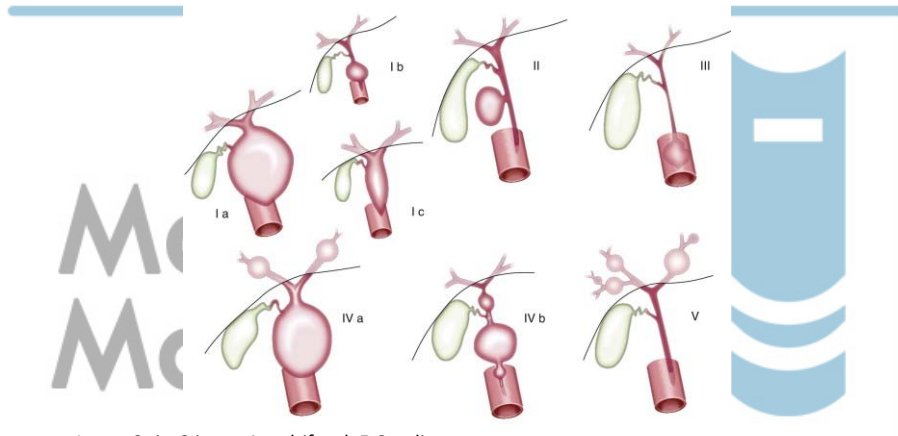


- **Choledochal Cysts**

- o Def: congenital cystic dilation of extra and/or intrahepatic ducts likely 2/2 anomalous jxn of PD and CBD with high insertion of CBD into the pancreatic duct leading to pancreatic juice reflux and subsequent inflammation and distal duct obstruction w/ proximal dilation and cyst formation
- o Epidemiology: F>M, Incidence: 1/15k in US vs 1/1k births in Japan
- o S/S: p/w triad of (1) cholestatic jaundice, (2) ab pain and (3) ab mass during the first few months of life but 20% present into adulthood with vague Sx for years
- o Complication (f/u is imperative even after Tx)
 - Cholangiocarcinoma (refer)
 - CHF
 - Portal HTN
 - Hepatic Abscess
 - Cyst Rupture
 - Recurrent Cholangitis
 - Pancreatitis
 - Cholelithiasis
 - Spontaneous Perforation
 - Biliary Stricture
 - Bleeding due to erosion into adjacent vessels
- o Todani Modification of the Alonso-Lej Classification (based on appearance and location)



- 1 cyst, 2 tic, 3 intra, 4 multifocal, 5 Caroli
- Type I **Choledochal Cyst** (extrahepatic CBD cyst, 1a = saccular, 1b = round, 1c = fusiform, **most common, 80%**)
 - Tx: cyst excision w/ Roux-en-Y anastomosis of bile duct to jejunum
- Type II **Choledochal Cyst** aka **Choledochal Diverticulum** (extrahepatic CBD diverticulum, 5%)
 - Tx: same as Type I
- Type III **Choledochal Cyst** aka **Choledochoceles** (intrahepatic CBD cyst, 5%)
 - Tx: rarely develop into cancer therefore excision is not mandatory unless large (can actually be Tx endoscopically by “unroofing” the cyst)
- Type IV **Choledochal Cyst** (4a = multiple intra/extrahepatic or 4b = multiple extrahepatic, 10%)
 - Tx: excision w/ partial hepatectomy
- Type V **Choledochal Cyst** aka **Caroli's Dz** (1%, intrahepatic)
 - NB some consider it a separate entity from choledochal cysts
 - NB can be associated w/ renal problems (PCKD, medullary sponge kidney, renal tubular ectasia) and liver problems (APBDJ, congenital hepatic fibrosis)
 - NB presents at 30yo w/ recurrent cholangitis w/ liver abscess and hepatolithiasis
 - Tx: conservative treatment with transplant as last resort

Other

- **Sump Syndrome**

- o Occurs in pts who had a choledochoduodenostomy for bile duct stones (before the era of ERCP)
- o Eventually the SO malfunctions and then the distal CBD b/c a “sump” collecting and storing duodenal material that refluxes back in to the CBD causing Sx of pain, fever, jaundice
- o Xray/US (pneumobilia and RUQ calcification), UGI (reflux into biliary tree), ERCP (dilated ducts proximal to anastomosis and distal narrowing to papilla)

Biliary Dysmotility

- **Gallbladder Dyskinesia/Dysfunction/Stasis/Delayed-Emptying**
 - o Etiology: 2/2 mild acute cholecystitis or chronic cholecystitis
 - o S/S: dyskinesia leads to sludge and then stone formation which can cause Sx BUT whether Sx can occur when no sludge/stones form is unclear, it is important to know that these pts often have concurrent functional ab pain
 - o Dx: EF% after CCK administration during HIDA Scan (>35% EF, avg is 75%), pain often occurs during CCK infusion but this is not a positive finding b/c CCK stimulates intestinal motility which can cause pain
 - o Tx: cholecystectomy (always confirm that chronic cholecystitis was present on pathology)
- **Sphincter of Oddi Dysfunction (SOD)**
 - o Anatomy: PD joins CBD forming the ampulla of Vater (nl angle is 5°-30°), the duodenal mucosal bulge that the ampulla/sphincter makes is called the papilla (ampulla length range 1-12mm w/ median 4.5mm, ~75% common channel, ~20% separate opening, ~5% septum, this is unlike APBDJ)
 - Ampulla is surrounded by the sphincter of Oddi (discovered by Ruggero Oddi a medical student in 1887) which has four parts
 - (1) sphincter choledochus = circular muscle surrounding the CBD (basal contraction prevents flow of bile b/t feeds)
 - (2) sphincter pancreaticus = circular muscle surrounding the PD (basal contraction prevents flow of pancreatic secretions b/t feeds)
 - (3) sphincter ampulla = circular muscle that surrounds ampulla (phasic contraction prevents duodenal reflux b/t feeds during duodenal MMC)
 - (4) fasciculus longitudinales = longitudinal muscle running b/t CBD and PD (contraction promotes flow of bile during feeds)
 - +: ACh, Motilin
 - -: CCK, Secretin, VIP, NO
 - NOT regulated by nerves
 - o Def: non-calculous obstruction of the SO (the two types below are not mutually exclusive)
 - Functional/Active (eg. spasming/dyskinesia/hypertension from long term opiate use (VERY BIG PROBLEM, ADVISE TO STOP), et al) = usually Type III Dz
 - Structural/Passive (eg. fibrosis, inflammation, etc from prior passage of stone, et al) = usually Type I Dz
 - NB intra-ampullary neoplasm may simulate SOD and should be suspected if there is excess tissue in the ampulla after sphincterotomy
 - o Epidemiology: middle aged women, ~10% of postcholecystectomy syndrome, pts often have concurrent functional disorders
 - o S/S: (biliary and/or pancreatic)
 - (1) postcholecystectomy syndrome (1% of cholecystectomies, why? either SOD is what they had all along or when they lost their GB it could no longer accommodate the increased pressure or when the GB was removed some of the inhibitory nerve pathways were also cut)
 - (2) idiopathic recurrent acute pancreatitis (causes pancreatitis by promoting reflux of bile into the PD or by obstructing PD outflow)
 - (3) biliary pain w/ an intact GB and no stones (most controversial)
 - Associations (controversial): s/p OLT, AIDS, DL, chronic pancreatitis
 - o Dx
 - ERCP w/ Sphincter of Oddi Manometry (SOM)
 - + when mean basal pressure is >40mmHg above duodenal baseline for >30sec on two separate pull thrus (other parameters that are looked at include contractile frequency >8/min, amplitude >350mmHg, retrograde propagation >50%)
 - How? water perfusion aspirating triple lumen 5F catheter passed thru the working channel of the ERCP scope, the catheter is attaches to external transducers and recordings are displayed, obtain a duodenal baseline to calibrate zero (elevator down and catheter not touching wall), then enter sphincter aspirate to determine biliary vs pancreatic (avoid placing wires or contrast b/c may affect pressure measurements but afterwards it is good to inject contrast to make no other pathology), perform measurements via orifices spaced 2mm apart moving back 1-2mm via a standard station pull-through technique measuring base pressure and contraction pressures, repeat for the other duct, stent PD b/c of high r/o PEP, monitor pts for several hours afterwards
 - avoid for >12hrs any drugs which can relax (CCB, nitrates, anticholinergics, glucagon, octreotide) or contract (morphine, cholinergics) the SO
 - o NB general anesthesia, propofol, benzo and meperidine <1mg/kg do NOT affect SO
 - pts often have high complication rates after ERCP w/ pancreatitis in up to 20% therefore ERCP w/ SOM should be reserved for pts w/ severe Sx
 - May miss SOD if 2/2 intermittent spasming
 - Empiric Placement of Biliary/Pancreatic Stent or BoTox Injection SO to see if Sx improve
 - Non-Invasive Tests (all lack sens/spec therefore often not used)
 - Nardi Test: reproduction of Sx after SC injection of morphine/neostigmine which increases SO pressure and pancreas secretion
 - Fatty Meal or CCK/Secretin US: >2mm dilation of the CBD after eating a fatty meal or administration of CCK

