
بسم الله الرحمن الرحيم

Gallbladder stone

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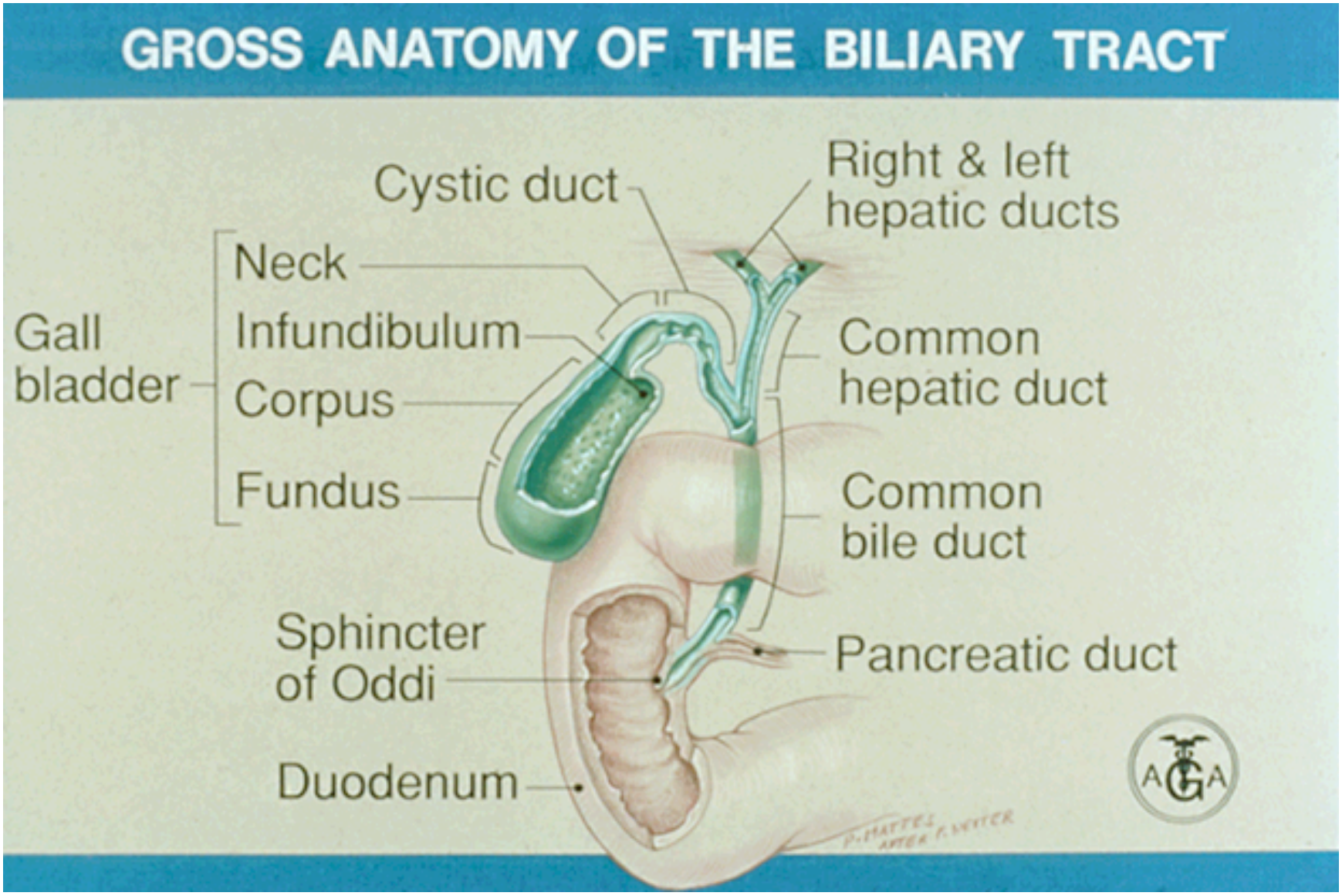
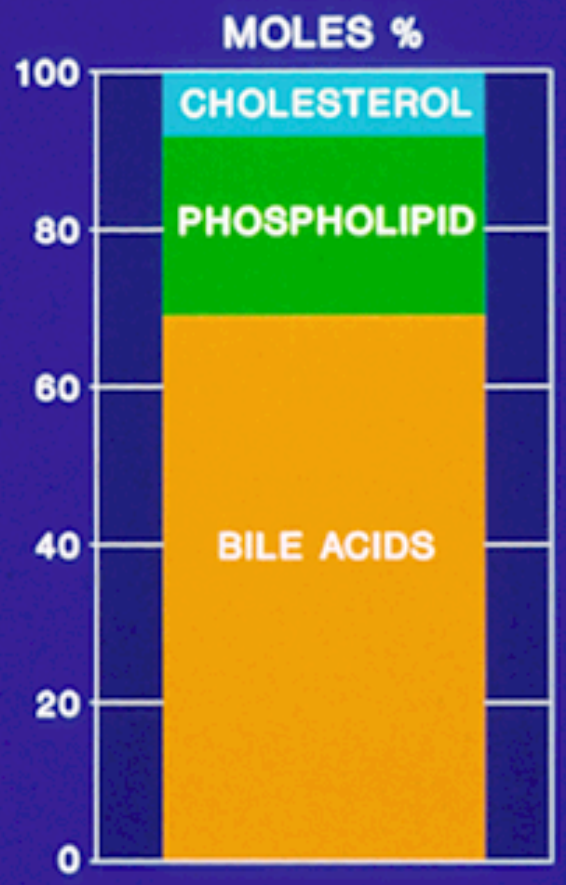

GROSS ANATOMY OF THE BILIARY TRACT
Cystic duct
Right & left
hepatic ducts
Neck
Gall
bladder
Infundibulum
Corpus
Fundus
Common
hepatic duct
Common
bile duct
Sphincter
of Oddi
Pancreatic duct
Duodenum
AGA

THERE ARE 3 MAJOR BILIARY LIPIDS

	MOLAR RATIO
BILE ACIDS — Mixture of Primary & Secondary	9
PHOSPHOLIPIDS — About 97% as Phosphatidylcholine (lecithin)	3
CHOLESTEROL	1



- A third important mechanism in cholesterol gallstone formation is **gallbladder hypomotility** .

- A high percentage of patients with gallstones exhibit abnormalities of gallbladder emptying.

