

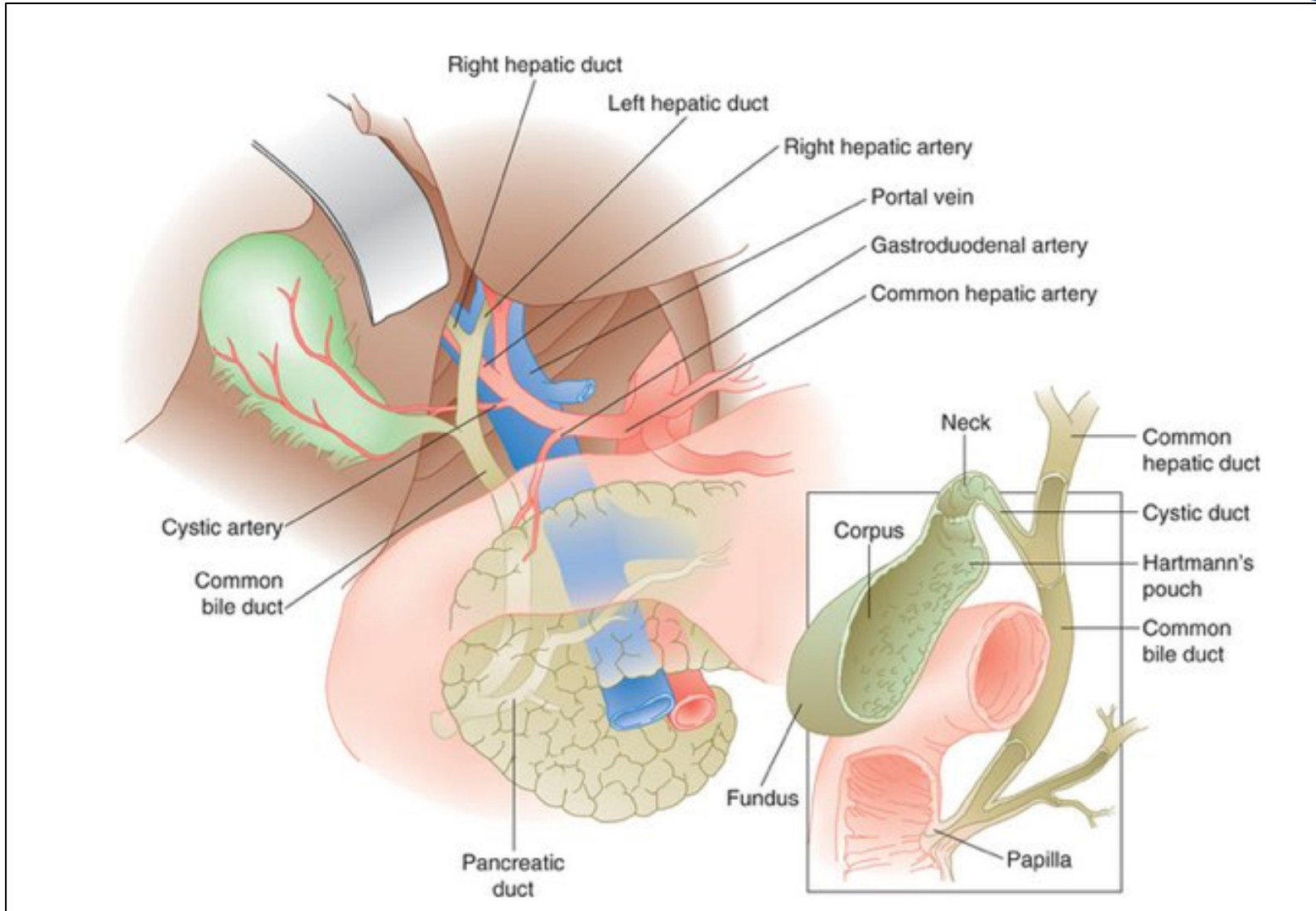
Biliary Tract Disease

Randolph L. Schaffer, MD
Scripps Center for Organ Transplant
Scripps Green Hospital

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- Anatomy and physiology
- General pathophysiology
- Benign and Malignant conditions
 - Extrahepatic bile ducts
 - Intrahepatic bile ducts
 - Gall bladder
- Diagnostic approach to suspected biliary tract disease.

- Signs and symptoms of gallstones and extrahepatic biliary obstruction have been recognized for centuries
- History of interventions is relatively recent:
 - 1867—1st documented biliary tract operation
 - 1880—1st biliary bypass
 - 1882—1st cholecystectomy
 - 1950s—transhepatic and endoscopic cholangiography
 - 1986—1st lap chole



