

# Gall Stone Disease

Pathogenesis  
Various Modes of Presentation  
Management

**Dr. Manish Madnani**

# Gallstones

## Types

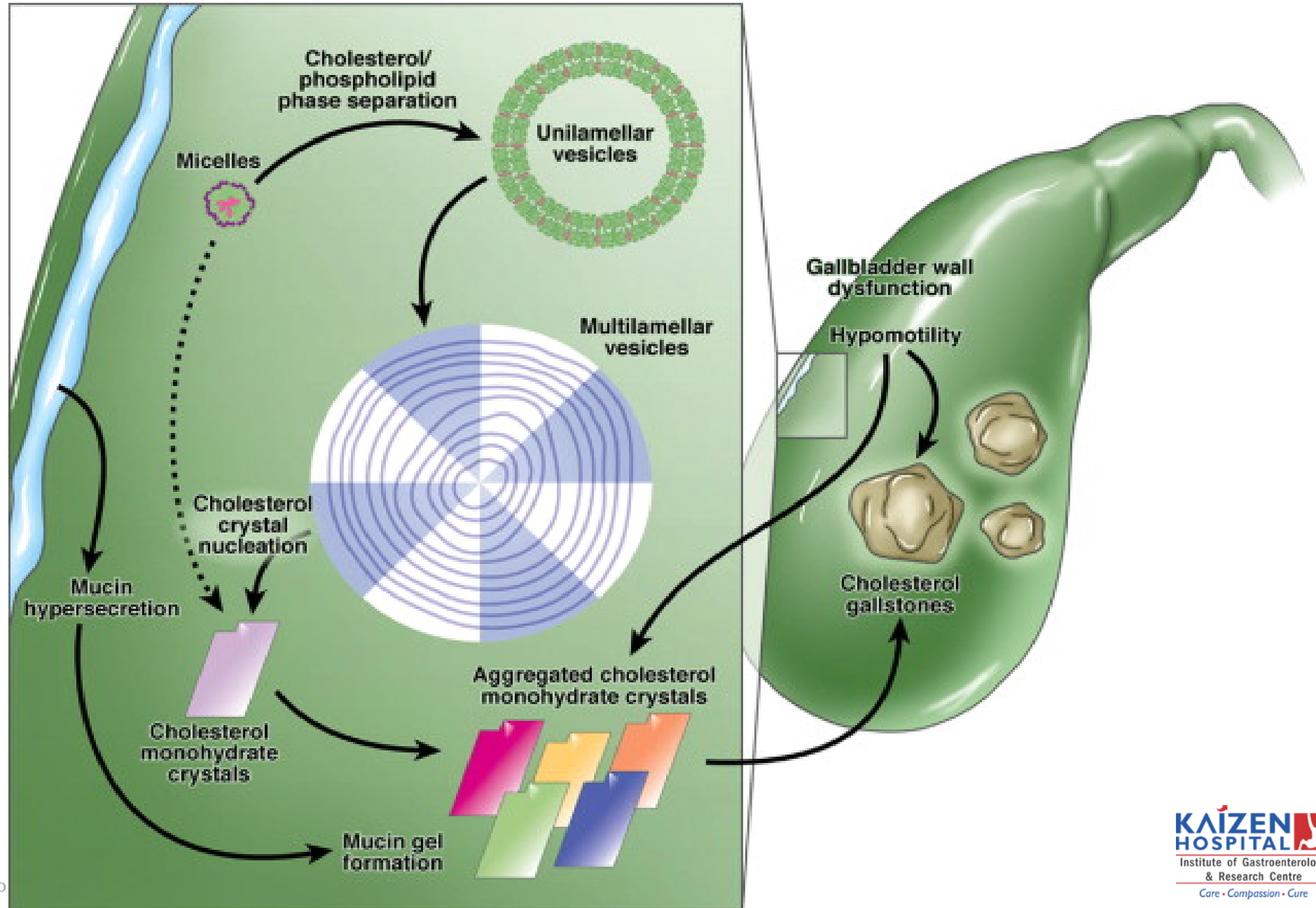
- Cholesterol stones
- Pigment stones
  - black stones
  - brown stones

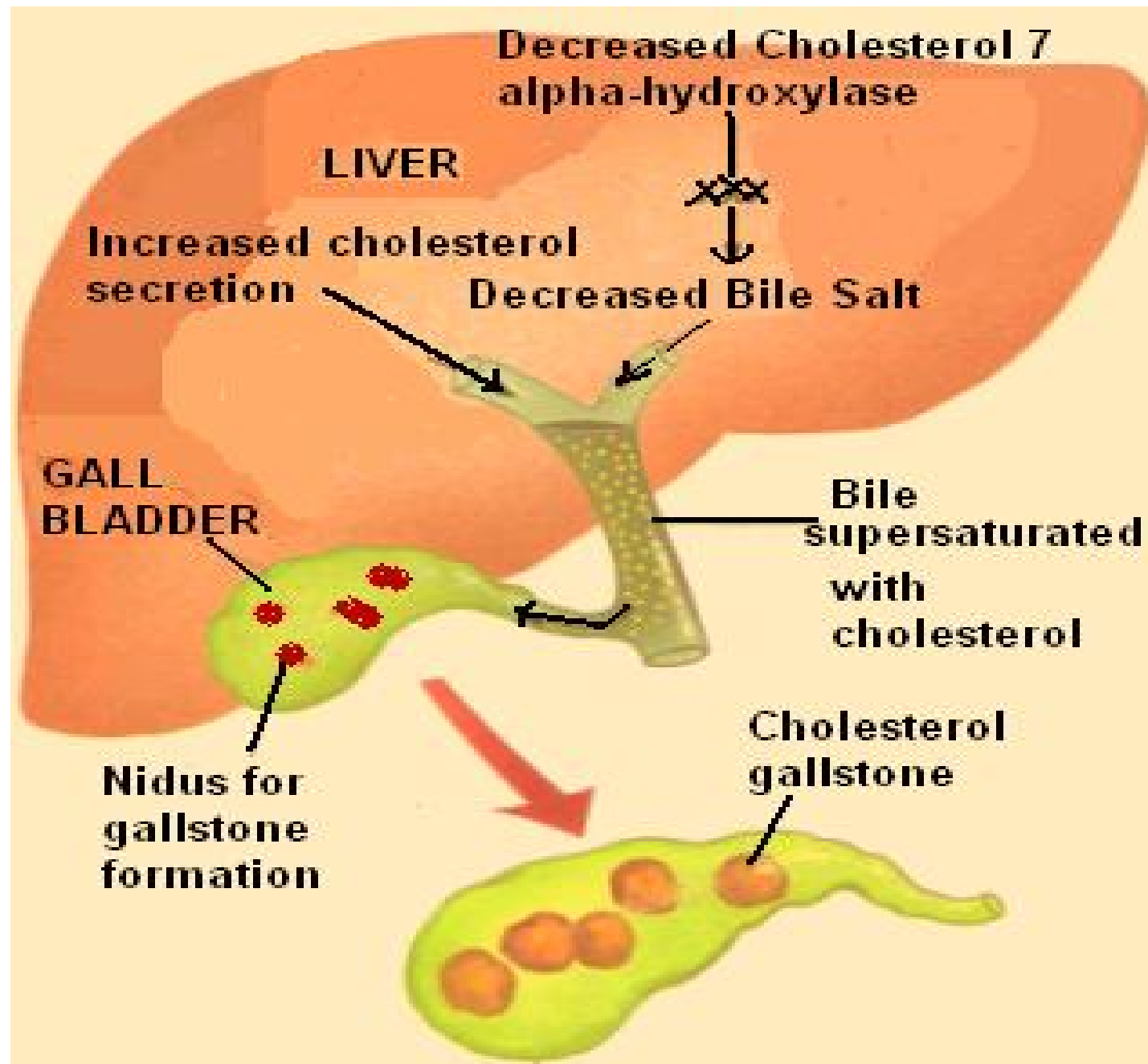
# Cholesterol gallstones

## Pathogenesis

- Supersaturated bile with cholesterol due to enhanced hepatic synthesis
- Low bile salt pool
- Poor contractility of gallbladder
- Excessive bile mucus glycoprotein

# Pathogenesis





## **Black stones**

Shiny

Resistant to crushing

Found in gallbladder

Bile sterile

A trace of calcium palmitate

< 20% cholesterol

## **Brown stones**

Dull brown

Soft

Found in bile duct

Bile infected

15% calcium palmitate

20-80% cholesterol

# Those who are most at risk.

- These are all adjectives to describe the person most at risk of developing symptomatic gallstones.

