Anesthesia Review

HIGHLIGHTS

- Extensive coverage of surgical and anesthetic aspects of management of individual diseases
- Covers most important examination topics

2nd Edition

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JAYPEE

Contents

7 CHAPTER

Anesthesia and Liver

FUNCTIONS OF THE LIVER

Introduction

Liver is a vital organ and performs myriad metabolic functions.

I. Reservoir for Blood Volume

❖ Vasculature of the liver:
- Most vascular organ in the body
- Receives almost one-third of the total cardiac output
- 1 mL blood is supplied per gram of liver tissue
- This large volume of blood forms the splanchnic reservoir
- Low resistance of the hepatic sinusoids allows it to store large volumes of blood
- Has a *unique dual blood supply*
- Approximately 75% of the total hepatic flow is through the portal vein
- Remaining 25% of the blood flow is supplied through hepatic artery
- Hepatic artery originates in the celiac trunk of abdominal aorta
- Portal vein is formed by union of superior mesenteric vein and splenic vein
- Portal vein transmits entire venous drainage of pre-portal splanchnic beds to the liver

❖ Mechanisms of intrinsic regulation of hepatic blood flow:
- ***Hepatic arterial buffer response (HABR):***
  - Most important intrinsic mechanism
  - Changes in portal vein flow cause reciprocal changes in hepatic artery flow
  - Mediated through adenosine from peripor-tal system
  - Adenosine in a potent vasodilator
  - By manipulating levels of adenosine, hepatic arterial tone can be altered
  - At its maximum, HABR can double hepatic arterial flow
  - Endotoxemia and splanchnic hypoperfusion can abolish HABR
- Metabolic control:
  - Mediated by changes in pH or pO_2 of portal venous blood
  - This causes increase or decrease in hepatic arterial flow
  - Metabolic and respiratory changes in acid base balance also can modulate hepatic blood flow
- Pressure-flow autoregulation:
  - Myogenic responses of vascular smooth muscle also regulate hepatic flow
  - Hypertensive responses cause an increase in myogenic tone
  - This regulates detrimental increases in hepatic flow
  - Hypotensive responses likewise cause a decrease in myogenic tone
  - This regulates decreases in hepatic flow
  - Thus, hepatic flow is maintained during hypotensive episodes

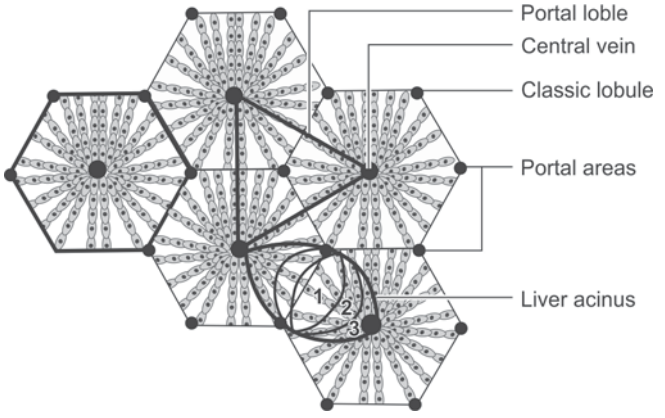


Fig. 1: Portal microstructure.

- ❖ Mechanisms of extrinsic regulation of hepatic blood flow:
  - Neural control:
    - Neural control is exerted via:
      - Vagus nerve
      - Phrenic nerve
      - Splanchnic nerve (post-ganglionic sympathetic fibres from T_5-T_{11})
    - Decreases in sympathetic tone increases splanchnic reservoir volume
    - Increases in sympathetic tone decreases splanchnic reservoir volume
    - Hepatic arterial system has α_1, α_2, β_2 and D_1 receptors
    - Portal venous system has only $\alpha_{1\ and}$ D_1 receptors
  - Humoral control:
    - Exerted via glucagon, angiotensin II and vasopressin
    - Glucagon causes relaxation of hepatic arterial smooth muscle
    - Angiotensin II causes constriction of hepatic and portal beds
    - Vasopressin increases hepatic arterial and decreases portal venous resistance
    - Due to this profile, vasopressin maybe used in treating portal hypertension