- Biliary Scintigraphy
 - Secretin MRCP: if there is PD dilation >2mm for >30min then positive
- o Modified Milwaukee Classification (predictive of the Hz of abnormal SOM and symptomatic response to sphincterotomy)
- Type I: pts w/ biliary pain and 3 of the following two
 - (1) AST or AP $\geq 1.1 \times$ ULN (although not necessary labs should correlate w/ clinical episodes and normalize b/t episodes)
 - (2) CBD ≥ 9 mm
 - Type II: pts w/ biliary pain and 1 of the above two
 - Type III: pts w/ biliary pain only
 - NB the critical thing is that the pt truly has “biliary-type” pain
 - NB a similar classification for the pancreas exists in which there is pancreatic-type pain, Amylase or Lipase $>1.1 \times$ ULN, PD >6 mm at head or >5 mm at body
 - NB delayed drainage (>45 min) of contrast from the CBD after ERCP was an old criterion that is no longer looked at
 - NB a new test called HIDA w/ CCK Stimulation SOD protocol looks at various parameters and calculates a score that correlates w/ risk of SOD (<4 nl vs >5 abnl)

Milwaukee Type	Abnormal SOM	Symptomatic Response to Sphincterotomy	
		if Abnormal SOM	if Normal SOM
Type I	$>90\%$	$>90\%$	$>90\%$
Type II	55-65%	85%	35%
Type III	25-60%	55-65%	$<10\%$

Milwaukee Type	Diagnostic Approach	Treatment
Type I	No further w/u is needed b/c SOM will assuredly be abnl therefore go ahead w/ Tx (even if nl SOM then likely false negative hence just skip SOM)	Endoscopic Sphincterotomy • NB if sphincterotomy does NOT resolve Sx then consider another cause of pain, inadequate sphincterotomy, restenosis, concomitant pancreatic sphincter hypertension • Surgical sphincterotomy/plasty • Intersphincteric BoTox Injection or BoTox injection not effective
Type II	SOM	If +SOM then sphincterotomy If -SOM then trial of conservative Tx • Decrease Pancreaticobiliary Stimulation: low fat diet • Lower SO Pressure: meds (nifedipine, nitrates, anticholinergics, glucagon, octreotide) NB avoid meds that increase SO pressure ESPECIALLY OPIATES
Type III	Cholecystectomy if not already done then search for other causes of pain (NASH, functional ab pain, etc) then as last resort do SOM Consider HIDA SOD Protocol to provide pt objective but non invasive evidence that they don't have SOD	“ “

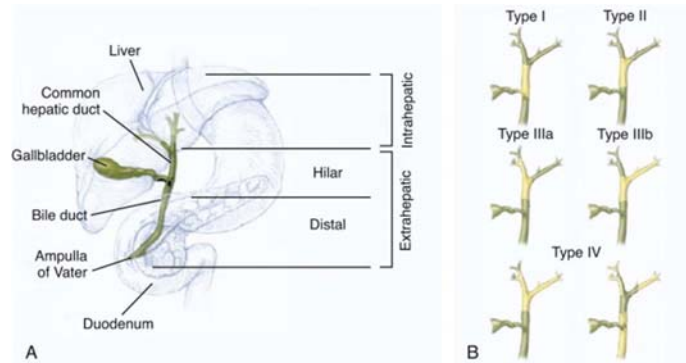
Ampullary Tumors

- Types: adenoma to AC (most common), NET to NEC (second most common), lymphoma, lipoma, fibroma, leiomyoma, hamartoma, etc
- Epidemiology: rare, 1/80,000/yr, ~60yo, slight M>F, White>Hispanic>AA
- RFs: most are sporadic but some are associated w/ other conditions: FAP (refer), NF (1/4 of ampullary NETs), Chronic Parasitic Liver Fluke Infections
- S/S: obstructive jaundice $\pm$ complications (stones, double duct sign, cholangitis, pancreatitis, Courvoisier) + GIB (Sx often present early in dz b/c of location)
- Gross: unlike AC of the remainder SI ampullary tumors usually arise from large/villous/sessile adenomas w/ higher malignant potential