**FAIR**



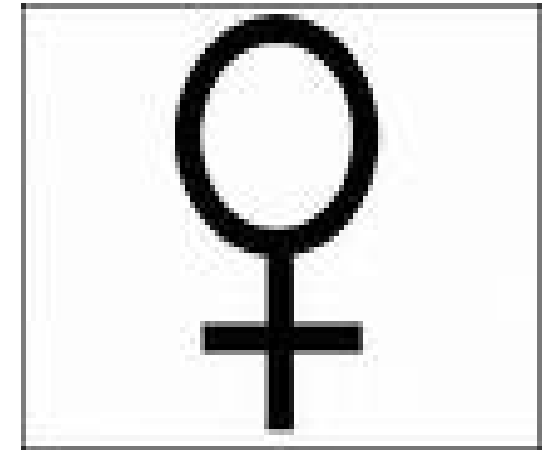
**FAT**



**FORTY**



**FEMALE**



# Factors associated with black pigment stones formation

- Chronic liver disease (increased frequency with severity)
- Ileal resection
- Chronic haemolysis
  - sickle cell anaemia
  - hereditary spherocytosis
  - thalassemia major
- Total parenteral nutrition
- Vagotomy



# Reasons for gallstone formation in cirrhosis

- Cirrhotic liver unable to convert all unconjugated bilirubin into bilirubin mono- and di-glucuronides
- Small fraction of unconjugated bilirubin spills into bile
- Unconjugated bilirubin precipitated with calcium

