

## Biliary tract infections and liver abscesses

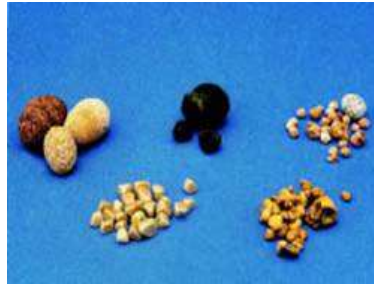
By  
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 Prof. of Hepatic biliary-pancreatic  
 Surgery and Laparo-endoscopy



- Cholecystitis
- Cholangitis
- Liver abscesses
  - pyogenic liver abscess
  - amoebic liver abscess

### Acute cholecystitis

- Acute inflammation of the gall bladder wall
- Female > male
- Other risk factors increasing age, obesity, pregnancy, certain ethnic groups etc.



### Pathogenesis

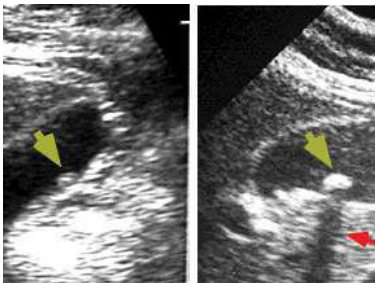
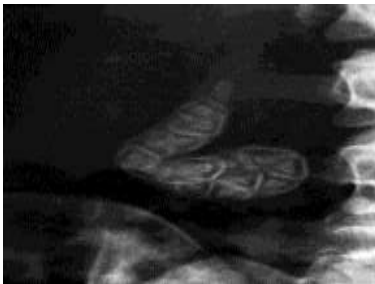
Impact of gallstones in the cystic duct > 90% cases  
 ↓  
 Obstruction and dilatation of gall bladder  
 ↓  
 Vascular congestion and oedema  
 ↓  
 Necrosis of wall, bacterial proliferation  
 ↓  
 Complications: sepsis, gangrene, perforation, liver abscess, cholangitis, bacteraemia etc.

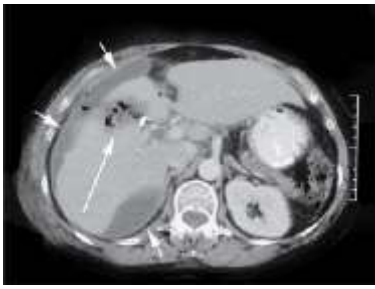
### Clinical features

- Epigastric or RUQ pain
- Nausea, vomiting
- Fever, anorexia, chills, sweats
- Moderate pyrexia
- Local peritonitis, RUQ tenderness (Murphy's sign)
- Palpable gall bladder (30-40%)
- Jaundice unusual

### Diagnosis

- Moderate leucocytosis
- LFT: ↑ bilirubin (50%), transaminases (40%) & alk phos (25%)
- Culture of aspirate/biopsy specimens
  - not usually available
  - enteric organisms (Gram-neg bacilli, anaerobes, enterococci etc)
- Imaging studies: ultrasound, CT scan





### Cholelithiasis in Gallbladder Cancer: Coincidence, Cofactor, or Cause!

EPHO 26 (2016), 514-520

- While gallstones are associated with concerns of the gallbladder, the actual nature of their relationship needs to be clarified. This would aid the recommendations on the need for prophylactic cholecystectomy.
- The evidence at the current time indicates that gallstones are a cofactor in the causation of gallbladder cancer. Absolute proof of their role as a cause for gallbladder cancer is lacking. The recommendation for prophylactic cholecystectomy in countries reporting a high incidence of gallbladder cancer and associated gallstones, needs to be tailored to the epidemiological profile of the place.

### Cholelithiasis in Gallbladder Cancer: Coincidence, Cofactor, or Cause!

EPHO 26 (2016), 514-520

In the case of gallstones, despite the lack of evidence to support a recommendation, large stones (>3 cm) or a gallbladder packed with stones (high stone:GB volume ratio) could serve as potential indications for prophylactic cholecystectomy.

### Differential diagnosis of cholecystitis

Common

- Appendicitis
- Perforated peptic ulcer
- Acute pancreatitis

Uncommon

- Acute pyelonephritis
- Myocardial infarction
- Pneumonia – right lower lobe

Ultrasound scan aids diagnosis

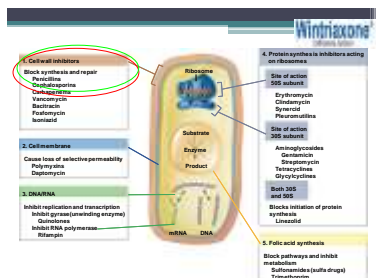
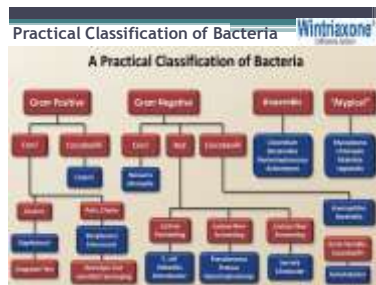
Uncertain diagnosis – do CT scan

### Complications

- Bacteremia - derelops in 50% cases
- Gasymen/empyema
- Perforation (10-15%)
- Obstructive jaundice, cholangitis, pancreatitis
- Liver abscess
- Peritonitis
- Bacteremia

**Treatment**

- Medical for IV fluids, IV antibiotics, analgesia, anti-emetics, bowel rest (NPO)
- Surgical for urinary cholecystectomy (laparoscopic cholecystectomy)



**Cephalosporin Agents by Generation**

Generation	First Of Appearance	Agents Trade Name & Manufacturer
1 <sup>st</sup> Generation	FD	Cephalexin (Keflex) GSK Cefadroxil (Duricef) GSK Cephadrine (Vedol) GSK
2 <sup>nd</sup> Generation	FD	Cefuroxime (Zinnat) Janssen Cefprozil (Ceftin) Janssen Cefaclor (Ceclor) Janssen
3 <sup>rd</sup> Generation	FD	Ceftriaxone (Rocephin) Hoffmann-La Roche Cefepime (Maxipime) Hospira Cefotaxime (Claforan) Hospira Cefixime (Suprax) Abbott
4 <sup>th</sup> Generation	Rocephin	Cefepime (Maxipime) Hospira
5 <sup>th</sup> Generation	Rocephin	Ceftazidime (Tazid) Hospira

**Cephalosporin Coverage**

Generation	Primary Coverage	Secondary Coverage
1 <sup>st</sup>	Gram positives (except MRSA)	None
2 <sup>nd</sup>	Aerobes	Gram positives (except MRSA) Gram negatives (except Pseudomonas)
3 <sup>rd</sup>	Gram negatives (very effective brain Penetration)	Gram positives (except MRSA)
4 <sup>th</sup>	Pseudomonas	Gram positives (except MRSA) Gram negatives
5 <sup>th</sup>	MRSA	Other gram positives Gram negatives

**3rd generation Cephalosporins**

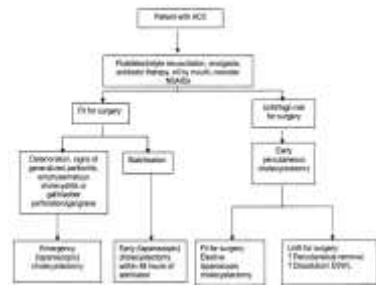
- 3rd generation Cephalosporin provide new therapeutic approaches to difficult infectious disease problems.
- Currently available 3rd generation Cephalosporins differ in their anti-microbial spectrum, pharmacokinetic profile, side effects and costs.
- 3rd generation Cephalosporins are 10-100 fold more active against most aerobic Gram negative organisms than 1st generation.

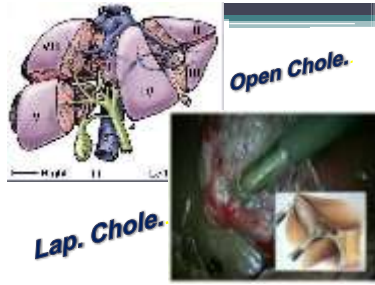
**Important definitions**

- C<sub>max</sub> : Peak plasma concentration of the drug.
- T<sub>max</sub>: The time after administration of a drug to reach peak plasma concentration.
- Bioavailability : The percentage of an administered dose which enters the systemic circulation as indicated by the area under the plasma concentration vs time curve.
- Plasma elimination half-life (t<sub>1/2</sub>) : Is the amount of time required for the plasma concentration of an antibiotic to decrease by half.