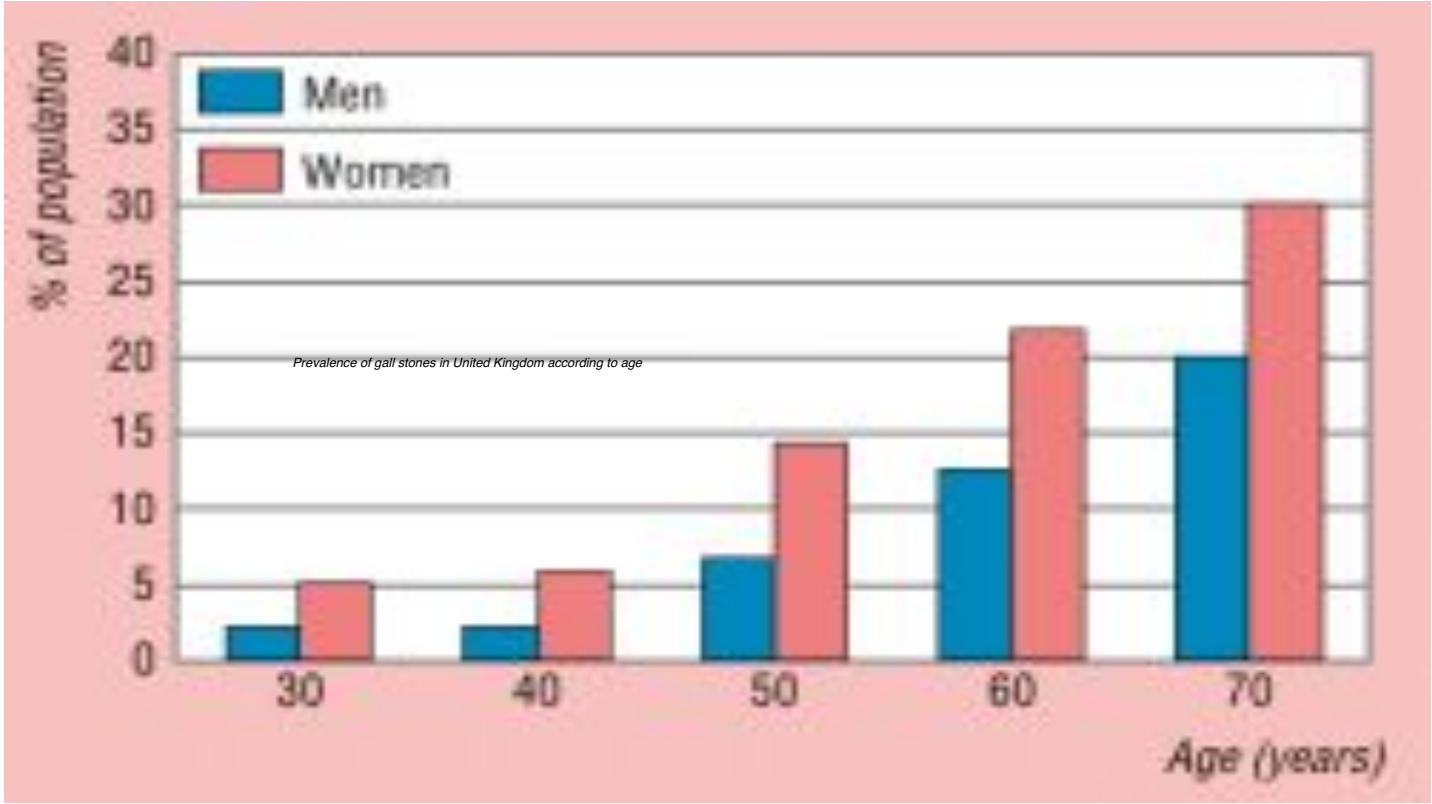
Mechanisms in the formation of lithogenic bile

The most important is **increased biliary secretion of cholesterol**.

This may occur in association with obesity,
the metabolic syndrome,
high-caloric and cholesterol-rich diets,
drugs (e.g., clofibrate) may result from increased activity of HMG-CoA reductase and increased hepatic uptake of cholesterol from blood.

Gallstone Disease

- At least 10% of the general population have gallstones.
- In general, gallstones are approximately two times more common in women than in men.
- Estimated prevalence of gallstone disease in variant populations is different.



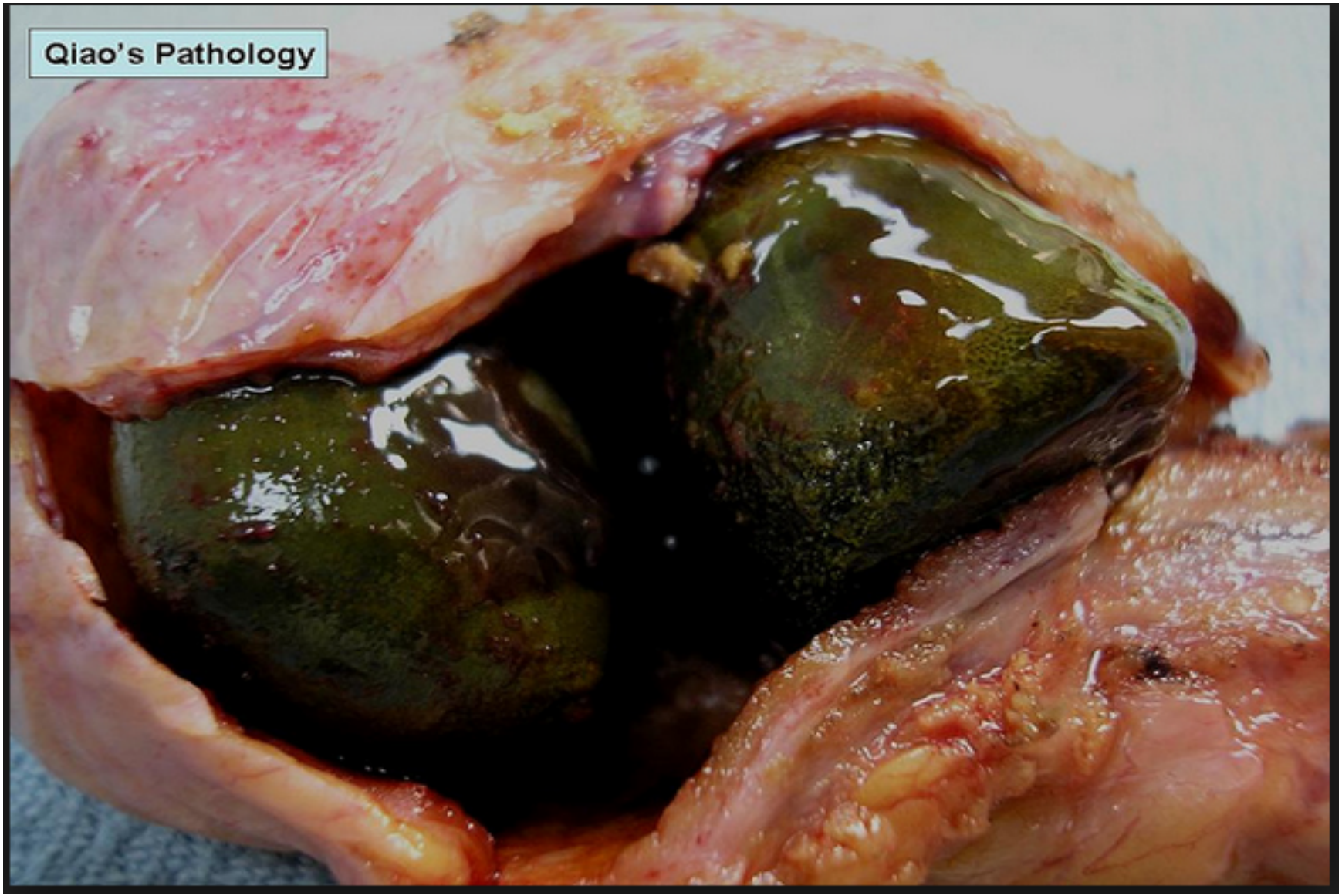
Prevalence of gall stones in United Kingdom according to age

Composition of gallstones

- Cholesterol stones (80%)
- Pigment stones (20%)
  - Black
  - Brown

pigment stones

comprising less than 20% and are composed primarily of calcium bilirubinate; they contain <20% cholesterol and are classified into “black” and “brown” types, the latter forming secondary to chronic biliary infection.


Qiao's Pathology

Risk Factors of Cholesterol Gallstones

- **Age**
- **Female gender**
- **Obesity**
- **Weight loss**
- **Total parenteral nutrition**
- **Pregnancy and parity**
- **Drugs**

Clofibrate
Oral contraceptives
Estrogen treatment in women
Progestron
Ceftriaxone
Octreotide

- **Genetic predisposition**
- **Native Americans**
- **Apolipoprotein E4/E4 alleles**
- **Diseases of the terminal ileum**
- **Decreased HDL**
- **Increased triglycerides**

Major risk factors

Major risk factors for the development of gallstones

Age
Female sex
Genetic
Pima Indians and certain other Native Americans
Chileans
Pregnancy
Obesity
Rapid weight loss
Very low calorie diet
Surgical therapy of morbid obesity
Cirrhosis
Hemolytic anemias
Hypertriglyceridemia
Medications
Estrogen and oral contraceptives
Clofibrate
Ceftriaxone
Octreotide
Terminal ileal resection
Gallbladder stasis
Diabetes mellitus
Total parenteral nutrition
Postvagotomy
Octreotide or somatostatinoma
Spinal cord injury
Reduced physical activity (at least in men)

Thyroid dysfunction and choleduocholithiasis.