# Brown pigment stones formation

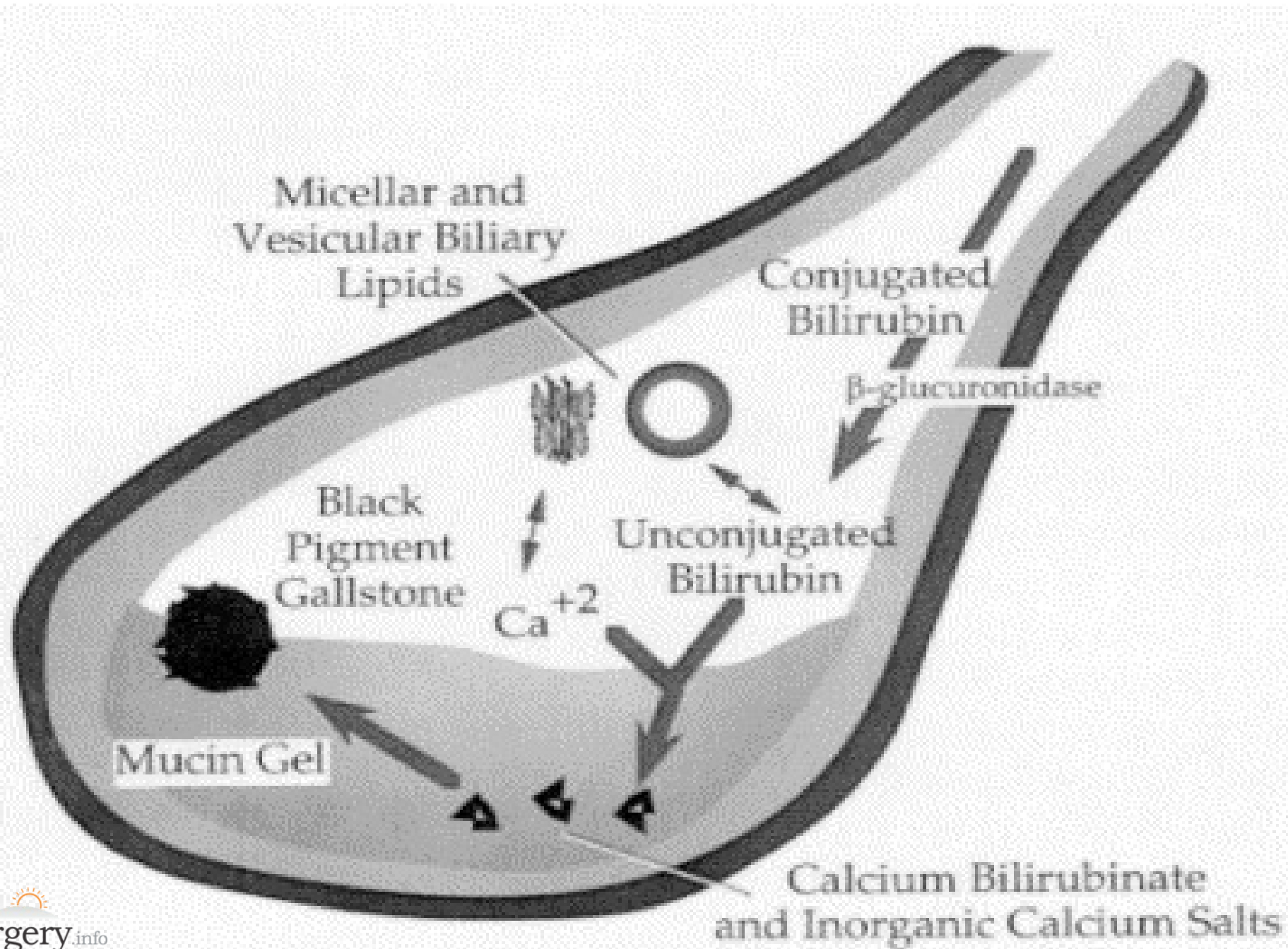
Bilirubin diglucuronide

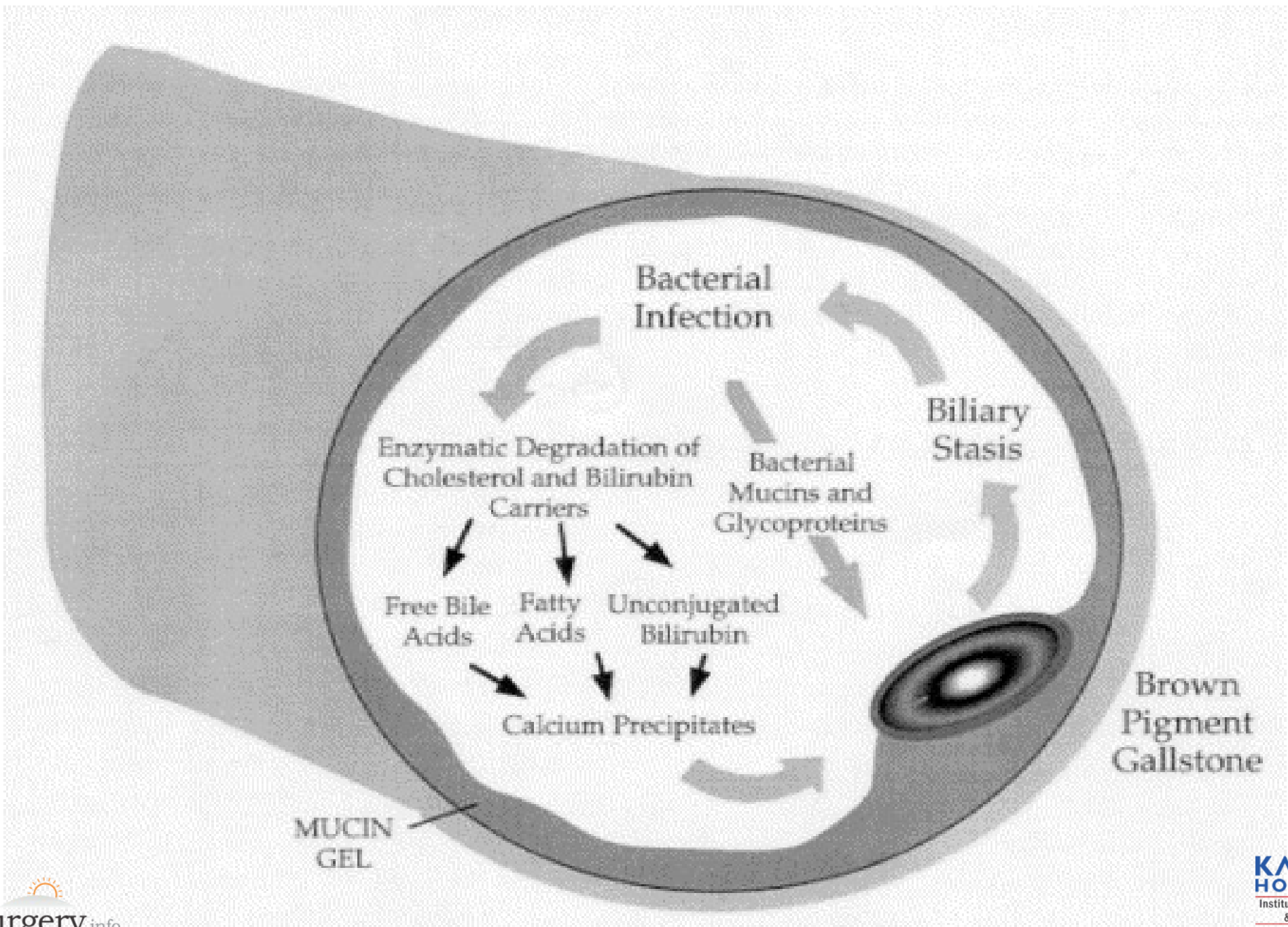
hydrolysis by  $\beta$ -glucuronidase

Unconjugated bilirubin

+Ca ion

Calcium bilirubinate

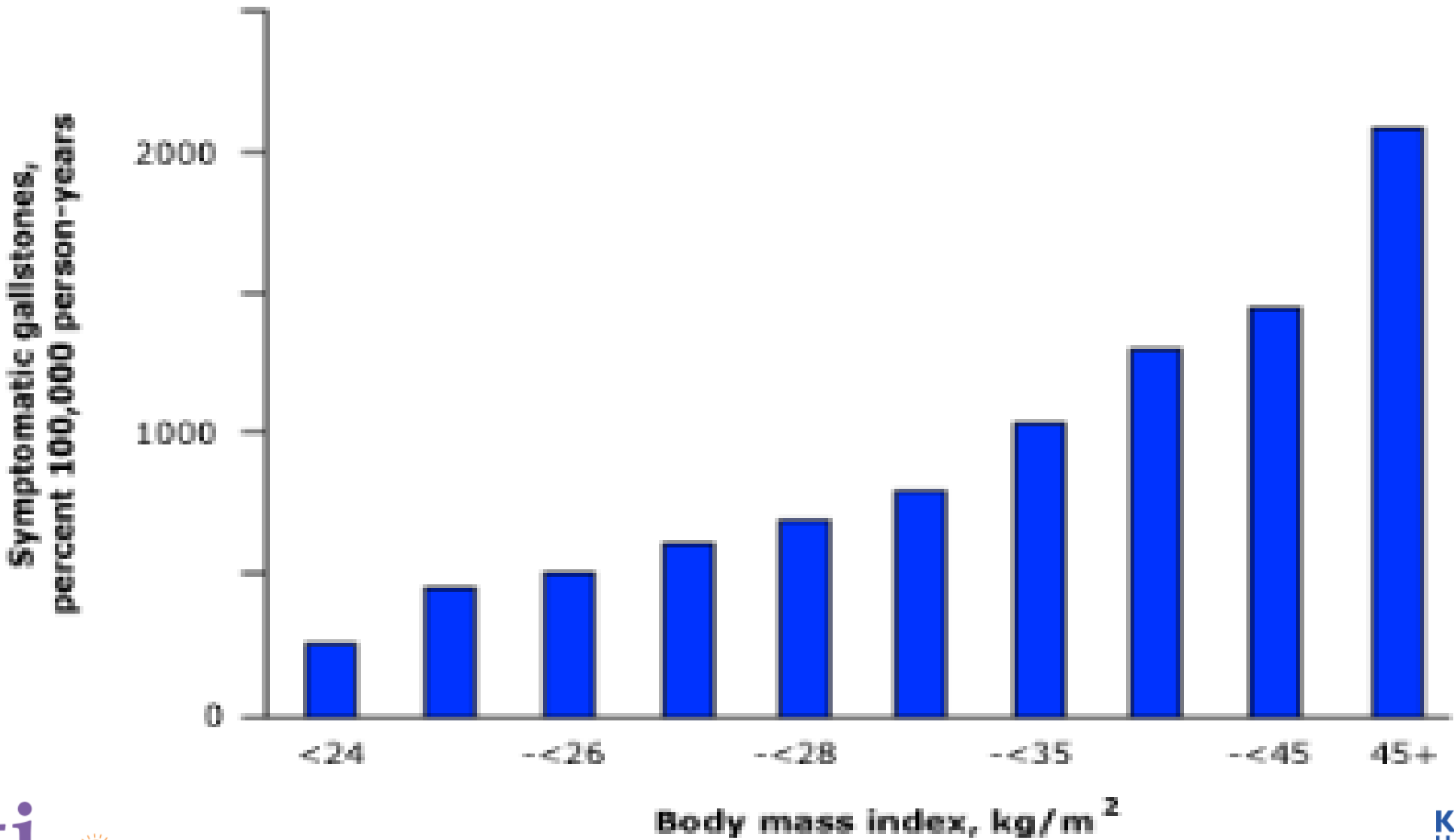




- Major risk factors for the development of gallstones
- Age
- Female sex
- Genetic
- Pima Indians and certain other Native Americans
- Chileans
- Pregnancy
- Obesity
- Rapid weight loss
- Very low calorie diet
- Surgical therapy of morbid obesity
- Cirrhosis
- Hemolytic anemias
- Hypertriglyceridemia

- 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)

# Relationship between body mass index (BMI) and gallstones



# Protective Factors

- Statins
- Vitamin C
- Moderate amount of coffee
- PUFA/MUFA
- Vegetable Protein

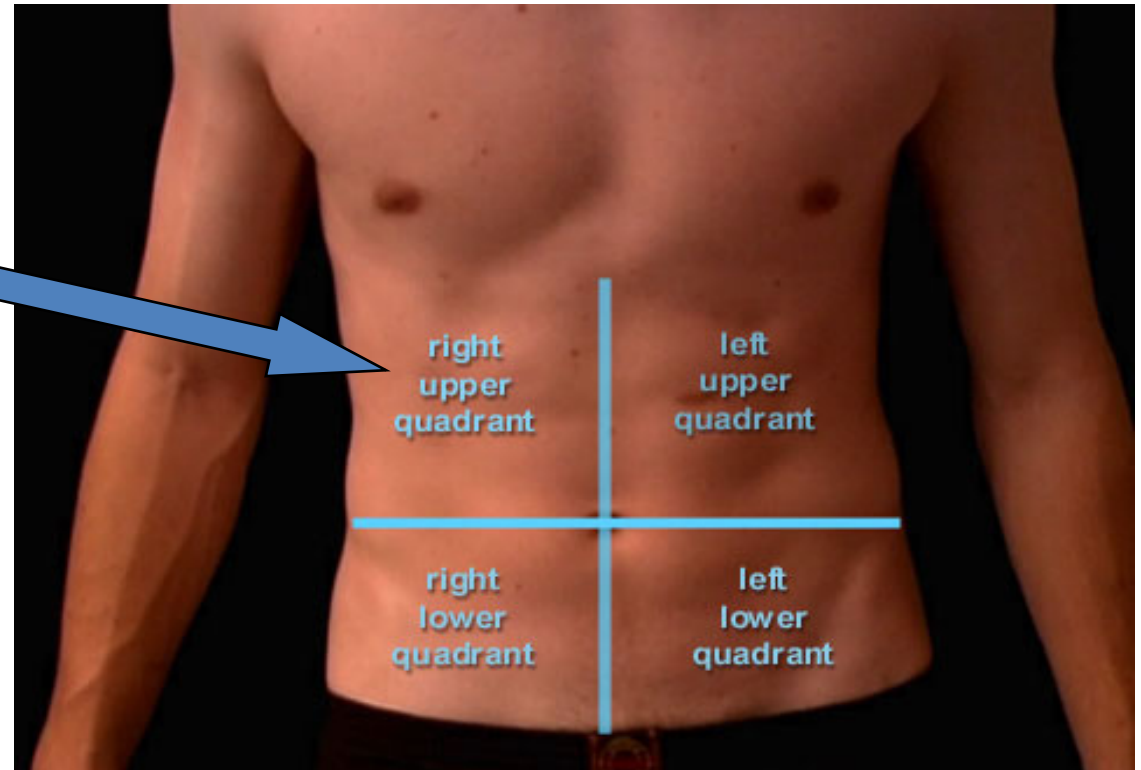


# Various Modes of Presentation

- Asymptomatic
- Symptomatic
  - Biliary colic
  - Acute Cholecystitis
  - Chronic Cholecystitis
  - *Complications*
  - Gangrenous Cholecystitis
  - Xanthogranulomatous Cholecystitis
  - Emphysematous Cholecystitis
  - Empyema
  - Mucocoele

# Biliary Colic

- Complaints of indigestion after eating high fat foods.
- Localized pain in the right-upper quadrant epigastric region.
- Anorexia, nausea, vomiting and flatulence.



- Increased heart and respiratory rate – causing patient to become diaphoretic which in turn makes them think they are having a heart attack.

# Biliary Colic

- Pain in the RUQ
  - Most common and typical symptom
  - May last for a few minutes to several hours
  - Mostly felt after eating a heavy and high-fat meal
- Pain under right shoulder when lifting up arms
- Colic - Misnomer

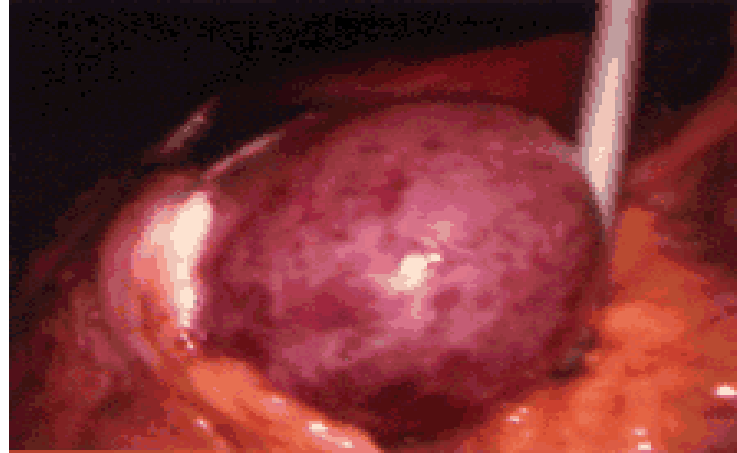
# Acute Cholecystitis

- Biliary Colic- Persistent
- Inflammatory component (fever, increased white cell count)
- Murphy's Sign
- Boas' Sign
- Ortner's Sign

# Stages of Acute Cholecystitis.



- Gallbladder has a grayish appearance & is edematous.
- There is an obstruction of the cystic duct and the gallbladder begins to swell.
- It no longer has the "robin egg blue" appearance of a normal gallbladder.



