Cases in Gastroenterology and Liver disease

25-2-2015 Revision Course

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Introduction

- Discuss a few cases
- Emphasise common and difficult problems
- Cannot cover everything you need to know

SIMPLY GASTRO

Acknowledgements/Conflicts of interest

All taken from:

Kumar and Clark's Clinical Medicine 8th edition 2012

- Essentials of Clinical Medicine - Ballinger
- Pass Finals - Smith, Carty and Langmead

- **Kumar and Clark's Medical Management and Therapeutics**
- Kumar and Clark's Clinical cases

Thanks to Dr Andrew Smith and Dr William Dooley

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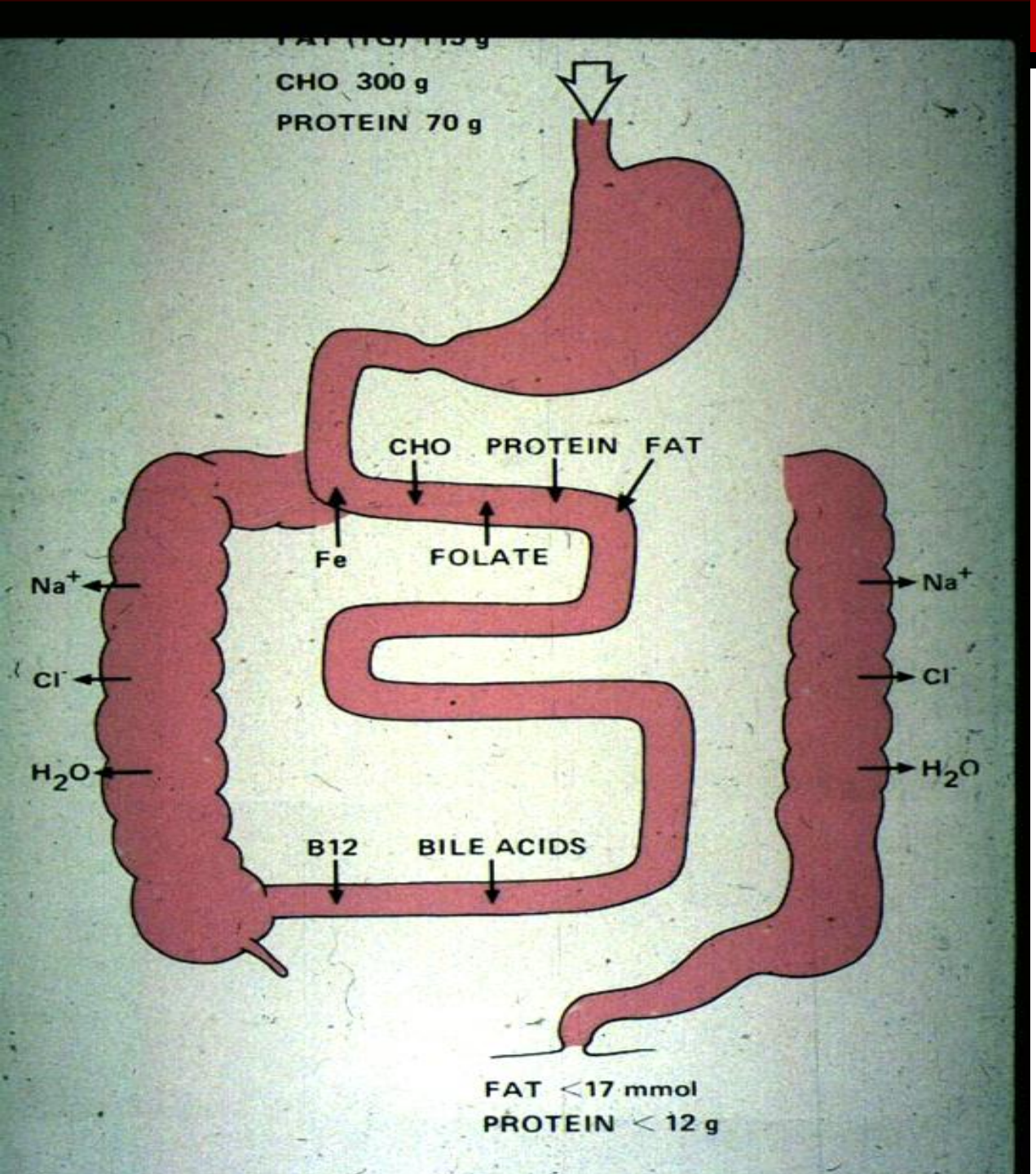
Introduction



Diseases

- GORD
  PUD
- Coeliac disease
- Inflammatory Bowel disease
  Crohn's
  Ulcerative Colitis
- Irritable Bowel syndrome
- Diverticular disease
- Carcinoma

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Case 1

- A 47 year old man attends A&E with worsening abdominal and chest pain. It's a sharp, burning pain and is worse after eating. This evening, he vomited and noticed some fresh red blood.

- PH: Nil

- DH: 75mg Aspirin daily bought OTC

- SH: Works as an accountant, married with 2 children.
  Drinks 1 bottle of wine a week.
  Ex-smoker (10 pack year history)

- *What more do you want to know?*

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What should you think of?

- ***Chest and abdo pain***

  Pneumonia/abdo /?systemic

- ***Burning*** GORD
- ***Vomiting blood*** Is he hypovolaemic?

  Resus

- ***Where is he bleeding from?***

  Oesophagus/stomach

NB ALARM symptoms?

Dysphagia
GI bleeding
Abdominal mass

Weight loss
Vomiting

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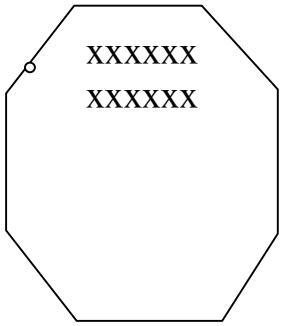
Case 1 Continued

- Obs: P89, BP 127/85,
  RR 16 T36.8 Sats 98% in air

- Examination:

CVS/Resp/Neuro NAD

Abdo: Epigastric tenderness, no peritonism. BS present.



PR normal, no melaena

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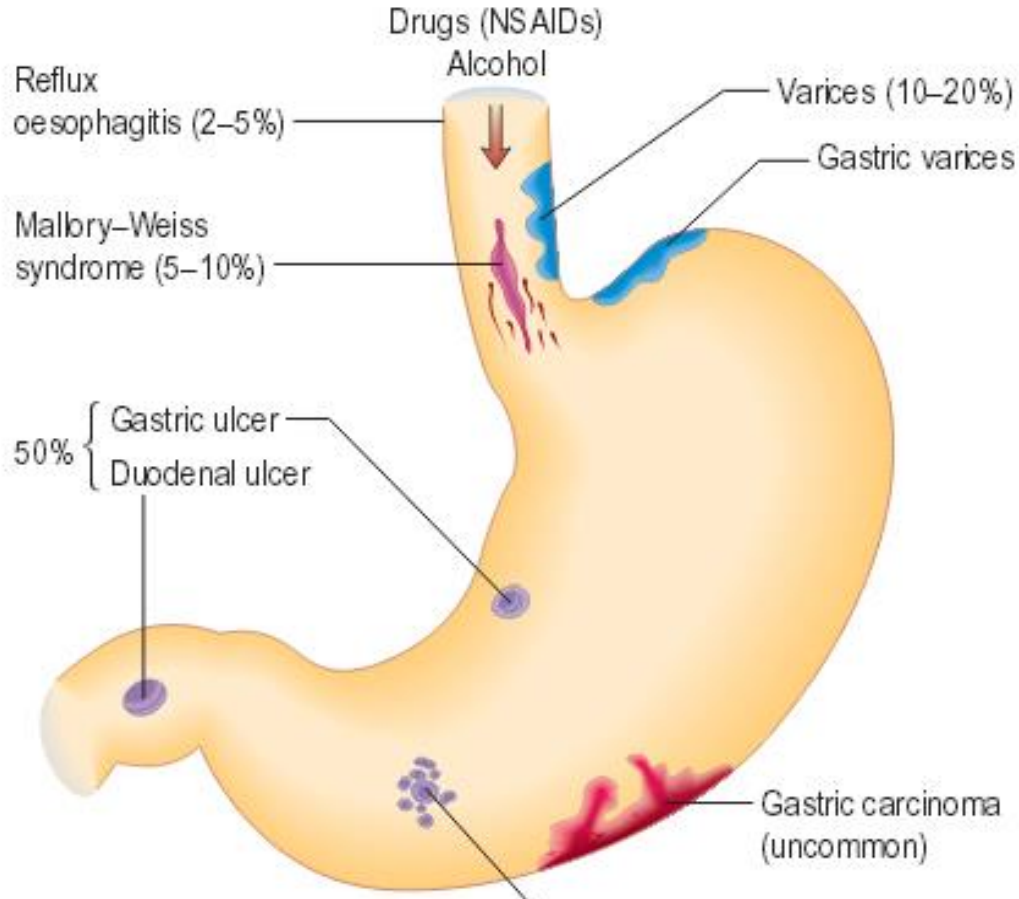
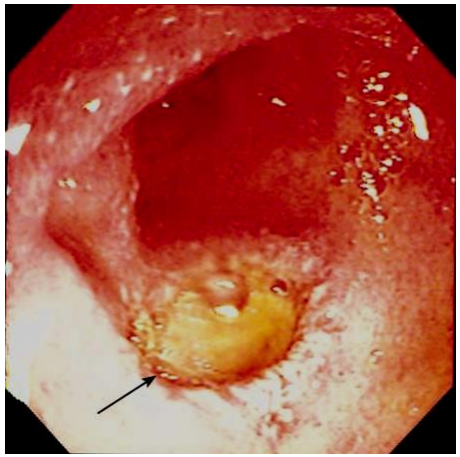
Causes of Upper GI Bleeds

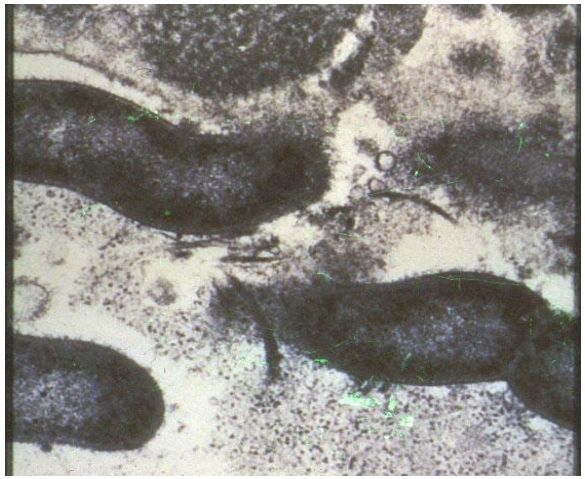


Other uncommon causes

Gastric antral vascular ectasia (GAVE)
Hereditary telangiectasia (Osler–Weber–Rendu syndrome)
Pseudoxanthoma elasticum
Blood dyscrasias
Dieulafoy gastric vascular abnormality
Portal gastropathy
Aortic graft surgery with fistula

Our patient found to have a GU





Helicobacter Pylori positive on CLO test on biopsy

- **Class I carcinogen**
- **Risk of Gastric carcinoma 3-6x**
- **Almost all PUs**
- **60% of un-investigated dyspepsia have NUD**

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H. pylori

Table 3.3 Diagnosis of *Helicobacter pylori* infection

	Method	Main use	Comments
Non-invasive tests			
^{13}C-Urea breath test	Hydrolysis of ingested ^{13}C-Urea by *H. pylori* to produce ^{13}C in expired air	Diagnosis of infection Monitoring of infection after eradication	Highly sensitive and specific False-negative results after recent use of PPIs or antibiotics
Stool antigen test	Immunoassay using monoclonal antibodies		
Serology	Serum antibody detection	Diagnosis of infection Epidemiological studies	Inaccuracy limits use Antibodies remain positive after infection cleared

SIMPLY GASTRO

H. pylori

Table 3.3 Diagnosis of *Helicobacter pylori* infection

Method	Main use	Comments
Non-invasive tests		
Invasive tests (endoscopic gastric mucosal biopsy)		
Rapid urease (CLO) test	Urease from *H. pylori* breaks down urea to produce ammonia causing a pH-dependent colour change in the indicator present	Diagnosis of infection in patients already undergoing endoscopy	Highly sensitive and specific False-negative results after recent upper gastrointestinal bleeding and recent use of PPIs or antibiotics
Histology	Direct visualization of the organism		Subject to sampling error and observer variability

PPI, proton pump inhibitors.