Ajdarkosh H1, Khansari MR1, Sohrabi MR1, Hemasi GR1, Shamspour N1, Abdolahi N1, Zamani F1

Middle East J Dig Dis. 2013 Jul;5(3):141-5.

Clinical Manifestations of Gallstones

- Asymptomatic Gallstones
- Symptomatic Gallstons
  - ➢ Biliary Colic
  - ➢ Acute Cholecystitis
  - ➢ Choledocholithiasis
  - ➢ Acute Cholangitis
- Complications (acute pancreatitis)

Biliary Pain

- Intermittent obstruction of the cystic duct
- No inflammation of the gallbladder
- Epigastric or RUQ visceral pain growing in intensity over 15 minutes and remaining constant for 1-6 hours, often with nausea
- Frequency of attacks varies from days to months
- Mild to moderate epigastric/RUQ tenderness during an attack.
- Often findings are normal

Biliary colic

The classic description of biliary colic is:

- An intense, dull discomfort located in the RUQ, epigastrium, or (less often) substernal area that may radiate to the back
- Despite its name, the pain is usually steady and not colicky.
- The pain is often associated with diaphoresis, nausea, and vomiting, not associated with position or motion
- The pain typically lasts at least 30 minutes, plateauing within an hour and then gradually decrease, lasting less than six hours

Hepatology. 1999;30:839–846Gastroenterology. 2011 Feb;140(2):508-16.

CLINICAL FEATURES

- the chance of recurring biliary colick is 30 % per year in the first two years
- the chance of developing complications is approximately 2 to 3% per year.
- once a complication develops, the chance of having additional, often more severe, complications is 30% per year

CLINICAL FEATURES

- Eating a fatty meal is a common trigger for gallbladder contraction, and many patients report postprandial pain.

- However, an association with meals is not universal, and in a significant proportion of patients the pain is nocturnal

*J Clin Gastroenterol. 1990;12:409–14, Best Pract Res Clin Gastroenterol. 2006;**20** (6): 1017–29.*
Surg Endosc. 2008;22(7):1620.

Atypical symptoms

- Chest pain
- Nonspecific abdominal pain
- Belching
- Fullness after meals/early satiety
- Fluid regurgitation
- Abdominal distension/bloating
- Epigastric or retrosternal burning
- Nausea or vomiting without biliary colic

Biliary Pain Cont.

- Laboratory findings
  - Usually normal,
  - Elevated serum bilirubin, alkaline phosphatase, or amylase levels suggest coexisting CBD stones
- Diagnostic studies
  - Ultrasonography
  - Oral cholecystography
- Natural history
  - After the initial attack, 30% of patients have no further symptoms
  - Symptoms develop in the remainder at a rate of 6% per year, and severe complications at a rate of 1% to 2% per year

DIFFERENTIAL DIAGNOSIS

- Esophageal chest pain
- Gastroesophageal reux disease
- Peptic ulcer disease
- Nonulcer dyspepsia
- Hepatitis
- Functional gallbladder disorder
- Sphincter of Oddi dysfunction
- Chronic pancreatitis
- Irritable bowel syndrome
- Ischemic heart disease
- Pyelonephritis
- Ureteral calculi
- acute cholecystitis, choledocholithiasis, acute pancreatitis, and acute cholangitis

Scand J Gastroenterol. 2000;35(1):70.
Surg Endosc. 2008;22(7):1620.
Practitioner.2015 Jun;259(1783):15-9, 2.

CATEGORIZATION OF PATIENTS

- Category 1: Gallstones on imaging studies but without symptoms
-
- Category 2: Typical biliary symptoms and gallstones on imaging studies with no evidence of complications
-
- Category 3: Atypical symptoms and gallstones on imaging studies
-
- Category 4: Typical biliary symptoms but without gallstones on ultrasound

BMJ. 2014;349:g6241. N Engl J Med. 1982;307(13):798.

CATEGORIZATION OF PATIENTS

- category 1 should generally be left alone
- category 2 should undergo cholecystectomy
- Optimal approaches for categories of 3 and 4 are less clear.

J Gastroenterol Hepatol.2010 Apr;25(4):719-24. *PLoS One2013; 8(10): e74887. Practitioner.2015 Jun;259(1783):15-9, 2.*

MANAGEMENT

Category 2 patients (typical biliary symptoms and gallstones)

Pain management : During an acute attack of biliary colic, management is focused on pain control.
Pain control can usually be achieved with NSAID, opioids and Ketorolac
Those with prolonged attacks should also receive intravenous hydration.

MANAGEMENT

- Although meperidine may be a narcotic of choice in patients with biliary colic or gallstone pancreatitis because it has less of an effect on sphincter of Oddi motility than morphine
- However, a systematic review found that all opioids result in increased sphincter of Oddi pressure when measured using sphincter of Oddi manometry
- Thus, there are insufficient data to suggest that morphine should be avoided in patients with biliary colic.
- In addition, morphine has the benefit of having a longer half-life than meperidine.

MANAGEMENT

- Category 3 patients (gallstones but atypical symptoms)

- Some patients with atypical symptoms and gallstones respond to cholecystectomy, but the response rates are lower than those seen for patients with typical biliary colic.

- An empiric trial of oral dissolution therapy with ursodeoxycholic acid (UDCA) may help identify patients who will benfiet from cholecystectomy

Ann Intern Med. 1994;121(3):207. ;Hepatology. 1999;30(1):6. J Am Coll Surg. 2016 Apr;222(4):377-84

MANAGEMENT

- Category 4 patients (typical biliary symptoms but without gallstones on ultrasound)

- If cholecystokinin stimulated cholescintigraphy reveals a low gallbladder ejection fraction,(a finding that is suggestive of functional gallbladder disorder,) the appropriate treatment is cholecystectomy.