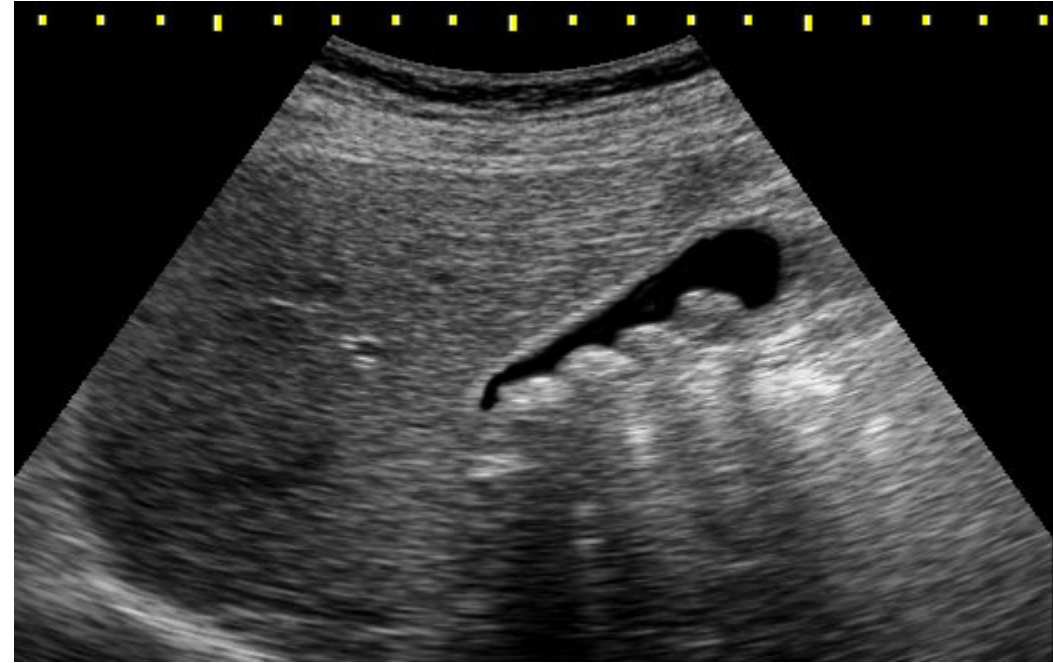
- As acute cholecystitis progresses, the gallbladder begins to become necrotic and gets a speckled appearance as the wall begins to die.



- Gallbladder undergoes gangrenous change and the wall becomes very dark green or black.
- This is the stage when perforation occurs.

# Diagnosis

- Ultrasound
  - Most sensitive and specific test for gallstones
- Computerized tomography (CT) scan
  - May show gallstones or complications, such as infection and rupture of GB or bile ducts
- Cholescintigraphy (HIDA scan)
  - Used to diagnose abnormal contraction of gallbladder or obstruction of bile ducts
- Endoscopic retrograde cholangiopancreatography (ERCP)
  - Used to locate and remove stones in bile ducts
- Blood tests
  - Performed to look for signs of infection, obstruction, pancreatitis, or jaundice





