Jaundice (NIH: national library of medicine)2024-2023 د. شذى كاظم عطوه/ ت. تحرير / م. رابعة/

Jaundice, also known as **hyperbilirubinemia**, is **defined** as a yellow discoloration of the body tissue resulting from the accumulation of excess bilirubin.

Deposition of bilirubin happens only when there is an excess of bilirubin, and this indicates **increased production** or **impaired excretion**. The normal serum levels of bilirubin are less than **1 milligram per deciliter** (mg/dL).

Bilirubin is a yellow chemical pigment present in the haemoglobin. Bilirubin pigment is produced by the hemolysis (breakdown of red blood cells) in the body and it is excreted by the liver. But in the case of liver dysfunction, the pigment is not excreted and gets accumulated in the **blood**, giving rise to **jaundice.**
Bilirubin has two components: **unconjugated(indirect)** and **conjugated(direct)**, and hence elevation of any of these can result in jaundice. **Icterus** acts as an essential clinical indicator for liver disease, apart from various other insults.
Yellowing of skin sparing the sclerae is indicative of carotenoderma which occurs in healthy individuals who consume excessive carotene-rich foods.
However, the **clinical presentation** of jaundice with peripheral **yellowing** of the **eye sclera,** also called "**scleral icterus**", is best appreciated when serum bilirubin **levels exceed 3 mg/dl.** With further increase in serum bilirubin levels, **the skin** will progressively discolor ranging from lemon yellow to apple green, especially if the process is long-standing; the green color is due to **biliverdin**. This activity reviews the evaluation and differential diagnosis of jaundice and highlights the role of an interprofessional team in evaluating and improving care for patients with this condition.

The liver is the body's **main** internal organ. It is **situated** below the diaphragm in the right upper quadrant of the abdominal cavity and **weighs** approximately 1.4 kg in women and 1.6 kg in men. It **performs** a variety of **important functions**, including bile production, plasma protein synthesis (e.g., clotting factors), drug metabolism, and vitamin, mineral, and glucose storage.

Liver disease (hepatic cause) is a multisystem condition that is classified as acute or chronic depending on the length of time between the onset of symptoms and the triggering event. **Acute liver failure** is characterized as the emergence of symptoms of serious liver injury with encephalopathy and diminished synthetic function in a patient who has no prior liver disease and has been sick for less than 26 weeks.

The frequency and prevalence of **chronic liver disease** are unknown, but best estimates suggest that they are much higher. Cirrhosis (**Chronic liver diseases** a result of hepatitis C (HCV), hepatitis B (HBV), alcohol, and non-alcoholic fatty liver disease (NAFLD).) , viral hepatitis, and hepatocellular carcinoma are estimated to cause 2 million deaths worldwide per year, with the vast majority of these deaths due to complications of cirrhosis, viral hepatitis, and hepatocellular carcinoma.

In a large proportion of patients with **well-compensated** or **occult cirrhosis**, **general anesthesia** and **surgery** **can cause complications**, which can result in significant morbidity and mortality

Objectives:

- *Describe the etiology and pathophysiology of jaundice.*
- *Outline the approach to performing a history and physical examination for patients with jaundice.*
- *Summarize the treatment and management options available for patients with jaundice.*
- *Explain the interprofessional team strategies for improving care coordination to advance the management of jaundice and improve outcomes.*

Etiology

I)Conjugated hyperbilirubinemia

1) ***Defect of canalicular organic anion transport***
- Dubin-Johnson syndrome

2)Defect of sinusoidal reuptake of conjugated bilirubin
- Rotor syndrome

3)Decreased intrahepatic excretion of bilirubin[8]
- Hepatocellular disease - Viral hepatitis A, B, D; alcoholic hepatitis; cirrhosis, nonalcoholic steatohepatitis, EBV, CMV, HSV, Wilson, autoimmune
- Cholestatic liver disease-Primary biliary cholangitis, primary sclerosing cholangitis
- Infiltrative diseases (e.g., amyloidosis, lymphoma, sarcoidosis, tuberculosis)
- Sepsis and hypoperfusion states
- Total parenteral nutrition
- Drugs & Toxins - oral contraceptives, rifampin, probenecid, steroids, chlorpromazine, herbal medications (e.g., Jamaican bush tea, kava kava), arsenic
- Hepatic crisis in sickle cell disease
- Pregnancy

4)Extrahepatic cholestasis (biliary obstruction)
- Choledocholithiasis
- Tumors (e.g., cholangiocarcinoma, head of pancreas cancer)
- Extrahepatic biliary atresia
- Acute and chronic pancreatitis
- Strictures
- Parasitic infections (e.g., Ascaris lumbricoides, liver flukes)

II)Unconjugated hyperbilirubinemia

1)***Excess production of bilirubin***
- Hemolytic anemias, extravasation of blood in tissues, dyserythropoiesis

2)Reduced hepatic uptake of bilirubin
- Gilbert syndrome

3)Impaired conjugation
- Crigler–Najjar syndrome type 1 and 2
- Hyperthyroid
- Estrogen

Epidemiology

The prevalence of jaundice differs among patient populations; **newborns and elderly** more commonly present with the disease.

Around **20 percent of "term babies"** are found with jaundice **in the first week of life,** primarily due to **immature hepatic conjugation process.**

Congenital disorders, overproduction from hemolysis**,** defective bilirubin uptake**,** and defects in conjugation are also responsible for jaundice in **infancy or childhood**.

