Diseases of the gall bladder and the biliary tract

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Diseases of gallbladder and biliary tract

- Cholelithiasis (stones in GB),
- Cholecystitis (inflammation of GB),
- Cholangitis,
- Choledocholithiasis,
- Carcinoma
- Functional gallbladder disorder
Gallstone disease may be thought of as having the following 4 stages:

- Lithogenic state, in which conditions favor gallstone formation
- Asymptomatic gallstones
- Symptomatic gallstones, characterized by episodes of biliary colic
- Complicated cholelithiasis (cholecystitis, cholangitis, choledocholithiasis)

Symptoms and Complications depend on where stuck the gallstones.
Gallstones Causes

- **The bile contains too much cholesterol.** Normally, the bile contains enough chemicals to dissolve the cholesterol excreted by the liver. But if the liver excretes more cholesterol than the bile can dissolve, the excess cholesterol may form into crystals and eventually into stones.

- **The bile contains too much bilirubin.** Certain conditions cause the liver to make too much bilirubin, including liver cirrhosis, biliary tract infections and certain blood disorders. The excess bilirubin contributes to gallstone formation.

- **The gallbladder doesn't empty correctly.** If the gallbladder doesn't empty completely or often enough, bile may become very concentrated and this contributes to the formation of gallstones.
Gallstones

• Gallstones are common with prevalences as high as and 10% to 15% in adults of developed countries.

• Types of gallstones, it contains
  • Cholesterol gallstones
  • The most common type of gallstone, called a cholesterol gallstone 75%
  • Pigment gallstones
  • These dark brown or black stones form when the bile contains too much bilirubin
  • Mixed gallstones
Gallstones
Gallstones Diagnosis

- Diagnosis (Imaging modalities that may be useful include the following)
- Abdominal UH, CT, MRI
- Lab
- ERCP
50 yr. old slightly overweight male pts. (referred by a family doctor). Complaints: Right upper quadrant pain, which developed after a meal. Shoulder blade radiating pain, nausea, abdominal discomfort.

US: cholelith (2 cm), normal gallbladder wall thickness, bile ducts were not wider. Dg: (biliary colic)? Cholelit,? gastritis?, pancreatitis? The pts. was hospitalized for observation inf. Iv spasmolytic, selected time LC?

- Lab: Sebi: 37, gGT: 56
- ALP 200, WBC: 9, CRP: 6
Gallstones Symptoms

Gallstones may cause no signs or symptoms 20-50%

- **Biliary colic**
  - Typically after meals
  - Sudden and rapidly intensifying pain in the upper right portion of the patient's abdomen
  - Back pain between the patient's shoulder blades, pain in the right shoulder, nausea-vomiting, sweating.
  - Gallbladder spasms causing the pain (stone stuck in cystic duct)

- **Lab:** Patients with uncomplicated cholelithiasis or simple biliary colic typically have normal laboratory test results; laboratory studies are generally not necessary unless complications are suspected.
  - (sebi, ALP, gGT, urin bilirubin, WBC, CRP)
<table>
<thead>
<tr>
<th>References</th>
<th>Characteristic</th>
<th>No. of cases</th>
<th>Average follow-up period (years)</th>
<th>No. of acute cholecystitis cases (%)</th>
<th>Only those with remarkable jaundice cases (%)</th>
<th>Cholangitis</th>
<th>Cholecystitis</th>
<th>Gallbladder cancer</th>
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<td>Comfort et al.</td>
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<td>Friedman et al.</td>
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<td>344</td>
<td>9</td>
<td>20 (5.8)</td>
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<td>332</td>
<td>10</td>
<td>38 (11.4)</td>
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Review by Friedman [12]
Gallstones differential diagnosis

- Ulcer
- GERD
- Nephrolithiasis
- Colon disease: IBS, Diverticulitis, CRC
- Angina
- Ao. aneurysm dissection
- Neuralgia
- Pleurisy
- Pericarditis
- Acute intermittent porphyria
Cholecystectomy for asymptomatic gallstones may be indicated in the following patients:

- Those with large (>2 cm) gallstones
- Those who have a nonfunctional or calcified (porcelain) gallbladder on imaging studies and are at high risk of gallbladder carcinoma
- Those with spinal cord injuries or sensory neuropathies affecting the abdomen
- Those with sickle cell anemia in whom the distinction between painful crisis and cholecystitis may be difficult
Case report 2.