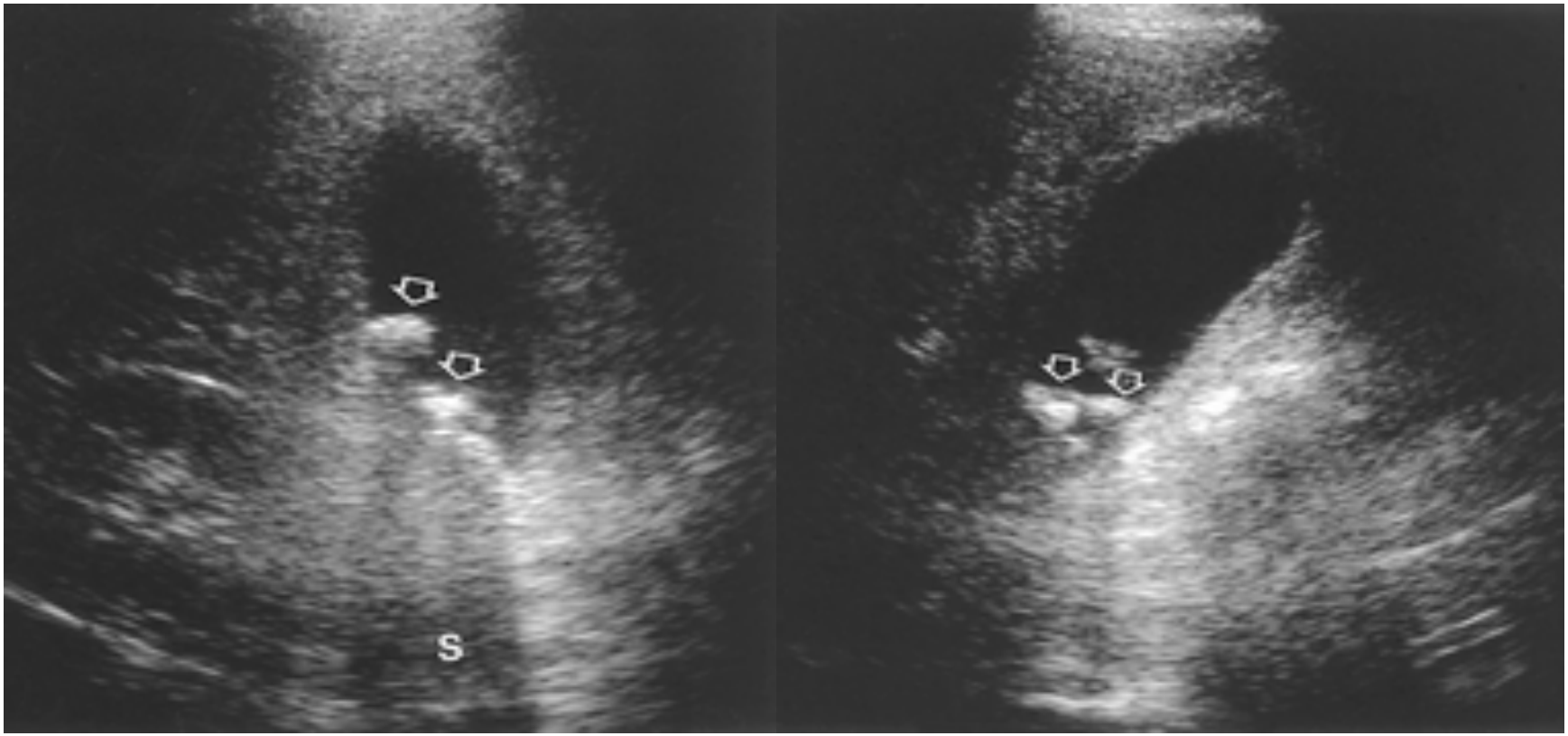
Nat Rev Dis Primers. 2016 Apr 28;2:16024.
World J Gastrointest Surg. 2016 Jan 27; 8(1): 65–76.

Imaging

- Gallstones are rarely seen on plain abdominal radiographs because only approximately 10% of gallstones contain enough calcium to make them sufficiently radio-opaque to be visible on a plain radiograph

Ann Surg 1983 Apr; 197(4): 464–469.
Ulster Med J2013 Sep; 82(3): 179–187

-Abdominal sonography



DIAGNOSIS

- Stone detection by sono:
  - sensitivity 84 %
  - specificity 99 %
  -
- Smaller stones may be missed, and the sensitivity falls to 50 to 60 % for stones less than 3 mm
- Modern sonographic equipment is able to detect stones as small as 1.5 to 2 mm

Gastrointest Endosc. 2010;71(1):1;
Gastrointest Endosc. 2011;74(2):378

DIAGNOSIS

In patients with typical biliary colic but no gallstones on ultrasonography, it should be repeat in a few weeks
If the repeat ultrasonography is negative, the patient may have microlithiasis or may have biliary symptoms without gallstones

Nat Rev Dis Primers.2016 Apr 28;2:16024, Practitioner. 2015 Jun;259(1783):15-9, National Institute for Health and Care Excellence (UK); 2014 Oct.

DIAGNOSIS

- **EUS:**
  - ➢ If the transabdominal ultrasound is negative in a patient with biliary colic, additional studies that may help with the diagnosis include endoscopic ultrasound (EUS)
  - ➢ The sensitivity and specifity of EUS for detecting cholelithiasis are 96 and 86 %, respectively

Cholescintigraphy (hepatobiliary scintigraphy; hydroxyiminodiacetic acid or diisopropyl iminodiacetic acid scans)

- Acute cholecystitis
  - ➢ Assesses patency of the cystic duct
  - ➢ Normal scan shows radioactivity in the gallbladder, CBD, and small bowel within 30-60 minutes
  - ➢ Positive result is defined as nonvisualization of the gallbladder with preserved excretion into the CBD or small bowel
  - ➢ Sensitivity rate is ≈95% and specificity rate ≈90%, with false-positive results seen in fasted, critically ill patients
  - ➢ With cholecystokinin stimulation, gallbladder "ejection fraction" can be determined
  - ➢ *Normal scan result virtually excludes acute cholecystitis*

Acute Cholecystitis

- Impacted stone in the cystic duct
- Acute inflammation of the gallbladder
- Secondary bacterial infection in ≈50%
- 75% of cases are preceded by attacks of biliary pain
- Severe, localized pain in the RUQ, back, right shoulder, or, rarely, chest
- Nausea with some vomiting is frequent
- Pain lasting >6 hours favors cholecystitis over biliary pain alone
- Febrile, but usually to <39°C unless complicated by gangrene or perforation
- Right subcostal tenderness with inspiratory arrest (Murphy's sign)
- Palpable gallbladder in 33% of patients, especially those having their first attack

Gallstone complication

- **Acute cholecystitis (most common)**
- **Rare complications include**
  - *Choledocholithiasis*
  - *Gallstone pancreatitis*
  - *Cholangitis*
  - *Mirizzi syndrome*
  - *Cholecystoduodenal fistula*
  - *Acalculous cholecystitis*
  - *Incidental gallbladder cancer*

World J Emerg Surg. 2016; 11: 52

Choledocholithiasis

- Intermittent obstruction of the common bile duct
- Often asymptomatic
- Symptoms (when present) are indistinguishable from biliary pain
- Predisposes to cholangitis and acute pancreatitis
- Jaundice with pain suggests stones;
- Painless jaundice and a palpable gallbladder favor malignancy

ERCP

Choledocholithiasis Cont.

- Laboratory findings
  - ➢ Elevated serum bilirubin and alkaline phosphatase levels are seen with CBD obstruction
  - ➢ A transient “spike” in serum aminotransferase or amylase (or lipase) levels suggests the passage of a stone

- Diagnostic studies
  - ➢ ERCP
  - ➢ EUS
  - ➢ MRI
  - ➢ PTC

- Natural history
  - ➢ Complications are more common and more severe than for asymptomatic stones in the gallbladder

Cholangitis

- Stone in the common bile duct causing bile stasis
- Bacterial superinfection of stagnant bile
- Pain may be mild and transient and is often accompanied by chills
- Fever in 95%
- RUQ tenderness in 90%
- Jaundice in 80%
- Charcot's triad (pain, jaundice, and fever) is present in 70% of patients

Cholangitis Cont.