" Hepatitis A" was found to be the most afflicting cause of jaundice among **children. Bile duct stones, drug-induced liver disease**, and **malignant biliary** obstruction occur in the **elderly population.**

Men have an increased prevalence of **alcoholic and non-alcoholic cirrhosis, chronic hepatitis B, malignancy of pancreas**, or **sclerosing cholangitis.**

In contrast, **women** demonstrate higher rates of **gallbladder stones, primary biliary cirrhosis**, and **gallbladder cancer.**

Complication of jaundice:

***Kernicterus** or ***Bilirubin-induced neurologic dysfunction (BIND)**, a complication of severe jaundice is a very rare cause of **death** in **neonates** with a **death rate of 0.28 deaths per one million live births.**

Pathophysiology

The pathophysiology of jaundice is best explained by dividing the metabolism of bilirubin into three phases: prehepatic, hepatic, and post-hepatic.

Pre-hepatic

1. **Production** - Bilirubin is the end product of heme, which is released by senescent or defective RBCs. In the reticuloendothelial cells of spleen, liver and bone marrow, heme released from the RBC undergoes a series of reactions to form the final product bilirubin:

Heme-->Biliverdin-->Bilirubin (insoluble due to tight hydrogen bonding)

Hepatic

1. **Hepatocellular uptake** - The bilirubin released from the reticuloendothelial system is in an unconjugated form (i.e., non-soluble) and gets transported to the hepatocytes bound to albumin which accomplishes solubility in blood. The albumin-bilirubin bond is broken, and the bilirubin alone is then taken into the hepatocytes through a carrier-membrane transport and bound to proteins in the cytosol to decrease the efflux of bilirubin back into the plasma.
2. **Conjugation of bilirubin** - This unconjugated bilirubin then proceeds to the endoplasmic reticulum, where it undergoes conjugation to glucuronic acid resulting in the formation of conjugated bilirubin, which is soluble in the bile. This is rendered by the action of UDP-glucuronosyl transferase.

Post-hepatic

1. **Bile secretion from hepatocytes**- Conjugated bilirubin is now released into the bile canaliculi into the bile ducts, stored in the gallbladder, reaching the small bowel through the ampulla of Vater and finally enters the colon.

2. **Intestinal metabolism and Renal transport**- The intestinal mucosa does not reabsorb conjugated bilirubin due to its hydrophilicity and large molecular size. The colonic bacteria deconjugate and metabolize bilirubin into urobilinogen's, 80% of which gets excreted into the feces and stercobilin and the remaining (10 to 20%) undergoes enterohepatic circulation. Some of these urobilin's are excreted through the kidneys imparting the yellow pigment of urine.

Dysfunction in pre-hepatic phase results in elevated serum levels of **unconjugated bilirubin** while insult in **post-hepatic phase** marks elevated **conjugated bilirubin**. **Hepatic phase** impairment can **elevate both unconjugated and conjugated bilirubin.**

Increased urinary excretion of **urobilinogen** can be due to increased production of bilirubin, increased reabsorption of urobilinogen from the colon, or decreased hepatic clearance of urobilinogen.

Toxicokinetics

As mentioned earlier, the serum level of bilirubin is a **balance between production and hepatic excretion**. After reaching the colon, the bacteria metabolize it into **urobilinogen**. A vast majority of urobilinogen is converted in **stercobilin and excreted in feces**. About 10 to 20% of urobilin gets reabsorbed by the action of beta-glucuronidase in the brush border of the gut and facilitates enterohepatic circulation and re-excreted by the liver; less than 3mg/dl escapes the hepatic uptakes and filters into the urine.

Owing to its **lipid soluble nature**, **bilirubin may cross the blood-brain barrier** and thus enter the brain. Its **clearance from the brain** is ensured by the presence of an enzyme on the **inner mitochondrial membrane,** which aids in the **oxidation of bilirubin,** thus protecting against its neurotoxic effects. The mechanism of toxicity is yet obscure, but bilirubin has a higher affinity to settle in **glia** and **neurons.**

However, in **newborns**, since the **blood-brain barrier(BBB) is yet to develop**, pathological **increase in serum levels of bilirubin** can result in death in the neonatal period or survival with disastrous neurological sequalae called **kernicterus**. Also, newborns are at increased risk **due to lack of colonic bacteria** resulting in deconjugation and enterohepatic reabsorption by b-glucuronidase enzymes resulting in hyperbilirubinemia.

Risk Factors

The risk factors for jaundice are :

1) Excessive consumption of alcohol
2) Using illicit medications
3) Taking drugs that may damage the liver
4) Exposure to viral infections like hepatitis A , hepatitis B , or hepatitis C
5) Vulnerability to certain industrial chemicals

Diagnosis of jaundice in infants

1) By doing **physical examinations** of the baby, paediatrics perform jaundice diagnosis in babies. Newborns should be examined for jaundice every 8 to 12 hours during the first 48 hours of life and continue it till they are 5 days old. The infant bilirubin tests include -
2) **Light Meter:** The paediatrician will use a light meter to check the transcutaneous bilirubin (TcB) level.
3) **Blood test**

Diagnosis of jaundice in adults

By examining the jaundice signs and symptoms, the gastroenterologist can conclude the diagnosis.Other diagnosis options include -

1) **Blood tests:** Various blood tests are used to diagnose jaundice, they are the complete blood count (CBC), liver function tests (LFT's), etc.
2) **Imaging Tests**
3) **Liver biopsy**
4) **Endoscopic Retrograde Cholangiopancreatography (ERCP)**
5) **Laparoscopy (uncommon)**

Treatment

The treatment approach for jaundice differs among **newborns and adults**. Also, based on every single condition and severity of the patient, the doctor adopts a more personalized treatment plan, which might vary in duration as well.