TRANS GB

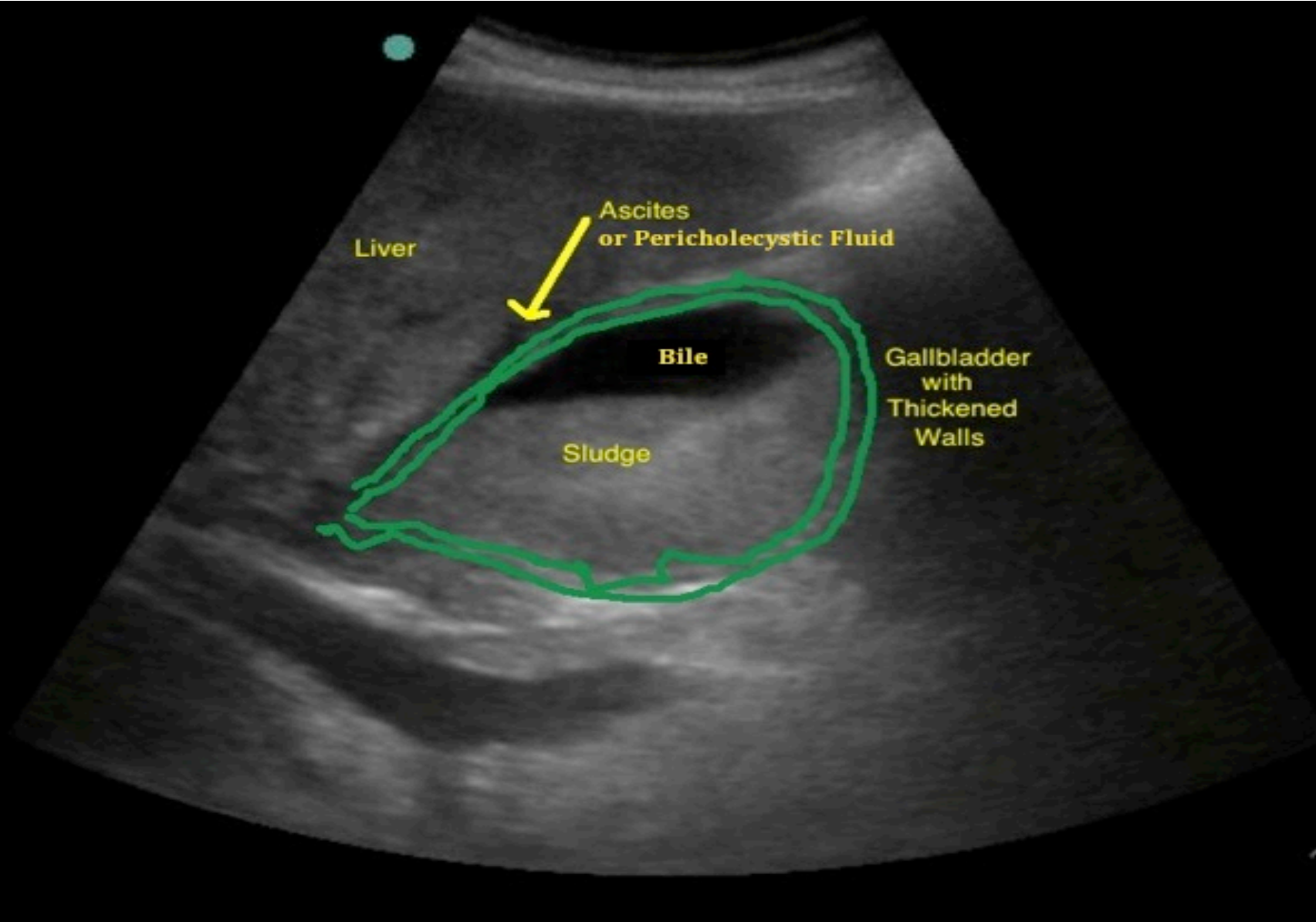
Thick wall

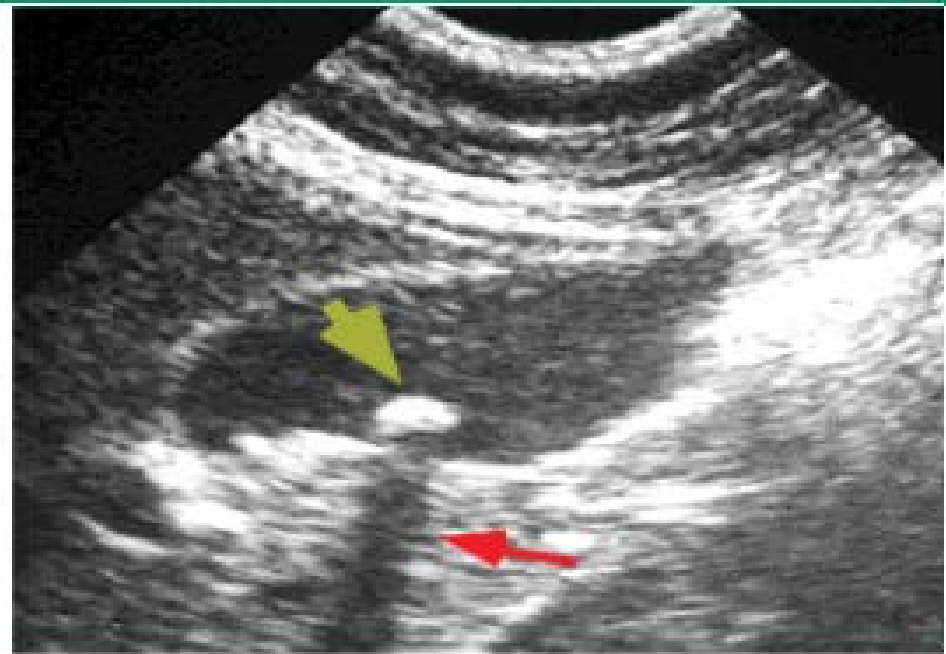
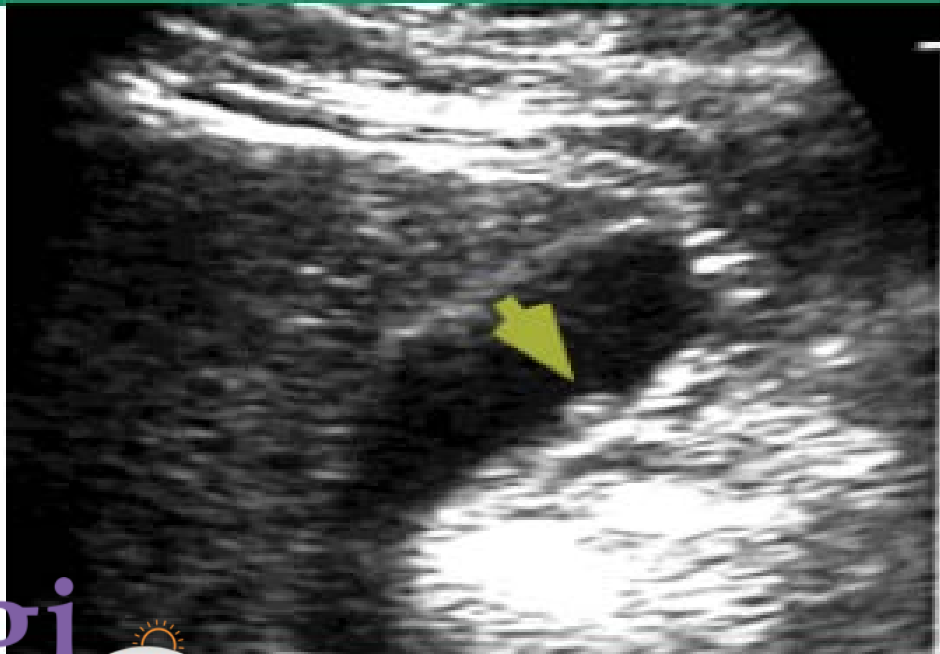
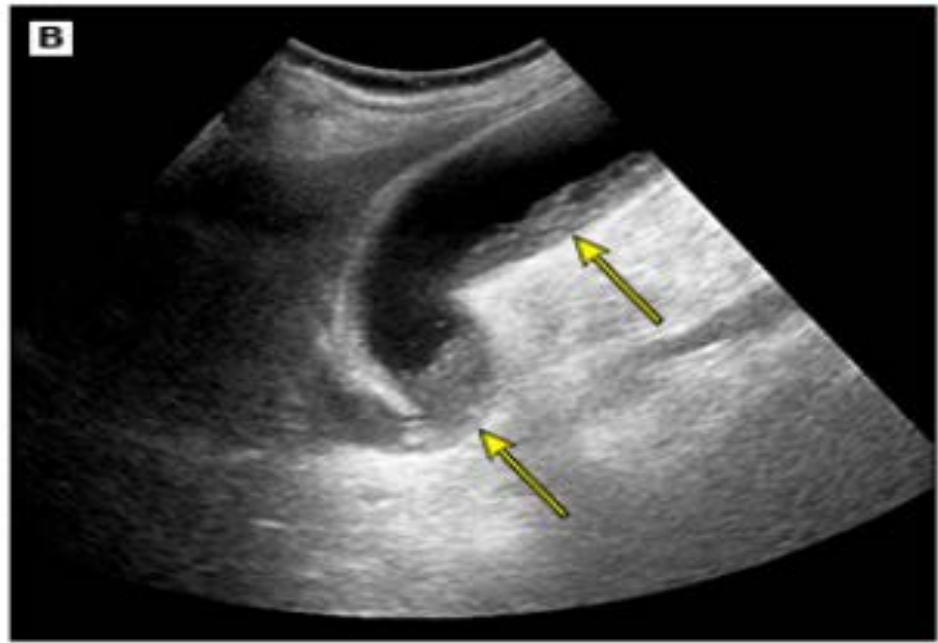
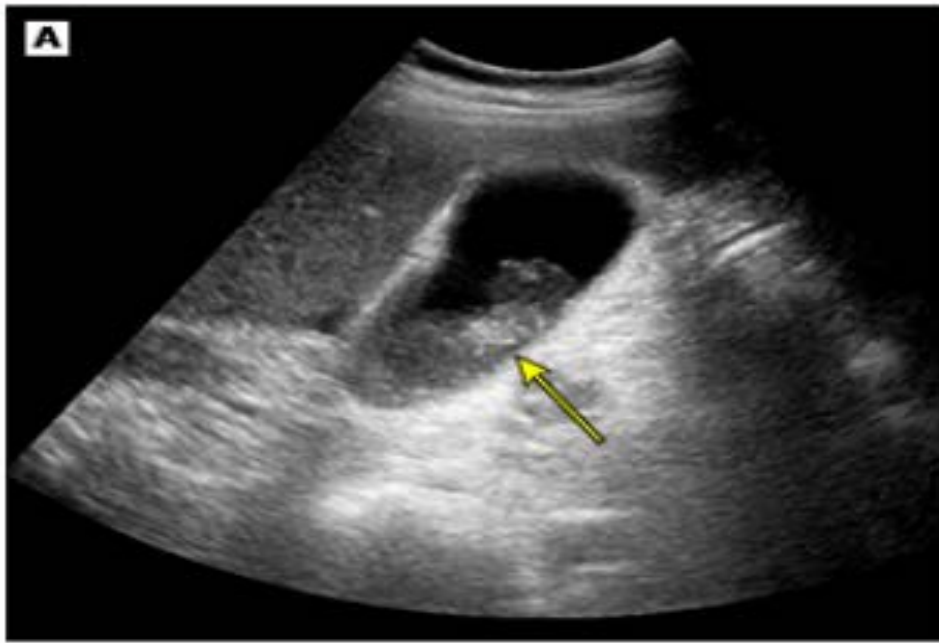
Free fluid

**Stones**

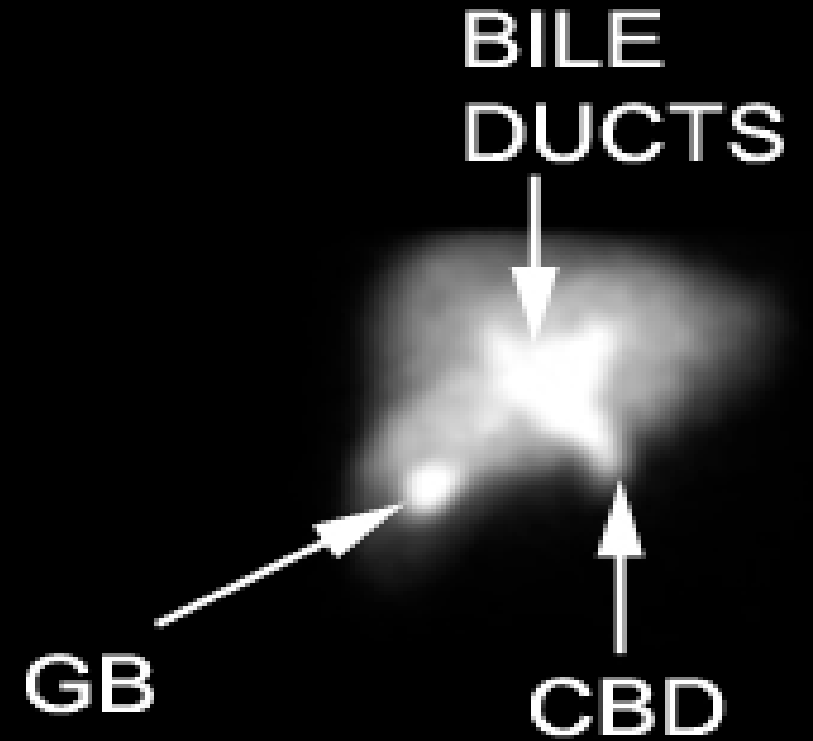
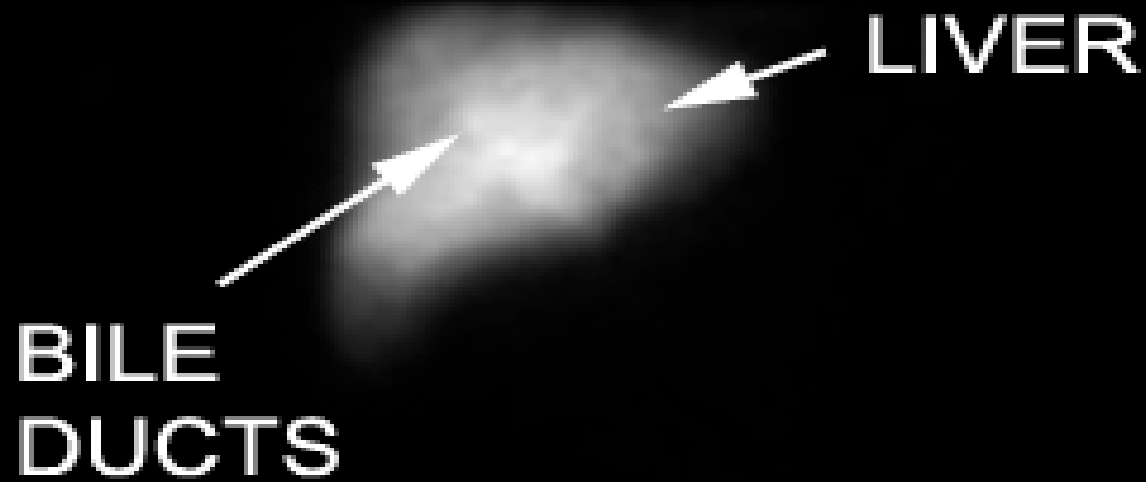
Absence of echoes posterior to the calculi  
**'Shadowing'**