- o Ampullary tumors can appear: (1) normal appearing if small intra-ampullary, (2) bulging but otherwise normal appearing ampulla if large intra-ampullary, (3) adenoma like if less advanced, (4) carcinoma like if more advanced
 - o NB periampullary tumors are 15x as common as true ampullary tumors
 - o Periampullary: Pancreas, CBD, Duodenum
- Dx:
 - o EUS (bx, size, wall invasion and duct involvement is suggestive of conversion to carcinoma)
 - o ERCP (re-bx to determine if there is intra-ampullary conversion to carcinoma which occurs in ¼ of cases THIS IS KEY!!!, confirm duct involvement)
- Staging for cancer
 - o T1d0 (sphincter only) T1d1 (to duodenal submucosa)
 - o T2 (to duodenal muscularis propria)
 - o T3 (to pancreas <2cm)
 - o T4 (to pancreas >4cm or adjacent organ/vessel involvement)
 - o N0-1
 - o M0-1
- Tx
 - o endoscopic ampullectomy (if adenoma, <4cm, no ductal involvement, NB T1d0N0M0 carcinomas can sometimes be managed alone w/ surgery but controversial)
 - inform pt that there are higher complication risks esp papillary stenosis and perforation
 - Pre-abx and 3d afterwards
 - Cannulate CBD/PD and do bilateral sphincterotomies (controversial, some leave wires in place)
 - Snare polypectomy (en-bloc better than piecemeal, submucosal lift not recommended) followed by thermal ablation of margins
 - Bilateral stent placement
 - Surveillance is imperative (Q3mo-1yr) and biopsy even if everything macroscopically looks normal
 - o surgical (if not above or ≥T1d1 carcinoma)
 - transduodenal resection to full Whipple if intraductal involvement
 - o NB even in the absence of FAP there is evidence that pts w/ ampullary adenomas/carcinomas have increased incidence of colon adenomas/carcinomas therefore consider frequent colonoscopies

Cholangiocarcinoma (CCA)

- Epidemiology
 - o Low Risk Areas (2% of all malignancies, USA w/ Hispanic>White>AA, incidence: 0.82-0.95/100,000 w/ increasing incidence of intrahepatic vs decreasing incidence of extrahepatic, slight M>F, rarely <40yo w/ median age 65yo except in pts w/ PSC)
 - o High risk areas (Asia likely b/c of parasitic infections and hepatolithiasis w/ incidence of 96/100,000, median age 50yo)
- Types (distinction b/t intra and extra is actually very important as they have different epidemiology, etiology, pathogenesis, molecular signatures and Tx)
 - o Tissue
 - Epithelial Adenocarcinoma 90% (10% are intestinal carcinoma, clear cell carcinoma, signet ring cell carcinoma, squamous cell carcinoma, small cell carcinoma, adenosquamous carcinoma, mucinous carcinoma, mets: colon/pancreas/stomach/breast/lung AC)
 - o Location
 - Intrahepatic (20%) = abdominal pain + general cancer Sx: cachexia, malaise, fatigue
 - proximal to 2nd order bile ducts
 - sometimes difficult to distinguish b/t liver mets and HCC and CCA (different enhancement phases are suggestive of one over the other (venous = CCA vs arterial = HCC) but IHC generally needed to confirm type)
 - present as a mass
 - Extrahepatic (80%) = painless biliary obstruction (jaundice, clay stools, dark urine, pruritus) ± bacterial cholangitis in 10% of cases
 - Hilar aka Klatskin's Tumor (50%) B-C classification has little clinical value
 - o Bismuth-Corlette I (below the confluence/bifurcation)
 - o Bismuth-Corlette II (confluence/bifurcation but not the R/L hepatic ducts)
 - o Bismuth-Corlette III (confluence/bifurcation AND a: R-HD vs b: L-HD)
 - o Bismuth-Corlette IV (multifocal OR like Type III but involving BOTH R and L-HD)
 - Distal (30%) below cystic duct



- RFs (70% are de novo and do not have an identifiable RF except for advancing age, if there is a RF it is usually due to cholestasis w/ inflammation which provides a microenvironment that promotes malignant transformation of cholangiocytes, certain RFs are more linked with extra-hepatic CCa vs intra-hepatic CCa and vice versa)

o Well Established

- 1° PSC (refer)
- Hepatolithiasis (stones proximal to the confluence of the R/L hepatic duct, rare in Western world more common in Asia, 2/2 prolonged irritation and bile stasis)
- Choledochal Cysts
 - esp Type I/V
 - 50yo have a 50% risk
 - mainly at cyst wall but 40% can occur at more distant sites including liver/pancreas/GB and thus pts are still at risk even after excision of cyst

o Less Well Established

- Biliary Tree Fluke Infections (refer)
- Toxins: Thorotrast, Dioxins, Polyvinyl Chloride
- IBD even in those w/o PSC
- HCV/HBV
- Cirrhosis of any cause
- Metabolic Syndrome: Diabetes, Obesity
- Toxins: Alcohol, Smoking
- Recurrent Choledocholithiasis
- Recurrent Infectious Cholangitis
- Biliary Enteric Anastomosis

• Dx

o Approach

- If clinical suspicion then check CA 19-9 and ERCP w/ brushing, cytology, FISH and if indeterminate then check MRI/PET otherwise if negative then just observe vs if positive then Tx for CCa

o Tumor Markers

- CA19-9
 - >129 U/mL: 80% sens 98% spec in PSC pts vs 50% sens 80% spec in non-PSC pts
 - variable sensitivity and non-specific including other malignancies including gastric/pancreatic and biliary stones and inflammation and cholangitis and if CA 19-9 does not fall after Tx of these conditions then consider CCA
 - 10% of the population who have a negative Lewis antigen do not express CA 19-9 and thus will have no CA 19-9
- Other: CEA, CA-125
- New Markers: Mac-2BP, Matrix Metalloproteinase-7, MUCIN-5AC

o Imaging (all are complementary)

- T-US (initial test demonstrating intra + extra hepatic duct dilation depending on location cancer)
- CT/MRI (good for TN staging but best for M staging specifically distant organ mets)
- EUS (best for TN staging and vascular involvement, malignancy is seen as a hypoechoic mass/thickening of the biliary wall, there is controversy whether FNA should be performed given r/o tumor seeding, there is 50% sens)
- PET (emerging as an important tool for determining the presence of malignancy in dominant stricture PSC and for small distant mets)
- ERCP
 - The difficult question: Is the stricture benign or malignant?
 - o Paucicellular, highly desmoplastic, inflammatory tumor making dx difficult (also it is difficult to accurately target the area of interest)
 - o Bile Sampling Cytology (20% sens), Brushing Cytology (40% sens), Biopsy Histology (50% sens), FISH (60% sens)

- Cytology + Histology (60% sens)
 - FISH: detect (1) trisomy 7 (helpful), (2) tetrasomy or duplication of any chromosome (helpful), (3) polysomy or amplification of any three chromosomes (diagnostic)
 - Most send for cytology and histology and if negative then send out for FISH
 - Site directed tissue acquisition using cholangioscopy and intraductal ultrasonography (hypoechoic asymmetric thickening w/ poorly demarcated borders and rough edges)
 - The next difficult question: If malignant stricture is it CCA or met?
 - Immunohistochemistry is helpful (CCA is uniquely + for cytokeratin-7 and K20)
 - Different growth patterns: mass forming, periductal-infiltrating, intra-ductal papillary
 - NB intra-ductal papillary spreads superficially along the mucosa w/in deep invasion and thus have a better prognosis
 - intrahepatic CC is usually mass forming while extrahepatic CC can be any of the three
- Staging
 - quite controversial and currently evolving
 - different staging systems should exist for intrahepatic and extrahepatic CCA as they are very different tumors
 - originally intrahepatic CCA was staged using the HCC TNM system however this approach was not predictive of prognosis, the AJCC system is based on the number of hepatic lesions, vascular involvement, LNs and mets