- 50 yr. old slightly overweight male pts. (referred by a family doctor)
  Complaints: Right upper quadrant pain, which developed after a meal.
  Shoulder blade radiating pain, chills, nausea, abdominal discomfort.

- + fever 38 C
- LAB:
  Sebi: 37, gGT: 56
  ALP 200, Fvs: 11, CRP: 33

UH: cholelith, gallbladder wall is thicker than normal, there is not larger bile ducts
The pts. was hospitalized, infusion, AB, diet selected time LC?
Dx: Cholecystitis acuta?,
Cholecystitis acuta

- Cholecystitis is inflammation of the gallbladder that occurs most commonly because of an obstruction of the cystic duct by gallstones arising from the gallbladder. (the gallbladder cannot be emptying + ascending bacterial overgrowth) Uncomplicated cholecystitis has an excellent prognosis; the development of complications such as perforation or gangrene the prognosis less favorable.
- Signs and symptoms
  - The most common presenting symptom of acute cholecystitis is upper abdominal pain and tenderness in the RUQ or epigastric region
  - Fever, tachycardia,
  - The physical examination
  - Palpable gallbladder or fullness of the RUQ (30-40% of patients)
  - Jaundice (~15% of patients)
  - Murphy's sign: If the patient stops breathing in for during an abdominal examination (gently placing the hand below the right costal margin)
- Lab:
  - GOT, GPT, sebi, gGT, ALP, CRP, levels may be elevated in cholecystitis or with common bile duct (CBD) obstruction
- UH
  - Gallstone, gallbladder wall thicker than normal, not larger bile ducts
  - fluid around the gallbladder
CHOLECYSTITIS, CHOLANGITIS

- **Gram-negative organisms**
  - Escherichia coli 31–44
  - Klebsiella spp. 9–20
  - Pseudomonas spp. 0.5–19
  - Enterobacter spp. 5–9
  - Acinetobacter spp. –
  - Citrobacter spp. –

- **Gram-positive organisms**
  - Enterococcus spp. 3–34
  - Streptococcus spp. 2–10
  - Staphylococcus spp. 0a
  - Anaerobes 4–20
  - Others –

J Hepatobiliary Pancreat Sci (2013) 20:60–70
Treatment of cholecystitis

- Supportive care: In acute cholecystitis, the initial treatment includes bowel rest, IV hydration, correction of electrolyte abnormalities, analgesia, and IV antibiotics, emesis can be treated with antiemetics and nasogastric suction.
- AB: Sanford guide – Piperacillin-tazobactam, ampicillin-sulbactam, or meropenem; in severe life-threatening cases, imipenem-cilastatin
- Laparoscopic cholecystectomy (standard of care for surgical treatment of cholecystitis)
When is the surgery?

- **Early**: Within 72 hours of the start of symptoms
- (the gallbladder wall is fragile after 72 hours)
- **UNFORTUNATELY** (surgery postponed)
- **Elective**: 6-12 weeks later
Fig. 1 Necrotizing cholecystitis. a Contrast-enhanced CT images show discontinuity of the gallbladder wall, suggesting possible presence of necrosis in a portion of the wall. b Resected specimen showing extensive falling-off of the gallbladder membrane, erosion, ulcer, and exposed fascia. Histologically, necrosis of the gallbladder wall and suppurative inflammation accompanying abscess (data not shown) were observed with fibrillation and regenerating hyperplastic epithelium as background.
Chronic cholecystitis

- Chronic cholecystitis is a long-standing gallbladder inflammation almost always due to gallstones.
- Chronic cholecystitis almost always results from gallstones and prior episodes of acute cholecystitis. Damage ranges from a modest infiltrate of chronic inflammatory cells to a fibrotic, shrunken gallbladder. Extensive calcification due to fibrosis is called porcelain gallbladder.
- Symptoms and Signs
  - Gallstones intermittently obstruct the cystic duct and so cause recurrent biliary colic. Such episodes of pain are not necessarily accompanied by overt gallbladder inflammation; the extent of inflammation does not correlate with the intensity or frequency of biliary colic. Upper abdominal tenderness may be present, but usually fever is not.
- Diagnosis: Ultrasonography
- Treatment: Laparoscopic cholecystectomy is indicated to prevent symptom recurrence and further biliary complications. This procedure is particularly appropriate for the porcelain gallbladder associated with gallbladder carcinoma.
Case Report 3.

