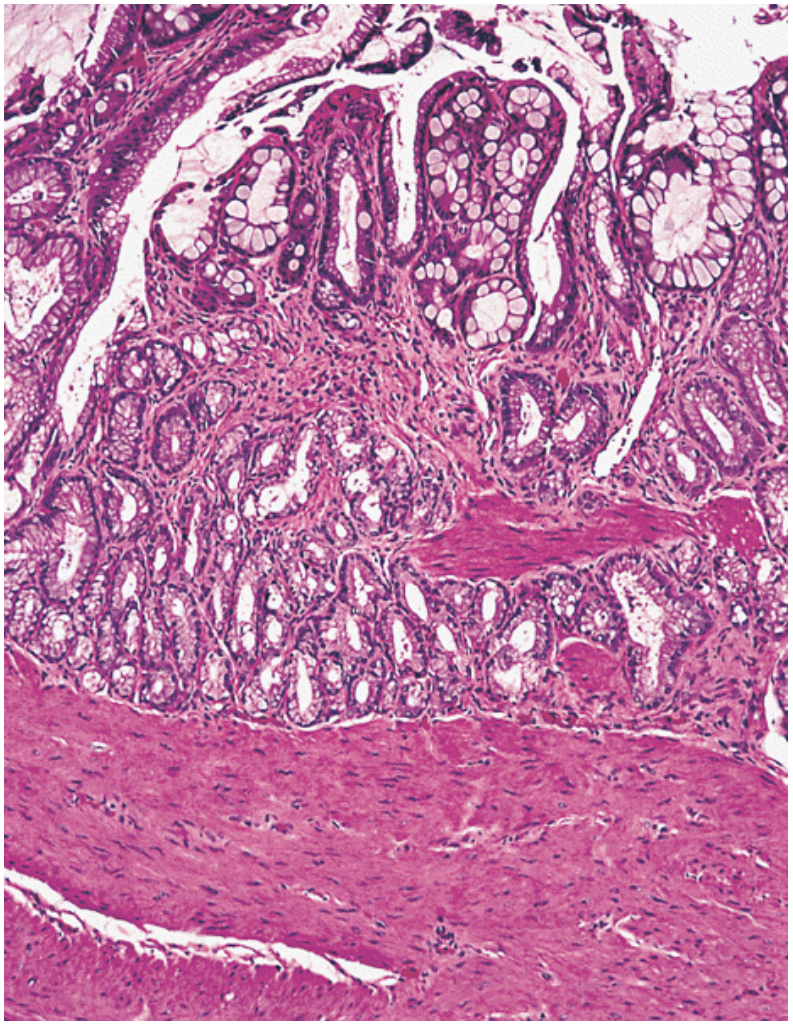


Figure 18-64 Chronic cholecystitis. **A,** The gallbladder mucosa is infiltrated by inflammatory cells. **B,** Outpouching of the mucosa through the wall forms Rokitansky-Aschoff sinus (contains bile).

Chronic cholecystitis



Both intestinal and pyloric gland metaplasia coexist in this gallbladder.

Fig. 10-6

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Cholangitis

- Fever a major component
- Sepsis may dominate course of illness
- Retrograde infection via Sphincter of Oddi
- Klebsiella-Enterobacter Species
- Group D Streptococci
- If with jaundice and biliary obstruction, stent may be required
- May lead to sclerosing cholangitis
- Carcinomas rarely diagnosed before surgery

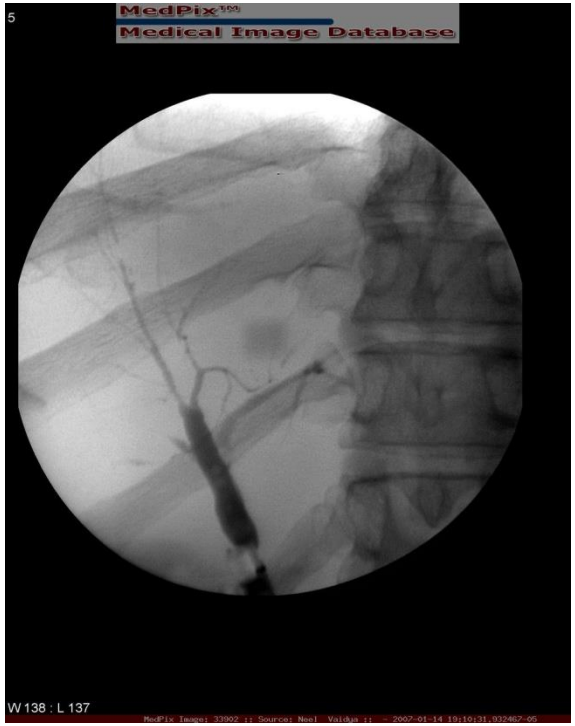
Primary sclerosing cholangitis

- Histopathology:
- Fibrosis of major ducts
- Periductular inflammation
- Portal tract edema
- Parenchymal cholestasis
- Intrahepatic duct obstruction
- Alternating strictures and dilatation with “beading” seen on ERCP.

Primary sclerosing cholangitis

- Anti-smooth muscle antibodies and an atypical p-ANCA (directed towards a nuclear envelope protein and not MPO) commonly found.
- IgG4 elevations noted in those who also have autoimmune pancreatitis.
- May be associated with ulcerative colitis.
- May progress to cirrhosis.
- 7% will develop cholangiocarcinoma.