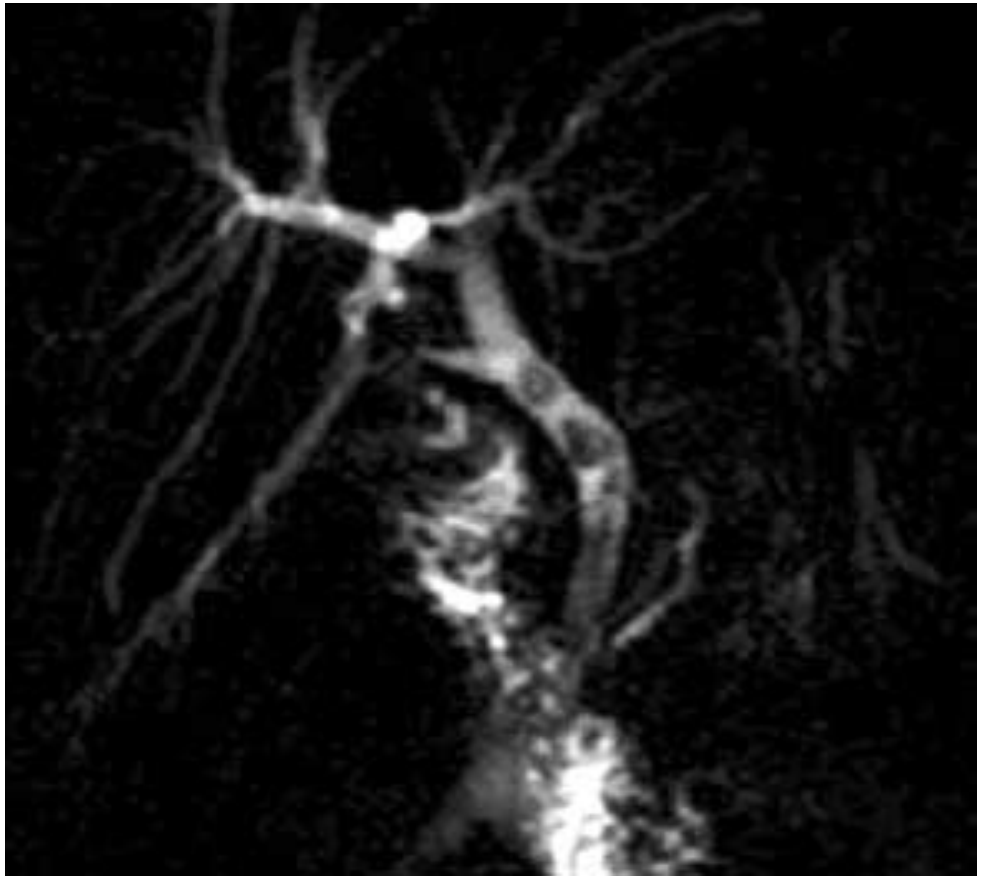
- Laboratory findings
  - Leukocytosis in 80%,
  - Serum bilirubin level >2 mg/dL in 80%
  - Serum alkaline phosphatase level is usually elevated
  - Blood cultures are usually positive, especially during chills or fever spike;

- Diagnostic studies
  - ERCP
  - PTC

- Natural history
  - High mortality rate if unrecognized, with death from septicemia
  - Emergency decompression of the CBD (usually by ERCP) improves

MRCP

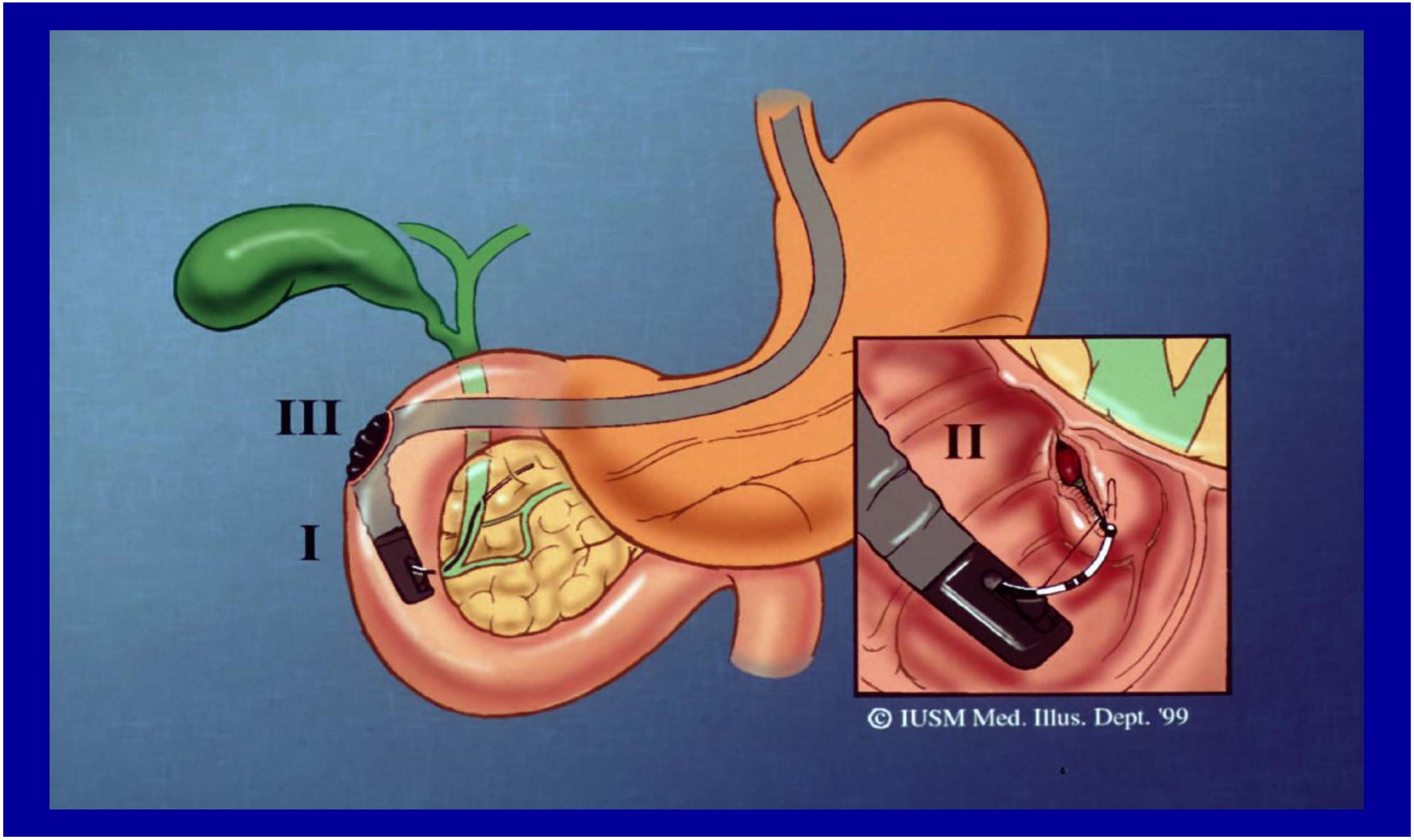
- Choledocholithiasis
  - ➢ Rapid, noninvasive modality that provides detailed bile duct and pancreatic duct images equal to those of ERCP
  - ➢ Sensitivity rate ≈93% and specificity rate ≈94%,
  - ➢ Useful for examining nondilated ducts, particularly at the distal portion, which often is not well visualized by ultrasonography
  - ➢ Adjacent structures such as liver and pancreas can be examined at the same time
  - ➢ *Recommended for patients with a low to moderate clinical probability of choledocholithiasis*



