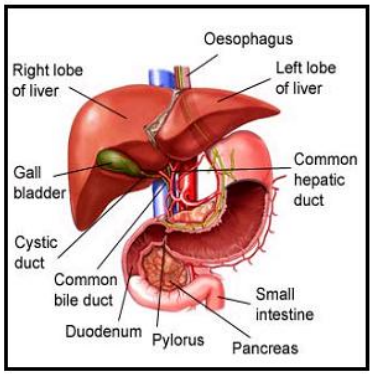
Liver Disease: Induction of Anesthesia

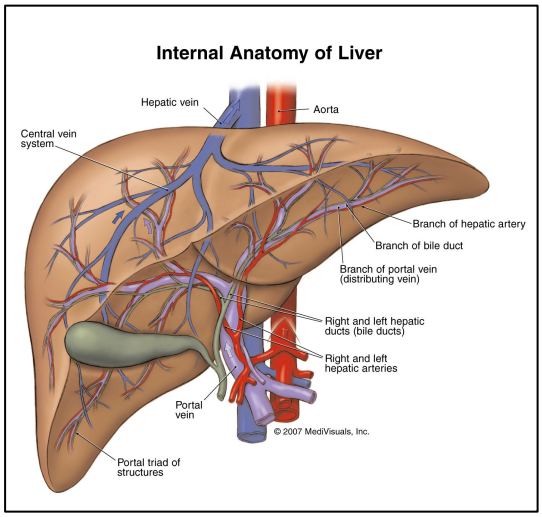
Anesthetic Pearls: The Anesthetic Implication of Liver Disease on the Induction of Anesthesia

- Hepatic dysfunction causes inconsistent changes in drug disposition.
- **Anesthetic titration to effect** is recommended for induction and maintenance.
- Anesthetic agents generally reduce hepatic blood flow.
- The cirrhotic liver is vulnerable to hypoxic damage and therefore careful attention must be given to maintain adequate hepatic perfusion and oxygen delivery.



A. Intravenous Induction Agents:

1. **Propofol** metabolized in the liver through conjugation to glucuronide and sulfate. Clearance of Propofol is through hepatic and extrahepatic metabolism. Liver disease prolongs Propofol elimination half-life but clearance appears to be unaffected.
2. Long and intermediate acting **Barbiturates** (Phenobarbital, Pentobarbital) have prolonged effects in liver disease because duration of action is determined by metabolism. However, short-acting barbiturates (Thiopental, Methohexital) duration of action is determined by redistribution. All barbiturates should be cautiously titrated with reduced bolus doses secondary to preexisting hypoalbuminemia that will reduce the degree of protein binding and increase active free fraction of the drug.
3. **Etomidate** metabolized by the liver through ester hydrolysis and N-dealkylation. Terminal half-life is decreased by drugs or conditions that reduce hepatic blood flow. Etomidate is 75% protein bound and may show an exaggerated pharmacologic response with hypoalbuminemia and should be carefully titrated with reduced bolus doses.
4. **Ketamine** is metabolized by the liver through demethylation to Nor-Ketamine. The clearance is approximated to hepatic blood flow (little data is available regarding Ketamine and liver disease).



B. **Benzodiazepines** metabolized by oxidative mechanisms (Diazepam, Midazolam) have increased half-lives in liver disease. However, benzodiazepines cleared by glucuronidation (Lorazepam) have normal half-lives.

C. **Opiods** may worsen hepatic encephalopathy and should be carefully titrated. Narcotic induced respiratory depression is more pronounced in liver failure. Meperidine (Demerol) clearance is significantly reduced in liver disease, however Morphine and Fentanyl clearance less impaired.

D. **Neuromuscular blocking drugs** such as Succinylcholine and short-acting NMBD's (Mivacurium) have prolonged duration of activity in severe liver disease due to decreased plasma cholinesterase levels. Intermediate acting NMBD's (Vecuronium and Rocuronium) have prolonged effects in liver disease because they are dependent on hepatobiliary excretion and metabolism. Long-acting NMBD's (Doxacurium, d-Tubocurarine, and Pancuronium) are predominantly excreted mostly unchanged in the urine and therefore do not have a change in duration of action. However, Atracurium and Cisatracurium do not have a change in metabolism (Hofmann elimination and plasma esterase degradation) or excretion and the duration of action is independent of hepatic function.

E. **Inhalation agents** do not significantly impair hepatic blood flow and hepatocyte oxygenation (Isoflurane, Desflurane, and Sevoflurane). However, Halothane can cause a significant decrease in both inlets of hepatic blood flow and can therefore reduce hepatocyte oxygenation.