- Treatment (resection remains the only curative treatment, neither neoadjuvant nor adjuvant chemoradiation has been shown to be effective in earlier studies but newer studies are suggesting that newer regimens may be effective, the more proximal typically the more advanced b/f diagnosis is made)
 - Resectable (<1/3)
 - Indications (all very controversial and evolving): no vascular invasion, no LNs, no adjacent organ, no mets, few medical comorbidities, no significant underlying liver dz, minimal involvement of the liver in intrahepatic CCA
 - Preoperative Stenting (refer)
 - Types
 - Intrahepatic: Lobar Resection (5yr survival 22-44%)
 - NB interestingly liver transplant has disappointing 5yr survival
 - Extrahepatic Hilar: en bloc resection w/ cholecystectomy, regional lymphadenectomy, Roux-en-Y hepaticojejunostomy for Type I/II vs “ ” + Partial Hepatectomy for Type III (5yr survival 11-41%)
 - NB preoperative portal vein embolization resulting in compensatory hyperplasia of the contralateral hepatic lobe is often done to allow for extended partial hepatectomy
 - NB liver transplantation was originally associated w/ rapid recurrence and poor survival rates however recent studies demonstrate better rates in bilateral extrahepatic hilar

CCa (Type IV) pre-treated w/ adjuvant chemoradiation (originally Type IV were universally unresectable)

- Extrahepatic Distal: Whipple (5yr survival 27-37%)
 - NB occasional end-to-end anastomosis
- NB PSC pts need to be transplanted
- NON-Resectable (>2/3, 50% die w/in 3-4mo of presentation)
 - Endoscopic/Percutaneous/Surgical Biliary Decompression
 - Endoscopic: refer
 - Percutaneous: refer
 - Surgical: hepaticojejunostomy or choledochojejunostomy
 - Ablation
 - Extrahepatic CCa: PDT (Photo Dynamic Therapy) = Systemic application of photosensitizing agent which is selectively taken up by tumor cells followed by localized illumination of the tumor with a specific wavelength of light resulting in the formation of toxic radicals in tumor cells and subsequent cytotoxicity
 - Intrahepatic CCa: TACE (Trans Arterial Chemo Embolization)

Gallbladder Lumen Disorders

- Polyps (5% of the population)
 - Neoplastic – 5% (solitary) Suggestive Factors: advancing age, sessile, coexistent gallstones, PSC
 - **Adenoma (5%)** = single (30% multiple) >1cm hypoechoic/isoechoic pedunculated polyp
 - NB unlike the colon in the GB it is interesting that adenoma are actually less common than adenocarcinoma
 - **Adenocarcinoma 5%** = similar to adenoma
 - Epidemiology
 - 2-6x F > 1x M
 - High Risk Areas: South Asia (esp India), South American (esp Chile), Eastern Europe (esp Slovakia), 21.5/100,000/yr, median age 55yo
 - NB leading cause of cancer death in Chilean and North Indian women!!!
 - Low Risk Areas: USA (esp Hispanic/American Indians), Australia, Western Europe, 1.2/100,000, median age 65yo
 - RFs (GB is exposed to various toxic substances secreted by the liver which are subsequently concentrated in the GB promoting their injury)
 - Pt: advancing age, female, certain ethnicities, poor socioeconomic status (refer above)
 - FHx: first degree relative w/ GBC
 - Gallstones: multiple, large (>2.5cm), chronic gallstones (most common RF but 25% do not have gallstones)
 - Precursor: adenoma, porcelain GB (reflects chronic inflammation), segmental adenomyomatosis
 - Carcinogens: smoking, methylcholanthrene, aminoazotoluene, nitrosamines
 - Chronic Infection: *Salmonelli typhi* and *paratyphi* (likely an important cause for Chile and India)
 - Metabolic: hyperestrogen state including pregnancy, HRT/OCPs, etc (aside from its risk in developing gallstones), DL w/ High TGL and Low LDL, obesity
 - Meds: methyldopa, isoniazide, estrogens
 - Other: Anomalous Pancreatico-Biliary Unions/Ductal-Junctions (APBU/DJs) results in increased reflux of pancreatic secretions into the gallbladder
 - Autoimmune: PSC!!!
 - Mechanism
 - Chronic Irritation/Inflammation (99% of cases) → proliferation (p-53 mutation) → intestinal metaplasia → dysplasia → carcinoma in situ
 - Hereditary (1% of cases) → proliferation (k-ras mutation) → adenoma → dysplasia → carcinoma in site
 - Other mutations: p16 inactivation, COX-2 over expression, microsatellite instability, VEGF induction, hypermethylation
 - Diagnosis
 - S/S: insidious/chronic symptoms similar to cholelithiasis + RUQ mass and B symptoms (night sweats, anorexia, chills)
 - Gross Pattern: focal mass (65%) vs focal/diffuse thickening (35%)
 - Location: fundus (60%), body (30%), neck (10%)
 - Spreads via direct invasion, lymphogenic/hematogenous spread, perineural invasion, intraperitoneal invasion, intraductal invasion
 - Markers: CA 19-9, CEA, CA-125 can each be variably elevated but CA-242 appears to have the best specificity and sensitivity
 - EUS provides the best information on GB lumen

- o CT provides the best information on adjacent organ involvement except for detecting small mets to liver surface and peritoneum (addition of PET and MRI may be helpful)

	2010 American Joint Committee on Cancer Staging System	T	N	M	Tx Surgery then Adjuvant Chemo	5yr Survival (overall median survival is 6mo!!!)
"Early"	0	is (Carcinoma <i>in situ</i>)	0	0	Open Cholecystectomy (not laparoscopic b/c of r/o trocar site tumor seeding)	95%
	I	1a (invades into lamina propria)	0	0		85%
		1b (invades into muscularis propria)			Radical Cholecystectomy (additional wedged resection of GB bed at liver segments IV/V and portal LN dissection)	80%
	II	2 (invades into connective tissue)	0	0	Extended Radical Chole (wider liver resection including segments IV/V/VI and greater LN dissection including hepato-duodenal LNs)	75%
"Late"	IIIA	3 (invades into serosa or into liver <2cm or <2 adjacent organs: colon or duodenum)	0	0	Controversial	5%
	IIIB	1-3	1 (cystic duct, common bile duct, hepatic artery, portal vein LNs)	0		
	IVA	4 (invades into liver ≥2cm or ≥2 adjacent organs or vessels: hepatic artery or portal vein)	0-1	0	Palliation (pruritus, cholangitis, pain, obstruction, etc)	1%
	IVB	#	# or 2 (periaortic, pericaval, superior mesenteric artery, celiac artery LNs)	1 or 0		