MRCP with stones in the duct

ERCP

- Choledocholithiasis
  - ➢ ERCP is the standard diagnostic test for stones in the CBD, with sensitivity and specificity rates of ≈95%
  - ➢ Use of ERCP to extract stones (or at least to drain infected bile) is life-saving in severe cholangitis
  - ➢ *Recommended for patients with a high clinical probability of choledocholithiasis*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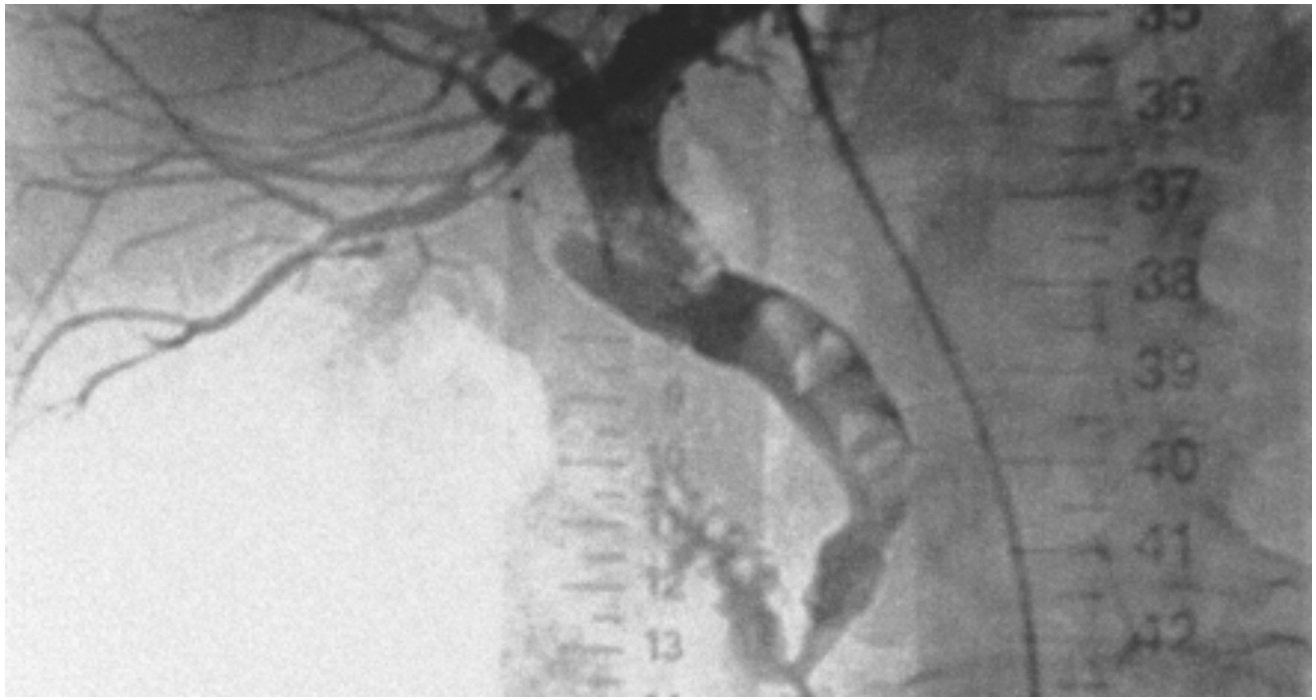
© IUSM Med. Illus. Dept. '99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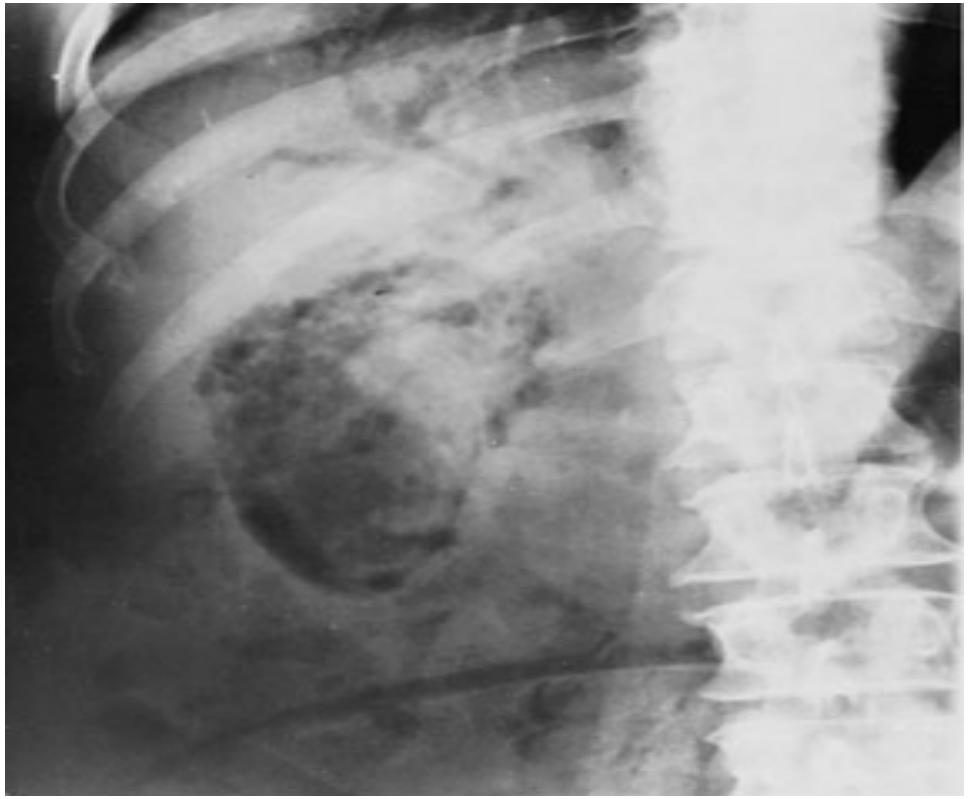
Uncommon Complications of Gallstone Disease

- Emphysematous cholecystitis
- Cholecystoenteric fistula
- Mirizzi's syndrome
- Porcelain gallbladder

abdominal flat-plate x-ray



Cholecystoenteric fistula

- Erosion of a (usually large) stone through the gallbladder wall into adjacent bowel, most often the duodenum, followed in frequency by the hepatic flexure, stomach, and jejunum
- Symptoms and signs similar to those of acute cholecystitis; although sometimes the fistula may be clinically silent
- Stones >25 mm, especially in elderly women, may produce a bowel obstruction, or “gallstone ileus”; the terminal ileum is the most common site of obstruction
- Plain abdominal films may show gas in the biliary tree and/or a small bowel obstruction in gallstone ileus
- Contrast gastrointestinal series may demonstrate the fistula
- A fistula from a solitary stone that passes may close spontaneously
- Cholecystectomy and bowel closure are curative