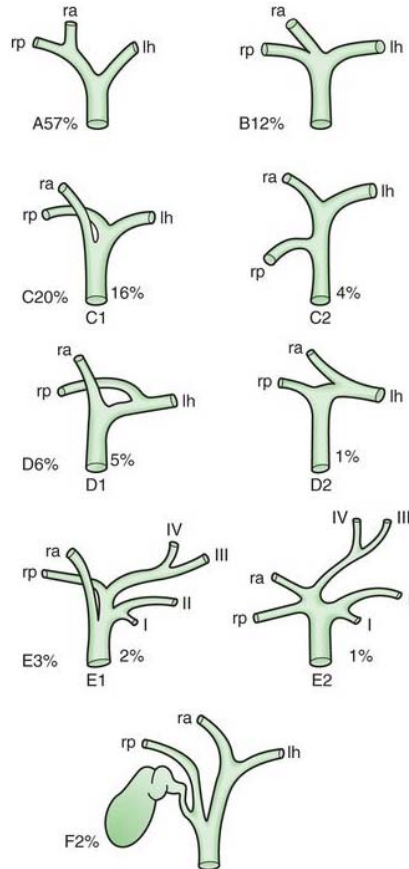


Figure 54-3 Variations in the confluence of the left and right hepatic ducts. **A**, Typical anatomy of the confluence. **B**, Trifurcation of left, right anterior, and right posterior hepatic ducts. **C**, Aberrant drainage of a right anterior (C1) or posterior (C2) sectoral hepatic

- Bile ducts, gallbladder and sphincter of Oddi modify, store and regulate bile flow
- 500-1000 mL of bile / day
- Bile flow responsive to neurogenic, humoral and chemical stimuli
 - Vagus: decreases flow
 - Secretin, CCK, gastrin increase flow
- Bile = water, electrolytes, proteins, bile salts, lipids and bile pigments

- GB stores and concentrates bile
- Enterohepatic circulation returns ~95% of bile acids to the liver via the portal venous system
- 5% of bile acids are excreted in the stool
- Color of bile comes from the breakdown of Hgb
- Bile pigments contribute to stool coloration

- Symptoms of biliary disease
 - Secondary to:
 - Obstruction
 - Internal
 - External
 - Infection
 - Compromised host
 - Inoculum
 - Stasis
 - Abdominal pain, jaundice, fever, nausea and vomiting

- Abdominal pain
 - Biliary colic
 - Constant pain that builds in intensity
 - May radiate to back, right shoulder or interscapular
 - Often described as “bandlike tightness”
 - Often triggered by fatty foods, but not always
 - Only about 50% associate with meals
 - May develop up to an hour after a meal
- Jaundice
 - Results from elevated serum bilirubin
 - Sclerae: > 2.5 mg/dL
 - Skin: > 5 mg/dL
- Nausea / vomiting
 - Typically result from contraction of a normal gallbladder against an obstruction (at any level)

- Charcot's Triad = ***acute cholangitis***
 - RUQ pain
 - Jaundice
 - Fever
- Reynauld's Pentad = ***severe ascending cholangitis***
 - Charcot's Triad *plus*
 - Altered mental status
 - Hypotension

- Common Bacteria in Biliary Infections
 - E. coli
 - Enterococcus
 - Klebsiella
 - Enterobacter
- Less common
 - Bacteriodes
 - Clostridium
 - Strep, Pseudomonas, Candida (rare)

Therapeutic abx in biliary tract infections should cover gram-neg aerobes, anaerobes and gram-pos organisms.

- Plain radiographs (15/85)
- Ultrasound / EUS
- CT
- MRI / MRCP
- Contrast cholangiography
 - ERCP, Percutaneous, intraoperative
- HIDA
- FDG-PET

- Gallbladder
 - Calculous disease
 - Biliary colic
 - Acute cholecystitis
 - Chronic cholecystitis
 - Acalculous cholecystitis
 - Polyps

- Risks
 - Female
 - Increasing age
 - Childbearing/multiparity
 - Obesity (>30)
 - Rapid weight loss
 - Ileal disease/resection/bypass
 - 1st degree relatives
 - Drugs (TPN, estrogen, ceftriaxone)
 - Ethnicity (Native American, Scandinavian)
- Pathogenesis
 - Pigment (20%) v. cholesterol stones (80%)
- Complications
 - Biliary cholic
 - Acute Cholecystitis
 - Chronic Cholecystitis
 - Emphysematous cholecystitis
 - Empyema of CB
 - GB perforation
 - Choledocholithiasis
 - GS pancreatitis
 - Acute cholangitis
 - Mirizzi's Syndrome
 - Gallstone ileus
 - Recurrent pyogenic cholangitis

