Abdominal Trauma

- **Aetiology**
  1. blunt trauma
    i. MVA's cause ~ 75%
       - associated splenic damage ~ 46%
         hepatic damage ~ 33%
         mesenteric damage ~ 10%
    ii. direct blows ~ 14%
       - some associated with CPR
    iii. falls ~ 10%
  2. penetrating trauma
    - majority are stabbings or gunshot wounds
    - simultaneous involvement of the thoracic cavity ~ 25%

- **Investigation**
  1. FBE, Hct
  2. Xrays
    - major trauma → CXR, Cx spine, SXR, AXR, Tx spine, pelvis
  3. peritoneal lavage
    - accuracy ~ 95%
    - complication rate ~ 1%
  4. CT scan
    - ideally should be performed prior to peritoneal lavage, so that interpretation is not obscured by introduced fluid/air
    - requires the patient to be haemodynamically stable prior to transport
    - allows diagnosis of organ damage prior to laparotomy
    - may provide additional diagnostic information → chest, Cx spine, Tx spine, etc.
  5. ultrasound
  6. nuclear scan
  7. contrast studies
    i. gastrograffin
      - 250 ml and right lateral position may confirm gastric/duodenal perforation
    ii. angiography
      - useful for continuous haemorrhage > 2 ml/min
      - allows selective embolisation of the bleeding vessel
  8. laparoscopy
  9. diagnostic laparotomy
Management

1. ABC / resuscitation
2. Laparotomy
   • < 20% of gunshot wounds are not associated with visceral injury
   i. Splenic injury
      • risks of overwhelming sepsis post-splenectomy, do not remove routinely
      • non-operative management of splenic trauma has a failure rate ~ 70%
      • success rate for conservative management in children is higher
      • operation with splenic conservation → Rx of choice
      • if repair not possible then require polyvalent pneumococcal vaccine
      • common infecting organisms - Pneumococcus
        - Meningococcus
        - Haemophilus influenzae
   ii. Hepatic injury
      • usually do not require operative repair
      • however, high incidence of associated injury and often require exploratory laparotomy to exclude other pathology
   iii. Renal injury
      • usually presents with haematuria
      • usually do not require operative repair
      • check IVP, cystogram
   iv. Hollow visceral injuries
      • more commonly follow penetrating trauma
      • require operative correction
Peritoneal Lavage

- sensitivity ~ 95%
- specificity ~ 85%
- complications ~ 1% *operator dependent
- positive result
  - aspiration
    - fresh blood ≥ 10 ml
    - faecal soiling or vegetable material
    - bile
  - lavage
    - appearance of lavage fluid in intercostal or urinary catheters
  - analysis
    - RBC count > 100,000/µl
    - 50,000/µl ≤ equivocal
    - 5,000/µl ≤ penetrating injuries
    - WCC > 500/µl
    - 200/µl ≤ equivocal
    - ALP§ > 3 IU/ml
    - amylase§ > 20 IU/ml

NB: §specificity for these is lacking → now rarely performed

- causes of false positives ~ 15%
  - traumatic lavage
  - retroperitoneal haemorrhage
  - pelvic haematoma - 2° fractures

- causes of false negatives ~ 5%
  - incorrectly performed
  - diaphragmatic rupture
  - retroperitoneal injuries - haemorrhage
    - duodenum, pancreas
    - renal injury
  - isolated hollow viscus perforation
**Indications**

a. multiple trauma patient in whom abdominal examination is,
   i. equivocal
   ii. unreliable - CHI, intoxication, cord injury
   iii. impractical - prolonged Xrays, angiography - requiring GA
b. unexplained fluid requirements in resuscitation
c. penetrating injuries - including lower thoracic
d. gunshot wounds

**Contraindications**

a. full bladder
b. pregnancy
c. recent abdominal surgery
d. obvious signs of intraperitoneal haemorrhage/infection

**NB:** ie., any indication for immediate laparotomy

**Complications**

a. haemorrhage
b. intestinal perforation
c. bladder perforation
d. infection

**Technique**

a. empty bladder, sterile technique, IV access
b. dialysis catheter introduced into pelvis via sub-umbilical incision
c. aspiration for frank blood | peritoneal fluid
d. 1000 ml of normal saline introduced over 5 minutes + ballotment
e. fluid drained sent for,
   i. red & white blood cell counts
   ii. urgent gram stain & culture
   iii. amylase
   iv. ? cytology
Acute Abdomen in ICU - Differential Diagnosis

a. adynamic ileus  - paralytic ileus, acute gastric dilatation
    - intestinal pseudo-obstruction
    - toxic megacolon

b. acalculous cholecystitis

c. pancreatitis

d. postoperative  - anastomotic leak
    - abscess formation

e. peritonitis
    i. secondary  - bacterial, chemical
    ii. primary   - *Pneumococcal, Streptococcal, Enterobacteriaceae*

f. trauma  - visceral perforation
    - laceration
    - haemorrhage, haematoma
    - post-CPR

g. splanchnic hypoperfusion  - mesenteric ischaemia

h. coincidental disease
    - appendicitis, cholecystitis
    - peptic ulcer
    - volvulus
    - diverticulitis
    - carcinoma
    - strangulated hernia

i. thoracic spinal trauma

### Medical Causes of the "Acute Abdomen"

a. endocrine  - Addisonian crisis
    - diabetic ketoacidosis

b. cardiac  - acute visceral congestion (CCF, tamponade, PE etc.)
    - lactic acidosis
    - mesenteric thromboembolism

c. neurological  - tabes dorsalis
    - herpes zoster
    - porphyria
    - epilepsy

d. autoimmune  - polyarteritis nodosa, SLE

e. metabolic  - hypercalcaemia
    - uraemia

f. respiratory  - lower lobe pneumonia
    - PTE
g. other
- Familial Mediterranean fever
- lead & other heavy metal poisoning
- lactose intolerance
- haemolytic crisis
- Henoch-Schönlein purpura.

h. allergy
- food allergy
- hereditary angioneurotic oedema

**Investigation - Acute Abdomen**

a. history of illness
b. physical examination - incl. temp., PR and PV
c. white cell count - nonspecific
d. AXR - supine & lateral decubitus
e. ultrasound
f. abdominal CT scan - with IV and enteral contrast
g. peritoneal lavage
h. diagnostic laparotomy

NB: untreated abdominal sepsis has a high mortality, whereas mortality is **unchanged** by a negative laparotomy

Acalculous Cholecystitis

- acute **necrotising** cholecystitis which may occur spontaneously in any critically ill patient
- multifactorial aetiology,
  1. reduced cystic artery perfusion
  2. ↑ bile viscosity 2° dehydration
  3. bile stasis - TPN, use of octreotide
  4. antibiotic precipitation - eg Ca++-salt of ceftriaxone

- may present as a tender RUQ mass, or as progressive jaundice with "sepsis"
- ultrasound may show an enlarged, oedematous gall-bladder, or may be **normal**
  - ie. a normal gallbladder and biliary tree ultrasound does not exclude the diagnosis
- high false positive rate for HIDA scans in ICU patients
- management is,
  1. **cholecystectomy**
  2. cholecystotomy, or
  3. radiological tube drainage
Intestinal Pseudo-Obstruction

- cause of acute abdominal distension and acute abdomen in the ICU patient
- ? due to alteration in neuromuscular function of the bowel

### Usual Presentation

- dilated loops of large and small bowel
- absence of signs of a site of mechanical obstruction
- may become grossly distended

### Complications

- splinting of diaphragms, respiratory embarrassment
- raised intra-abdominal pressure - adverse renal, respiratory, and CVS effects
- "toxic megacolon" and rupture > 6 cm diameter
- septicaemia
- pain and distension
- intolerance of enteral feed

### Aetiology *Multifactorial*

- autonomic neuropathy
- any cause
- drugs
- opiates
- β-agonists, antihypertensives
- anticholinergics, tricyclics, phenothiazines
- purgatives, barium, aluminium
- iron supplements
- electrolyte abnormalities - hypo-K⁺ / Ca²⁺ / HPO₄⁻
- neuromuscular
- Parkinson's disease
- myotonic dystrophy
- M.S.
- endocrinopathies
- myxoedema / hypothyroidism
- diabetes mellitus
- porphyria
- hypoparathyroidism
- amyloidosis
- autoimmune
- SLE, polyarteritis nodosa
- scleroderma, dermatomyositis
- ? IPPV causing reduced splanchnic blood flow
### Treatment

- **a. reverse potential causes** - e.g. cease narcotics
- **b. colonoscopy & decompression** - may need to be repeated daily ± flatus tube
- **c. operative decompression** - caecostomy
- **d. prokinetic agents** - ? cisapride

### Differential Diagnosis

- **a. adynamic / paralytic ileus**
- **b. toxic megacolon**
- **c. bowel obstruction- hernia, volvulus, adhesion, tumour**
- **d. ischaemic bowel**

### Adynamic Ileus

**Def'n:** any non-surgical impairment of the distal propulsion of intestinal contents

- traditional belief that all abdominal operations are followed by ~ 48 hr period of ileus
- SI is largely **unaffected** by laparotomy and may accommodate enteral feeding almost immediately
- however, other factors delaying function
  - a. gastric emptying impaired ~ 24 hrs
  - b. colonic activity impaired ~ 48 hrs

- therefore, postoperative ileus is predominantly a **colonic** problem
- with prolonged ileus, mechanical obstruction (faecal impaction) must be excluded
- propulsion may be aided by,
  - a. cisapride - 5-10 mg q8h
  - b. metoclopramide - 10 mg q6h
  - c. domperidone - 10 mg q8h
- **Metoclopramide**
  - structurally related to procainamide, but no LA activity
    - a. CNS
      - effects due to dopaminergic blockade →
        - i. antiemesis
        - ii. hyperprolactinaemia - galactorrhoea, breast tenderness
        - menstrual irregularity in females
        - used to promote milk production post-partum
    - no antipsychotic activity
    - may produce significant extrapyramidal symptoms
      Rx benztropine, diphenhydramine
  - b. GIT
    - ↑ smooth muscle activity, mainly stomach & proximal SI
    - ↑ LOS tone & ↓ pyloric tone
    - no effect on colonic activity or gastric acid secretion
    - mechanism of action not fully understood,
      - i. predominantly DA$_2$ receptor blockade
      - ii. ? stimulates release of ACh as 2° agonist
        - GIT effects blocked by atropine

- **Domperidone**
  - both prokinetic and antiemetic
  - also a dopaminergic blocking agent
  - effects on GIT →
    - a. same spectrum of activity cf. metoclopramide
      - but not blocked by atropine
      - efficacy for gastric motility equivalent
    - b. doesn't cross the BBB, ∴ CNS effects are supposedly less
    - c. less antiemetic activity

- **Cisapride**
  - effects on GIT = metoclopramide | domperidone
  - however, also increases colonic motility
  - mechanism poorly understood
  - like metoclopramide activity is blocked by atropine, ∴ partially due to myenteric ACh
## Body Fluids

<table>
<thead>
<tr>
<th>Body Fluids</th>
<th>Vol/day</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Cl⁻</th>
<th>HCO₃⁻</th>
<th>IVT</th>
<th>+ KCl</th>
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<tr>
<td>Plasma</td>
<td>136-144</td>
<td>3.5-5.0</td>
<td>95-110</td>
<td>25</td>
<td></td>
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<tr>
<td>Gastric</td>
<td>1-5 l</td>
<td>30-120</td>
<td>10-15</td>
<td>140</td>
<td>pH ~ 1.5</td>
<td>N.Sal</td>
<td>~20-50</td>
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<tr>
<td>Bile</td>
<td>&lt; 1000ml</td>
<td>145</td>
<td>5</td>
<td>100</td>
<td>35-70</td>
<td>Hart</td>
<td>20</td>
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<tr>
<td>Pancreas</td>
<td>&lt; 1000ml</td>
<td>140</td>
<td>5</td>
<td>60</td>
<td>90</td>
<td>Hart</td>
<td>20</td>
</tr>
<tr>
<td>SI</td>
<td>1-3 l</td>
<td>120</td>
<td>5-10</td>
<td>105</td>
<td>25</td>
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<td>100-500ml</td>
<td>&lt; 80</td>
<td>20-40</td>
<td>&lt; 50</td>
<td>&lt; 45</td>
<td>Hart</td>
<td>20-50</td>
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<tr>
<td>Sweat</td>
<td>~ 400ml</td>
<td>50</td>
<td>5-10</td>
<td>45</td>
<td>D,W-N/5</td>
<td>N/2 Sal.</td>
<td>20</td>
</tr>
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</table>
Diarrhoea

**Def’n:** ≥ 3 watery bowel actions per day

- a common problem, occurring in ~ 25% of enterally fed patients
- often independent of feeding regimen, often culture/toxin negative
- common aetiology of diarrhoea in ICU patients,
  a. part of primary illness
  b. drug induced
  c. recovery from ileus
  d. acquired hypoalbuminaemic "protein losing enteropathy"
  e. change in bowel flora - bacterial overgrowth
  f. hypo or hyper-osmotic feeds

