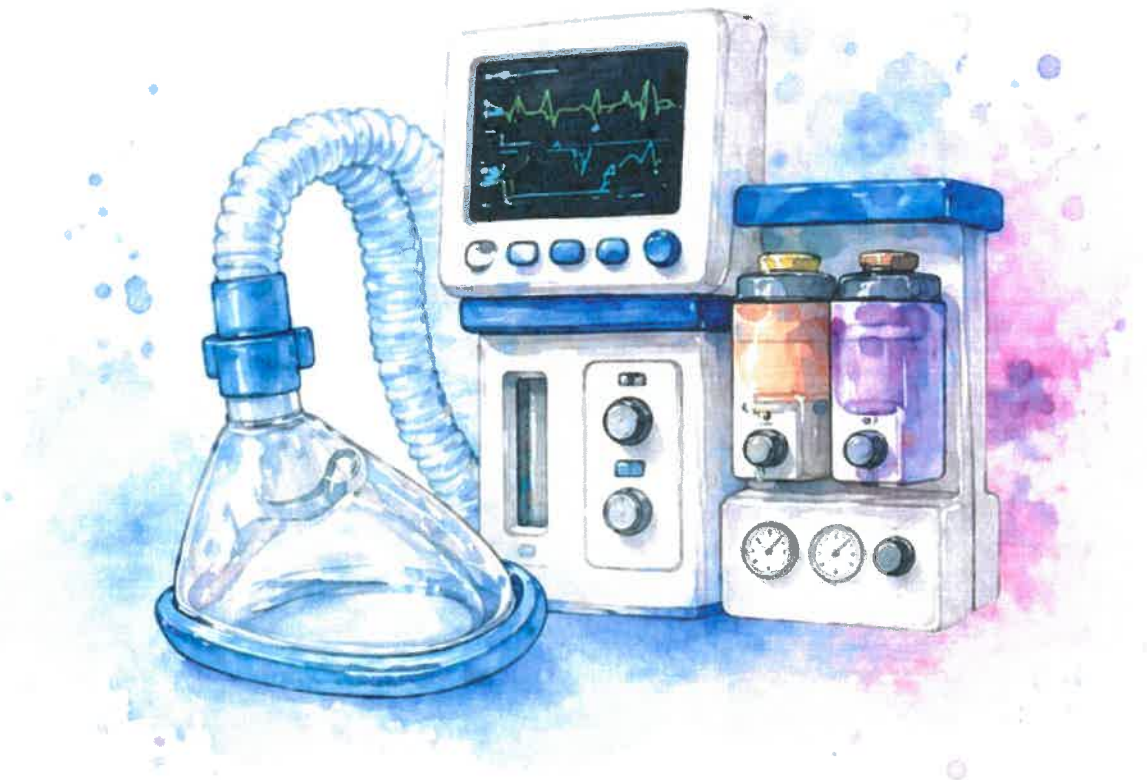
NEET SS ANESTHESIA

Updated Notes 2026



TRANSPLANT ANAESTHESIA

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LIVER ANATOMY

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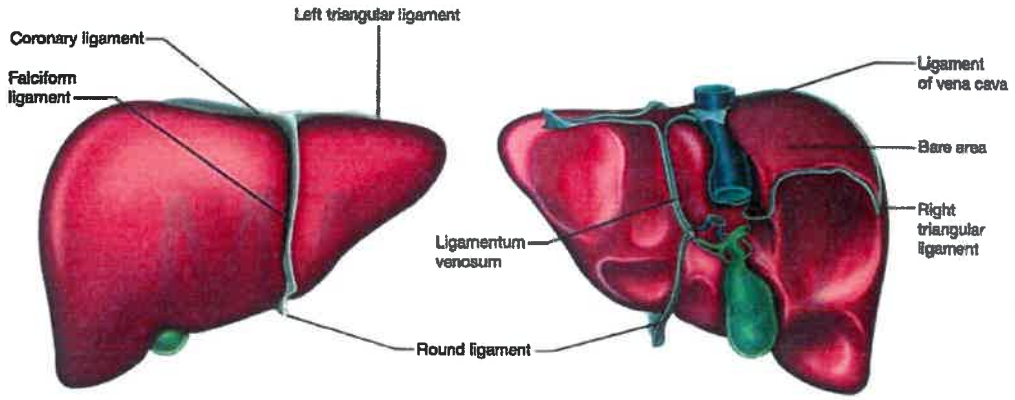
Introduction 00:00:49

Basics :

- The human liver is the largest solid organ, comprising 2% of total body mass.
- Weight : 1,500 g (600–1800).
  - Around 1.5–2% of adult body weight.
- Basic structures :
  - Coronary ligament.
  - Falciform ligament.
  - Left triangular ligament.
  - Round ligament.
  - Ligamentum venosum.
  - Ligament of venacava.
  - Right triangular ligament.