Acalculous Cholecystitis

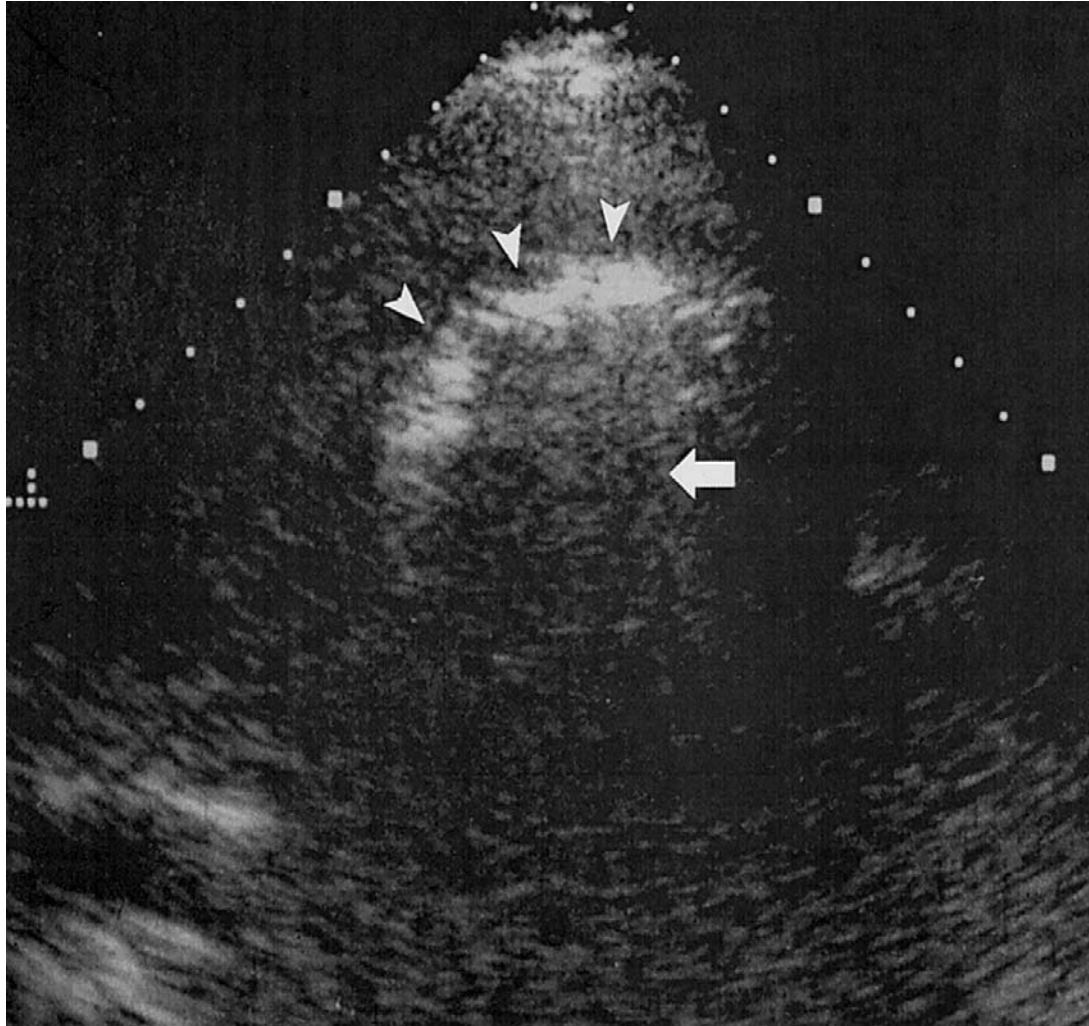
- Acute gallbladder inflammation in the absence of stones
- 5-10% of all acute cholecystitis
- 1-2% of cholecystectomies
- Generally more fulminant than calculous cholecystitis
- Associated with high morbidity and mortality

- At risk population:
 - Elderly
 - Critically ill
 - Immunocompromised
 - Examples:
 - Trauma, burns, following major surgery (e.g. open vascular or heart surgery), mechanical ventilation, sepsis/hypotension, Diabetes, immunosuppression (Txp, AIDS, chemotherapy), long-term TPN
- Exact etiology unknown
 - Stasis and ischemia of the GB
 - Visceral ischemia also commonly associated

- Presentation variable and insidious
- High incidence of gangrene and perforation of the gallbladder
- Labs test results are variable and non-specific so must have high index of suspicion
- Ultrasound (bedside, reliable)
 - HIDA if stable, but high false positive rate
 - CT to r/o other intra-abdominal pathology

- Ultrasound findings
 - Absence of stones or sludge
 - Thickening of GB wall (> 5mm) and pericholecystic fluid
 - Positive Murphy's sign
 - Failure to visualize GB
 - Emphysematous cholecystitis (Champagne sign)
 - Frank perforation with abscess