Sclerosing cholangitis



Fluroscopic ERCP image following contrast infusion in the common bile duct. Multifocal areas of constriction and dilatation in intrahepatic and extrahepatic ducts. Medpix image 33901. Contributed by Neel Vaidya. Accessed 08/12/2010

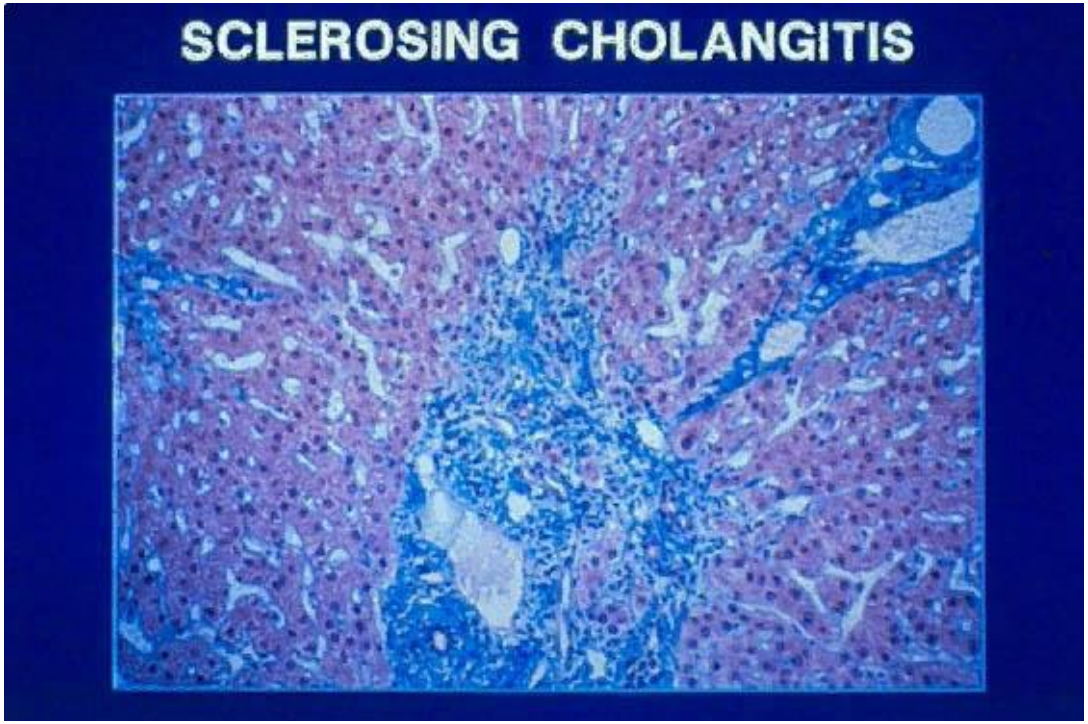
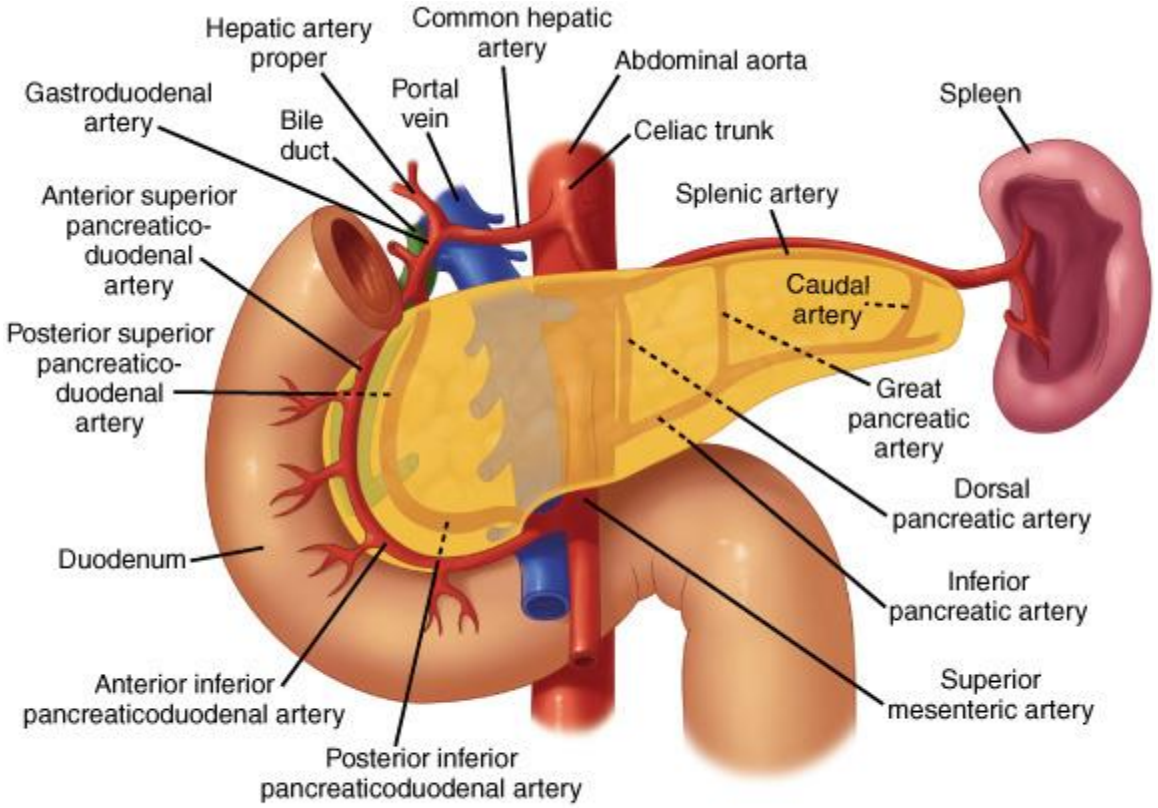


Figure 16-x.. In: McPhee SJ, Hammer GD. Pathophysiology of Disease: An Introduction to Clinical Medicine. 6th ed. New York, NY: McGraw-Hill; 2010. http://www.accessmedicine.com. Accessed February 1, 2010.

