The Gastroenterology Block

Peptic ulcer disease, acute and chronic viral hepatitis, decompensated cirrhosis, upper GI bleeding, inflammatory bowel disease and hepatocellular carcinoma.

Cases 34–40 · 9,176 words

This block covers the gastrointestinal and hepatological teaching of both internal medicine courses. The **first course** supplies cases 34 and 38; the **second course** supplies cases 39 and 40.

Case	Lecture it serves
System opener: the gastrointestinal history and examination	History taking in gastrointestinal; physical examination of the gastrointestinal system
Case 34 — Dyspepsia, reflux and peptic ulcer disease	Gastro-oesophageal reflux disease and peptic ulcer disease
Case 35 — Acute viral hepatitis	Hepatitis (acute)
Case 36 — Chronic viral hepatitis	Hepatitis (chronic)
Case 37 — Decompensated cirrhosis and portal hypertension	Cirrhosis and portal hypertension; hepatocellular failure and ascites seminars
Case 38 — Upper gastrointestinal bleeding	Gastrointestinal bleeding
Case 39 — Inflammatory bowel disease	Inflammatory bowel disease; approach to chronic diarrhoea
Case 40 — Hepatocellular carcinoma	Malignancies of the liver

System Opener · The Gastrointestinal History and Examination

The history

Characterise the cardinal symptoms

Symptom	What to establish
Abdominal pain	Site, character, radiation and relation to food. Epigastric pain related to meals suggests peptic disease; right upper quadrant pain radiating to the back or shoulder tip suggests biliary disease; epigastric pain boring through to the back and eased by sitting forward suggests pancreatic disease.
Dysphagia	Solids first, then liquids, progressively means a mechanical obstruction — stricture or carcinoma. Both from the outset suggests a motility disorder such as achalasia. Painful swallowing is odynophagia. Ask the patient to point to the level at which food sticks.
Dyspepsia and reflux	Heartburn, acid regurgitation, waterbrash; relation to meals, to lying flat and to bending. Ask also about cough, hoarseness and dental erosion, which are the extra-oesophageal manifestations.
Vomiting	Timing, volume and content. Vomiting of undigested food several hours after eating indicates gastric outlet obstruction. Bile, blood or coffee grounds each mean something different.
Change in bowel habit	Frequency and stool consistency; blood mixed through the stool, on its surface, or only on the paper; mucus; tenesmus; and nocturnal diarrhoea, which points to organic rather than functional disease.
Steatorrhoea	Pale, bulky, offensive stool that floats and is difficult to flush — malabsorption.
Jaundice	With pale stools, dark urine and itching, indicating cholestasis. Painless progressive jaundice with weight loss is malignancy until proved otherwise.

THE ALARM FEATURES

The presence of any one of these changes a case of dyspepsia into a case requiring urgent endoscopy:

Dysphagia · unintentional weight loss · anaemia · overt gastrointestinal bleeding · persistent vomiting · an abdominal or epigastric mass · new symptoms above the age threshold · a family history of upper gastrointestinal cancer.

Every dyspepsia consultation in this book, and on the ward, begins by asking about these.

Then the exposures

- **Alcohol, quantified in units per week** and over how many years — not "socially". **Non-steroidal anti-inflammatory drugs and aspirin**, including those bought without prescription. Smoking.
- **Liver risk:** blood transfusion before screening, tattoos and unsterile procedures, injecting drug use, needle-stick injury, sexual history, family history of hepatitis, and country of birth.
- **Travel, food and water exposure**, shellfish, and **unpasteurised dairy and animal contact** — brucellosis presents with hepatitis and fever in this region.
- **Drugs that damage the liver:** paracetamol, antituberculous therapy, methotrexate, anabolic steroids, and **herbal and traditional preparations**, which patients rarely mention unless asked directly.
- Family history of inflammatory bowel disease, coeliac disease, colorectal cancer and liver disease.

The examination

Before the abdomen

- **General:** cachexia and muscle wasting, **jaundice examined in the sclerae in natural light**, pallor, hydration, and mental state — a drowsy or disinhibited patient with liver disease has encephalopathy until proved otherwise.
- **Hands:** clubbing, leuconychia, koilonychia, palmar erythema, Dupuytren contracture, and **asterixis** — ask the patient to hold the wrists extended for thirty seconds.
- **Arms and chest: spider naevi** — more than five is abnormal, they occur in the distribution of the superior vena cava, and they fill from the centre outwards after blanching; bruising, scratch marks, gynaecomastia, loss of body hair, tattoos.
- **Face and mouth:** xanthelasma, parotid enlargement, fetor hepaticus, angular stomatitis, glossitis, aphthous ulceration, telangiectasia.
- **Neck:** the left supraclavicular node of Troisier, which points to an intra-abdominal malignancy.