Liver anatomy

Histology :

Zones :

- Hepatocytes are divided into ~~different~~ zones based on their proximity to the portal triad (Hepatic artery, portal vein and the bile duct).
  - Zone 1 is periportal.
  - Zone 3 is around the central vein (Perivenous or pericentral).
  - Zone 2 is in between zone 1 and zone 3 (mid zone).
- Zone 3 is furthest away from the portal tracts → Receives blood with a lower oxygen tension and nutrient content.

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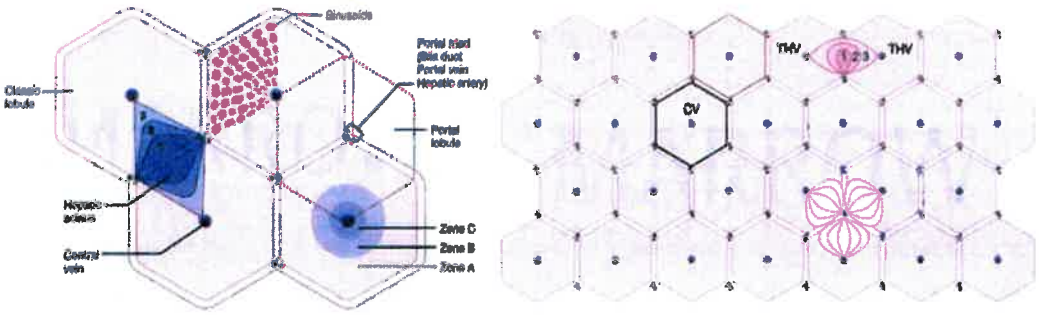


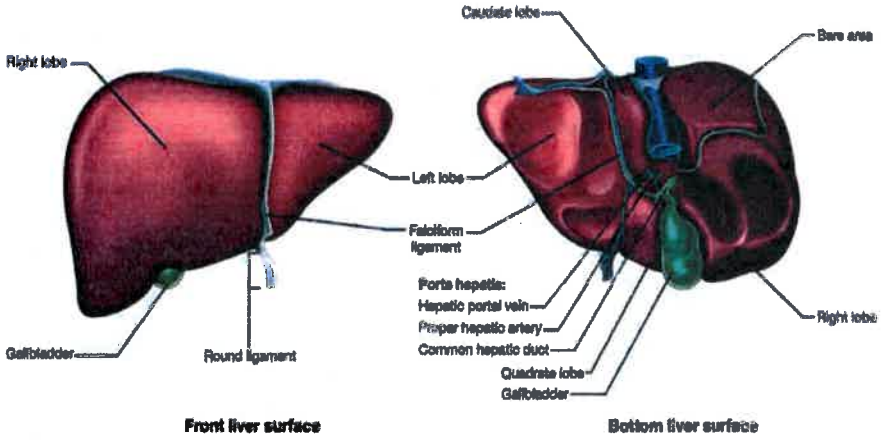
Zones of liver

Glisson's capsule :

- A thin connective tissue layer that covers liver.
- Attached to the diaphragm by the coronary ligaments.

Anatomy of liver :

Anatomically, the liver has four lobes : Right, left, caudate and quadrate lobes.



Anatomy of liver

- Porta hepatis contains : Hepatic portal vein, hepatic artery, & common hepatic duct.

Ligaments :

- Round ligament (Ligamentum teres hepatis) :
  - Remnant of left umbilical vein.
- Falciform ligament : Divides the liver into right and left lobe.
  - Sickle shaped.

Segmental anatomy of liver :

- Liver segmental anatomy was described by Claude Couinaud in 1954.
- Couinad segments :
  - Total of eight independent segments.
  - Each segment has its own blood supply and biliary drainage.

