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***IN THE NAME OF GOD***



# *Anesthesia and the Hepatobiliary System*

# *Hepatobiliary System*

- The liver is the largest organ in the body, and it plays a critical role in the:
- Homeostasis of many physiologic systems, including nutrient and drug metabolism,
- Synthesis of plasma proteins and critical hemostatic factors,
- Detoxification and elimination of many endogenous and exogenous substances.

# *VOLATILE ANESTHETICS*

- Although all volatile anesthetics decrease MAP and PBF,halothane has a more consistently dramatic impact on HABF.
- Halothane also reduces hepatic oxygen delivery and hepatic venous oxygen saturation.

# *Aminotransferases*

- ALT is a cytoplasmic enzyme that is highly specific to the liver, but the cytoplasmic and mitochondrial isoenzymes of AST are present in extrahepatic tissues as well.
- The AST/ALT ratio can be a useful measurement. When levels of both enzymes are elevated, a ratio of less than 1 is characteristic of nonalcoholic steatohepatitis.

# *Alkaline Phosphatase*

- Increases in serum alkaline phosphatase lack specificity as a diagnostic test for liver disease.
- However, in cholestatic disorders, an increased alkaline phosphatase concentration may indicate the bile salt–induced damage of hepatocyte membranes.
- Alkaline phosphatase has a serum half-life of approximately 1 week, so the level remains elevated for several days after resolution of biliary obstruction.

# *International Normalized Ratio*

- Prolongation of the international normalized ratio (INR) shows strong correlation with deteriorating hepatic function
- and has a reliable predictive value for survival of patients with liver disease.
- It can indicate impairment of hepatic synthetic function of coagulation factors, but evaluation of the entire coagulation cascade requires other testing.

# *Albumin*

- Albumin is the most abundant plasma protein. It is synthesized exclusively by hepatocytes and accounts for about 15% of all the protein synthesized by the liver.

# *Drug-Induced Hepatitis*

- A large variety of medications (analgesics, anticonvulsants, antibiotics, antihypertensives, and many others) can cause hepatic inflammation resulting from idiosyncratic reaction or dose-related toxicity.
- The onset of clinical signs is usually 2 to 6 weeks after exposure but can be delayed for as long as 6 months after starting the medication.
- Acetaminophen overdose is a well-known cause of hepatocellular toxicity and liver necrosis.
- Oral N-acetylcysteine administration within the first 8 hours after acetaminophen ingestion can dramatically reduce the extent of parenchymal injury