Jaundice treatment for infants

Mild jaundice subsides on its own after 1 or 2 weeks. Breastfeeding in infants should be done regularly. If the baby is not getting sufficient breast milk, the paediatrician may recommend supplementing with formula.
Other treatment options include -

1) **Fluids:** Giving fluids, as loss of fluids (dehydration) will cause high bilirubin levels
2) **Phototherapy**
3) **Exchange blood transfusion**
4) **Intravenous immunoglobulin (IVIg)**

Jaundice treatment for adults

Often, jaundice doesn't require treatment in adults, **but** it is a serious condition in newborns. Jaundice can be **treated for its underlying causes and effects**. Treatment for jaundice is the **management of the underlying hepatobiliary or haematological disease.**

Do's and Don'ts of Jaundice

Jaundice is a medical condition with high bilirubin levels in the bloodstream. It is more severe in neonates than in adults. By following the do's and don'ts, **it is easy to prevent or lessen the severity of its symptoms.**

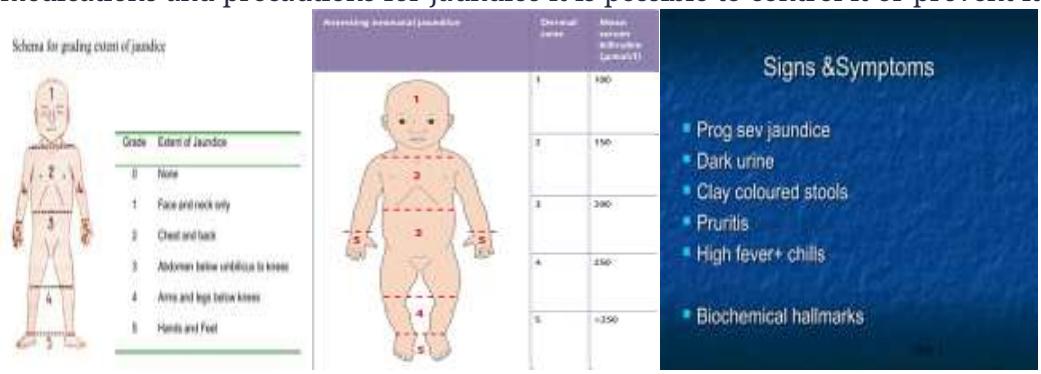
Do's	Don'ts
Limit alcohol intake	Eat canned, packaged, and spicy food
Eat nutritious food	Take drugs that harm the liver
Take enough rest	Take illicit medications
Regular health check-ups	Go out of your home
Stay away from industrial pollution	Skip jaundice medicines

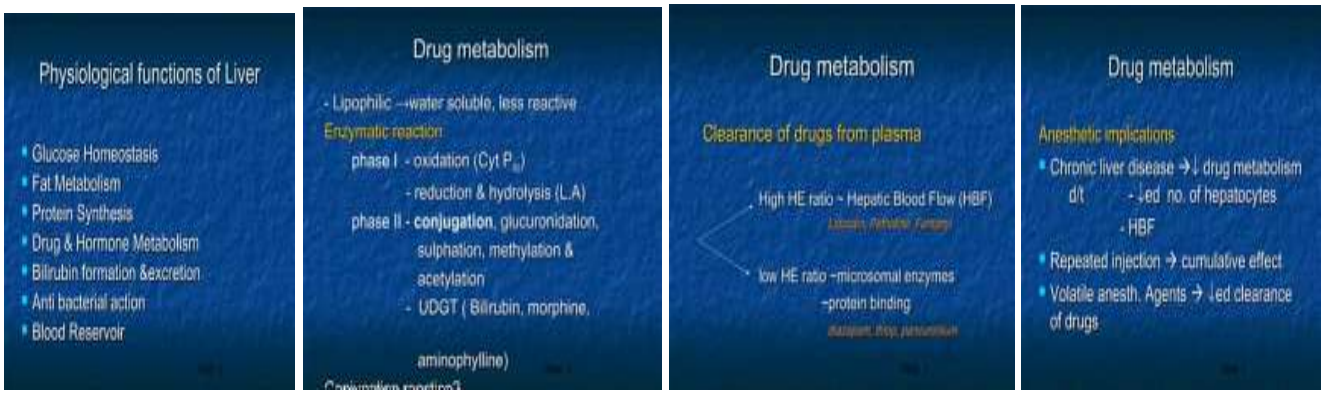
Foods play an important role in the **control and cure of jaundice**. There are specific **guidelines** regarding food when suffering from jaundice
Foods to eat and avoid during jaundice

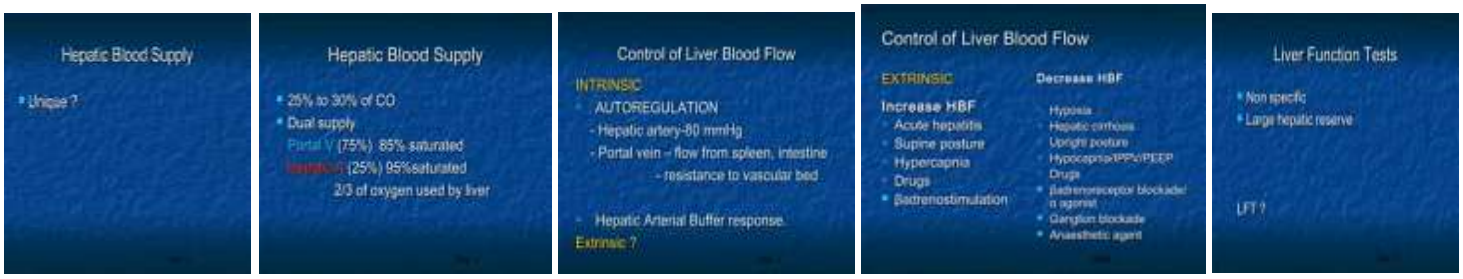
Foods to Eat	Foods to Avoid
Stay hydrated - Drink water, lemon, grape juice, etc.	Sugar
Fresh fruits and vegetables	Salt
Coffee and tea	Alcohol
Whole grains	High-fat and fried foods