II. Role in Metabolism

- ❖ Protein metabolism:
  - Protein breakdown:
    - Liver plays central role in production and breakdown of amino acids
    - Amino acids are broken down to ketoacids, glutamine and ammonia by transamination
    - ***Krebs- Henseleit cycle*** removes ammonia and other nitrogenous wastes from the body
  - Protein synthesis:
    - Almost 15% of the proteins synthesized by the liver is albumin
    - Healthy adults produce around 12–15 g of albumin per day
    - Factors affecting albumin synthesis include:
      - Plasma oncotic pressure (main regulator)
      - Dietary amino acids
      - Hormones
    - Liver also synthesizes other important proteins like:
      - Procoagulants
      - Hormones
      - Cytokines and chemokines
      - Acute phase reactants
      - Transport proteins
- ❖ Carbohydrate metabolism:
  - Glycogen:
    - Liver regulates carbohydrate metabolism mainly through glycogen
    - In the fed state, glucose is polymerized to glycogen and stored
    - This is mediated through glycogen synthase
    - In the starving state, glycogen is depolymerized to glucose
    - This is mediated via glycogen phosphorylase
  - Gluconeogenesis:
    - When glycogen stores are exhausted, hepatic gluconeogenesis is used
    - Substrates for gluconeogenesis:
      - Lactate
      - Glycerol from hydrolysis of triglycerides
      - Alanine, glutamine from protein catabolism
- ❖ Lipid metabolism:
  - Fatty acid synthesis:
    - Dietary fatty acids reach liver in the form of chylomicrons
    - These are processed into triglycerides through esterification
    - These maybe stored in the liver, in the form of triglycerides
    - Alternatively, they can be transported to other organs as lipoproteins
    - In the presence of sufficient glycogen, even glucose may be stored as triglycerides
  - Fatty acid metabolism:
    - Mainly via β-oxidation pathways
    - Glucagon activates this pathway and stimulates lipolysis
    - Insulin inhibits β-oxidation and fatty acid metabolism
    - Fatty acids are sequentially cleaved through β-oxidation to yield acetyl-CoA.

III. Enterohepatic Circulation

- ❖ Bile is formed by hepatocytes and is secreted eventually into the duodenum
- ❖ Bile plays an important part in absorption of molecules with minimal acqueous solubility

- Constituents of bile:
  - Water (97%)
  - Conjugated bile salts (< 1%)
  - Cholesterol, fatty acids, phospholipids
  - Lecithin
  - Conjugated bilirubins
  - Electrolytes, inorganic salts
  - Alkaline phosphatase
- Bile salts are formed from cholesterol by hepatocytes
- Primary bile salts are chenodeoxycholic acid and cholic acid
- These are secreted into the duodenum and travel through the intestine
- These are then absorbed from the terminal ileum and metabolized to secondary bile acids
- Both types of bile acids reach the liver again via portal venous blood
- This forms the enterohepatic circulation
- Through this system, about 95% of the bile acids are conserved

IV. Coagulation System

- Procoagulants:
  - Most of the procoagulants are synthesized in the liver
  - Factors synthesized in the liver are Factors I, II, V, VII, IX, X, XI, XII, XIII
  - *Exceptions* are factors III, IV (calcium) and VIII (von-Willebrand factor)
- Regulators of coagulation:
  - Liver also synthesizes regulators of coagulation
  - These are:
    - Protein C
    - Protein S
    - Protein Z
    - Plasminogen activator inhibitor (PAI)
    - Antithrombin III
- Posttranslational modification:
  - Vitamin K dependent factors undergo post translational modification in the liver
  - This involves γ-carboxylation of glutamate residues at the amino terminus
  - This process creates procoagulants capable of forming complexes with calcium
  - Thus, procoagulants are primed for participation in the coagulation cascade
  - Vitamin K dependent factors include:
    - Factor II
    - Factor VII
    - Factor IX
    - Factor X
    - Protein C and S

V. Bilirubin Metabolism

- Main source of bilirubin is heme metabolism
- Approximately 300 mg of bilirubin is produced by the body everyday
- 80% of bilirubin is derived from the phagocytosis of RBCs
- This is done by macrophages in the liver, spleen and bone marrow
- Reticuloendothelial cells extract protein from hemoglobin and convert heme to bilirubin
- Bilirubin is transported to the liver in conjugation with albumin
- Hepatocytes extract the bilirubin and conjugate it with glucuronic acid
- These conjugates are secreted in the bile for excretion via the gut