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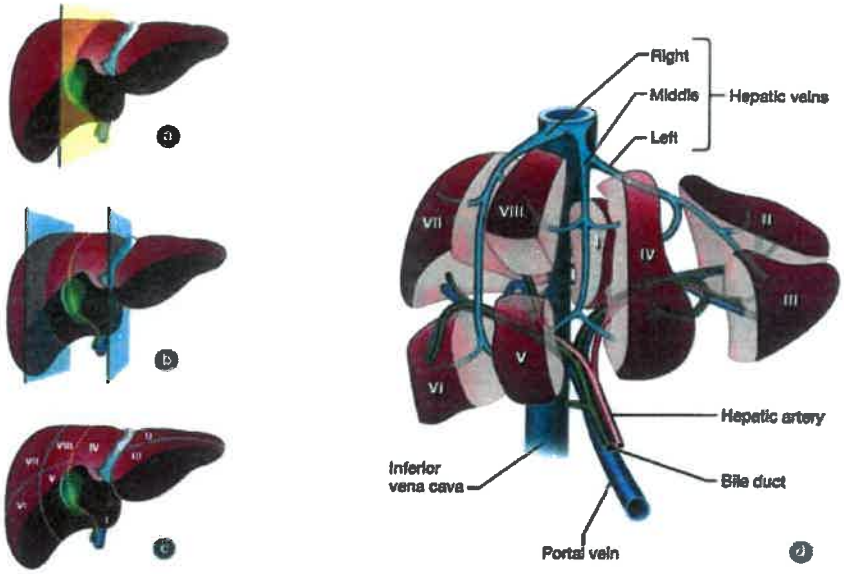
- Cantlie's line : Line connecting the gallbladder bed and IVC.
- Right lobe : Segments 5, 6, 7, 8.
- Left lobe : Segments 2, 3, 4.
- Segment 1 : Caudate lobe (Drains into the IVC directly).



Segmental anatomy of liver

Blood supply & micro-anatomy 00:18:42

Blood supply :

- Normal blood flow is from the portal vein through the liver (Hepatopetal flow).
- In the setting of cirrhosis and portal hypertension, blood flow reverses away from the liver (Hepatofugal flow) .
- Liver blood supply is 25% from the hepatic artery and 75% from the portal vein.
- The liver receives approximately 25% of the resting cardiac output.

Hepatic artery :

- High-pressure/ high-resistance system.
- Branch of the coeliac trunk (Branch of abdominal aorta).
- Carries oxygenated blood.
- 20%–30% of total blood supply to the liver is carried by hepatic artery.
- Responsible for 40%–50% of total oxygen supply to liver.
- Replaced left hepatic artery originates from left gastric artery.

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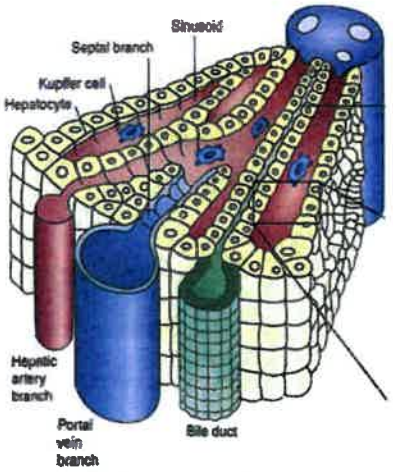
Portal vein :

- Low pressure/ low resistance system.
- Formed by the union of superior mesenteric vein and splenic vein behind the neck of pancreas.
- Carries oxygen-poor but nutrient-rich blood.
- 70%–80% of total blood supply to the liver is carried by portal vein.
- Responsible for 50%–60% of total oxygen supply.

Micro-anatomy :

Sinusoids :

- Hepatocytes are arranged within hepatic sinusoids surrounding a central hepatic vein.
- They are bordered by interlobular portal triad consisting of a biliary duct, hepatic artery, and portal vein.



Micro-anatomy

Arrangements :

- Based on direction of blood flow.
- Hexagonal structure with the central vein in the middle and portal triad (Branches of portal vein, hepatic artery, and bile duct) in the six corners.
- The hepatic arterial and portal venous blood flows from portal triad to the central vein.
- Kupffer cells : Macrophages.
- Stellate cells : Responsible for extracellular matrix production and capable of contractile function to regulate sinusoidal blood flow.
  - Significant in cases of portal hypertension.
- Pit cells : Lymphocytes.
- Venous drainage of the liver is through the hepatic veins directly into the inferior venacava (IVC).
- The perisinusoidal space of Disse : The space separating the sinusoids from hepatocyte.
- Bile is produced by hepatocytes and secreted into biliary canaliculi via canals of Hering.