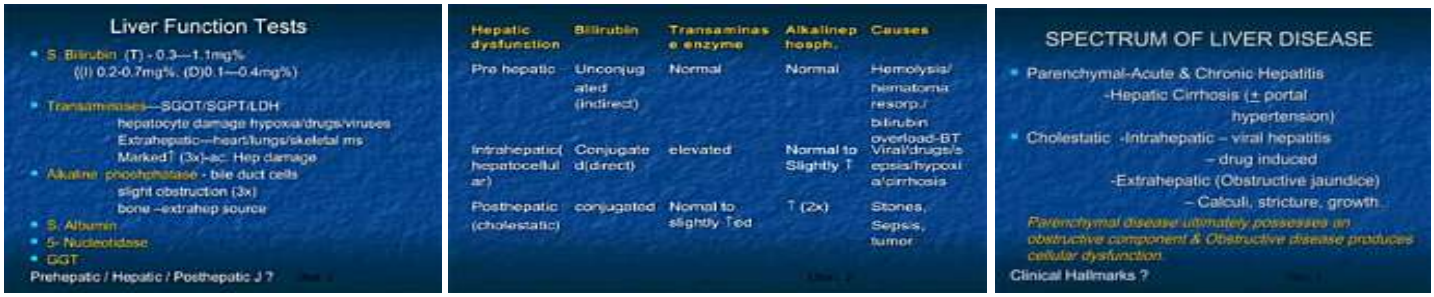
Nuts and legumes Iron consumption

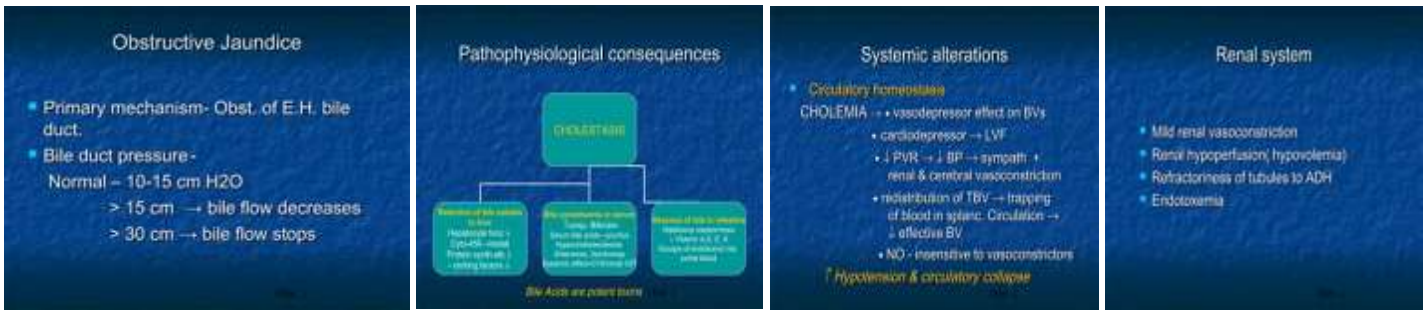
If jaundice is not treated on time, it can lead to **serious complications** or **even death**. By taking the right medications and precautions for jaundice it is possible to control it or prevent it completely.











Renal System

- Acute Renal Failure

- Hepatorenal Syndrome

Renal system

Hepatorenal Syndrome

- Oliguria
- Inability to excrete Na in urine(10mmol/l)
- Functional change
- Normal renal blood flow
- Treatment : Prevention-identify high risk patients

Systemic alterations

- Coagulopathy(low grade DIC)
  - Impaired platelet function
  - ↑ FDP---inhibition of fibrinolysis
  - ↑ Endotoxins
- Hm gastritis & stress ulcers
- Impaired wound healing

Anesthetic problems in Obstructive Jaundice ?

PROBLEMS

DUE TO DYSFUNCTION OF LIVER ITSELF :

- Low serum proteins
- Coagulopathy
- Drug metabolism and disposition
- Metabolic derangement - Hypoglycemia
  - Electrolyte imbalance
- Haematological - Anaemia
  - Thrombocytopenia
  - Leucopenia
  - DIC
- Deficiency of fat soluble vitamins (A, D, E, K)
- Increased serum cholesterol (atheromatous changes)

PROBLEMS

DUE TO INVOLVEMENT OF OTHER SYSTEMS

- CVS– TBV ↓, PVR ↓, ↑Circulatory collapse
- Renal - pre renal azotemia
  - Hepatorenal failure
- GIT - Hm gastritis & stress ulcers
- Resp.– Arterial Hypoxemia
  - vulnerability to pulmonary infection
- CNS – Hepatic encephalopathy

Problems related to surgery ?

Problems related to surgery

- Whipple's procedure---Carc. Head of panc
- Distal gastrectomy,PJ, HJ, GJ
- Major surgery---long duration
- Increased blood loss/fluid shifts
- Wide incision---Roof top---warrants good postoperative analgesia
- Extensive monitoring reqd for favourable outcome

Risk Factors

- Age > 60yrs
- Albumin < 30gm%
- Preop. renal dysfunction
- Long standing biliary obstruction → infection → sepsis
- Weight loss

↑Serum creatinine & Sepsis---prognostic factors
↑Periop CVS collapse & renal failure

Preoperative Assessment

OBJECTIVES

- Assess the type and degree of liver dysfunction.
- Assess effect on other system.
- To ensure – post operative facilities (High risk patient).

Preoperative Assessment

- History
- Clinical examination
- Investigations ???