VI. Regulation of Hematogenous Endocrine Mediators

- Liver plays an important role in metabolism of hormones and hormone binding proteins
- *Synthesis*: Hormones synthesized by hepatocytes are:
  - Angiotensinogen
  - Thrombopoietin
  - Insulin like growth factor I (IGF-I)
  - Activation of thyroxine (T4) to triiodothyronine (T3)
- *Inactivation*: Hormones inactivated by the liver are:
  - Aldosterone
  - Anti-diuretic hormone
  - Estrogens, androgens
  - Insulin
  - Thyroxine (T4)

VII. Modulator of Immune and Inflammatory Processes

- Liver is the largest reticuloendothelial organ in the body

- ❖ Kupffer cells play an important role in immune modulation
- ❖ Kupffer cells form almost 10% of the total liver mass
- ❖ Functions of Kupffer cells are:
  - Degradation of toxins
  - Phagocytosis of bacteria
  - Processing antigens
  - Attenuation of inflammatory response by removing inciting agents from bloodstream
  - Inciting inflammatory response by releasing cytokines, chemokines and leukotrienes

VIII. Metabolism and Excretion of Xenobiotic Molecules

- ❖ Hepatocytes eliminate drugs through 3 phase reactions:
- ❖ Phase I:
  - Uses CYP and mixed function oxidases
  - This increases polarity of the drugs by insertion of polar groups
  - Groups inserted include:
    - Hydroxide group
    - Amine group
    - Sulfhydryl group
- ❖ Phase II:
  - Conjugates phase I metabolites with water soluble substrates
  - This increases polarity of the drugs
  - Substrates used are:
    - Glucuronic acid
    - Glutathione
    - Sulphates
    - Acetates
- ❖ Phase III:
  - Involves excretion of the metabolites into biliary canaliculi
  - Uses specific molecules called *ATP-Binding Cassette (ABC) transport proteins*

LIVER FUNCTION TESTS

Introduction

- ❖ Refers to standard test panels used to detect hepatobiliary status
- ❖ Misnomer as none of the tests measure any specific liver function

I. Detection of Hepatic Injury

- ❖ Aminotransferases:
  - Refers to two enzymes:
    - Alanine aminotransferase (ALT, SGPT)
    - Aspartate aminotransferase (AST, SGOT)
  - These enzymes are involved in gluconeogenesis
  - ALT is highly specific, compared with AST as it is a cytoplasmic liver enzyme
  - AST isoenzymes are found in extrahepatic tissues like:
    - Brain, heart
    - Skeletal muscle
    - Kidney, pancreas
  - Both these enzymes are localized to acinar zone 1
  - These enzymes are released into circulation as a result of hepatocellular injury
  - Normal levels of these enzymes are:
    - AST 10–40 U/L
    - ALT 7–56 U/L
  - Mild elevation:
    - Levels between 100–249 IU/L
    - Causes of mild elevation:
      - Steatosis, alcohol consumption
      - Medications
      - Hemochromatosis
      - Cholestasis
      - Chronic viral hepatitis
      - Neoplasms, cirrhosis
  - Moderate elevation:
    - Levels between 250–999 IU/L
    - Causes of moderate elevation:
      - Acute viral hepatitis
      - Drug induced liver injury
      - Acute exacerbations of chronic liver disease
  - Severe elevation:
    - Levels between 1000- 1999 IU/L
    - Often due to acute hepatitis superimposed on chronic active liver disease
  - Extreme elevations:
    - Levels above 2000 IU/L
    - Often due to massive hepatic necrosis
    - Causes of extreme elevation:
      - Fulminant viral hepatitis
      - Paracetamol poisoning
      - Shock liver, hypoxic hepatitis
      - Autoimmune hepatitis
      - Acute biliary obstruction