SIMPLY GASTRO

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PPI, proton pump inhibitors.

H. pylori

Example eradication regimens are:

- Omeprazole 20 mg, clarithromycin 500 mg and amoxicillin 1 g all twice daily, *or;*
- Omeprazole 20 mg, metronidazole 400 mg and clarithromycin 500 mg – all twice daily.
- Quadruple therapy

- **These should be given for (7 or)14 days.**

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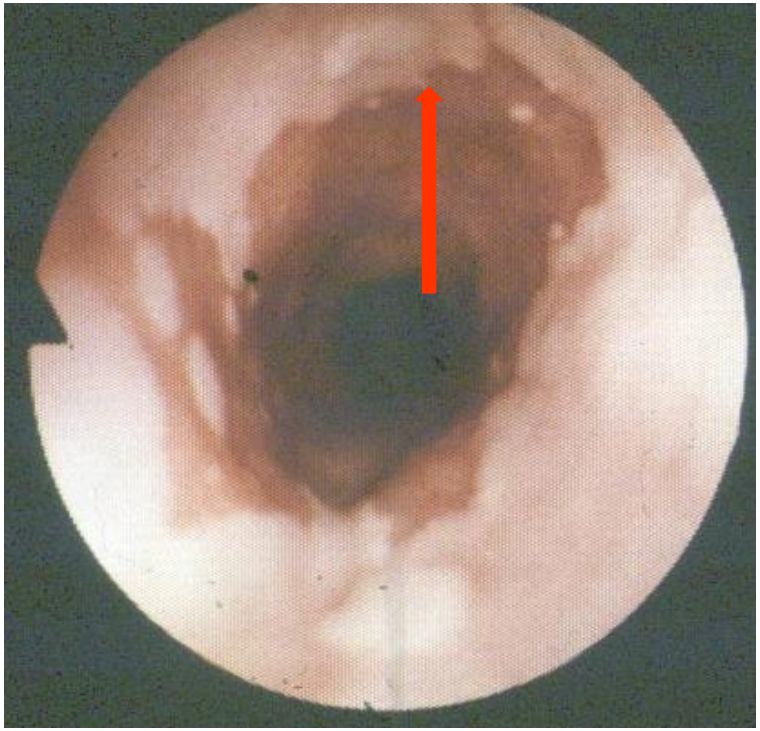
If GORD had been a problem …think of…..
Barrett's Oesophagus



- Long standing reflux
- Pre-malignant-adenocarcinoma
- Middle-aged men
- Histology-intestinal metaplasia→carcinoma
- Management

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Same case – different scenario….

- A 47 year old man attends A&E with worsening abdominal and chest pain. It's a sharp, burning pain and is worse after eating. This evening,

~~he vomited and noticed some fresh red blood~~.

He vomited **large quantities of fresh blood**

OE HR 120 bpm , BP 102/60, sweaty

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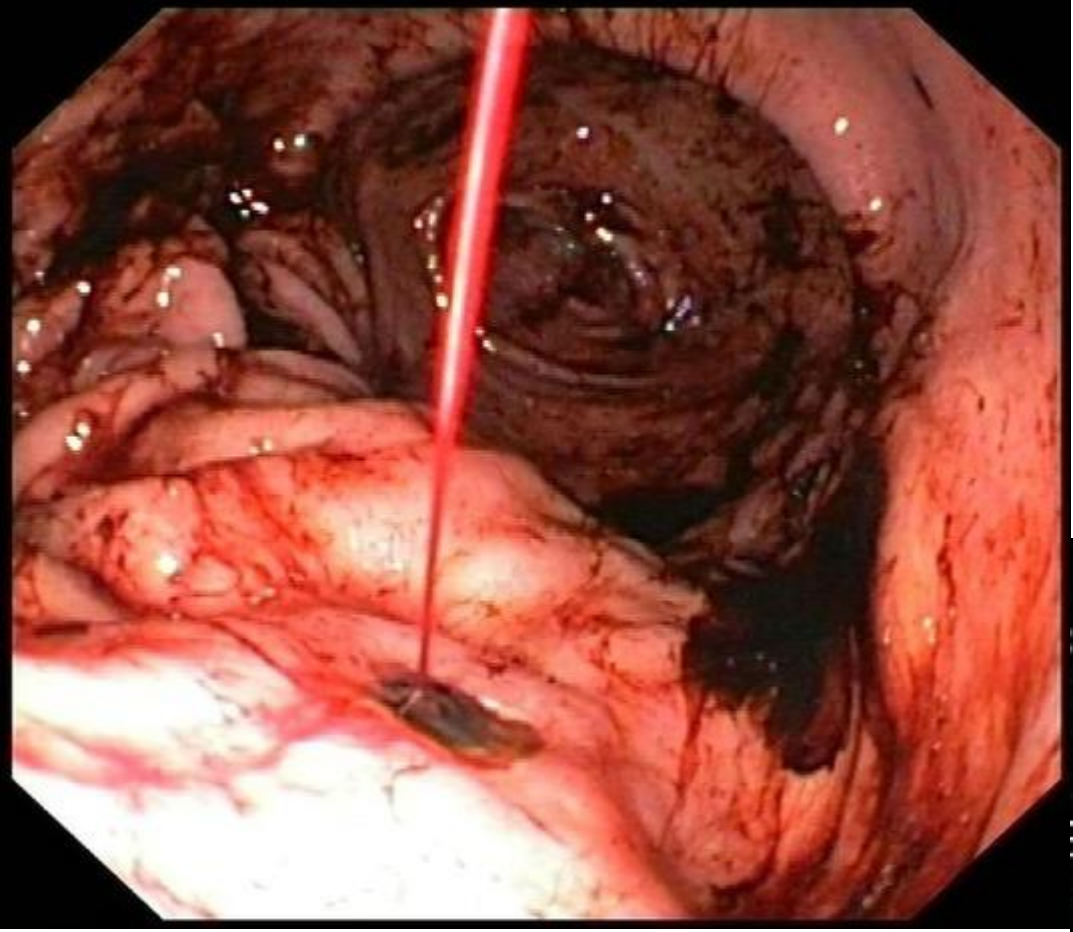
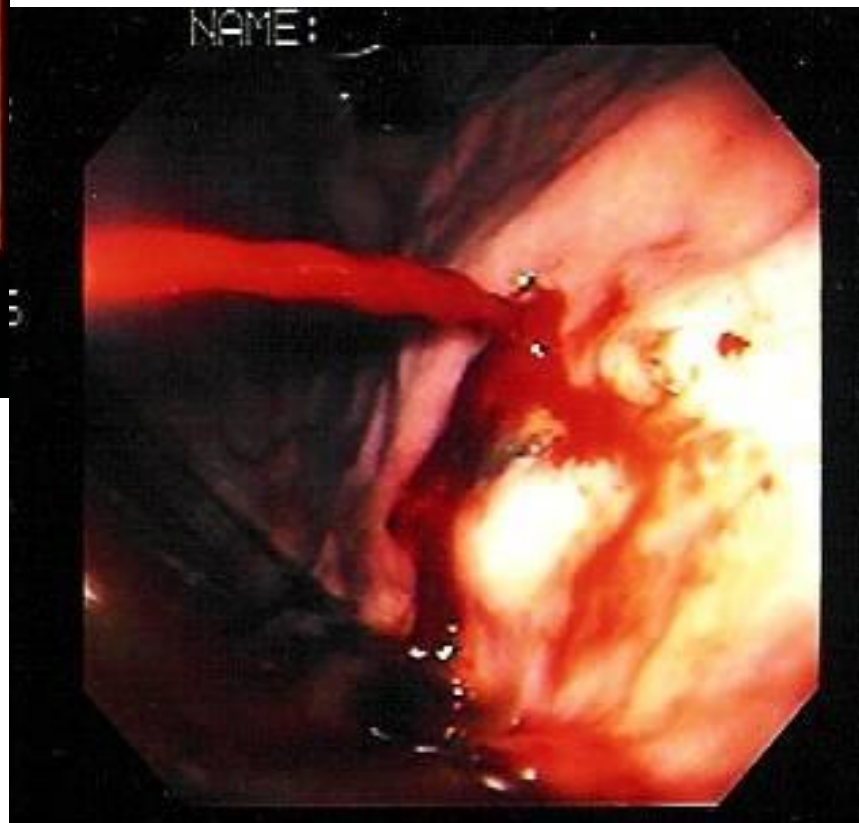
Management of acute gastrointestinal bleeding

- History and examination. Note co-morbidity
- Monitor the pulse and blood pressure half-hourly
- Take blood for haemoglobin, urea, electrolytes, liver biochemistry, coagulation screen, group and cross-matching (2 units initially)
- Establish intravenous access – 2 large bore i.v. cannulae

Management of acute gastrointestinal bleeding

- History and examination. Note co-morbidity
- Monitor the pulse and blood pressure half-hourly
- Take blood for haemoglobin, urea, electrolytes, liver biochemistry, coagulation screen, group and cross-matching (2 units initially)
- Establish intravenous access – 2 large bore i.v. cannulae
- Give blood transfusion/colloid if necessary. Indications for blood transfusion are:
  a. SHOCK (pallor, cold nose, systolic BP below 100 mmHg, pulse >100 b.p.m.)
  b. Haemoglobin <100 g/L in patients with recent or active bleeding
- Oxygen therapy
- Urgent endoscopy in shocked patients/liver disease
- Continue to monitor pulse and BP
- Re-endoscope for continued bleeding/hypovolaemia
- Surgery if bleeding persists




NAME:

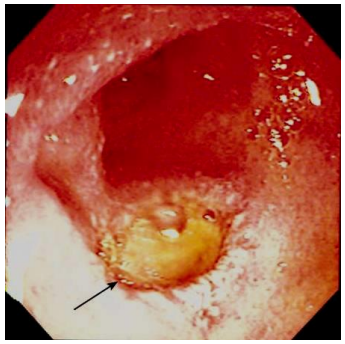
Upper GI bleeding cont

Endoscopy Treatments:

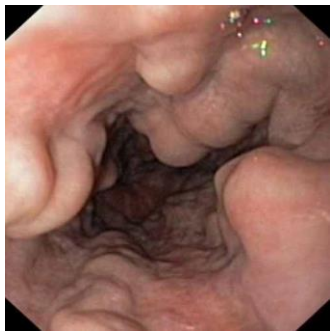
- Ulcers
  - Adrenaline injection
  - Sclerosant injection
  - Heat coagulation

  (DO dual therapy)

  New powder spray for bleeding



- Varices
  - Sclerosent Injection
  - **Banding**



Surgery is needed for uncontrolled bleeding

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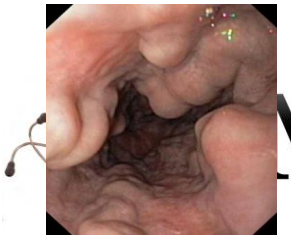
Oesophageal varices - liver disease



MPLY

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Rockall assessment score

Table 6.7 Risk assessment in non-variceal upper gastrointestinal haemorrhage

Rockall risk assessment score

Variable	Score			
	0	1	2	3
Age (years)	<60	60–79	>79	–
Circulation	BP >100 mmHg Pulse <100 b.p.m.	BP >100 mmHg Pulse >100 b.p.m.	BP <100 mmHg Pulse >100 b.p.m.	–
Co-morbidity	None		Cardiac disease, any other major co-morbidity	Chronic kidney disease, liver failure, disseminated malignancy
Endoscopic diagnosis	Mallory–Weiss tear, no lesion	All other diagnoses	Malignancy of the upper GI tract	–
Major SRH	None, or dark spots	–	Blood in the upper GI tract, adherent clot or spurting vessel	–

Rockall scores post-endoscopy

Risk score	Predicted mortality (%)	
	Rebleed	No rebleed
0	5	0
1	3	0
2	5	0
3	11	3
4	14	5
5	24	11
6	33	17
7	44	27
8+	42	41

BP, blood pressure (systolic); SRH, stigmata of recent haemorrhage.


