# Contents

# Overview Liver Function

- Mnemonic:
  - M etabolic
  - E endocrine
  - D etox/metab drugs
  - I mmune
  - C oag
  - A cid/base
  - B ile formation
  - R eservoir for blood
  - U rea formation
  - S torage function
  - H aematopoesis

# By Disease

## Acute Hepatic Disease

- = development of hepatocelluar dysfunction assoc with coagulopathy & encephalopathy in pts without prior liver disease
- assoc with high mortality rates (10-100%)

### Preoperative

#### TYPES (mortality)

- hyperacute – within 7 days (30%)
- acute – 7-28 days (33%)
- sub acute – 28 days – 6 months (14%)

#### HISTORY/CAUSES

- viral hepatitis (A->G, CMV, HSV, EBV)
- drugs (paracetamol, halothane, idiocyncratic)
- toxins
- fatty infiltration in pregnancy
- HELLP
- Wilsons
- Reye's
- NASH

#### FEATURES

- classic:
  - encephalopathy
  - cerebral oedema
  - severe coagulopathy with active fibrinolysis
  - metabolic derrangement: ↓BSL, ↓K, ↓Na, met acidosis
  - high cardiac output with ↓SVR
  - multiorgan failure: ↑ICP, ARDS, ARF

#### EXAMINATION

- jaundice
- vasodilated
- high cardiac output
- signs of raised ICP
- ascities
- hepatomegally
- bruising

### INVESTIGATIONS
- blds:
  - coag screen
  - electrolytes:
    - low urea (in adequate production by liver)
    - ↓K
    - ↓albumin
    - ↑LFTs
    - ↓BSL - ↓glycogen stores, ↓gluconeogensis in liver
  - virology: hepatitis serology
  - immunology:
    - antinuclear antibody (chronic active hepatitis)
    - smooth muscle antibody (primary biliary cirrhosis)
    - alpha-feto protein (hepatoma)
- Radiology:
  - U/S
  - CT/MRCP
- ERCP

### MANAGEMENT
- neuro orientated good ICU care
- active hepatitis = delay all elective surgery for 30 days until LFT's have normalised
- universal precautions
- support organ dysfunction
- intubate if has severe encephalopathy
- correct electrolytes & ↓BSL
- CVS support with noradrenaline if required
- NaHCO3 buffered haemofiltration
- ICP monitoring
- NAC in paracetamol OD
- do not routinely attempt to correct coagulopathy as PT is a marker of hepatic function & treatment
  ↳ reverse if active bleeding or invasive procedures
- liver transplant may be required

## Intraoperative
- PPI or H2 antagonists
- RSI
- beaware of exaggerated CNS effects of drugs
- iso, sevo and des preferred agents
- induction agents: propofol, thiopentone, etomidate
- relaxants: atracurium
- opioids: remi
- analgesics: paracetamol
- may need ascites drained
- treat bleeding aggressively

# Acute Fatty Liver of Pregnancy
- Unclear cause
- prodromal 1-2wk
- similare to PET/HELLP
- Bloods:
  - ↑WCC
  - Deranged LFTs ↑bili
  - ↓platelets
- Rx:

- Early delivery
- Concern about coal problems

# Chronic Liver Disease

- = any hepatitis lasting >6months
- inflammation ⟹ hepatic fibrosis ⟹ cirrhosis incl nodular regeneration & disruption of architecture ⟹ portal HTN
- 2 types of cirrhosis:
  - compensated = normal liver function
  - decompensated:
    - = deteriorating funciton
    - precipitant eg infection
    - need to Rx underlying cause
    - if untreatable need to consider transplant
- more prevelant than acture

## Preoperative

### HISTORY

- weakness & fatigue
- jaundice
- abdominal pain or swelling
- altered mental state
- pruritis

- durations of disease
- alcohol intake
- IV drug use
- blood transfusions
- tattoos
- overseas travel
- drugs (isoniazid)

### Causes of Severe Hepatic Disease (Cirrhosis)

- infection: viral hepatitis (chronic if infection > 6 months)
- drugs (isoniazide and methyldopa) & alcoholism
- biliary disease
- Vascular eg Budd Chiari, veno-occlusive disease
- inherited: haemochromatosis, α1 antitrypsin, Wilson's disease
- immune mediated: primary bilary cirrhosis, primary sclerosing cholangitis, autoimmune hepatitis
- Haemoglobinopathies: sickle cell disease