Arterial supply to pancreas



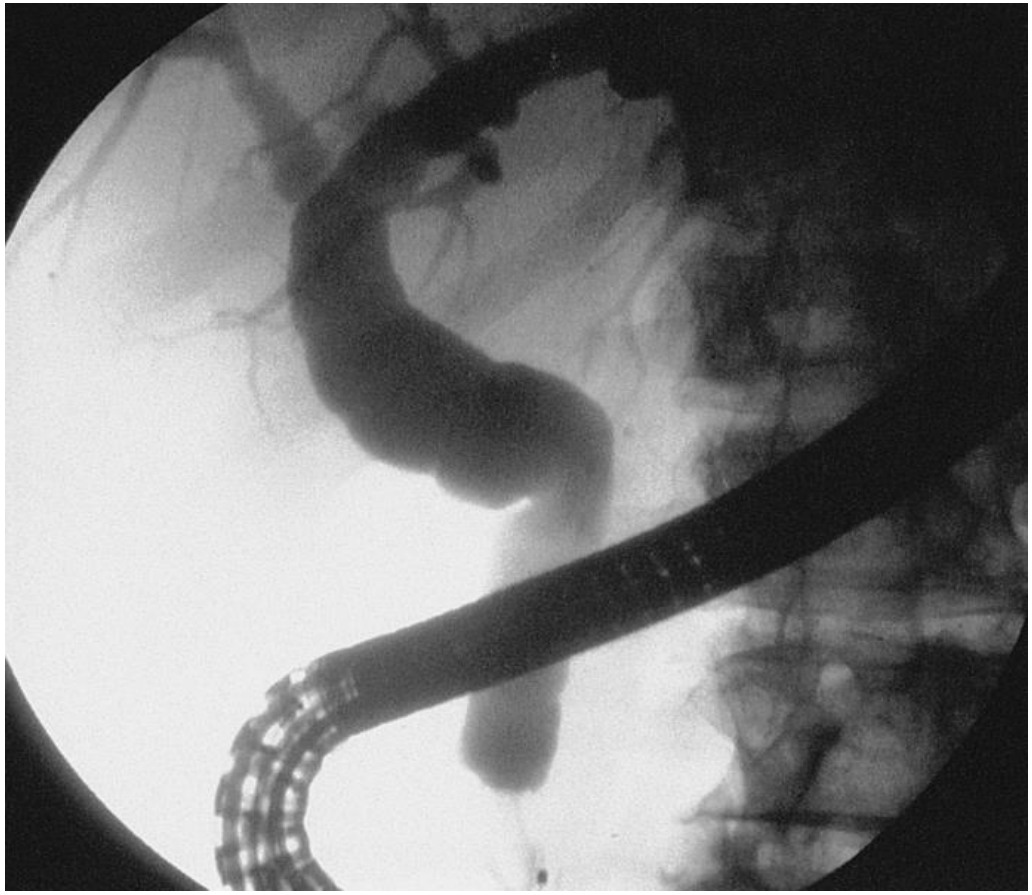
Source: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE: *Schwartz's Principles of Surgery, 9th Edition:* http://www.accessmedicine.com

Fig. 33-4 Accessed 02/01/2010

Biliary tract cancer

- Generally present with pain and right upper quadrant mass.
- Bile duct lesions generally present with obstruction
- Polyps >1cm diameter have the greatest malignant potential.
- MRI-cholangiopancreatography is the optimal imaging procedure to outline local anatomy.

Bile duct obstruction



The ERCP reveals a tight, irregular, distal common bile duct stricture caused by a well-differentiated adenocarcinoma.

Fig. 12-4

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Periampullary neoplasms

- Adenomas are <10% or periampullary neoplasms
- Duodenal adenoma only distinguished by site
- Generally occur in older individuals
- Usually asymptomatic but can cause gastric outlet obstruction or bleeding and rarely acute pancreatitis, biliary obstruction or intussusception
- Present as polypoid or exophytic mass
- May be seen with familial adenomatous polyposis