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Case 2

- A 75 year old lady presents to your GP practice with difficulty swallowing for 2 months.

- PH: GORD, Hypertension
- DH: Ramipril 5mg od, Gaviscon PRN
- SH: Retired widow. 5 cigarettes a day for 50 years. No alcohol.

- **O/E** Cachexic, nil else.

- *What more do you want to know?*

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Case 2

- A 75 year old lady presents to your GP practice with difficulty swallowing for about 2 months.

- PMHx: GORD, Hypertension
- DHx: Ramipril 5mg od, Gaviscon PRN
- SHx: Retired widow. 5 cigarettes a day for 50 years. No alcohol.

- **O/E** Cachexic, nil else.

- *Elderly, can't swallow, short history, lost weight++*
- *Social circumstances, ?Lives alone, ?family. Who is with her*

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Causes of Dysphagia

Disorders of the mouth and tongue	Extrinsic pressure
E.g. tonsillitis	Mediastinal glands
Neuromuscular disorders	Goitre
Pharyngeal disorders	Enlarged left atrium
Bulbar palsy	
Myasthenia gravis	**Intrinsic lesion**
	Benign stricture
Oesophageal motility disorders	Malignant stricture
Primary oesophageal disease	Oesophageal web or ring
Achalasia	Foreign body
Other oesophageal dysmotility	Pharyngeal pouch
Eosinophilic oesophagitis*	
Systemic disease	
Diabetes mellitus	
Chagas' disease	
Scleroderma	

**Increasingly apparent cause of dysphagia (? due to discoordination of longitudinal muscle of the oesophagus), characterized by eosinophil infiltration of the oesophagus and diagnosed on mucosal biopsies.*

??

?

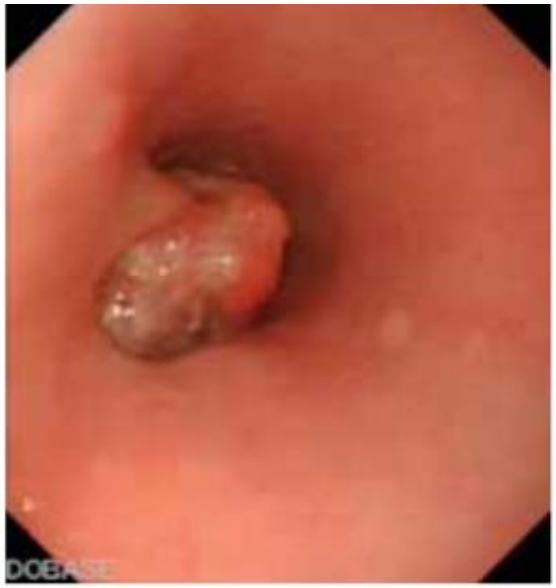
Table 6.5 Risk factors for cancer of the oesophagus

Squamous cell carcinoma	Adenocarcinoma
Tobacco smoking	Longstanding, heartburn
High alcohol intake	Barrett's oesophagus
Plummer–Vinson syndrome	Tobacco smoking
Achalasia	Obesity
Corrosive strictures	Breast cancer treated with radiotherapy
Coeliac disease	Older age
Breast cancer treated with radiotherapy	
Tylosis[a]	

[a]Tylosis is a rare autosomal dominant condition with hyperkeratosis of the palms and soles.

Oesophageal carcinoma

- OGD with biopsy
- + Staging scans



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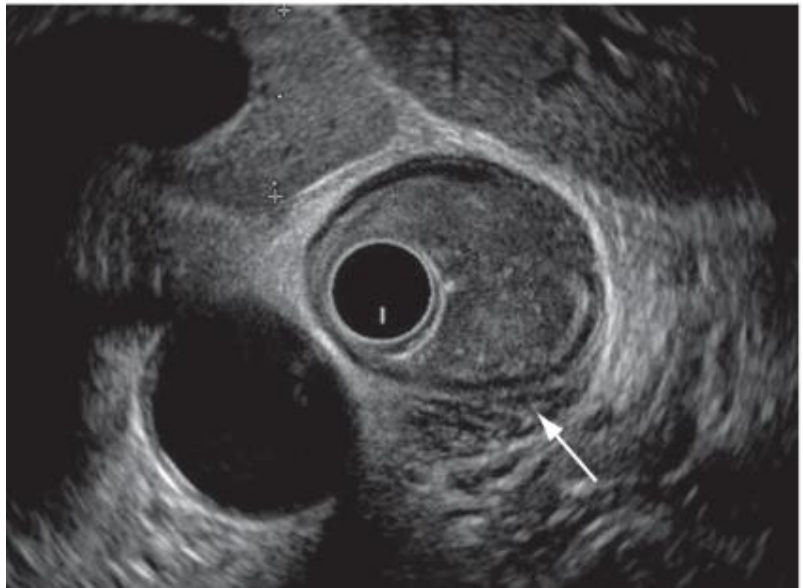

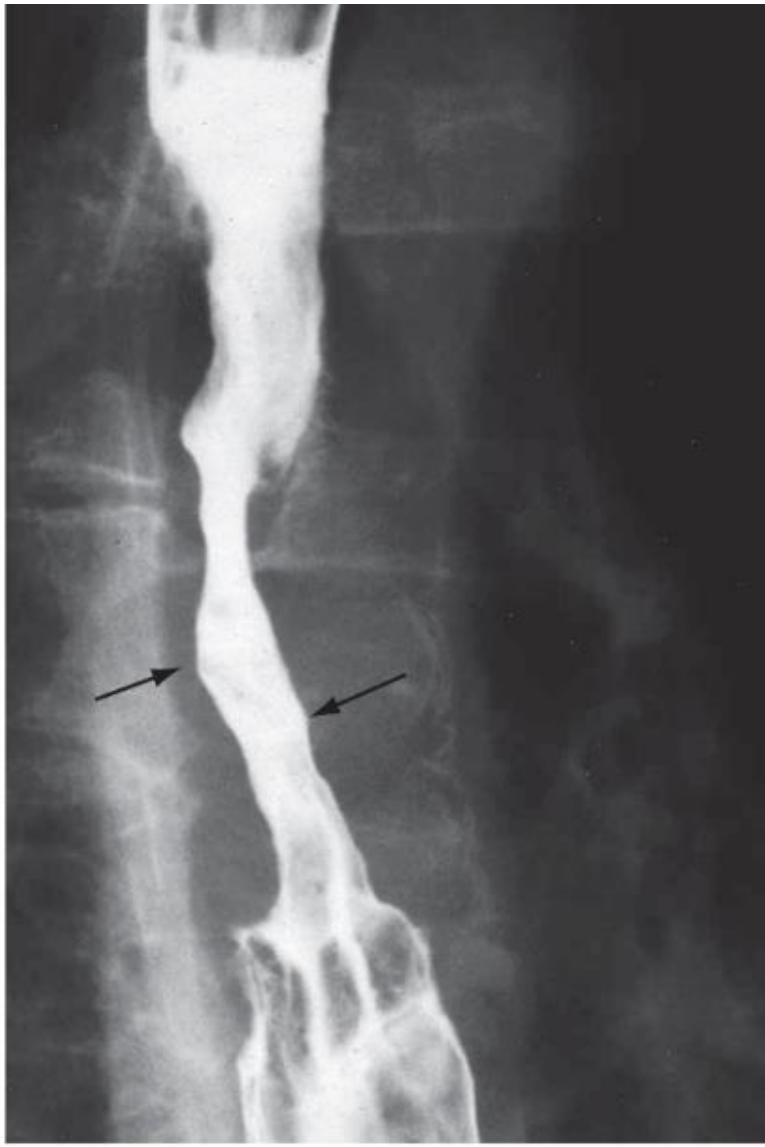

b

Tis	Carcinoma in situ	Nx	Nodes cannot be assessed
T1	Invading lamina propria	N0	No node spread
T2	Invading muscularis propria	N1	Regional Node Metastases
T3	Invading adventia	M0	No distant Spread
T4	Invading adjacent structures	M1	Distant Metastasis

Stage[a]		Standard treatment	5-Year survival rate (%)
Stage 0	(Tis N0 M0)	Surgery	> 90
Stage I	(T1 N0 M0)	Surgery	> 70
Stage IIA	(T2–3 N0 M0)	Surgery, chemoradiation therapy, or combination	15–30
Stage IIB	(T2–3 N0 M0 or T1–2 N1 M0)	Surgery, chemoradiation therapy, or combination	10–30
Stage III	(T1–2 N2 M0; T3 N1 M0; or T4 Any N M0)	Chemoradiation therapy with or without surgery	10–25
Stage IV	(Any T Any N M1)	Radiation therapy ± intraluminal intubation and dilation ± chemotherapy	Rare

[a] According to the AJCC TNM system definitions (see Table 1)
Note: Surgical results are based on the pathologic staging system, whereas patients treated with combined-modality therapy or neoadjuvant chemoradiation therapy are clinically staged.

>70% present at Stage III +


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Case 3

- A 28 year old man presents to A&E complaining of 3 weeks of loose stools, associated with abdominal pain. He opens his bowels 8-12 times a day. On occasion, there is some fresh red blood mixed in with the stools.

- PH: Appendicetomy aged 8
- Medic: Nil. Allergies: Penicillin
- SH: Non-smoker. Drinks 3-4 pints a week.
  He works as a holiday rep.

- ***What further questions would you ask?***

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Case 3

- A 28 year old man presents to A&E complaining of 3 weeks of loose stools, associated with abdominal pain. He is opening his bowels 8-12 times a day. On occasion, there is some fresh red blood mixed in with the stools.
- PMHx: Appendicetomy aged 8
- DHx: Nil. Penicillin Allergy.
- SHx: Non-smoker. Drinks 3-4 pints a week.
  He works as a holiday rep.

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Case 3 - interpretation

- Young
- Man
- 3 weeks (most G'enteritis self limiting 48hr)
- Abdo pain….? Helpful
- Blood in stools …
- 8-12 x/day (what about night ?)
- Holiday rep

Diff Diag?

Bloody D ….infective (travel), IBD

Immunosuppressed?

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Some Causes of Diarrhoea

- **Infective**
  - Bacterial
  - Viral
  - Protozoal
- **Inflammatory Bowel Disease**
  - Crohn's
  - Ulcerative Colitis
- Alcohol excess
- Irritable Bowel Syndrome
- Hyperthyroidism
- Malabsorptive States
- Diverticular Disease
- Constipation (with overflow)
- Drugs
- Ischaemic
- Radiation Colitis
- Malignancy
- Bacterial Overgrowth
- Fictitious

http://www.continence.org.au/data/images/bristol_stool_chart.gif

For stool gazers !