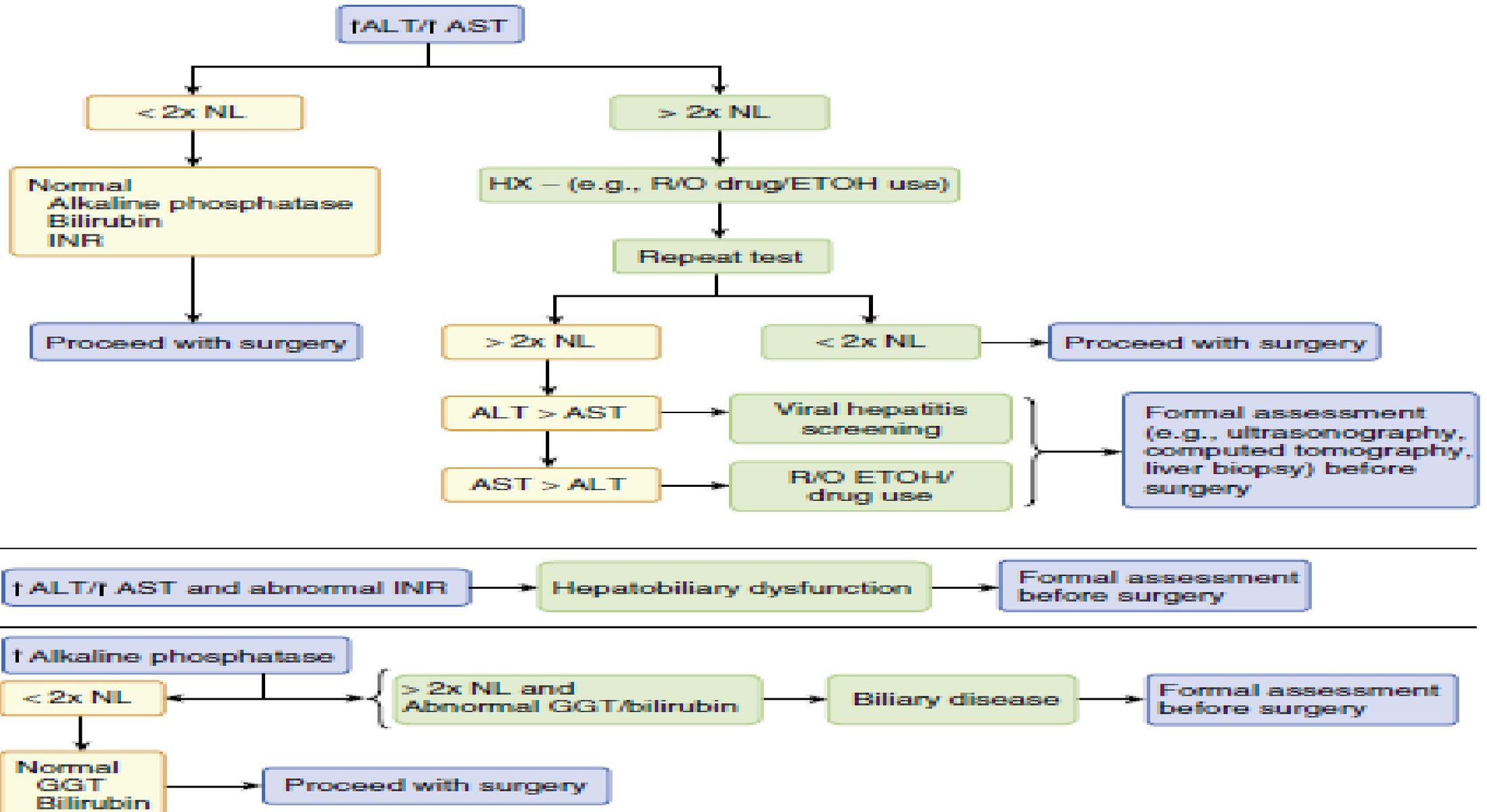
# *Halothane Hepatitis*

- In genetically susceptible individuals, certain volatile anesthetics (halothane, enflurane, isoflurane, desflurane) can elicit an immune-mediated hepatotoxic reaction.
- The most compelling evidence for this is the presence of circulating immunoglobulin G antibodies in the majority of patients with a diagnosis of halothane hepatitis.

# *Halothane Hepatitis*

- Halothane is the most common volatile anesthetic to cause hepatitis,
- Sensitized individuals may show cross-reactivity with other fluorinated volatile anesthetic agents.
- Sevoflurane is an exception

## Asymptomatic Patient with Abnormal Liver Test Results



## The most appropriate initial approach to a surgical patient with abnormal liver enzyme test results consists of:

- A detailed history and physical examination.
- Symptoms of fatigue, anorexia, nausea, vomiting, biliary colic, pruritus, fever, or dark-colored urine
- If, however, the patient is asymptomatic, the significance of abnormal enzyme test results can be questioned.
- The patient should be further asked about a history of associated diseases such as chronic hepatitis, a family history of Wilson disease, hemochromatosis,  $\alpha$ 1-antitrypsin deficiency, diabetes mellitus, hyperthyroidism or hypothyroidism, and previous transfusion history.
- All medications, including vitamins and herbal or other homeopathic remedies, should be reviewed for potential hepatotoxic side effects.
- The patient should be further questioned regarding alcohol, the presence of tattoos.

# PERIOPERATIVE MANAGEMENT OF PATIENTS WITH ASYMPTOMATIC OR CHRONIC LIVER DYSFUNCTION

- The goal of perioperative management of patients with asymptomatic elevations in aminotransaminase, alkaline phosphatase, or bilirubin levels or in patients with preexisting chronic liver disease is prevention of acute liver failure or further hepatic deterioration.

- Perioperative risks should be identified, and therapy should be directed to minimize hepatotoxicity and maximize hepatic oxygen delivery.

- In patients with cholelithiasis and biliary tract obstruction, the use of opiates should be limited preoperatively because these drugs can cause spasm of the choledochoduodenal sphincter (sphincter of Oddi) and a subsequent increase in intrabiliary tract pressure.
- These effects appear to be more pronounced for fentanyl, morphine, and meperidine and less severe for opiate agonist-antagonists.