### Diarrhoea - Classification

a. **infective**
   i. viral
   - rotavirus, enteroviruses
   - Hepatitis A & B, CMV
   ii. bacterial **toxins**
   - enterotoxigenic *E. coli*
   - *Klebsiella sp.*
   - *Enterobacter*
   - *Staph. aureus*
   - *Bacillus cereus*
   - *Vibrio cholerae*
   - *Cl. perfringens*
   - *Cl. difficile* (pseudomembranous colitis)
   - *Cl. botulinum*
   iii. bacterial **invasion**
   - enteropathogenic *E. coli*
   - *Campylobacter sp.*
   - *Vibrio parahaemolyticus*
   - Salmonella
   - Shigella
   - Staphylococci
   iv. fungal
   - Candidiasis
   v. protozoal
   - Giardiasis
   - *Entamoeba histolyticum*
b. non-infective
i. drugs - antibiotics
- Mylanta and other antacids
- osmotic agents, cathartics
- cholinergics
- antimetabolites
- chemotherapy
- common non-specific side effect

ii. bowel disease - diverticulitis
- ulcerative colitis
- Crohn's disease
- enterocolic fistula
- ischaemic colitis
- pelvic abscess
- villous adenoma
- carcinoma
- faecal impaction + overflow incontinence

iii. malabsorption - lactose intolerance
- hypoalbuminaemia
  (acquired "protein losing enteropathy")
- tropical sprue
- pancreatic insufficiency
- enteral feeds

iv. post-GIT surgery - short bowel
- blind loop
- post-gastrectomy
- recovery from paralytic ileus, or obstruction

v. endocrine / metabolic - thyrotoxicosis
- diabetes
- hypoparathyroidism
- carcinoid
- hypoadrenalism
- autonomic neuropathy
- heatstroke

- **Causes of Antibiotic-Induced Diarrhoea**

  a. direct irritation, decreased transit time
  b. altered microflora - decreased anaerobes
  - increased gram (-)ves
  c. resistant organisms - Candidiasis
  - Staphylococcal overgrowth
  d. pseudomembranous colitis - *Cl. difficile*
- **Diagnosis**

  a. history - medical/surgical problems, drugs
  b. examination - fluid status, nature of feeding
  - abdominal signs, PR, sigmoidoscopy
  c. serum electrolytes and albumin
  d. feces for microbiology - M,C & S
  - ova & paracytes
  - Cl. difficile toxin
  e. AXR - erect and supine
  f. sigmoidoscopy / colonoscopy

- **Short Bowel Syndrome**

  - SI resection,
    a. \( \leq 50\% \) is usually tolerated without impairment
    b. \( \geq 75\% \) usually results in malabsorption of nutrients
    c. with remaining bowel 15-20% (60-80 cm), refeeding should be progressive, with a view to attaining a normal dietary intake

  - clinical sequelae & management,
    1. diarrhoea - loperamide, codeine, \( H_2 \)-blockers, cholestyramine, octreotide
    2. malabsorption
      - calcium - calcium salts, \( 1,25(OH)_2D_3 \)
      - magnesium, zinc, other trace elements
      - folate, \( B_{12} \), iron
      - fat soluble vitamins
    3. nephrolithiasis / hyperoxaluria - cholestyramine
      - hyperoxaluria 2° ↑ colonic absorption with extensive ileal loss
    4. gastric acid hypersecretion - \( H_2 \)-blockers, omeprazole, octreotide, ketanserin
      - peptic ulceration
      - diarrhoea
    5. metabolic acidosis
      - SI bacterial overgrowth
      - \( d \)-lactic acidosis - metronidazole, vancomycin
      - \( HCO_3 \) losing diarrhoea - sodium citrate / acetate
    6. gall stones
      - ↓ bile salt pool & ↑ lithogenicity of bile
UPPER GASTROINTESTINAL HAEMORRHAGE

**Aetiology**

1. oesophageal
   i. varices
   ii. Mallory-Weiss syndrome
   iii. oesophagitis

2. gastric & duodenal
   i. peptic ulceration / acute stress ulceration
   ii. gastritis
   iii. hiatus hernia
   iv. tumours - benign, malignant
   v. AV malformation, telangetasia

3. aorto-enteric fistula

4. coagulation disorders

**Investigation**

1. laboratory investigation
   i. FBE/Coags - [Hb], platelets, INR/APTT
   ii. EC&U, LFT, CaP, BSL, Mg
      • *urea:creat. ratio* > 100 in 87% with upper GI bleeding
      < 100 in 95% with lower GI bleeding

2. *endoscopy*
   • potential bleeding site identified ~ 90%
   • multiple potential bleeding sites ~ 33%
   • performed within 12 hrs, active bleeding ~ 45%

3. contrast studies
   • less sensitive / specific cf. endoscopy
   • Gastrograffin / barium swallow will only detect bleeding site in ~ 50%

4. angiography
   • may be of value with continued bleeding > 0.5-2 ml/min

**Management**

1. ABC / resuscitation → priority
2. 85% will stop bleeding *spontaneously*
3. specific management per lesion
Stress Ulceration

- distinguish stress erosions (75-100%), stress ulcers and stress haemorrhage (~ 5%)
- stress ulcers occur within minutes to hours → sign of *splanchnic ischaemia*
- incidence in the 1970's,
  - a. erosions ~ 75-100%
  - b. ulcers ~ 50%
  - c. macroscopic bleeding ~ 25%
  - d. *serious bleed* ~ 5% → ~ 50-70% mortality
  - e. perforation rare

**NB:** markedly reduced with antacids / H₂ blockers → universal use

- *overt bleeding* occurred with,
  - a. placebo ~ 15%
  - b. antacids ~ 3.3%
  - c. H₂ blockers ~ 2.7%

- the incidence in the 1980's,
  - a. erosions ~ 40-50%
  - b. ulcers ~ 5% ∝ 10x ↓ incidence
  - c. macroscopic bleeding ~ 5% ∝ 5x ↓ incidence
  - d. serious bleed → rare but still a *high mortality*

**NB:** Reusser *et al.* CCM 1990
**RCT** of endoscopically detected stress ulceration in neurosurgical patients (n = 40) prophylaxis and non-prophylaxis groups → *no significant difference*
therefore queried whether antacids / H₂ blockers are still necessary !

- **Risk Factors**
  - a. previous ulcer disease
  - b. coagulopathy
  - c. mechanical ventilation > 48 hrs
  - d. previous factors → now questioned
    - i. head injury, multiple trauma
    - ii. severe burns
    - iii. sepsis / SIRS
    - iv. hypotension, hypovolaemia
    - v. renal failure
    - vi. hepatic failure
Prophylaxis

- proven measures,
  a. gastric pH control → antacids > H₂-blockers
  b. cytoprotective drugs → sucralfate ≡ antacids / PG-analogues
  c. nutrition → enteral > TPN

- the reduced incidence is also probably due to,
  a. better ICU management
  b. better O₂ & fluid management
  c. early NG feeding
  d. improved analgesia
  e. Rx of coagulopathy
  f. ? dopamine → improved gut blood flow

Pathology

- the site is usually the fundus and body
- rarely in the antrum, duodenum, or oesophagus
  1. mucosal ulceration
     • superficial, eroding through to the muscularis mucosae only
     → results in little bleeding & heals rapidly
  2. acute peptic ulceration
     • deep, through the muscular layer where the larger arteries reside
     → greater bleeding and slower to heal

- damage to mucosal defences is caused by,
  a. alcohol
  b. aspirin, NSAID’s
  c. vasoconstrictors
  d. steroids

- factors which increase the risk of haemorrhage,
  a. aspirin, NSAID’s
  b. anticoagulants
  c. dextrans
  d. antibiotics → vit K deficiency, platelet defect
local defence mechanisms include,

a. the mucus barrier
b. surfactants & HCO$_3^-$ - secreted by mucosal cells
c. H$^+$ reabsorbed by the mucosa is neutralised by blood derived HCO$_3^-$ and washed away by rich mucosal blood flow

- shock states result in,
  a. mucosal ischaemia
     • TNF results in thrombosis within gastric mucosal vessels
     • sympathetic redistribution of blood flow away from the splanchnic bed
  b. H$^+$ / pepsin / bile seep in and damage intracellular components
  c. mucosal necrosis → ulcer formation

- pepsin is still active unless pH > 7
  1. pH ~ 5-7 → pepsin still dissolves clot, and
  2. pH < 5.4 → pepsin prevents clot formation

**NB:** but alkaline gastric contents are not necessary for prevention, and there is no evidence that hypersecretion per se is responsible for erosions

- intracellular pH is probably more important than intra-gastric pH

- prostaglandins result in,
  a. ↑ blood flow
  b. ↑ mucus production, and ? mucus secretion
  c. ↓ ulcer incidence and promotion of healing

- bile salt disruption of the mucosal barrier occurs, and prevention of duodenal reflux is associated with a significant reduction in gastric ulceration

<table>
<thead>
<tr>
<th>Acid/Pepsin Production reduced by</th>
<th>Mucosal Resistance increased by</th>
</tr>
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<tbody>
<tr>
<td>enteral feeds</td>
<td>enteral feeds</td>
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<tr>
<td>prostaglandins</td>
<td>? prostaglandins</td>
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<tr>
<td>antacids</td>
<td>sucralfate</td>
</tr>
<tr>
<td>H$_2$ blockers</td>
<td></td>
</tr>
</tbody>
</table>
**Prevention**

a. treat stress factors → improve gut $O_2$ delivery  
   - normovolaemia, adequate $O_2$ / ventilation  
   - maximise cardiac output & GIT perfusion pressure  

b. NG feeds ASAP  
   - especially high risk groups  
     - head injury, major trauma, burns  
     - prolonged IPPV  
     - renal failure, hepatic failure  
     - sepsis  

c. sucralfate $| H_2$-blockers where  
   - NG aspiration of blood / "coffee grounds"  
   - no NGT and "at risk"  
   - previous peptic ulcer disease  

d. omeprazole  
   - clinical bleed on $H_2$-blockers  
   - endoscopically proven ulceration not healing with $H_2$-blockers

**Treatment: Mild Bleed**

a. maximise coagulation status / remove precipitants  
   i. vit K  
   ii. stop heparin, NSAID's etc  
   iii. blood transfusion, FFP, platelets etc  
   iv. DDAVP for patients on aspirin, or with liver or renal failure  

b. antacids - pH > 3.5 (ideally > 7)  

c. sucralfate  

d. $H_2$-blockers  
   - cimetidine, *ranitidine* and famotidine are competitive antagonists  
   - ↑ GI gram negative colonisation does not increase nosocomial pneumonia ??  

e. *omeprazole*  
   - absorbed in SI, short plasma $t_{1/2}$ but effective for 24 hrs  
   - binds irreversibly to fundic parietal cell $H^+/K^+\text{-ATPase}$  
   - 20 mg → 65% inhibition at 4-6 hrs  
     25% inhibition at 24 hrs  
   - 40 mg → 100% inhibition of mean 24 hr gastric acid secretion  
   - results in *hypogastrinaemia* & potential enterochromafin hyperplasia  

f. prostaglandins - PGE$_{1,2,3}$  

g. *aminocaproic acid* - 5g stat & 1 g/hr for 24 hrs IV  
   - ~ 20-30% reduction in rebleeding  
   - ~ 40% reduction in mortality
h. **endoscopy** for assessment

**NB:** if **major bleed** then proceed with,

1. **octreotide infusion** ~ 100 µg stat, then 12.5-25 µg/hr
   - some data now to say 50 µg stat, then 50 µg/hr equally effective to **sclerotherapy**
2. **pitressin infusion** *questionable benefit*
3. **endoscopic haemostasis** - laser coagulation, electrocoagulation
   *questionable benefit in stress ulceration*
4. **surgery**
   - partial or total gastrectomy in the setting of uncontrolled GI haemorrhage
   \[\rightarrow \text{mortality} \sim 70\%\]

**Cushing's Ulcer**
- lesions in the oesophagus, stomach & duodenum, initially described by Cushing in association with **coma** from any cause
- now accepted as acute peptic ulceration in association with severe **head injury** and raised ICP
- results from increased vagally mediated gastric acid secretion & responds to **H₂-blockade**

**Curling's Ulcer**
- circumscribed (≤ 2 cm) duodenal ulcer in patients with ≥ 35% **burns**
- also results from gastric acid hypersecretion & responds to **H₂-blockade**
Ulcer Prophylaxis

- early 1970's Rₓ → hourly gastric pH, plus mylanta 30 ml/hr to keep pH > 5
- this resulted in a large reduction in GIT bleeding
- problems with high dose Mylanta included,
  1. diarrhoea / constipation
  2. electrolyte abnormalities → hypo-PO₄⁻³
     hyper-Mg²⁺ / hyper-Al¹
  3. ↓ drug absorption
  4. bowel obstruction

- following the introduction of H₂-blockers, Rₓ →
  1. hourly gastric pH
  2. if pH < 5 add antacids

- problems of H₂-blockers (*cimetidine*),
  1. CNS side effects
  2. drug interactions - P₄₅₀ inhibition
  3. thrombocytopenia, leukopenia
  4. bradycardia, hypotension
  5. jaundice, renal failure
  6. GIT side effects
  7. rash / fever
  8. endocrine effects

*N'B*: cimetidine >> ranitidine, famotidine

- very few proper studies comparing the efficacy of *antacids vs H₂ blockers*
- faecal occult blood test useless,
  a. cimetidine → false (+)ve
  b. antacids → false (-)ve

- problems of antacids and H₂ blockers,
  1. diarrhoea
  2. drug interactions
  3. microaspiration ? gram (-)'ve pneumonia
  4. sepsis
Sucralfate

- Sucrose-Al(OH₃)-sulphate, with added H⁺ → paste formation which results in,
  a. coating of cells
  b. ↓ back-diffusion of H⁺
  c. ↑ prostaglandin secretion

- therefore, must avoid simultaneous use of antacids and H₂-blockers

- problems of Sucralfate include,
  1. blockage of NG tube
  2. nausea, vomiting, constipation - rarely obstruction with high dose
  3. hypo-PO₄²⁻ and increase Al⁺
  4. prevents drug absorption
  5. overt bleeding - same incidence as antacids and H₂-blockers
  6. nosocomial pneumonia - cf H₂ blockers
    i. German → 10% vs 34%
    ii. Boston → 9% vs 23%

