

Bazeliuc iurii

GENERATION OF BILIRUBIN

1. □ Bilirubin has no function in the body and excreted through bile the senescent RBC's break down liberating the Hemoglobin. □ From hemoglobin, the globin chains are separated, they are hydrolysed and aminoacids are channeled in to the body - aminoacid pool. □ The Iron liberated from Heme is re utilized. (The Fe^{+2} liberated is oxidized to Fe^{+3} and taken up by transferrin.
2. □ The porphyrin Ring is broken down in Reticuloendothelial (RE) cells of liver, spleen and bone marrow to bile pigments, mainly bilirubin. □ 6 grams of HB is broken down per day from which about 250 mg of bilirubin is formed. □ From myoglobin and other heme containing proteins another 50mg of bilirubin is formed. □ Approximately 35 mg of bilirubin is formed from 1gm of HB. □ A total of 300 mg of bilirubin is formed every day of which 80% is from distruction of old RBC's, 10% from ineffective erythropoisis and rest 10% from degradation of Myoglobin and HEME containing proteins.

TRANSPORT TO LIVER

□ The liver plays the central role in the further disposal of the bilirubin. The bilirubin formed in the RE cells is insoluble in water. the lipophilic bilirubin is there fore transported in plasma, bound to Albumin. □ One molecule of Albumin can bind 2 molecules of bilirubin.100ml of plasma can transport up to 25mg of bilirubin. □Albumin binds bilirubin forms Albumin-Bilirubin complex, It reaches at the sinusoidal surface of the liver,The bilirubin is taken up , The uptake is a Carrier mediated Active process.

CONJUGATION IN LIVER

The bilirubin is conjugated with glucuronic acid, to make it water soluble.

□ The first carbon of glucuronic acid is combined with the carboxyl group of the propionic acid of bilirubin molecule. 80% of bilirubin in Di-glucuronide form, 20% are in Monoglucuronide form.

the water soluble conjugated bilirubin is excreted in to the bile by an active process and this occurs against a concentration gradient. It is rate limiting step in catabolism of HEME

The conjugated bilirubin reaches the Intestine through the bile. Intestinal bacteria Deconjugate the conjugated bilirubin to free Bilirubin.[beta glucuronidase] □ This free bilirubin (36 Hydrogen Atoms) is further reduced to a colourless tetrapyrrole Urobilinogen (UBG). □ Further reduction of the Vinyl substituent groups of UBG leads to formations of Mesobilinogen and stercobilinogen (SBG). □ The stercobilinogen [SBG] is mostly excreted through feces (250– 300mg/day)

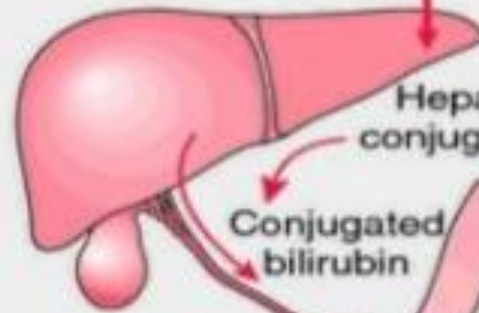
Red cell
destruction

Heme protein
catabolism

Bone marrow
erythropoiesis

Bilirubin

Circulating albumin -
bilirubin (unconjugated)



Hepatic
conjugation

Conjugated
bilirubin

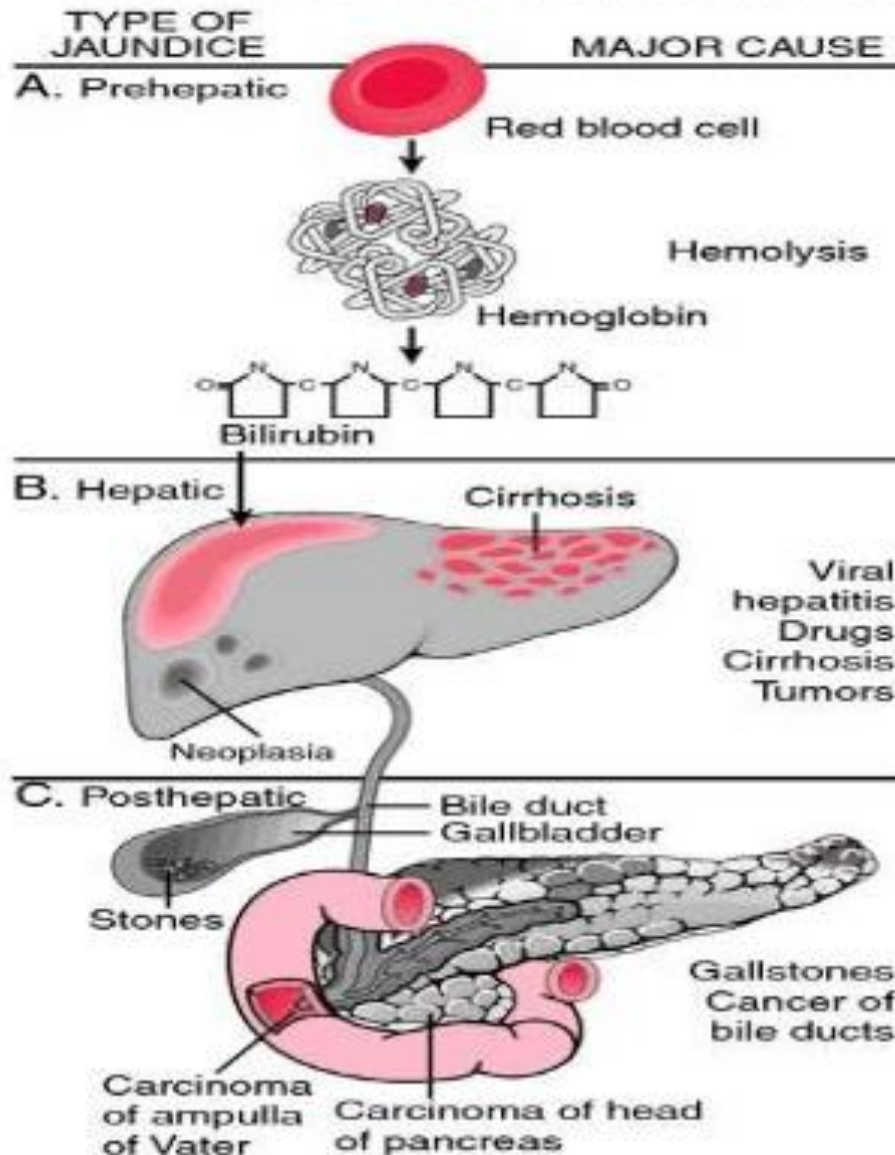
(Circulating
conjugated
bilirubin)



Bacterial deconjugation

Fecal stercobilinogen

Causes of Jaundice





Causes of Obstructive Jaundice

Obstructive jaundice is caused by conditions that block the normal flow of bile from the liver into the intestines including:

- Cholelithiasis (gallstones)
- Cholangiocarcinoma
- Carcinoma pancreas
- Biliary stricture (mainly iatrogenic)
- Cholangitis (inflammation of the common bile duct)
- Congenital structural defects
- Choledochal cysts (Cysts of the bile duct)
- Lymph node enlargement
- Pancreatitis
- Parasitic infection
- Trauma, including surgical complications

DEFINITION

- The presence of gallstones in the gallbladder is called cholelithiasis.
- The presence of gallstones in the common bile duct is called choledocholithiasis