Unexplained jaundice of 4wks duration or longer will prove to be caused by obstruction in nearly 75% patients

Blumgart L

Preoperative Investigations

To know the pattern of disease :

- S. Bilirubin
- SGOT, SGPT 90% predictive
- alk. phosphatase

Preoperative Investigations

To judge the synthetic ability of liver

- Serum albumin– < 2.5 gm% - severe damage
- Albumin/globulin ratio – reversed
- Prothrombin time –> 1-5 sec. Over control
  – INR - > 1.3

(D/D – Par enteral Vit. K – Obst. Jaundice)

To assess general condition of patient

(i) Haematological
- Hb
- TLC, DLC
- Platelet Count
- Clotting factors (PT, PTTK)
- BT

(ii)Cardiorespiratory
- Chest X-ray
- ECG
- Blood gases

(iii) Metabolic-
- Serum proteins
- Serum glucose
- Electrolyte
- Urea / Creatinine
- Urinary-Ureal Creatinine
- -Electrolyte

(iv) Hepatic imaging

(v) Microbiological -
- Culture
- Hep. B marker
- Viral antibodies

Preoperative management

- Avoid prolonged hyperbilirubinemia
- Treat infection –cholangitis
- Use Aminoglycosides carefully
- Avoid pre renal failure
- Correct Anaemia\Coagulation\hypoalbuminemia
- Avoid all NSAIDS
- I/V saline & mannitol pre & postop

Premedication

- Anxiolytic – oral short acting BDZ
- Oral H2 antagonist
- Vit. K (Obst. J) – 10 mg B D X 3 day
- If Bilirubin > 8 mg% –
  - I/V fluid - 1-2 ml/kg/hr.
  - Mannitol – 100 ml of 20% 2 hrs preop.
- Order morning PT / S. Electrolyte
- Preop urinary catheter & CVP

Anaesthetic Management

General Considerations

Minimize physiological insult to liver & kidney

- Maintain O2 supply – demand relationship in liver.
  →Adequate pulmonary ventilation and cardiovascular fn.
- Maintain renal perfusion
  →Avoid Hypotension, hypoproteinemia & Hypoxia
  → meticulous fluid balance

Choose appropriate anaesthetic agent
Metabolism of drugs + Effect on HBF.

Induction ?

Anesthetic technique

- General anesthesia
- Preoxygenation
- Induction - Thiopentone
  Propofol
- Muscle relaxant –
  Suxamethonium
  Vecuronium 0.15mg/kg
  Rocuronium0.6mg/kg
  Atracurium(DOC)
- Opioids ?

Anesthetic technique

- Opioids – Well tolerated
  smaller doses
  Morphine—ph-II reac.
  fentanyl(DOC)
  spasm of sphincter of Oddi

Anesthetic technique

Spasm of sphincter of Oddi

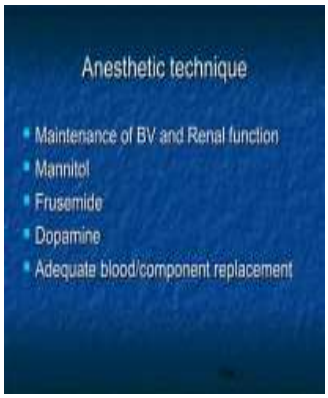
- Interpretation of operative cholangiography & biliary pressures
- All patients do not show this response
- Incidence of spasm is very low
- Intraop manipulation of BD system → spasm
- Treatment

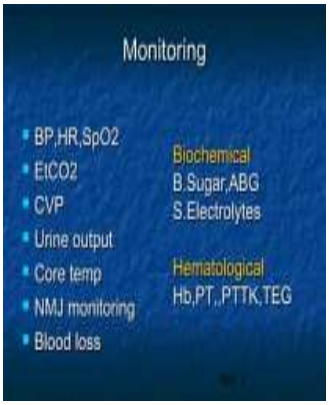
Anesthetic technique

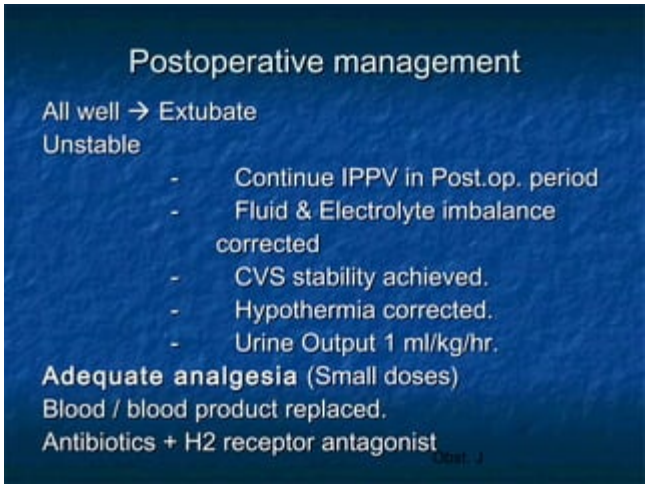
Volatile Anesthetics

- Useful & well tolerated
- Can be entirely eliminated
- Disadv- CVS instability → vasodilation → ↓perf. Press. → ↓ blood velocity →↑ oxygen extraction → ↓ HBF & oxygen supply
- Isoflurane—best maint. of HBF & oxygen

IPPV ?