The abdomen

- **Inspect** for distension, scars, caput medusae, striae, visible peristalsis and hernias, with the patient lying flat and the abdomen fully exposed from nipples to knees.
- **Palpate** lightly through all regions watching the patient's face, then deeply. **Liver:** begin in the right iliac fossa and move up towards the costal margin, asking the patient to breathe in; measure the extent below the costal margin and describe the edge, consistency, tenderness and any pulsatility. **Spleen:** begin in the right iliac fossa and move towards the left costal margin; if not felt, roll the patient into the right lateral position. A spleen has a notch, you cannot get above it, it moves with respiration and it is dull to percussion — a kidney is none of these things.
- **Percuss** the liver span, the Traube space, and for **shifting dullness**; test for a fluid thrill if the ascites is tense.
- **Auscultate** for bowel sounds and for bruits.
- **Complete the examination:** hernial orifices, external genitalia, **rectal examination**, and urinalysis. In an examination you may offer these; on the ward you perform them.

Stigmata of chronic liver disease	Signs of portal hypertension	Signs of decompensation
Spider naevi, palmar erythema, leuconychia, clubbing	Splenomegaly	Jaundice
Gynaecomastia, testicular atrophy, loss of body hair	Ascites	Ascites
Dupuytren contracture, parotid enlargement	Caput medusae, dilated abdominal veins	Encephalopathy — asterixis, altered sleep pattern, confusion
Bruising, scratch marks	Varices — not visible externally	Variceal bleeding

The distinction matters. Stigmata tell you the liver is chronically diseased. Signs of decompensation tell you it is failing now, and it is decompensation — not the stigmata — that determines admission, prognosis and the need for transplant assessment.

Case 34 · Dyspepsia, Reflux and Peptic Ulcer Disease

CLINICAL VIGNETTE

A **38-year-old man** describes four months of burning discomfort behind the sternum, worse at night and when he lies flat, sometimes waking him with a sour taste at the back of his throat. Separately, he describes a gnawing epigastric pain that comes on two to three hours after meals and is **relieved by eating**.

He takes ibuprofen most days for back pain, bought from the pharmacy. He smokes 15 cigarettes daily and drinks strong coffee through the day.

He has lost no weight, swallows normally, has never vomited blood and has no family history of gastric cancer.

On examination: body mass index 29 kg/m^2, mild epigastric tenderness, no mass, no lymphadenopathy. **Stool antigen for *Helicobacter pylori* is positive.**

1. Focused History

- **Separate the two symptom patterns**, because he has both. Retrosternal burning worse on lying flat is reflux. Epigastric gnawing pain with a clear relation to meals is peptic ulceration — classically **relieved by food in duodenal ulcer** and **provoked by food in gastric ulcer**, although the distinction is far from reliable in practice.
- **Screen for every alarm feature** listed in the system opener. Their absence in a man under the age threshold is what permits a non-invasive approach.
- **Drugs:** non-steroidal anti-inflammatory drugs and aspirin, corticosteroids, anticoagulants, bisphosphonates, and potassium supplements. Ask about what is bought over the counter — that is where the anti-inflammatory almost always comes from.
- Alcohol, smoking, caffeine, late meals, and weight. Previous eradication therapy and whether it was completed.
- **Extra-oesophageal reflux symptoms:** chronic cough, hoarseness, sore throat, worsening asthma, dental erosion.

2. Differential Diagnosis

Diagnosis	The feature that discriminates it
Functional dyspepsia	The commonest cause overall. Normal endoscopy, no alarm features, often with other functional symptoms. A positive diagnosis after exclusion, not a shrug.
Gastro-oesophageal reflux disease	Retrosternal burning, regurgitation, worse lying flat and bending, relieved by antacids.
Peptic ulcer disease	Epigastric pain with a meal relationship; *Helicobacter pylori* or anti-inflammatory drug exposure.
Gastric carcinoma	Alarm features — weight loss, anaemia, vomiting, mass, dysphagia. This is the reason the alarm list exists.
Biliary colic	Severe right upper quadrant pain in discrete episodes lasting hours, often nocturnal, radiating to the back.
Chronic pancreatitis	Boring epigastric pain to the back, steatorrhoea, weight loss, alcohol history.
Myocardial ischaemia	Epigastric discomfort with exertion, sweating or radiation. Always consider it in an older patient with vascular risk factors — patients with infarction are routinely treated for indigestion.