Choledocholithiasis

- It is estimated that common bile duct stones are present in anywhere from 1-15% of patients with cholelithiasis

Effects of Gallstones In the common bile duct(CBD):

- Obstructive jaundice
 - Cholangitis
 - Pancreatitis
 - Mirizzi syndrome



GALL BLADDER STONE



CBD STONE

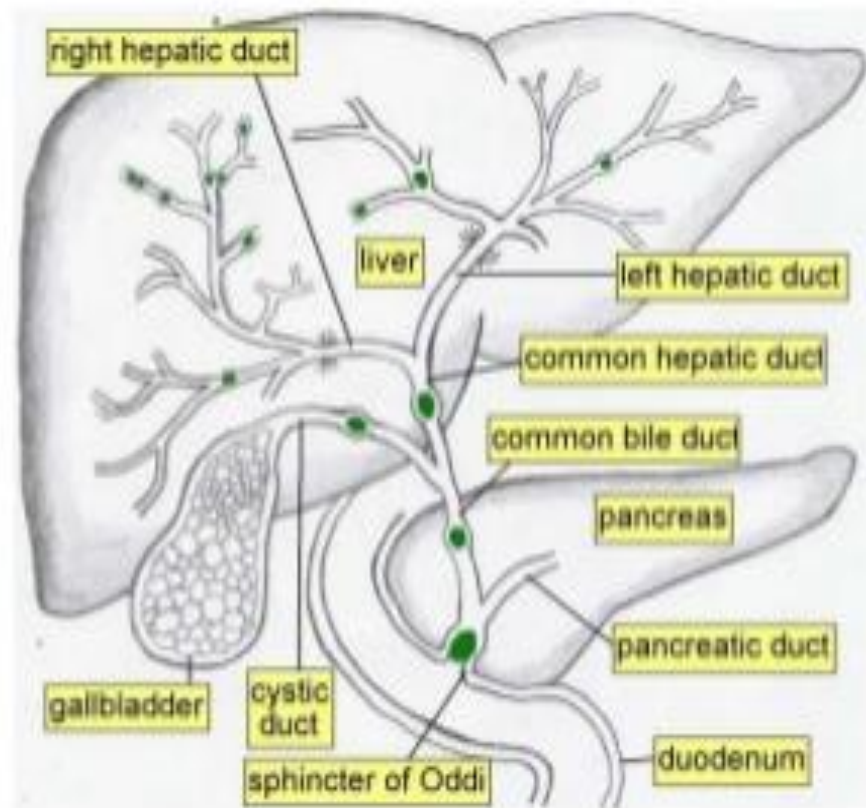
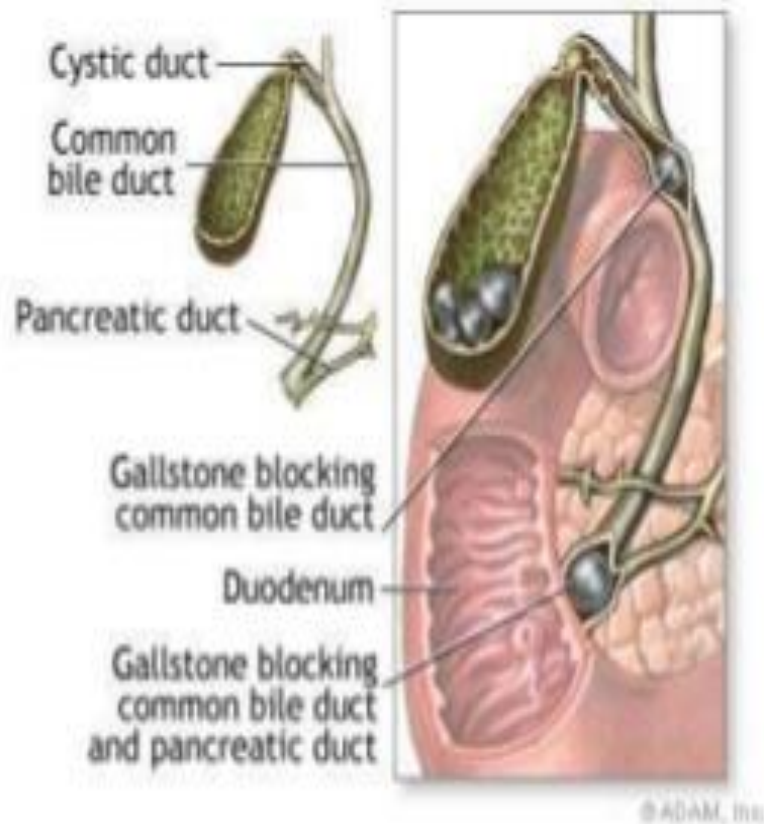
CLASSIFICATION

PRIMARY STONES

Bile stasis, bactibilia, chemical imbalances, increased bilirubin excretion, pH imbalances, and the formation of sludge are some of the factors which lead to the formation of these stones.

2. **Secondary**: They are from gallbladder (gall stones), pass through Cystic Duct to CBD. Less commonly, stones are formed in the intrahepatic biliary tree, termed primary hepatolithiasis, and may lead to choledocholithiasis.

Choledocholithiasis-Etiology



CLINICAL FEATURES

□ 50% asymptomatic

Common bile duct stones may be silent and are often discovered incidentally. • In these patients, biliary obstruction is transient, and laboratory tests may be normal.

- Biliary colic because of CBD obstruction by stone – pain in Right Hypochondrium & Epigastrium
- Jaundice due to choledocholithiasis more likely to be painful with rapid distension of biliary duct Stimulating pain fibres.
 - Clinical Manifestations of jaundice like scleral icterus, clay coloured stool, Dark coloured urine, pruritis etc..
- Jaundice most common symptom of choledocholithiasis.
- Fever with chills & rigor also common ..

CT Scan:

- It shows stones , location, ductal stricture or block , ductal dilatation, intra hepatic biliary changes & stones.
- Helical CT cholangiography is also useful but bilirubin level should be normal which is the limitation.

MRCP (Magnetic Resonance Cholangiopancreatography)

Non contrast non invasive imaging
method better than ERCP in Diagnostic
tool in biliary & pancreatic diseases

- It delineates biliary tree anatomy & pathology clearly
- but not therapeutic
- Highly(>90%) sensitive & almost 100% specific..

Endoscopic Ultrasound

☐ Procedure:

- USG probe passed through an upper GI endoscope and kept in pylorus/duodenum area

- High frequency used - 20-40Mhz

- ☐ Evaluates Pancreato-biliary system.

- ☐ Detection of microlithiasis

- ☐ Choledocholithiasis

- ☐ Evaluation of benign and malignant strictures.

- ☐ Detects regional lymphnodes

- ☐ Relationship to vascular structures.

Endoscopic Ultrasound Advantages:

- High resolution imaging.
- Less invasive.
- No exposure to radiation.
- Aspiration of a cyst or FNAC.

Disadvantages:

- Higher operator dependency.
- Cost and availability.
- Visualization is limited to 8 cm.

EUS – Stone Impacted at Ampulla



USG of choledohus – the stone inside it

УЗИ

Эхограмма холедоха, в просвете –
единичный конкремент



ERCP More of a therapeutic than diagnostic technique.