### Complications:

1. **bleeding** (decreased production of factors, thrombocytopaenia, platelet dysfunction)
2. **encephalopathy** (sedation, high protein diet, infection, trauma, hypokalaemia, constipation -> accumulation of toxic products, grade 0 = alert and orientated, grade IV = unresponsive to deep pain)
3. **hypoglycaemia** (decreased glycogen stores)
4. **ascites** (from portal hypertension and fluid retension)
5. **infection** (immunosuppression)
6. **renal failure** (from cause of liver failure or increased renovascular resistance or impaired tubular function)
7. **cholecystitis**
8. **pancreastitis**

### EXAMINATION

- general – abdominal distension, jaundice, cachexia, bruises
- palmar erythema
- bruising
- spider naevi

- yellow sclerae
- fetor
- gynaecomastia

- abdomen: masses, distension, bruising, scars
- hepatosplenomegally
- ascites
- bruits

## INVESTIGATIONS

- FBC - anaemia
- U+E – hepatorenal syndrome
- BSL
- LFT's – active damage
- Albumin – synthetic function
- COAGs – bleeding
- ABG – lactate acidaemia
- ascitic fluid – cytology, microscopy, culture and biochemisty
- liver biopsy
- endoscopy – varices

## MANAGEMENT

1. Daily vitamin K injections 10mg IV
2. Daily FBC
3. Adequate access to blood products
4. Monitor glucose closely -> 10% dextrose as required
5. Monitor K+
6. No nephrotoxic agents
7. protein and fluid restriction

## SURGICAL RISK

- liver cirrhosis is highest RF for peri-op mortality of any disease
- 2 risk scoring systems for surgery:
  - Child-Pugh
  - MELD
- mortality due to sepsis, renal failure, bleeding, worsening liver failure ⟹ encephalopathy

**Child-Pugh:**

| **Mortality @ 1yr** | **< 5%** | **5-50%** | **>50%** |
|---|---|---|---|
| Bilirubin(mol/L) | <25 | 25-40 | >40 |
| Albumin (g/L) | >35 | 30-35 | <30 |
| Ascities | none | moderate | marked |
| Nutrition | excellent | good | poor |
| INR | <1.7 | 1.7-2.3 | >2.3 |
| Encephalopathy | grade 0 | 1-2 | 3-4 |

## MELD = model for end stage liver disease

- developed to predict survival in cirrhotic pt undergoing liver transplant
- but may be more accurate in non transplant setting than Child-Pugh

MELD uses bili, INR & creatinine

$$\text{MELD} = 3.78\left[\log_e \text{serum bilirubin (mg/dL)}\right] + 11.2\left[\log_e \text{INR}\right] + 9.57\left[\log_e \text{serum creatinine (mg/dL)}\right] + 6.43$$

- scores:
  - 5-6 = low risk elective surgery (<5% mortality)

- 7-9 = intermediate (5-50% mortality)
- >10 = unacceptable mortality ⟹ postpone all non essential surgery (>50% mortality)

# Postoperative

- monitor closely: sepsis, renal failure, bleeding, worsening of liver function

# Complications of Liver Disease

## Bleeding

- liver synthesises all factors incl protein C & S & ATIII (does not make XII)
- several mechanisms of coagulopathy:
  - ↓synthesis of factors
  - ↓platelets & ↓platelet function
  - ↓clearance of activated clotting factors
  - hyperfibrinolysis
- TEG very useful to assess coagulation
  ↳ better than lab coag screen

### Treatmemt

- jaundice ⟹ vit K deficiency ∴ trial empirical vit K useful to assess effect on PT
- blood products: FFP, cryoprecipitate, platelets

## Encephalopathy

- occurs in severe liver failure
- toxic products build up (esp ammonia) ⟹ progressive encephalopathy
- precipitants:
  - sedatives = opioids/benzo's
  - GI bleeding
  - infection = spent bacterial peritonitis
  - operations
  - trauma
  - ↓K
  - constipation
- must be intubated if ↓GCS to protect airway

**Box 7.1 Grades of hepatic encephalopathy**

| | |
|---|---|
| Grade 0 | Alert and orientated |
| Grade I | Drowsy and orientated |
| Grade II | Drowsy and disorientated |
| Grade III | Rousable stupor, restlessness |
| Grade IV | Coma—unresponsive to deep pain |