3. Investigations

THE DECISION THAT STRUCTURES THE WHOLE CONSULTATION

Under the age threshold and with no alarm features: test non-invasively for *Helicobacter pylori* and treat if positive. Endoscopy is not required.

Any alarm feature, new symptoms above the age threshold, or failure of treatment: endoscopy.

- **Urea breath test or stool antigen** are the tests of choice — both detect **active** infection. **Serology cannot distinguish current from past infection** and is of little use where prevalence is high.

THE PRACTICAL POINT STUDENTS GET WRONG

Stop proton pump inhibitors for two weeks and antibiotics and bismuth for four weeks before testing — for both the initial test and the test of cure.

Acid suppression suppresses the organism as well as the acid, and produces false negative breath and stool tests. A patient sent for a breath test while taking omeprazole has had a wasted test, and will be told they do not have an infection that they do have.

- **At endoscopy:** biopsy for a rapid urease test and histology. **Every gastric ulcer must be biopsied**, because gastric ulcers may be malignant.
- **Repeat endoscopy after 6–8 weeks to confirm healing of a gastric ulcer.** Duodenal ulcers do not require this — they do not become malignant. This asymmetry is a favourite examination question.
- **Confirm eradication** with a urea breath test at least four weeks after completing therapy, in complicated ulcer disease, persistent symptoms or a bleeding ulcer.
- Complete blood count and ferritin for iron deficiency, coeliac serology where the picture fits, liver function and an ultrasound if biliary disease is possible.

- **Fasting gastrin** where ulcers are multiple, distal to the duodenal bulb, refractory or recurrent — the Zollinger–Ellison syndrome.

4. Management

Address the causes

- **Stop the ibuprofen.** If an anti-inflammatory is genuinely necessary, use the lowest effective dose with proton pump inhibitor cover, and reconsider the underlying back problem.
- Smoking cessation, weight reduction, avoiding meals within three hours of lying down, elevating the head of the bed, and reducing alcohol and caffeine.

Eradicate the organism

- Standard first-line therapy is a **proton pump inhibitor with amoxicillin and clarithromycin for 14 days**. Where clarithromycin resistance is high — and it is high in much of this region — **bismuth-based quadruple therapy or a levofloxacin-containing regimen** is preferred. **Follow local resistance data rather than the textbook default.**
- Emphasise completing the full course; failure is usually a failure of adherence.

Acid suppression

- A proton pump inhibitor for 4–8 weeks for reflux or ulcer healing, then **step down to the lowest effective dose or on-demand use**.
- **Review long-term proton pump inhibitor use annually.** Prolonged therapy is associated with vitamin B12 and magnesium deficiency, enteric infection including *Clostridioides difficile*, and fracture. Many patients continue them for years without anyone reconsidering the indication.

When it does not settle

- Reconsider the diagnosis, confirm eradication, and check adherence. Then oesophageal pH studies and manometry, and consideration of anti-reflux surgery in carefully selected patients.
- **Complications to know:** bleeding, perforation, gastric outlet obstruction, and **Barrett oesophagus** — intestinal metaplasia of the lower oesophagus which carries a risk of adenocarcinoma and enters a surveillance programme.

5. Teaching Points and Viva Questions

- The alarm features decide whether this is a prescription or an endoscopy.
- Stop the acid suppression before testing for *Helicobacter pylori*, or the result is worthless.
- Biopsy and re-scope gastric ulcers. Duodenal ulcers need neither.
- The anti-inflammatory drug is almost always bought, not prescribed, so it will not be on the medication list.
- Epigastric pain in an older patient with vascular risk factors deserves an electrocardiogram before an antacid.

Questions you should be able to answer:

- List the alarm features and explain what each one is a marker for.
- He has been taking omeprazole for three weeks. How does that affect your testing?
- Why must a gastric ulcer be re-scoped but not a duodenal one?
- Eradication fails and he remains positive. What are the three explanations, in order of likelihood?
- What are the risks of leaving him on a proton pump inhibitor for ten years?