- 50 yr. old slightly overweight male pts. (referred by a family doctor) Complaints: Right upper quadrant pain, which developed after a meal. Shoulder blade radiating pain, chills, fever, icterus, nausea, vomiting, abdominal discomfort.
- + icterus
- Lab: Sebi: 55, gGT: 120
  - ALP 450, WBC: 15, CRP: 70,
  - Amilaz: 76

UH: cholelith, choledocholith, gallbladder wall thickness is normal, larger bile ducts
The pts. was hospitalized, inf. AB, diet Control UH: not larger bile ducts
Dx: choledocholithiasis, stones in CBD
Choledocholithiasis

– Choledocholithiasis is the presence of gallstone in the common bile duct.
– (gallstones pass from the gallbladder)

**Symptoms:**
– Pain in the right upper or middle upper abdomen for at least 30 minutes. The pain may be constant or cramping. It can feel sharp or dull.
– Fever
– Yellowing of skin and whites of the eyes (jaundice)
– Loss of appetite
– Nausea and vomiting
– Clay-colored stools
– Lab:
  – Elevated (ALP, gGT), bilirubin

• UH: larger bile duct, stone
• Treatment
  – Endoscopos Retrograd Cholangio et Pancreatographia **ERCP**
  – Endoscopic Sphincterotomy – EST
  – Surgery
Cholangitis

- Etiology:
  - Biliary stone spontaneously migrate from gallbladder into the common bile duct where the stone trapped and cause blockage and bacterial infections

- Symptoms
  - Right upper quadrant pain, fever, jaundice mechanical (Charcot's triad)

- Lab
  - Inflammatory markers, elevated cholestatic liver enzymes
  - UH: wide bile ducts

- Treatment
  - Antibiotic (well secreted in bile)
  - Remove stones if stones are in the background: primarily ERCP
<table>
<thead>
<tr>
<th>Etiology of acute cholangitis</th>
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</thead>
<tbody>
<tr>
<td>Cholelithiasis</td>
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<tr>
<td>Benign biliary stricture</td>
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<td>Congenital factors</td>
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<td>Post-operative factors (damaged bile duct, strictured choledochojunostomy, etc.)</td>
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<td>Inflammatory factors (oriental cholangitis, etc.)</td>
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<td>Malignant occlusion</td>
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<td>Bile duct tumor</td>
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<td>Gallbladder tumor</td>
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<tr>
<td>Ampullary tumor</td>
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<td>Pancreatic tumor</td>
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<td>Duodenal tumor</td>
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<tr>
<td>Pancreatitis</td>
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<td>Entry of parasites into the bile ducts</td>
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<td>External pressure</td>
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<td>Fibrosis of the papilla</td>
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<td>Duodenal diverticulum</td>
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<td>Blood clot</td>
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<tr>
<td>Sump syndrome after biliary enteric anastomosis</td>
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<td>Iatrogenic factors</td>
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Reviewed by Kimura et al. [1]
Case Report

A 36-year-old woman comes to the office because of a 3 day history of yellow skin, fever and abdominal pain. RUQ and her right shoulder. She has had several similar episode in past, but they were not accompanied by fever, and yellow skin.

A: acute cholangitis  
B: acute cholecystitis  
C: acute hepatitis  
D: acute pancreatitis  
E: biliary colic

Lab:  
- Sebi: 55, gGT: 120  
- ALP 450, Fvs: 15, CRP: 70,  
- Amilaz: 76
ERCP

- Biliary tract disease including:
  - Choledocholithiasis
  - Malignant and benign biliary strictures
  - Bile-duct injuries or leaks
  - Sphincter of Oddi dysfunction
- Pancreatic disease including:
  - Recurrent acute pancreatitis
  - Chronic pancreatitis
  - Pancreatic duct leaks
  - Pancreatic fluid collections such as acute pseudocysts, chronic pseudocysts, and pancreatic necrosis
  - Pancreatic cancer and other pancreatic malignancies
- Ampullary adenomas

ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. 2007
Contraindication

- **Absolute contraindication:**
- The uncooperative patient.
- Recent attack of acute pancreatitis, within the past several weeks.
- Recent myocardial infarction.
- Inadequate surgical back-up
- History of contrast dye anaphylaxis

- **Relative contraindications:**
- Poor health condition for surgery.
- Severe cardiopulmonary disease.
- Ascites.
Major complications of ERCP and endoscopic sphincterotomy

- **Pancreatitis**  Amylase at least three times normal at more than 24 hours after the procedure, requiring admission or prolongation of planned admission to two to three days Hospitalization of 4 to 10 days Hospitalization of more than ten days, hemorrhagic pancreatitis, phlegmon or pseudocyst, or intervention (percutaneous drainage or surgery)

- **Bleeding**  Clinical, not just endoscopic evidence of bleeding, hemoglobin drop <3 g, and no need for transfusion Transfusion (four units or less), no angiographic intervention or surgery Transfusion (five units or more), or intervention (angiographic or surgical)

- **Cholangitis**  >38ºC for 24 to 48 hours  Febrile or septic illness requiring more than three days of hospital treatment or endoscopic or percutaneous intervention Septic shock or surgery

- **Perforation**  Possible, or only very slight leak of fluid or contrast, treatable by fluids and suction for three days or less Any definite perforation treated medically for 4 to 10 days Medical treatment for more than 10 days, or intervention (percutaneous or surgical)

Stones in cystic duct
Choledocholithiasis
Cholelith
Sludge
STONE REMOVAL
Vater papilla stenosis
MIRIZZI SYNDROME

Fig. 4 Mirizzi syndrome, a MRCP showed the obstructed common hepatic duct but failed to visualize the gallbladder. b Cholangiography with an ENBD tube showed the stenosed common hepatic duct but failed to visualize the gallbladder. c Coronal images by contrast-enhanced CT clearly showing that stones impacted in the gallbladder duct have expanded the common hepatic duct, thereby inducing stenosis.

Estimated to occur in 0.7-1.4% of cholecystectomies.
Gallbladder cancer

- Gallbladder cancer is a relatively uncommon cancer. (The gallbladder cancer is fifth in gastrointestinal cancer)
- Gender—approximately twice more common in women than men, usually in seventh and eighth decades.
- In our country the incidence is (6-7 / 100,000).
  Incidentally discovered gallbladder cancer (adenocarcinoma) following a cholecystectomy. (2-3%)
  Compared CRC (70/100,000)
Case report

- 68 years old, minimally overweight males. Patient
- Complaints: Steady pain in the upper right abdomen
- Indigestion, Dyspepsia (gas)
- Weakness, Loss of appetite
- Weight loss
- LAB: not typical
- Sebi: 47, gGT: 56
- ALP 280, Fvs: 11, CRP: 11
Gallbladder Cancer: Risk Factors

• **Gallstones.** Gallstones are the most common risk factor for gallbladder cancer. However, less than 1% of people with gallstones develop gallbladder cancer. There is no evidence of a direct causal relationship between gallstones and gallbladder cancer. (porcelain gallbladder)

• **Gallbladder polyps.** Doctors often recommend gallbladder removal for people who have polyps larger than 1 centimeter because these are more likely to be cancerous.

• **Age.** Most people diagnosed with gallbladder cancer are older than 70.

• **Gender.** Women are about twice as likely to develop gallbladder cancer as men.

• **Obesity** increases the risk for gallbladder cancer.

• **Smoking.** Tobacco use may increase the risk of gallbladder cancer.

• **Family history.** A family history of gallbladder cancer slightly increases a person’s risk of developing gallbladder cancer.
Gallbladder cancer symptoms

• (Sometimes, gallbladder cancer is found unexpectedly after removal of the gallbladder for another reason, such as gallstones.)
• When symptoms do occur, they include the following:

  • Jaundice (yellowing of the skin and whites of the eyes)
  • Abdominal pain
  • Nausea and vomiting
  • Bloating
  • A lump in the abdomen
  • Fever
Diagnosis

- **UH**: CT represents external compression by gallbladder cancer.
- **MRI**
- **ERCP**: that represents external compression by gallbladder cancer.
Five-year survival data