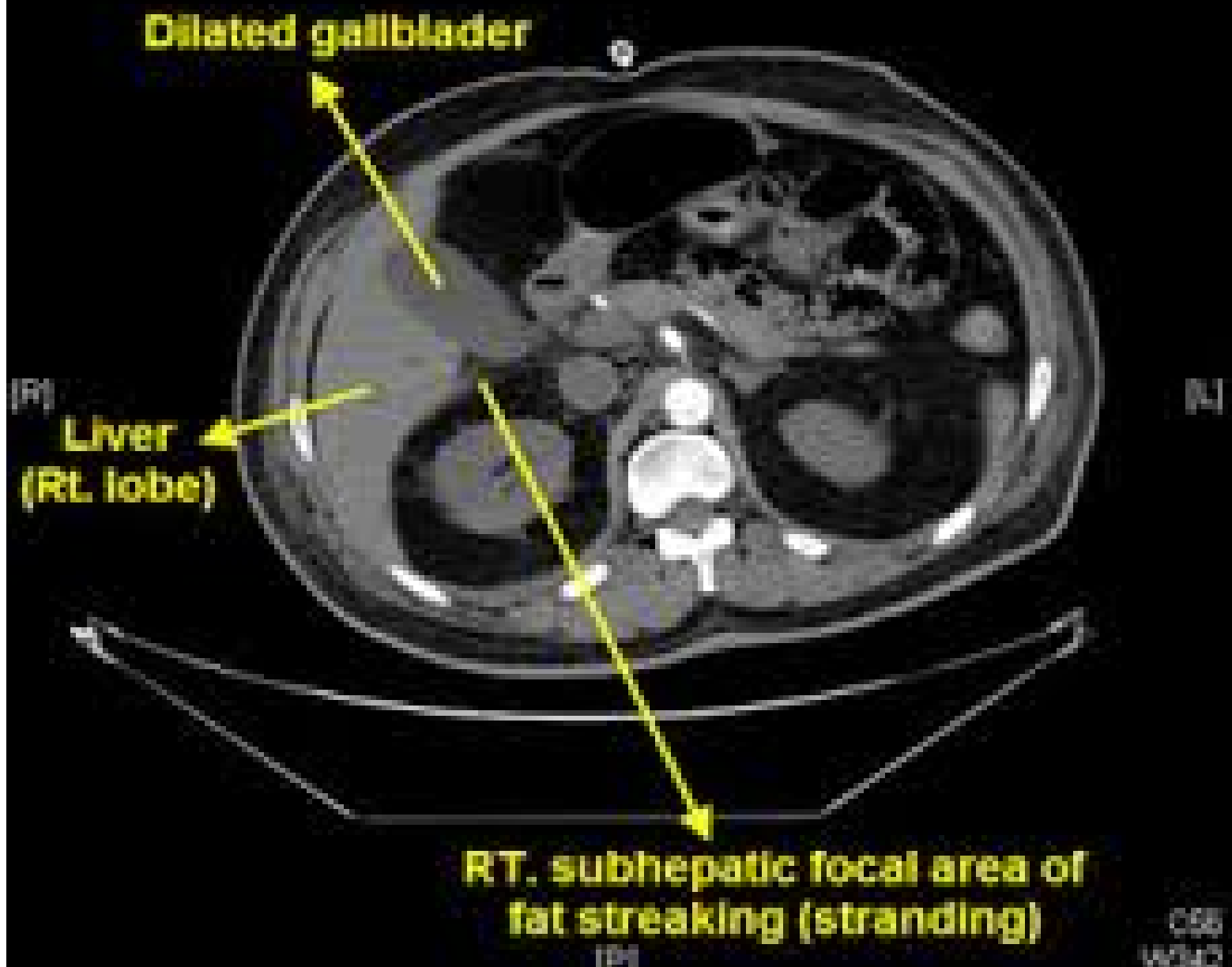






# NORMAL HIDA SCAN





# Chronic Cholecystitis

- Nonspecific
- Intermittent attacks of pain
- Mistaken for colitis/ Peptic Ulcer / Hiatus Hernia

# Emphysematous Cholecystitis

- Clostridial Cholecystitis
- Symptoms similar to acute cholecystitis
- Less chances of nausea , vomiting
- Early gangrene / perforation



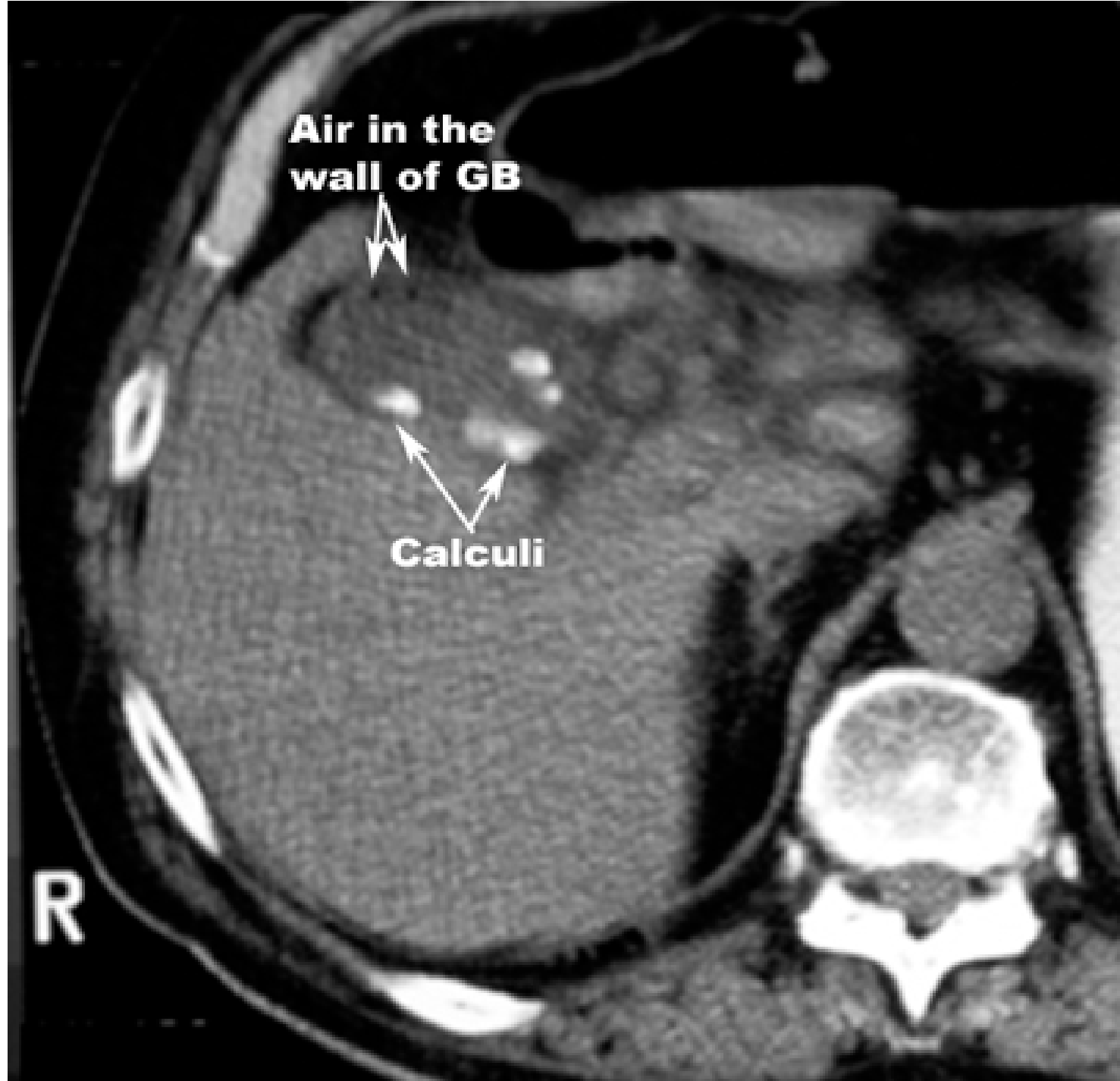


Air in the wall is bright like a stone but has no shadow posteriorly, and has ring down artifact.