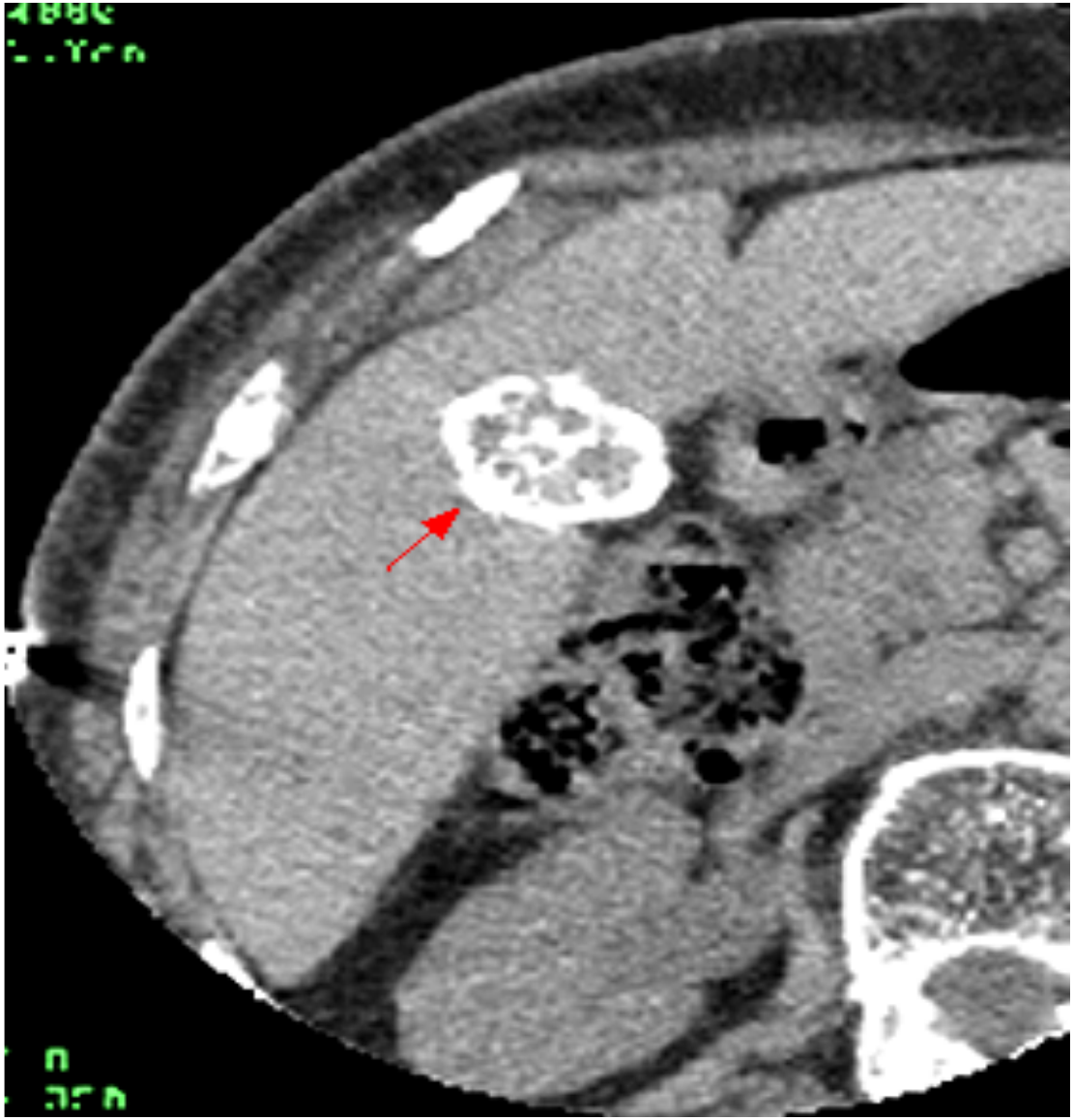
Mirizzi's syndrome

- Impacted stone in the gallbladder neck or cystic duct with extrinsic compression of the common hepatic duct from accompanying inflammation
- Jaundice and right upper quadrant pain
- ERCP demonstrates extrinsic compression of the common hepatic duct and fistula
- Preoperative diagnosis is important to guide surgery and minimize the risk of CBD injury

Porcelain gallbladder

- Intramural calcification of the gallbladder wall, usually in association with stones
- No symptoms attributable to the calcified wall per se, but carcinoma of the gallbladder is a late complication in ≈20%
- Plain abdominal films or CT shows intramural calcification of the gallbladder wall
- Prophylactic cholecystectomy is indicated to prevent carcinoma

Porcelain GB

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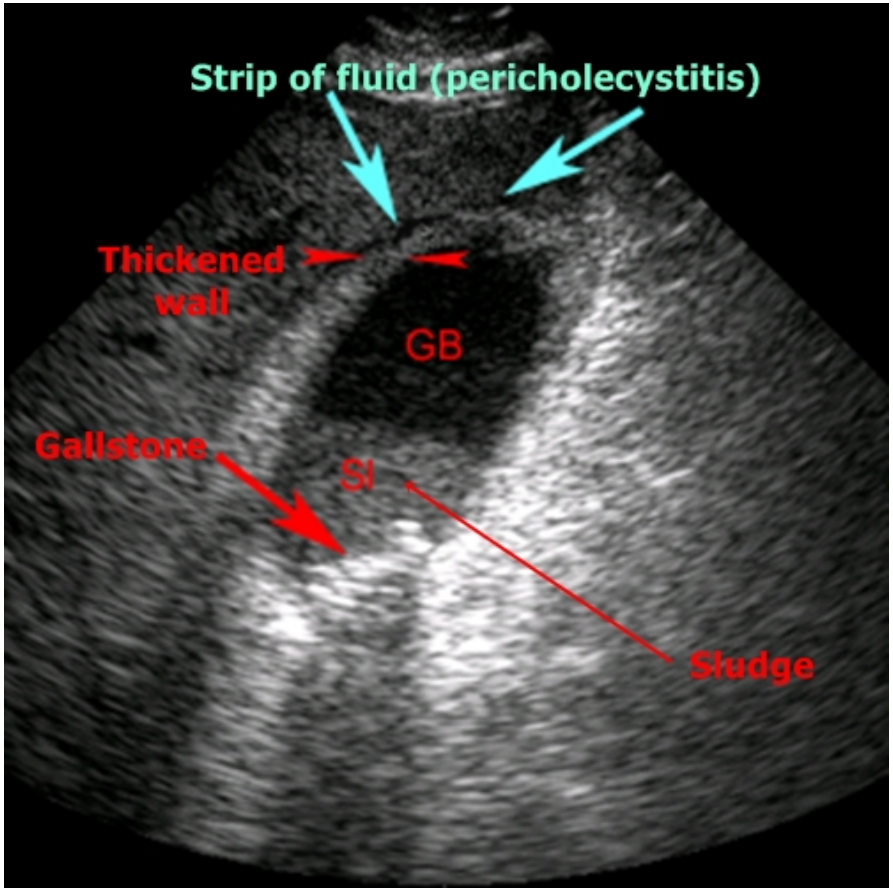
Laboratory Interpretation

- Acute Cholecystitis
  - WBC < 15
  - AST and ALT 2-3x's normal
  - Total Bilirubin mild elevated
  - LFT elevation not common
- Cholangitis
  - WBC > 15
  - Significant AST/ALT elevation
  - Total Bilirubin > 4
  - Modest elevation Alk-Phos
- Choledocholithiasis
  - Normal labs unless stone impaction
  - When obstruction occurs labs reflect either cholangitis, pancreatitis or both
- Gallstone Pancreatitis
  - Elevated WBC
  - Elevated lipase and amylase
  - Concomitant biliary obstruction
- Biliary Colic
  - Normal labs

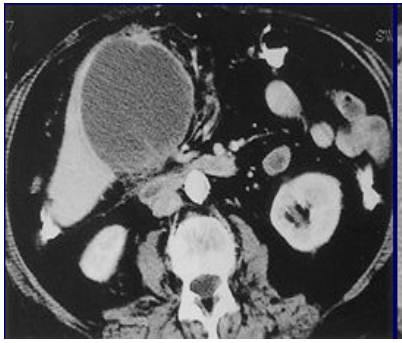
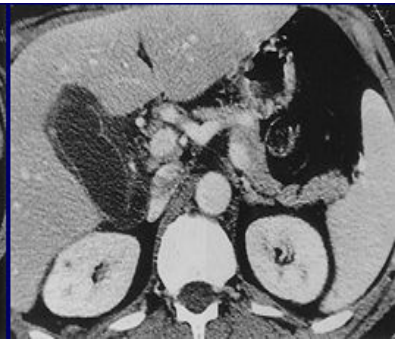
sonography


Strip of fluid (pericholecystitis)
Thickened wall
GB
Gallstone
SI
Sludge

CT and MRI

- High resolution
- More accurate
- Expensive
- Show the stone ,tumor, dilated duct
- MRCP show the entire biliary tree



Imaging Studies of the Biliary Tract

- Ultrasonography
- EUS
- Oral cholecystography
- Cholescintigraphy (hepatobiliary scintigraphy; hydroxyiminodiacetic acid or diisopropyl iminodiacetic acid scans)
- ERCP
- MRCP
- CT

CT

- Complications of gallstones
  - ➢ Not well suited for detecting uncomplicated stones, but excellent for detecting complications, such as:
    - o Abscess,
    - o Perforation of the gallbladder or CBD
    - o Pancreatitis

TREATMENT

- SURGICAL THERAPY

- MEDICAL THERAPY—GALLSTONE DISSOLUTION

Oral Bile Acid therapy

- Ursodeoxycholate (UDCA)
  - ➢ 10 mg/kg/d

- Effective in dissolution of GS
  - ➢ Non-calcified, cholesterol GS & Mild symptom
  - ➢ Functioning GB, patent cystic duct
  - ➢ Single or small stones < 10 mm

  - ➢ Reduce biliary cholesterol secretion
  - ➢ Complete dissolution in 30-40%
  - ➢ Recurrence rate high with cessation of drug

Indications for prophylactic cholecystectomy (Harrison)

- The presence of a prior complication of gallstone disease, i.e., history of acute cholecystitis, pancreatitis, gallstone fistula.
- Calcified or porcelain gallbladder.
- Previous attack of acute cholecystitis.
- Patients with very large gallstones (>3 cm in diameter)
- Patients having gallstones in a congenitally anomalous gallbladder.
- Although young age is a worrisome factor in asymptomatic gallstone patients, few authorities would now recommend routine cholecystectomy in all young patients with silent stones.