NB: enteral feeds partially buffer gastric acid, the increased energy supply to the mucosa improves defences, ∴ sucralfate is not necessary

Cook et al. JAMA 1996

- metaanalysis of 63 PRCT’s assessing efficacy of sucralfate, H₂-antagonists and antacids in the prevention of,
  1. overt bleeding
    • H₂-antagonists → significant ↓ cf. placebo | no therapy | antacids
    • sucralfate → significant ↓ cf. no therapy
    • no evidence for differential efficacy of sucralfate versus antacids | H₂-antagonists
  2. clinically significant bleeding
    • H₂-antagonists → significant ↓ cf. placebo | no therapy
    • sucralfate no difference from antacids | H₂-antagonists
  3. pneumonia *diagnostic criteria variable & suspect
    • sucralfate was associated with a trend toward lower incidence cf. H₂-antagonists
  4. mortality
    • sucralfate was associated with reduced mortality cf. antacids | H₂-antagonists
    • OR = 0.73 (CI: 0.54-0.97)
Peptic Ulceration

- **Duodenal Ulceration**
  - 95% occur in 1st part
  - chronic and recurrent disease
  - approximately 2x the normal parietal cell mass & secrete ≤ 40 mmol/hr of H⁺
  - seen with increased frequency in,
    a. smoking
    b. NSAID use
    c. chronic renal failure / renal transplantation
    d. alcoholic cirrhosis
    e. hyperparathyroidism
    f. COPD

- *Helicobacter pylori* (GN spiral bacterium) produces a urease, which splits urea producing ammonia which neutralises H⁺ in the stomach, blocking the negative feedback on the antral production of gastrin
  - colonisation has been reported in up to 100% of DU patients

- all H₂-blocking agents are equally efficacious,
  a. 75% healed at 4 weeks
  b. 90% at 8 weeks
  c. high 12 month recurrence rate → ~ 33% without symptoms
  d. ∴ all should receive 12 months maintenance therapy - 150 mg ranitidine nocte

- **omeprazole** 20 mg/day is efficacious in 5-10% of DU patients not responsive to H₂-blockers
  - if not healed at 8 weeks, then 2-4 weeks of omeprazole 40 mg/day
  - while more efficacious, omeprazole induced hypergastrinaemia results in
    1. hypertrophy of enterochromafin-like cells
    2. carcinoid tumours in animals

- levels of gastrin are generally less than those found in pernicious anaemia
  - however, therapy is generally limited to 4-8 weeks, followed by maintenance ranitidine

- **pirenzpine** is a selective M₁-antagonist → ↓ acid secretion ~ 50-60%
  - minimal anticholinergic side-effects (blurred vision, dry mouth, constipation, urinary retention)
  - equally effective to H₂-blockers in healing, but slower resolution of ulcer pain

- **sucralfate** shows similar rates of ulcer healing to H₂-blockers
- **colloidal bismuth subcitrate** promotes healing as a cytoprotective agent, cf sucralfate
- also inhibits *H. pylori* and has a lesser relapse rate cf. *H₂*-blockers & sucralfate

- **surgery** is indicate for,
  1. patients > 60 years of age
  2. bleeding ulcer not controlled by medical therapy

  **NB:** truncal vagotomy & oversew of ulcer ± pyloroplasty

- **Gastric Ulceration**
  - peak incidence ~ 60 years, cf. DU at 40-50 years
  - requires endoscopy & **biopsy** to exclude carcinoma
  - other therapy is cf. DU
Oesophageal Varices

- systemic / splanchnic anastomoses occur at,
  1. gastro-oesophageal junction
  2. retroperitoneal space, between kidneys & spleen
  3. mesenteric / gonadal veins
  4. diaphragm
  5. umbilicus
  6. rectum

- portal venous pressure,
  a. normal ~ 5-10 mmHg
  b. portal hypertension > 12 mmHg
  c. bleeding varices ~ 12-40 mmHg

- of patients with cirrhosis,
  a. 60% develop oesophageal varices
  b. 66% of these bleed → ~ 40% of cirrhotics develop bleeding varices

**Poor Prognostic Factors**

a. severity of liver disease ≥ Child's grade C
   - ascites, encephalopathy
b. severity of haemorrhage ≥ 2000 ml, or ≥ 5⁰ transfusion
   - continuing / recurrent haemorrhage
c. age > 60
d. associated disease - IHD, respiratory or renal disease
   - coagulopathy
   - malignancy

**Treatment Aims**

1. resuscitation
2. control of haemorrhage
3. prevention of encephalopathy
4. correction of complications
**Therapy Options**

a. endoscopic *variceal sclerosis*
   - Rx of choice for acute haemorrhage and control of rebleeding
   - greater efficacy \(\sim 80-90\%\) control of haemorrhage
     - cf. \(\sim 60\%\) for balloon tamponade
   - better survival \(\sim 84\%\) at 6 months
     - cf. \(\sim 45\%\) for balloon tamponade
   - gastric varices also regress following eradication of oesophageal varices
   - *prophylactic* sclerotherapy, in those who have not bled,
     - is of *no value* and is associated with *increased mortality*
   - complications
     - retrosternal pain, strictures, dysphagia
     - fever, bacteraemia, mediastinitis, empyema
     - aspiration, pneumonia, ARDS

b. variceal banding
   - some suggest more effective than sclerotherapy, \(\therefore\) procedure of choice if experienced operator

c. Vasopressin
   - 0.2-0.8 U/min
   - reduces portal pressure and temporary control of bleeding
   - efficacy \(\rightarrow\) \(\equiv\) placebo \(\sim 30-50\%\) controlled
   - \(\pm\) GTN for systemic effects
     - \(\sim 20\%\) side effects, \(3\%\) mortality
     - hypertension, coronary & bowel ischaemia
     - diarrhoea, colic

d. *Somatostatin*
   - 250-500 \(\mu\)g/hr
   - controlled trial vs vasopressin showed *more effective* & less complications
     - Jenkins *et al.* BMJ 1985
   - no trials with *octreotide* (12.5-25 \(\mu\)g/hr) but probably equally effective

e. *balloon tamponade*
   - \(\sim 80-90\%\) control of haemorrhage
     - \(\rightarrow\) but *50\% rebleed*
   - reserved for acute haemorrhage not controlled by sclerotherapy
   i. Linton-Nachlas
      - single gastric lumen
   ii. Sengstaken-Blakemore
      - oesophageal & gastric balloons, gastric suction
   iii. *Minnesota*
      - 4 lumens, 2 balloons, gastric & oesophageal suction
      - intubate if required, tube may be inserted nasally or orally to 60 cm
      - inflate gastric balloon with 250-500 ml of air & apply traction \(\leq 1\,\text{kg}\)
      - seldom necessary to inflate oesophageal balloon if gastric correctly placed
      - continuously aspirate stomach to assess bleeding control
      - if required, inflate oesophageal balloon with air to a pressure \(\leq 40\,\text{mmHg}\)
      - check position on CXR

f. TIPS
   - transjugular intrahepatic porta-systemic shunt
   - successful in reducing portal pressure \(\rightarrow\) \(< 12\,\text{mmHg}\)
   - likely to become procedure of choice, irrespective of patient's Child's classification
g. porta-systemic shunt  ~ 90% control  
   ~ 20-40% mortality  
   • 4 RCT's showing PSS reduces rebleeding, but no decrease long-term mortality  
   • high incidence encephalopathy  

h. distal / selective shunts - spleno-renal (Warren)  
   • effectively divides the splanchnic circulation into portomesenteric and gastrosplenic  
   • incidence of post-shunt encephalopathy is greatly reduced  
   • does not prevent later liver transplantation  
   • no difference in mortality cf central shunts  

i. transhepatic embolisation  

j. oesophageal transection  

k. orthoptic liver transplantation  

- **Current Recommendations**  

1. resuscitate  
2. early endoscopy, if ongoing bleeding, then  
   i. Minnesota tube ~ 150-200 ml air in gastric balloon  
      ~ 0.75-1.0 kg traction  
      ± 30-40 mmHg in oesophageal balloon  
   ii. variceal sclerosant ± variceal banding  
3. octreotide infusion  
4. TIPS  

- β-blockade in contraindicated in the acutely bleeding patient  
- however, does reduce portal pressure and rebleeding once bleeding is controlled
HEPATIC DISORDERS

- **Functional Anatomy**

  1. **hepatic lobule**
     - central hepatic venule | sinusoids | peripheral portal triad
     - traditional unit

  2. **hepatic acinus**
     - **zone 1** - portal vein & hepatic artery supplying sinusoids
     - **zone 2** - follows sequentially
     - **zone 3** - drains to hepatic venule
       - arrangement produces gradient of all nutrients, etc from zone 1 to 3
       - zone 3 is most susceptible to hypoxic injury

  3. blood flow ~ 1500 ml/min
     - **hepatic artery** ~ 33% of flow & ~ 60% of DO₂
     - **portal vein** ~ 66% of flow & ~ 40% of DO₂

- **Liver Functions**

  1. **bile production** ~ 500 ml/day secreted
     - fat digestion & excretion of drugs, toxins and bilirubin
     - bile salts, lecithen, cholesterol, bilirubin & electrolytes
     - **bile salts**
       - Na⁺/K⁺-salts of cholic & chenodeoxycholic acids
       - ~ 95% reabsorbed in terminal ileum
       - daily synthesis ~ 0.2-0.4g of total pool of ~ 3.5g
       - absence results in ~ 25% fat malabsorption & ADEK deficiency
     - **bilirubin**
       - ~ 7.5g of Hb are catabolised per day → 250 mg (440µmol)/day
       - ~ 80% old RBCs, remainder from young RBCs, myoglobin, enzymes
       - liver capacity ~ 15g Hb/day
       - conjugated in microsomes in 2-step process
       - normal excretion → ~ 85% diglucuronide / 15% glucuronide
         - energy dependent and rate limiting step

  2. **protein synthesis**
     - albumin, some globulins
     - coagulation & fibrinolytic factors
     - prekallikrein, kininogen
     - serum proenzymes / enzymes
     - carrier proteins
     - **acute phase reactants** - C-reactive protein, complement, coagulation
       - haptoglobins, plasminogen
       - α₁-antitrypsin, α₂-macroglobulin, caeruloplasmin
3. **CHO and intermediary metabolism**
   i. amino acids - protein synthesis  
   - gluconeogenesis  
   - transamination  
   ii. glucose - production and storage  
   - conversion to fat, AA's  
   - glucuronidation  
   - energy source  
   - NADPH production  
   iii. fat - metabolism  
   - lipoprotein for transport  
   - cholesterol, ketones

4. **hormone synthesis & metabolism**

5. **biotransformation**
   i. ammonia & **urea cycle**
   ii. drugs & toxins

6. **storage**
   i. glycogen ~ 80-100g  
   ii. fat ≤ hepatic weight  
   iii. Fe++, B₁₂, folate, Cu

7. **immune defence** - against agents entering the portal circulation

---

**Post-operative Jaundice**

**Aetiology**

a. **increased bilirubin load**
   i. haemolysis  
   ii. haematoma - reabsorption  
   iii. transfusion - old cells, incompatibility, sepsis

b. **hepatocellular dysfunction**
   i. congenital  
      • Gilbert's disease - **ligandin** deficiency → ↓ uptake  
      • Crigler-Najjar Type I & II - low or absent **glucuronyl transferase**  
      • Rotor's & Dubin-Johnson - low biliary excretion  
   ii. acquired *see hepatitis*  
      • hepatitis - hypoxia/ischaemia, infective, sepsis, drugs, trauma, etc  
      • cholestasis - hypoxia/ischaemia, drug-induced, TPN, pregnancy

c. **obstructive**
   i. bile duct trauma, oedema, ligation  
   ii. cholangitis  
   iii. cholelithiasis
Hyperbilirubinaemia

- **Predominantly Unconjugated**

  1. **overproduction**
     i. haemolysis
     ii. reabsorption of haematoma
     iii. ineffective erythropoeisis
  2. decreased hepatic **uptake**
     i. sepsis
     ii. prolonged fasting
     iii. RV failure
     iv. drugs - rifampicin, probenecid
  3. decreased **conjugation**
     i. hepatocellular disease - hepatitis, cirrhosis
     ii. sepsis
     iii. drugs - chloramphenicol
     iv. inherited glucuronyl transferase deficiency
        - Gilbert's syndrome - actually *ligandin* deficiency
        - Crigler-Najjar - types II & I

- **Predominantly Conjugated**

  1. impaired hepatic **excretion**
     i. sepsis
     ii. post-operative state
     iii. hepatocellular disease
        - hepatitis - viral, ischaemic, drug-induced
        - cirrhosis
     iv. drug-induced cholestasis - OCP, methyltestosterone
     v. inherited disorders - Dubin-Johnson, Rotor syndrome - benign familial recurrent cholestasis
     vi. cholestasis of pregnancy
  2. biliary **obstruction**
     i. biliary cirrhosis - primary | secondary
     ii. sclerosing cholangitis
     iii. extrahepatic obstruction - stone, tumour, stricture
Intrahepatic Cholestasis

**Def’n:** severe form ~ "ICU liver"
mild form ~ "benign postoperative intrahepatic cholestasis"
- common after major, abdominal, or emergency surgery
- especially if associated with hypotension & hypoxia

**Pathogenesis**

- liver hypoxia / ischaemia
- sepsis
- inflammatory mediators - endotoxin, TNF, IL-1, free radicals
- ↑ bilirubin load - haematoma, transfusion
- TPN induced hepatic steatosis
- ↓ renal excretion
- drugs
  - flucloxacillin, rifampicin, erythromycin estolate
  - chlorpromazine, phenytoin, carbamazepine, valproate
  - steroids, OCP