- **Stage I**
- Gas is present in the gallbladder lumen. There is a dense band of hyperreflective echoes with distal reverberations when the gallbladder is full of gas or a band of reverberations in the gas-filled portion of the gallbladder with the usual signs of cholecystitis in the bile-filled portion when the gallbladder is partially full of gas.
- **Stage II**
- Gas is present in the gallbladder wall. There is an area of high reflectivity in the gallbladder wall with reverberations that may change position with patient movements or a bright hyperreflective ring emanating from the entire gallbladder circumference.
- **Stage III**
- Gas is present in the pericholecystic tissue and is seen inside the gallbladder, within its wall and outside the gallbladder in the surrounding tissues, indicating gangrene and perforation.

- **Effervescent gallbladder**
- In some cases, there may be multiple tiny echogenic foci in the gallbladder lumen, arising from the dependent part of the gallbladder and "floating" to the nondependent wall, reminiscent of bubbles rising in a glass of champagne.
  
- **Ring-down effect/comet tail**
- Curvilinear gaseous artifacts in the gallbladder, the "ring-down effect" or "comet tail," are diagnostic of emphysematous cholecystitis, but the frequency with which these are observed is not clear



# Xanthogranulomatous Cholecystitis

- Focal or diffuse destructive inflammatory process, with accumulation of lipid laden macrophages, fibrous tissue, and acute and chronic inflammatory cells
- Among patients with symptomatic gallbladder disease ranges from 0.7 percent in the United States to up to 10 percent in India and Japan
- M:F 2:1 in western studies in India 1:9
- extravasation of bile into the gallbladder wall from rupture of Rokitansky-Aschoff sinuses or by mucosal ulceration



- Acute or chronic cholecystitis
- Mass in Right Hypochondrium
- 20% Obstructive Jaundice
- *No features of Malignancy –anorexia, weight loss*
- Mirizzi / Biliary Stricture
- High rate of Perforation
- Confirmation -Histopathology

- Diffuse gallbladder wall thickening: sensitivity 89 percent, specificity 65 percent
- Continuous mucosal line: sensitivity 67 percent, specificity 82 percent
- Intramural hypoattenuated nodules: sensitivity 61 percent, specificity 71 percent
- Absence of macroscopic hepatic invasion: sensitivity 72 percent, specificity 77 percent
- Absence of intrahepatic bile duct dilatation: sensitivity 67 percent, specificity 71 percent





# Asymptomatic Gallstones (AsGS) – To Treat or Not to?

Anu Behari and V. K. Kapoor

- Indian J Surg. 2012 February; 74(1): 4–12.
- Published online 2011 December 3. doi: [10.1007/s12262-011-0376-5](https://doi.org/10.1007/s12262-011-0376-5)

# Natural History of Gall Stones

Series	Patients	Years of follow-up	Biliary pain (%)	Biliary complications (%)	Annual risk of biliary pain
Gracie and Ransohoff [6]	123	15	18	2	2
McSherry et al. [9]	135	4	10	0	–
Friedman et al. [7]		20	18		2.5–5
Cucchiaro et al. [14]	125	5	25	3	–
Wada and Imamura [12]	680	13	20	–	–
Haldestam et al. [13]	123	7	6	4.8	–

Advantages	Disadvantages
Expectant Management	
Avoids overtreatment	Potential for development of a serious complication while waiting
Avoids anaesthesia/surgery-related morbidity/mortality	Need to operate on an older patient (with co-morbidities) or in an emergent setting may increase morbidity and mortality
Avoids unnecessary cost/workload for the health care system	
Routine Cholecystectomy	
Definitive cure	Overtreatment of a large number of patients
	Potential morbidity/mortality of anaesthesia/surgery
Generally a safe procedure with low morbidity and mortality, especially when performed in absence of complications	Increased cost/workload for the health care system
Selective Cholecystectomy	
Theoretically ideal – only subgroups at higher risk for development of symptoms or complications would be treated	Practically difficult – clear identification of high-risk subgroups still far from easy

- Category 1: Patients with gallstones but no symptoms
- Category 2: Patients with typical biliary symptoms and gallstones
- Category 3: Patients with gallstones but atypical symptoms
- Category 4: Patients with typical biliary symptoms but without gallstones on ultrasound

- increased risk of conversion from asymptomatic to symptomatic disease.
- increased risk of developing complications.
- increased suspicion/risk of developing GBC.

- Age <55 years
  - Smoking
  - Female sex
  - Greater body weight
  - Presence of three or more GS
  - Floating stones
- 
- Life expectancy >20 years
  - Calculi >2 cm in diameter
  - Calculi <3 mm and patent cystic duct
  - Non-functioning GB
  - Perioperative detection of incidental stones
- 
- Polyps >1 cm, calcified
  - Gb (13–22%)
  - Large stones >3 cm (10 times risk)
  - GB packed with stones
  - Ethnic groups in high-incidence GBC areas

# Hemolytic anemias

- Curro G, Meo A, Ippolito D, Pusiol A, Cuninotta A. Asymptomatic cholelithiasis in children with sickle cell disease. Early or delayed cholecystectomy? *Ann Surg.* 2007;245:126–129. doi: 10.1097/01.sla.0000242716.66878.23.

# Transplant recipient

- Sianesi M, Capocasale E, Ferreri G, Mazzoni MP, Dalla Valle R, Busi N. The role of cholecystectomy in renal transplantation. *Transplant Proc.* 2005;37(5):2129–2130. doi: 10.1016/j.transproceed.2005.03.028.
- Jackson T, Treleaven D, Arlen D, D'Sa A, Lambert K, Birch DW. Management of asymptomatic cholelithiasis for patients awaiting renal transplantation. *Surg Endosc.* 2005;19:510–513. doi: 10.1007/s00464-004-8817-x.



# Perioperative Discovery

- Thompson JS, Philben VJ, Hodgson PE. Operative management of incidental cholelithiasis. *Am J Surg*. 1989;124:821–824.
- Juhasz ES, Wolff BG, Meagher AP, Kluiber RM, Weaver AL, Heerden JA. Incidental cholecystectomy during colorectal surgery. *Ann Surg*. 1994;219:467–472. doi: 10.1097/00000658-199405000-00004.
- Bragg LE, Thompson JS. Concomitant cholecystectomy for asymptomatic cholelithiasis. *Arch Surg*. 1989;124:460–462. doi: 10.1001/archsurg.1989.01410040070016.
- Wolf BG. Current status of incidental surgery. *Dis Colon Rectum*. 1995;38:435–441. doi: 10.1007/BF02054237.

# Diabetes Mellitus

- Babineau TJ, Booth A., Jr General surgery consideration in the diabetic patient. *Infect Dis Clin North Am.* 1995;9:183–193.
- Aucott JN, Cooper GS, Bloom AD, Aron DC. Management of gallstones in diabetic patients. *Arch Intern Med* 1993;153:1053–1058. doi: 10.1001/archinte.1993.00410090019003.
- Landau O, Deutsch AA, Kott I , Rivlin E, Reiss R. The risk of cholecystectomy for acute cholecystitis in diabetic patients. *Hepatogastroenterology.* 1992;39:437–438

# Cirrhosis Of Liver

- Orozco H, Takahashi T, Mercado MA, Prado E, Borunda D. Long-term evolution of asymptomatic cholelithiasis diagnosed during abdominal operations for variceal bleeding in patients with cirrhosis. *Am J Surg.* 1994;168(3):232–234. doi: 10.1016/S0002-9610(05)80192-8

- [Trop Gastroenterol.](#) 2011 Jul-Sep;32(3):196-203.
- **Asymptomatic gall stones--revisited.**
- [Supe A.](#)
  
- Patients should be counseled about the natural history and available management options, their advantages and disadvantages, and should be part of the decision making process. Prophylactic routine cholecystectomy for asymptomatic stones is not recommended. However, laparoscopic cholecystectomy should be performed selectively or concomitantly in a specific subgroup of patients.