Case 35 · Acute Viral Hepatitis

CLINICAL VIGNETTE

A **22-year-old student** presents with ten days of malaise, anorexia, nausea and a low-grade fever. He describes a striking aversion to cigarettes, which he previously smoked daily. Three days ago his urine turned dark, his stools became pale, and his family noticed he was yellow. He has a dull ache under the right ribs.

He returned three weeks ago from a trip during which he ate frequently from street stalls. He has had no tattoos, injections or transfusions, and takes no regular medication.

On examination: clearly jaundiced. Temperature 37.6 °C. The liver is **palpable 3 cm below the costal margin and tender**. There is no splenomegaly, no ascites, and **no spider naevi, palmar erythema or clubbing**. He is fully alert with no asterixis.

Alanine aminotransferase 1840 U/L · aspartate aminotransferase 1320 · bilirubin 180 µmol/L · alkaline phosphatase 160 · albumin 40 g/L · INR 1.1.

1. Read the Liver Tests First

Before any serology, decide which of three patterns you are looking at. It narrows the differential more than anything else you will do.

Pattern	Definition	Points to
Hepatitic	Aminotransferases raised far out of proportion to alkaline phosphatase	Viral hepatitis, drugs and toxins, autoimmune hepatitis, ischaemia
Cholestatic	Alkaline phosphatase and gamma-glutamyl transferase raised out of proportion	Biliary obstruction — stones, tumour, stricture — or intrahepatic cholestasis
Mixed	Both raised comparably	Drug reactions, infiltration, sepsis

WHEN THE AMINOTRANSFERASE IS ABOVE 1000

An alanine aminotransferase above 1000 U/L has a **short** differential, and you should be able to recite it:

Acute viral hepatitis · drugs and toxins, above all paracetamol · ischaemic hepatitis, the "shock liver" · autoimmune hepatitis · acute biliary obstruction from a passing stone · acute Budd–Chiari syndrome · Wilson disease in a young patient.

2. Focused History

- **The prodrome** — malaise, anorexia, nausea, fever, and the characteristic **aversion to cigarettes** — followed by jaundice, at which point the patient often begins to feel better.
- **Route of exposure, matched to the virus:** hepatitis **A and E** are faecal–oral, from contaminated food and water, shellfish, and for E also undercooked meat; hepatitis **B, C and D** are parenteral, sexual and vertical.
- **Every drug, including herbal, traditional and slimming preparations, and anabolic steroids.** Ask specifically about paracetamol — total dose and over how many days, including staggered overdose and therapeutic excess in a malnourished patient.
- Alcohol; mushroom ingestion; occupational exposure; contacts with similar illness; vaccination status; and, in a woman, pregnancy.

WHAT TO LOOK FOR, AND WHAT ITS ABSENCE MEANS

The absence of ascites and of chronic stigmata in this patient is a positive finding, not merely a negative one. It tells you this is acute disease in a previously normal liver, rather than an acute deterioration on a background of cirrhosis — which has a different management and a far worse prognosis.

Red flags for acute liver failure: confusion, altered sleep pattern or any change in personality; persistent vomiting; bleeding or bruising; a **shrinking liver**; hypoglycaemia; and a **rising prothrombin time**.

3. Physical Examination

- Depth of jaundice; a tender smooth hepatomegaly; **splenomegaly and lymphadenopathy**, which suggest Epstein–Barr or cytomegalovirus infection rather than a hepatitis virus.
- A deliberate search for **stigmata of chronic liver disease** and for ascites, as above.
- **Mental state and asterixis, formally assessed and repeated.** Encephalopathy is what converts acute hepatitis into acute liver failure, and it is a clinical diagnosis.
- Bruising and bleeding from puncture sites.

4. Investigations

THE DISTINCTION THAT DECIDES WHO IS IN DANGER

Bilirubin and aminotransferases measure **damage**. They tell you cells are dying; they do not tell you how much liver is working, and a falling aminotransferase in a deteriorating patient is a bad sign, not a good one.

The tests of liver function, and therefore of severity, are: the prothrombin time or INR, the blood glucose, and the mental state. Check all three, and repeat them.