# *ANESTHESIA FOR PATIENTS WITH DECREASED LIVER FUNCTION*

- Risk Assessment
- Patients with liver disease have a diminished physiologic reserve with which to respond to surgical stress and, as a result, are at increased risk for bleeding, infection, hepatic decompensation, and death.
- The extent of liver damage and the type of surgery are the two main determinants of perioperative risk.

# *Perioperative Care*

- Malnutrition and malabsorption are common in patients with advanced liver disease.
- Vitamin deficiencies and hypoalbuminemia have consequences for a number of organ functions and for pharmacokinetics as well.

# *Perioperative Care*

- Blood glucose monitoring is warranted, and a glucose infusion may be required during surgery.
- Hyponatremia despite an increased total body sodium content is common, because the degree of free water retention exceeds the degree of sodium retention.
- Administration of an aldosterone antagonist combined with consumption of a low-sodium diet help to correct this abnormality.
- In patients receiving diuretic therapy creatinine and electrolyte levels should be monitored.

# *PULMONARY COMORBIDITIES*

- Evaluation for the possible presence of hepatopulmonary syndrome and/or portopulmonary hypertension,
- Measurement of oxygen saturation with the patient breathing room air,
- Pulmonary function testing
- Measurement of pulmonary artery pressure

# *AIRWAY MANAGEMENT*

- Patients with chronic liver disease, especially those with ascites, frequently have:
  - increased gastric volumes and delayed gastric emptying.
  - Therefore, rapid-sequence induction of general anesthesia with cricoid pressure is prudent to facilitate endotracheal intubation and airway protection.

# *RENAL FUNCTION*

- Patients with cirrhosis are at increased risk of developing renal dysfunction.
- Gastrointestinal bleeding, hypotension, hypo perfusion, and administration of potentially nephrotoxic medications all increase the likelihood of acute renal deterioration.
- However, maintenance of euvolemia and renal replacement therapy are essential while the patient tries to recover from the underlying hepatic dysfunction.
- Patients benefit from monitoring for the presence of metabolic acidosis, particularly lactic acidosis, and correction of acid-base and electrolyte imbalances

# *CIRCULATION*

- The decreased systemic vascular resistance
- However, hypoalbuminemia and the resulting decrease in plasma oncotic pressure can cause fluid to shift to the interstitial space, so edema is common.
- In hypotensive patients, invasive monitoring (arterial line, cardiac output measurement), intravascular volume replacement, and vasopressor therapy may be necessary.
- In euvolemic, vasodilated patients, vasopressor administration can help restore blood pressure without compromising tissue perfusion.

# *COAGULATION*

Reduced procoagulant factor production typically result in excessive bleeding.

- Laboratory testing of clotting factor concentrations, fibrinogen levels, platelet counts, and other parameters, combined with clinical observation of bleeding and thromboelastography may be particularly helpful in diagnosing the cause of the bleeding and an optimal treatment plan.

# COAGULATION

- If malnutrition is present, vitamin K administration is helpful to enhance hemostasis via production of vitamin K–dependent clotting factors.
- Transfusion of fresh frozen plasma, cryoprecipitate, platelets, or a combination of these products may be indicated.
- A dysfunctional liver has a diminished capacity to metabolize citrate,, so monitoring of ionized calcium concentration is necessary.
- Intravenous calcium administration is often indicated.

# *EFFECT OF HEPATIC DYSFUNCTION AND HEPATOBILIARY DISEASE ON ANESTHETIC DRUG PHARMACOKINETICS*

- Liver disease may have a significant impact on drug metabolism and pharmacokinetics as a result of :
- Alterations in protein binding,
- Reduced levels of serum albumin and other drug-binding proteins,
- Altered volume of distribution because of ascites and increased total-body water compartments,
- Reduced metabolism secondary to abnormal hepatocyte function

- Cirrhosis and other forms of advanced liver disease predictably reduce the elimination of vecuronium, rocuronium, and mivacurium and prolong the duration of neuromuscular blockade, especially after repeated doses or the use of prolonged infusions.
- Atracurium and cisatracurium are not dependent on hepatic elimination and can be used without modification of dosing in patients with end-stage liver disease.
- Careful monitoring of neuromuscular function is recommended whenever muscle relaxants are used in this patient population.

★Thank you for your  
Attention★