- ❖ Lactate dehydrogenase:
  - Normal levels 70–250 IU/L
  - Elevation in LDH levels can be due to hepatic and extrahepatic causes
  - Concomitant elevation of ASL and ALT when due to hepatocellular injury
  - Thus, rarely yields more information than that provided by AST and ALT levels
  - Hepatic causes of elevated LDH:
    - Fulminant hepatitis
    - Paracetamol poisoning
    - Hypoxic hepatitis
    - Malignancies
  - Extrahepatic causes of elevated LDH:
    - Hemolysis, rhabdomyolysis
    - Tumor necrosis, renal infarction
    - Acute cerebrovascular accident
    - Myocardial infarction
- ❖ Glutathione-S-transferase:
  - Specific for some patterns of drug induced liver injury
  - Released rapidly after hepatocellular injury
  - Has a brief plasma $T_{1/2}$ of 90 minutes
  - GST localizes in acinar zone 3 (centrilobular region)
  - This zone has cells with highest susceptibility to injury from hypoxia or drugs
  - More sensitive than AST and ALT for centrilobular necrosis

II. Assessment of Protein Synthesis

- ❖ Serum albumin:
  - Indicates effectiveness of protein synthetic function of the liver
  - Normal serum concentration is 3.5-5.5 g/dL
  - In chronic liver diseases, protein synthetic function is diminished
  - This causes low plasma albumin levels
  - Plasma albumin has a $T_{1/2}$ of nearly 3 weeks
  - Changes in albumin level is seen days after cessation of protein synthetic function
  - Other causes of hypoalbuminemia:
    - Increased albumin catabolism
    - Circulatory overload states
    - Maldistribution of albumin
    - Renal albuminuria (nephrotic syndrome)
    - Protein losing enteropathies
- ❖ Prothrombin time:
  - Prothrombin time is used to monitor patients with acute liver dysfunction
  - Only 20–30% of normal factor activity is required for normal coagulation
  - Thus prolonged PT usually reflects severe liver disease
  - Procoagulants derived from the liver have a shorter $T_{1/2}$ compared with albumin
  - Factor VII has the shortest $T_{1/2}$ among hepatic procoagulants (4–6 hours)
  - This is reflected as a high PT, occurring soon after onset of hepatic dysfunction
  - Thus, PT start to fall within 24 hours of onset of severe liver dysfunction
  - Prolongation of PT more than 3–4 sec from control is significant
  - This usually corresponds to an INR> 1.5

III. Detection of Cholestatic Disorders

- ❖ Alkaline phosphatase:
  - Lacks specificity for hepatobiliary diseases
  - Normal values range from 40–112 IU/L
  - Extrahepatic sources of ALP are:
    - Bone, leukocytes
    - Intestines, kidneys
    - Placenta, neoplasms
  - Usually is only mildly elevated or normal in liver parenchymal diseases
  - Marked elevation of ALP suggests conditions causing biliary obstruction
  - ALP has a $T_{1/2}$ of almost 1 week
  - Thus, serum ALP levels remain elevated for days after bile flow has normalized
- ❖ Gamma glutamyl transpeptidase (GGT):
  - It is a canalicular enzyme
  - Normal range between 10–48 IU/L
  - Compared with ALP, it remains normal in disorders of the bone
  - Thus, elevated GGT suggests that elevated ALP is of hepatic origin
  - Conditions causing elevated GGT levels:
    - Alcoholism
    - Medications: anticonvulsants, H2 receptor blockers
    - Prostrate disease
    - Obesity, diabetic nephropathy, HTN

- Bilirubin:
  - Normal serum bilirubin is less than 1.5 mg/dL
  - Jaundice is readily discernible at serum bilirubin levels above 4 mg/dL
  - Scleral icterus can be demonstrated at bilirubin levels above 3 mg/dL
  - Conjugated hyperbilirubinemia:
    - Occurs when conjugated bilirubin is not effectively eliminated
    - Conjugated bilirubin is water soluble
    - Thus, this is associated with presence of urinary urobilinogen
    - Causes:
      - Dubin- Johnson syndrome
      - Rotor syndrome
      - Acquired intrahepatic cholestasis
      - Extrahepatic biliary obstruction
  - Unconjugated hyperbilirubinemia:
    - Seen when bilirubin production exceeds ability of liver to conjugate it
    - Unconjugated bilirubin is not water soluble
    - Thus, urinary urobilinogen is absent
    - Causes:
      - Gilbert syndrome
      - Crigler-Najjar syndrome
      - Hemolysis
      - Acquired defects in bilirubin conjugation