- hyperbilirubinaemia (≥ 100 µmol/l) disproportionate to enzyme levels, common at 2-14^{th} day
  - usually > 80% conjugated and may rise as high as 600 µmol/l
  - mild ALP elevation 3-10x increase → "obstructive jaundice" pattern (ie. biliary stasis)
  - this is often delayed 5-10 days after the rise in bilirubin
  - mild increase in AST/ALT
  - prolonged form also has severe hypoalbuminaemia → INR ≥ 1.4
  - associated reduction in protein synthesis, reduced AA clearance, & low redox potential
  - differential diagnosis,
    1. acalculous cholecystitis
    2. calculus colecystitis
    3. hepatic abscess
    4. drug induced cholestasis
Liver Function Tests

1. albumin
   - spectrophotometric absorption of bromocresol green at pH = 4.2
   - BCG also bound to acute phase reactants, \( \therefore \) Alb actefactually elevated (up to 10g/l)
   - \(~ 50\% \) resides in intravascular space

2. globulins
   - usually not measured, but calculated from total protein - albumin
   - increases either,
     i. polyclonal - cirrhosis, infection, autoimmune diseases
     ii. monoclonal - myeloma, lymphomas
   - decreased with malignancy, malnutrition, plasmapheresis

3. gamma-glutamyl transferase
   - resides in cells of the bile canaliculi, responsible for AA transport
   - also present in the pancreas and brush border of renal tubules
   - nonspecific indicator of hepatic dysfunction
   - levels usually highest with obstructive disorders
   - most common causes for elevation - chronic ethanol abuse
     - antiepileptic medication

4. alkaline phosphatase
   - originates from liver, bone, placenta, and intestine (? brain)
   - occasionally from malignancies - indistinguishable from placental isoenzyme
   - normal plasma ALP \( \sim \) 80% liver / 20% GIT
   - in children/adolescents, major source is growing bone (osteoblasts)
   - resides on luminal surface of bile canalicular cells
   - elevated in obstructive/cholestatic disorders
   - however \( \sim 20\% \) of patients with a cholestatic disorder \( \rightarrow \) \(< 250 \text{ IU/l}\)
     i. hepatic - cholestatic disorders
     ii. bone - physiological
        - Paget's disease
        - recent fracture(s)
        - carcinoma, primary / secondary
        - hyperparathyroidism, \( 1^\circ, 2^\circ, 3^\circ \)
        - osteomalacia, \( 2^\circ \) calcium/phosphorus deficiency
          \( \rightarrow \) Vit.D, malabsorption, RTA
     iii. placenta - \( 3^{\text{rd}} \) trimester pregnancy


5. lactic acid dehydrogenase
- exists as 5 isoenzymes: LDH\textsubscript{1,2} → haemolysis, myocardial damage
  - LDH\textsubscript{3,4,5} → hepatic, skeletal muscle
- also produced by lung (LDH\textsubscript{2,3}) and kidney (LDH\textsubscript{1,2}) but these are rare causes
- normal LDH\textsubscript{1}:LDH\textsubscript{2} < 1 → > 1 in - myocardial infarction
  - renal infarction
  - haemolysis

6. transaminases
   i. aspartate amino-transferase
      - AST, cytosolic & mitochondrial - also called SGOT
      - liver, kidney, cardiac & skeletal muscle
   ii. alanine amino-transferase
      - ALT, cytosolic - also called SGPT
      - predominantly liver, some skeletal m., brain & pancreas
      - both elevated in hepatocellular disorders *see hepatitis
      - degree of elevation does not correlate well with the degree of liver damage
        → ie. they have no predictive value
      - infective / toxic hepatitis → ↑ lasting weeks
        → ↑ AST:ALT ~ 1.5:1
      - ischaemic hepatitis → ↑ lasting days
        → ↑ AST:ALT ~ 1.5:1
      - alcoholic hepatitis → ↑ AST:ALT > 2:1 (rarely > 500 IU/l)
      - false lowering of the AST may occur with azotaemia

7. prothrombin

8. ammonia < 30 mmol/l normal
   - absolute elevation correlates poorly with encephalopathy, but may be used as a
     guide to therapy response in an individual patient

9. urobilinogen
   - formed by intestinal bacteria acting on conjugated bilirubin
   - 80% excreted in feces, 20% reabsorbed in terminal ileum
   - 90% of reabsorbed urobilinogen re-excreted in bile, 10% → urine (~ 2%)
   - complete absence in urine suggests absence of intestinal bilirubin & obstruction
   - ↑ urinary urobilinogen - liver in unable to excrete absorbed urobilinogen
     - increased excretion of bilirubin, haemolysis

10. urinary bilirubin
    - normally absent
    - excretion occurs in conjugated hyperbilirubinaemia
Liver Function Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Hepatocellular injury</th>
<th>Obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartate transaminase(^1)</td>
<td>AST / SGOT (\uparrow) to (\uparrow\uparrow\uparrow)</td>
<td>(\uparrow)</td>
</tr>
<tr>
<td>Alanine transaminase (\uparrow)</td>
<td>ALT / SGPT (\uparrow\uparrow\uparrow\uparrow\uparrow)</td>
<td>(\uparrow\uparrow\uparrow)</td>
</tr>
<tr>
<td>Alkaline Phosphatase (\uparrow)</td>
<td>(\uparrow) (\uparrow\uparrow\uparrow\uparrow)</td>
<td>(\uparrow\uparrow\uparrow)</td>
</tr>
<tr>
<td>Gamma-glutamyl transpeptidase (\uparrow)</td>
<td>GGT (\uparrow\uparrow\uparrow\uparrow)</td>
<td>(\uparrow\uparrow\uparrow)</td>
</tr>
<tr>
<td>5-Nucleotidase (\uparrow)</td>
<td>ALP (\uparrow\uparrow\uparrow\uparrow\uparrow)</td>
<td>(\uparrow\uparrow\uparrow)</td>
</tr>
<tr>
<td>Albumin (\downarrow)</td>
<td>(\downarrow\downarrow\downarrow)</td>
<td>(\uparrow)</td>
</tr>
<tr>
<td>Prothrombin time (\uparrow)</td>
<td>(\uparrow\uparrow\uparrow\uparrow)</td>
<td>(\uparrow)</td>
</tr>
<tr>
<td>Bilirubin (\uparrow)</td>
<td>(\uparrow\uparrow\uparrow)</td>
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</table>

1. **AST** also in heart, rbc’s, muscle. **ALT** is more specific for liver, enzyme rise reflects extent & acuteness of cellular injury, but does not correlate with prognosis.
2. Origins of **ALP** include: liver, bone, intestine, placenta & lung.
3. Increase does have worse prognosis. Shorter half-life & more rapid change cf. albumin.
4. Correctable with vitamin K.

**Sequelae of Liver Dysfunction**

- **Hypoalbuminaemia** - low COP, increased tendency to **oedema** formation
- **Coagulopathy** - ↓ vit K dependent factors
  + May bleed or have thromboses
- **Septicaemia** - immune dysfunction
- **Toxaemia** - metabolites, bacteria, toxins
- **Amino-acid imbalance** - low branched-chain / high aromatic
- **Drugs** - altered pharmacodynamics & kinetics, \(\uparrow\) \(t_{\text{half}}\)
- **Hyperammonia** - not cleared
- **Severe hypoglycaemia** - impaired glucose & AA metabolism
- **Citrate toxicity** - impaired metabolism with large volume transfusions
  + Especially the anhepatic phase of transplantation
  - \(R_X\) CaCl₂
Hepatitis

1. **infective**
   - Hepatitis A, B, C, Delta, E, NANBNC
   - EBV, CMV, HSV, Coxsackie, Yellow fever

2. **drugs**
   i. **cholestasis**
      - alcohol
      - chlorpromazine, chloramphenicol, chlorpropamide
      - tetracyclines, erythromycin, rifampicin
      - oestrogens, OCP, androgens
   ii. **hepatitis**
      - $\alpha$-methyl-dopa $\rightarrow$ 5% abnormal LFT's
      - 1% hepatitis
      - 0.15% CAH
      - paracetamol, phenytoin, isoniazid, rifampicin
      - **halothane**, enflurane, & ? isoflurane

3. **toxins**
   - CCl$_4$, vinyl chloride, chloroform
   - *Amanita phalloides* (mushroom)

4. **cardiovascular**
   i. **ischaemic**
      - hypovolaemic shock, ischaemia
   ii. **congestive**
      - cor pulmonale, RV failure, CCF
      - Budd-Chiari syndrome

5. **metabolic**
   - alcohol
   - parenteral nutrition
   - Wilson's disease (hepatolenticular degeneration)
   - Haemochromatosis
   - $\alpha_1$-antitrypsin deficiency

6. **autoimmune**
   - chronic active hepatitis
   - drug induced
   - vasculitis, SLE, UC, PN
   - 1° biliary cirrhosis

7. **pregnancy**
   - acute fatty liver of pregnancy

8. **hyperthermia**

---

**Ischaemic Hepatitis**

- centrilobular necrosis (acinar zone 3) secondary to liver ischaemia, hypotension, hypoxia, sepsis, MODS, pancreatitis, etc.

a. mild to moderate hyperbilirubinaemia

b. $\uparrow$ liver enzymes $\rightarrow$ ratio AST:ALT $<$ 1.5:1
   - cf. ETOH hepatitis, AST:ALT $>$ 2:1
   - often rapid rise to high levels (10x) followed by dramatic fall with recovery

**NB:** DD$_x$: viral hepatitis (Hepatitis A/B/C, CMV, EBV)
- drug induced hepatitis
Hepatitis C Infection

- positive stranded RNA virus of classified within the Flaviviridae family (heterogeneous group)
- the most widely used nomenclature comprises six major genetic groups and a number of recognised subtypes that are more closely related
- numbered from 1 and the subtypes a, b, and c in order of discovery
- possibility that different genotypes may respond differently to interferon alfa

Diagnosis

- no tests for HCV-Ag
- diagnosed by HCV-Ab based immunoassay
- HCV-IgM antibody doesn't differentiate persistent viraemia from an episode of resolved viraemia
- supplemental tests → recombinant immunoblot assay
- confirmatory tests are invariably positive in HCV-Ab positive patients with chronic hepatitis
  a. serum ALT
  b. HCV antibody tests
  c. HCV RNA, genotypes, and HCV RNA concentrations

- infection is usually monitored by serum ALT, but nonspecific
- young patients without evidence of cirrhosis have a generally indolent course of the infection
- with development of cirrhosis → frequently complicated course
- older patients may present with complications of cirrhosis or hepatocellular carcinoma

- there is evidence that alcohol and HCV may synergistically aggravate hepatic injury
- there are no vaccines available
- sexual transmission has been described but is a comparatively infrequent
- mother to infant transmission of HCV has been recorded but seems to be unusual
- transmission of HCV from infected surgeons to patients has been verified by molecular epidemiological evidence
Interferon Alfa

1. acute HCV
   - acute icteric HCV has become comparatively rare
   - HCV infection is clinically mild and subclinical disease is common
   - only 25% of cases are icteric, and the peak serum ALT activities are less than those in acute hepatitis A or B
   - the mean incubation period of HCV is 6-12 weeks
   - diagnosis in these cases requires confirmation by HCV RNA testing
   - severe or fulminant HCV is rare but may occur, especially in immunosuppressed

2. chronic HCV
   i. advantages
      - inhibits HCV replication in some patients with chronic disease
      - sustained response in some patients
      - important component of combined antiviral treatment
      - can improve histological hepatitis
   ii. disadvantages
      - given by injection
      - low sustained response rates in many patients with type 1 hepatitis and higher levels of viraemia
      - high relapse rates
      - side effects
      - neutralising antibodies in some patients
      - relative expense

3. ribavirin and combination antiviral therapy
   - several therapeutic trials of interferon alfa for acute HCV have been completed
   - most indicate that amelioration of the severity of the chronic hepatitis lesion or even a reduction in the rate of chronic disease is possible with at least six months of treatment
   - require HCV confirmation and exclusion of other causes → ↑ ALT,
     a. obesity
     b. alcoholism, drug induced hepatotoxicity
     c. biliary tract disease
     d. autoimmune hepatitis *treated differently, ∴ test autoantibodies
        - dividing line between this and chronic HCV is not always clear
        - a high proportion of HCV patients have low titres of anti-Sm & ANA
     e. thyroid disease must be excluded → T_{3/4}, TSH, and antithyroid antibodies
     f. inborn errors of metabolism
- Side Effects of Interferon Alfa

1. early
   i. flu-like illness, chills, fever, malaise, muscle aches, headache
   ii. poor appetite

2. later - common
   i. weight loss
   ii. increased need for sleep
   iii. psychological side effects - irritability, anxiety, depression
   iv. hair loss
   v. thrombocytopenia, leucopenia

3. unusual or severe
   i. seizures
   ii. acute psychosis
   iii. bacterial infections
   iv. autoimmune reactions
   v. hyperthyroidism or hypothyroidism or transient thyroiditis

4. rare
   i. proteinuria
   ii. myocardopathy
   iii. rashes
   iv. interstitial lung disease
   v. retinal changes
   vi. ototoxicity

- Summary Points

1. the natural course of chronic HCV is not fully defined
2. a range of disease exists
   • from mild asymptomatic infection to serious disease with dire sequelae
3. assessment of viral load and genotype/serotype may help in predicting response
4. difficult to indicate the prognosis for younger patients with mild disease
   • they may need to be considered for treatment, so that the opportunity to avoid later disease is not forfeited
5. it is not yet clear whether patients who are more responsive to interferon have a better prognosis
HEPATIC FAILURE

**Def'n:** *fulminant hepatic failure*, is a clinical syndrome resulting from massive hepatic necrosis, in an individual with previously normal liver function, characterised by,