Champagne sign



Grayson D E et al. *Radiographics* 2002;22:543-561

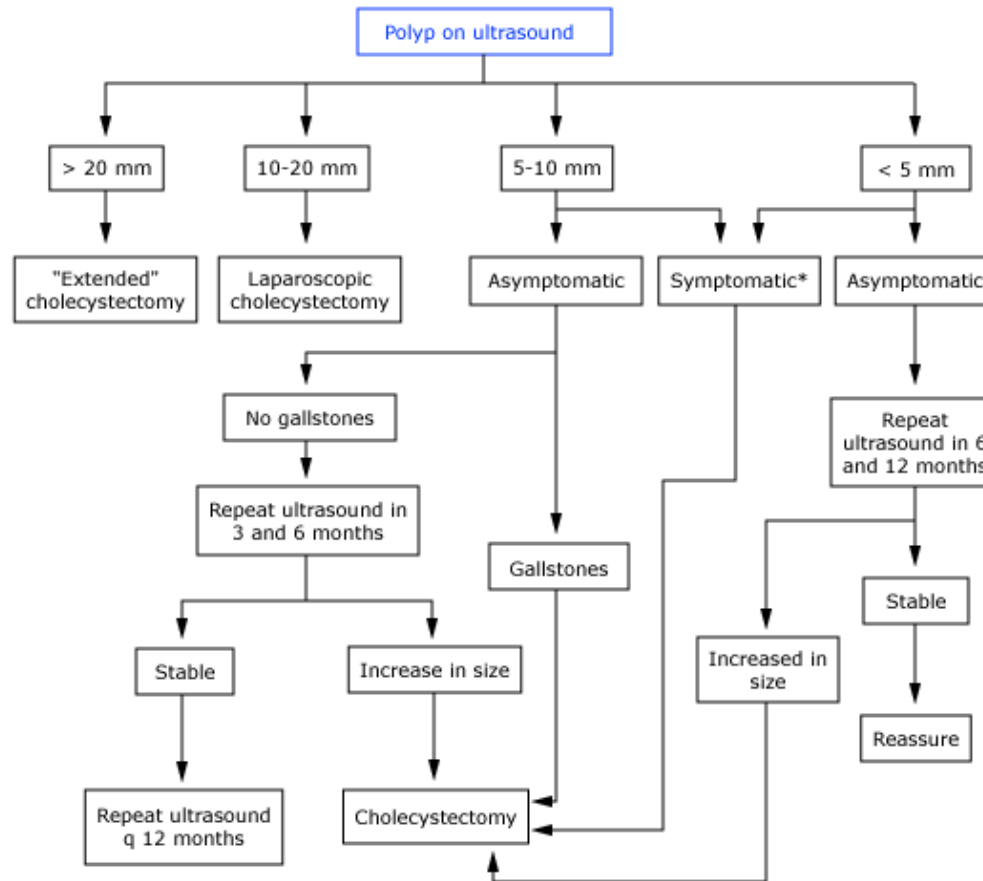
- Treatment:
 - Supportive care
 - Hemodynamic support and antibiotics (+ antifungal)
 - ***plus***
 - Surgery if stable enough
 - More often open v. laparoscopic if critically ill
 - Percutaneous cholecystostomy
 - If diagnosis uncertain
 - Successfully treats in ~90% of cases

- Usually found incidentally on ultrasound
 - Reported in 1.5 - 4.5% of GB by U/S
- Majority are non-neoplastic
 - Hyperplastic
 - Lipid deposits (cholesterolosis)
- GB adenomas quite rare (less than 0.5%)
- Imaging alone cannot discern non-neoplastic polyps from adenomas or carcinomas

- Can be associated with
 - biliary pain
 - chronic dyspeptic pain
- Cholecystectomy frequently improves or resolves these symptoms
- Risk of malignancy
 - 1-2 cm possibly malignant (40-70%)
 - > 2cm almost always malignant

Gallbladder Polyps

A suggested algorithm for managing gallbladder polyps



* Symptoms: Biliary type pain, common duct obstruction, cholangitis, or recurrent pancreatitis. Dyspepsia is not an indication for surgery.

- Incidence: uncommon
 - Fewer than 5000 cases/yr in the US
 - 1-2 cases / 100,000 population
- Epidemiology:
 - Elderly (75% > 65), female (2-6 x), caucasian
- Prognosis: poor
 - 5-year survival 5% - 38%
 - Similar to Pancreas Adenocarcinoma

- Risk factors
 - Gallstones present in 70 - 90% of GBC
 - Porcelain Gallbladder (12 - 60%)
 - Adenomatous GB polyps
 - Chronic infection (*Salmonella typhi*)
 - Congenital biliary cysts (Choledochal cysts)
 - Anomalous pancreaticobiliary junction
 - Obesity
 - (Medications, carcinogen exposure, Diabetes)

- Clinical presentation
 - Often mimics cholecystitis
 - Weight loss, jaundice and a palpable mass are less common
- Diagnosis
 - Ultrasound (often 1st)
 - Irregular GB wall
 - Heterogeneous mass replacing the lumen
 - CT / MR / EUS
 - Extending into adjacent organs (liver, colon) or
 - Involving vascular structures (Portal vein, hepatic A.)

- Additional evaluation
 - PET/CT
 - Main utility is identifying radiographically occult metastatic disease to avoid unnecessary surgery
 - Labs
 - CEA, CA 19-9 are often elevated, but lack sensitivity and specificity
 - ERCP / MRCP
 - May help in surgical planning (intra-hepatic anatomy and intra-ductal tumor extension)

- Surgical management
 - Majority found incidentally at exploration for presumed benign biliary disease
 - If GBC suspected (e.g. porcelain GB) then open cholecystectomy recommended
 - Laparoscopic port site recurrences have been reported, but resection of the port site no longer necessary, as not associated with change in outcome

TNM staging of gallbladder cancer

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor invades lamina propria or muscular layer
T1a	Tumor invades lamina propria
T1b	Tumor invades muscular layer
T2	Tumor invades perimuscular connective tissue; no extension beyond serosa or into liver
T3	Tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as the stomach, duodenum, colon, pancreas, omentum, or extrahepatic bile ducts
T4	Tumor invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastases to nodes along the cystic duct, common bile duct, hepatic artery, and/or portal vein
N2	Metastases to periaortic, pericaaval, superior mesenteric artery, and/or celiac artery lymph nodes
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

- Simple cholecystectomy
 - Appropriate for T1a lesions
- Radical cholecystectomy
 - T1b or greater
 - GB with partial hepatectomy and regional lymph nodes
- Radical chole with hepatic resection
 - Typically T3/4
 - If extension into liver or proximity to major vascular structures