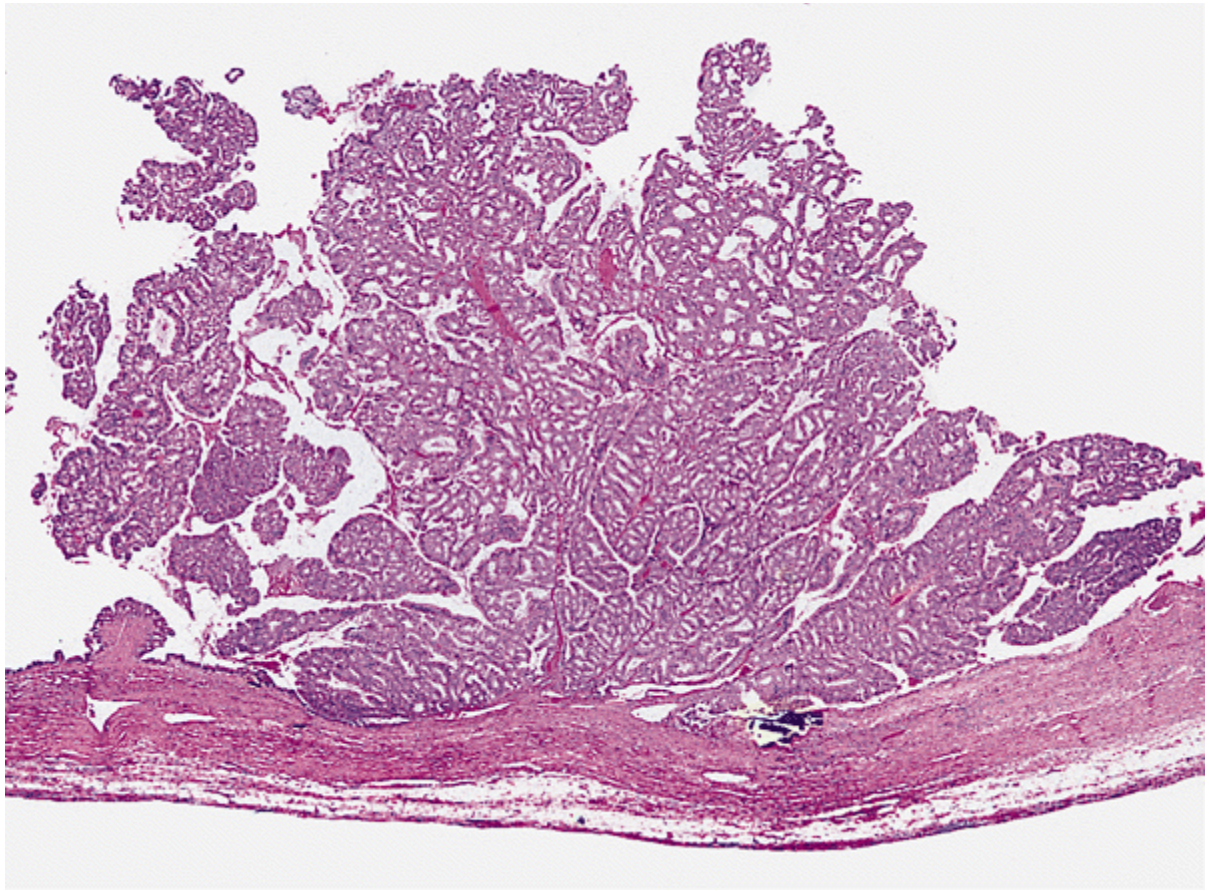
Periampullary neoplasms

- Microscopically:
- Tubular or villous or mixed tubular/villous adenomas as in colon
- Paneth cells, endocrine cells, goblet cells noted
- May have pancreatobiliary epithelium
- BRAF mutations, p53 alterations and DNA mismatch repair abnormalities are rare
- KRAS and APC mutations are more common, both in sporadic cases and in those from patients with familial adenomatous polyposis.

Periampullary neoplasms

- Resection may be curative in early or relatively confined lesions
- If not confined, may require pancreatoduodenectomy

Pyloric gland adenoma

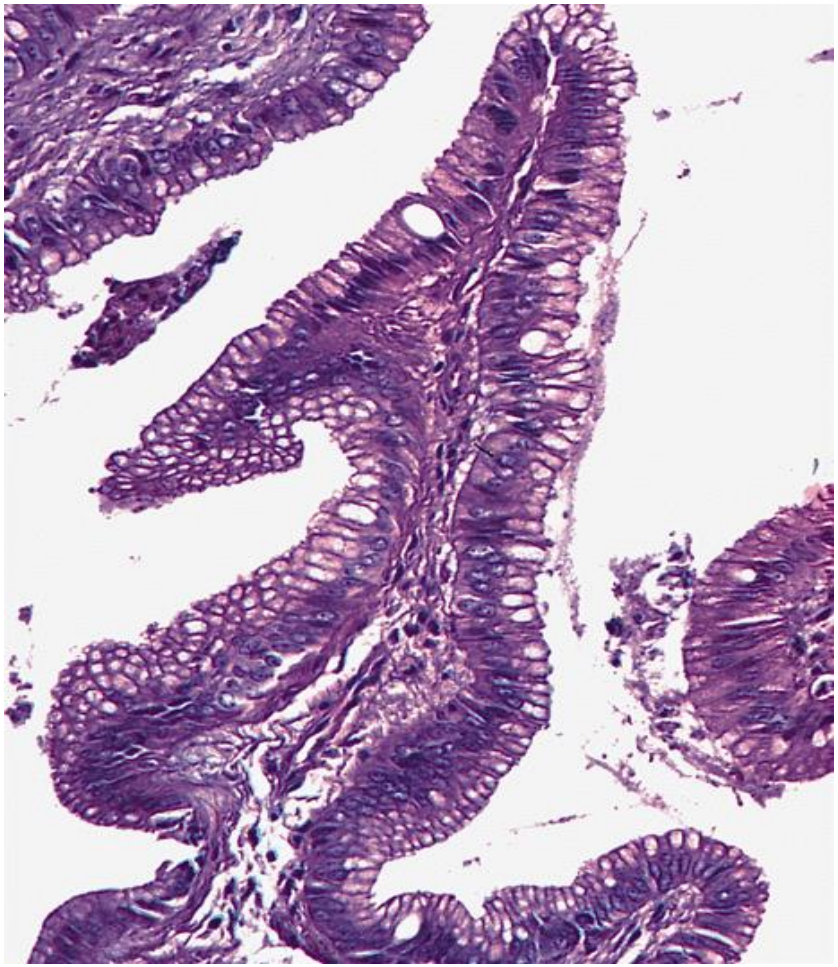


Low- power view of a sessile pyloric gland adenoma containing some dilated glands.

Fig. 3-5L

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Biliary adenoma



A papillary adenoma is composed of fibrovascular stalks that extend outward into the lumen of the gallbladder. They are lined by tall, columnar, mucus- secreting cells.

Fig. 3-19

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Gallbladder adenocarcinoma

- Generally present with pain and right upper quadrant mass.
- 3:1 women
- 50-60 years of age
- Prevalent among Native American populations (particularly in Southwest), Bolivia, Chile, and in North India
- Primarily affects the fundus (60%), body (30%) or neck (10%) of gallbladder

Gallbladder adenocarcinoma

- Cholelithiasis, Salmonella, E. Coli, and H. pylori infections predispose.
- Porcelain gallbladder can be associated with cancer in 20% of patients.

Gallbladder adenocarcinoma

- Up to 50% are detected incidentally in routine cholecystectomy specimens due to absence of gross abnormalities
- Peritoneal seeding is uncommon.
- Noninvasive papillary carcinomas, regardless of size and differentiation, do not metastasize
- Invasive papillary carcinomas have the most favorable prognosis
- Aggressive cancer, with an overall 5 year survival rate of < 10%