1. severe progressive **encephalopathy**
2. **jaundice**, hepatic foetor, asterixis
3. **hypotension**, tachycardia, oliguria
4. coagulopathy, hypoglycaemia
5. high mortality ~ 80% with grade 4 coma

**Classification King's**

1. hyperacute - encephalopathy within *7 days* of the onset of jaundice
2. acute hepatic failure - 8-28 days from jaundice to encephalopathy
3. subacute hepatic failure - 29-72 days from jaundice to encephalopathy

**Causes**

a. viral hepatitis* - Hepatitis A, B, C, D, E
   - CMV, EBV, HSV, ? HIV
   - yellow fever virus, echovirus
b. drugs - paracetamol*
   - anti-TB drugs, rifampicin, isoniazid
   - MAOI, α-methyl dopa
   - halothane ± enflurane
c. chemicals - carbon tetrachloride, vinyl chloride
   - hydrocarbons, chloroform, phosphorus
   - mushroom poisoning (*Amanita*)
d. acute steatosis syndromes - fatty liver of pregnancy
   - tetracyclines
   - Reye's syndrome
e. ischaemic liver necrosis - Budd-Chiari, CCF
   - hypoxia, shock, sepsis syndrome, MODS*
f. massive infiltration - lymphoecticular tumours | acute leukaemia
   - transplant rejection

**NB:** *commonest causes*

note differences cf. chronic liver failure / cirrhosis later
**Acute-on-Chronic Liver Disease**

a. alcoholic cirrhosis  
b. primary biliary cirrhosis  
c. chronic active hepatitis  
d. chronic persistent hepatitis  
e. Wilson's disease  
f. haemochromatosis  
g. α₁-antitrypsin deficiency

---

## Child's Classification

**Severity of Chronic Liver Disease**

<table>
<thead>
<tr>
<th>Class</th>
<th>A</th>
<th>B</th>
<th>C</th>
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<tbody>
<tr>
<td>• albumin</td>
<td>&gt; 35 g/l</td>
<td>&gt; 30 g/l</td>
<td>&lt; 30 g/l</td>
</tr>
<tr>
<td>• total bilirubin</td>
<td>&lt; 35 µmol/l</td>
<td>35-60 µmol/l</td>
<td>&gt; 60 µmol/l</td>
</tr>
<tr>
<td>• ascites</td>
<td>absent</td>
<td>controlled</td>
<td>uncontrolled</td>
</tr>
<tr>
<td>• encephalopathy</td>
<td>absent</td>
<td>absent</td>
<td>present</td>
</tr>
<tr>
<td>• nutrition</td>
<td>good</td>
<td>fair</td>
<td>poor</td>
</tr>
<tr>
<td><strong>surgical risk</strong></td>
<td><strong>5%</strong></td>
<td><strong>10%</strong></td>
<td><strong>50%</strong></td>
</tr>
<tr>
<td>prothrombin time²</td>
<td>+ 1 1-4 s</td>
<td>+ 2 4-6 s</td>
<td>+ 3 &gt; 6 s</td>
</tr>
</tbody>
</table>

1. Child *et al.* 1964 surgical cohort undergoing *portasystemic shunting*

2. Pugh *et al.* 1973 increased risk for each group, according to ↑ PT
- **Prognostic Factors**

1. age
2. severity of 1° illness
3. underlying cause
4. complications
   i. sepsis
   ii. cerebral oedema
   iii. renal failure
   iv. ARDS
5. duration and severity of coma

- **Shellman CCM 1988**

1. Child's classification - severity
2. mechanical ventilation - respiratory failure
3. high creatinine - renal failure
4. other significant factors - coagulopathy
   - hypo/hyper-Na⁺
   - sepsis

- Bihari, 1987, *tissue hypoxia* important
- Gazzard, 1975, causes of death,
  a. neurological (*cerebral oedema*) ~ 67%
  b. GIT haemorrhage ~ 13%
  c. haemodynamic (shock) ~ 8%
  d. respiratory failure
  e. renal failure
Organ System Involvement

**Liver**

- hypoalbuminaemia: low COP, increased tendency to oedema formation
- coagulopathy: ↓ vit K dependent factors
- septicaemia: immune dysfunction
- toxaemia: metabolites, bacteria, toxins
- amino-acid imbalance: low branched-chain / high aromatic
- drugs: prolonged effect
- hyperammonia: not cleared
- severe hypoglycaemia: impaired glucose metabolism

**Central Nervous System**

**Def'n:** hepatic encephalopathy: a neuropsychiatric syndrome in a patient with advanced liver disease or porto-systemic shunting, characterised by,

1. early frontal area impairment (behaviour/motor/sensory) with **brainstem sparing**
2. followed by varying degrees of **coma**, with brainstem dysfunction resulting in
   i. respiratory failure
   ii. vasomotor imbalance: vasodilatation, arrhythmias
3. Wernicke-Korsakoff syndrome
4. ↑ muscle tone early
5. very high sensitivity to sedatives, narcotics, general anaesthetics
6. EEG:
   - slowing of rhythm
   - low frequency theta rhythm
   - high amplitude delta waves (deep coma)
7. **asterixis**
   - flapping tremor usually found in grade 2-3 coma
   - nonspecific finding, also seen in hypercarbia, hypokalaemia
   - severe CCF, polycythaemia
8. **cerebral oedema** often without clinical or CT signs
   - NB: CT is **unreliable** for diagnosis, ∴ require pressure monitoring
   - predominantly **cytotoxic** and responds to mannitol & STP
   - recent work suggests also a vasogenic component 2° endothelial dysfunction
**Renal / Electrolytes**

*NB:* hyponatraemia, hypokalaemia, hypophosphataemia, hypomagnesaemia & hypoglycaemia

- **a.** 2° hyperaldosteronism - hypokalaemia
  * hyponatraemia cf. expected hypernatraemia
- **b.** renal failure - hypotension / hypovolaemia, haemorrhage
  - sepsis
  - hepatorenal syndrome
- **c.** respiratory alkalosis - central hyperventilation
- **d.** later metabolic alkalosis - renal 2° aldosterone, vomiting
- **e.** metabolic acidosis with hypoxia, hypoglycaemia

**Respiratory System**

- **a.** foetor hepaticus \( \propto \) methylmercaptan and present in all grades of coma
- **b.** central hyperventilation \( \rightarrow \) respiratory alkalosis
- **c.** vasodilatation / ↓ HPV \( \rightarrow \) ↑ shunt fraction & hypoxaemia / cyanosis
- **d.** aspiration, infection
- **e.** intra-abdominal hypertension due to ascites
  - i. ↓ chest wall compliance
  - ii. ↓ FRC / TV
  - iii. may result in pleural effusion
- **f.** central respiratory failure occurs late
- **g.** rarely hepatopulmonary syndrome

**Cardiovascular System**

- **a.** initially high cardiac output with *peripheral vasodilatation*
- **b.** central *vasomotor depression* *low HR, CO and SVR
- **c.** arrhythmias
  - hypo-K⁺, hypoxia
  - cerebral oedema
**Coagulation Disorders**

- fall in production of coagulation factors
  - i. **VII** - shortest t½ ~
  - ii. vit K dependent factors - II, VII, IX, X
  - iii. low factor V implies liver impairment other than vit K lack
  - iv. fibrinogen falls last *↓FI → probably DIC
- also fall in coagulation inhibitors - protein C & S
- **DIC** is usually secondary to sepsis, severe hypovolaemia and rarely to the liver failure

**Gastrointestinal Tract**

- gastric erosions ~ 50%
- oesophageal, gastric or duodenal haemorrhage
- bacterial breakdown of protein → ↑encephalopathy
- enteric bacteria are (? maybe) a source of septicaemia
- spontaneous bacterial peritonitis

**Reticuloendothelial**

- pneumonia
- spontaneous gram negative septicaemia
- often associated with hypothermia, low WCC, hypodynamic circulation
Treatment Principles

a. remove precipitating cause where possible
b. manage / prevent infection
c. manage / prevent respiratory failure
d. normalise vasomotor instability
e. maintain urine output * central hypovolaemia / arterial underfilling
f. minimise and treat cerebral oedema
g. prevent hypoglycaemia
h. identify high risk patients early → liver transplantation

Treatment Hepatic Encephalopathy

a. minimise protein load
i. dietary protein restriction
ii. avoid GIT bleeding
iii. lactulose ~ 30 mg q8h
   • synthetic nonabsorbable disaccharide → large bowel
   • metabolised by GI bacteria → lactate, formate, acetate & CO₂
   • ↓ GIT pH → inhibits gram (-)'ve bacteria (proteolytic)
     favours the growth of lactobacilli,
     traps NH₃ in the gut, and cathartic
iv. neomycin ~ 1 g q6h
   • additive effect with lactulose
   • may be absorbed in patients with chronic encephalopathy, ∴ not used
     → nephrotoxic & ototoxic effects
   • FMC use enteral gentamicin & claim added efficacy to lactulose
v. MgSO₄ enema

b. treat and prevent electrolyte disturbances
i. Na⁺, K⁺, osmolality
ii. pH, especially alkalosis

c. avoid narcotics, sedatives, etc.

d. experimental
i. alter amino-acid balance in favour of branched-chain amino-acids
ii. infusion of neurotransmitter precursors (L-dopa)
iii. charcoal haemoperfusion / haemofiltration * no survival benefit
iv. flumazenil
   • improves EEG & clinical markers of encephalopathy, but effects are
     short-lived & has no effect in patients with cerebral oedema
**Treatment Cerebral Oedema**

- a. regular neurological assessment
- b. early institution of controlled ventilation to maximise $P_{aO2}$ & lower $P_{aCO2}$
- c. ICP monitoring *all patients with grade 4 coma* → CPP > 50 mmHg
- d. diuretics
  - i. mannitol ~ 0.25 g/kg q2h
  -  
    - ICP > 25 mmHg for > 15 min
    - > 30 mmHg for > 1 min
  - ii. ± frusemide
  - iii. fluid restriction - however, often intravascularly deplete
  - iv. ultrafiltration - if in ARF and on CVVHD
- e. thiopentone ~ 10 mg/kg over 30 mins
  - ~ 5 mg/kg/hr for 5 hrs
  - ~ 1 mg/kg/hr
  - may be used in cases of CSF hypertension refractory to all other therapy
- f. ? cranial decompression for resistant cases
- g. ? CVVHF to clear middle-molecules
- h. high dose steroids of **no benefit**

**Treatment Nutrition**

- a. low total protein
  - with high ratio of branched-chain amino-acids ? no benefit
- b. high glucose intake, no fats / intralipid
- c. vitamin supplements
  - i. Vit K ~ 15-20 mg/day
  - ii. thiamine ~ 200 mg/day
  - iii. folate ~ 1-2 mg/day ± folinic acid for coagulopathy
  - iv. Vit C ~ 500 mg/day

**Treatment Liver**

- a. maintain adequate oxygen and blood supply
- b. minimise complications
- c. ? insulin/glucagon infusion to stimulate hepatic regeneration
- d. orthoptic liver transplantation
Keays King’s College J-Hepatol. 1993

- 36 of 68 consecutive patients with FHF progressing to grade 4 encephalopathy → extradural ICP monitors inserted
- only minor complications were encountered,
  1. local wound bleeding at the burrhole site in 4 patients
  2. a small cerebral hemorrhage in relation to the monitor in one patient
  3. no significant long-term sequelae were related to the operative procedure
- monitoring identified rises in ICP unaccompanied by clinical signs and treatment was given to the monitored patients more often than the non-monitored group (p < 0.01)
- survival from the onset of grade 4 encephalopathy was significantly greater in the ICP monitored group (median 60 vs. 10 h, p < 0.01) although overall survival was unchanged
- monitoring also provided important prognostic information since the peak ICP was higher in non-survivors than in survivors (median 45 vs. 35 mmHg, p = 0.051)

N-Acetylcysteine

- will prevent paracetamol-induced FHF if given within 8 hrs in most cases
- lower efficacy at > 8 hrs, and generally ineffective if > 15 hrs
- however, even though it does not prevent FHF, it does improve the outcome of patients by reducing encephalopathy & renal failure associated with paracetamol FHF

Forbes et al Hepatology 1989

- FHF & intracranial hypertension in the presence of renal failure → mortality > 90%
- incremental IV thiopental in 13 patients until ICP (extradural) fell to within normal limits or adverse hemodynamic changes occurred
- 5 patients made a complete recovery, there were 3 deaths from intracranial hypertension

NB: "the response of otherwise intractable intracranial hypertension and the 38% survival rate was remarkable for a group of patients with such a poor prognosis"
### Other Therapies

- therapies *not* altering mortality in FHF,
  1. heparin
  2. corticosteroids
  3. exchange transfusion / plasmapheresis
  4. BCAA
  5. bromocriptine
  6. charcoal haemoperfusion / polyacrylonitrile-membrane haemodialysis
  7. L-dopa
     - improves conscious level temporarily
     - however, both L-dopa & carbidopa are no better than placebo in PRCT

### Orthoptic Liver Transplantation

- 1 year survival ~ 80% in non-FHF cases
- grade 4 coma,
  1. medical therapy $\rightarrow$ ~ 20%
  2. OLT $\rightarrow$ ~ 60% survival at 1 year
Hepatic Encephalopathy

**Def'n:** complex organic brain syndrome characterised by,

1. evidence of advanced hepatocellular failure
2. disturbance of CNS function - esp. mentation, awareness, memory
3. fluctuating neurological signs - tone, reflexes, extensor plantar response - occasionally seizures
4. EEG - symmetrical high-voltage, slow-wave (2-5Hz)