Management of Asymptomatic Stones

- Several studies have suggested that many of such patients remain asymptomatic (about 2 to 3% develop biliary colic annually).
- In the absence of antecedent symptoms, complications of gallstone disease, such as acute cholecystitis, develop at a rate of less than 1% per year.
- Also, in 90% of people with asymptomatic gallstones in whom symptoms develop the initial clinical presentation is biliary pain and not a biliary complication.

Prophylactic cholecystectomy

- *calculi >3 cm or < 3 mm in diameter,*
- *high prevalence of GBC &calcified (porcelain) GB*
- *Young adults and children because of risk of GBC*
- *Larger stones, more than 3 cm*
- *Those with higher GB stone to GB volume ratios.*
- *large polyps, anomalous pancreatico biliary channels.*

Indian J Surg Oncol. 2015 Sep; 6(3): 251–255.

MANAGEMENT

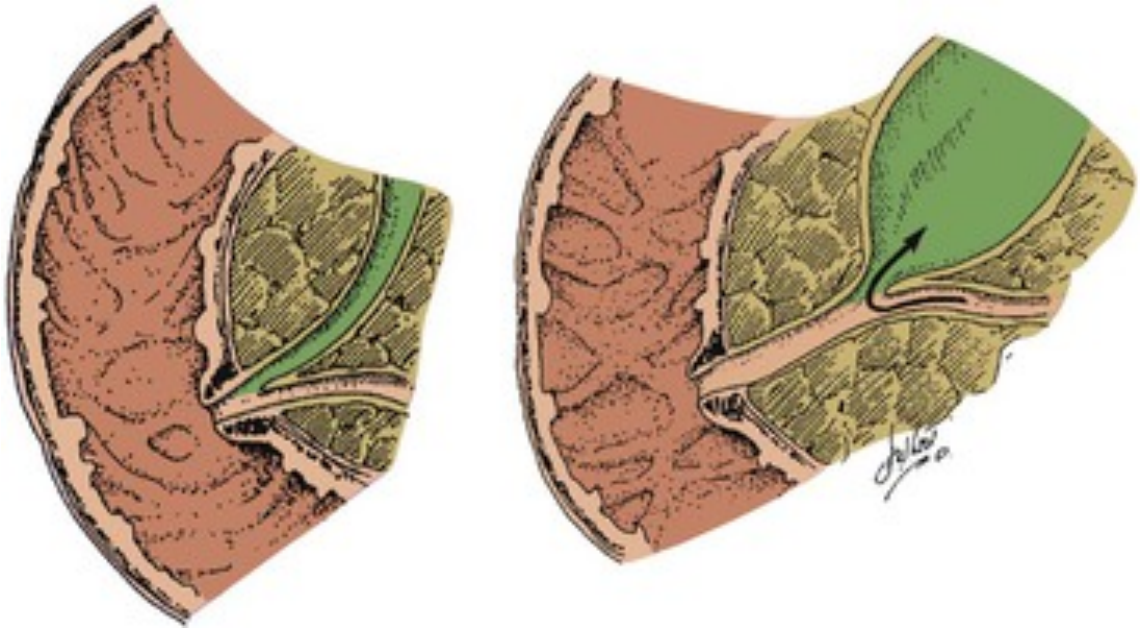
- Prophylactic Cholecystectomy is indicated for:
  - ➢ Patients at increased risk for gallbladder cancer
    - Anomalous pancreatic ductal drainage (in which the pancreatic duct drains into the common bile duct)
    - Gallbladder adenomas
    - Porcelain gallbladder
    - Large gallstones (if larger than 3 cm)
    -
  - ➢ some patients with hemolytic disorders

  - ➢ Gastric bypass

MANAGEMENT GS

- Prophylactic cholecystectomy is **not** indicated for most asymptomatic pts. cholecystectomy if ,
- gallbladder cancer
- Anomalous pancreatic ductal drainage
-
- Gallbladder adenomas , polyps , cholestrolosis
- Porcelain gallbladder
- Hemolysis, gastric bypass

Abnormal pancreatobiliary junction



MANAGEMENT

- Hemolytic disorders :

Patients with sickle cell disease and hereditary spherocytosis have a high incidence of forming pigment gallstones (50 % or more)

➢ perform a cholecystectomy if the patient has gallstones and a splenectomy for hereditary spherocytosis.

MANAGEMENT

Gastric bypass :

- Morbidly obese patients who have undergone gastric bypass surgery have a high incidence of developing gallstones (greater than 30%)

➢ A **prophylactic cholecystectomy** at the time of the bypass is recommended by some (regardless of whether gallstones are present)

MANAGEMENT

- Patients with diabetes mellitus may be at increased risk for the development of severe gangrenous cholecystitis

- However, the magnitude of the risk and the risks and costs of cholecystectomy do not warrant prophylactic cholecystectomy in patients with asymptomatic gallstones.

Indications for prophylactic cholecystectomy (Harrison)

- The presence of a prior complication of gallstone disease, i.e., history of acute cholecystitis, pancreatitis, gallstone fistula.
- Calcified or porcelain gallbladder.
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- gallbladder cancer
- Anomalous pancreatic ductal drainage
-
- Gallbladder adenomas , polyps , cholestrolosis
- Porcelain gallbladder
- Hemolysis, gastric bypass

Should prophylactic cholecystectomy be performed duringbariatric surgery in obese subjects undergoing rapid weightloss?

***Prophylactic cholecytectomy is not** routinely indicated*

during.bariatric surgery

Oral Bile Acid therapy

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  - ➢ Complete dissolution in 30-40%
  - ➢ Recurrence rate high with cessation of drug

Gallstones in pregnancy

- After acute appendicitis, acute cholecystitis is the second most common non-obstetrical indication for surgery in pregnant women

Gallstones in pregnancy

- Gallstones are more common during pregnancy due to:
  - ➢ decreased gallbladder motility (progesterone)
  - ➢ increased cholesterol saturation of bile:
    - Estrogen: increases cholesterol secretion
    - Progesterone: reduces bile acid secretion

- **These changes normalize one to two months following delivery.**

Management

- In first episode of biliary colic only supportive care , lead to resolution of symptoms in most cases, but the symptoms frequently recur later in pregnancy
- Recurrent biliary colic suggest cholecystectomy
- *Cholecystectomy can be performed safely and electively during any trimester of pregnancy.*

Is surgery indicated for gallbladder polyps?

Cholecystectomy should be performed in patients with gallbladder polyps ≥1 cm without or with gallstones

regardless of their symptoms

Cholecystectomy should also beconsidered in patients with asymptomatic gallbladder stones and gallbladder polyps 6-10 mm and in case of growing Polyps.

Cholecystectomy may be recommended for asymptomaticpatients with primary sclerosing cholangitis .polyp more than 8mm in

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- **Does gall stone is the cause of GB cancer ?**

although diabetic patients are at increased risk for the development of severe gangrenous cholecystitis,but prophylactic cholecystectomy in asymptomatic gallstones do not warrant.


Thank you