IV. Quantitative Liver Function Tests

- Hepatic clearance:
  - Hepatic clearance of a substance reflects the total hepatocellular mass
  - Substances used are indocyanine green and bromsulphalein
- Caffeine clearance:
  - Patients take an oral dose of caffeine (150- 300 mg)
  - Caffeine metabolites in saliva are measured for upto 24 hours
- Aminopyrine breath test:
  - Not commonly used in clinical practice
  - Patient is asked to inhale ^{14}C- labeled aminopyrine
  - Amount of ^{14}C-labelled CO_2 in patients breath is measured for 2 hours
  - Low levels of carbon dioxide indicates impaired liver function
- Monoethylglycinexylidide (MEGX) assay:
  - IV lidocaine is given in a dose of 1mg/kg
  - 15 minutes later, a blood sample is obtained and assayed for MEGX
- Other tests:
  - Galactose elimination capacity
  - Antipyrine clearance

V. Measurement of Hepatic Blood Flow

- Clearance techniques:
  - Uses indirect Ficks principle to approximate hepatic blood flow
  - Valid for substances with a high hepatic clearance
  - Substances used to study clearance are:
    - Indocyanine green dye
    - Propranolol
    - Lidocaine
    - Colloidal particles- gold 198
  - Indocyanine green extraction is one of the *most reliable* techniques
  - After injection of the substance, time- radioactivity curve is plotted
  - Area under the curve is used to estimate hepatic blood flow
  - Severe liver disease renders these tests as unreliable
- Indicator dilution techniques:
  - Unlike clearance techniques, these tests are reliable in a severe liver disease
  - Radiolabeled indicator like iodinated albumin is injected into the spleen
  - Indicator dilution is measured from samples obtained from the hepatic vein
  - Indicator dilution curve is used to estimate hepatic blood flow
- Direct measurements:
  - Uses electromagnetic flow probes placed on hepatic A or portal V
  - Surgical access is used to place the probes
  - Probe is left in-situ after implantation procedure
  - Telemetry is then used to measure hepatic blood flow

VI. Radiological and Endoscopic Methods

- Procedures used commonly to evaluate hepatobiliary disorders are:
  - Percutaneous transhepatic cholangiography (PTHC)
  - Endoscopic retrograde cholangiopancreatography (ERCP)
- Percutaneous transhepatic cholangiography (PTHC):
  - Evaluates intrahepatic bile ducts of patients with unexplained hepatic cholestasis
  - Dilated intrahepatic ducts suggest mechanical occlusion of these ducts
  - When dilatation is absent, most likely cause is parenchymal disease
- Endoscopic retrograde cholangiopancreatography (ERCP)
  - ERCP provides intraductal access to biliary tree and pancreatic duct
  - Mainly used to diagnose and treat extrahepatic biliary disorders
  - Less invasive compared with surgery
- Esophagogastroscopy:
  - Used to evaluate submucosal varices in those with portal hypertension
  - Varices may be treated with banding if indicated
- Splenoportography:
  - Evaluates splenic and portal veins
  - Allows evaluation of extent of portosystemic shunts

VII. Tests for Specific Diseases

- Serological tests to identify microbial and autoimmune causes:
  - Viral etiology:
    - Hepatitis A, B, C, D, E and F
    - Hepatotropic viruses A, B, C, E
    - Cytomegalovirus
    - Epstein-Barr virus
  - Autoimmune etiology:
    - Anti-asialoglycoprotein antibodies useful for autoimmune hepatitis
    - Anti-mitochondrial antibodies characteristic in primary biliary cirrhosis
    - Primary sclerosing cholangitis:
      - Anti-smooth muscle antibodies
      - Anti-nuclear antibodies
- Genetic tests to identify hereditary metabolic disorders
- Tumor marker assays for malignancies:
  - Plasma α-fetoprotein (AFP):
    - Highly specific for hepatocellular carcinoma (HCC)
    - Sensitivity ranges from 50–90%
  - Plasma γ-carboxylated prothrombin levels:
    - HCC cells make procoagulants without γ-carboxylating them
    - High levels of des-γ-carboxylated, vitamin K dependent procoagulants occurs in HCC

POSTOPERATIVE JAUNDICE

Introduction

- Most cases of postoperative jaundice manifest within 3 weeks of surgery
- Most common causes of postoperative jaundice are:
  - Resorption of hematomas
  - Hemolysis following blood transfusion