**Wintrioxone Pharmacokinetic Properties**

- IV ceftriaxone 0.5, 1 or 2g produces mean peak plasma concentrations of C<sub>max</sub> of 32, 151 and 297 mg/L
- IM ceftriaxone 0.5 or 1g achieves C<sub>max</sub> concentrations of 38 and 76 mg/L respectively within 2 to 3 hours
- 24 hours after IV ceftriaxone 2g, mean plasma concentrations range from 12 to 20 mg/L
- The peak to trough IV and IM ratio for ceftriaxone 2g results in a 34:1 increase in mean C<sub>max</sub> and a 2.5 fold increase in the level of free drug available to the drug
- Ceftriaxone binds reversibly to albumin and the level of free drug decreases with increasing plasma protein concentrations (30% at 100 mg/L to 58% at 600 mg/L)
- Ceftriaxone distributes widely in the body fluid and tissue. The volume of distribution for plasma is relatively low and increases with dose from 53 to 155 L
- Ceftriaxone preferentially binds to albumin and mean concentrations of 125 and 100 mg/L are achieved at 1 and 3 hours respectively after intravenous administration of 2g dose.





### Anatomy and congenital malformation

The classic description of the extra hepatic biliary tree and its arteries applies only in about one third of patients.

Molmenti EP, Pinto PA, Klein J, et al: Normal and variant arterial supply of the liver and gallbladder. *Pediatr Transplant* 7:80, 2003. [PubMed: 12581334]  
 Chan TH, Shyu JF, Chen CH, et al: Variations of the cystic artery in Chinese adults. *Surg Laparosc Endosc Percutan Tech* 10:154, 2000. [PubMed: 10672977]  
 (Schwartz's Principles of Surgery , Ninth edition)

Golden rules for safe cholecystectomy:

- (1)-Decide the best approach, then dissect the cholecysto-hepatic triangle for good anatomical identification especially of cystic artery and duct.
- (2)-Good dissection and identification of the gall bladder cystic junction prior ligation and cutting to avoid CBD injury or ligation.
- (3)-Avoid clipping, ligation, or even clamping of any unidentified structure as it always ends in biliary injury.
- (4)-Avoid unnecessary use of diathermy in general, and in the vicinity of CBD in particular.
- (5)-Ligation of the cystic artery nearby the gall bladder neck to avoid hepatic artery injury.

- (6)-Do not misplace in myth, if in doubt consult, shift lap to open procedure, or use cholangiogram if possible.
- (7)-Any subtle duct structure connected to the bladder bed should be identified then assessed by cholangiogram, if necessary it is ligated to avoid postoperative leak, if major duct, it must be repaired or transposed.
- (8)-Any bile leak in the field should be taken seriously and searched for its source and managed accordingly without reluctance with cholangiogram visualization.
- (9)-Do not skeletonize the CBD aiming for good identification as it is almost always in its ischemic structure.
- (10)-Do not attempt to close the patient till you are extremely sure about all details, and consult if in doubt as most of biliary injuries discovered intraoperatively and managed mainly cure in 80% of cases.

- (11)-If you do not have the facility to manage complications, drain the subhepatic area and refer the patient immediately to the competent center with full details report about the procedure without hesitancy.
- (12)-CBD exploration should be attempted if in doubt about obstruction, or the cause of biliary dilatation.
- (13)-Cholecystectomy is done in supra duodenal CBD anterior wall with clear cut edge, without laceration of the tissue or massive diathermy use.
- (14)-Do not use flexible testing of CBD clearance using metal dilator or scopes.
- (15)-T-shaped tube application is the standard after CBD exploration, with upper end apart from the carm, and lower end above the sphincter of Oddi.

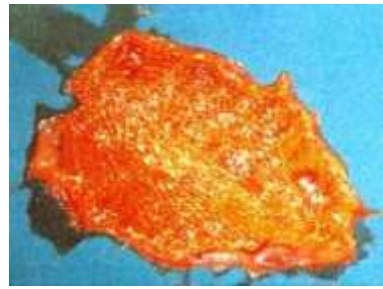
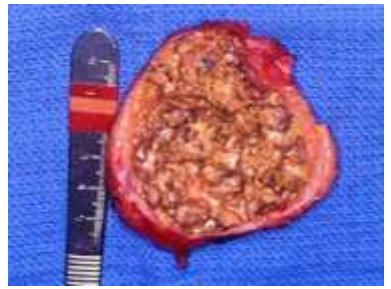
- (16)-Cholecystectomy in case of large necrotic stones with above and below T-tube external limb extension for better healing and less complications safer extraction.
- (17)-Do not hesitate to open the duodenum if stone is impacted in the papilla with operative papillotomy.
- (18)-Lower down CBD obstruction is not managed symptomatically with side to side cholecysto-oduodenostomy without good intraoperative diagnosis of its nature and shape, extend the pylorus if needed then managed accordingly.
- (19)-Cholecysto-oduodenostomy with J-tube or Y-loop end to side or side to side is the operation of choice in securing the biliary tract to the gut with the least morbidity.
- (20)-Almost always fashion the biliary stoma as large as possible (at least 3 cm in diameter) by all possible techniques for better outcome without stricture formation later on, and split the anastomosis in smaller caliber externally, or internally by internal orifice, or T-tube.

**PROPHYLACTIC CHOLECYSTECTOMY**

- Prophylactic cholecystectomy may be considered in those patients with high rates of complications:
  - Calculated (postulated) gallbladder (high cancer risk)
  - Bile fistulas
  - Liver transplantation, stable cell disease
  - Children
  - Mutual obesity/gastronomy
  - Cholelithiasis
  - Immunosuppressed
  - Chronic hemolysis/splenoectomy
  - Large stone > 2.5cm
  - Gall polyp

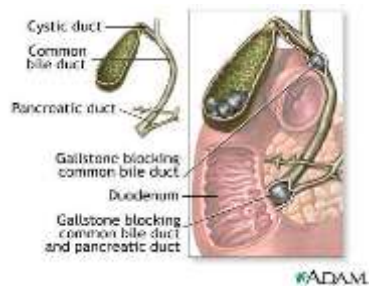
**TREATMENT SYMPTOMATIC GS**

- Elective cholecystectomy is the preferred treatment of patients with symptomatic GS
  - Biliary colic: Cholecystitis, Cholelithiasis, Cholangitis, GB perforation
- Overall mortality for cholecystectomy 0.5%
  - Significantly lower for elective operations
  - Higher in emergencies
  - 2-3x higher for CBD exploration



**Cholangitis**

- Inflammation involving the hepatic and common bile ducts
- Pathogenesis similar to that of cholecystitis
- Obstruction of common bile duct → oedema, congestion, necrosis of walls → bacterial proliferation within biliary tree
- Causes of obstruction
  - gallstones
  - biliary tract surgery, tumour, parasitic infection, calcification etc.



**Etiology**

- Obstruction of the common bile duct due to
  - gallstones
  - benign strictures
  - malignant strictures
  - sclerosing cholangitis
  - parasites

**Clinical features**

- High fever
- RLQ pain
- Jaundice (usually prominent)
- Charcot triad: present in 85% cases
- Chills, rigors
- RLQ tenderness, pale stools
- Sepsis, septic shock

**History of Cholangitis**

- 1877 – Dr. Jean-Martin Charcot recognized triad of symptoms
- 1958 – Dr. Benedict Reynolds recognized a more severe form



**Charcot's Triad**

- Jaundice, fever, and RUQ pain

**Reynold's Pentad**

- Abdominal tenderness, mental status, and hypotension

**Risk factors**

- Age > 50 years
- Cholelithiasis/stenosis of gallstones
- Benign strictures
- Malignant strictures
- Postoperative injury of bile ducts
- History of sclerosing cholangitis

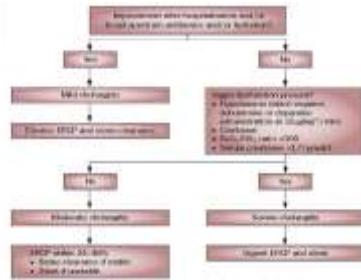
**Box 1.2 Differential diagnosis of common causes of severe acute epigastric pain**

- Biliary colic
- Peptic ulcer disease
- Oesophageal spasm
- Myocardial infarction
- Acute pancreatitis

**Tokyo guidelines**

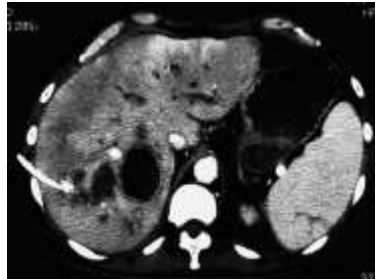
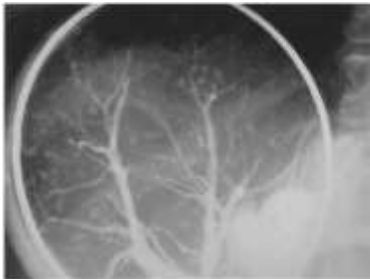
**Key laboratory studies, which should be done**