- Surgery is the only potentially curative treatment
 - T2 lesions
 - Radical resection or re-resection after simple chole improves long-term DFS
 - From 24 – 40% 5-yr survival to >80%
 - Locally advanced T3/4 lesions
 - Still overall poor long-term prognosis
 - T3 survival increases from 15% to >50%
 - T4 survival increases from 7% to 25%
- Chemo +/- XRT
 - Unresectable disease (majority of cases)
 - Poor surgical candidates

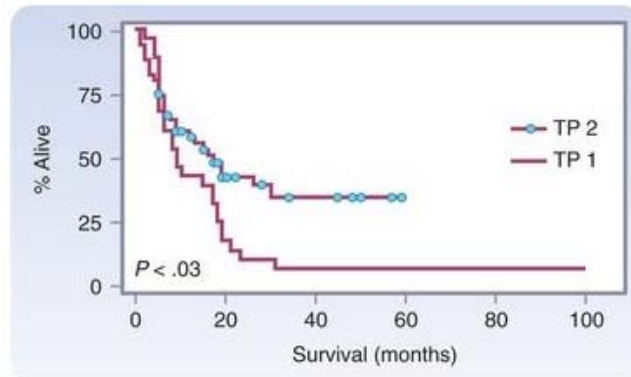


Figure 54-33 Improved survival due to an aggressive approach to gallbladder cancer comparing two time periods (TPs), 1990-1996 and 1996-2002 (circles) ($P < .03$).

(From Dixon E, Vollmer CM, Sahajpal A, et al: An aggressive surgical approach leads to improved survival in patients with gallbladder cancer: A 12-year study at a North American Center. Ann Surg 241:385-394, 2005.)

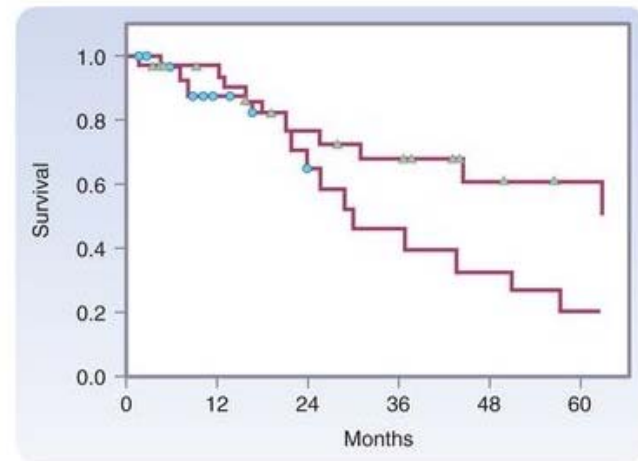
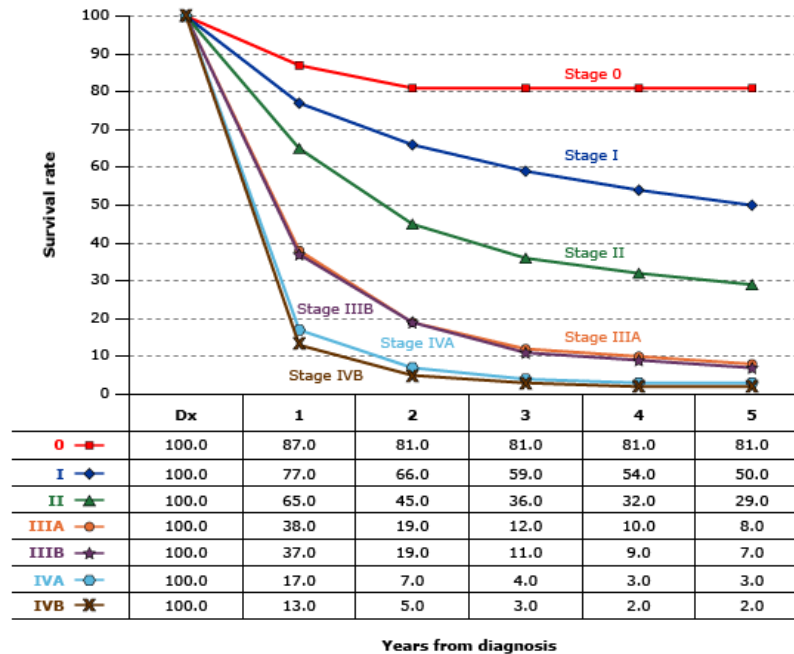


Figure 54-34 Survival following surgical resection for T2 gallbladder cancer. Patients undergoing radical resection (triangles) are compared with patients undergoing simple cholecystectomy (circles) ($P > .05$).

(From Fong Y, Jarnigan W, Blumgart LH: Gallbladder cancer: Comparison of patients presenting initially for definitive operation with those presenting after prior noncurative intervention. Ann Surg 232:557-569, 2000.)