- Tx

- o if surgeon suspects malignancy during routine lap chole then the operation should be converted to an open chole and frozen sections should be sent off and if confirmed consider radical chole and perform port site excision
- o have pathologist review surgical specimen in T1a tumors to make sure it is not T1b and thus would require a radical surgical approach
- o if found incidentally after lap chole then no further action is needed if ≤T1a
- o adjuvant chemotherapy is generally provided to every pt however data is limited to few phase II trials, the most common agents used are nucleoside analogues and platinum agents
- o there is even less data on radiation but is often offered to pts w/ "late" GBC
- o with our understanding of the underlying intracellular events involved in tumor growth more targeted therapy is being investigated including antibodies against EGFR, VEGF, HER-2, various kinases

- Prognosis

- o Why are most dx at an advanced stage?
 - (1) few, late, non-specific symptoms
 - (2) behaves aggressively (compared to other tumors including CCA/ampullary cancer) resulting in rapid spread
 - (3) GB lives in an anatomically "busy area" w/ close continuity to bile duct, portal vein, duodenum, colon
 - (4) GB is a thin (<3mm) organ
 - thin epithelium, lamina propria and discontinuous muscularis propria
 - absent muscularis mucosa, submucosa and serosa

- continuous w/ liver w/ some cholecystic veins draining into the liver bed
 - o Why prognosis poor? (generally incidence rates reflects mortality rates)
 - (1) dx at advanced stage
 - (2) poor understanding of genetics rendering chemotherapeutics not very effective
 - o mortality rate has been decreasing in the US mainly b/c of the increased rates of cholecystectomy and advanced imaging
 - o those w/ long term survival are those detected incidentally during routine cholecystectomy for gallstones (unfortunately this only represents 2% of cases)
 - o some recommended prophylactic cholecystectomy in high risk pts (eg. young Chilean women w/ asymptomatic gallstones, pts w/ gallstones >2cm, pts w/ porcelain GB)
- o Non-Neoplastic – 95% (multiple)
 - **Cholesterol Polyps 2/2 Cholesterolosis (65%)** = multiple (20% single) <1cm hyperechoic pedunculated polyps
 - Mech: accumulation of cholesterol w/in macrophages (lipid laden foamy) which collect in the lamina propria resulting in four types of mucosal hyperplasia w/ elongated villi: (1) diffuse (80%), (2) polyps (10%), (3) diffuse + polyp (10%), (4) focal (rare)
 - o NB unclear why the GBs of some pts absorb biliary cholesterol
 - o NB sometimes small yellow particles can be seen floating in bile and represent a detached collection of macrophages
 - o NB creates pale, yellow linear streaks running longitudinally on the inner surface
 - Epidemiology: incidence (20% resected GB vs 10% autopsy GB), same RFs as gallstones but usually they do not occur together
 - Dx: can detect polyps on US but the diffuse form cannot be dx on US
 - Tx: remove if polyp (refer below)
 - **Adenomyoma Polyps 2/2 Adenomyomatosis (25%)** = single 1-2cm sessile isoechoic polyp usually in the fundus
 - Mech: as the GB ages the epithelium normally penetrates/invaginates the muscular layers creating intramural diverticula aka “Rokitansky-Aschoff sinuses” → in adenomyomatosis the process is much more extensive b/c of increased intraluminal pressure w/ sinuses becoming deeper and more branched and the muscular layer hypertrophying creating three patterns: (1) diffusely thickening, (2) annular segmental thickening, (3) polyps
 - o NB unlike the intestine the GB has no muscularis mucosa rather the lamina propria abuts directly onto the muscular layers
 - Epidemiology: incidence (1% resected GB)
 - Dx: US (thickened wall w/ intramural diverticula, 65% sens), CT/MRI (different enhancement of a thickened wall, 75/95% sens)
 - Complication: may be associated w/ AC but if it is it is usually far removed from the area of adenomyomatosis suggesting that the link is purely coincidental and not causal except in cases of segmental adenomyomatosis where is AC is found at that site
 - Tx: remove if polyp (refer below) or segmental form
 - **Inflammatory Polyps (5%)** = multiple (50% single) <1cm sessile ?-echoic polyps
 - Mech: chronic inflammation resulting in granulation and fibrous tissue formation
 - **Other: Liver/Pancreatic/Gastric Heterotopic Mucosa, Lipomas, Hemangiomas, Leiomyomas, Neurofibromas, Carcinoids**
- o Dx
 - AB-US: fixed, non-mobile, non-shadowing mass (difficult to make a dx if concurrent gallstones are present)
 - NB EUS is much better
- o S/S: generally asymptomatic and often an incidental finding on lap chole but can cause biliary colic
 - NB some can detach and act like stones w/ its accompanying complications
 - NB some can bleed and cause hemobilia
- o Tx
 - Problems
 - (1) you can’t confidently determine type of polyp based on imaging (US is only 20% specific in determining type of polyp) w/o histology hence you have to determine whether a polyp has malignant features or not
 - (2) GB cancer is rare but has a devastating prognosis
 - (3) benign polyps are common
 - NB any GB polyp in a PSC pt should be resected
 - Symptomatic: resect w/ lap chole
 - Asymptomatic (some emerging evidence is stating that a better cut-off is 0.6cm and not 1cm)
 - >1cm
 - o malignant appearing (solitary, sessile, symptomatic, rapid increase in size) or RFs for malignancy (refer above): resect w/ lap chole
 - o not malignant appearing or no RFs for malignancy: EUS