- Haematology responses, for example:**
  - Abnormal white blood cell count
  - Elevated C-reactive protein level
- Abnormal liver test results, for example:**
  - Alkaline phosphatase
  - γ-Glutamyl transaminase
  - Aspartate aminotransferase
  - Albumin and total bilirubin
- Imaging evidence of stones, for example:**
  - Stone
  - Stricture
  - Stenosis



**Complications**

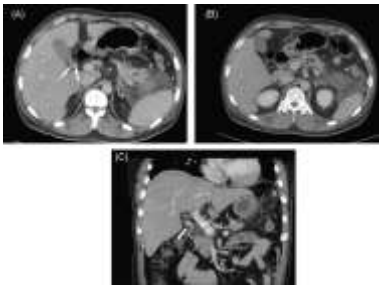
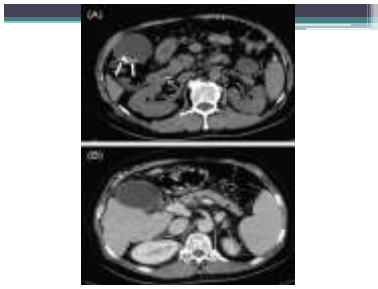
- Bacteremia about 50% cases
- Liver abscesses
- Septic shock



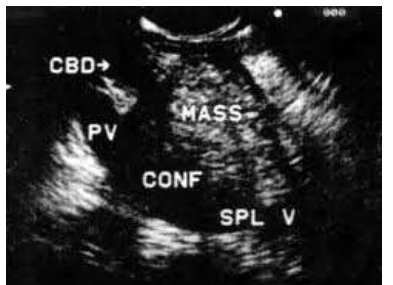
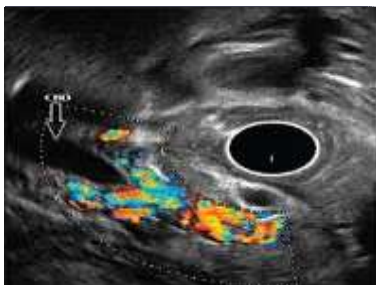
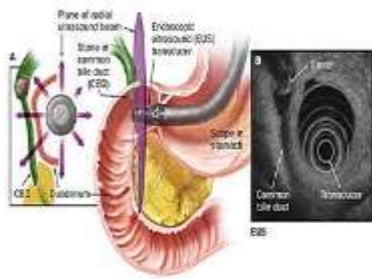
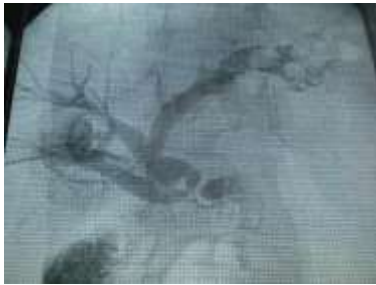
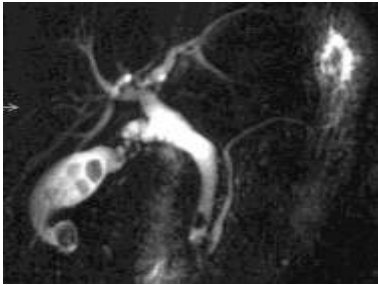


Diagnosis

- *Marked leukocytosis*
- *Marked ↑ bilirubin, alkaline phosphatase; moderate ↑ transaminases*
- *Blood cultures*
  - *enteric GAD and aspergillus frequently isolated*
- *Imaging studies*
  - *ultrasound; CT scan*
  - *ERCP, endoscopic retrograde cholangiopancreatography, PTC (percutaneous transhepatic cholangiography)*







### EUS OR MRCP FOR CHOLEDOCHOLITHIASIS ?

Parameter	EUS	MRCP
Accuracy	92%	92%
Specificity	92%	92%
Sensitivity	92%	92%
Cost	Low	High
Availability	High	Low
Time	Short	Long
Contraindications	None	Renal failure, Gadolinium allergy

Dr. Laghmani 1392



### ENDOSCOPIC ULTRASOUND: EUS

**Advantages:**

- Comparable accuracy to ERCP
- less complications
- less costly (diagnostically)

**Disadvantages:**

- no therapeutic capability

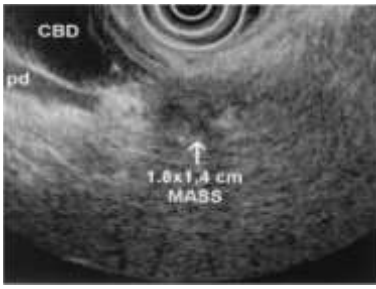
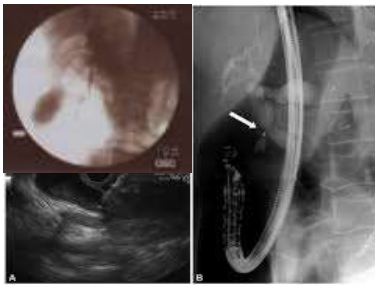
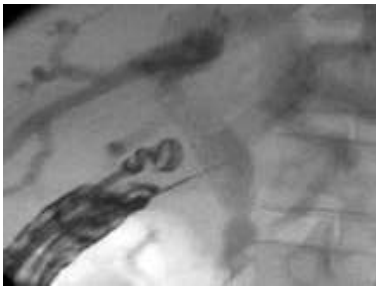
**Recommended use:**

- low pretest probability of stones or need for therapeutic intervention
- prior unsuccessful ERCP
- contraindications for ERCP

### ACCURACY OF EUS

A meta-analysis of 27 studies (with a total of 2673 patients) estimated an overall sensitivity of 94 percent (95% CI 92-96%) and specificity of 95 percent (95% CI 94-96%) of EUS compared with ERCP, intraoperative cholangiography, or surgical exploration as the reference standard.

ERCP EUS: a meta-analysis of test performance in suspected cholelithiasis





**PREDICTING CBD STONES-1**

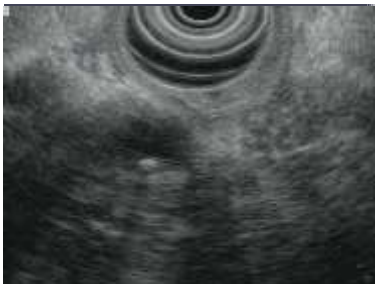
Risk	Clinical	LFT	CBD diameter	Risk CBD stones
Low	well	N	≤ 7mm	2-2%
Intermediate	Cholangitis/ pancreatitis	↑ < 2x	8-10mm	10-50%
High	Cholangitis; jaundice	↑ > 2x	>10mm	50-80%

Cotter 2002, LBD      Pritsker 2011 with Ann Askin de laing

**HIGH PROBABILITY OF CHOLEDOCHOLITHIASIS**

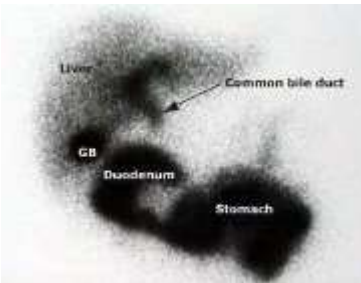
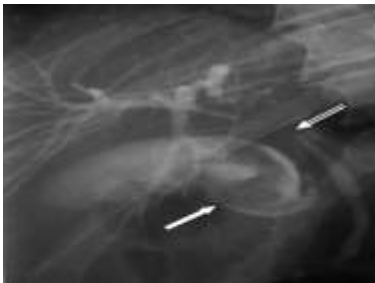
Patients were considered to have a high probability of cholelithiasis if they had:

- 1- CBD stone on US or CT or
- 2- At least **three** of the following:
  - Distal CBD on US (>7 mm)
  - Fever
  - Bilirubin > 2 mg/dL
  - Elevated alkaline phosphatase
  - Serum ALP > twice normal



ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

- Gold standard
- Cholelithiasis, unresolving cholangitis or gallstone pancreatitis
- Both diagnostic, and therapeutic potential
- Sensitivity - 95%
- Specificity - 95%



Tests

- Transabdominal ultrasound
- Endoscopic ultrasound
- CT
- Magnetic resonance cholangiopancreatography (MRCP)
- Endoscopic retrograde cholangiopancreatography (ERCP)
- Lab tests
  - abnormal LFTs, elevated CRP, WBC



**Diagnosis of acute cholangitis has traditionally been made by the Charcot triad criteria that is, clinical findings of fever, right upper quadrant tenderness and jaundice.**

- Approximately 80% of patients with acute cholangitis respond to broad-spectrum antibiotics alone while the remainder require early biliary drainage in addition to antibiotic therapy.
- Endoscopic retrograde cholangiopancreatography (ERCP) and stent placement are considerably safer than surgical biliary decompression.
- Endoscopic stenting should be performed after resolution of acute cholangitis in patients with an intact gallbladder.