Gallbladder Cancer

Observed survival rates for 10,705 gallbladder cancers



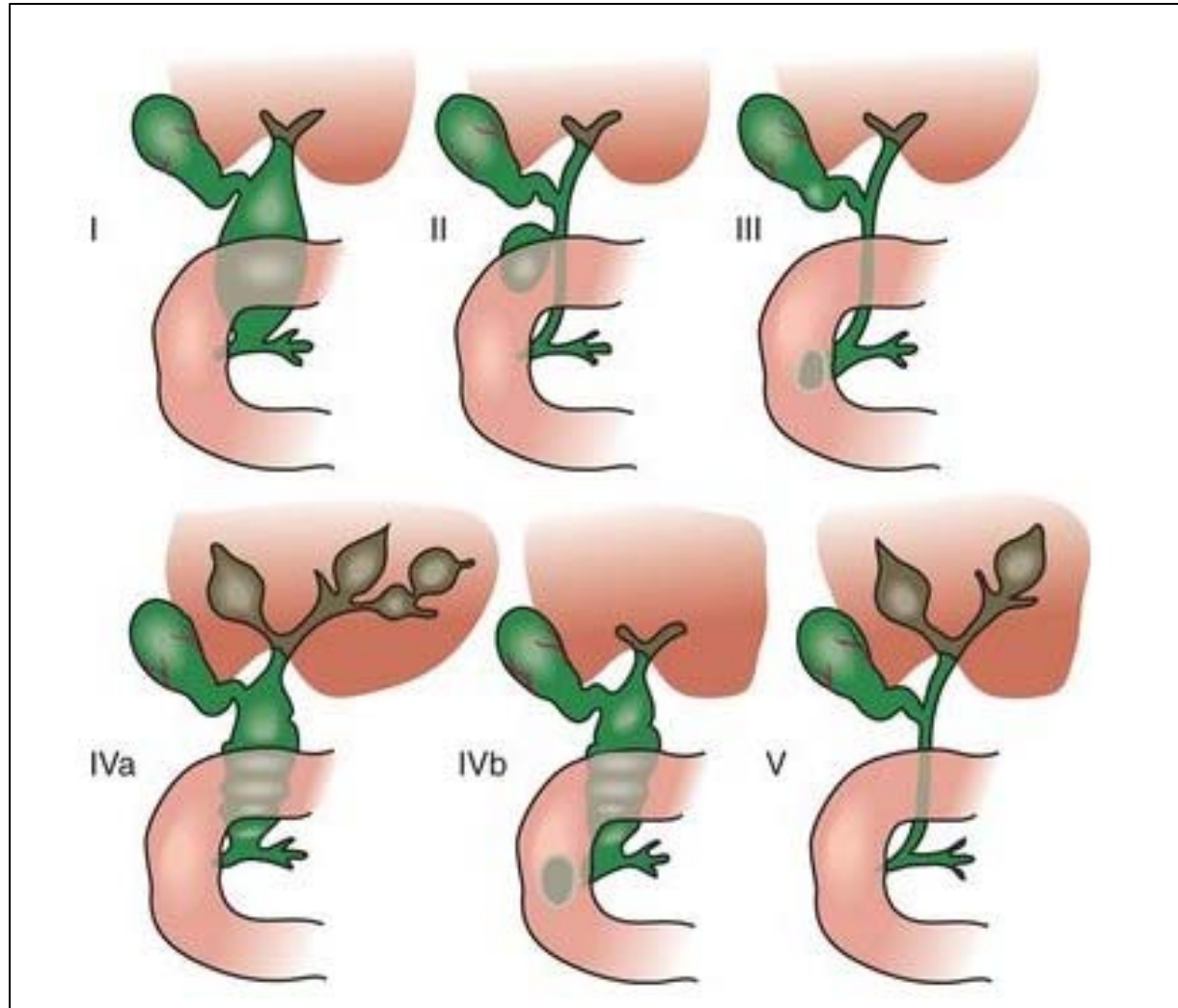
Data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) diagnosed in years 1989-1996.

- Less than 15% of all patients with GBC are alive at 5 years
- Median survival for Stage IV patients from presentation is 1-3 mos.

- Benign conditions
 - Choledocholithiasis
 - Benign strictures (stones, procedures)
 - Intraductal Papilloma / adenoma
 - PSC
 - Biliary (Choledochal) cysts
 - Cystadenomas
- Malignant conditions
 - Cholangiocarcinoma
 - Cystadenocarcinoma

- Type I (50-85%)
 - IA – cystic dilatation of the entire extrahepatic duct
 - IB – focal dilatation of the extrahepatic duct
 - IC – smooth, fusiform dilatation of the entire extrahepatic duct
- Type II (2%)
 - True diverticula
- Type III (1-5%)
 - Limited to intraduodenal portion of the CBD (multiple subtypes)
- Type IV (15-35%)
 - IVA – both intra and extrahepatic cysts
 - IVB – multiple extrahepatic cysts
- Type V (20%)
 - Caroli's disease
 - Intrahepatic ducts without extrahepatic involvement

Classification of Biliary (Choledochal) Cysts



- Various proposed etiologies, though no one mechanism accounts for all
- Types 1A and 1C are associated with anomalous pancreaticobiliary junction (APBJ)
- Genetic, environmental factors
- Fetal viral infection (reovirus)
- Associated with a 2.5 – 30 fold increased with of cholangiocarcinoma