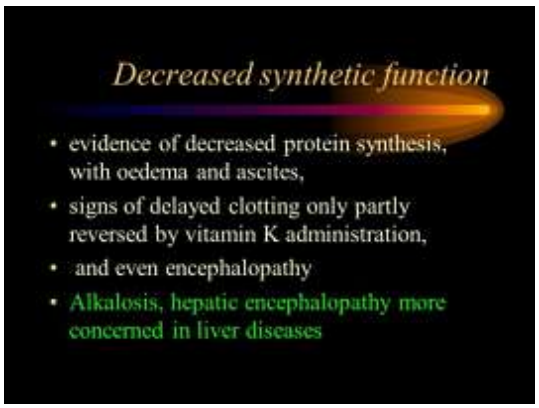


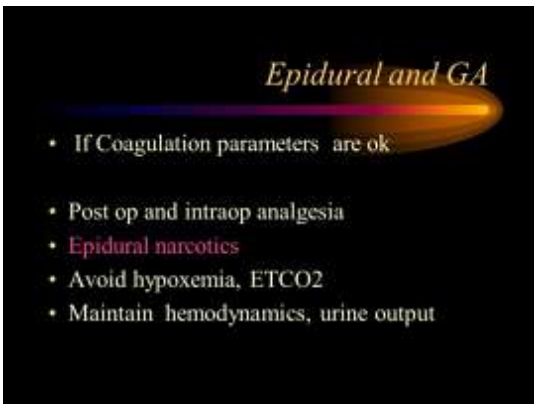
Pre-op optimization

- Avoid prolonged hyperbilirubinemia, consider drainage stent
- Treat infection
- Prophylactic antibiotics to prevent sepsis
- Correct anemia, coagulation abnormality, hypoalbuminemia, dyselectrolytemia
- Inj-Vitamin K 10 mg IM OD for 3 days atleast 48-72 hrs before surgery

Anesthetic goals

- ❑ Minimize physiological insult to liver & kidney
- ❑ Maintain O2 supply demand relationship in liver
- ❑ Adequate pulmonary ventilation and cardiovascular function
- ❑ Maintain renal perfusion
- ❑ Avoid hypotension, sympathetic stimulation, hypoxia & hepatic venous congestion
- ❑ Meticulous fluid balance
- ❑ Choose appropriate anesthetic agent - Metabolism of drugs+ Effect on HBF





Most surgical procedures result in small elevations in serum liver biochemical test levels, whether performed under general, spinal, or epidural anesthesia.

In patients without underlying liver disease, minor postoperative increases in serum aminotransferase, alkaline phosphatase, or bilirubin levels are not clinically important.

Surgery, on the other hand, can hastenاسرع hepatic decompensation in patients with underlying liver disease, especially those with compromised hepatic synthetic function. The intensity of the operation is related to the operational risk.

In patients with elevated liver enzyme levels, anesthesia and surgery may deteriorate liver function; thus, choosing anesthetics with less hepatotoxicity may be critical in these patients.

Preoperative evaluation is critical for elective procedures to ensure a proper risk benefit calculation for elective surgery and to direct optimization.

The emphasis of postoperative treatment should be on patient rehabilitation and close monitoring for liver decompensation. Non-hepatic surgery is more common in general and occurs often in the course of acute care surgery

In summary: .A full blood count, coagulation profile, liver function tests, serum electrolytes, and creatinine should be included in a minimum range of blood tests. Cirrhotic patients often experience coagulopathy, electrolyte disruptions, and renal dysfunction, all of which have clear perioperative consequences.

Treatment / Management

Patients with liver disease presenting with non-hepatic **surgery** might have postoperative complications that can lead to death. There are predictors of outcome in these patient population like preoperative Child's class. So **that efforts** should be expended to favorably alter a patient's preoperative Child's class before undertaking an elective operation. In these patients anesthesia and surgery may deteriorate liver function; thus, **choosing anesthetics with less hepatotoxicity could be helpful for good outcome.**

Treatment of choice for jaundice is the correction of the underlying hepatobiliary or hematological disease, when possible.

Pruritis associated with cholestasis can be managed based on the severity. For mild pruritis, warm baths or oatmeal baths حمامات دقيق الشوفان can be relieving. Antihistamines can also help with pruritis.

Patients with moderate to severe pruritis respond to bile acid sequestrants such as **cholestyramine** or **colestipol.**

Other less effective therapies include **rifampin, naltrexone, sertraline, or phenobarbital**. If medical treatments **fail, liver transplantation** may be the only effective therapy for **pruritis.**

Jaundice is an indication for **hepatic decompensation** التعويض الكبدي (Overall, decompensated cirrhosis has worse symptoms, complications, and outlook. Compensated cirrhosis is usually asymptomatic and sometimes reversible. If left untreated, it can progress to decompensation. If caught early, it is a less serious condition.) and may be an indication for **liver transplant** evaluation depending on the severity of the hepatic injury.

Differential Diagnosis

The differential for **yellowish discoloration of the skin** is narrow. Healthy individuals with high consumption of vegetables and fruits that contain carotene, such as carrots can present with carotenoderma which classically spares the sclerae.

Quinacrine leads to yellowish discoloration of the skin in up to one-third of patients treated with it.

Prognosis

Prognosis of jaundice **depends on the etiology.**

Etiologies of jaundice with excellent prognosis include jaundice from *resorption of hematomas, *physiologic jaundice of newborn, *breastfeeding, *breast milk jaundice, *Gilbert syndrome, *choledocholithiasis.

As a general rule, **malignant biliary obstructions and cirrhosis** with jaundice predict a poorer prognosis**.**

Complications

Indirect (insoluble) bilirubin is harmful to cells and cellular structures. Due to the physiologic mechanisms that protect against elevated bilirubin, the toxic effects are limited to neonates due to the **poorly developed blood-brain barrier.** High levels of bilirubin are neurotoxic and can lead to **permanent neurologic injury (kernicterus) (Bilirubin-induced neurologic dysfunction).**

Consultations

Specific challenging patients may require specialty consultations for further workup and management. Gastroenterology specialists most frequently consult on undiagnosed cases of jaundice.