**NB:** exclusion of the differential causes below essential

- **Differential Diagnosis**
  a. acute alcoholic intoxication
  b. other drug overdose - esp. sedatives, narcotics
  c. Wernicke's encephalopathy
     - nystagmus, ataxic gait, confusion ± peripheral neuropathy
     - later cranial nerve III & VI paralysis, conjugate gaze abnormalities
     - seen in alcoholics & AIDS patients \( \propto \downarrow \text{thiamine} \)
     - IV glucose prior to thiamine may worsen symptoms
  d. Korsakoff's psychosis - defect of retentive memory
     * same disease process, stages of evolution
  e. subdural haematoma
  f. meningitis | sepsis
  g. hypoglycaemia
  h. respiratory failure - hypercapnia | hypoxaemia
  i. uraemia

### Hepatic Encephalopathy Grading

<table>
<thead>
<tr>
<th>Grade</th>
<th>Asterixis</th>
<th>Foetor</th>
<th>Conscious state</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>rare</td>
<td>moderate</td>
<td>minor lapses in attention</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>impaired coordination of fingers, hands</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>impaired arithmetic and complex functions</td>
</tr>
<tr>
<td>2</td>
<td>occasional</td>
<td>severe</td>
<td>lethargy, disorientation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>behaviour or irregular personality change</td>
</tr>
<tr>
<td>3</td>
<td>frequent</td>
<td>severe</td>
<td>confused or very drowsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>respond to stimuli, or bizarre behaviour</td>
</tr>
<tr>
<td>4</td>
<td>continuous</td>
<td>severe</td>
<td>coma, unresponsive to stimuli</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>decerebrate or decorticate posturing</td>
</tr>
</tbody>
</table>
Summary of Coma Grades

1. confused, speech alteration
2. drowsy
3. sleeps but rousable
4. coma with response to pain
5. deep coma without response to pain ~ 80-90% mortality
6. coma with flat EEG

Investigations

a. neurological examination - exclude focal lesion
b. serum chemistry
   i. glucose
   ii. E,C,&U - exclude other metabolic disturbances
   iii. LFTs, CaP
   iv. blood gases
c. blood picture
   i. Hb - evidence of GIT bleeding
   ii. WCC - may be low with infection
   iii. platelets - ETOH associated thrombocytopenia / hypersplenism
d. septic screen
   i. blood cultures
   ii. T/Aspirate ± BAL
   iii. ascitic culture
   iv. lumbar puncture * exclude raised ICP first
e. drug screen
f. CT head scan

Precipitating Factors

a. acute fulminating hepatic failure
b. GIT bleed
c. high protein load
d. sedatives, narcotics, general anaesthesia, alcoholic binge
e. acute infections / sepsis
f. electrolyte disturbance, esp. alkalosis
### Pathogenesis

#### a. hyperammonaemia
- ~ 40-50% from GIT organisms degrading protein/urea
- ~ 50-60% from deamination/deamidation of AA's
- urinary excretion ~ 460 mmol/d, 400 as urea, 40 as ammonia, 20 as other
- urinary ammonia excretion may increase up to 300 mmol/d in acidosis
- in CNS: $\alpha$KG + $\text{NH}_3 \rightarrow$ glutamate + $\text{NH}_3 \rightarrow$ glutamine
- results in CNS depletion of citric acid cycle intermediate $\alpha$KG
- clinical picture of hyperammonaemia differs from hepatic encephalopathy
- also, *poor correlation with coma level??
- FFAs and mercaptans enhance the encephalopathic effects of ammonia
- alkalosis & hypokalaemia $\rightarrow$ ↑[NH$_3$]$_{ICF}$

#### b. $\alpha$-ketoglutarate
- can 'mop up' excess NH$_3$
- may be toxic in its own right
- serum & CSF levels $\equiv$ coma level

#### c. glutamine ($\alpha$KG + NH$_3$)
- CSF levels high with encephalopathy
- degree of correlation reasonably good
- neurotoxic in animals

#### d. amino-acid imbalance
- * aromatic > branched-chain
- ammonia liberates glucagon $\rightarrow$ ↑gluconeogenesis $\rightarrow$ skeletal muscle catabolism & plasma AA's
- hyperinsulinism $\rightarrow$ ↑uptake of BCAA by skeletal muscle
- common AA carrier, $\therefore$↑ plasma aromatic:BCAAs $\rightarrow$ ↑CNS aromatic AA's
- ↑CNS tyrosine & phenylalanine $\rightarrow$ ↓dopamine & noradrenaline
- ↑CNS tryptophan $\rightarrow$ ↑serotonin (inhibitory)

#### e. tryptophan / serotonin
- CNS toxic
- CSF level $\equiv$ coma level

#### f. false neurotransmitters
- animal studies $\rightarrow$ - GABA, glycine, octopamine, 5HT
- histamine, catechols, phenylethylamine

#### g. "GABA-like" substances
- synthesised by the GIT flora and are normally cleared by the liver
- an endogenous benzodiazepine has been postulated (GABA receptor facilitator)
- benzodiazepine-like immunoreactivity is increased in CSF in encephalopathy
- flumazenil $\rightarrow$ unpredictable ↑CNS state

#### h. methionine (mercaptan)
- serum level $\equiv$ coma level

#### i. short-chain FA
- poor correlation
- displaces tryptophan

#### j. impaired BBB
- becomes 'leaky' with HE
Management of Proven Benefit

a. prevention
b. empty gut
   • lactulose \(\rightarrow\) osmotic agent, cathartic, acidification, NH\(_3\) trapping
   • and/or Neomycin/Gentamicin (oral or rectal)
   • MgSO\(_4\) enema
c. protein restriction
d. \(\alpha\)-keto-analogues of non-essential amino-acids
e. branched-chain AA's - effective nutrition, costly
   - no decrease in mortality
f. Bromocryptine, Levodopa - increase arousal but side effects
g. charcoal haemoperfusion / CVVHF
   • improves early haemodynamics, but no alteration in mortality
h. cross-circulation
i. minimise complications
   i. hypoglycaemia
   ii. hyper/hypo-Na\(^+\), hypo-K\(^+\)
   iii. coagulopathy / haemorrhage
   iv. infection / sepsis
   v. renal failure - hepatorenal syndrome, ATN
   vi. sedatives / narcotics
   vii. alkalosis
Ascites

**Def'n:** generalized swelling of abdomen, especially in the flanks, which gives a *fluid thrill* and *shifting dullness*

**Aetiology**

- a. cirrhosis ± portal hypertension
- b. congestive cardiac failure
- c. nephrotic syndrome
- d. pancreatitis ± pseudocyst
- e. Budd-Chiari - hepatic vein thrombosis
- f. infective - pyogenic, TB (with or without AIDS)
- g. malignancy - lymphoproliferative, metastatic, Kaposis sarcoma, DXRT
- h. rare causes - lymphatic leiomyomatosis, vagotomy, sarcoidosis - Bechets syndrome, trauma, retroperitoneal vascular surgery - lymphatic cyst rupture, lymph node biopsy

**NB:** poor prognostic indicator ~ 40% 24 month survival

**Pathophysiology  Cirrhosis**

1. portal hypertension / raised sinusoidal pressure
2. hypoalbuminaemia
3. renal retention of salt & water *cause unknown (?? not hyperaldosteronism)*
   - peripheral arteriolar vasodilatation
   - studies have shown *increased* intravascular volumes in these patients
   - however, head-out water immersion still produces natriuresis
4. excess hepatic lymph formation - "overflow" phenomenon

**Investigation**

- a. history - alcohol, IHD
- b. examination
  - i. periphery - chronic liver disease
  - CCF (JVP, heart size, oedema, etc.)
  - ii. abdominal - liver/spleen, pelvic tumour, pancreatitis
  - iii. nephrotic syndrome - kidney size, hypertension, urinalysis
- c. investigations - ascitic tap
  - urinalysis
  - U+E's, LFT's, FBE, INR/APTT
  - CXR
Management

1. bed rest
2. fluid/salt restriction ~ 10-20 mmol of Na+/day
3. spironolactone ~ 100-600 mg/day
   • urine Na:K ratio > 1 generally respond to smaller doses (100-150 mg)
   < 1 require higher doses (ie. ↑ plasma aldosterone)
4. frusemide
   • risks of volume depletion and renal failure
   • diuresis should be ≤ rate of absorption of abdominal lymph ~ 600-900 ml/d
   • weight-loss of ~ 0.5 kg/day is generally satisfactory
5. NSAIDs are *contraindicated*
6. paracentesis & IV albumin replacement
7. peritoneovenous (LeVeen) shunt if intractable
   • shunt malfunction, peritonitis, endocarditis, DIC, SVC obstruction

Budd-Chiari Syndrome

*Def'n:* acute liver disease secondary to *hepatic vein thrombosis*

Clinical Features

a. sudden or gradual onset
b. grossly enlarged liver
c. splenomegaly
d. portal hypertension
e. intractable ascites
f. absence of right heart failure

Aetiology

a. polycythaemia
b. hyperviscosity syndromes
c. renal carcinoma invading IVC
d. rarely congenital fibrous webs in hepatic veins
e. ? association with OCP in women

*NB:* biopsy → centrilobular congestion, necrosis & sinusoidal dilatation
Spontaneous Bacterial Peritonitis

- classically develops in patients with cirrhosis & ascites
- may also occur in ascites with,
  1. nephrotic syndrome
  2. cardiac failure
  3. peritoneal carcinomatosis
  4. immunosuppression

- organisms,
  1. *E.coli, Klebsiella pneumoniae*
  2. other *Enterobacteriaciae*
  3. Pneumococcus
  4. Streptococci

- diagnosis,
  1. WCC > 500 / mm$^3$
     PMN > 250 / mm$^3$ → high suspicion of bacterial infection
     commence antibiotic therapy
  2. positive culture
  3. absence of a primary source of infection

*NB:* WCC > 500/mm$^3$ & negative culture may →
  i. peritoneal carcinomatosis
  ii. pancreatitis
  iii. perforated ulcer

- mixed aerobic/anaerobic infections *do not* normally occur without visceral perforation
- initial antibiotic therapy,
  1. amoxicillin 1g tds IV
  2. gentamicin 3.5 mg/kg/d IV
Cirrhosis

**Def’n:** chronic disease of the liver, characterised by,

1. fibrosis
2. disorganisation of the lobar and vascular architecture
3. nodular regeneration of hepatocytes

■ **Aetiology**

a. alcohol*

b. congestive cardiac failure* *most common causes

c. infection - HBV*, HCV*, CMV
   - brucellosis
   - toxoplasmosis, schistosomiasis

d. drugs / toxins - pyrrolidizine alkaloids
   - α-methyldopa
   - isoniazid
   - halothane, enflurane

e. autoimmune - chronic active hepatitis
   - primary biliary cirrhosis
   - inflammatory bowel disease

f. metabolic - glycogen storage disease
   - α1-antitrypsin deficiency
   - haemochromatosis
   - Wilson's disease
   - Fanconi syndrome

g. cystic fibrosis ??

h. familial

i. idiopathic

**NB:** differences cf. acute hepatic necrosis

many idiopathic cases were probably HCV
Clinical Signs

NB: great variation in severity → from asymptomatic to fulminant hepatic failure
~ 10% diagnosed incidentally at laparotomy

- jaundice
- ascites
- tender hepatomegaly, or a firm nodular liver
- encephalopathy
- splenomegaly
- clubbing of the fingers
- palmar erythema
- Dupuytren's contractures
- spider naevi
- parotid & lacrimal swelling
- weight loss, generalised muscle wasting
- peripheral oedema, thin skin
- males - decreased body hair
- testicular atrophy
- females - virilisation
- menstrual irregularities
- signs of chronic renal insufficiency
### Chronic Active vs. Chronic Persistent Hepatitis

<table>
<thead>
<tr>
<th>CAH¹</th>
<th>CPH²</th>
</tr>
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<tbody>
<tr>
<td>PHx acute viral hepatitis</td>
<td>30%</td>
</tr>
<tr>
<td>recurrent episodes</td>
<td>yes</td>
</tr>
<tr>
<td>other organs involved</td>
<td>yes</td>
</tr>
<tr>
<td>prognosis</td>
<td>variable</td>
</tr>
<tr>
<td>liver necrosis</td>
<td>yes</td>
</tr>
<tr>
<td>end-stage cirrhosis</td>
<td>yes</td>
</tr>
<tr>
<td>ALT increase</td>
<td>2-10x</td>
</tr>
<tr>
<td>albumin</td>
<td>low</td>
</tr>
<tr>
<td>autoimmune features</td>
<td>yes</td>
</tr>
</tbody>
</table>

*autoantibodies*

- elevated IgG ~ 70%
- anti-smooth muscle ~ 80%
- anti-nuclear factor ~ 50%
- anti-mitochondrial ~ 20%

¹ Chronic active hepatitis ~ autoimmune hepatitis
² Chronic persistent hepatitis ~ prolonged viral hepatitis ≥ 6/12

---

### Complications of Hepatitis B

- a. massive hepatic necrosis ± encephalopathy
- b. cirrhosis with portal hypertension ~ 15-30%
- c. carrier state (HBsAg / HBcAb) ~ 5%
- d. chronic active hepatitis ~ 3-5%
- e. hepatocellular carcinoma
- f. immune complex syndromes - serum sickness
  - polyarteritis
  - glomerulonephritis
  - urticaria

**NB:** many of the complication previously ascribed to HBV may well be due to *concurrent* HCV infection
LIVER TRANSPLANTATION

- first performed 1963 but limited survival
- current 5 year survival in USA ~ 60%
- **fulminant hepatic failure** is increasingly an indication for transplantation
- 1 year survival with medical Rx ~ 20-30%, cf. following transplantation ~ 65%