- **Viral serology:** hepatitis A IgM; hepatitis B surface antigen with **core IgM**; hepatitis C antibody **and HCV RNA**, since the antibody may still be negative in early infection; hepatitis E IgM; Epstein–Barr and cytomegalovirus serology.
- **Paracetamol level in every patient**, whatever the history says.
- Autoimmune screen — antinuclear and anti-smooth muscle antibodies, immunoglobulin G. **Caeruloplasmin and copper studies in any patient under 40.**
- **Brucella serology** where there has been exposure to unpasteurised dairy or livestock, which is a realistic cause of fever with hepatitis in this region.
- Complete blood count, renal function, glucose, INR repeated at least daily, and **ultrasound with Doppler** to exclude biliary obstruction and hepatic vein thrombosis.

5. Management

- **Supportive care is the treatment for uncomplicated acute viral hepatitis.** Rest, hydration, adequate nutrition, and avoidance of alcohol and hepatotoxic drugs.
- **Monitor INR, glucose, creatinine and mental state.** Deterioration in any of these changes the plan entirely.

- **N-acetylcysteine** for paracetamol toxicity, and it is also used in non-paracetamol acute liver failure.
- **Notify public health.** Advise on hand hygiene and food handling for hepatitis A; vaccinate close contacts; test and vaccinate contacts where hepatitis B is found. Advise abstaining from unprotected sex and from donating blood.

WHEN TO REFER TO A LIVER UNIT

Discuss with a transplant centre early — before the patient is critically ill, not after.

Transfer for **any degree of encephalopathy**, a rising INR, hypoglycaemia, metabolic acidosis, or renal impairment.

King's College criteria — paracetamol: arterial pH below 7.3 after adequate resuscitation, **or** the combination of INR above 6.5, creatinine above 300 µmol/L and grade 3–4 encephalopathy.

Non-paracetamol: INR above 6.5 alone, or three of — unfavourable aetiology, age under 10 or over 40, jaundice for more than 7 days before encephalopathy, INR above 3.5, bilirubin above 300 µmol/L.

6. Outcome by Virus

Virus	Course
A	Self-limiting, never chronic. More severe with increasing age. Vaccine available.
E	Usually self-limiting, but carries a mortality of up to one in five in pregnancy, particularly in the third trimester. Can be chronic in the immunosuppressed.
B	Becomes chronic in about 5% of infected adults but in around 90% of infected neonates — which is why perinatal prevention matters so much. Vaccine available.
C	Becomes chronic in around three-quarters. Now curable with oral antiviral therapy.
D	Only in the presence of hepatitis B; co-infection or superinfection, and it worsens the course.

7. Teaching Points and Viva Questions

- Measure liver function with the INR, the glucose and the mental state — not with the bilirubin.
- A falling aminotransferase in a patient who is getting worse means there is little liver left to leak enzymes.
- Check a paracetamol level in every jaundiced patient regardless of the history.
- Chronic stigmata in an apparently acute hepatitis means the liver was already diseased.
- Hepatitis E in pregnancy is a genuine obstetric emergency.

Questions you should be able to answer:

- Give the differential for an alanine aminotransferase of 1840.
- Which three measurements tell you how sick he is, and why those three?
- His INR rises to 2.4 on day three and he seems muddled. What do you do?
- Why does the absence of spider naevi matter here?

- His sister is pregnant and has been exposed. What is your concern?

Case 36 · Chronic Viral Hepatitis

CLINICAL VIGNETTE

A **45-year-old man** is found to be **hepatitis B surface antigen positive** at a pre-employment screening. He feels entirely well and has never been jaundiced. He was born in a country with high endemic prevalence; his mother died of liver disease in her fifties and a brother has "a liver problem".

He drinks no alcohol. Body mass index 31 kg/m^2.

Alanine aminotransferase 68 U/L · bilirubin normal · albumin 41 g/L · INR 1.0 · platelets 138 × 10^9/L · hepatitis B e antigen negative, anti-HBe positive · hepatitis B DNA 24,000 IU/mL.

1. Reading the Hepatitis B Panel

Students find this confusing because they try to memorise combinations. Learn instead what each marker **means**, and the combinations decode themselves.