- high risk features on EUS (vascular): resect w/ lap chole
 - low risk features on EUS: serial US Q6mo-1yr
 - <1cm: serial US Q6mo-1yr
- **Cholelithiasis (stone in gallbladder usually cholesterol), Hepatolithiasis (stone in liver ducts, usually brown pigment), Choledocholithiasis (stone in CBD, usually mixed)**
 - o NB acalculous biliary pain (young female w/ similar RFs as gallstones, just like symptomatic cholelithiasis but nl US/labs, consider sludge, chronic cholecystitis, gallbladder dysmotility, gallbladder dyskinesia in which gallbladder contracts normally but not in coordination w/ SO relaxation, visceral hypersensitivity)
 - o Types
 - **Cholesterol Stones = single, large, yellow/white, hard/granular, radiolucent stone vs Mixed = multiple, small, 20% calcified aka seen on xray (75%)**
 - Cholesterol Stones: slowed intestinal transit → increased exposure of bile salts to bacteria → bacteria converts cholic acid to deoxycholic acid → increased deoxycholic acid promotes increased intestinal absorption and biliary secretion of cholesterol → RFs below → bile becomes supersaturated w/ cholesterol → cholesterol monohydrate crystals precipitate aka “nucleates” around a nidus of calcium carbonate/phosphate and unconjugated bilirubin → stone “grows” utilizing mucin as an architectural framework
 - RFs (The F’s)
 - o Age: **Forty** (aka older age)
 - o FHx: positive **FHx**, genetic mutations (CYP7A1, ABCB4, APOE)
 - o Lipids: High TGL, Low HDL (NB LDL is not associated!!!)
 - o Drugs: Estrogens (**Female, Fertile** aka pregnant (Why? estrogen increases cholesterol secretion and reduces GB motility ESPECIALLY POST PARTUM), Fibrates, Octreotide, Ceftriaxone (secreted into bile reaching 200x concentration that of serum exceeding saturation level in bile resulting in it complexing with calcium creating a nidus for cholesterol stones)
 - o Ethnicity: Pima Native Americans, Mexican Americans, Scandinavians, Alaskans, Canadians, Bolivians, Chileans (general high risk areas: N/C/S Americas, Europe, Australia) Indians/Hispanics>White>AA>
 - o Diet: high calorie and cholesterol
 - o Metabolic Syndrome: **Fat** (aka obese), DM
 - o **Gallbladder Stasis 2/2 decreased CCK 2/2 fasting states: TPN, ICU stay, rapid weight loss, octreotide use, spinal cord injuries**
 - o Other: AIDS, Cirrhosis, BMT, ApoE4 genotype
 - **Black/Brown Pigment aka Unconjugated Bilirubin Stones (25%) = single, large, 50% calcified aka seen on xray**
 - Black Stones = **Polymer** Calcium Bilirubinate (20%) **form in gallbladder**
 - o Mechanism #1: **excess heme breakdown from chronic hemolytic anemia OR elderly OR cirrhosis** → bilirubin overloads glucuronidation = excess unconjugated bilirubin
 - o Mechanism #2: **TI failure** (Crohn’s, Ileectomy, Surgery, etc) → impaired bile salt absorption → bile salts enter colon and solubilize unconjugated bilirubin allowing it be reabsorbed = excess unconjugated bilirubin
 - NB Crohn’s pts also get cholesterol stones
 - Brown Stones = **Monomer** Calcium Bilirubinate (5%) **form in bile duct**
 - o Mechanism: **Bile Stasis** (Stricture, etc) + **Bile Infection** (Bacteria, Liver Flukes esp in Asia, Roundworm, etc) = glucuronidases from these infections unconjugates bilirubin = excess unconjugated bilirubin
 - o S/S (10% of the US population has gallstones)
 - Asymptomatic (3/4)
 - most are incidental findings
 - check if pt has the exemptions noted below
 - you need to educate the pt telling them that 2% convert to symptomatic cholelithiasis each year and if symptoms arise they need to see a doctor (risk decreases over time)
 - Symptomatic (1/4)
 - NO Constitutional Sx
 - NO Lab Abnormalities
 - Biliary Pain as gallbladder tries to squeeze stone into cystic duct (50% will have another episode at 1yr but 30% will never have another episode therefore some wait till 2nd episode before cholecystectomy)
 - o Increases quickly over 15min and then last <6hrs and is usually constant but can be “colicky”
 - o poorly localized (unlike cholecystitis) RUQ/MEG pain
 - o episodic w/ frequency varies from daily to yearly
 - o pain elicited after fatty meal esp at night
 - o occurs esp during periods of weight reduction or being inactive

- NB cholelithiasis does not cause dyspeptic Sx like gas, bloating, etc
 - NB if atypical Sx but + gallstones on imaging look for other causes and in mean time Tx w/ URSO
 - NB if typical Sx but – gallstones on imaging look again via EUS b/c likely small stones
- Complications (generally occur in pts who already are having symptomatic gallstones and who are elderly, 1% risk of developing complications per year if pt is already symptomatic, risk stays the same over time)
 - **Cholelithiasis and its accompanying complications** (10%)
 - **Cholecystitis and its accompanying complications** (10%, instead of stone intermittently obstructing the cystic duct and causing biliary pain the stone is impacted in the cystic duct causing acute cholecystitis)
 - **Cholecystoenteric Fistula** (stone erodes thru gallbladder neck into bowel w/ drainage of bile to adjacent organs esp hepatic flexure colon → stomach → jejunum and entry of air/bacteria to biliary tree, barium study will show barium entering the GB)
 - **Bouveret's Syndrome**
 - Mechanism: gallstones enters the duodenal bulb obstructing the stomach
 - **Gallstone Ileus**
 - Epidemiology: seen esp in the elderly females
 - Mechanism: gallstone enters the bowel via cholecysto-duodenal/colonic fistula → gallstone causes *intermittent* obstruction (the term "ileus" is a misnomer b/c there is actual obstruction) often delaying dz until it lodges at the distal duodenum or ICV causing overt obstruction
 - NB occurs when stone is >2.5cm
 - NB represents 2% of bowel obstruction
 - Dx when you see pneumobilia, obstruction and a stone that changes locations over time in the RLQ
 - Tx: stone removal via small enterotomy
 - **Mirizzi's Syndrome**
 - Types
 - I: large stone impacted in cystic duct or GB neck
 - II: a fistula b/t GB & CBD
 - III: no stone but severe edema/inflammation from cholecystitis compressing the CBD
 - S/S: repeated bouts of obstructive jaundice
 - Complications: increased r/o GB cancer
 - Tx
 - I/III: cholecystectomy and if not able to draw out stone during operation then ERCP (difficult to place basket or balloon above stone therefore laser lithotripsy is often needed)
 - II: partial cholecystectomy and cholecystocholedochoduodenostomy
 - **Gallbladder Adenocarcinoma** (refer)
- Dx
 - RUQ US: + if an acoustic shadow forms and it moves to dependent position, best if pt has been fasting >8hrs b/c ensures that the gallbladder is distended (95% sens and 95% spec for stones >2mm, smaller ones are confused for sludge) BUT if pt is obese the sensitivity drops hence some people move to EUS if obese b/c the gallbladder is right next to duodenum
 - KUB: + opaque stone seen in area of gallbladder
 - EUS: if RUQ US is negative and you are convinced of cholelithiasis, pt might have sludge which can be picked up by EUS
- Px
 - Prevention of Sx: physical activity
 - Prevention of Gallstone Formation: URSO
- Tx
 - Asymptomatic: no surgery b/c most develop symptoms before complications occur but there are exceptions (only take out the gallbladder if already do an operation for another reason): >2.5cm gallstones, SCD, pre-transplant for only heart/lung not other organs, immunosuppressed pts, extreme remote future like space travel, concern for cancer, children, morbidly obese or pts undergoing gastric bypass b/c hard to reach ampulla if cholelithiasis occurs, hereditary spherocytosis, NB originally diabetics were believed to be at increased risk for complications but no longer
 - Symptomatic
 - Surgical Candidate: elective (aka non-urgent) Laparoscopic Cholecystectomy ("Lap Chole") vs Open Cholecystectomy ("Open Chole") via Right Subcostal Kocher Incision
 - 75% are laparoscopic w/ 3% converting to open
 - "Intra Operative Cholangiogram" (IOC) visualize the patency of the ducts during surgery so as to r/o cholelithiasis (occurs in 10% of cases) and to delineate anatomy
 - Indications: jaundice, hyperbilirubinemia, increased alkaline phosphatase
 - Complications
 - General: bleeding, wound infection, seroma