**Considerations  Preoperative**

1. malnutrition
2. liver failure
   i. coagulopathy
      - factor deficiency < 20% V → ↑ intraoperative haemorrhage
      - thrombocytopaenia ∝ splenomegaly | Ab's
      - splenectomy → ↑ portal vein thrombosis, ::*not* an option
      - ± ? relationship to transfusion requirements
   ii. immunosuppression - spontaneous bacterial peritonitis
   iii. metabolic derangement - hypoglycaemia, hyponatraemia, hypokalaemia
3. CNS failure - hepatic encephalopathy
   * acute cerebral oedema
4. respiratory insufficiency - ↑ shunt / ↓ compliance / central drive failure
   - infection, aspiration
5. cardiovascular insufficiency - ↓ effective blood volume despite ascites (????)
   - ↓ LV function masked by ↓ afterload
6. renal failure * hepatorenal syndrome

**Intraoperative**

1. aspiration risk - RSI
2. cerebral oedema - ↑ ICP ∝ ↑ permeability of BBB & toxins
   - steroids *not effective*
   - limit use of volatile agents, vasodilators
   - ICP monitoring
3. high risk of VAE ? avoid using N₂O
   - monitoring
4. prolonged procedure ~ 8 hrs
5. massive transfusion ~ 25 units average
   - IV access & fluid warmers
   - monitoring: CVP/PAP, IABP, CUD, core T.
   - *citrate* toxicity & ↓ Ca²⁺ when *anhepatic*
6. electrolyte disturbances - ↓ Na⁺, ↓ K⁺, ↓ Mg²⁺
   * BSL usually OK
   - progressive metabolic acidosis
   ± NaHCO₃ ~ 50 mmol prior to unclamping

7. coagulopathy - INR, APTT, fibrinogen & platelets hourly

8. fibrinolysis - ↑↑ tissue plasminogen activator
   - treat with Amicar (EACA)
   - monitor with thromboelastography

9. maintenance of renal perfusion

10. venovenous bypass - used by some institutions
    - ↓ CVS compromise, inotropes & blood loss
    - no difference in morbidity / mortality

11. unclamping - H⁺ & K⁺ load, plus cold fluid
    - highest risk of VAE
    - arrhythmias (↓ HR), ↑ PAOP, ↓ CO
    - risk of PTE

Postoperative Considerations

1. pain relief / sedation
2. fluid requirements
3. hypothermia
4. transfusion - blood, FFP, platelets
5. electrolyte changes
   i. hyper- - Na⁺, osmolarity
   ii. hypo- - Mg²⁺, K⁺
   iii. glucose - usually hyperglycaemic
   iv. uraemia
   v. metabolic alkalosis
6. pulmonary → - elective ventilation
   ± ARDS, pneumonia
7. 1° graft non-function - small percentage, ? reperfusion injury
8. renal failure - ATN*, persistence of hepatorenal syndrome
   - cyclosporin nephrotoxicity
   ± CVVHD
9. CNS - IC haemorrhage, hypertension
   - seizures
   - cyclosporin neurotoxicity
10. graft rejection / liver failure ~ 5-20%
Complications

a. **pre-operative**
   i. malnutrition
   ii. coagulopathy
   iii. metabolic derangement
   iv. renal failure
   v. acute cerebral oedema & raised ICP
   vi. nosocomial infection / sepsis

b. **intraoperative**
   i. prolonged procedure \( \geq 8 \text{ hrs} \)
   ii. massive transfusion \( \sim 25 \text{ units average} \)
   iii. coagulopathy
   iv. electrolyte disorders
   v. VAE
   vi. hypothermia

c. **postoperative**
   i. fluid requirements
   ii. transfusion - blood, FFP, platelets
   iii. hypothermia
   iv. renal failure - cyclosporin nephrotoxicity
      - ATN*, hepatorenal syndrome
   v. electrolyte changes - hyper-Na\(^+\)
      - hyperosmolarity
      - hyperglycaemia / hypoglycaemia
      - hypo-Mg\(^+\) / Ca\(^++\) (citrate)
      - hypo-K\(^+\)
      - uraemia
      - *metabolic alkalosis*
   vi. pulmonary - oedema, pneumonia, ARDS
   vii. CNS - seizures
      - IC haemorrhage
      - cyclosporin neurotoxicity
   viii. liver failure
Aetiology of Renal Dysfunction

a. pre-existing renal dysfunction - HRS, pseudo-HRS
b. hypovolaemia, hypoperfusion
c. IVC obstruction
d. inefficiency of venovenous bypass
e. poor graft
f. nephrotoxins - cyclosporin, aminoglycosides
g. intra-abdominal hypertension
h. septicaemia

NB: \( R_x \rightarrow \) IV fluids, reduce Cyclosporin dose, ? dopamine

Transplant Rejection

a. 1° graft rejection \(~2\%\) → - ↑GGT, fever & tachycardia
   - later ↑ALP
b. 'preservation injury' - reversible centrilobular lesion
c. vascular thrombosis - ↑AST & ALT first
d. intrahepatic cholestasis - common, spontaneous remission
e. biliary tract complications
f. chronic rejection

NB: Acute rejection \( R_x \) - pulse steroids
   - monoclonal Ig OKT\(_3\)

Maintenance \( R_x \) - azathioprine
   - cyclosporin A, steroids
HEPATORENAL SYNDROME

**Def'n:** potentially reversible renal failure associated with severe liver failure, characterised by,

1. oliguria with - low urine Na⁺
   - high urine osmolality
2. unresponsive to fluids/inotropes
3. may progress to ATN

**Clinical Features**

- mortality ~ 95%
  * recovery associated with improvement of liver function
- oliguric renal failure with H₂O/Na⁺ retention
- high urine osmolality with [Na⁺] < 10 mmol/l
- low SVR, low cardiac output, hypotension
- hypervolaemia
- decreased response to vasopressors
- high circulating renin, angiotensin II, aldosterone
  - these may decrease with the onset of HRS
- increased renal excretion of noradrenaline & TBX₂
- decreased renal production / urinary excretion of PGE₂
  - normally increased in cirrhosis with ascites
  - ie. intrarenal PG's protect GFR against high circulating angiotensin/aldosterone

**Precipitating Factors**

1. paracentesis - probably 2° association
   - ie., the syndrome is associated with ascites
2. diuretics
3. hypovolaemia
4. sepsis
5. NSAID's
Proposed Mechanisms

- **Secondary Tubular Dysfunction**
  - completely reversible with return of liver function
  - successful transplantation of HRS kidneys
  - enzymuria & $\beta_2$-microglobulinuria seen in HRS not seen in ATN or pre-renal failure
  - but, absence of histological tubular damage in some studies & able to conserve Na$^+$
  - other studies show ATN-like changes, bile vacuoles in tubular cells and hypertrophied JGA

- **Mediator Imbalance**
  - xenon studies show maldistribution of RBF
    a. $\downarrow$ renin-angiotensin activity - $\downarrow$ renin substrate in HRS
       - improved filtration with FFP or AII infusion
    b. $\downarrow$ "glomerulopressin"
       - hormone, MW ~ 500, synthesized in the liver
       - increased by AA infusion & glucagon
       - reduces afferent aa. tone and increases GFR
       - synthesis blocked by NSAID's
    c. $\downarrow$ PGE$_2$ / PGI$_2$
       - $\downarrow$ substrate & enzyme activity
       * normal in ATN
    d. $\uparrow$ TBX$_{A2}$
       ? 1° or 2° to hypovolaemia & high circulating catecholamines
       * little evidence to support this (Maxwell & Kleeman)

- **Other Factors**
  1. intra-abdominal hypertension
     - increased renal vein pressure
     - improved filtration with paracentesis and colloid infusion, or peritovenous shunt
  2. high SNS tone $\rightarrow$ reversible cortical ischaemia

  - factors probably not involved,
    a. fall in ANF - levels are only marginally reduced
       - infusion does not improve filtration
    b. high renin-angiotensin II ?
    c. aldosterone - levels correlate poorly with the degree of Na$^+$ retention

  **NB:** however, plasma renin activity correlates with survival in cirrhosis,
  those with, (Maxwell & Kleeman)
  i. high PRA $\rightarrow$ ~ 6 months mean survival
  ii. normal PRA $\rightarrow$ ~ 28 months
Treatment

- **a. prevention**
- **b. optimise volume status**
- **c. paracentesis + FFP, HSA-20%**
- **d. ?? LeVeen shunt**
  - ↑ preload & cardiac output
  - ↑ RBF & GFR
  - high operative mortality → no improved survival
  - problems with **thrombocytopenia**
- **e. liver transplantation**

**• other modalities tried with little or no success,**
- **a. vasodilators - dopamine**
- **b. lumbar sympathectomy**
- **c. vasopressors - transient improvement**
- **d. A-II inhibitors - marked hypotension**
  - no increase in GFR
- **e. Ca**++ entry blockers - transient effect
- **f. PGE$_2$ infusion**
- **g. selective TBX$_{b2}$ inhibitors**
- **h. water immersion - increases venous pressure**
- **i. dialysis**
- **j. plasma exchange**

**Pseudo-Hepatorenal Syndrome**

- occurs where primary disease process involving the liver also affects the kidneys,
  1. autoimmune - SLE, PAN, systemic sclerosis
  2. drugs
  3. toxins - CCl$_4$, amanita poisoning
  4. severe sepsis
  5. cardiogenic shock
Intra-Abdominal Pressure / Hypertension

**Aetiology**

- a. haemorrhage - intra-abdominal / retro-peritoneal
- b. ascites
- c. severe pancreatitis
- d. bowel obstruction
- e. gas insufflation - laparoscopy
- f. external pressure - eg. abdominal binder

**Methods of IAP Measurement**

- a. intra-vesical pressure
- b. intra-gastric pressure
- c. direct intra-peritoneal pressure
- d. rectal or vaginal pressure

**Complications of Raised IAP**

- a. CVS - ↓ venous return & cardiac output
  - ↑ SVR
- b. renal - ↓ RBF/GFR resulting in oliguria
- c. respiratory - ↓ FRC, respiratory impairment, high P_{IP}
  - ↑ V/Q mismatch, hypoxia
- d. GIT - ↑ intra-gastric pressure
  - regurgitation and aspiration
- e. opening of congenital pleuroperitoneal connection
Clinical Effects

- normal IAP $\sim 0.5$ mmHg
- post-operatively levels $\leq 12$ cmH$_2$O (9 mmHg) occur without renal impairment
- as IAP is raised $\geq 25$ cmH$_2$O (20 mmHg) there is,
  i. $\uparrow$ venous return and cardiac output, but
     - later followed by $\downarrow$ VR
  ii. $\uparrow$ SVR $\sim 30$
  iii. $\uparrow$ renal-VR $\leq 500\% \rightarrow 25\% \downarrow$ RBF/GFR

NB: the dramatic rise in renal vascular resistance and oliguria lead to anuria at IAP $\geq 30$ mmHg

- mechanisms of renal failure with intra-abdominal hypertension,
  a. $\downarrow$ venous return + $\uparrow$ afterload $\rightarrow$ $\downarrow$ cardiac output
  b. $\uparrow$ RVR + $\downarrow$ cardiac output $\rightarrow$ $\downarrow$ RBF
  c. renal vein compression
  d. redistribution of RBF, cortical $\rightarrow$ medullary

Cullen CCM 1989

- syndrome of massively increased IAP $\sim 30-80$ cmH$_2$O
- all patients had,
  a. hypovolaemia but high filling pressures
  b. good EF $\sim 55\%$ but low stroke volume & cardiac output
  c. oliguria $\leq 10$ ml/hr
  d. hypoxia - all patients required IPPV
  e. small improvement with volume challenge (10ml/kg)
  f. considerable improvement in cardiac, renal and respiratory function with decompression

NB: similar picture to cardiac tamponade

Jacques AIC 1988

- case report of traumatic retroperitoneal haematoma causing oliguria and high IAP $\sim 32$ cmH$_2$O
- no response to volume, mannitol, or dopamine
PANCREATITIS

- **Aetiology**
  - a. ethanol*
  - b. gallstones* *(a + b) account for ~ 85%
  - c. idiopathic ~ 7%
  - d. traumatic
  - e. post-ERCP
  - f. familial / hereditary
  - g. cystic fibrosis
  - h. SIRS, ARDS, MODS ? ischaemic pancreatitis
  - i. metabolic
    - hyperlipidaemia
    - hyperparathyroidism, hypercalcaemia
    - renal failure
    - acute fatty liver of pregnancy
    - haemochromatosis
  - j. infections
    - viral hepatitis, mumps
    - Coxsackie, Echovirus and other viruses
    - Mycoplasma, Ascariasis
  - k. autoimmune diseases → "pancreatic vasculitis"
    - SLE, TTP, necrotising vasculitis
  - l. drugs
    - thiazides, frusemide, valproate
    - vit D, oestrogens
    - sulphonamides, tetracyclines, azathioprine
    - possible associations
      - steroids, methyl dopa, procainamide, chlorthalidone,
      - ethacrynic acid, β-blockers, cimetidine, clonidine,
      - rifampicin, phenformin, paracetamol
  - m. toxins
    - methanol
    - scorpion envenomation
    - organophosphate poisoning
  - n. renal transplant
    - surgery
    - hypercalcaemia
    - steroids (?), diuretics
    - viral infections, immunosuppressives
  - o. GIT disease
    - duodenal ulcer, penetration / perforation
    - Crohn's disease
    - obstruction of the Ampulla of Vater
    - pancreas divisum
Pathophysiology

- **exocrine** gland secretes ~ 1500-2000 ml fluid/d
  ~ 150-200 mmol HCO₃⁻/d \( \propto \) **secretin**
- also secretes lipolytic & proteolytic enzymes \( \propto \) **cholecystokinin** muscarinic ACh stimulation

- proenzymes: trypsinogen \( \rightarrow \) trypsin
  + other enzymes \( \rightarrow \) kallikrein, elastase, phospholipase
  under the influence of **enterokinase** secreted by the duodenal mucosa