Gallbladder adenocarcinoma

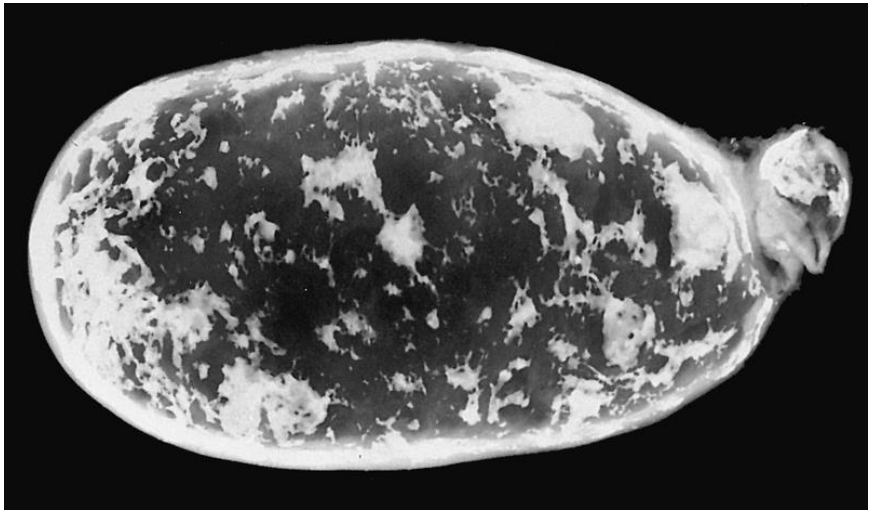
- Histologic types:
- (1) Biliary type adenocarcinoma
- 75% of cases:
- (2) Intestinal type adenocarcinoma:
- (3) Mucinous carcinoma:
- Comprised of > 50% extracellular mucin
- (4) Clear cell carcinoma:
- Sheets of clear cells in an alveolar arrangement separated by blood vessels

Gallbladder adenocarcinoma

- (5) Signet ring cell carcinoma:
- Signet ring cells are the predominant or exclusive component
- (6) Hepatoid carcinoma:
- (7) Sarcomatoid carcinoma (carcinosarcoma)

- 30-60% ERBB2 over expressed

Porcelain gallbladder

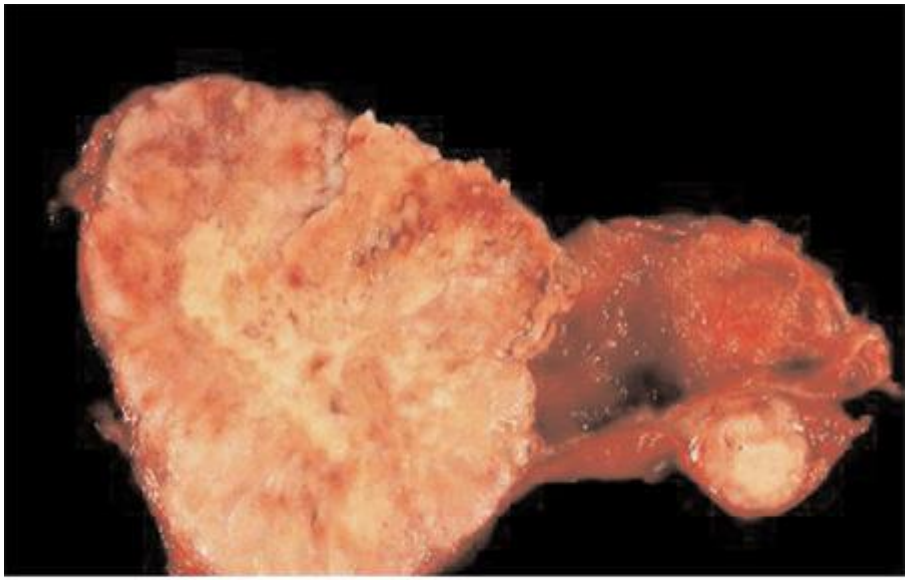


The wall of this large distended gallbladder is rigid and calcified. A stone found in the neck had been previously removed.