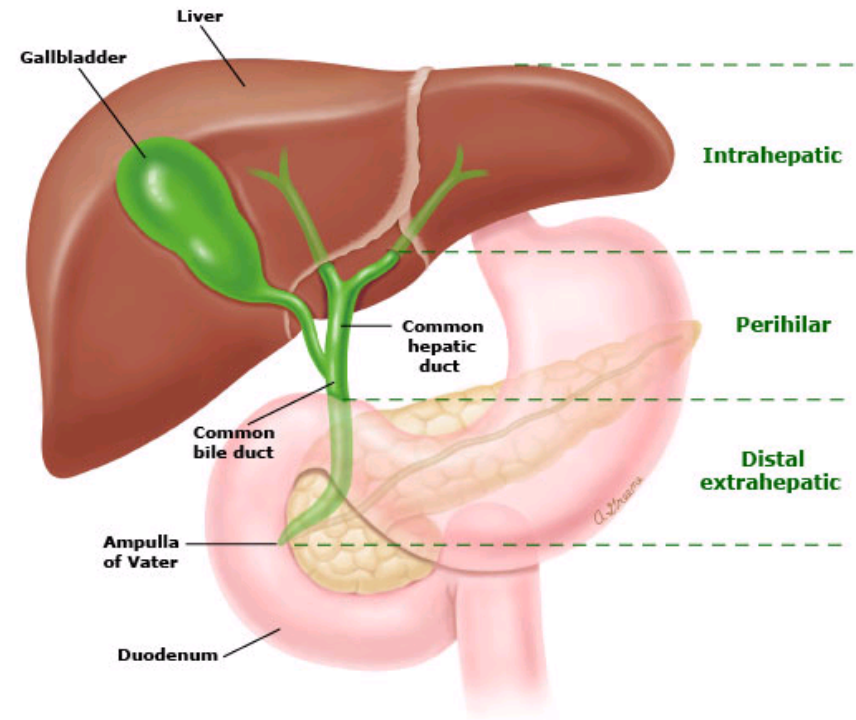
- Risk of cholangiocarcinoma*
 - Risk increases with age
 - <10 years – 0.7%
 - 11-20 yrs – 6.8%
 - > 20 yrs – 14.3%
 - Overall incidence 10-30% (mean age at Dx = 32)
 - Incidence as high as 50% in older patients
 - Most occur in Type I (68%) and Type IV (21%)
 - Lowest risk in Type III (2%)

* Risk in normal population is <<1%

- Bile duct cancers arising in
 - Intrahepatic
 - Perihilar
 - Distal (extrahepatic) biliary tree

*excludes gallbladder & Ampulla of Vater

Anatomic classification of cancers of the human biliary tract



- Incidence similar to GBC
 - 1 – 2 cases per 100,000 population
 - Exact incidence hard to define because intrahepatic lesions used to be grouped with liver cancers.
- Increases with age
 - Typical patient 50-70
 - Nearly 2 decades earlier with PSC and choledochal cysts
- More common in men (unlike GBC)
- Prognosis poor
 - Unresectable: median survival <6 months, 5-yr < 5%

- Risk factors
 - PSC
 - Nearly 30% of cholangiocarcinomas (w/wo UC)
 - Annual incidence of 0.6% - 1.5%
 - Lifetime incidence of 10-15%
 - More difficult to diagnose
 - Biliary (Choledochal) cysts
 - (15% risk of malignant change)
 - Hepatolithiasis / Recurrent pyogenic cholangitis
 - 5-10% of patients will develop cholangiocarcinoma.
Much higher in certain Asian populations
 - Parasitic infections
 - Liver flukes Clonorchis and Opisthorchis

- Risk factors
 - Thorotrast exposure
 - 30+ years later
 - Lynch syndrome
 - Biliary papillomatosis
 - Chronic liver disease
 - Viral (HBV, HCV)
 - Non-viral
 - Prior biliary procedures
 - Recurrent episodes of cholangitis

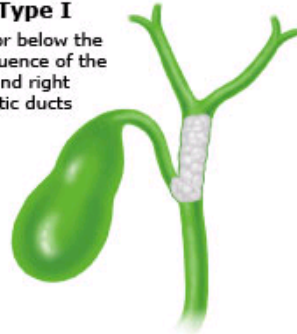
- Clinical features
 - Jaundice (90%)
 - Pruritis (66%)
 - Abdominal pain (30-50%)
 - Weight loss (30-50%)
 - Fever (up to 20%)
 - 2° to associated cholangitis
 - Acholic stools, dark urine, hepatomegaly, abdominal mass, palpable gallbladder (Courvoisier's sign)

- **Diagnosis**
 - RUQ Ultrasound
 - Dynamic CT
 - MRI / MRCP
 - ERCP with brushing/biopsy
 - Tumor markers (CA 19-9, CEA)
 - Tissue confirmation still lacking
 - US- or CT-guided biopsy
 - EUS with FNA
 - Surgical exploration
 - PET/CT