Etiology

- Prehepatic causes:
  - Transfusion related:
    - Senescent RBC breakdown
    - Hemolytic reactions
    - Multiple blood transfusions
  - Hemolysis due to prosthetic valves:
    - Caged ball valves- Starr- Edwards valve
    - Multiple prosthetic valves
    - Prosthetic valve endocarditis
    - Periprosthetic leaks
  - Resorption of massive hematomas:
    - Retroperitoneal hematomas
    - Intraabdominal hematomas
  - Drug induced erythrocyte lysis:
    - Thiopentone
    - Acetaminophen, ibuprofen
    - Penicillin and derivatives
    - Cephalosporins
    - Ranitidine
    - Procainamide, hydralazine
    - Insulin
    - Intravenous contrast media
- Hepatic causes:
  - Preexisting liver disease

- Gilberts syndrome, Crigler-Najjar syndrome
- Dubin- Johnson syndrome, Rotor syndrome
- Drug induced hepatitis:
  - Allopurinol, bleomycin, cyclosporine, cisplatin
  - Amiodarone, phenytoin, propylthiouracil
  - Amoxicillin, erythromycin, ketoconazole
  - Diclofenac, naproxen, indomethacin, piroxicam
  - Statins
  - Halothane hepatitis
  - Total parenteral nutrition
- Ischemic or hypoxic injury
- Viral hepatitis
- Intrahepatic cholestasis:
  - Sepsis
  - Total parenteral nutrition
  - Acalculous cholecystitis

❖ Posthepatic causes:
- Postoperative cholecystitis
- Extrahepatic cholestasis:
  - Retained common bile duct stone
  - Bile duct injury
- Postoperative pancreatitis

Pathophysiology

❖ Three events lead to postoperative jaundice
❖ Overproduction of bilirubin:
- Prehepatic cause of postoperative jaundice
- Occurs as bilirubin production exceeds livers ability to conjugate it
- Thus, associated with unconjugated hyperbilirubinemia
- Hemolysis can lead to anemia, hemoglobinuria and renal failure
- Usually occurs as a result of:
  - Drug induced erythrocyte destruction
  - Mechanical RBC destruction
- Laboratory findings:
  - Anemia
  - Peripheral smear shows:
    - Fragmented RBCs
    - Reticulocytosis
  - Indirect hyperbilirubinemia
  - Positive direct antiglobulin test
  - Low serum haptoglobin
  - Urinary haptoglobin

❖ Direct hepatocellular injury:
- Hepatic cause of postoperative jaundice
- It is associated with conjugated hyperbilirubinemia
- Marked elevations in serum aminotransferases is also seen
- Usually occurs as a result of:
  - Drug induced hepatitis
  - Cardiogenic, non-cardiogenic shock
  - Sepsis, systemic inflammatory response syndrome
  - Viral hepatitis
- Laboratory findings:
  - Grossly elevated serum transaminases
  - Conjugated hyperbilirubinemia
  - Increased GGT, 5′ nucleotidase
  - Increased alkaline phosphatase

❖ Extrahepatic obstruction:
- Posthepatic cause of postoperative jaundice
- Occurs due to obstruction of the bile duct, preventing bilirubin excretion
- Ability of the liver to conjugate bilirubin, however, is preserved
- Thus, it is associated with conjugated hyperbilirubinemia
- Ultrasonography useful in diagnosing extrahepatic obstruction
- Acute renal failure:
  - High incidence of acute renal failure seen with obstructive jaundice
  - Seen in almost 8- 10% patients with postoperative obstructive jaundice
  - Incidence of ARF coincides with the degree of hyperbilirubinemia
  - Obstructive jaundice results in low levels of intestinal bile acids
  - This causes increased resorption of gut endotoxins
  - This stimulates release of inflammatory mediators like endothelin
  - Endothelin causes potent renal vasoconstriction
  - Thus, renal perfusion is reduced, causing ARF

- Laboratory findings:
  - Conjugated hyperbilirubinemia
  - Increased GGT, 5′ nucleotidase
  - Increased alkaline phosphatase
  - Minimal or no elevation in Transaminases
  - Presence of bilirubin in urine

Grading of Severity

- Mild postoperative jaundice: Serum bilirubin < 4 mg/dL
- Severe postoperative jaundice: Serum bilirubin >4 mg/dL.