### 5 éves túlélési adatok

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**III./3.4. Epehólyag tumorok** Somlai Krisztián, Dank Magdolna, Harsányi László
**Bile duct cancer (cholangiocarcinoma)**

**Risk factors:**
Although most patients present without any known risk factors evident, a number of risk factors for the development of cholangiocarcinoma have been described. (PSC, IBD, parasitic liver Diseases, alcoholic liver disease, viral hepatitis)

**Sign and symptoms:**
The most common physical indications of cholangiocarcinoma are abnormal liver function tests, jaundice, abdominal pain (30%–50%), generalized itching (66%), weight loss (30%–50%), fever (up to 20%), and changes in stool or urine color.
Prognosis

Surgical resection offers the only potential chance of cure in cholangiocarcinoma.

For non-resectable cases, the 5-year survival rate is 0%. Overall median duration of survival is less than 6 months in inoperable, untreated, otherwise healthy patients.
Cholangiocarcinoma

ERCP: Distalis epeúti tumor

Klatskin tumor = MRCP: Cholangiocarcinoma of junction of right & left hepatic ducts
Surgical resection

- Roux-en-Y Hepaticojejunostomy
Cholangiocarcinoma

- For non-resectable cases:
- Stent (palliative)
- Chemo +/- Radio treatment
- Only (chemo / radio) survival time is 12 - 18 month
Bile duct palliative treatment
Antireflux metal stent of biliary malignancies

- Endoscopic insertion of an ARMS is technically feasible, safe, and effective in patients with distal malignant biliary obstruction. The impact of ARMSs in prolonging stent patency and life expectancy deserves further randomized evaluation.

Antireflux valve

EUS Transgastric endoscopic ultrasonography-guided biliary drainage

Functional gallbladder disorder

- Functional gallbladder disorder is defined as biliary pain resulting from a primary gallbladder motility disturbance in the absence of gallstones, sludge, microlithiasis, or microcrystal disease. The diagnosis is considered in patients with typical biliary-type pain who have had other causes for the pain excluded. The prevalence of functional gallbladder disorder among patients with biliary-type pain and a normal transabdominal gallbladder ultrasound is up to 8 percent in men and 21 percent in women.
Functional gallbladder disorder

- Rome IV criteria for functional gallbladder disorder require:
  - Biliary pain
  - Absence of gallstones or other structural pathology
  - In addition, the criteria that are supportive of functional gallbladder disorder, but are not required, include:
    - Low ejection fraction on scintigraphy (gallbladder ejection fraction, GBEF)
    - Normal liver enzymes, conjugated bilirubin, and amylase/lipase.
Functional gallbladder disorder management

- Patients with functional gallbladder disorder are candidates for cholecystectomy if they have typical biliary-type pain and a low GBEF (<40 percent).
Sphincter of Oddi dysfunction

Sphincter of Oddi dysfunction refers to a group of functional disorders leading to abdominal pain due to dysfunction of the Sphincter of Oddi: functional biliary sphincter of Oddi and functional pancreatic sphincter of Oddi disorder.
Oddi sphincter

The sphincter of Oddi is a sphincter muscle, a circular band of muscle at the bottom of the biliary tree which controls the flow of pancreatic juices and bile into the second part of the duodenum.
Sphincter of Oddi dysfunction

- If all of the above criteria are met, individuals are classified as having a functional biliary sphincter of Oddi disorder, if the testing of pancreatic enzymes (amylase and lipase) is normal.

- The Milwaukee classification of biliary sphincter of Oddi dysfunction (SOD) further divides the condition into three subtypes:
  
  - Type I biliary SOD: biliary-type abdominal pain, with all of altered liver enzymes on blood testing, dilated biliary ducts on ultrasound or ERCP, and delayed bile clearance on HIDA scan.

  - Type II biliary SOD: biliary-type abdominal pain associated with one or two of the following: altered liver enzymes on blood testing, dilated biliary ducts on imaging tests, and delayed bile clearance on HIDA scan.

  - Type III biliary SOD: biliary-type abdominal pain with none of the following: altered liver enzymes on blood testing, dilated biliary ducts on imaging tests, and delayed bile clearance on HIDA scan.
Sphincter of Oddi dysfunction treatment

- ERCP- EST
THANK YOU FOR YOUR ATTENTION!