## Hypoglycaemia

- ↓hepatic glycogen storage

## Ascites

- caused by combo of:
  - portal HTN
  - hyperaldosteronism ⟹ Na/water retention
  - splanchnic vasodilation
  - low serum albumin
- spironolactone used but need to monitor electrolytes & renal function

## Infection

- ↓immune function:
  - resp
  - urinary
  - spont bacterial peritonitis
- intraop Abx

## CVS

- shunting (porotsystemic, pulmonary, cutaneous) ⟹
  - hyper dynamic high cardiac output state (can hide underlying cardiac dysfunction)

        - ↓SVR ⟹ ↓MAP
        - ↑HR
        - fluid overload 2nd to RAAS
- alcohol excess ⟹ cardiomyopathy
- portal HTN ⟹ varices:
    - engorgement of anastomoses between portal & systemic circulations:
        - oesophageal/gastro-oesophageal junction
        - haemorrhoids
        - abdo wall - caput medusae

# Renal

- impairement commonly caused by:
    - dehydration
    - sepsis
    - nephrotoxic drugs
- renal & liver failure together ⟹ high mortality
- prevention:
    - adequate hydration
    - goal directed fluid therapy
    - drain tense ascites - may ↓renal blood flow & falsely ↑CVP
    - avoid hypotension
    - avoid nephrotoxic drugs
    - aim UO 1ml/kg/hr
- hepatorenal syndrome:
    - end stage problem
    - diagnosis of exclusion. Criteria:
        - urinary Na <10mmol/L
        - Urine:plasma osmolality & creatinine ratios >1
        - normal CVP & no diuresis on central volume expansion
        - underlying chronic liver disease & ascites
    - exclusively in cirrhotic liver disease
    - due to altered renovascular tone - permanent vasodilation ⟹ ↓GFR
    - 2 types:
        - 1 = rapidly progressive
        - 2 = slower onset with diuretic resistant ascites
    - difficult to Rx & may require liver transplant
        ↳ terlipressin/albumin ⟹ splanchnic vasoC

# Respiratory

- hypoxia is common & multifactorial:
    - ascites ⟹ splinting diaphragm, atelectasis & collapse
    - hepatopulmonary syndrome:
        - ↓ed production or clearance of pulmonary vasodilators eg N2O
        - ⟹ ↑shunt ⟹ V/Q mismatch
        - liver transplant required
    - pHTN (portopulmonary syndrome):
        - seen in 0.25-4% cirrhotic pts
        - due to local pulmonary production of vasoconstrictors
            ↳ all while systemic vasoD predominates

# Blood

- ↓PPBs:
    - ↓albumin & other proteins
        ↳ best chronic marker of liver function
    - ascites & oedema
- Anaemia - caused by:
    - chronic blood loss
    - hypersplenism
    - haemolysis
    - chronic illness

- malnutrition

## GI

- Varices - oesophageal
- delayed gastric emptying
- Spent bacterial peritonitis

# Treatment End Stage Liver Disease

- protein restriction ⟹ ↓ammonia
- Lactulose ⟹ ↓ammonia uptake
- Abx - ↓gut flora + SBP prophylaxis
- Diuretics - spiro & frusemide
- Na restriction
- Rpt therapeutic paracentesis
- Propanolol - varices
- TIPSS

# Practical Anaesthesia

## Drugs in Liver Disease

- causes of altered pharmacokinetcs:

**Table 7.4** Causes of altered drug pharmacokinetics in liver failure

| Liver problem | Pharmacological effect |
|---|---|
| Decreased portal blood flow in hepatic fibrosis | Decreased first-pass metabolism |
| Hypoalbuminaemia | Increased free drug in plasma |
| Ascites and sodium/water retention | Increased volume of distribution |
| Biotransformation enzymes | Activity may increase or decrease |
| Reduced liver cell mass | Reduced activity |
| Obstructive jaundice | Decreased biliary excretion of drugs |

- alcoholic liver disease:
  - early phase: P450 system induced ⟹ ↑rapid metab of drugs
  - late phase: reversed ⟹ ↓metab
- end stage disease:
  - systems usually preserved until now due to large reserve
  - altered pharmacodynamics ⟹ coma easy to induce
  - specific drugs: ↑half life & potentiation of effects:
    - opioids - alfentanil & morphne
    - vec, roc & mivacurium
    - benzo's
    - (sux - due to ↓plasma cholinesterase)