Classification of Postoperative Jaundice

- Early postoperative jaundice (< 3 weeks):
  - Hemolysis
  - Blood transfusions
  - Resorption of hematoma
  - Gilberts syndrome
  - Hypotension, hypovolemia
  - Infection, sepsis
  - Drug induced
  - Acute viral hepatitis
  - Bile duct injury
  - Hepatic artery ligation
  - Postoperative cholecystitis
  - Postoperative pancreatitis
- Delayed postoperative jaundice (> 3 weeks):
  - Drugs
  - Blood transfusion
  - Total parenteral nutrition.

Treatment

- Prehepatic causes: Treat underlying cause
- Hepatic causes:
  - Broad spectrum antibiotics
  - Adjustment of TPN
  - Restoration of hepatic perfusion
  - Removal of offending medications
  - Antiviral agents
  - Supportive care
- Posthepatic causes:
  - ERCP, sphincterotomy and stone removal for common bile duct stones
  - ERCP, balloon dilatation, stent placement for biliary strictures
  - Surgical correction for those strictures not amenable to endoscopic interventions

HALOTHANE HEPATITIS

Definition

Jaundice occurring in a patient who is previously exposed to halothane within 3 weeks with fever, rashes and lab evidence of raised liver enzymes like SGOT, SGPT and antibodies.

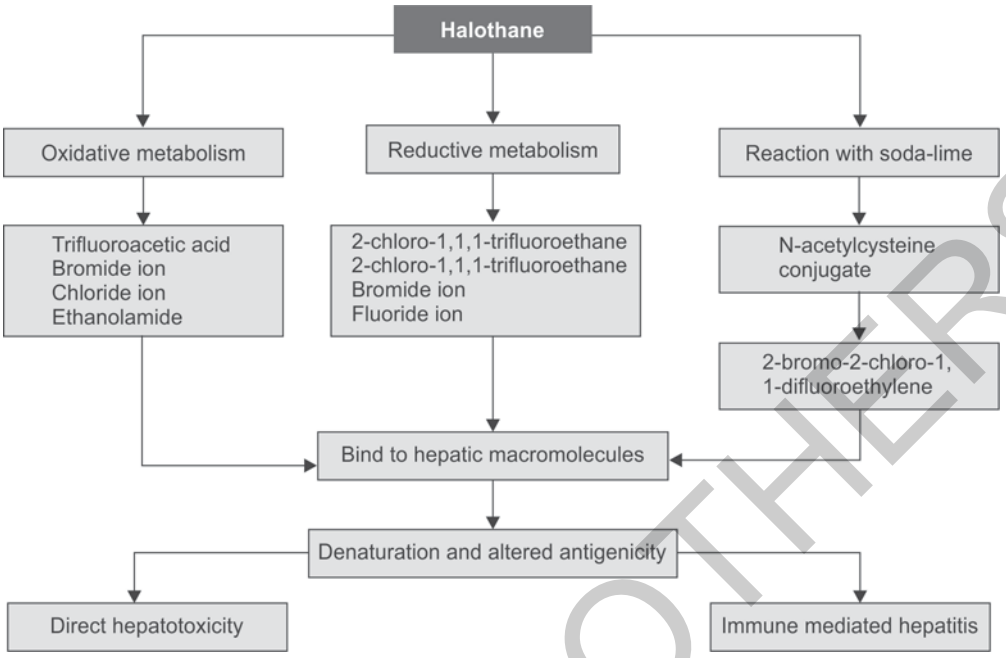
Incidence

- Male:female: 1:2
- Most commonly seen in middle age group
- Relatively rare in children
- Incidence in children: 1:1,00,000–2,00,000 patients
- Type I halothane hepatitis: 25–30%
- Type II halothane hepatitis: 1:6000–35000 patients

Classification

- Type I halothane hepatitis:
  - Mild form
  - Relatively common (25–30% of those who receive halothane)
  - Results from reductive (anaerobic) biotransformation of halothane
  - Benign features
  - Self limiting disease
  - Mild rise in serum transaminase and glutathione-S-transferase
  - Altered postoperative drug metabolism
  - Not characterized by jaundice or clinically evident hepatocellular disease
  - Does not occur after exposure to other inhalational agents
- Type II halothane hepatitis:
  - Severe form
  - Relatively uncommon
  - Appears to be immune mediated
  - Occurs due to antibody formation to oxidative metabolites of halothane
  - Fulminant features
  - Causes massive centrilobular necrosis
  - Clinically fever, jaundice, grossly elevated serum transaminases
  - Results in fulminant liver failure
  - Fatality rate of 50%
  - Can occur after exposure to other volatile anesthetics like enflurane.