ERCP – Diagnostic

- Gold standard of imaging for biliary tree.
- Detects stones or malignant strictures
- Identifies the cause and level of obstruction

Normal ERCP

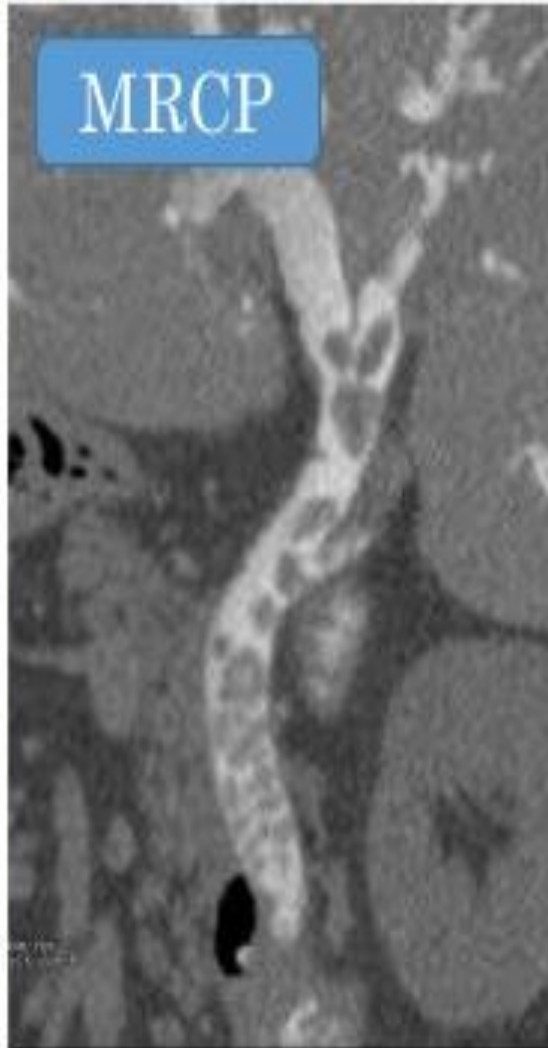


Investigations-Imaging

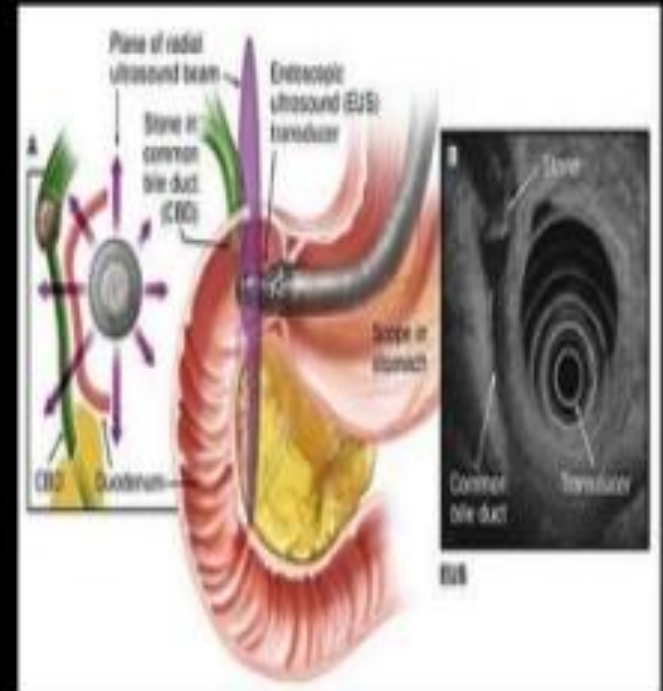
ERCP



MRCP



Endoscopic Ultrasound



Percutaneous Transhepatic Cholangiography (PTC)

- More of a palliative technique.
- Bile ducts are cannulated directly. •

Demonstrates areas of stricture/obstruction.

- Effective in pts with a dilated biliary ductal system
- Indications:

- When ERCP fails or is not possible. •

Stenting for biliary drainage.

- Prior to biliary drainage procedure.

Contraindications:

- bleeding tendency,
- Unfit for surgery,
 - Hydatid Cysts,
 - Ascites,
- CLD (chronic liver disease)

differential diagnoses of choledocholithiasis:

Bile duct cancer

- Klatskin tumor
- Bile duct stricture
- Choledochal cyst
- Peptic ulcer disease
- Acute cholecystitis
- Sphincter of Oddi dysfunction
- Functional gallbladder disorder

Choledocholithiasis and its treatment can lead to several complications, such as:

- Post-ERCP Pancreatitis
- Sepsis
- Cholangitis
- Retained and impacted stones
- Gallstone pancreatitis
- Respiratory insufficiency
- Biliary duct injury
- Renal failure
- Liver failure and cirrhosis
- Hepatic vascular injury

CHOLEDOCHOLITHIASIS treatment

ERCP sphincterotomy with a balloon sweep and extraction of the stone followed by Laparoscopic cholecystectomy in the same admission.

Various applications:

- Endoscopic sphincterotomy/papillotomy
- Removal of stones
- Insertion of stents
- Dilation of strictures
- Extraction of worms

Contra-indications of ERCP

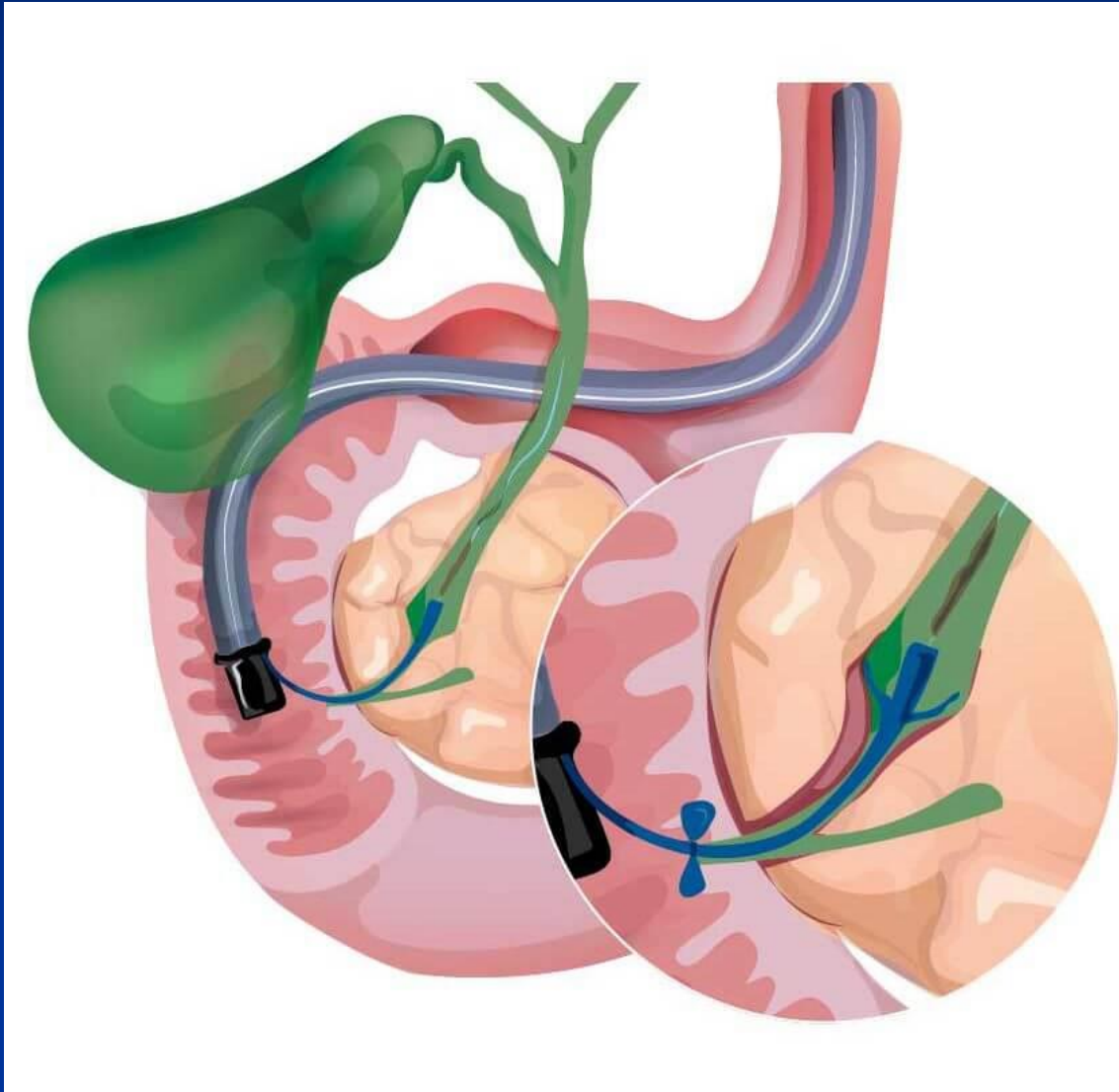
- Acute Pancreatitis
 - Pancreatic Pseudocyst
- Previous Pancreato-duodenectomy
 - Coagulation disorders
 - Recent Myocardial Infarction
 - H/o contrast dye anaphylaxis
 - Not fit for surgery