- Bile Acid Diarrhea (80% - refer)
- Right Sided CRC (2x increased risk 2/2 mucosal exposure to carcinogenic secondary bile acids)
- Bowel Injury (0.1%)
- Artery Injury w/ bile duct ischemia (0.1%)
- Bile Duct Thermal Injury w/ Stricture (0.5%)
 - Types: (1) Right Hepatic Duct (most common): usually occult injury, can eventually result in right lobe atrophy and cholangitis w/ intrahepatic brown stones and (2) CHD/CBD (less common): can eventually result in secondary biliary cirrhosis
 - Tx: can just follow or if complicated then attempt ERCP Tx but often a hepaticojejunostomy is needed
- Bile Leak +/- Biloma (0.5%)
 - Types: (1) cystic duct leak from ineffective placement of ligatures (most common), (2) GB fossa leak from ducts of Luschka or aberrant R hepatic duct that goes directly into GB rather than joining L hepatic duct and forming the CHD (rare), (4) CHD injury, Tx: surgery (rare)
 - Post-cholecystectomy, transplant, trauma
 - Dx: US showing fluid collection which can be confirmed w/ biliary scintigraphy and drainage (TB fluid/serum >5)
 - Complicated: infected biloma
 - Approach

- o Asymptomatic, small perihepatic bile collections, seen in 50% of pts after chole!!!, typically w/in 24hrs, resolve spontaneously, require no Tx
- o Symptomatic w/ F, ab pain, large biloma, abnl LFTs, rare, typically b/t 2-10d, require abx and percutaneous drainage catheter (should be removed after biliary stent) and ERCP (sphincterotomy $\pm$ 10F plastic biliary stent x1-3mo (bridge the leak site if possible but not necessary as its effectiveness is mainly b/c it facilitates drainage thru CBD by eliminating sphincter pressure and this promotes closure) which should be removed at 4-8wks (NB CBD leaks require surgery)
- o Large bilomas >3cm need percutaneous drain

- Post-Chole Syndrome (30%)
 - 1st assess for complications above esp if Sx are new and not persistent from before the operation
 - 2nd pt didn't have GB dz in the first place but something entirely different
 - 3rd there is a biliary problem

- o **Choledocholithiasis** (if <2yrs from operation then likely residual stones from GB vs if >2yrs from operation then likely de novo brown pigmented stone)
- o **Cystic Duct Remnant Syndrome** (new controversial concept, pathology has revealed in some cases stones, fistulas, granulomas, and neuromas, if you suspect then surgical resection of the cystic duct remnant)
- o **SOD**

- NON Surgical Candidate (only effective in pts w/ cholesterol stones, significant calcium makes stones non-dissoluble hence must be radiolucent on xray and iso/hypodense on CT, stones will return unless the lithogenic disturbance that caused the stone formation in the first place is Tx)
 - o **URSO**: 60% effectiveness, 50% recurrence rate at 5yrs
 - great for multiple small <6mm stones
 - only stop if two consecutive US are normal 1mo apart
 - decrease in size 0.7mm/mo
 - NB make sure GB is functioning fine w/ HIDA scan
 - NB percutaneous instillation of methyl-tertiary-butyl was similarly effective but there were lots of SEs hence not used anymore
 - o **Extra-Corporeal Shock Wave Lithotripsy**: 80% effectiveness, 40% recurrence rate at 5yrs
 - great for single large <20mm stone
 - concurrently give URSO, sedate, prone position, multiple Tx are needed
 - SEs: petechial, hematuria, liver hematoma, complications of stone passage
 - o **Percutaneous Cholecystostomy w/ Drainage Tube**

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- NB GB prokinetic agents (alpha adrenergic agonists, clarithromycin, etc) have not studied but in theory may be helpful

Cholecystitis

- Types
 - Acute Calculus Cholecystitis (90%, 1% mortality)
 - Stone impacted at cystic duct → toxic bile (one of the most noxious agents in the human body) backs up into gallbladder → mucosal phospholipases hydrolyze lecithin to toxic lysolecithins → mucus layer is disrupted → epithelium exposed to detergents → inflammation → secondary infection w/ GN bacteria and anaerobes
 - Acute Acalculus Cholecystitis (10%, usually a very sick ICU pt, 10-50% mortality)
 - **Ischemia** (post-op, trauma, vasculitis, cholesterol emboli, GB torsion, shock, burns, post-partum, cystic artery thrombosis, cytotoxic chemo thru hepatic artery)
 - NB because the cystic artery has no collateral circulation any cause of ischemia can cause damage and inflammation
 - NB can occur in an outpt specifically elderly males w/ PVD and young males w/ HIV/AIDS
 - **Fasting State → Decreased CCK → GB Stasis → Sludge may obstruct cystic duct** (parenteral nutrition, ICU stay, rapid weight loss)
 - **Reflux of Pancreatic Secretions** (opioids)
 - **BM Tx**
 - **Infection** (*Salmonella typhi*, *Staph aureus*, EBV in children, CMV in immunocompromised pts)
 - **NB some pts have no identifiable RFs!!!**
- S/S
 - Constitutional Sx: F, N, V, anorexia, tachycardia, diaphoretic, slight jaundice (important to know)
 - Lab Abnormalities: leukocytosis, TB <4, A/L mildly high, LFTs should be normal or slightly elevated b/c of adjacent inflammation on the liver
 - Cholecystitic Pain as the gallbladder becomes inflamed b/c of constant obstruction of cystic duct
 - NB most pts had prior attacks of biliary colic but now this episode is similar in quality EXCEPT pain lasts >6hrs
 - if pt has one attack they will likely have several more therefore Tx
 - Boas' Sign (referred pain to right shoulder)
 - Murphy's Sign (inspiratory arrest during deep palpation b/c during inspiration the gallbladder is brought into contact with the examiner's hand)
 - Courvoisier's Sign (palpable gallbladder)
 - NB for acalculus cholecystitis there can be just fever to symptoms similar to acute cholecystitis except that the pain is insidious not sudden and the patient is usually VERY SICK b/c of the underlying cause
- Complications
 - NB much more common if pt is a diabetic and in acalculus cholecystitis (75% of acalculus cholecystitis)
 - Perforation with peritonitis and biloma (intraperitoneal bile)
 - Empyema (6%)
 - Perforation (3%)
 - Gangrenous Cholecystitis (7%, inflammation resulting in thrombosis of cystic artery resulting in necrosis)
 - Emphysematous Cholecystitis (1%, gangrenous cholecystitis + infection w/ gas forming bacteria aka *Clostridium* = gallbladder fills with gas, NB there must be no evidence of fistula, very high r/o perforation therefore abx coverage against anaerobes and urgent cholecystectomy)
 - Porcelain Gall bladder (calcified gallbladder seen on KUB, very high r/o cancer, prophylactic cholecystectomy is indicated)
 - Hydrops of the Gallbladder (if untreated the GB lumen b/c distended w/ mucoid material)
 - Xanthogranulomatous Cholecystitis (?)
 - Chronic Cholecystitis
- Diagnosis
 - RUQ US (80% sens and 80% spec)
 - thickened edematous wall >3-5mm (false + hypoalbuminemia)
 - pericholecystic fluid (false + ascites)
 - distended gallbladder
 - cholelithiasis
 - sonographic Murphy's
 - If US evidence of inflammation is equivocal then do a 99m-Tc Tagged HIDA (Hepato IminoDiacetic Acid) Scan
 - 95% sens and 90% spec significantly higher than US nonetheless US is first TOC b/c so easy to use, absence of radiation, etc therefore only used in the 20% of cases where US is equivocal
 - IV injection of radiolabeled HIDA which is selectively taken up by liver at 5min then secreted into biliary tree w/ 1/3 to GB and 2/3 to bowel if everything is alright at 30min
 - Positive findings
 - If the GB is inflamed HIDA cannot enter into the GB (b/c of the inflammation and b/c the cause is usually a calculus in the cystic duct, NB sensitivity for acalculi is slightly less ~90%) and thus is not visualized within GB at 1-4hr after injection, to confirm you can give morphine at this point to constrict SOD and promote bile back into GB