Bismuth-Corlette classification of biliary tract cancers

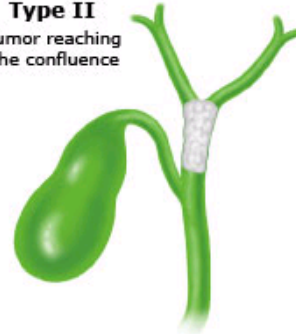
Type I

Tumor below the confluence of the left and right hepatic ducts



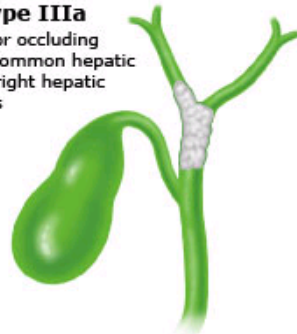
Type II

Tumor reaching the confluence



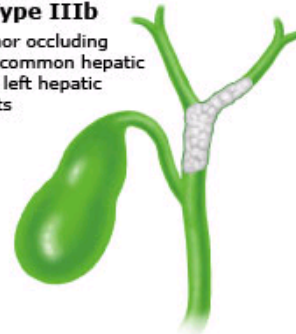
Type IIIa

Tumor occluding the common hepatic and right hepatic ducts



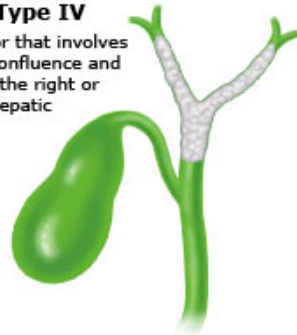
Type IIIb

Tumor occluding the common hepatic and left hepatic ducts



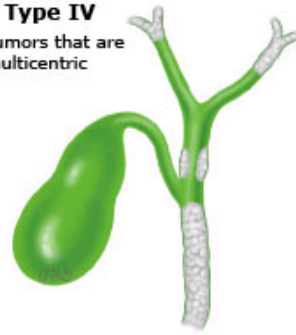
Type IV

Tumor that involves the confluence and both the right or left hepatic duct



Type IV

Tumors that are multicentric

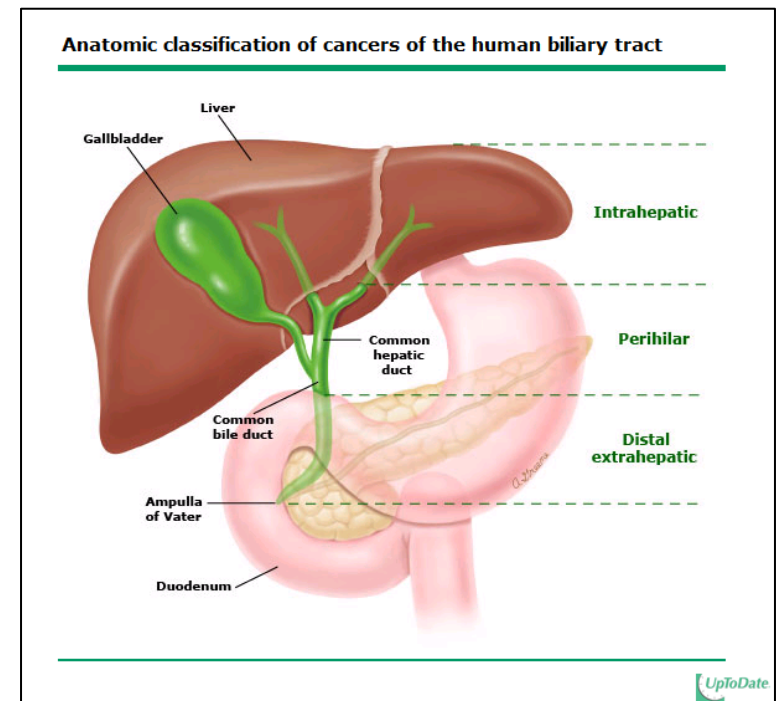


The Bismuth-Corlette classification of biliary tract. White areas represent tumor and green areas normal bile duct.
Modified from de Groen PC, Gores GJ, LaRusso NF, et al. *N Engl J Med* 1999; 341:1368.

- Surgery represents best chance for cure
 - Distal tumors
 - Most likely to be resectable (90%)
 - 5-year survival rates 15%-50%
 - May include Ampullary CA (favorable) and pancreatic (poor)
 - Perihilar (Klatskin tumor)
 - Resectable about 60% of the time
 - High rate of local recurrence without radical resections. 5-yr survival ranges 20% - 50%
 - Intrahepatic lesions
 - Resectable about 57% of the time
 - Broad range of outcomes based on stage
 - 3-yr survival rates: 66% (Stage 1) to 7% (node positive)

- Criteria for resectability:
 - Extent of both right and left duct involvement
 - Absence of extended regional LN mets
 - Absence of liver mets
 - Absence of vascular invasion (PV, main HA)
 - Absence of extrahepatic adjacent organ invasion
 - Absence of disseminated disease

- Surgical approaches
 - Distal bile duct
 - Whipple
 - Perihilar bile duct
 - Bile duct resection with partial liver resection
 - Liver transplant*
 - Intrahepatic bile duct
 - Liver resection
 - Liver transplant*



- Liver transplant for unresectable CCA
 - Mixed results
 - Best if incidental (sub-clinical) finding (as might occur in PSC)
 - Historically, poor results with known tumor
 - >50% recurrence
 - One-year survival 58% (v 87.7% for OLT in general*)
 - 3-year survival 22% (v 79.9% for OLT)
 - 5-year survival 13% (v 74.3% for OLT)
 - Mayo study
 - Highly selective enrollment criteria
 - Neoadjuvant chemo/XRT
 - 1-, 3-, 5-year survival of 82, 63, and 55%
 - Generally not recommended outside of study protocol

- Reviewed general anatomy, physiology and pathophysiology
- Selected Benign and Malignant conditions
 - Intra- and Extra-hepatic bile ducts
 - Gall bladder
- Diagnostic approach to suspected biliary tract disease

Thank you