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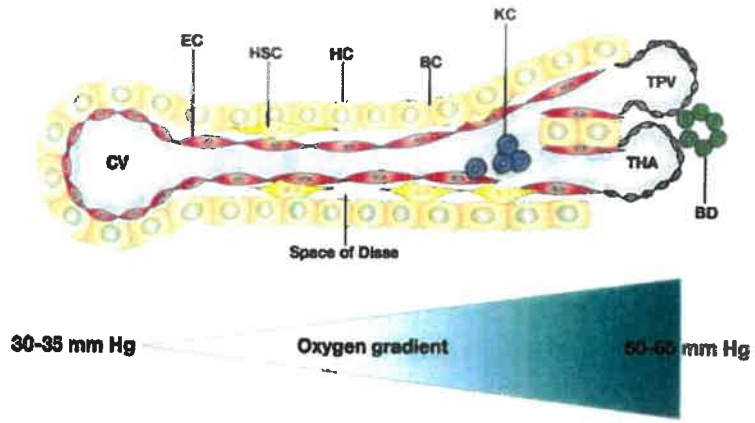

Cross section of portal triad

Zones :

- Zone 1 :
  - Periportal (Zone 1) hepatocytes are the major sites of aerobic metabolism, and process such as glycogen synthesis and sulfation.
  - Blood supply is the highest.
  - Is susceptible to damage by blood-borne toxins and infection.
- Zone 3 :
  - Perivenous (Zone 3) hepatocytes are the major sites of anaerobic metabolism, glycolysis and glucuronidation.
  - Zone 3 hepatocytes are most sensitive to hypoxia.
  - Zone 3 is closer to the central vein.
  - This area is higher in CYP 450 levels.
  - Gets the least blood supply and is susceptible to ischaemia.
- Zone 2 or intermediate zone.

Note :

- Replaced left hepatic artery originates from left gastric artery.

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HEPATIC BLOOD FLOW

Liver blood flow and oxygen delivery :

- Liver receives 25% of resting cardiac output.
- It receives 20% of resting oxygen consumption.
- Liver & splanchnic circulation together contain 10 to 15% of total blood volume.

Dual blood supply :

- Hepatic artery : Contributes 25% of hepatic blood flow.
- Portal vein : Contributes 75% of hepatic blood flow.
- Oxygen delivery from each source is equivalent at 50%.

Total hepatic blood flow (THBF) :

- THBF = PBF + HABF.
- PBF : Portal blood flow.
- HABF : Hepatic artery blood flow.

Facts :

- Portal vein acts as a valveless capacitance vessel.
- Hepatic artery is a resistance vessel.
- Hepatic artery blood flow depends on systemic arterial pressure and flow.
- Liver acts as an autologous reservoir of blood.

Factors effecting hepatic blood flow 00:03:48

Regulation of hepatic blood flow – Types :

Intrinsic :

1. Hepatic artery buffer response (HABR).
2. Myogenic autoregulation.
3. Metabolic control.

Extrinsic :

1. Neural.
2. Humoral.

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Intrinsic :

Hepatic artery buffer response (HABR) :

- When portal blood flow decreases, hepatic artery blood flow is upregulated so that total hepatic blood flow remains constant.
- THBF = PBF + HABF.
- Hepatic artery flow changes according to portal flow.
- It has an inverse relationship.
- Mediated by adenosine which causes vasodilatation.
- Endotoxins and splanchnic vasoconstriction can abolish HABR.
- This inverse relationship is called the hepatic arterial buffer response.
- The hepatic artery buffers changes in portal venous flow to maintain a steady state.

Adenosine wash out hypothesis :

- Elevations in portal venous flow wash out locally produced adenosine, thereby decreasing hepatic arterial flow.
- Adenosine acts as a vasodilator.

Volatile anesthetics and HABR :

- HABR is preserved by isoflurane, sevoflurane and desflurane.
- Volatile anesthetics decrease MAP and CO.
- Hepatic artery blood flow is decreased by halothane and enflurane through direct vasoconstriction.

Metabolic control :

- Decrease in O_a content or pH of portal venous blood increases hepatic arterial blood flow.
- Postprandial hyperosmolarity increases hepatic blood flow.

Myogenic autoregulation :

- Vascular smooth muscle stretch during hypertension protects the liver.

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Extrinsic :

Neural :

- Parasympathetic and sympathetic nerves regulate vascular tone.
- Blood volume is shifted to systemic circulation.
- Hepatic artery has α_1, α_2, and β_2 receptors.
- Portal vein has only α receptors.

Humoral :

- Glucagon causes hepatic artery vasodilation.
- Angiotensin II causes vasoconstriction.
- Vasopressin reduces portal venous pressure and is used in portal hypertension.