Figs. 4-2 and 4-3

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

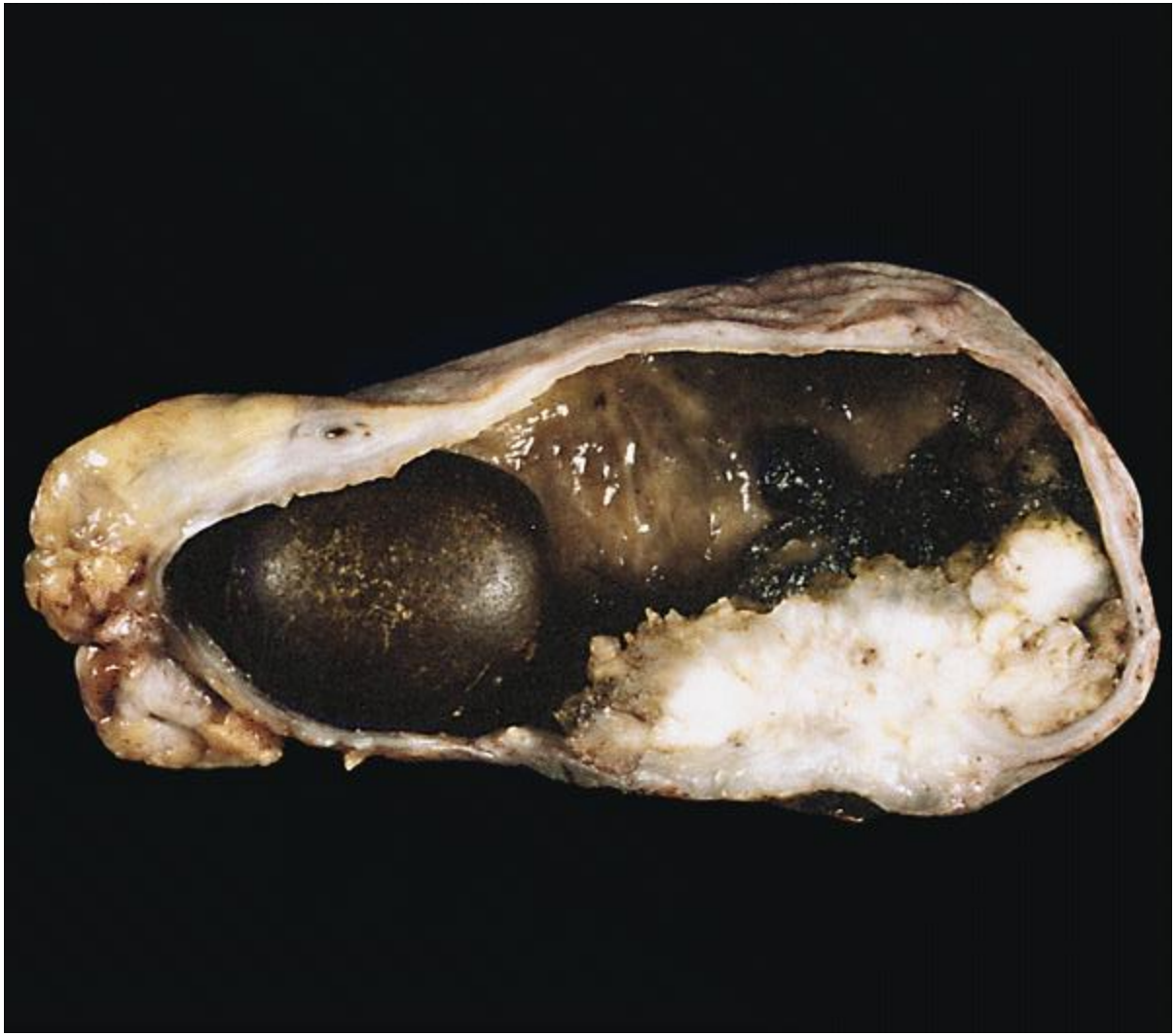
Gallbladder carcinoma



Gallbladder lumen is filled with tumor.

Fig.15-12 Accessed 04/10/2010

Adenocarcinoma

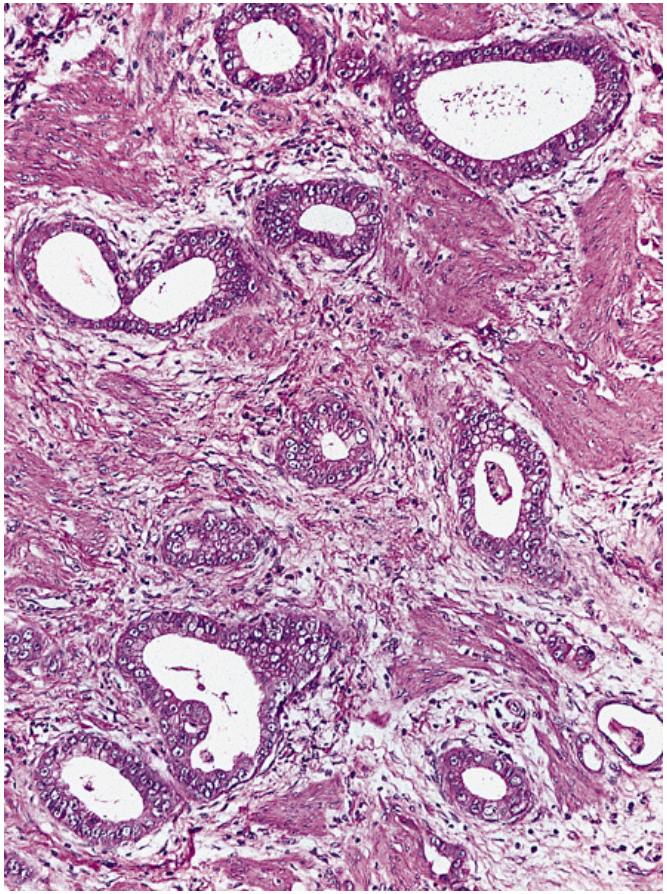


Gallbladder excised for cholelithiasis. A small infiltrating carcinoma was found in a thickened area of the fundus. Early changes may be mistaken for cholecystitis.

Fig. 6-3

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Adenocarcinoma



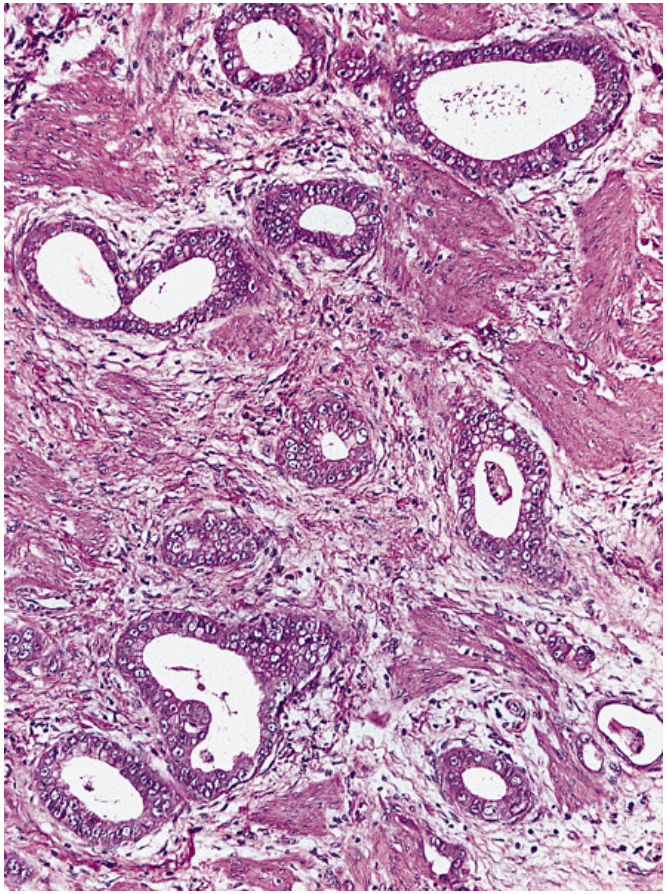
A well-differentiated adenocarcinoma is composed of variable sized glands that infiltrate the muscular wall of the gallbladder.

Fig. 6-9

Albores-Saavedra, J, Henson DE, Klimstra ,DS, “Tumors of the extrahepatic bile ducts, and ampulla of Vater.” Atlas of Tumor Pathology, Third Series, Fascicle 27. Armed Forces Institute of Pathology, Washington, D.C. 2000.