- bile contents, especially lipase \( \rightarrow \) more specific for pancreas cf. amylase
- kinins \( \rightarrow \) proteolysis
- activation of these enzymes results in,
  a. connective tissue & fat necrosis
  b. pancreatic destruction
  c. vasodilatation
  d. shock, haemorrhage
  e. trypsin \( \rightarrow \) **complement activation**, C₃ & C₄
     activation of coagulation, kinin system & fibrinolytic cascades

- mechanisms for activation,
  1. duodenopancreatic reflux
     - allows duodenal **enterokinase** to activate trypsinogen, which in turn activates phospholipase A₂ \( \rightarrow \) lysolethecin which causes duct damage
  2. hypersecretion
     - rare cause \( \rightarrow \) scorpion envenomation, organophosphate poisoning
  3. pancreatic duct 'hypertension'
     - not supported by animal studies of obstruction \( \rightarrow \) **atrophy**
     - pancreatic obstruction by a gallstone is rare in pancreatitis (4% of 2653 pts)

Presentation

a. severe central abdominal **pain**, nausea and vomiting
b. paralytic **ileus**
c. jaundice
d. systemic inflammatory response syndrome, coagulopathy
e. hypovolaemic **shock**
f. respiratory failure - pain, pleural effusion - ARDS
g. tetany from hypocalcaemia and hypomagnesaemia
### Clinical Signs

a. Cullen's sign - blue discoloration of the periumbilical area
   - haemoperitoneum
b. Gray-Turner's sign - blue discoloration of the flanks
   - retroperitoneal haematoma, usually > 48 hrs
c. petechiae ± purpura
d. thrombophlebitis
e. warm, dry erythema of SIRS
f. jaundice
g. Peach's retinopathy - retinal artery fat emboli

### Investigations / Diagnosis

a. clinical * high suspicion in critically-ill
b. serum *amylase* $\geq 3x$ rise (> 600 IU/l), usually > 3 hrs, **P-type** cf. S-type
   - peaks at 12-24 hrs and returns to normal by 3-5 days, cleared by GFR
   - *poor* correlation with disease severity & outcome
   - if elevated > 5 days then $\rightarrow$ **pseudocyst**
   - also found in the liver, lung, prostate, fallopian tubes, and ovaries
     $\rightarrow$ different amylase (S-type), cleared by non-renal mechanisms
   i. false negative - early mild, or severe necrotising pancreatitis
   ii. false positive ~ 300-600 IU/l
     - perforated or ischaemic bowel, salivary disease or biliary colic
     - tumours of lung, ovary, or pancreas
     - pregnancy, acidaemia, DKA, ARF
c. urinary amylase > 750 IU/l (N: 10-300)
   peritoneal amylase * grossly elevated, may be > 50,000 IU/l
d. amylase:creatinine ratio $\frac{[\text{Cr}]_{\text{p}}}{[\text{Cr}]_{\text{u}}}$ x $\frac{[\text{Ams}]_{\text{p}}}{[\text{Ams}]_{\text{u}}}$
   - $< 5$ $\rightarrow$ non-pancreatic amylase
   - $\sim 5-10$ $\rightarrow$ pancreatitis
   - invalid in the presence of renal failure
e. serum *lipase* - more specific for pancreas, elevated in $\sim 75$
   - remains elevated for 10-14 days
f. FBE / blood film
   i. leukocytosis $\sim 15-20,000/\mu$l
   ii. haemolysis - free Hb, $\downarrow$ haptoglobin, $\uparrow$ methaemalbumin
   iii. thrombocytopenia - ? DIC
   iv. methaemalbuminaemia
g. biochemistry - ↑ AG metabolic acidosis
   - hypocalcaemia, hypomagnesaemia, hypokalaemia
   - hyperglycaemia
   - hypertriglyceridaemia (~ 15%, may normalise amylase)
   ± rising creatinine/urea
h. LFT's - high bilirubin / low albumin
   ± alcoholic hepatitis  |  obstructive jaundice
i. AGA's ~ 25% will be hypoxaemic
j. ECG - non-specific ST/T wave changes, tachycardia
k. AXR ~ 50% - regional ileus → "sentinal loop"
   ± gallstones  |  pancreatic calcification  |  ascites
l. CXR ~ 40% - basal atelectasis, pleural effusions
   - raised left hemidiaphragm
   ± cardiac failure  |  ARDS
m. U/Sound < 60% - often fails to visualise pancreas
   - assessment of biliary tracts / gallbladder
n. CT Scan - good sensitivity for oedematous pancreatitis
   - identification of late complications
   * grading of severity
o. diagnostic laparotomy

**Electrolyte Disorders**

a. hypocalcaemia
b. hypomagnesaemia
c. hypo/hyper-K⁺
d. hyperglycaemia
e. hyperlipidaemia
f. high anion gap metabolic acidosis
g. elevated urea and creatinine

**Acidosis in Pancreatitis**

a. lactic acidosis - types I & II
b. diabetic ketoacidosis
c. alcoholic ketoacidosis
d. renal failure
e. respiratory failure
f. rarely 2° to ingested toxin
Respiratory Dysfunction / Failure

a. mechanical
   - pain, sputum retention
   - pleural effusion, increased IAP
   - often pre-existing lung disease

b. V/Q mismatch
   - kinin, C' activation

c. central depression
   - analgesics, sedatives, treatment of DT's

d. acute lung injury / ARDS

e. infection
   - nosocomial pneumonia, aspiration

Investigation of Cause

a. history
   - alcohol, gallstones, drugs

b. examination

c. baseline investigations
   i. FBE
   ii. U,C&E's, Ca++, Mg++, glucose
   iii. amylase, LFT's
   iv. CXR, AXR
   v. CT scan

d. other investigations
   • serum lipids
   • hepatitis and other viral serology
   • ANF, ANA
   • cholecystogram

<table>
<thead>
<tr>
<th>CT Grading of Pancreatitis</th>
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<tbody>
<tr>
<td>Grade A</td>
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<td>Grade B</td>
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<td>Grade C</td>
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<tr>
<td>Grade D</td>
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<td>Grade E</td>
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</table>
Treatment Principles

a. rest the pancreas/gut
   i. nil orally - on recovery, low fat, low protein diet
   ii. NG tube and suction - only if severe, otherwise just nil orally
      * no therapeutic value in controlled studies of mild disease
   iii. analgesia - parenteral narcotics
      - epidural analgesia (exclude coagulopathy)
   iv. aprotinin - inhibitor of proteolytic enzymes
      * no proven benefit

b. prevent / treat complications
   i. IV fluids - large deficit may be present
      - crystalloids / colloids
   ii. O₂ therapy - all but mild cases
      - ABG's if clinical respiratory failure
   iii. monitor vital signs - fluid balance, urine output, CVP
      - PA catheter PRN
   iv. maintain urine output ≥ 0.5 ml/kg/hr
      - fluids / inotropes (?? mannitol, dopamine)
   v. electrolyte shifts - give K⁺, Ca++, Mg++ if low
      * calcium replacement is rarely if ever required and may exacerbate disease
   vi. TPN - with additional insulin
   vii. antibiotics - not for uncomplicated cases
      - suspected cholangitis or septicaemia
      - pancreatic abscess
   viii. peritoneal lavage
      * tried in severe cases - 2l isotonic dialysate + Heparin 1000U
      * stabilises haemodynamics & reduces early mortality
      * however, no decrease in overall mortality
      - drain every hour & continue 24-48 hrs
      - suspected cholangitis or septicaemia
      - pancreatic abscess
   ix. CT guided drainage - pseudocyst, not abscess
   x. surgery
      * diagnosis uncertain
      * pancreatic abscess - persistent high WCC, (+)ve cultures
      * pancreatic pseudocyst ~ 10%
      * biliary tract disease - fever and pain > 1-3 weeks, CT scan
      * ? peritoneal debridement to prevent progressive deterioration

b. prevent relapse
   i. avoid precipitating factors
   ii. drain pseudocyst
Peritoneal Lavage

- proposed advantages,
  a. decreased sepsis & sepsis-related mortality
  b. decreased overall mortality
  c. improved early haemodynamic stability
  d. decreased severity

- technique,
  a. 2000 ml isotonic dialysate + Heparin 1000U
     + Amoxicillin 250 mg
  b. drain every hour
  c. continue 2-7 days

- variables,
  a. volume
  b. frequency
  c. additives (antibiotics, antiproteases)
  d. duration

  NB: reduces early mortality and stabilises haemodynamics
  however, no long-term decrease mortality

- SGO, 1980 controlled multi-centre British trial showed,
  a. no improvement in outcome
  b. increased protein loss
  c. higher incidence bacterial peritonitis

- SGO, 1990 Perderzoli, uncontrolled, unblinded study of 191 pts all given peritoneal, or retroperitoneal lavage
  - method = 1000 ml 4-6 hrly, hypertonic solution + aprotinin
  - three groups, commenced on day ≤ 2, 2-4 days, or > 4 days
  - decreased mortality with early lavage, and (-)ve blood cultures

- SGO, 1990 Ranson, uncontrolled study with 2 days vs 7 days lavage,
  a. decreased overall mortality 43% vs 27%
  b. decreased incidence of sepsis 83% vs 33%
  c. decreased mortality associated with sepsis 20% vs 0%
Prognosis

- overall mortality ~ 20%
- poor prognostic factors defined by Ranson 1976
- predictive criteria for severe pancreatitis ≥ 3 of the following,

<table>
<thead>
<tr>
<th>Multiple Prognostic Scales</th>
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<tbody>
<tr>
<td><strong>Ranson - 1976</strong></td>
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<tr>
<td><strong>On Admission</strong></td>
</tr>
<tr>
<td>- age &gt; 55 yrs</td>
</tr>
<tr>
<td>- glucose &gt; 11 mmol/l</td>
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<tr>
<td>- WBC &gt; 16,000</td>
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<tr>
<td>- AST &gt; 120 U/l</td>
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<tr>
<td>- LDH &gt; 350 U/l</td>
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<tr>
<td><strong>During the First 48 hrs</strong></td>
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<tr>
<td>- IVT &gt; 6000 ml</td>
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<td>- ↓ Hct &gt; 10%</td>
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<tr>
<td>- ↑ urea &gt; 10 mmol/l</td>
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<tr>
<td>- HCO(^3)- &lt; 20 mmol/l</td>
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<tr>
<td>- ↓ ( P_{aO2} ) (air) &lt; 60 mmHg</td>
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<tr>
<td>- ↓ calcium &lt; 2.0 mmol/l(^3)</td>
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<tr>
<td>- Alb &lt; 32 g/l</td>
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**NB:** amylase level not useful as a predictor of severity

1. Ranson's original criteria was SGOT (AST) > 250 Frankel Units
2. Severe Acute Pancreatitis if > 2 criteria met in first 48 hours
3. uncorrected plasma calcium

<table>
<thead>
<tr>
<th>Surg Gynaecol Obstet, 1990</th>
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<tbody>
<tr>
<td>&quot;Ranson&quot; score</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>0 - 2</td>
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<tr>
<td>3 - 5</td>
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<tr>
<td>≥ 6</td>
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</table>
• another factor associated with high mortality is (+)ve blood cultures (2x)
• more recent studies assessing validity of APACHE II scores showed 77% predictive value
• if re-evaluated for first 48 hours, then,
  a. APACHE II prediction ~ 88% ? Tan et al.
  b. Ranson score ~ 69%
    Imrie score ~ 84%

**NB: severe acute pancreatitis** → admission APACHE II > 9

### Complications

1. **local**
   i. pancreatic
      • phlegmon
      • pseudocyst ~ 4% of patients
    ~ 30% develop complications
      • abscess ~ 100% mortality without surgery
      • haemorrhage
      • necrosis
   ii. ascites
      • may respond to somatostatin / octreotide
   iii. retroperitoneal - abscess
    - haemorrhage
   iv. venous thrombosis - splenic, renal, or portal vv.

2. **systemic**
   i. pulmonary - effusion, atelectasis
    - ARDS
    - chylothorax
    - mediastinal abscess
   ii. cardiovascular - hypotension | shock
    - tachycardia
    - pericardial effusion
    - ST/T changes \( \equiv \) AMI
   iii. DIC
   iv. gastrointestinal - acute stress ulceration / peptic ulceration
    - oesophageal variceal haemorrhage
    - ileus
   v. renal - ARF
   vi. CNS - encephalopathy
    - seizures
    - psychosis
    - sudden blindness (Purtscher's retinopathy)
PSEUDOMEMBRANOUS COLITIS

Def'n: infective colitis due to Clostridium difficile cytopathogenic toxin

- uncommon but reversible cause of infective diarrhoea
- causative agents,
  a. cephalosporins → most common case
  b. Clindamycin ~ 2-10%
  c. Lincomycin
  d. Amoxicillin
  e. Chloramphenicol*
  f. tetracyclines*
  g. Cotrimoxazole* *rarely

Clinical Features

- onset within 2-25 days of antibiotic use,
  a. profuse watery diarrhoea, bleeding uncommon
  b. cramping abdominal pain
  c. dehydration, hypoalbuminaemia
  d. dilated bowel, toxic megacolon
  e. sigmoidoscopy - oedematous friable mucosa
    - white-yellow raised plaques (fibrin, cells, polymorphs, mucus)
    ± ulceration or sloughing
  f. Barium study - dilated bowel
    - distortion of haustra
    - ulcers
    - thumb-printing
    - cobblestone appearance

Treatment

a. removal of causative antibiotic
b. correction of fluid and electrolyte deficiencies
c. Vancomycin or Metronidazole orally
d. ? cholestyramine - binds toxin

NB: steroids no use
recovery usual within 3 weeks