Treatment

- Prompt institution of appropriate antimicrobial therapy is essential:
  - initial choice usually empirical
  - eg. 3<sup>rd</sup> gen cephalosporin/quinolones/co-amoxiclav + metronidazole.
- Biliary drainage
  - ERCP
  - Percutaneous transhepatic cholangiography (PTC)
  - EUS guided drainage
  - Open surgical drainage



**Wintrioxone Pharmacokinetic Properties**

- IV ceftriaxone 0.5, 1 or 2 g produces mean peak plasma concentrations of 10, 20 and 40 mg/L
- IM ceftriaxone 0.5 or 1 g achieves C<sub>max</sub> values of 38 and 76 mg/L, respectively, after 2 to 3 hours
- 24 hours after IV ceftriaxone 2 g, mean plasma concentrations average from 12 to 20 mg/L
- It is paired to nearly daily IV dosing of ceftriaxone 2 g results in a 34% increase in mean C<sub>max</sub> and a 60% increase in mean C<sub>min</sub> by making the accumulation of the drug
- Ceftriaxone binds to albumin and the level of binding decreases with increasing albumin concentrations. 90% at 10 mg/L, 88% at 100 mg/L
- Ceftriaxone distributes readily in the body fluids and tissues. The volume of distribution of ceftriaxone is relatively constant ranging from 23 to 25 L.
- Ceftriaxone preferentially binds to albumin and mean concentrations of 125 and 100 mg/L are achieved in 2 to 3 hours, respectively, after intravenous administration of 2 g dose.

**Cephalosporin Agents by Generation**

Generation	First Of Generation	Agents Trade Name & Manufacturer
1 <sup>st</sup> Generation	FD	Cephalexin (Duricef, GSK) Cephazolin (Cepazolin, GSK) Cephadrine (Vice, GSK)
	Parenteral	(Keflin, Lilly)
2 <sup>nd</sup> Generation	FD	Cefuroxime (Ceftin, Lilly) Cefepim (Ceftin, GSK)
	Parenteral	Cefuroximol (Moxel, Lilly)
3 <sup>rd</sup> Generation	FD	Cefixime (Spectro, Sunovion) Cefprozim (Ceftin, Pfizer) Cefprozim (Ceftin, Sunovion) Cefprozim (Ceftin, Sunovion)
	Parenteral	Ceftriaxone (Rocefin, Boehringer)
4 <sup>th</sup> Generation	Parenteral	Cefepime (Maxipime, GSK)
5 <sup>th</sup> Generation	Parenteral	Ceftazidime (Tazid, Takeda)

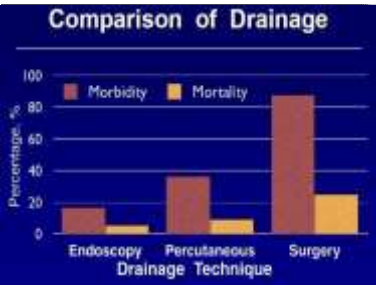
**ERCP**

➤ Treatment of choice

Dye is injected through a catheter into the pancreas to identify ducts.

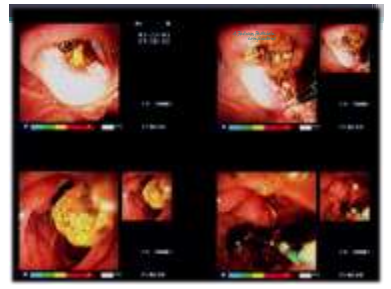
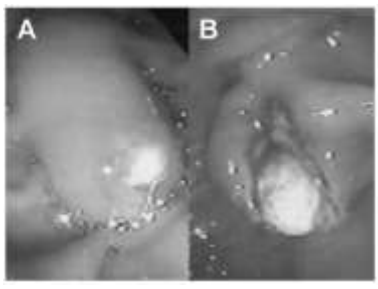
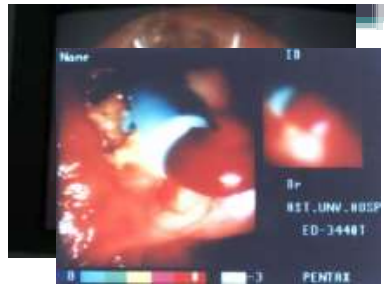
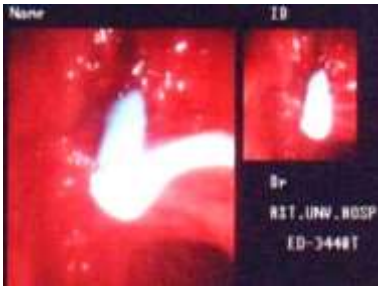
**Surgical Decompression**

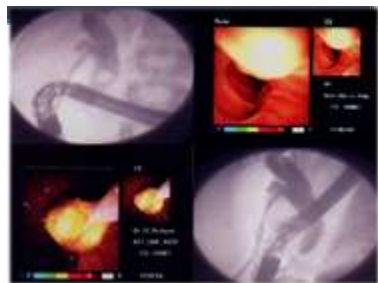
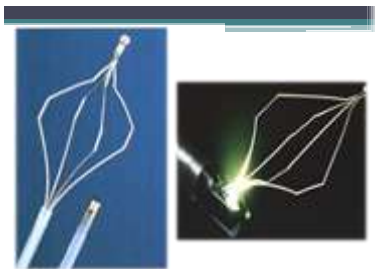
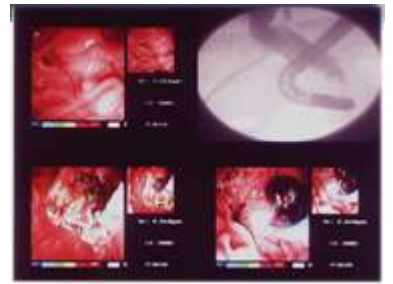
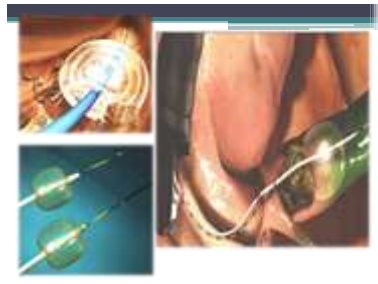
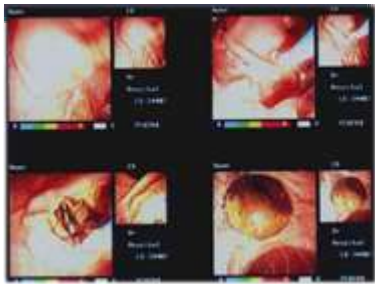
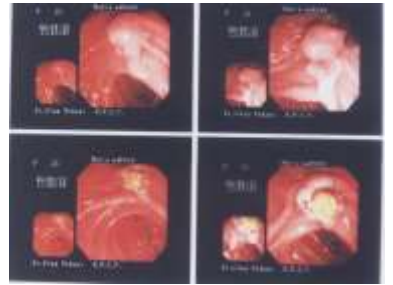
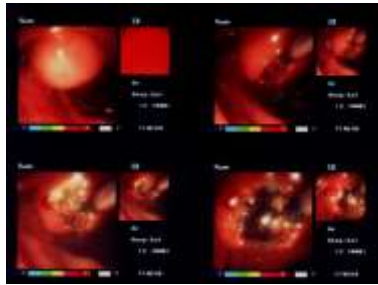
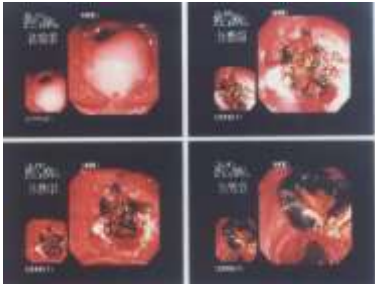
- Rarely performed
- CBD exploration for difficult stones
- Choledochotomy + T-tube for emergency
- Lower mortality rate than CCY + CBD exploration