Hepatic blood flow measurement 00:12:30

Clearance technique :

- Based on Fick's principle.
- Determined by the rate of disappearance of a substance that is exclusively cleared by the liver.
- High extraction ratio substances include indocyanine green (ICG), propranolol and lidocaine.
- Dual cholate test :
  - measures the clearance of cholate, a bile salt.
  - Cholate is administered in both oral and intravenous form.

Indicator dilution technique :

- Can measure hepatic blood flow even in the presence of liver dysfunction.
- Hepatic blood flow is calculated by creating indicator dilution curves.
- The substance used should be resistant to hepatic clearance.
- Primarily used as a research tool.

Direct measurements

- Ultrasonography probes or electromagnetic probes are used.
- Radiological methods :
  - Doppler ultrasonography demonstrates diminished portal flow and portal venous flow reversal.
  - Contrast enhanced CT and MRI provide quantitative assessment.
  - Elastography is used to assess fibrosis.

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Halothane hepatitis :

- Halothane undergoes extensive hepatic metabolism compared to other volatile anesthetics.
- Breakdown products include trifluoroacetic acid and trifluoroacetic chloride.
- These metabolites bind to liver proteins and are recognized as antigens by the immune system.
- The immune response results in halothane hepatitis.
- Characterized by fulminant hepatic necrosis with a fatality rate of 50 to 75%.
- multiple exposures increase the likelihood of this immune-mediated reaction.
- Halothane hepatitis is 10 to 30 times more common in adults than in children.

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HEPATIC DRUG METABOLISM

Pharmacokinetics 00:01:00

Bioavailability :

- Drugs administered intravenously have 100% bioavailability because the original form of the drug reaches the systemic circulation unchanged.
- When taken orally, the intestines and liver absorb and process drugs thereby decreasing the effective dose that enters systemic circulation.

Drug metabolism :

Xenobiotics :

- Drugs, natural, and synthetic substances are metabolised by the liver.
- Goal : To render the compounds more hydrophilic so that renal elimination of the modified drug or its metabolites occurs easily.

Phases of drug metabolism :

- There are two main phases : Phase 1 and Phase 2.
- They may occur alone or in combination.
- Phase 1 :
  - Alters existing functional groups to make the molecule more polar thereby increasing its water solubility.
  - Phase 1 enzymes consist of cytochrome P450 (CYP superfamily) of enzymes that hydrolyze, oxidize, or reduce the parent compound.
- Phase 2 :
  - Acts primarily to conjugate polar compounds and increase their hydrophilicity.
  - These enzymes can be inhibited and are inducible.
  - Reactions include glucuronation, acetylation, sulfation, and methylation.
- Phase 3 :
  - Involves the excretion of compounds into bile by molecular transporters.
  - Molecular transporters : multidrug resistance protein, cystic fibrosis transmembrane conductance regulator, multidrug resistance related protein, and ATP binding cassettes (ABC).

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Clinical significance :

- Absence or dysfunction of phase I or II enzymes can result in hyperbilirubinemia and encephalopathy.
- Gilbert's syndrome : mutation in bilirubin UGT leading to reduced conjugation of bilirubin with glucuronide and unconjugated hyperbilirubinemia.
- Depletion of molecules involved in conjugation reactions can result in liver injury.
- Acetaminophen toxicity : Relative depletion of glutathione and accumulation of N-acetyl-p-benzoquinone-imine (NAPQI), the unconjugated toxic acetaminophen by-product leading to zone 3 necrosis.
- Cytochrome 2C19 (CYP 2C19) is the enzyme that activates the prodrug of clopidogrel and also metabolises proton pump inhibitors.
- Competition for this enzyme causes decreased activation of clopidogrel and increased risk of acute coronary syndrome.

Conjugation :

- Phase II biotransformation reaction.
- Activated drugs are conjugated with polar species such as glutathione, sulphate, glycine, or glucuronic acid to render them water soluble and easily excretable by the kidneys.

Drug clearance :

Hepatic drug clearance depends on three factors.

1. The intrinsic ability of the liver to metabolize a drug depending on the presence of the appropriate drug metabolising enzyme.
2. Hepatic blood flow.
3. Extent of binding of the drug to blood components such as albumin.

Extraction ratio :

- Substances that undergo significant first pass elimination are said to have a high extraction ratio.
- Elimination of these drugs is largely determined by hepatic blood flow.
- The liver removes the entire drug entering the liver in one pass.