Marker	What it means
HBsAg — surface antigen	The virus is present now. Present for more than six months means chronic infection.
Anti-HBs — surface antibody	Immunity. Alone, it means vaccination.
Anti-HBc IgG — core antibody	The patient has met the real virus at some point. Vaccination does not produce this, which is how you distinguish vaccination from past infection.
Anti-HBc IgM	Recent infection, or a flare of chronic infection.
HBeAg — e antigen	High viral replication and high infectivity.
Anti-HBe	Lower replication — but not necessarily inactive disease, because e-antigen-negative chronic hepatitis exists and is common in this part of the world.
HBV DNA	The actual viral load, and the number that drives treatment decisions.

Combination	Interpretation
Anti-HBs positive alone	Vaccinated
Anti-HBs positive with anti-HBc IgG positive	Past infection, resolved, immune
HBsAg positive, anti-HBc IgM positive	Acute infection
HBsAg positive for over 6 months, anti-HBc IgG positive	Chronic infection — then define the phase
Anti-HBc IgG positive alone	Occult infection, remote infection with waning antibody, or the window period. Matters because immunosuppression can reactivate it.

Chronic infection is not one disease but a sequence of phases — immune tolerant, immune active, inactive carrier, and e-antigen-negative chronic hepatitis. **Treatment depends on the phase, not on the positive test**, which is why a positive surface antigen is the beginning of the assessment rather than the end of it.

2. Focused History

- **Probable route and duration:** birth in an endemic area and a mother with liver disease strongly suggest **vertical transmission in infancy**, which means decades of infection and a much higher lifetime risk of cirrhosis and liver cancer.
- **Family history of hepatitis and of hepatocellular carcinoma** — the latter independently raises his own risk and lowers the threshold for surveillance.
- **Cofactors that accelerate fibrosis:** alcohol, obesity, diabetes and fatty liver, and co-infection with hepatitis C, D or human immunodeficiency virus.
- Previous treatment; symptoms suggesting established cirrhosis; and — critically — **any planned or current immunosuppression, chemotherapy or biologic therapy**.
- Household and sexual contacts, and their vaccination status. In a woman, pregnancy plans.

3. Investigations

- Liver enzymes, **albumin, INR and platelet count**. A **falling platelet count is often the earliest laboratory clue to portal hypertension**, appearing long before ascites or varices, and it is easy to overlook on a routine blood count.
- **HBV DNA and e-antigen status**; hepatitis D serology in every surface-antigen-positive patient; hepatitis C, human immunodeficiency virus, and hepatitis A immunity.
- **Assess fibrosis non-invasively.** Transient elastography where available; otherwise the **FIB-4 and APRI scores**, which are calculated from age, aminotransferases and platelet count and therefore cost nothing. Liver biopsy is now reserved for uncertain cases.
- Ultrasound of the liver, alpha-fetoprotein, and cross-sectional imaging for any nodule.
- **Hepatitis C:** the antibody is the screening test, but **HCV RNA is required to confirm active infection**, since the antibody persists after clearance.

4. Management

Hepatitis B

- **Nucleoside or nucleotide analogues — tenofovir or entecavir — suppress the virus but do not cure it**, and are usually continued long term. Treatment is indicated according to a combination of viral load, aminotransferase level, fibrosis stage, family history of liver cancer and extrahepatic disease.
- **Counsel that suppression is not cure**, so that adherence does not lapse when the patient feels well and the tests normalise.

THE SCREENING STEP THAT PREVENTS DEATHS

Screen for hepatitis B before starting any significant immunosuppression — chemotherapy, rituximab in particular, high-dose or prolonged corticosteroids, biologic agents, transplantation.

Reactivation in an unprotected patient can cause fulminant hepatic failure and death. It is entirely preventable with prophylactic antiviral therapy. **This applies to patients who are core-antibody positive with a negative surface antigen as well**, not only to those with active infection.

This is one of the few places in medicine where a routine blood test taken before treatment prevents a death, and it is frequently omitted.

- **In pregnancy:** antiviral therapy in the third trimester where the viral load is high, plus **hepatitis B immunoglobulin and vaccination for the neonate at birth** — together these reduce vertical transmission to near zero. Given that neonatal infection becomes chronic in around nine of ten cases, this is among the highest-value interventions in hepatology.

Hepatitis C

- **Direct-acting antiviral therapy cures over 95% of patients with 8–12 weeks of oral treatment**, with few side effects. This has transformed the disease within a decade. Check for drug interactions before prescribing.
- **Cure does not abolish the risk of hepatocellular carcinoma in a patient who already has cirrhosis.** Surveillance continues after successful treatment, which surprises patients and must be explained.