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

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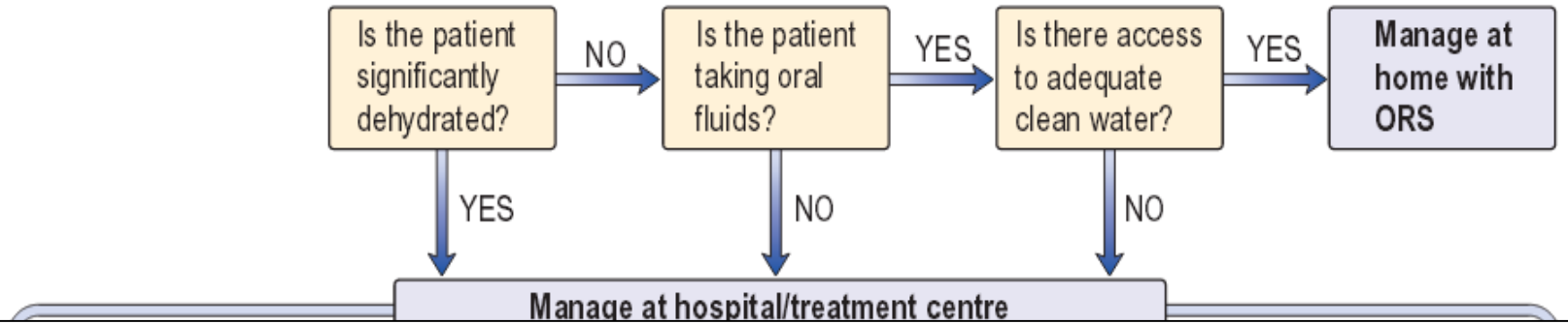
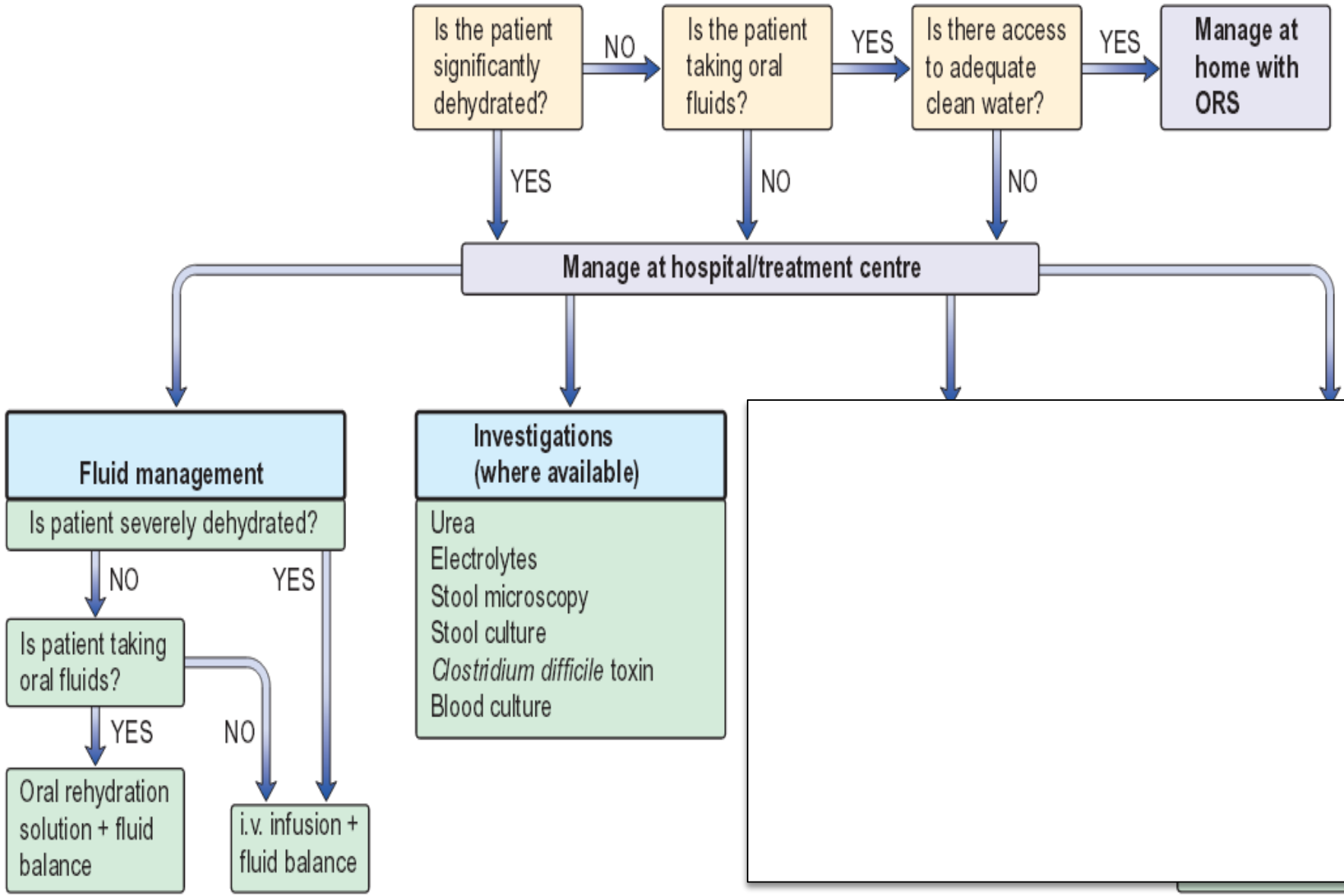
Causes of Travellers' Diarrhoea

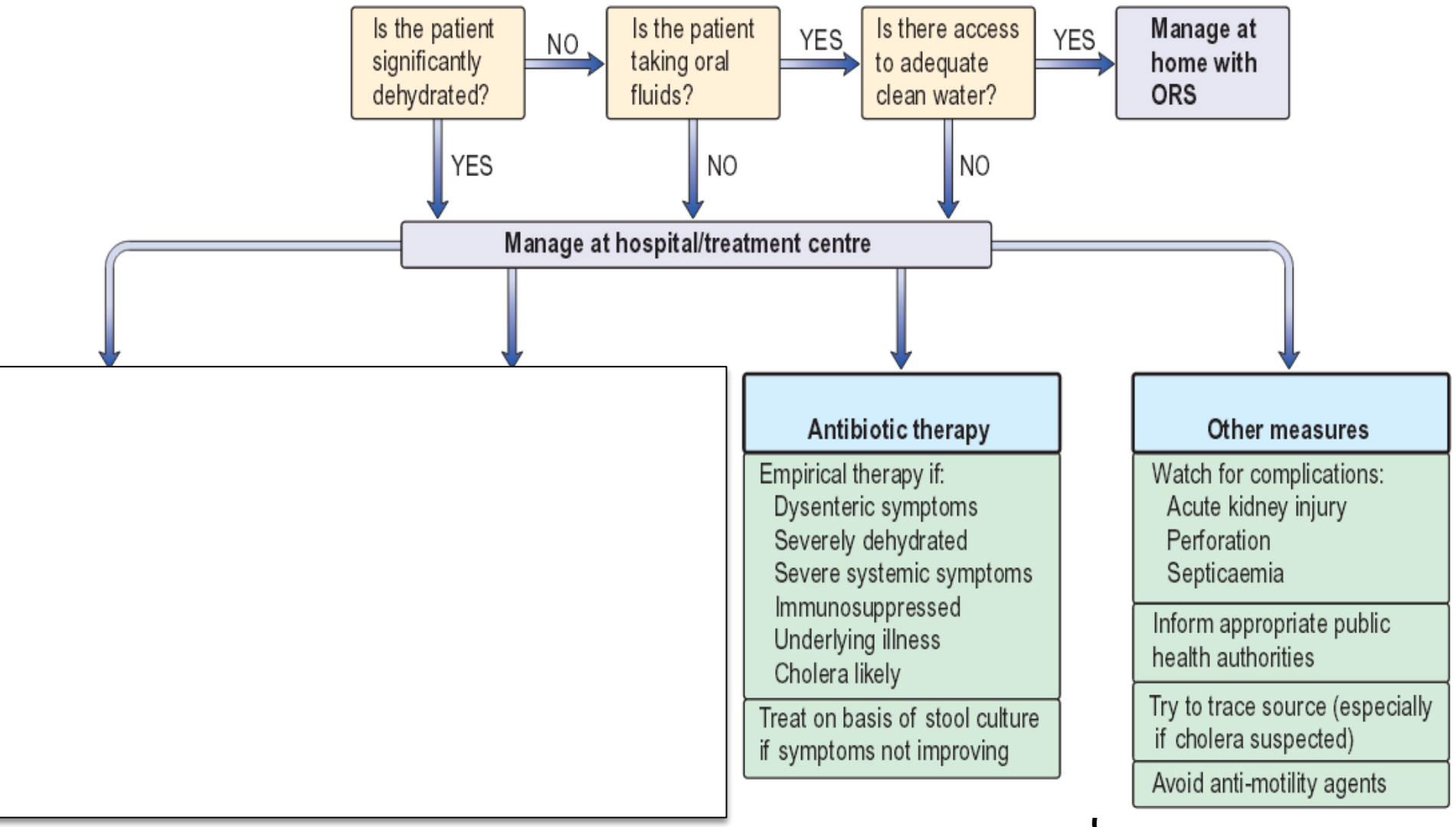
Bacteria – 70–90% of cases	*E. coli* (enterotoxigenic)
	E. coli (enteroaggregative)
	Shigella spp.
	Salmonella spp.
	Campylobacter jejuni
	Aeromonas and *Plesimonas* spp.
	Vibrio cholera
Viruses – 10%	Rotavirus
	Noroviruses*
Protozoa – <5%	*Giardia intestinalis*
	Entamoeba histolytica
	Cryptosporidium parvum
	Cyclospora cayetanensis

Note: Co-infection with multiple pathogens occurs in approximately 10% of cases.
**Often associated with outbreaks of diarrhoea or cruise ships and in holiday resorts.*


Is the patient significantly dehydrated?
NO
Is the patient taking oral fluids?
YES
Is there access to adequate clean water?
YES
Manage at home with ORS
YES
NO
NO
Manage at hospital/treatment centre

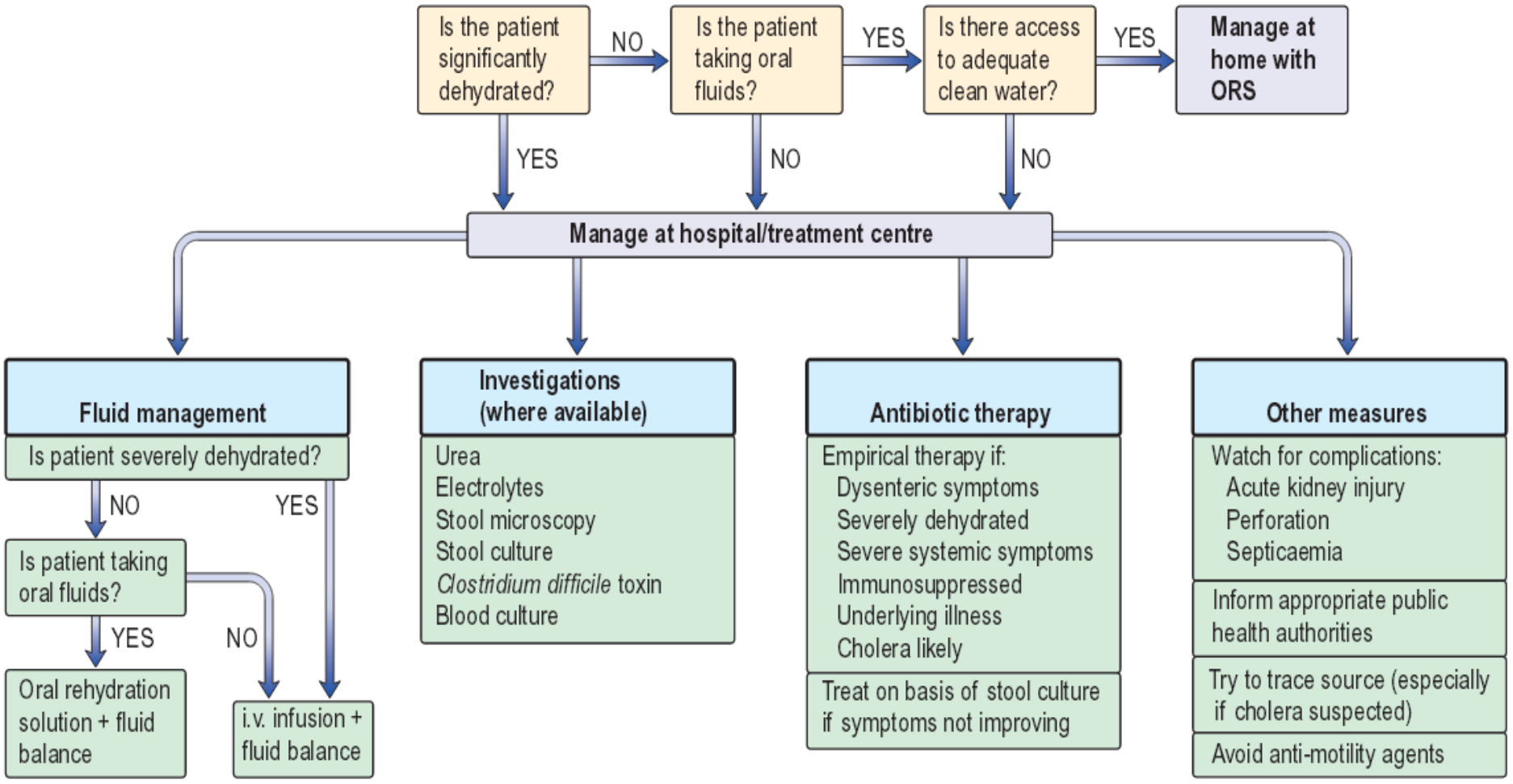


Gastroenteritis Management Algorithm



IMPLY GASTRO

Gastroenteritis Management Algorithm



IMPLY GASTRO

Case 3 Continued

- The patient's stool and blood cultures are negative.