Metabolism and Mechanism



Risk Factors

- Multiple exposures at intervals < 6 weeks (most important)
- Prior history of post anesthetic fever/jaundice
- Duration: prolonged exposure, major surgeries
- Obesity, middle age, pregnancy
- Female sex
- Genetic predisposition
- Enzyme induction (alcohol/barbiturate abuse)
- Drug allergy, recent viral hepatitis.

Predisposing Factors

- Pregnancy
- Viral hepatitis
- Burns
- Hypoxia, hypercarbia.

Clinical Features

- Type I hepatotoxicity is usually clinically silent
- Type II hepatotoxicity:
  - Onset 5-7 days following exposure
  - Onset can occur upto 4 weeks post surgery
  - High grade fever lasting for 3–14 days
  - Jaundice:
    - Onset usually occurs 7–10 days after exposure
    - Onset can occur earlier within 1-2 days, if prior exposure to halothane
  - Nausea, vomiting, anorexia
  - Chills, myalgia, rash
  - Moderate liver enlargement with tenderness
  - Fulminant liver failure ensues.

Lab Findings

- Leucocytosis, eosinophilia
- Raised serum bilirubin
- Raised serum ALT, AST and alkaline phosphatase
- Increased prothrombin time
- Increased GST > 2 is specific index
- ELIZA may detect halothane related antibodies
- Liver biopsy: widespread centrilobular hepatocellular necrosis.

Guidelines for Safe Use

- Prefer TIVA
- Avoid halothane if:
  - Age more than 70 years
  - Obese females
  - Preexisting liver disease/biliary surgery
  - If family history of unexplained jaundice after halothane
  - Recent halothane exposure within 6 weeks.

Anesthesia Review

Salient Features

- Incorporatiom of latest guidelines
- Inclusion of new chapters on transplant anesthesia, ophthalmic anesthesia and renal disorders
- Comprehensive coverage of anesthetic management of various clinical conditions and surgeries
- Easy to replicate pattern for exams
- Details of salient trials for each topic have been added.

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He completed his schooling from National Public School, Bengaluru in 2001 as school topper. He was given a special award for his outstanding performance in biology by Sri Murali Manohar Joshi, the then Minister for Science and Technology, sponsored by the Department of Biotechnology, Government of India. He was also awarded a scholarship by the Central Board of Secondary Education for being the top 50 students in the country during academic year 2000-01.

After completing his undergraduation in medicine from Sri Devaraj Urs Medical College, Kolar, Karnataka, he went on to pursue postgraduation from Sri Sathya Sai Institute of Higher Medical Sciences, Puttaparthi. Subsequently, he joined Manipal Hospitals, and completed his cardiac anesthesia fellowship with a special focus on pediatric cardiac anesthesia. He then joined G Kuppuswamy Naidu Memorial Hospital and working till the present.

It was during his postgraduate years in Puttaparthi, that he realized what a strong influence a teacher can have on his students in motivating them and also shaping their character. The pursuit of DNB as a postgraduation degree had been an arduous task in the past, owing to the difficult work schedule and high expectations from the student at the time of examinations. This textbook has been written to make life easier for those students taking the DNB examination.

A simple person by nature and habit, it is his love and dedication to his profession that has earned him the respect of his colleagues and peers. An academician at heart, the art of teaching only naturally comes to him. His analytical approach to problems and sheer hard work has enabled him to be a successful clinician and academician. His fundamental and basic approach to clinical problems parallels his belief in life, that of "Simple Living, High Thinking". He has been a source of constant motivation for his friends and juniors and has guided many of them successfully in their academic pursuits.

Apart from his academic and professional achievements, he is also a talented sportsperson and has represented his city, college and school at various levels in cricket and basketball. He is also an artist and a budding wildlife photographer. Having so many parallel interests, he is well known among the people close to him for his ability to multitask responsibilities.

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