## Anaesthetic Management

### Preoperative

- History:
  - anorexia
  - malaise
  - weight loss
  - easy brusing
  - itching
  - RUQ pain
- signs:
  - jaundice
  - palmar erythema
  - spider naevi
  - caput medusae
  - gynaecomastia
  - ascites
  - hepatosplenomegaly
  - testicular atrophy
- RFs:
  - alcohol excess
  - IVDA
  - obese
  - autoimmune conditions
  - haemodialysis

- haemophilia

- Investigations:
  - Bloods:
    - FBC & coag screens
    - electrolytes - urea often falsely low due to ↓production
    - BSL
    - LFTs:
      - PT, albumin & bili = sensitive markers of liver function
      - AST, ALT = sensitive to liver damage but do not predict mortality
      - ALK = bilary obstruction
    - hepatitis screening
  - Urine
  - US, ERCP, CT, MRI
  - ECHO - cardiomyopathy (esp in alcohol excess), effusions (cirrhosis)
  - ECG - cardiomyopathy & arrhythmias
  - CXR & ABG

| | | |
|---|---|---|
| Bilirubin | 2–17 micromoles/L | Haemolysis<br>Gilbert's syndrome<br>Acute and chronic liver failure<br>Biliary obstruction |
| Aspartate transaminase (AST) | 0–35IU/L | Non-specific (found in liver, heart, muscle, etc.)<br>Hepatocellular injury |
| Alanine aminotransferase (ALT) | 0–45IU/L | Specific<br>Hepatocellular injury<br>Degree of elevation can point to aetiology:<br>>1000: acute viral hepatitis, drugs, autoimmune hepatitis, and ischaemia<br>100–200: acute viral hepatitis, alcohol and non-alcoholic fatty liver disease |
| Alkaline phosphatase (ALP) | 30–120IU/L | Physiological (pregnancy, adolescents, familial)<br>Bile duct obstruction (stones, drugs, cancer)<br>Primary biliary cirrhosis<br>Metastatic liver disease<br>Bone disease |
| γ-glutamyl transpeptidase (γ-GT) | 0–30IU/L | Non-specific (found in heart, pancreas, kidneys)<br>Useful to confirm hepatic source for ↑ ALP (always raised if liver source of ↑ ALP)<br>Alcoholic liver disease |
| Albumin | 40–60g/L | Non-specific (affected by nutritional status, catabolism, and urinary and GI losses)<br>Prognostic in chronic liver disease |
| Prothrombin time and international normalized ratio (INR) | 10.9–12.5s (INR 1.0–1.2) | Non-specific (vitamin K deficiency, warfarin therapy, DIC)<br>However, best prognostic marker in acute liver failure |

- optimise nutrition

- ?presence of varices
- plan for coagulopathy

# Perioperative

- drug choices:

**Table 7.6** Anaesthetic drugs in liver failure

| | Drugs safe in liver failure | Drugs to be used with caution (may need reduced dosage) | Drugs contraindicated in liver failure |
|---|---|---|---|
| Premedication | Lorazepam | Midazolam, diazepam | |
| Induction | Propofol, thiopental, etomidate | | |
| Maintenance | Desflurane, sevoflurane, isoflurane, nitrous oxide | Enflurane | Halothane (possibly)[1] |
| Muscle relaxants | Atracurium, cisatracurium | Rocuronium, vecuronium, suxamethonium | |
| Opioids | Remifentanil | Fentanyl, alfentanil, morphine, pethidine | |
| Analgesics | Paracetamol ↓dose | lidocaine, bupivacaine | NSAIDs |

[1] Halothane has been rarely reported to cause hepatitis (see p. 142).