- His pain and diarrhoea persist. He looks ill.
- Hb 98g/L MCV 78fl CRP 86

What further investigations would you consider?

- *Immediate AXR*
- *IV infusion*
- *Unprepared sigmoid/colonoscopy + biopsy*

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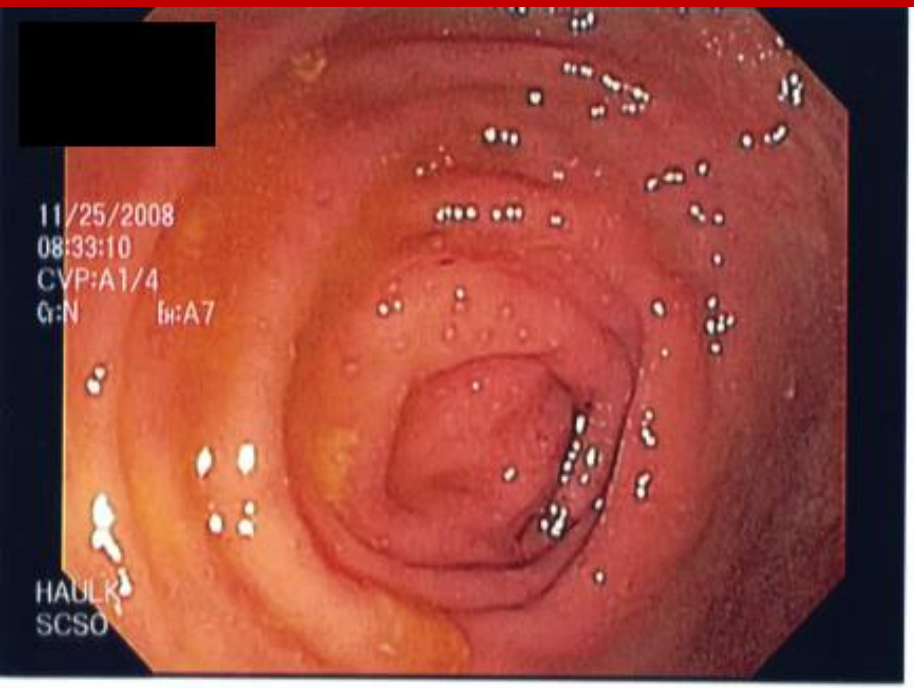

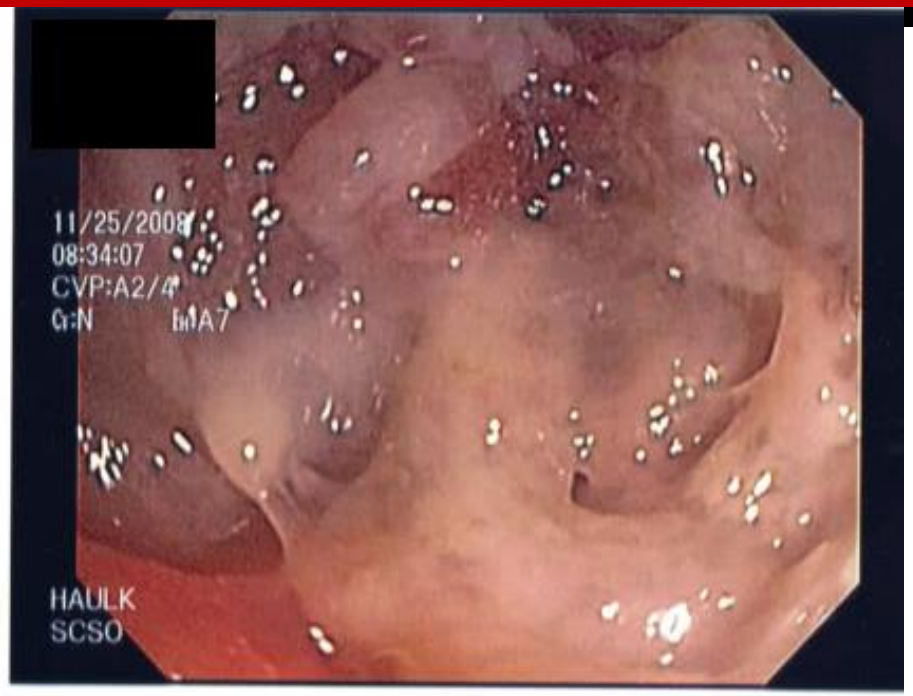

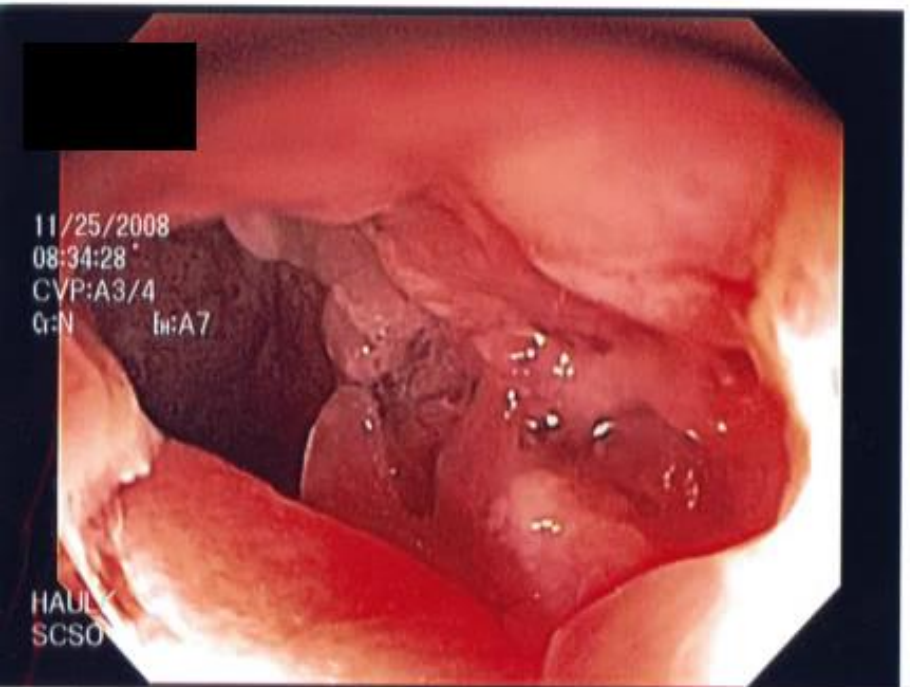

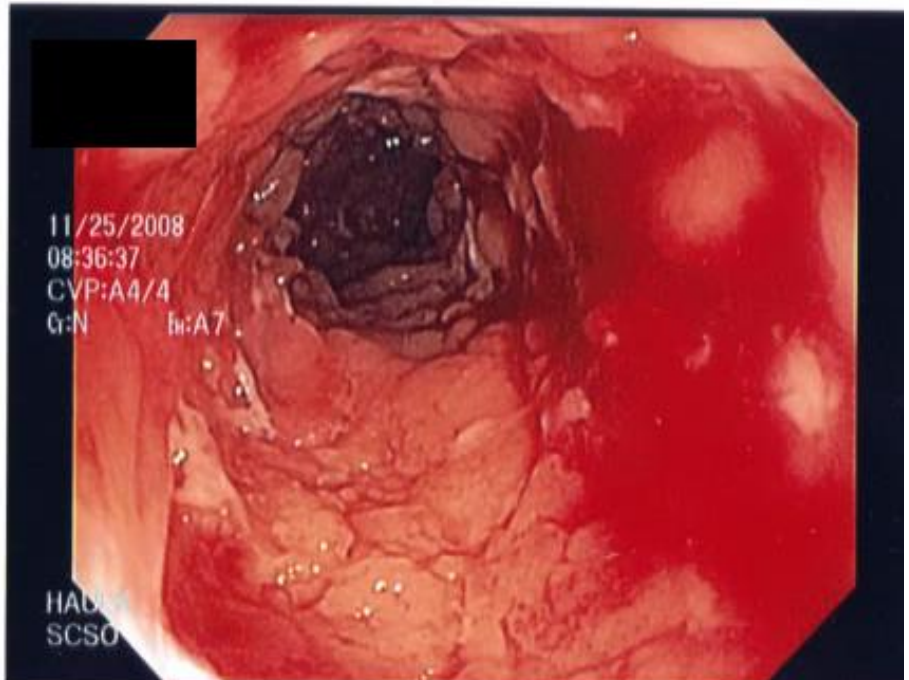

http://www.crohnsforum.com/showthread.php?t=4727

Management of acute severe colitis

Admit to hospital

- Joint inpatient management between gastroenterologist and colorectal surgeon

Investigations

- FBC, CRP, liver biochemistry, serum albumin and electrolytes
- Blood cultures (Gram-negative sepsis occurs)
- Plain abdominal X-ray looking for colonic dilatation (transverse colon diameter >5 cm), and mucosal islands
- Stool cultures (× 3) and *Cl. difficile* toxin to exclude coincidental infection (do not delay steroids while awaiting result)

Management of Acute Colitis (contd)

Treatment

- Stop drugs that may precipitate colonic dilatation (anticholinergics, antidiarrhoeals, non-steroidal anti-inflammatory drugs, opioids)
- i.v. hydrocortisone 100 mg 6-hourly
- Correct electrolyte and fluid imbalance
- Low molecular weight heparin to reduce the risk of venous thrombosis
- Consider i.v. ciclosporin (2 mg/kg over 24 hours) or infliximab if no response after 4 days of i.v. hydrocortisone. Colectomy may be necessary.

Monitor

- Stool chart: frequency, type and presence of blood
- Vital signs at least four times daily
- Daily bloods and abdominal X-ray if admitting film abnormal

Differences between Crohn's and UC

	Crohn's disease	Ulcerative colitis
Macroscopic	Affects any part of gastrointestinal tract	Affects only the colon
	Oral and perianal disease	Begins in rectum and extends proximally in varying degrees
	Discontinuous involvement ('skip lesions')	Continuous involvement
	Deep ulcers and fissures in mucosa: 'cobblestone appearance'	Red mucosa, bleeds easily
		Ulcers and pseudopolyps (regenerating mucosa) in severe disease
Microscopic	Transmural inflammation	Mucosal inflammation
	Granulomas present in 50%	No granulomata
		Goblet cell depletion
		Crypt abscesses

Summary of treatments for Crohn's and UC

Induction of remission

- Oral or i.v. glucocorticosteroids
- Enteral nutrition
- Anti-TNF antibodies

Maintenance of remission

- Azathioprine, 6MP, methotrexate, mycophenolate mofetil
- Anti-TNF antibodies

Perianal disease

- Ciprofloxacin and metronidazole
- Azathioprine
- Anti-TNF antibodies

Get off steroids asap , if you can

Disease severity	Medication	Indications
Mild/moderate	Oral 5-ASA	First line for left sided/extensive
	Rectal 5-ASA/steroids	For proctitis or proctosigmoiditis
	Oral prednisolone	Second line, if inadequate response to 5-ASA
Severe	Oral prednisolone	
Severe with systemic features	Hydrocortisone	See Emergency Box 3.2
	Ciclosporin	
	Infliximab	
Maintain remission	5-ASA	Most patients require maintenance treatment
	Azathioprine/6-mercaptopurine	For patients who relapse frequently despite ASA or are ASA-intolerant

5-ASA, aminosalicylic acid; left sided disease, up to splenic flexure; proctitis, rectal inflammation.