ERCP

If stones are present in the common bile duct, an endoscopic sphincterotomy must be performed to remove them BEFORE a cholecystectomy is done.

- A number of various instruments are inserted through the endoscope in order to "cut" or stretch the sphincter.
- Once this is done, additional instruments are passed that enable the removal of stones and the stretching of narrowed regions of the ducts.

ERCP



Желчный пузырь с камнем

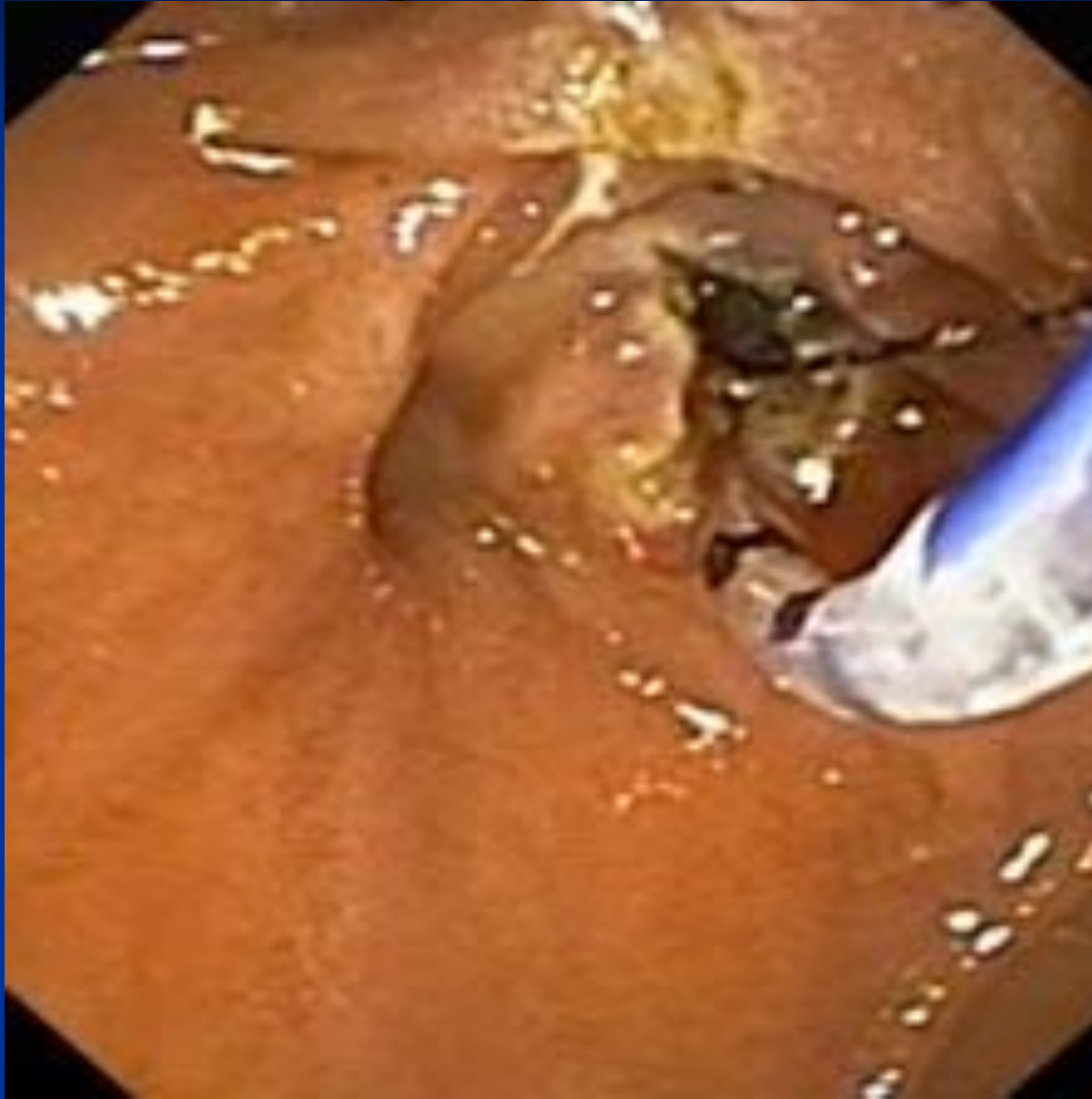


Общий желчный проток

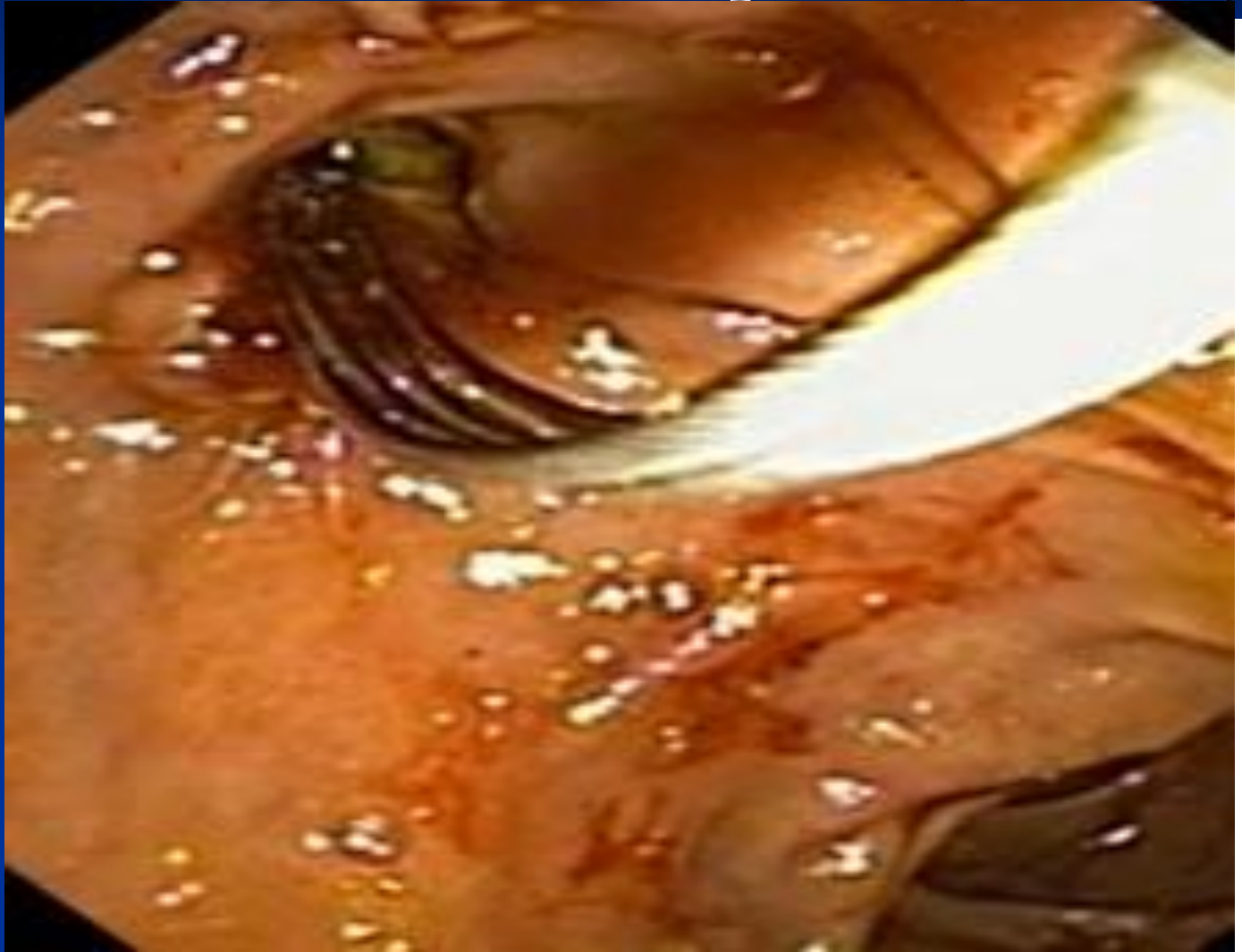
*Камень блокирующий
общий желчный проток*



After endoscopic papilosphincterotomy



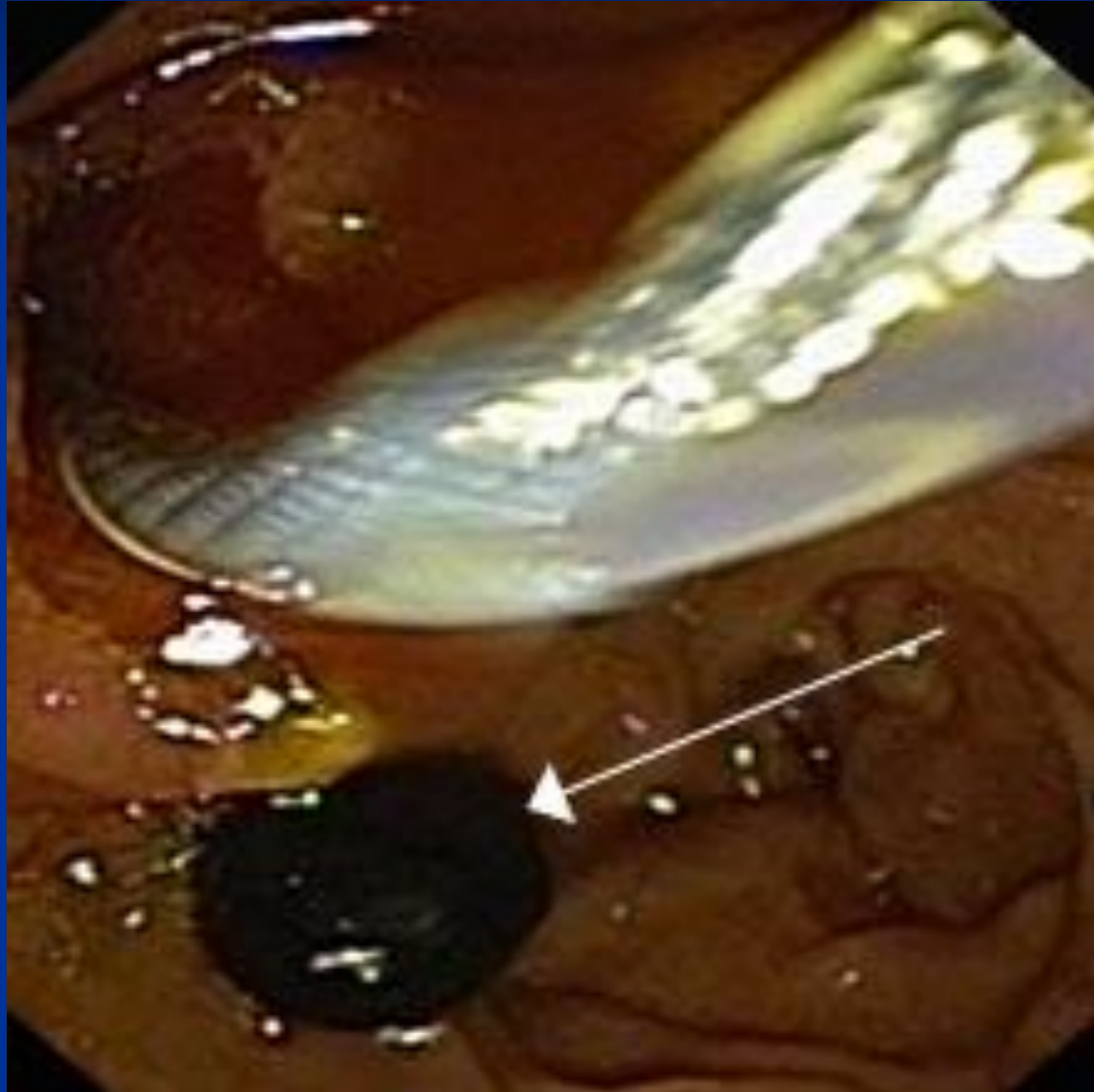
Endoscopic papiloshincterotomy with stone remove with Dormia probe (catheter)