Figure 18-65 Gallbladder adenocarcinoma. **A,** The opened gallbladder contains a large, exophytic tumor that virtually fills the lumen. **B,** Malignant glands are seen infiltrating a densely fibrotic gallbladder wall.

Adenocarcinoma



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Cholangiocarcinoma

- 10% of all hepatic cancers
- Second most common cancer of hepatobiliary tree
- 50-70 years of age
- Associated with:
- Fluke infection (Asia)
- Primary sclerosing cholangitis
- HCV infection
- Caroli's disease (congenital fibropolycystic disease of the biliary system).

Cholangiocarcinoma

- Peritoneal seeding is uncommon.
- Cholangiocarcinoma is subdivided into:
- Proximal extrahepatic (perihilar or Klatskin tumor, 50-60%)
- At the hilum (bifurcation of right and left ducts).
- Distal extrahepatic (20-25%)
- Intrahepatic (peripheral, 20-25%).
- 10% exclusively intrahepatic

Cholangiocarcinoma

- Extrahepatic origin
- Tumors appear as firm, gray nodules within the bile duct wall
- Some may be diffusely infiltrative lesions
- Others are papillary, polypoid lesions.
- Intrahepatic origin
- Occur in the non-cirrhotic liver and may track along the intrahepatic portal tract system creating a branching tumor within a portion of the liver
- Cholangiocarcinomas do not make bile, but they do make mucin

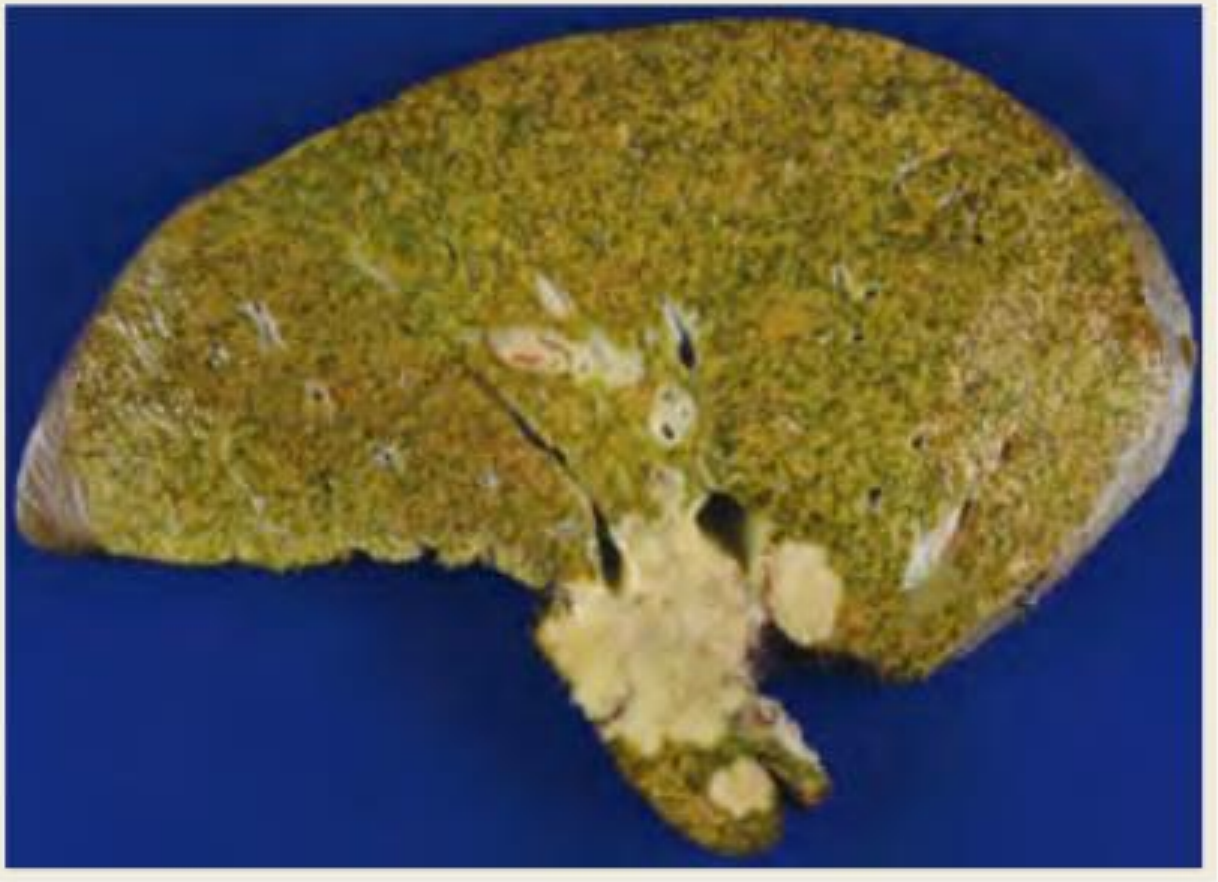
Cholangiocarcinoma

- IL-6 overexpression and AKT activation
- IL-6 drives JAK/STAT signaling
- The anti-apoptotic protein MCL-1 is increased.
- KRAS and TP53 mutations are common
- COX2, ERBB2, C-MET expression increased.
- Amplification of EFGR and diminished function of p16/ink4A have also been noted.
- FGFR2 mutation at 10q26.13 gives rise to a gene fusion product
- Targeted by futibatinimib
- KMT2C mutation at 7q36.1 common in Asians