Extra-intestinal manifestations of IBD

Eyes	Uveitis, episcleritis, conjunctivitis
Joints	Arthralgia*, small joint arthritis, monoarticular arthritis (knees and ankles), ankylosing spondylitis, inflammatory back pain
Skin	Erythema nodosum, pyoderma gangrenosum (necrotizing ulceration of the skin, commonly on lower legs)
Hepatobiliary	Fatty liver*, sclerosing cholangitis, chronic hepatitis, cirrhosis, gallstones*
Renal calculi	Oxalate stones in patients with small bowel disease or after resection
Venous thrombosis	

All uncommon, occur in less than 10% of patients other than those marked.*

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Complications of IBD

Toxic dilatation of the colon + perforation
Stricture formation*
Abscess formation (Crohn's disease)
Fistulae and fissures (Crohn's)*
Colon cancer

**Surgical intervention only necessary if symptomatic and not responding to medical treatment.*


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Case 4

- A 56 year old man comes to his GP with a 6 week history of constipation. He occasionally notices some red blood in the stools.

- *What further questions would you ask him?*

NB

Older, recent change in bowel habit, blood PR

?weight loss

?change in medication

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Causes of Constipation

General

Pregnancy, inadequate fibre intake, immobility

Metabolic/endocrine

Diabetes mellitus, hypothyroidism, hypercalcaemia, porphyria

Functional

Irritable bowel syndrome, idiopathic slow transit

Drugs

Opiates, antimuscarinics, calcium channel blockers e.g. verapamil,
Antidepressants, e.g. tricyclics, iron

Neurological

Spinal cord lesions, Parkinson's disease

Psychological

Depression, anorexia nervosa, depressed urge to defecate

Gastrointestinal disease

Intestinal obstruction (e.g. by colon cancer) and pseudo-obstruction
Painful anal conditions, Hirschsprung's disease

Defecatory disorders

Rectal prolapse, pelvic floor dyssynergia
Megarectum, large rectocele

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Causes of Rectal Bleeding

Colonic

Haemorrhoids

Anal fissure

Neoplasms: benign and malignant

Colitis: ulcerative colitis, Crohn's, infective, ischaemic

Angiodysplasia (abnormal collections of blood vessels)

Diverticular disease

Small intestine

Neoplasms

Ulcerative disease: Crohn's disease, vasculitis, NSAIDs

Angiodysplasia

Meckel's diverticulum

Case 4 contd

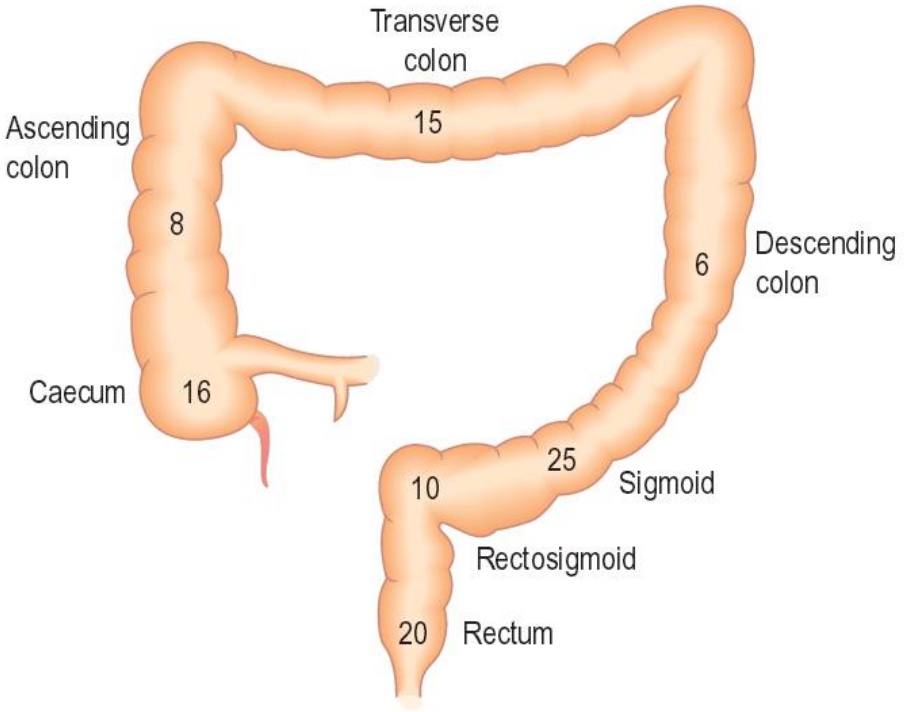
On Examination:

- He looks thinner than when you last saw him.
- CVS and Resp examinations normal.
- Abdo – Bowel sounds present. No organomegaly.
- PR – A mass is felt in the posterior aspect of the rectum. There is some blood on the finger on removal.

Risk Factors and Distribution (%) of Colorectal Ca.

Increased risk
- Increasing age
- Animal fat (saturated) and red meat consumption
- Sugar consumption
- Colorectal polyps
- Family history of colon cancer or colonic polyps
- Chronic inflammatory bowel disease
- Obesity (body and abdominal)
- Smoking
- Acromegaly
- Abdominal radiotherapy
- Ureterosigmoidostomy

Decreased risk
- Vegetable, garlic, milk, calcium consumption
- Exercise (colon only)
- Aspirin (including low dose) and other NSAIDs



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Investigations

The purpose of investigation is to confirm the diagnosis and stage the tumour.

- **Colonoscopy** with biopsy is gold standard.
  - CT colonography and barium enema can be used.

- **Blood tests**
  - FBC may show anaemia. LFTs may be abnormal in metastases.
  - Carcinoembryonic antigen (CEA) are often raised

- **Radiology**
- CT scan of the chest, abdomen and pelvis is the initial staging investigation to look for local spread and metastatic disease.
- MRI and endoanal ultrasound are used to locally stage rectal cancer.

- **(Do NOT do Faecal occult blood** tests…… **Only used** in population screening studies but are not of value diagnostically)

Treatment and Staging

- Treatment is primarily surgical (avoiding stomas if possible)
- Adjuvent chemotherapy increases survival in Stage II and III tumours
- Radiotherpy can be used in low rectal tumours.
- Chemoradiotherapy may be used in palliation

TNM stage	Description	5-year survival (%)
Stage 0	Tumour confined to the mucosa	>95
Stage 1	Tumour invades submucosa (T1) or muscularis propria (T2). No involved nodes (N0) or distant metastases (M0)	80–95
Stage II	Tumour invades into subserosa (T3) or directly into other organs (T4). No involved nodes (N0) or distant metastases (M0)	65–85
Stage IIIa	T1/T2 and 1–3 regional lymph nodes involved (N1).	55–65
Stage IIIb	T3, N1 or T4, N1	35–42
Stage IIIc	Any T, ≥4 regional lymph nodes (N2)	25–27
Stage 4	Any T, any N + distant metastases	5–7


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Case 5

- A 34 year old woman attends your GP practice complaining of feeling generally unwell for a couple of weeks. She complains of nausea and has had a temperature during this time.

- On examination, you notice she is jaundiced and has 4 cm smooth hepatomegaly.

- *Anything else you would like to know?*
- *What would you like to do next?*

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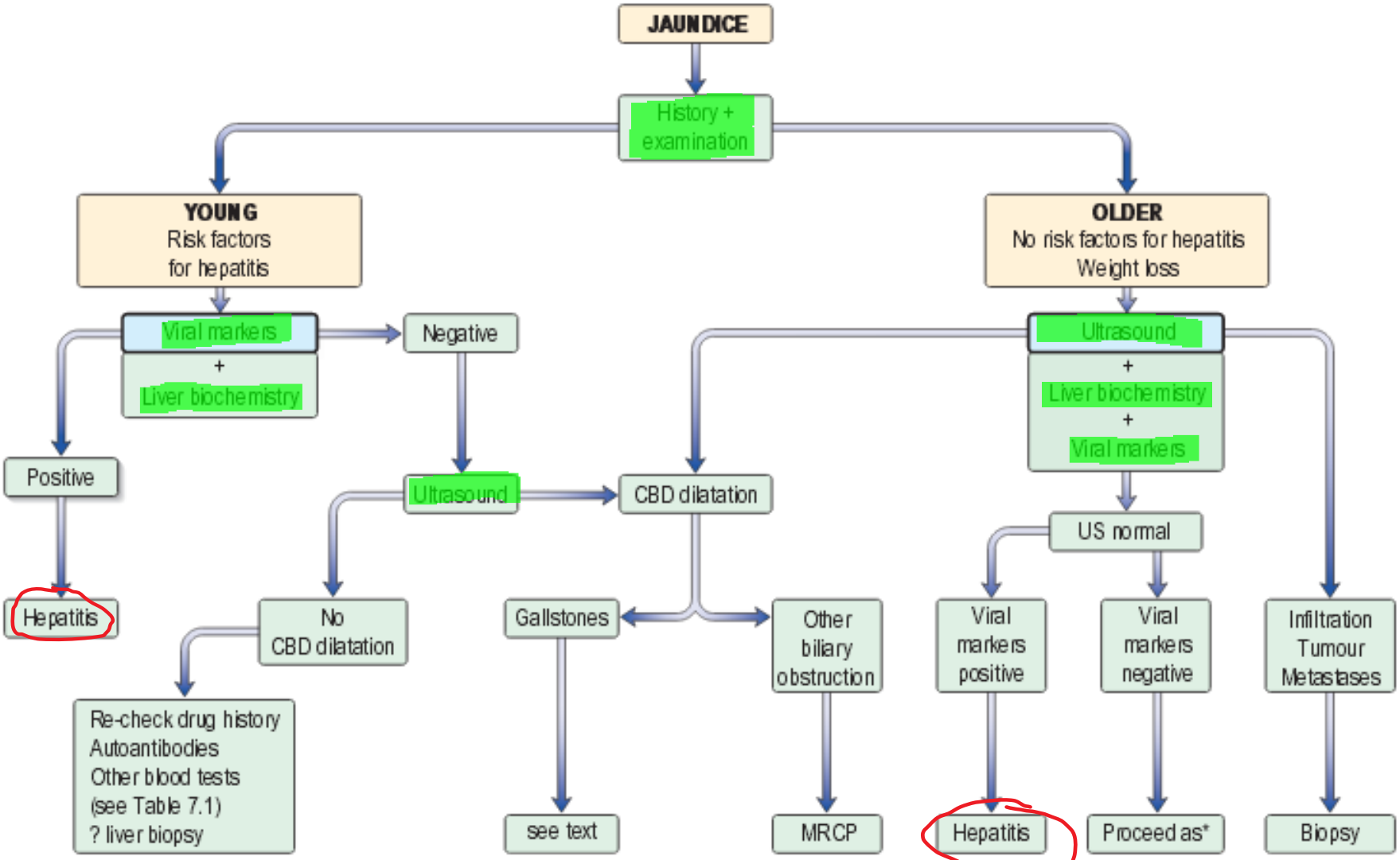
Causes of Jaundice

Types	HAEMOGLOBIN → BILIRUBIN	Causes
Prehepatic		Haemolysis
Cholestatic	CONJUGATION	
Intrahepatic		Viral hepatitis Drugs Alcoholic hepatitis Cirrhosis – any type Pregnancy Recurrent idiopathic cholestasis Some congenital disorders Infiltrations
Extrahepatic	GALL BLADDER PANCREAS	Common duct stones Carcinoma – bile duct – head of pancreas – ampulla Biliary stricture Sclerosing cholangitis

Gilberts



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Causes of Hepatomegaly		Causes of Splenomegaly	
Infective	Viral Hepatitis EBV Malaria Leishmaniasis	**Infective**	EBV Malaria Leishmaniasis
Malignant	Hepatocellular Ca. Leukaemia Lymphoma Secondary Ca.	**Malignant**	Leukaemia Lymphoma
Metabolic/ Infiltration/ Inflammatory	Fatty Amyloid Haemochromatosis Storage Diseases Sarcoid	**Metabolic/ Infiltration/ Inflammatory**	Amyloid Sarcoid Storage Diseases Haemolytic Anaemia Haemoglobinopathies SLE
Cardiovascular	Right Heart Failure Budd-Chiari	**Cardiovascular**	Portal Hypertension
Other	Reidel's Lobe Low Diaphragm		

Case 5 Continued

FBCs and U+Es: Normal

Liver Biochemistry: AST 1134, ALT 1456, ALP 145
GGT 188 Bil 34

Liver function: Alb 36 **INR** 1.1

Autoantibody screen: ASMA, ANCA and ANA negative

HBsAg +
HBeAg +
Anti-HBs –
Anti-Hbe –
Anti-HBc IgM +
Anti-HBc IgG +

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	A	B	C	D	E
Virus	RNA 27 nm Picorna				
Spread					
Faeco-oral	Yes				
Blood/blood products	Rare				
Vertical	No				
Saliva	Yes				
Sexual	Rare				
Incubation	Short (2–3 weeks)				
Age	Young				
Carrier state	No				
Chronic liver disease	No				
Liver cancer	No				
Mortality (acute)	<0.5%				
Immunization					
Passive	Normal immunoglobulin serum i.m. (0.04–0.06 mL/kg)				
Active	Vaccine				

[a]Chronic hepatitis in immunosuppressed patients.