- If there is a biliary tree obstruction only the liver (and possibly the GB will light up depending on where the obstruction is) and not bowel will light up (NB if the obstruction is partial you will see the tree and bowel but it is delayed aka >1-4hr)
 - If there is a biliary leak then HIDA will pool around liver (seen after trauma or surgery, sometimes the biloma can collect near the GB fossa falsely looking like a GB or coat the liver increasing the activity of the liver when it should be decreasing over time)
 - If pt has cirrhosis no HIDA will be taken up by liver
 - Sometimes if everything is looking normal and the pt has S/S of RUQ pain consider that your test was a False- and thus you can give CCK and see if the GB contracts normally (**>35% EF, avg is 75%**) and if it doesn't then pt has Gallbladder Dyskinesia 2/2 mild acute cholecystitis or chronic cholecystitis buy whether this alone w/o stones/sludge causes Sx is controversial!!!
 - Remember that food stimulates GB contraction therefore if pt has eaten HIDA might not enter GB appearing as if pt has cholecystitis, on the contrary, pts who have not eaten for a long while or are ill have GB filled w/ bile and thus might have a false+ as HIDA cannot enter an already distended GB
 - Sometimes a duodenal diverticula, etc can mimic a GB giving a false-
 - NB Oral Cholecystography (not done anymore, replaced by HIDA scan, ingest radiopaque contrast (iopanoic acid) that is absorbed and secreted by liver and collects in GB like bile)
- Tx
 - First calm the gallbladder down before surgery w/ hydration, bowel rest w/ NPO and NGT decompression, analgesics then determine surgical/abx course based on severity:
 - Mild Case: Cefoxitin + Early (1-7d) Lap Chole (the early approach has been shown to have shorter hospitalizations, less M&M, less cost)
 - Mod Case: Either Abx + Delayed (6-8wks) Lap Chole (the delayed approach has been shown to have less biliary tree injury)
 - Severe Case: Zosyn or 3rdCeph/Flagyl + Percutaneous Cholecystostomy w/ Draining Tube OR ERCP Cystic Duct placement of nasobiliary drain (or if not surgical candidate then leave in place until cholangiogram shows normal drainage, you can also instill 1% NAC to dissolve sludge) then Delayed Lap Chole
 - NB ERCP Guided Transpapillary or EUS Guided Transduodenal GB Drainage followed by stent placement

Choledocholithiasis (stone in duct)

- Etiology
 - Primary: begin in the CBD often proximal to stricture w/ concurrent cholangitis and within liver aka hepatolithiasis (brown pigment stones) 5%
 - RF: biliary sphincterotomy b/c it allows for cholangitis which leads to formation of brown stones (12% risk)
 - Secondary: begin in the gallbladder and then pass into CBD (cholesterol stones) 95%
- S/S
 - Asymptomatic (50%)
 - Symptomatic (50%)
 - similar pain to cholelithiasis
 - obstructive LFTs w/ jaundice, pain, N/V, pruritus, etc (50% asymptomatic)
 - transient spike in AT and A/L suggests recent passage of stone!!!
- Complications
 - Obstructive Jaundice
 - Acute Pancreatitis
 - Ascending Cholangitis
 - Secondary Biliary Cirrhosis
 - Fibrosis of Sphincter of Oddi
- Dx/Tx is based on suspicion
 - First you always do a RUQ US (NB RUQ US is not sensitive unlike for cholelithiasis only picking up 50% of stones but can detect dilated ducts if >6mm increasing sensitivity to 75%) to assess cholelithiasis b/c 95% of choledocholithiasis comes from gallstones and it is cheap and easy to do
 - If + RUQ US for cholelithiasis and you are suspecting choledocholithiasis based on S/S and labs then proceed with one of three tests (ERCP, IOC, EUS/MRCP/CT) based on your degree of suspicion (refer to acute pancreatitis)
 - If you take out a stone with ERCP you should do a cholecystectomy w/in a few weeks

Cholangitis (inflammation of duct)

- Etiology
 - any lesion that obstructs bile flow resulting in stagnant bile proximal to obstruction becoming secondarily infected with bacteria (*E.coli*, *Klebsiella*, *Pseudomonas*, *Proteus*, *Enterococci*) from duodenum
 - almost always choledocholithiasis (85%) but sometimes due to
 - stents, catheters or other foreign objects
 - tumors (ampullary carcinoma, cholangiocarcinoma, et al)
 - surgical strictures
 - Recurrent Pyogenic Cholangitis, Oriental Cholangiohepatitis, Hong Kong Disease, Biliary Obstruction of the Chinese

- Epidemiology: rural Asia but incidence is decreasing
 - Mechanism: chronic infection w/ *Clonorchis sinensis*, *Opisthorchis spp*, *Ascaris lumbricoides* → chronic obstruction → recurrent bacterial cholangitis + intrahepatic pigment stones + biliary strictures (esp left hepatic duct)
 - Complications: cirrhosis, cholangiocarcinoma
- S/S
 - o Charcot's Triad: F + Jaundice + RUQ Pain (seen in 75% of pts)
 - o Reynold's Pentad: Triad + Septic Shock + AMS (seen in 15% of pts) NB 100% mortality if emergent decompression is not done
 - NB sepsis is directly related to the biliary pressure
 - Dx
 - o 80% respond to conservative management but 20% need biliary decompression
 - o medical emergency
 - o stabilize w/ fluids and pressor support if septic shock
 - o broad-spectrum antibiotics (Cefoxitin, Zosyn, Merrem) NB not ceftriaxone b/c causes biliary stasis
 - o Dx is essentially clinical but if stable then ERCP or percutaneous transhepatic cholangiography (PTC)

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