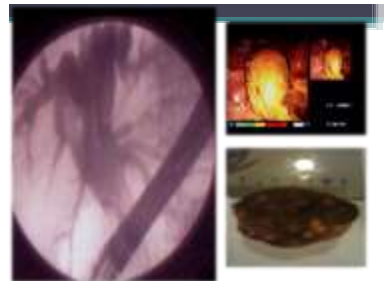
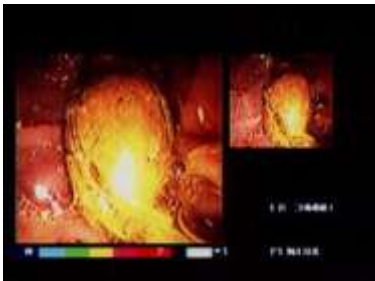
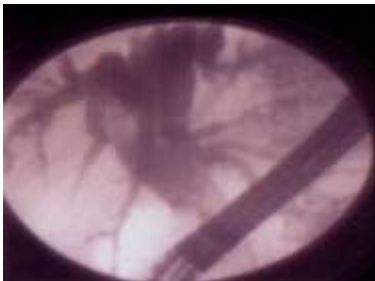
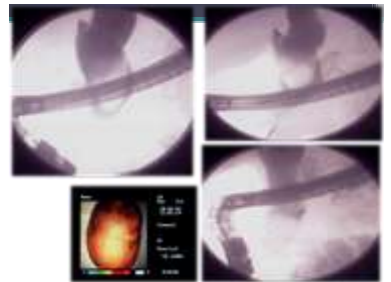
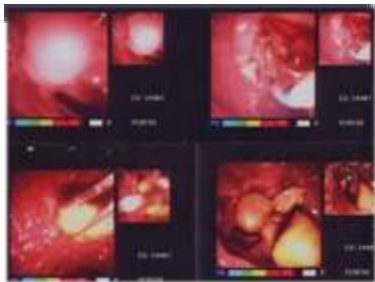
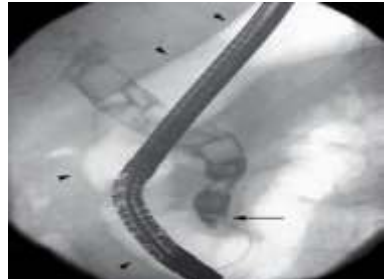
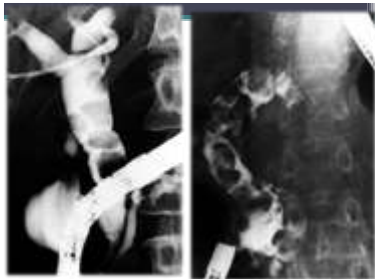
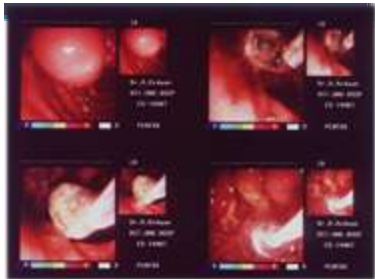


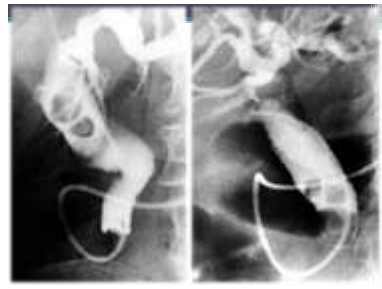
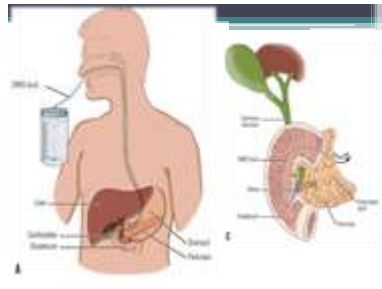
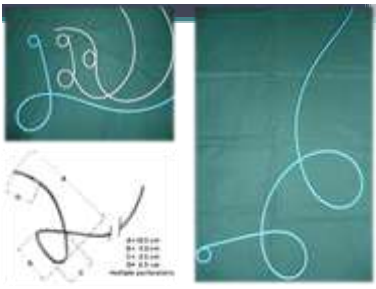
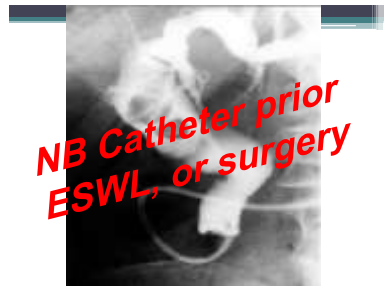
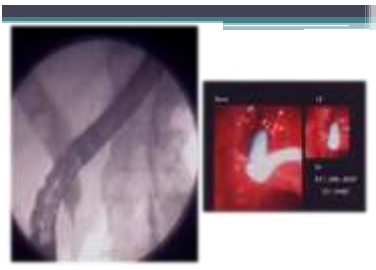
- > Result of biliary stasis & infection
- > 80% respond to conservative therapy
- > ERCP first line drainage therapy
- > CBD stones removed in 90-95% after sphincterotomy

# Biliary Blokage









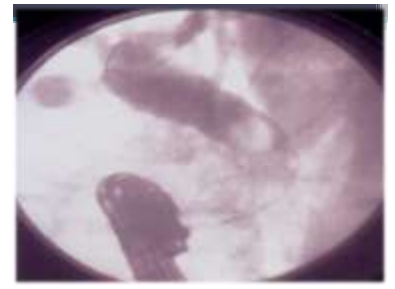
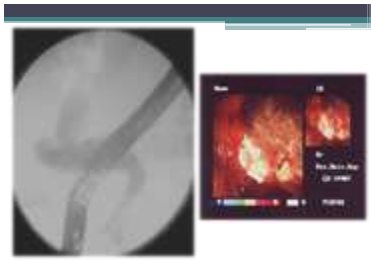
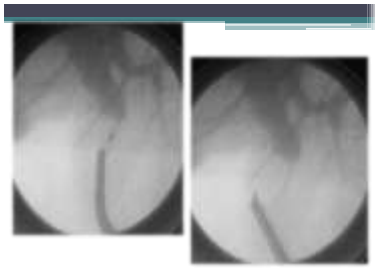
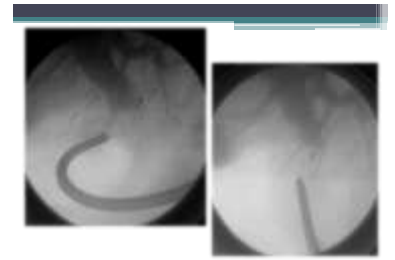
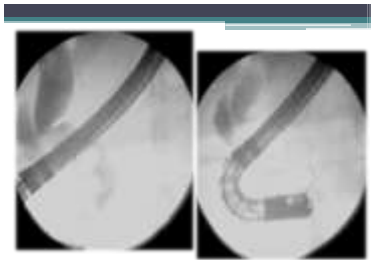
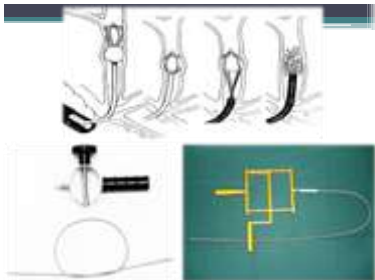
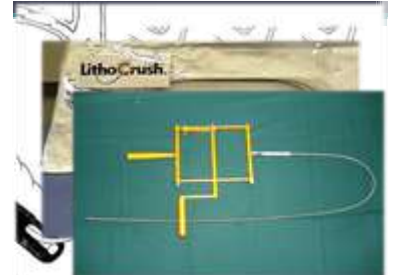
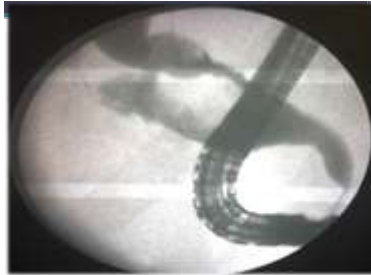
**Lithotripsy**  
 Mechanical manual lithotripsy (internal or external)  
 Electrohydraulic shockwave lithotripsy (ESWL)  
 Chemical lithotripsy (Dissolution treatment)  
 Electrohydraulic lithotripsy  
 LASER lithotripsy (Smart LASER)

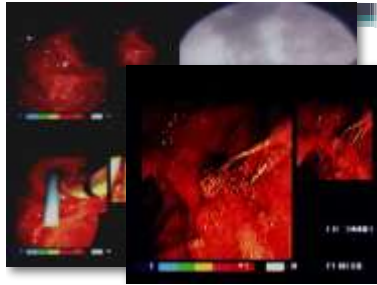
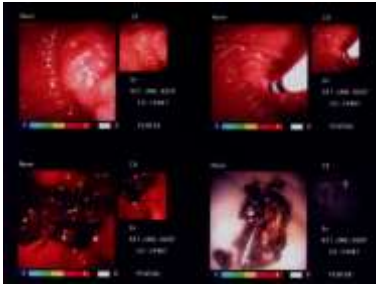




### Stone Removal and Lithotripsy

Either via the transorally inserted duodenoscope or via a percutaneous laparocholangioscope, these methods have yielded highly acclaimed success in the removal or destruction of stones in the common bile duct, without the burden of a laparotomy procedure. This endoscopic approach can also be performed intra- or post-operatively to confirm the removal of all stones, thereby preventing cases of retained stones.