Summary of the Viral Hepatitis Viruses

	A	B	C
Virus	RNA 27 nm Picorna	DNA 42 nm Hepadna	RNA approx. 50 nm Deltaviridae
Spread			
Faeco-oral	Yes	No	No
Blood/blood products	Rare	Yes	Yes
Vertical	No	Yes	Rare
Saliva	Yes	Yes	Yes
Sexual	Rare	Yes	Yes (rare)
Incubation	Short (2–3 weeks)	Long (1–5 months)	Long
Age	Young	Any	Any
Carrier state	No	Yes	Yes
Chronic liver disease	No	Yes	Yes
Liver cancer	No	Yes	Rare
Mortality (acute)	<0.5%	<1%	
Immunization			
Passive	Normal immunoglobulin serum i.m. (0.04–0.06 mL/kg)	Hepatitis B immunoglobulin (HBIg)	No
Active	Vaccine	Vaccine	HBV vaccine

[a]Chronic hepatitis in immunosuppressed patients.

Summary of the Viral Hepatitis Viruses

	A	B	C	D	E
Virus	RNA 27 nm Picorna	DNA 42 nm Hepadna	RNA approx. 50 nm Deltaviridae	RNA 36 nm (with HBsAg coat) Flavi	RNA 27 nm Herpesvirus
Spread					
Faeco-oral	Yes	No	No	No	Yes
Blood/blood products	Rare	Yes	Yes	Yes	No
Vertical	No	Yes	Rare	Occasional	No
Saliva	Yes	Yes	Yes	? No	?
Sexual	Rare	Yes	Yes (rare)	Rare	No
Incubation	Short (2–3 weeks)	Long (1–5 months)	Long	Intermediate	Short
Age	Young	Any	Any	Any	Any
Carrier state	No	Yes	Yes	?	No[a]
Chronic liver disease	No	Yes	Yes	Yes	No[a]
Liver cancer	No	Yes	Rare	Yes	No
Mortality (acute)	<0.5%	<1%		<1%	1–2% (pregnant women 10–20%)
Immunization					
Passive	Normal immunoglobulin serum i.m. (0.04–0.06 mL/kg)	Hepatitis B immunoglobulin (HBIg)	No	No	No
Active	Vaccine	Vaccine	HBV vaccine	No	Vaccine

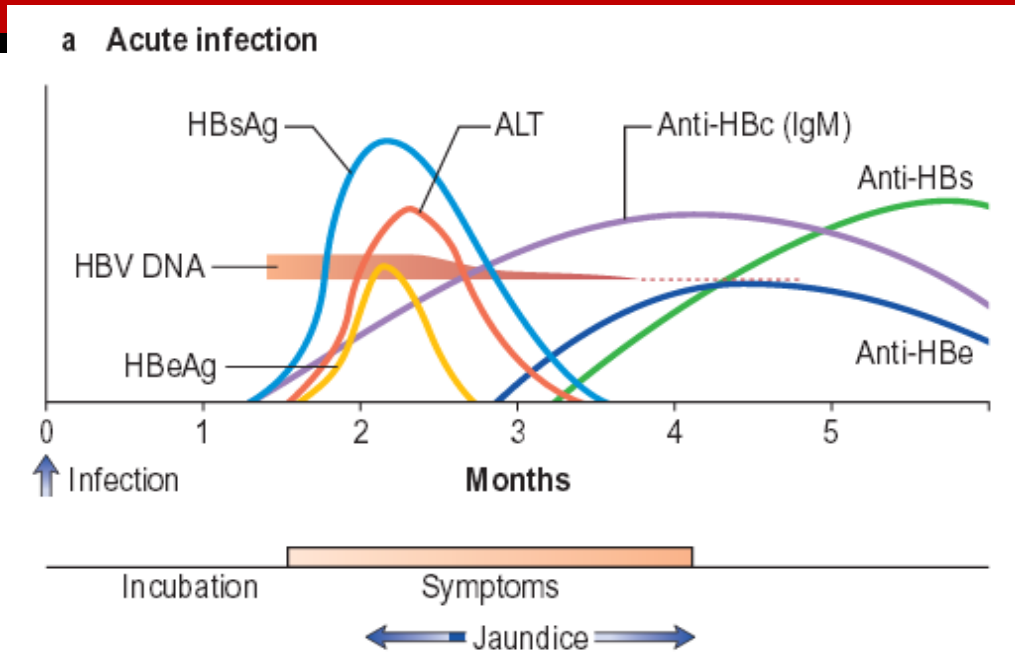
[a]Chronic hepatitis in immunosuppressed patients.

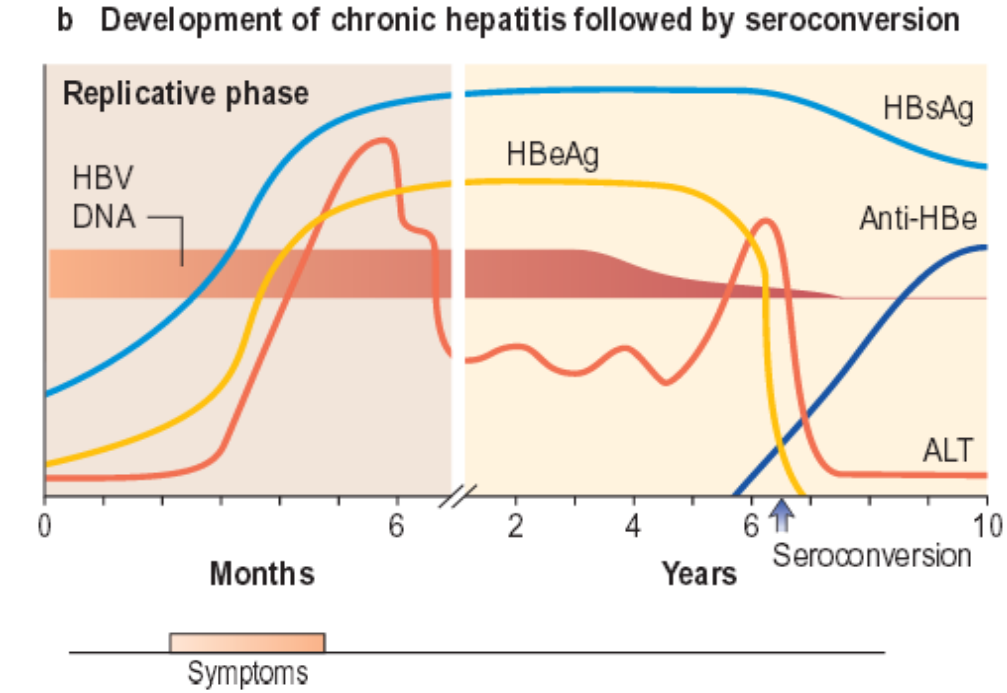
Hepatitis B

Antigens	
HBsAg	Acute or chronic infection
HBeAg	Acute hepatitis B Persistence implies: Continued infectious state development of chronicity Increased severity of disease
HBV DNA	Implies viral replication Found in serum and liver Levels indicate response to treatment
Antibodies	
Anti-HBs	Immunity to HBV; previous exposure; vaccination
Anti-HBe	Seroconversion
Anti-HBc	
IgM	Acute hepatitis B (high titre) Chronic hepatitis B (low titre)
IgG	Past exposure to hepatitis B (HBsAg-negative)

Hepatitis B virus

Serology and Course





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Treatment of HBV Infection

Acute – Mainly symptomatic. The majority (>90%) will recover and clear the virus.

Chronic Infection – May be inactive or show chronic hepatitis.

- Criteria for treatment is based on:
  - Presence of HBeAg,
  - HBV DNA level (>20000)
  - serum ALT (> x2 normal)
  - Liver histology (biopsy is not indicated if the above features are present)

Treatment options:

- ***Pegylated α-interferon*** given subcutaneously, once weekly. Response rate of 25-45% at 1 year.
- ***Entecavir*** – Nucleoside analogue 1-5mg oral x1/day Response rate of 67-90% at one year.
- ***Tenofovir*** – Reverse Transcriptase Inhibitor –300mg oral x1/day Response of 76-93 at one year.

Hepatitis C

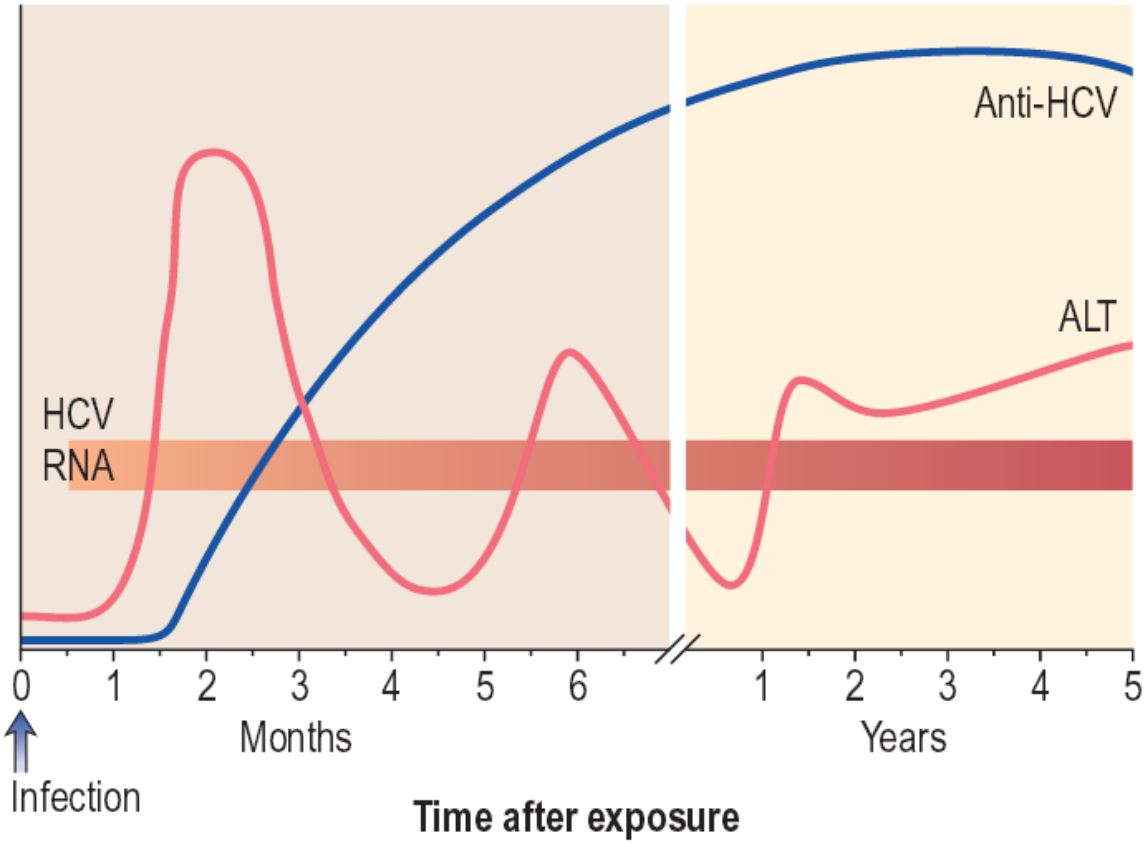

Figure 7.19 Time course of the events and serological changes seen following infection with hepatitis C virus.