For both

- Complete alcohol avoidance; weight and metabolic control; vaccination against hepatitis A and B as appropriate; screening and vaccination of household and sexual contacts.
- **Six-monthly ultrasound surveillance for hepatocellular carcinoma** in all patients with cirrhosis, and in hepatitis B also in selected patients without cirrhosis on the basis of age, family history and origin.
- **Screening endoscopy for varices** once cirrhosis is established.

5. Teaching Points and Viva Questions

- Interpret the panel, not the single test. Anti-HBc separates vaccination from past infection.
- A normal aminotransferase does not mean absent disease, and e-antigen-negative chronic hepatitis is common here.
- The platelet count is the cheapest early marker of portal hypertension.
- Screen for hepatitis B before immunosuppression, including in core-antibody-positive patients.
- Cure of hepatitis C does not end cancer surveillance once cirrhosis exists.

Questions you should be able to answer:

- A patient is anti-HBs positive and anti-HBc negative. Explain.
- Why does this man's platelet count of 138 concern you?

- He is about to start rituximab for lymphoma. What must be done?
- His wife is pregnant and also surface antigen positive. What are the steps to protect the baby?
- How would you assess his fibrosis without a biopsy or elastography?

Case 37 · Decompensated Cirrhosis and Portal Hypertension

CLINICAL VIGNETTE

A **54-year-old man** with cirrhosis presents with three weeks of increasing abdominal distension and ankle swelling. For the past two days his family report that he has been sleeping through the day, awake and restless at night, and confused about where he is.

He takes spironolactone and furosemide, and bought ibuprofen last week for backache.

On examination: jaundiced, with spider naevi, palmar erythema, gynaecomastia and multiple bruises. Temperature 37.6 °C, blood pressure 98/58 mmHg, heart rate 96/min. **Asterixis is present** and he is disorientated in time. The abdomen is distended with **shifting dullness**; there is mild generalised tenderness. The spleen is palpable. There is pitting oedema to the thighs.

Sodium 128 · creatinine 132 µmol/L (baseline 78) · bilirubin 78 µmol/L · albumin 24 g/L · INR 1.8 · platelets 78 × 10^9/L.

1. Focused History — Find the Precipitant

A patient with compensated cirrhosis does not decompensate spontaneously. **Something did this**, and the something is usually treatable while the cirrhosis is not.

Precipitant	How to find it
Infection, especially spontaneous bacterial peritonitis	Often with no fever and no abdominal pain. The only way to find it is to tap the ascites.
Gastrointestinal bleeding	Melaena, haematemesis, or a haemoglobin drop. Blood in the gut is a large protein load.
Constipation	Simple, common, and easily corrected.
Dehydration and over-diuresis	Weight loss, rising creatinine, low sodium.
Drugs	Sedatives and opioids; and non-steroidal anti-inflammatory drugs, which this patient has taken and which precipitate both renal failure and fluid retention.
Electrolyte disturbance, alcohol, portal vein thrombosis, hepatocellular carcinoma	Biochemistry, history, imaging with Doppler and alpha-fetoprotein.

- Also establish: the cause of the cirrhosis; previous variceal bleeding or banding; **previous spontaneous bacterial peritonitis**, which mandates lifelong prophylaxis; previous paracentesis; nutritional state; ongoing alcohol use; and whether transplantation has ever been discussed.

2. Physical Examination

- Full stigmata, as set out in the system opener, and **grade the ascites and the encephalopathy** rather than merely noting their presence.
- **Grades of encephalopathy:** I — altered sleep pattern, mild confusion, reversed day and night; II — lethargy, disorientation, obvious asterixis; III — somnolent but rousable, gross disorientation; IV — coma.
- Search deliberately for infection: chest, urine, skin, and the abdomen — remembering that **peritonitis in cirrhosis is frequently silent**.
- Assess **nutrition and muscle bulk**. Sarcopenia is common, is a strong adverse prognostic marker, and is routinely ignored.

- Examine for a hard nodular liver or a hepatic bruit suggesting hepatocellular carcinoma, and for hernias, which are common with tense ascites.

3. Investigations

THE INVESTIGATION THAT MUST NOT BE SKIPPED

Every patient admitted with ascites has a diagnostic tap, whether or not infection is suspected. Spontaneous bacterial peritonitis is present in around one in ten such admissions and is frequently asymptomatic.