The stones of CBD



The stone was remove inside
duodenum



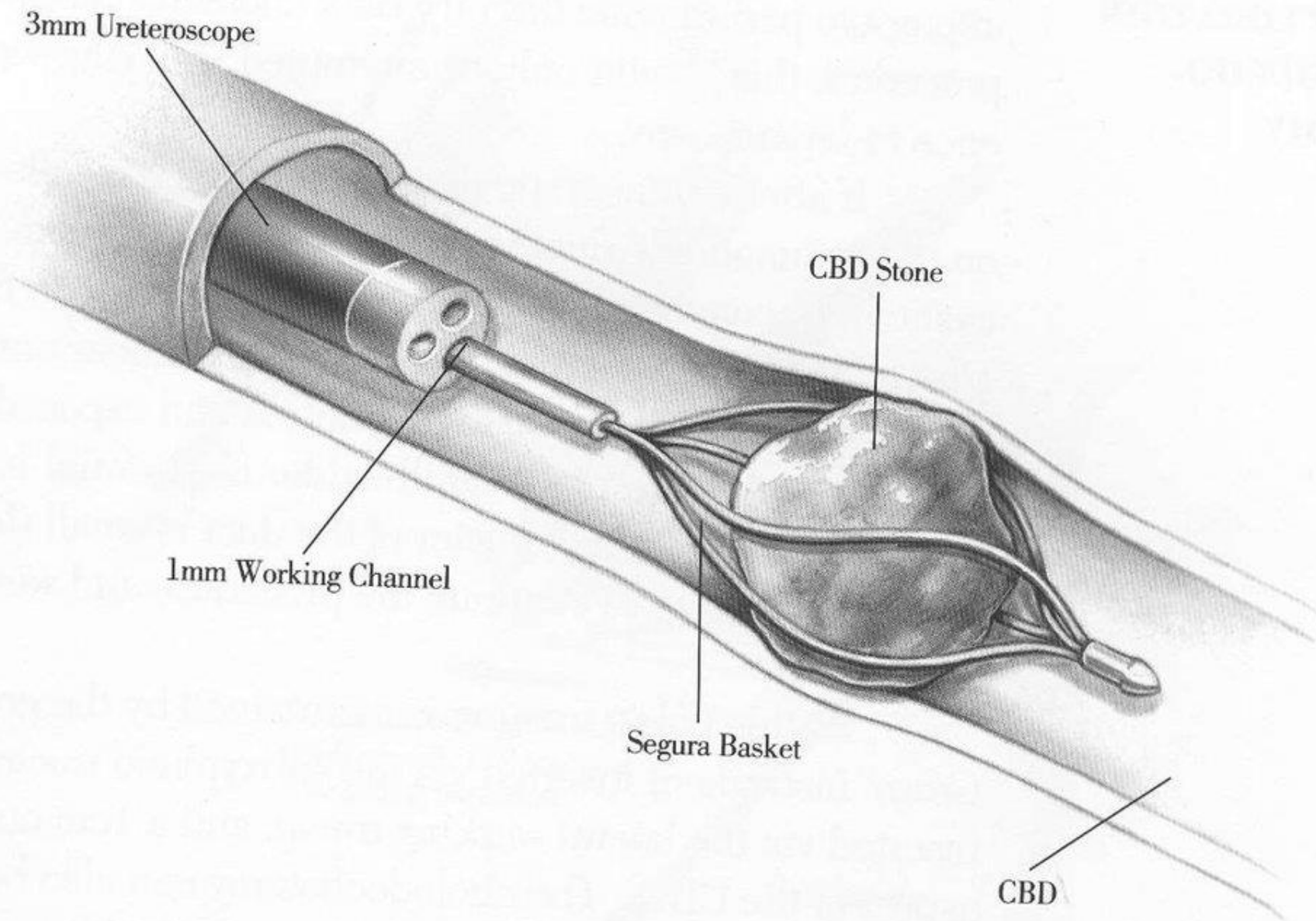
3mm Ureteroscope

1mm Working Channel

CBD Stone

Segura Basket

CBD



ERCP

Drains (stents) can also be used to prevent a narrowed area from rapidly returning to its previously narrowed state.

Complications of ERCP

- Pancreatitis
- Duodenal perforation
 - Bleeding
- Cholangitis
- Dye related allergic reactions

LAPAROSCOPIC CBD EXPLORATION

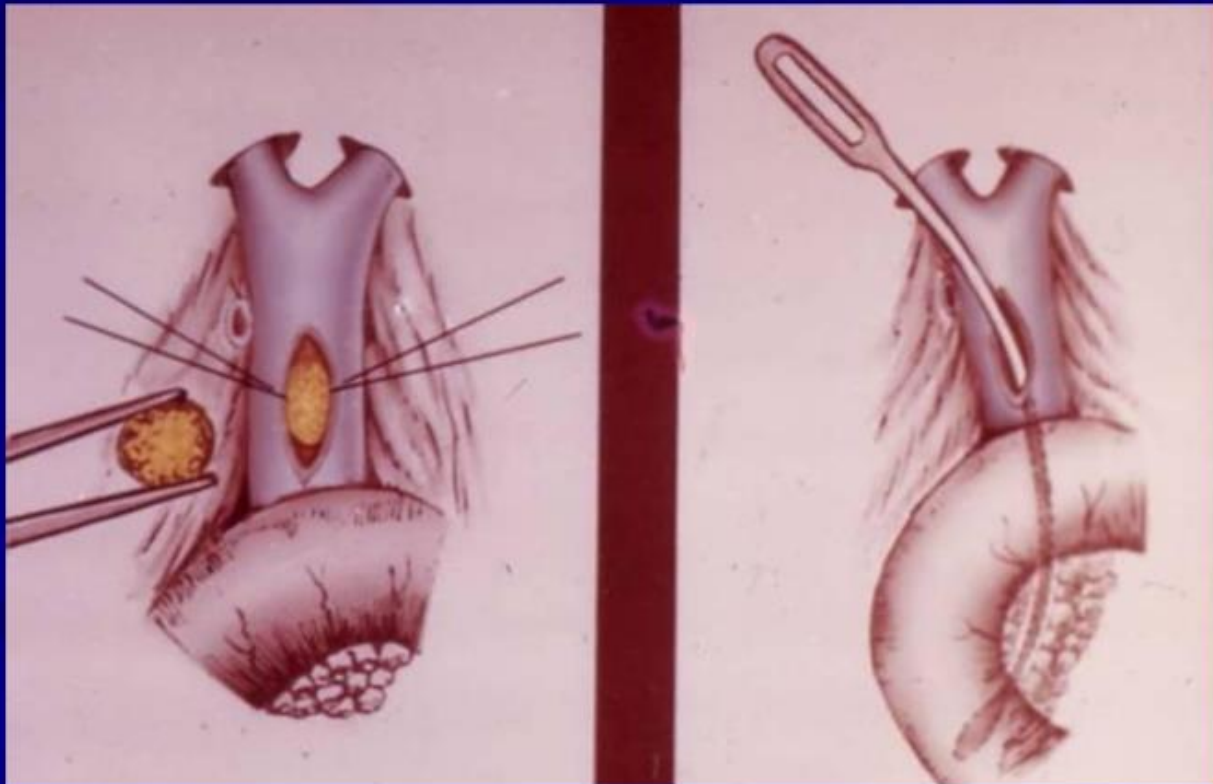
- Laparoscopic common bile duct exploration through: (choledochoscope)
 - cystic duct or □with formal choledochotomy allows the stones to be retrieved during the same procedure.
- If the expertise and instrumentation for laparoscopic common bile duct exploration are not available: □a drain should be placed and left adjacent next to the cystic duct & □ERCP with stone extraction is performed the following day.

Open Common Bile Duct Exploration

- An open common bile duct exploration should be performed if endoscopic intervention is not available or not feasible because of anatomic restrictions or expertise.
 - If a choledochotomy is performed, a T tube is left in place.
 - The purpose of the T tube is to provide access to the biliary system for postoperative radiologic stone extraction.
- Completion cholangiography via the T tube documents stone removal.