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Case 6

- A 63 year old man is brought into hospital by his family who are concerned with his drinking. He has been drinking more and more since his wife passed away 2 years ago; he is currently having a large bottle of whisky every 1-2 days.

- Family say he seems to be more confused today and has recently developed a number of unexplained bruises.

- ***Are you concerned? What would you like to do?***

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Case 6 ? Differential diagnosis

- Alcohol
- Confusion
  - Subdural?
  - Encephalopathy?
  - Other cerebral event?
  - Wernicke- Korsakoff ?

Bruising - coagulopathy? due to falls? Low platelets

ALCOHOL

1 unit	1.5 units	2 units	3 units	9 units	30 units
 Normal beer half pint (284ml) 4%	 Small glass of wine (125ml) 12.5%	 Strong beer half pint (284ml) 6.5%	 Strong beer large bottle/can (440ml) 6.5%	 Bottle of wine (750ml) 12.5%	 Bottle of spirits (750ml) 40%
 Single spirit shot (25ml) 40%	 Alcopops bottle (275ml) 5%	 Normal beer large bottle/can (440ml) 4.5%	 Large glass of wine (250ml) 12.5%	Government advises alcohol consumption should not regularly exceed:  Men 3-4 units daily  Women: 2-3 units daily	
		 Medium glass of wine (175ml) 12.5%			

SOURCE: Office for National Statistics

http://news.bbc.co.uk/1/hi/in_depth/629/629/7202183.stm

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Central nervous system
- Epilepsy (p. 1114)
- Wernicke–Korsakoff syndrome (p. 1091)
- Polyneuropathy (p. 1147)

Muscles
- Acute or chronic myopathy

Cardiovascular system
- Cardiomyopathy (p. 771)
- Beriberi heart disease (p. 209)
- Cardiac arrhythmias
- Hypertension

Metabolism
- Hyperuricaemia (gout)
- Hyperlipidaemia
- Hypoglycaemia
- Obesity

Endocrine system
- Pseudo-Cushing syndrome

Respiratory system
- Chest infections

Gastrointestinal system
- Acute gastritis (including bleeding p. 254)
- Carcinoma of the oesophagus or large bowel
- Pancreatic disease
- Liver disease (fatty liver, hepatitis, cirrhosis; p. 342)

Haemopoiesis
- Macrocytosis (due to direct toxic effect on bone marrow or folate deficiency)
- Thrombocytopenia
- Leucopenia

Bone
- Osteoporosis
- Osteomalacia

Physical Effects of Excessive Alcohol Use

← MCV

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Case 6 cont:

On Examination

His Mini-mental score is 5/10.
He is jaundiced with a number of bruises. He has a course flapping tremor.
Cranial nerves normal.
HS 1+2+nil. Chest is clear.

Abdomen is mildly distended with shifting dullness.
No organomegaly is felt.

PR – empty rectum

What would you do now?

SIMPLY GASTRO

Case 6 cont:

On Examination
His Mini-mental score is 5/10.
He is jaundiced with a number of bruises. He has a course flapping tremor.
Cranial nerves normal.
HS 1+2+nil. Chest is clear.

Abdomen is mildly distended with shifting dullness.
No organomegaly is felt.

PR – empty rectum

So he is :
Yellow
Encephalopathic
Ascites
ie **Complications of Chronic liver disease**

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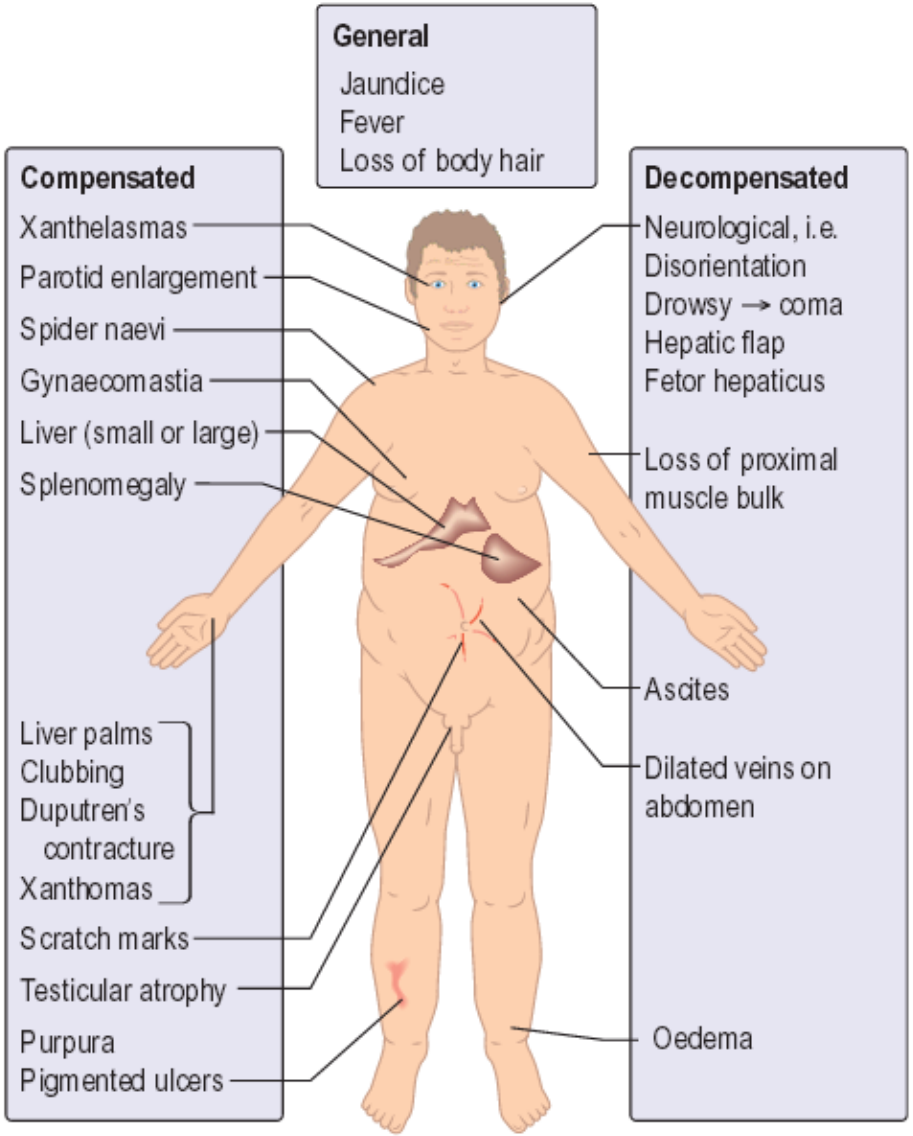
Signs of Chronic Liver Disease and Causes of Ascites



Transudate	Exudate
Portal hypertension, e.g. cirrhosis	Peritoneal carcinomatosis
Hepatic outflow obstruction	Peritoneal tuberculosis
Budd–Chiari syndrome	Pancreatitis
Hepatic veno-occlusive disease	Nephrotic syndrome
Cardiac failure	Lymphatic obstruction (chylous ascites)
Tricuspid regurgitation	
Constrictive pericarditis	
Meig's syndrome*	

**Meig's syndrome is the triad of benign ovarian fibroma, ascites and pleural effusion.*

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Case 6 contd:

FBCs: Hb 108 MCV 102 WCC 8.2 Plt 156

U+Es: Na 130 K 4.6 Urea 8.9 Creat 265

LB: AST 1467 ALT 677 ALP 137 GGT 237
Bil 38

LFTs: Alb 24 **INR** 1.8 **PT** 22 seconds

α-fetaprotein – normal

Viral and Autoimmune Screen Negative

Septic Screen Clear

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Management of alcohol withdrawal in hospital

- Prevent or treat established Wernicke's encephalopathy by administration of intravenous B vitamin complex (see p. 605). Give before administration of glucose-containing i.v. fluids.
- Correct dehydration and electrolyte imbalance. Hypophosphataemia and hypomagnesaemia is common.
- Chlordiazepoxide 30 mg four times daily decreasing to zero over 7 days. With very heavy alcohol intake and severe withdrawal symptoms the dose is increased up to 60 mg four times a day decreasing to zero over 10 days.
- Oxazepam is the drug of choice for alcohol detoxification in patients with severe liver disease as it is not metabolized by the liver.

Grading of Hepatic Encephalopathy

Grades	Detailed Description
I	Mild confusion, euphoria, anxiety or depression, reversed sleep rhythm, slurred speech.
II	Drowsiness, lethargy, gross deficits in the ability to perform mental tasks, relatively moderate confusion.
III	Somnolent but arousable, severe confusion, inability to perform mental tasks
IV	Coma with (IVa) or without (IVb) response to painful stimuli.

Causes of Fulminant Liver Failure

Fulminant Liver Failure

Defined as severe hepatic failure in which hepatic encepthalopathy is present within 2 weeks

Viruses
- A, B, (D), E

Other viruses

Drugs (examples)
- Analgesics (e.g. paracetamol)
- Monoamine oxidase inhibitors
- Halogenated anaesthetics
- Antituberculosis (e.g. isoniazid)
- Antiepileptic (e.g. valproate)
- 'Social' drugs (e.g. 'Ecstasy')

Toxins
- *Amanita* poisoning
- Halohydrocarbons

Miscellaneous
- Wilson's disease
- Acute fatty liver of pregnancy
- Reye's syndrome
- Budd–Chiari syndrome
- Autoimmune hepatitis

Causes of Cirrhosis

Common	Others
Alcohol	Biliary cirrhosis:
Hepatitis B ± D	Primary
Hepatitis C	Secondary
Non-alcoholic fatty liver disease	Autoimmune hepatitis
	Hereditary haemochromatosis
	Hepatic venous congestion
	Budd–Chiari syndrome
	Wilson's disease
	Drugs (e.g. methotrexate)
	α_1-Antitrypsin deficiency
	Cystic fibrosis
	Galactosaemia
	Glycogen storage disease
	Veno-occlusive disease
	Idiopathic (cryptogenic)
	? Other viruses

Child-Pugh Score for Cirrhosis

Score	1	2	3
Ascites	None	Mild	Moderate/severe
Encephalopathy	None	Mild	Marked
Bilirubin (µmol/L)	<34	34–50	>50
Albumin (g/L)	>35	28–35	<28
Prothrombin time (seconds over normal)	<4	4–6	>6

Add above scores for your patient for survival figures below

Grade (scores)	% survival		
	1 year	5 years	10 years
Child's A (<7)	82	45	25
Child's B (7–9)	62	20	7
Child's C (10+)	42	20	0

Cirrhosis Outcomes

Indicators of Poor Prognosis

Blood tests
- Low albumin (<28 g/L)
- Low serum sodium (<125 mmol/L)
- Prolonged prothrombin time >6 s above normal value
- Raised creatinine >130 µmol/L

Clinical
- Persistent jaundice
- Failure of response to therapy
- Ascites
- Haemorrhage from varices, particularly with poor liver function
- Neuropsychiatric complications developing with progressive liver failure
- Small liver
- Persistent hypotension
- Aetiology (e.g. alcoholic cirrhosis, if the patient continues drinking)

Complications

Portal hypertension and gastrointestinal haemorrhage
Ascites
Portosystemic encephalopathy
Acute kidney injury (hepatorenal syndrome)
Hepatopulmonary syndrome
Hepatocellular carcinoma
Bacteraemias, infection
Malnutrition
Osteoporosis

Average 5 year survival is 50%

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Liver Failure Management

- Liaise with specialist liver centre. Manage in high-intensity ward.

- Treat the cause
- Nutritional Support (high carb, low to high protein, vitamins)
- Watch for sepsis
- Strict fluid status, daily weights and observations.
- Ovoid sedatives and drugs metabolised in liver

- **Treat Symptoms:**
  - Ascites: Na and fluid restriction. Spironolactone (then furosemide can help. Paracentesis and replacement of albumin may be needed.
  - Bleeding – Vitamin K
  - Laxatives
  - Cerebral oedema – mannitol, hyperventilate

- **Always think of liver transplantation early**

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The End

Any Questions?

Bibliography

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Essentials of Clinical Medicine - Ballinger

Pass Finals – Smith, Carty and Langmead

Kumar and Clark's Medical Management and therapeutics

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