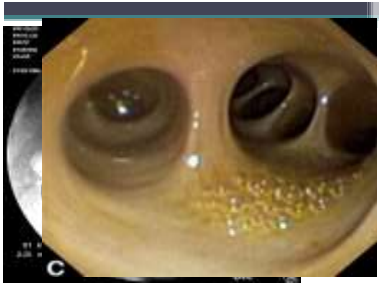
**Mother and baby  
scope technique**



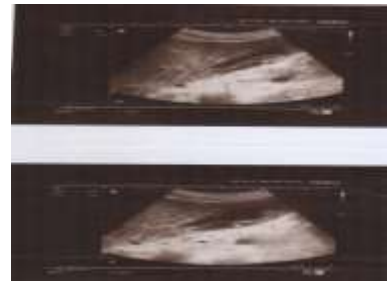
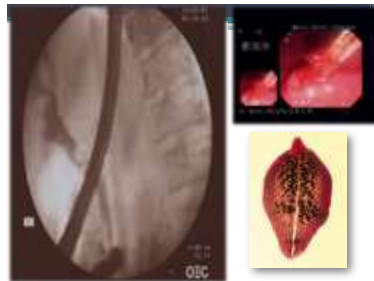
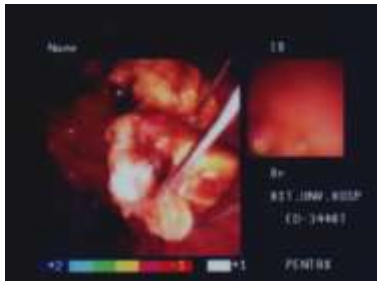
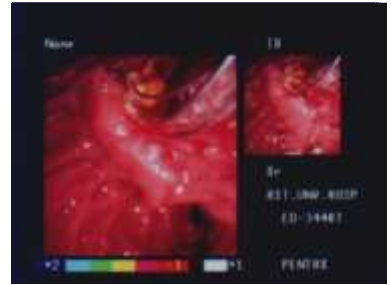
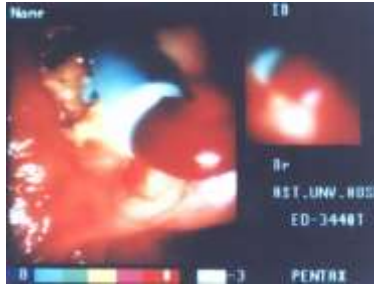
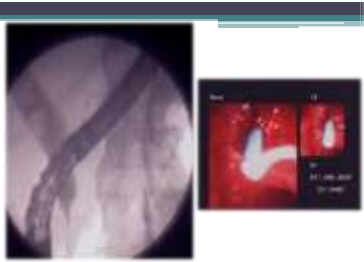
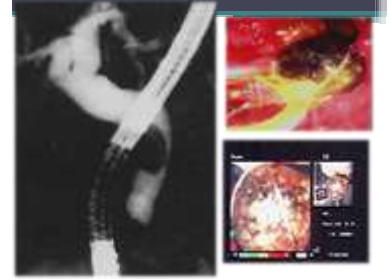
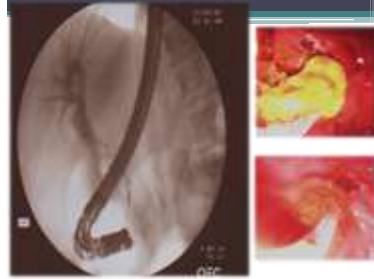
**Spyglass  
technique**

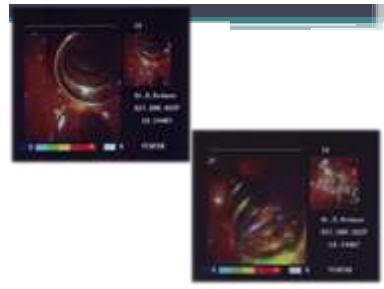
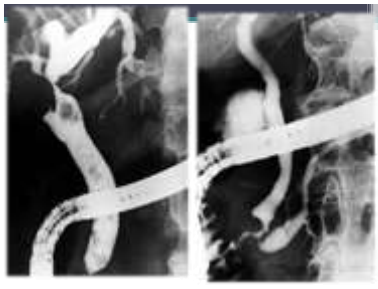
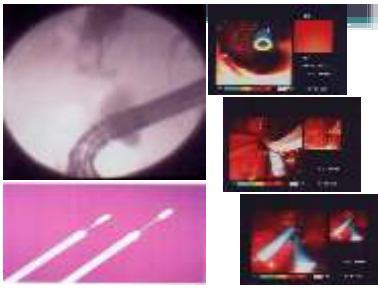
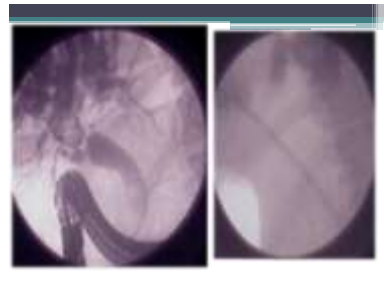
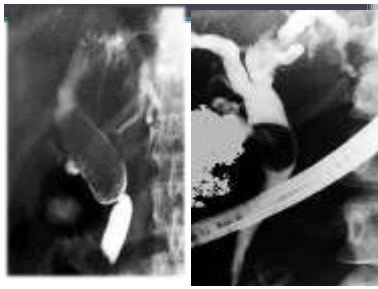
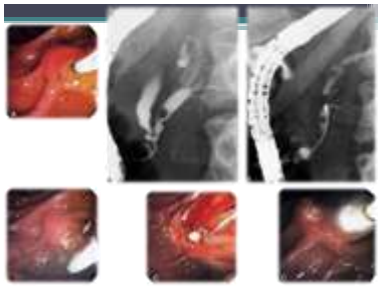
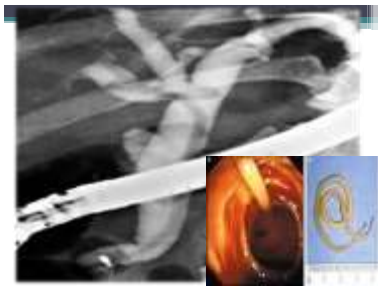


**PER ORAL  
CHOLANGIOSCOPY**

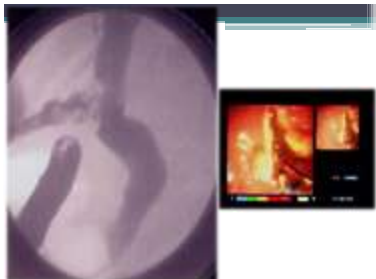
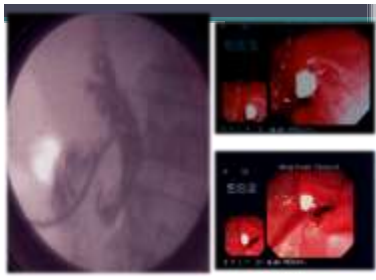
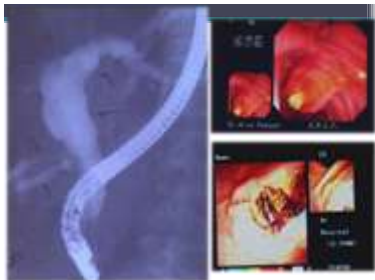


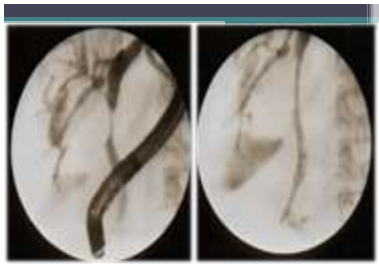
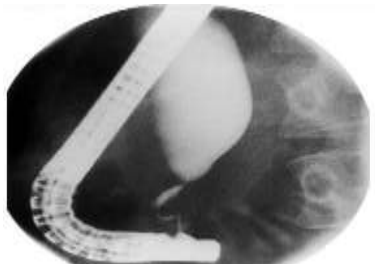
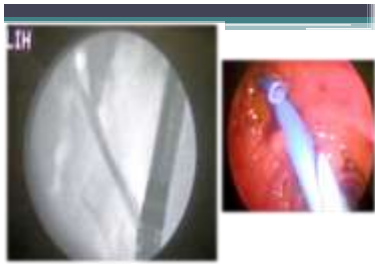
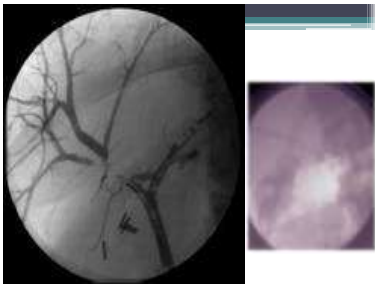
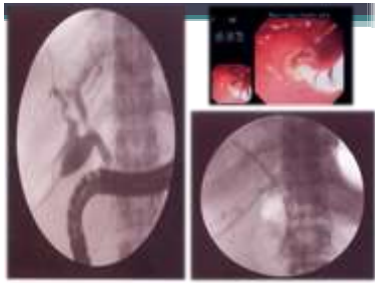
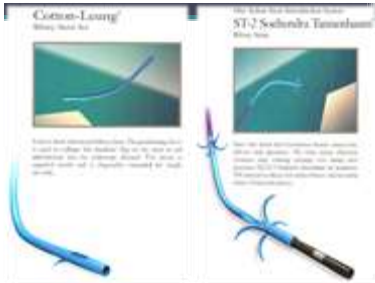
Very  
Interesting  
Rare Cases