Deterrence and Patient Education

Most cases of jaundice can be effectively prevented by following a few simple recommendations which include:

1. Avoid herbal medications without consulting with a physician, most herbal supplements are toxic to the liver and can cause irreversible liver damage leading to jaundice
2. Avoid smoking, consumption of alcohol, and intravenous drugs
3. Avoid exceeding the recommended dose on prescribed medications
4. Visit your doctor if you notice yellowish discoloration of body tissue
5. Encourage safe sex practices
6. Always get the recommended vaccines before traveling to a foreign country

Perioperative management of patients with liver disease for non-hepatic surgery

Liver disease is a multisystem condition that is classified as **acute or chronic** depending on the **length of time.** **Cirrhosis** patients are expected to undergo surgery in the l**ast two years of their lives,** according to estimates. In patients with **elevated liver enzyme levels**, anesthesia and surgery **may deteriorate liver function. Preoperative identification, optimization and anesthetic management** are essential for optimum outcomes in patients with liver disease undergoing surgery.

Patients with liver disease presenting with non-hepatic surgery might have postoperative complications that can lead to death.

Highlights

1) Liver disease is a multisystem condition that is classified as acute or chronic.
2) Preoperative assessment and risk stratification are paramount for optimization.
3) Nephrotoxic drugs should be avoided.

Anesthetic agents

An evidence based guideline recommends that anesthetics can reduce hepatic blood flow by 30–50%; therefore: isoflurane, desflurane, sevoflurane, and propofol are recommended for patients with liver disease because they cause less disruption in hepatic arterial blood flow than other inhaled anesthetics

Anesthetic agents are chosen based on factors like *protein binding, *distribution, and *drug metabolism. Propofol is favored over benzodiazepines for sedation procedures because it has a quicker onset of sedation and recovery time in cirrhotic patients. Because of its rapid redistribution, propofol is the preferred induction agent for general anesthesia due to its rapid redistribution; however, it can induce vasodilation, which can reduce liver perfusion.

An evidence-based guideline recommends that Halothane, 20% of which is metabolized by the liver, is no longer widely used and should be avoided by people who have liver disease. Enflurane, on the other hand, is just 4% metabolized by the liver. Isoflurane, desflurane, and sevoflurane have very little hepatic metabolism (0.2%), making them the best anesthetic options for patients with liver disease, along with nitrous oxide

In general, **propofol** is **favored** as a **narcotic** over benzodiazepines. **Sufentanil and remifentanil** are the **opioids** of choice for liver insufficiency.

Since the **muscle relaxants** **vecuronium and rocuronium** are only metabolized by the liver, they **should be avoided**. In patients with liver disease, **atracurium and cisatracurium** are favored because they are not metabolized by the liver**.**

A retrospective cohort recommended that in patients with **preoperatively elevated liver transaminase** levels who underwent non-hepatic surgeries, the improvement in ALT level was significantly lower after total **intravenous anesthetics (TIV)** than after inhalational (INHA); this indicates that in these patients, TIVA might be a better option than INHA. Despite this, the majority of patients in both groups had relatively **stable livers** following surgery, with lower AST and ALT levels than before. These**.**

When compared to **halothane,** newer agents including sevoflurane and desflurane undergo less hepatic metabolism and are thus safer in cirrhotic patients. The majority of **available analgesics** are metabolized in the liver and removed via the kidneys, which can be troublesome for patients with chronic liver disease (CLD). While most patients tolerate **acetaminophen** well, the dosage should be decreased in those with decompensated hepatitis**.** Because of **their** adverse effects, such as gastrointestinal bleeding and renal damage, non-steroidal anti-inflammatory drugs are **not recommended.**
Long-acting opioids like morphine should be avoided, but titrated doses of **fentanyl or sufentanil** are well tolerated in cirrhotic patients**.**

Finally, in **liver disease,** decreased doses of opioids with increased intervals prevent drug accumulation. Long-acting opioids, such as morphine and mepiridine, should be **avoided**, but shorter-acting opioids, like fentanyl is well tolerated when used in lower doses and titrated to effect.

Nephrotoxic drugs and non-steroidal anti-inflammatory drugs should be **avoided**, and caution should be practiced. even though acetaminophen is generally well tolerated, it should be used with caution in patients with advanced cirrhosis, especially those who are malnourished. Because of the risk of gastrointestinal bleeding and kidney failure, nonsteroidal anti-inflammatories should be used with caution .

Benzodiazepines should be **avoided** in general, When midazolam and propofol were compared in cirrhotic patients, **propofol was consistently found to be sa**fer due to its faster removal longer half-lives and higher levels of unbound (i.e. free) medication, cause increased sedative impact and duration of circulating benzodiazepines, which may precipitate encephalopathy. Shorter-acting agents like midazolam are preferred at lower doses and with close monitoring.

patients with cirrhosis and liver disease cannot be considered auto-ant coagulated, since there is clear evidence of thrombotic events, including an appreciable frequency of DVT and PE comparable to other chronic diseases, despite irregular standard coagulation tests. As a result, thromboprophylaxis should be prescribed in patients with liver cirrhosis that are at high risk for thrombotic complications, at the very least. In this category of patients, LWMHs seem to be reasonably safe; however, if there are significant risk factors for bleeding, graduated compression stockings or intermittent pneumatic compression should be considered

on the assessment and treatment of coagulopathy in critically ill patients with liver failure found that patients with liver failure are at high risk for both bleeding and clotting complications at any level of LT. Increased mortality and morbidity are linked to these complications. There is currently no approved procedure for thrombosis prevention.

Risk stratification

The Child-Pugh (Table 3) classification and the model for end-stage liver disease (MELD) score are valuable methods for predicting peri-operative morbidity and mortality in patients. Child A patients are acceptable candidates for elective procedures with special intra-operative care. Child B should undergo pre-operative optimization to convert to Child A, and Child C or with a MELD score greater than 20, are at a high risk for anesthesia, and should be postponed to elective surgeries.