- A recent Cochrane Database Systematic Review (2007) observed the following:
  - There are no randomized trials comparing cholecystectomy versus no cholecystectomy in patients with silent (asymptomatic) GS.
  - Further evaluation of observational studies, which measures outcomes such as obstructive jaundice, GS-associated pancreatitis and/or GBC for sufficient duration of follow-up, is necessary before randomized trials are designed in order to evaluate whether cholecystectomy or no cholecystectomy is better for asymptomatic GS.
- ‘The availability of laparoscopic cholecystectomy should not expand the indications for gall bladder removal’.
- NI H Consensus Conference Report 1993 [8]

**Table 1: Probabilities used in preparing Markov Model**

<b>Variable</b>	<b>Value</b>
Number of patients developing mild symptoms (from asymptomatic gall stones) every year	2% <sup>1</sup>
Number of patients developing moderate and severe symptoms (from asymptomatic gall stones) every year	1.3% and 0.2%
Operative Mortality	5/10000
Complications	1/1000
Persistent symptoms after surgery	15%
Other causes of mortality	6.4/1000 per year

(India Population Project)

# FATE OF ASYMPTOMATIC GALLSTONES: THE NATURAL HISTORY OF LEAVING GALLSTONES BEHIND DURING BARIATRIC PROCEDURES

Nestor Pulido, Vicky Ka Ming Li, Pedro Martinez-Duarte, Patricio Fajnwaks, Samuel Szomstein and Raul Rosenthal  
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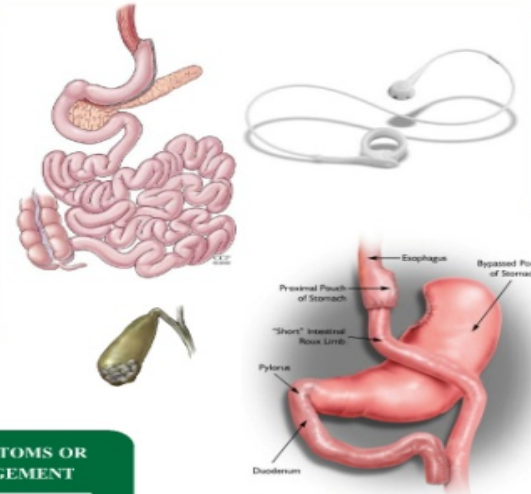


**Background:** The incidence of gallstones in the morbidly obese is up to 45%.<sup>11</sup> Our data showed that the risk of developing de novo symptomatic gallstones is 7.8% in a mean time of 10.2 months after bariatric procedures, 1.9% presented as complications on initial presentation. In normal population, 1-4% of patients with asymptomatic gallstones develop symptoms or complications within one year of diagnosis<sup>12</sup>. However, after bariatric procedures, the risk of patients with asymptomatic gallstones to become symptomatic remains unknown. Knowing the potential difficulties and related complications of concomitant cholecystectomy at bariatric procedure, expectant management has been suggested for those with asymptomatic gallstones<sup>13,14</sup>.

**Objectives:** To elucidate the risk and risk factors of developing subsequent symptoms or complications in those with expectant management for asymptomatic gallstones during bariatric procedures

## Method:

- A retrospective review of a prospectively collected database for 796 consecutive patients who underwent laparoscopic Roux-en-Y gastric bypass, adjustable gastric banding or sleeve gastrectomy between January 2004 and June 2006.
- Patients who were diagnosed with gallstones or sludge on routine preoperative transabdominal ultrasound and who did not have concomitant cholecystectomy were included in the study.
- Statistical evaluation was performed using a univariate and multivariate analysis. Risk factors including age, gender, preoperative BMI, BMI >45, Diabetes Mellitus, hyperlipidaemia, and weight loss > 25% of their original weight were analyzed for their association with development of symptoms or complications.



## PATIENT DEMOGRAPHICS

Mean age (range)	45 (23-71)
Male/female, %	25.4/74.6
Diabetes Mellitus, n (%)	14 (27.5)
Hyperlipidaemia, n (%)	13 (25.5)
Mean preoperative BMI (range)	47.8 (37-68)
BMI > 45, n (%)	28 (55)
Postoperative weight loss > 25%, n(%)	39 (76.5)

## PATIENT INCLUSION

Total no. of patients	796
No. of patients with previous cholecystectomy (%)	135 (17)
No. of patient with gallstones identified on preoperative transabdominal ultrasound (%)	65 (8.2)
No. of patient with concomitant cholecystectomy	14
No. of patient included for analysis	51

## UNIVARIATE VARIATE ANALYSIS OF RISK FACTORS FOR SYMPTOMS OR COMPLICATIONS OF GALLSTONES AFTER EXPECTANT MANAGEMENT

Factors	* Group 1 vs Group 2	p- value
Mean age, years	41.2 vs 41.6	0.349
Female gender, n (%)	6 (100) vs 32 (71.1)	0.318
Preoperative BMI, Kg/m <sup>2</sup>	47.3 vs 48.1	0.807
BMI >45, n (%)	3 (50) vs 25 (55.6)	1.000
Diabetes Mellitus, n (%)	0 (0) vs 14 (31.1)	0.170
Hyperlipidaemia, n(%)	2 (33.3) vs 11(24.4)	0.638
Weight loss > 24 %	5 (83.3) vs 33 (73.3)	1.000

## Reference

- Orna HE. Pitfalls in the diagnosis of gallbladder disease in clinically severe obesity. *Obes Surg* 1998; 8:444-51.
- Gurusamy, KS; Samraj, K. Cholecystectomy versus no cholecystectomy in patients with silent gallstones *The Cochrane Library*. Copyright 2007, Volume (2), 2007.
- Portenier DD, Grant JP, Blackwood HS, Pryor A, McMahon RL, Demaria E. Expectant management of the asymptomatic gallbladder at Roux-en-Y gastric bypass. *Surg Obes Relat Dis* 2007 Apr 17.
- Swartz DE and Felix EL. Elective cholecystectomy after Roux-en-Y gastric bypass: why should asymptomatic gallstones be treated differently in morbidly obese patients? *Surg Obes Relat Dis* 2005;1(6):555-60.

## OUTCOMES AFTER EXPECTANT MANAGEMENT OF GALLSTONES

Symptoms/Complications of gallstones	n (%)
Biliary colic	4 (7.8)
Acute cholecystitis	1 (2)
Obstructive jaundice	1 (2)
Total	6 (11.8)

\* Symptoms/complications developed over a mean period of 15.5 (2 -31) months. Three (5.9%) patients had symptoms within 1 year after surgery. All underwent subsequent cholecystectomy

## Conclusion:

Expectant management of asymptomatic gallstones at the time of bariatric surgery will leave a significant proportion of patients requiring subsequent cholecystectomy. No risk factor was identified to predict subsequent biliary symptoms or complications. Risk of proceeding to concomitant cholecystectomy should be balanced carefully with the harm of leaving it before a decision is made.

# Open above Lap

- Suspected or confirmed gallbladder cancer
- [Type II mirizzi syndrome](#) (cholecystobiliary fistula)
- Gallstone ileus
- Severe cardiopulmonary disease.
- Xanthogranulomatous Cholecystitis
- Pregnant Patients
- Cirrhosis with Bleeding disorder



# Medical(± ESWL) above Surgical

- Patients with complications or with frequent and severe attacks of biliary colic are not suitable candidates.
- Patients with mildly symptomatic gallstones are the best candidates.
- Patients with increased surgical risks or those who do not want to undergo surgery due to personal preferences should be considered for medical dissolution therapy.
- Asymptomatic patients are currently not treated.
- For medical therapy to be effective, the gallbladder needs to fill and function. Finally, only cholesterol stones can be dissolved by bile acids, and any significant calcification of the stones will render them nondissolvable.

- optimal lean patient with small (< 5 mm) radiolucent stones (approximately 3% of all symptomatic patients) will have a 90% likelihood of complete dissolution within 6 months.
- In contrast, patients with 5- to 10-mm radiolucent stones (approximately 12%) will have only a 50% chance of successful dissolution within 9 months.
- Pregnancy, rapid weight loss, and convalescence from abdominal surgery are recognized transient risk factors.
- Several reports have suggested that bile-acid treatment may improve dyspepsia as well as biliary colic in patients with gallstones, even when there is no evidence of stone dissolution

## Table 3. Oral Bile Acid Dissolution Agents

Agent	Dosage	Therapy Duration	Adverse Effects (>10%)
Ursodiol (Actigall)	8-10 mg/kg/day (in 2-3 divided doses); prophylaxis: 300 mg bid	Symptom relief occurs in 3-6 wk; results may take 6-24 mo	Headache, dizziness, diarrhea, constipation, dyspepsia, nausea, vomiting, back pain, upper respiratory tract infection
Chenodiol (Chenodal)	Initial: 250 mg bid for 2 wk; increase by 250 mg/day per wk until 13-16 mg/kg/day (in 2 divided doses) or maximum tolerated dose reached	Discontinue therapy if no dissolution has occurred in 18 mo; use beyond 24 mo not established	Hypercholesterolemia, dose-dependent diarrhea, leukopenia, increased serum aminotransferase

Source: References 5, 14.

- A mixture of cyclic monoterpenes in olive oil –menthol
- fatty-acid-bile-acid conjugates (FABACs) have been shown to be cholesterol solubilizers and to prevent cholesterol crystallization in vitro as well as in vivo
- Statins
- Petroni ML, Jazrawi RP, Pazzi P, et al. Ursodeoxycholic acid alone or with chenodeoxycholic acid for dissolution of cholesterol gallstones: a randomized multicentre trial. *Aliment Pharmacol Therapeut.* 2001;15:123-128.

# PCC

- Cholecystostomy is used as a temporizing measure in critically ill patients with acute cholecystitis who cannot undergo cholecystectomy. After the symptoms resolve and the patient's condition is stabilized, definite treatment is still gallbladder removal.
- In acalculous cholecystitis, percutaneous drainage may be the only treatment required.

- Gold Standard – Laparoscopic Cholecystectomy

Thank you