Cholangiocarcinoma: classification

Bismuth–Corlette classification

TYPE I	TYPE II	TYPE IIIa	TYPE IIIb	TYPE IV
				



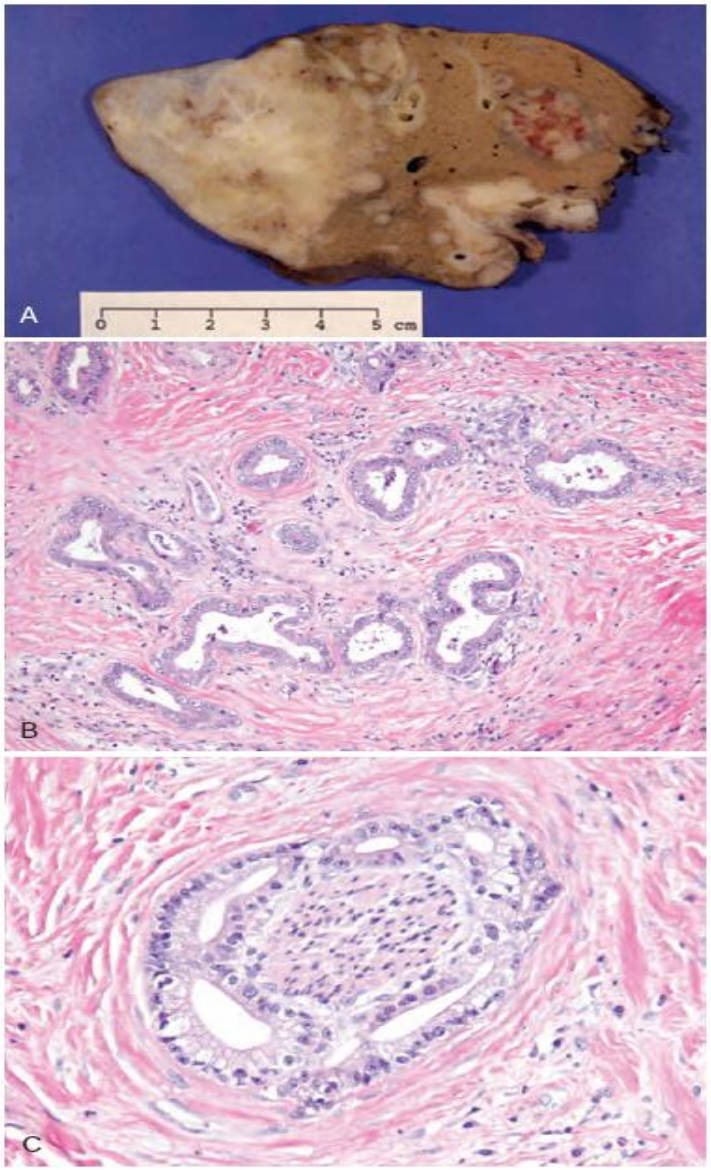
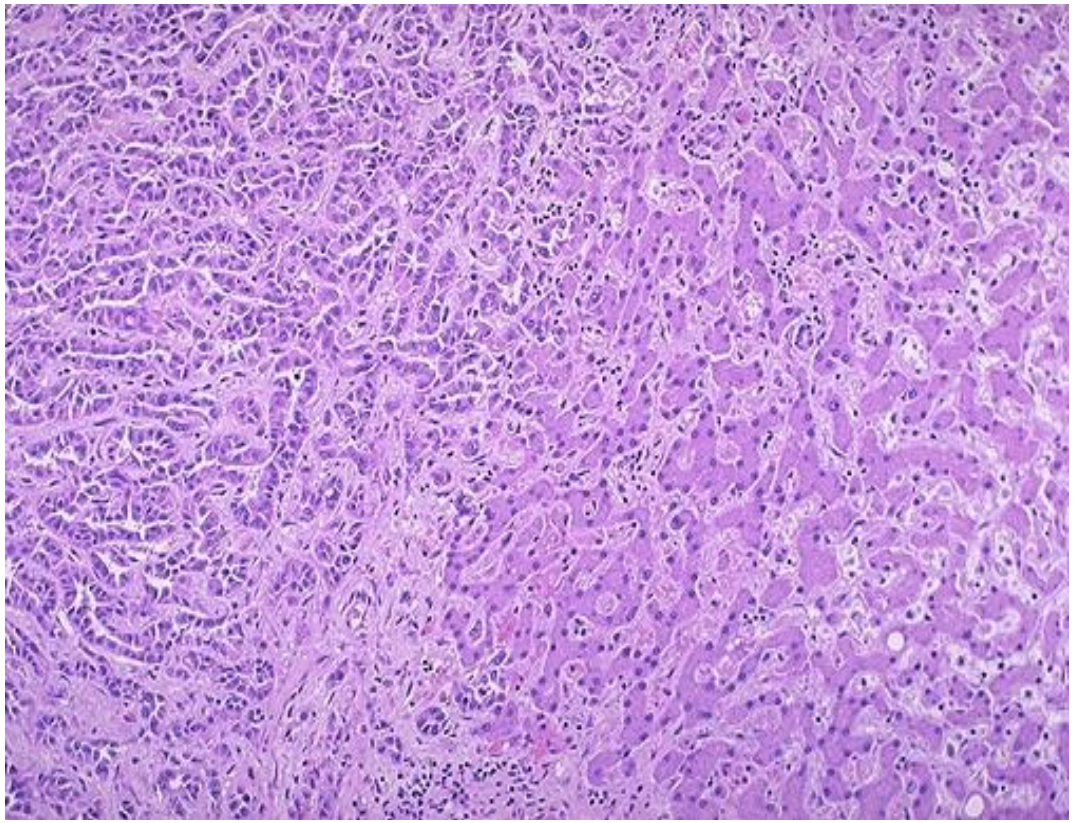


Figure 18-60 Cholangiocarcinoma. **A,** Multifocal cholangiocarcinoma in a liver from a patient with infestation by the liver fluke *Clonorchis sinensis*. **B,** Invasive malignant glands in a reactive, sclerotic stroma. **C,** Perineural invasion by malignant glands, forming a wreathlike pattern around the central, trapped nerve. (**A,** Courtesy Dr. Wilson M.S. Tsui, Caritas Medical Centre, Hong Kong.)

Cholangiocarcinoma



The carcinoma at the left has a glandular appearance that is most consistent with a cholangiocarcinoma.

There is a disorderly arrangement of ducts lined by neoplastic biliary epithelium.

A liver cancer may have both hepatocellular as well as cholangiolar differentiation.

https://webpath.med.utah.edu/LIVEHTML/LIVER032.html
Accessed 12/10/2019