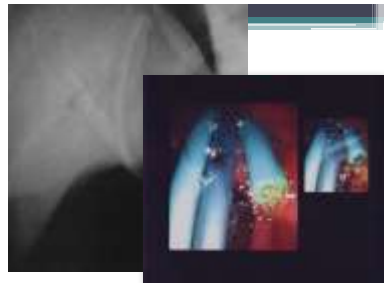
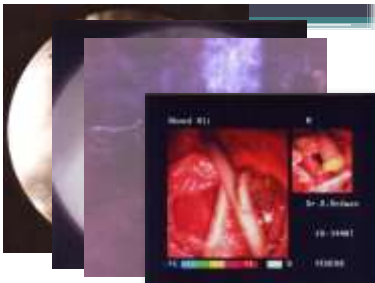
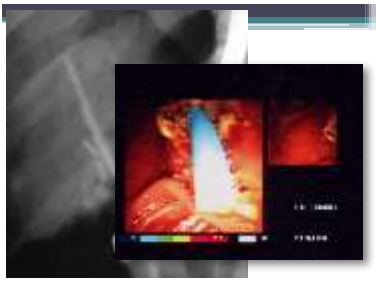
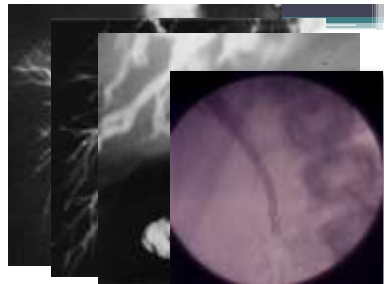
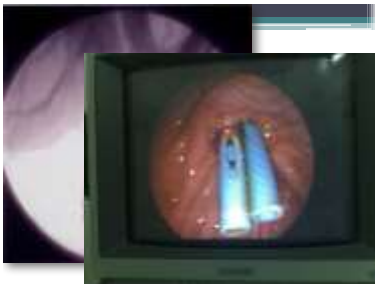
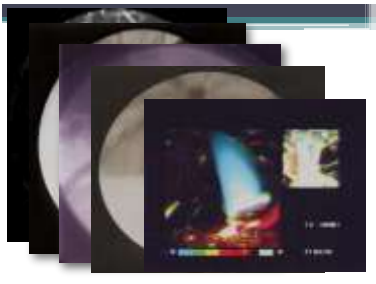
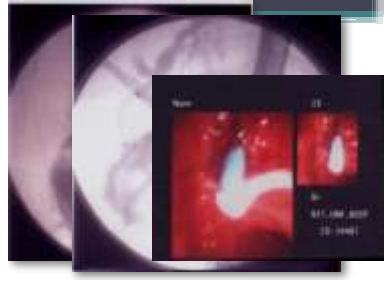
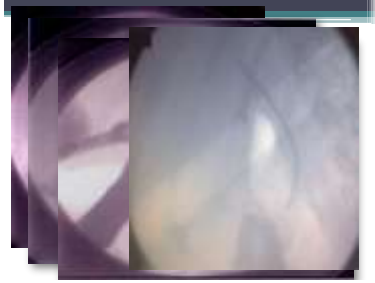


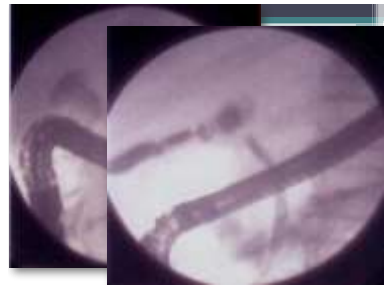
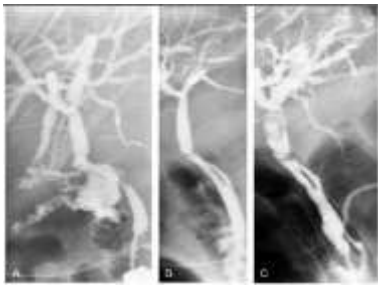
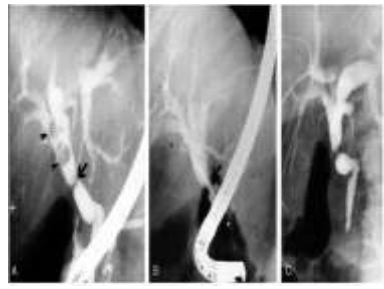
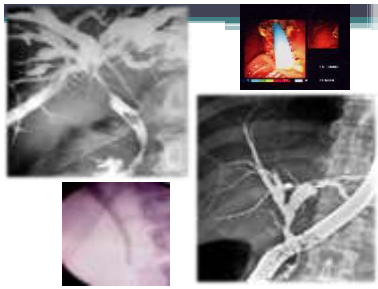
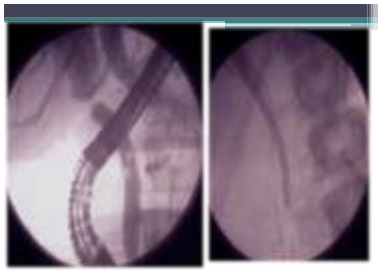
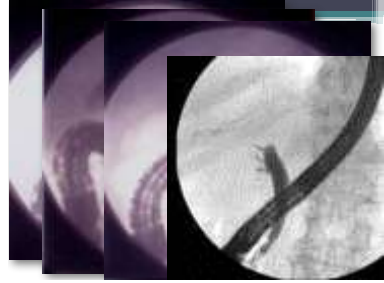
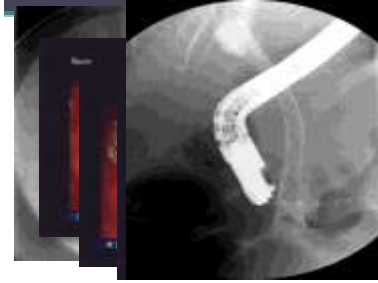
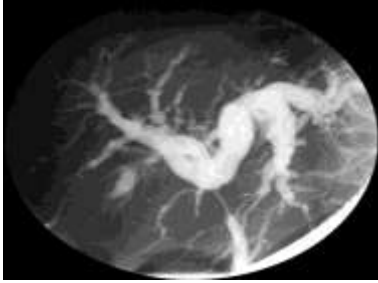


# Biliary Injury

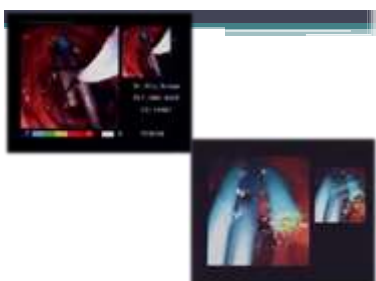
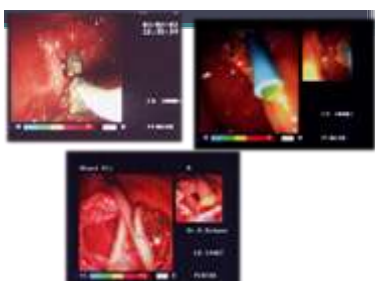
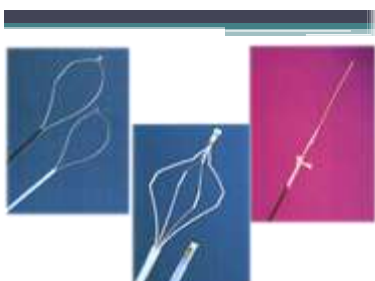
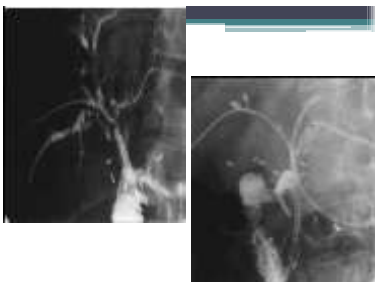
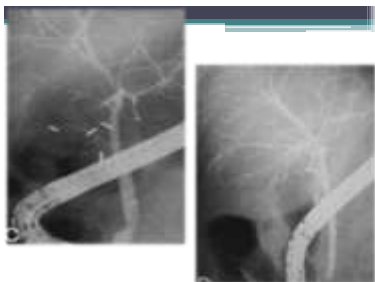
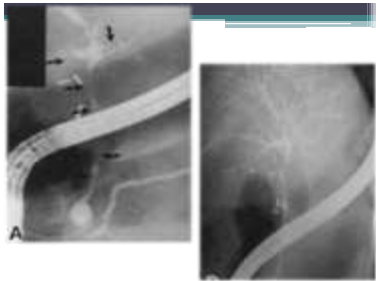
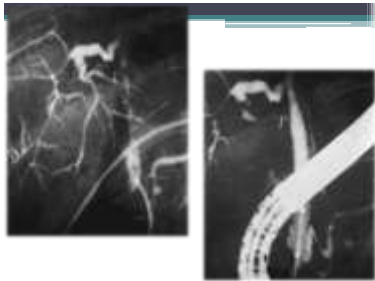
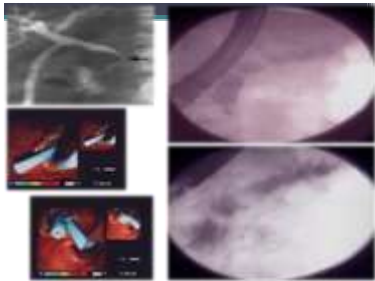