Table 3

Child—Turcotte–Pugh (CTP) classification.

A. Classification

Clinical parameter	1 point	2 points	3 points
Total bilirubin (mg/dL)	<2	2–3	>3
Serum albumin (g/dL)	>3.5	2.8–3.5	<2.8
INR	<1.7	1.7–2.3	>2.3
Ascites	None	Mild	Moderate to severe
Hepatic encephalopathy	None	Grade I or II	Grade III or IV

B. Interpretation

Points	Class	Mortality
5–6	A	10%
7–10	B	30%
10–15	C	76–82%

3.4. Intraoperative anesthetic management

A systematic **review on perioperative evaluation and management of patient with cirrhosis** concluded that the overall intraoperative objectives are **to preserve hepatic blood flow and oxygen supply** **while minimizing exposure to hepatotoxic drugs to prevent more liver harm**(6)**1a.**

According to the **Intravenous Hypnotic Regimens (IHR)** in patients with liver disease guideline, opioids are successfully used in patients with liver diseases, and **fentanyl is the medication of choice** for these patients when used at an average dose, liver oxygen content and liver blood flow are not impaired [18]**1a.**

Analgesics are often metabolized in the liver and removed by the kidneys. **To avoid drug accumulation** in patients with liver disease, **lower opioid doses** with longer periods should be used. Long-acting opioids like morphine and mepiridine should be avoided, but **shorter-acting opioids like live fentanyl** are well tolerated when given in small doses and titrated to effect [2]**1a.**

Avoid mepiridine in patients with liver disease because it reduces clearance and increases the risk of **seizures.** **Morphin**e has been shown to have reduced clearance and improved oral bioavailability in patients with liver disease, and it should be avoided to prevent accumulation and increased risk of adverse reactions. If morphine is needed, the intervals between doses should be increased [23]**1a.**

For patients with **liver failure**, a few opioids are favored. At lower doses and longer dosing times, tramadol should be used with caution. Fentanyl is the safest drug because it does not have a toxic metabolite and it does not normally need dosage changes [23]**1a.**

Perioperative risk factors in patient with liver disease **undergoing non-hepatic surgery** guideline concluded that **Inhalational agents isoflurane, desflurane and sevoflurane** undergo hepatic metabolism, extent of which is 0.2% for isoflurane, 2%–4% for enflurane, and 20% for halothane presumably, this **leads to a lesser incidence of drug-induced hepatitis.** Therefore, isoflurane has become the inhalation **agent of choice** in patients with liver disease. Remembering that halothane can cause lethal hepatitis in patients who undergo general anesthesia, so; this drug should be avoided.

Rocuronium and vecuronium, amino steroid neuromuscular agents, are metabolized in part by the liver, and their term of action can be extended in liver failure. **Peripheral nerve stimulators** should be used to titrate these drugs to impact. **Atracurium and *cis*-atracurium**, two benzylisoquinolinium neuromuscular agents, are unaffected by liver disease**.** Succinylcholine is metabolized by plasma cholinesterase, a liver enzyme; despite the fact that succinylcholine has a long time of action, it is not clinically important

In cases of **advanced liver cirrhosis**, the dose of intravenous anesthetic agent **thiopental** should be decreased and propofol is the preferred intravenous anesthetic agent.

Normal monitoring of arterial blood gases, lactate, glucose, electrolytes, and coagulation status is recommended for all patients (as recommended by the AAGBI), but intrusive monitoring of both arterial and central venous pressure are recommended for major surgery and regular monitoring of arterial blood gases, lactate, glucose, electrolytes, and coagulation status are also recommended for major surgery. It's also a good idea to keep track of patients core body temperature, neuromuscular block, and urine production [22]**1a.**

4. Postoperative anesthetic management

An evidence based guideline on surgery in patients with liver disease **concluded** that urine **output must be monitored carefully as intra-operative fluid shift** can lead to poor renal perfusion which if not detected early and treated aggressively can lead to acute renal failure. In these patients, it is important to monitor the CVP, pulse, BP, and oxygen saturation.

An evidence-based guideline on **non-hepatic abdominal surgery** in patients with **cirrhotic liver disease** suggested that many of the postoperative cirrhotic patient's treatment techniques are similar to those used before surgery**: avoid liver-metabolized drugs**, **control intravascular volume**, **avoid metabolic disturbances**, and use **lactulose for hepatic encephalopathy (HE) and opioid-induced constipation.** If the patient will remain null per os (NPO), parenteral feeding should be started as soon as possible.

Opioid-induced constipation should be avoided with the use of laxatives, and these patients should be closely monitored for symptoms of sedation and encephalopathy. In patients who are intolerant to opiates due to advanced disease and a high risk of HE, regional analgesia in the form of local infiltration or transverse abdominis plane block is a choice. Only after coagulopathy has been corrected with INR 100 000/mm3, epidural analgesia can be considered.

According to a guideline on the outcome of **abdominal surgery** in patients with cirrhosis, postoperative management should preferably be done in the ICU, at least for the first 24 h, particularly in CTP B and C. It's crucial to monitor for potential complications, which vary depending on the severity of the LC and the type of operation.

Any drug that is nephrotoxic should be avoided. Starting oral feeding as soon as possible is recommended to help avoid SBP. Following surgery, the patient's liver, renal, and coagulation profiles, as well as blood sugar levels, should be closely monitored in order to diagnose early liver or renal failure. Any decline in liver or renal function could indicate sepsis, and broad-spectrum antibiotics should be given to these patients with a low threshold. Since the liver metabolizes the bulk of opioids, their dosage should be decreased.