Choledocholithotomy with the revision of choledochus

Холедохолитотомия и ревизия холедоха
зондом

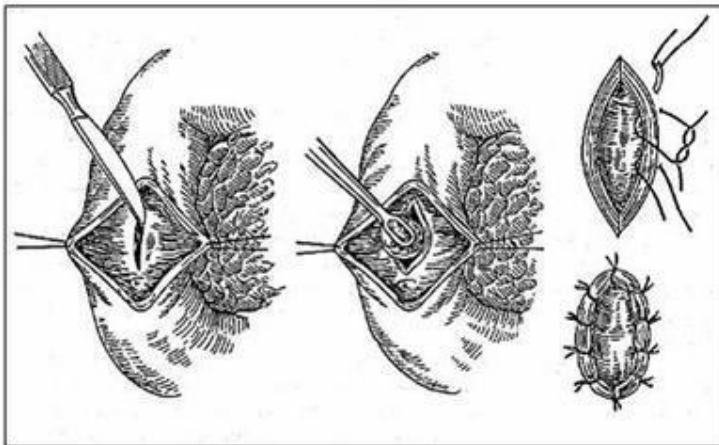


- Stones impacted in the ampulla may be difficult for both endoscopic ductal clearance and common bile duct exploration.
- In these cases, transduodenal sphincteroplasty and stone extraction should be performed; if this is not successful,
 - a choledochoduodenostomy or a Roux-en-Y choledochojejunostomy should be performed.
 - Sump syndrome associated with choledochoduodenostomy

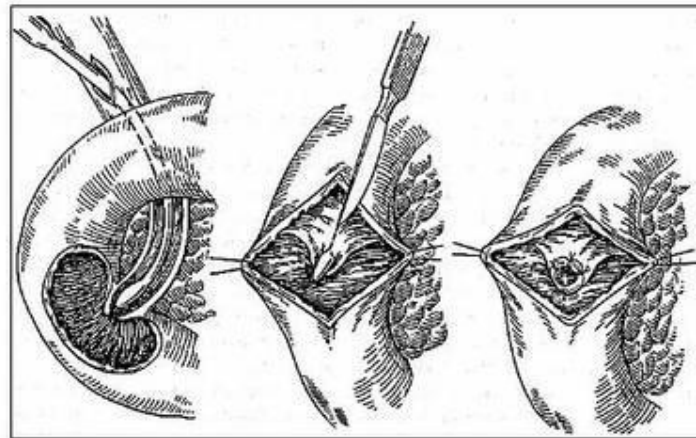
Transduodenal papilosphincterotomy

**Открытые оперативные вмешательства в лечении
механической желтухи**

**Внутренняя
трансдуоденальная
холедоходуоденостомия**

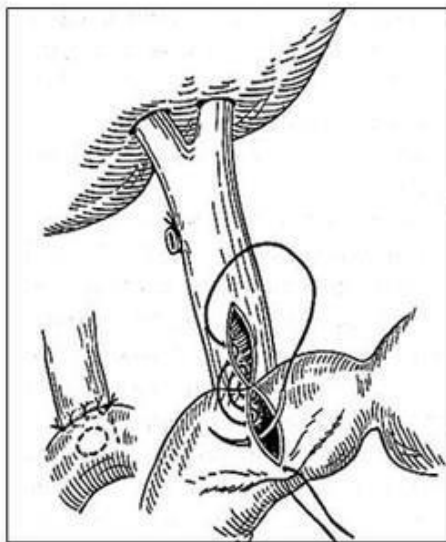


**Трансдуоденальная
папилосфинктеротомия и
папилосфинктропластика**

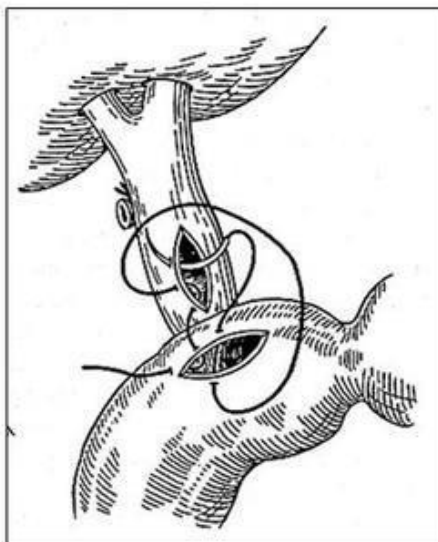


Choledochoduodenostomy

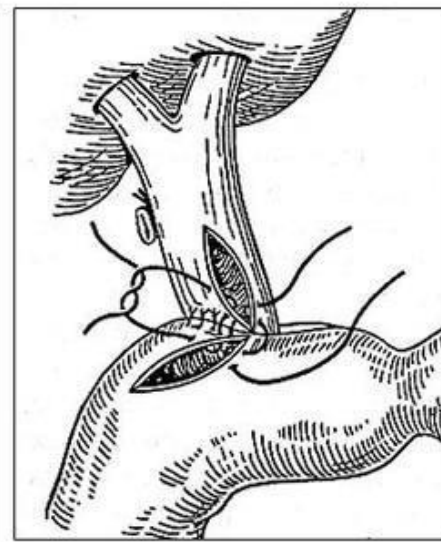
Холедоходуоденостомия



ХДА по Юрашу

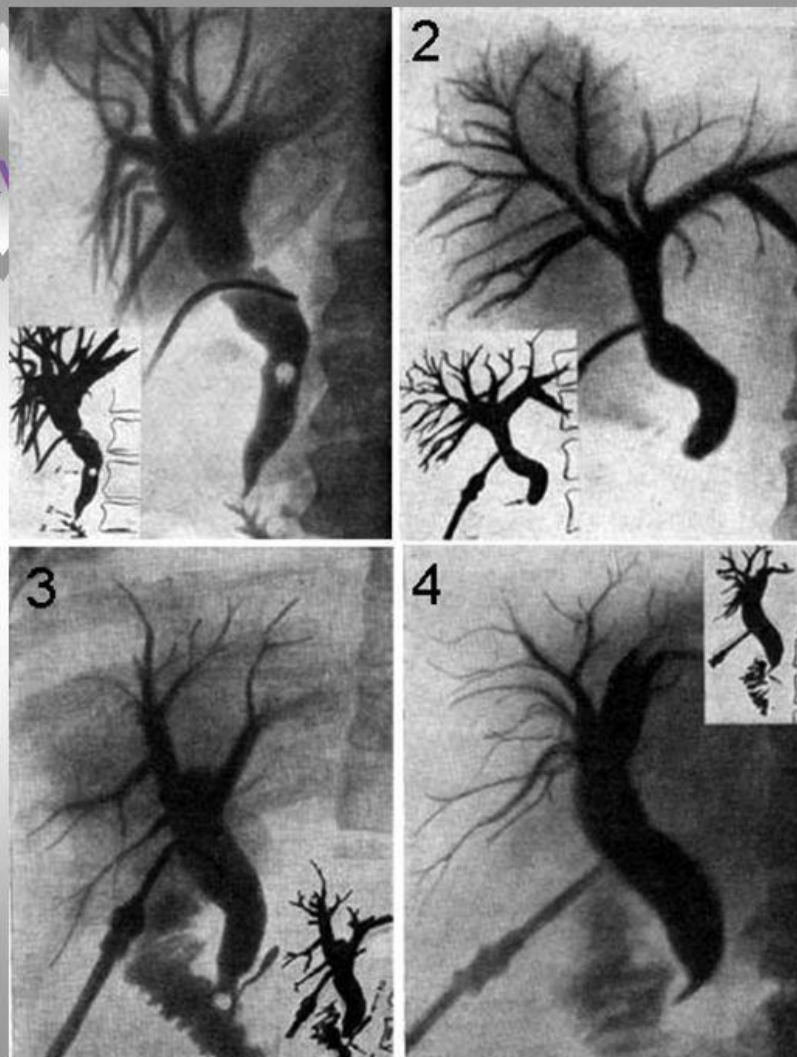


ХДА по Флеркену



ХДА по Финстереру

Intraoperation cholangiogram



Операционные
холангиограммы

REASONS FOR FAILURE OF ERCP

- multiple stones,
 - intrahepatic stones,
- impacted stones,
 - difficulty with cannulation,
- duodenal diverticula,
 - biliary stricture