- anaesthetic effects on hepatic blood flow:
  - drugs - vasopressors, volatiles (↓s blood flow)
  - IPPV & PEEP
  - surgical technique

## Induction

- antacid prophylaxis/RSI
- invasive monitoring - to maintain adequate perfusion pressures 10-20% baseline

## Maintenance

- des best choice:
  - least metabolised
  - best preservation of hepatic blood flow
  - quicker emergence time
- 4% albumin good fluid choice
- use TEG not INR
- regional good option but:
  - coagulopathy
  - all LAs metab'ed by liver
- careful positioning

## Postop

- ICU if advanced disease - ?need ICP monitor for cerebral oedema
- constipating drugs must be given with laxatives to ↓risk of encephalopathy
- ileus ⟹ encephalopathy
- UO 1ml/kg/hr

## Special Points

- post op complications:
  - ↓wound healing
  - sepsis
  - renal impairement
  - bleeding

# Post Op Liver Dysfunction

- post op jaundice common
- hepatitis 2nd to volatiles now thing of past
- common causes:
  - intra/post op hypoxia/hypotension ⟹ hepatic ischaemia
  - benign intrahepatic cholestasis:
    - mimicks bilary obstruction
    - assoc with ↓bp, ↓SpO2, blood transfusion
  - surgical cause eg haematoma

**Table 7.7** Causes of post-operative liver dysfunction or jaundice

| | |
|---|---|
| Bilirubin overload (haemolysis) | Blood transfusion<br>Haematoma resorption<br>Haemolytic anaemia (sickle-cell, prosthetic heart valve, glucose-6-phosphate dehydrogenase deficiency) |
| Hepatocellular injury | Exacerbation of pre-existing liver disease<br>Hepatic ischaemia: hypovolaemia, hypotension, cardiac failure<br>Septicaemia<br>Drug-induced (antibiotics, halothane)<br>Hypoxia<br>Viral hepatitis |
| Cholestasis | Intrahepatic (benign, infection, drug-induced, e.g. cephalosporins, carbamazepine, erythromycin)<br>Extrahepatic (pancreatitis, gallstones, bile duct injury) |
| Congenital | Gilbert's syndrome |

## Volatiles

- halothane hepatitis
  - 20% metabolised
  - 2 diff syndromes:
    - 1st =
      - transient LFT rise,
      - post 1st exposure
      - low risk
    - 2nd =
      - repeated exposure
      - immune mechanism
      - fulminant hepatic failure & high mortality
      - rare
- enflurane:
  - 2% metab
  - theortical cross reactivity for pts with prev halothane hepatitis
- isoflurane:
  - 0.2% metab
  - theoretical risk
  - considered safe though as is sevo & des

## Fluid

- avoid dextrose - hypo-osmolar (cerebral oedema) & does not expand volume
- Hartmans - external lactate load
- avoid NSL - high sodium load ⟹ worse ascites
- 4% albumin - perfect colloid
- IV terlipressin + daily albumin may improve renal function
- peri-op removal of ascites ⟹ post op re-accumulation

# By Surgery

## Acute Oesophageal Variceal Haemorrhage

- =medical emergency
- significant CVS compromise & coagulopathic
- 30% varices bleed with mortality 40%

### Management

- aims:
  - correct hypovolaemia
  - stop bleeding
  - reverse coagulopathy: pot >50, INR <1.5, fib >1.5
  - restrictive transfusion regime - aim Hb 80 (if not severe ongoing bleeding)
- Large access + Aline
- stop anticoagulants/antiplatelets
- early endoscopy for banding: RSI
- vaso-actives -
  - terlipressin 2mg 6hrly or vasopressin infusion for 1-2days
  - constriction of mesenteric beds
  - may cause coronary constriction ⟹ angina (use GTN patch/infusion)
    ↳ terlipressin causes less angina
- somatostatin 250mcg/hr and octreotide 50mcg/hr for 2-5days
  ↳ start both while waiting for scope
- balloon tamponade bleeding but only use if endoscopy has failed
  ↳ high complication rate: oesophageal tear/airway obstruction

### PostOp

- failed banding should have transjugular intrahepatic portosystemic shunt (TIPSS)
- start propanolol - ↓portal pressure ⟹ ↓re-bleed rate from 70-50%

## TIPSS

- indications:
  - refractory variceal bleeding
  - ascites resistant to diuretics
- stent placed rdiologically between hepatic & portal veins ⟹ blood bypass dilated oesophageal & gastric veins
- volume resus patient & balloon tamponade oesophageal bleed
- complications:
  - PTX
  - arrhythmias
  - massive bleeding 2nd to hepatic artery puncture or hepatic capsule tear
  - cardiac failure ⟹ sudden ↑VR & preload esp if cardiomyopathy
  - ↑liver dysfunction: ↑jaundice, ↑encephalopathy
- contraindications:
  - clinical or EEG encephalopathy
- requirements:
  - stable patient
  - good IV access + A line
  - inotropes & blood products