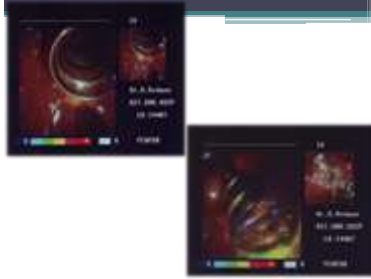
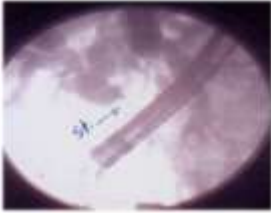




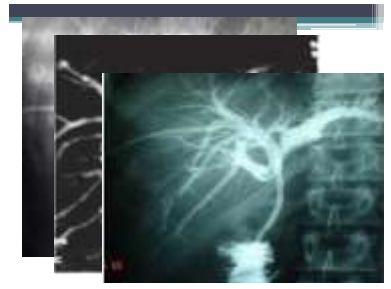
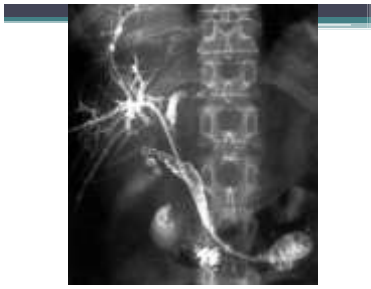
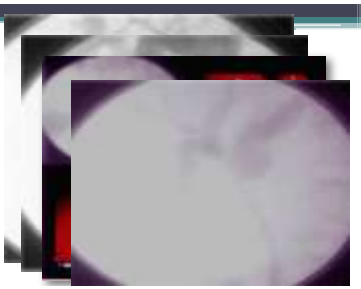


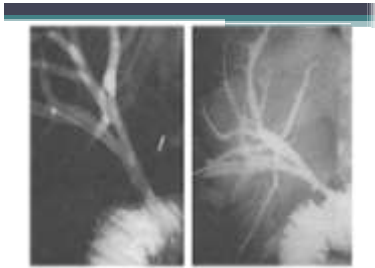




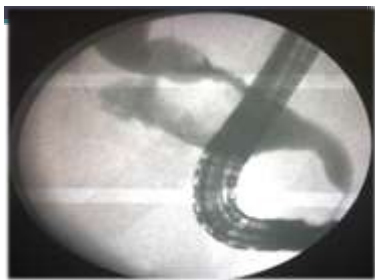


*percutaneous manipulations*



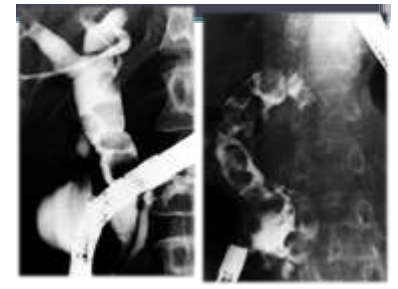
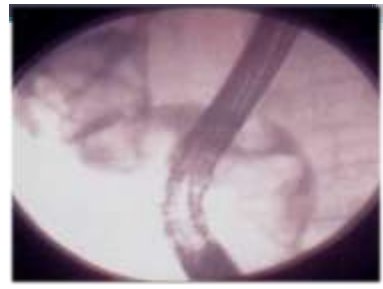
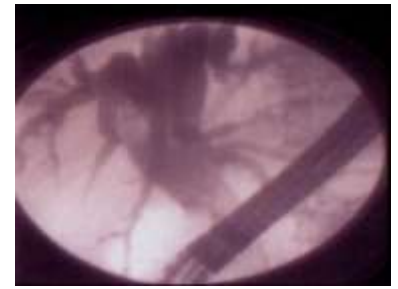
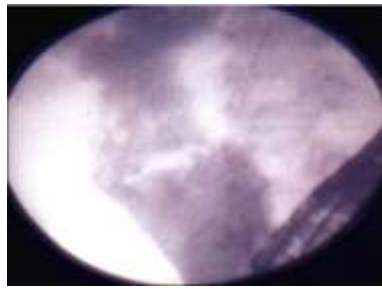
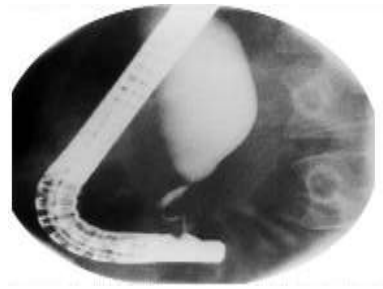


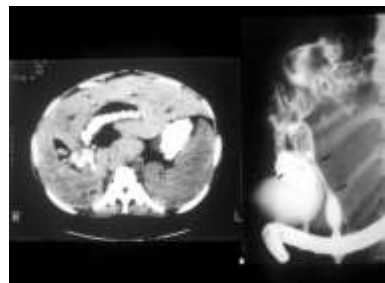
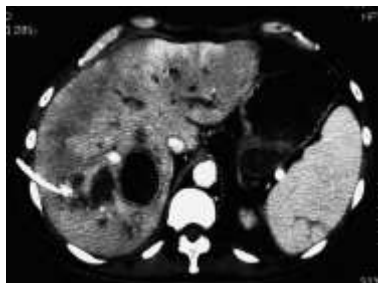
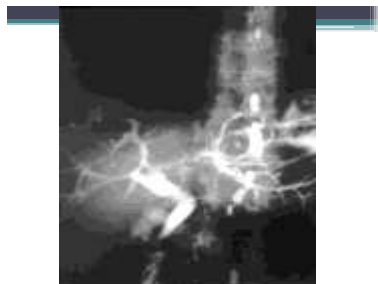
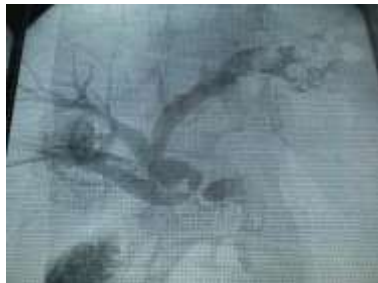
**Surgery**

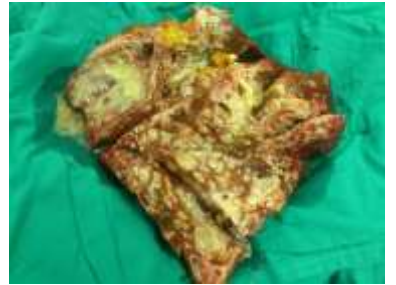
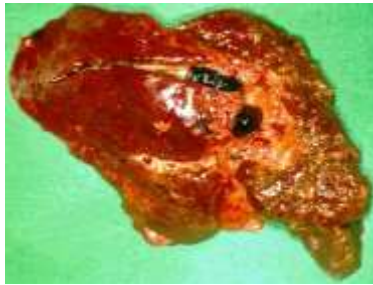


Operations in quiescent phase  
Complicated cases

- *Hepatocutaneous jejunostomy*
- *Strictureplasty*
- *Partial hepatectomy*







**Hepatico / choledocho jejunostomy**



**Hepaticocutaneous jejunostomy**

- For repeated or limited access to the biliary tract by cholecystoscopy
- Reopening of stoma for recurrence of stones and strictures