Low extraction ratio :

- Drugs that require a prolonged time for biotransformation have a low extraction ratio.
- Such drugs are often protein bound in the circulation.
- They are not readily available to drug metabolising enzymes in the liver.

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Common anaesthetic drugs :

High Clearance (high extraction ratio that is blood flow dependent)	Intermediate Clearance	Low Clearance (low extraction ratio that is blood flow independent)
Morphine	Aspirin	Warfarin
Lidocaine	Quinine	Phenytoin
Propofol	Codeine	Rocuronium
Propranolol	Nortriptyline	Methadone
Fentanyl	Vecuronium	Diazepam
Sufentanil	Alfentanil	Lorazepam

Note :

- Drugs with a high intrinsic clearance such as lignocaine, opioids, etomidate, and propofol have a hepatic clearance dependent on hepatic blood flow.
- They are unaffected by enzyme induction because of their already high extraction ratio.

Cytochrome P450 00:28:15

Features :

- Group of enzymes predominantly located in the liver.
- Responsible for metabolism of various drugs.
- Involved mainly in phase I reactions.
- CYP450 are proteins containing haem as a co-factor.
- The term P450 refers to the spectrophotometric wavelength absorption maxima for the enzyme in the reduced state (450 nm).
- Drug drug interactions can result in induction or inhibition of CYP450 enzymes.
- CYP450 enzymes are located throughout the body but are highly concentrated within the smooth endoplasmic reticulum of hepatocytes in the liver, gut, and kidneys.

Importance in anaesthesia :

- CYP2E1 is mainly responsible for oxidative metabolism of volatile anaesthetics.
- CYP3A is responsible for metabolism of intravenous anaesthetics.
- Polymorphism refers to genetic mutations that give rise to enzymes with different abilities to metabolise drugs.
- The expression of CYP450 enzymes varies between populations and influences drug metabolism and response.

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- Inducers increase the expression level of CYP450 enzymes resulting in increased metabolism of drugs.
- This reduces the therapeutic concentration & may cause treatment failure.
- Expression and function of phase I and II enzymes are reduced in neonates.
- Activities of some CYP450 enzymes are ↑ed in women compared to men.
- Genetic polymorphism plays an important role in inter-individual variability of drug response.

CYP450 inducers :

- Anticonvulsants : Phenytoin, carbamazepine, phenobarbitone.
- Steroids : Dexamethasone, prednisolone, glucocorticoids.
- Antibiotics : Rifampicin, griseofulvin.
- Others : Nicotine, alcohol, cigarette smoke, St John's Wort.

CYP450 inhibitors :

- Inhibitors prevent CYP450 enzymes from working or reduce the rate of enzyme catalysed reactions.
- This decreases drug metabolism and increases the potential for toxicity.
- Azoles : Ketoconazole, fluconazole.
- Antibiotics : Sulfonamides, metronidazole, ciprofloxacin, chloramphenicol, macrolides, isoniazid.
- Cimetidine.
- Omeprazole.
- Sodium valproate.
- Grapefruit.

Note :

- Phase I biotransformations : CYP3A4 is the single most important enzyme responsible for 40% to 45% of all CYP mediated drug metabolism.

Morphine metabolism :

- Undergoes glucuronidation.
- Morphine is metabolised to morphine 3 glucuronide (Inactive) and morphine 6 glucuronide (Active).

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LIVER FUNCTION TESTS

Introduction 00:00:36

Basic interpretation :

- ALST is more sensitive than ALT to liver damage, but ALT is more liver specific than AST.
- Reduction in albumin concentration is more likely to be as a result of protein catabolism than decreased synthesis.
- ALP increases occur with biliary tract dysfunction.

Functions of liver :

- Multi functional organ.
- Metabolic functions : Carbohydrate, lipids, proteins, minerals and vitamins.
- Excretory function : Bile pigments, bile salts → Bile → Intestine.
- Detoxification : Ammonia → Urea, antibiotic metabolism.
- Protective function : Kupffer cells.
- Storage function : Glycogen, Vitamin A, D, B_{12}.
- Synthetic functions : Plasma proteins → Albumin, prothrombin, hormones.
- Conjugates bilirubin with glucuronic acid to form water soluble bilirubin that is excreted in bile.
- Production of cholesterol and lipoproteins.
- Vitamin K dependent coagulation factors (II, VII, IX, and X).

Tests of liver function 00:05:22

Overview :

Approach to assessment of liver function include :

- Clinical findings.
- Radiological studies.
- Laboratory :
  - Static.
  - Dynamic : measures functional pathways.