Cholangitis

is bacterial infection on biliary obstruction

First described by Jean-Martin Charcot in 1850s as a serious and life-threatening illness

Causes

Choledocholithiasis

Obstructive tumors

Pancreatic cancer

Cholangiocarcinoma

Ampullary cancer

Porta hepatis

Pathophysiology

- Bile duct develops an obstruction
 - Obstruction may be incomplete (more common) or complete
 - Causes: Gallstones (most common), malignancy, benign stricture, iatrogenic (i.e. ERCP), biliary parasites, primary sclerosing cholangitis (PSC)
- Elevated intraluminal pressure in the gallbladder leads to translocation of bacteria
 - Bacteria may gain access via lymphatics, portal venous blood or retrograde from the duodenum
 - Common pathogens: *E. coli*, *Klebsiella*, *Streptococcus*, *Enterobacter*, *Pseudomonas* Other causes: HIV/AIDS cholangiopathy, parasitic infections (*Ascaris lumbricoides*)

CLINICAL FEATURES CONTD.

- Charcot's Triad.:
 - □ Intermittent Fever with chills
 - □ Intermittent jaundice &
 - □ Intermittent colicky pain....
- Feature of Ascending Cholangitis.. If untreated may progress to Septic Shock..

Reynold's pentad

- ☐ *hypotension +*
- ☐ *altered mental status with Charcot's Triad.*
- ☐ Both evidence of shock from a biliary source.. Found in Suppurative Cholangitis.

Obstructive jaundice

Occasionally, a small stone passes into the bile duct and impacts at the ampulla, causing pain and jaundice. The severity of the jaundice depends on the duration of the obstruction, but as the stone passes on the jaundice spontaneously resolves. A solitary stone may disappear from the biliary tree in this way, but normally some stones remain in a thick-walled gallbladder to support the diagnosis. Such patients need a cholecystectomy and a preoperative cholangiogram is essential to confirm that no stones remain in the duct.

a larger stone or stones within a dilated bile duct.

More commonly there is a larger stone or stones within a dilated bile duct. Sometimes the number of stones in the duct leads to a significant impairment of bile flow. At other times a stone moves up and down within the duct and acts as a ball valve, causing pain and jaundice when it impacts but allowing the symptoms to resolve spontaneously when it moves away. The site of impaction is usually immediately above the ampulla, but it may be above a fibrotic narrowing in the bile duct caused by the stones themselves. Complete impaction of a stone causes severe, progressive jaundice.

Stones in the bile duct usually cause pain.

However, from the pain alone it is not easy to distinguish obstructive jaundice due to stones from that due to malignant disease. Clinical examination normally reveals nothing except a jaundiced patient, and possibly some scratch marks from the intolerable itching.



Xanthomas



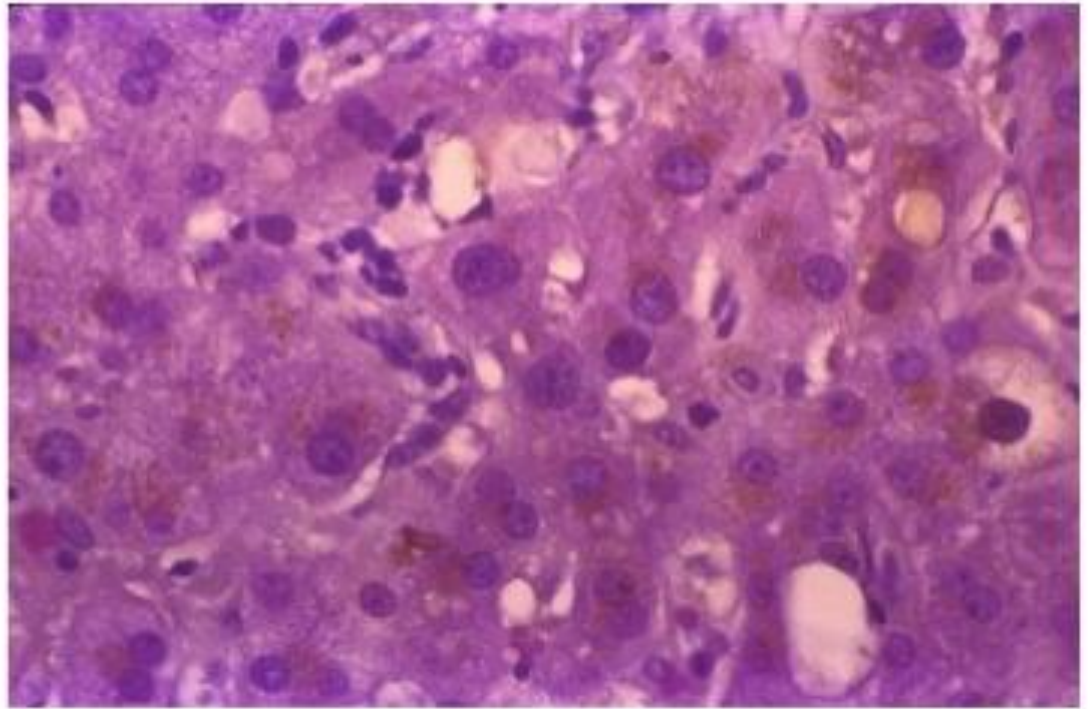
Scleral icterus



Scratch marks & pruritus

Cholestasis:

Retained bile pigments & bilirubin in hepatocytes



Tests

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

Treatment

The obstructed bile duct must be drained adequately, by the most effective route, and as quickly as possible.

However, the patient must first be resuscitated with intravenous fluids and antibiotics.

Antibiotic treatment of septicaemia will produce improvement for a short period, but it will not cure unless the obstruction is relieved.

Nowadays this can usually be achieved by an endoscopic sphincterotomy

If this is not possible then percutaneous transhepatic drainage should be tried.

Surgery to drain the bile duct is a last resort.

The septic process can develop in two different ways.

Sometimes intrahepatic abscesses appear. They can be seen on a cholangiogram as cavities in association with intrahepatic ducts. Repeated examinations are required.

Hepatic abscesses may rupture through the hepatic capsule and give rise to intraperitoneal perihepatic collections. The liver is often swollen and there is tension within the biliary tree. There is often a gush of purulent bile into the duodenum when the obstructing stone is released endoscopically.

Complications of cholangitis

Alternatively the **sepsis** may become systemic. Progressive renal and cardiac impairment ensues, and patients develop septic shock. Dialysis or haemofiltration may well be required. Occasionally the presenting feature of cholangitis is complete renal failure or cardiovascular collapse; such patients frequently die.

Prognosis of cholangitis

- Acute cholangitis has a high mortality (7-40%),
- Higher mortality in patients with co-morbidities, e.g. elderly, renal failure, cirrhosis, metastatic disease, failure to respond to antibiotics