Send: cell count and differential, **culture in blood culture bottles inoculated at the bedside**, albumin, total protein, glucose, lactate dehydrogenase, cytology, and acid-fast staining where tuberculosis is a possibility.

The diagnosis is made on the neutrophil count: 250 cells/mm^3 or more is spontaneous bacterial peritonitis, whether or not the culture grows anything, and whether or not the patient has fever or pain.

- **Serum-ascites albumin gradient** — serum albumin minus ascitic albumin. **A gradient of 11 g/L or more indicates portal hypertension** (cirrhosis, heart failure, Budd–Chiari). Below 11 points elsewhere — peritoneal malignancy, tuberculous peritonitis, pancreatitis, nephrotic syndrome.
- Full biochemistry, complete blood count, C-reactive protein, blood and urine cultures, chest radiograph, glucose.
- **Ammonia is of limited value.** Do not use it to diagnose or to exclude encephalopathy, which is a clinical diagnosis. A normal level in a confused cirrhotic patient does not let you off finding the cause.
- **Ultrasound with Doppler:** liver texture and nodules, **portal vein patency**, spleen size and ascites volume. Alpha-fetoprotein; cross-sectional imaging for any nodule.
- Endoscopy for varices. Score severity with **Child–Pugh** (bilirubin, albumin, INR, ascites, encephalopathy) and **MELD**, which also drives transplant prioritisation.

4. Management — One Problem at a Time

Ascites

- **Dietary sodium restriction** to about 2 g of sodium daily, which is the single most important measure and the one most often not explained properly.
- **Spironolactone with furosemide**, conventionally in a 100 mg to 40 mg ratio. **Daily weights** — aim for 0.5 kg loss per day without peripheral oedema, up to 1 kg with oedema. Monitor sodium, potassium and creatinine.
- **Large-volume paracentesis for tense ascites, with intravenous albumin replacement of 6–8 g for every litre removed**, to prevent post-paracentesis circulatory dysfunction.
- **Refractory ascites:** consider a transjugular intrahepatic portosystemic shunt, and refer for transplant assessment.
- **Avoid absolutely: non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors and receptor blockers, and aminoglycosides.**

Spontaneous bacterial peritonitis

- A third-generation cephalosporin, adjusted to local sensitivities.
- **Intravenous albumin, 1.5 g/kg on day 1 and 1 g/kg on day 3.** This is not supportive fluff — it substantially reduces the incidence of hepatorenal syndrome and reduces mortality.
- **Lifelong secondary prophylaxis** with a quinolone after a first episode.

Hepatic encephalopathy

- **Find and treat the precipitant.** This is the treatment; lactulose is the adjunct.
- **Lactulose titrated to two or three soft stools daily** — not to a fixed dose. Rifaximin is added for recurrent episodes.
- Avoid sedatives. Nurse in a well-lit place with orientation cues; assess swallowing before giving oral medication to a drowsy patient.

> **DO NOT RESTRICT THE PROTEIN**
>
> Older teaching restricted dietary protein in encephalopathy. **This is wrong and it is harmful.**
>
> Patients with cirrhosis are catabolic and frequently sarcopenic, and protein restriction worsens both the malnutrition and the outcome. **Give adequate protein**, roughly 1.2–1.5 g/kg daily, with frequent small meals and a **late evening snack** to shorten the overnight fast.

The rest

- **Varices:** a non-selective beta blocker such as propranolol or carvedilol, or endoscopic band ligation, for primary prophylaxis.
- **Hyponatraemia** is usually dilutional — fluid restriction, and reduce or stop diuretics if it is severe. Do not give saline.
- **Hepatorenal syndrome** — a diagnosis of exclusion, made after withdrawing diuretics and nephrotoxins and giving an albumin challenge. Treat with terlipressin and albumin; transplantation is the definitive treatment.
- **Transplant assessment**, alcohol abstinence with support, vaccination, six-monthly cancer surveillance, and an honest conversation about prognosis and preferences.

5. Teaching Points and Viva Questions

- Tap the ascites in every admission. Peritonitis in cirrhosis is usually silent.
- Two hundred and fifty neutrophils makes the diagnosis, with or without a positive culture.
- Albumin with peritonitis and with large-volume paracentesis changes outcomes.
- Feed the patient. Protein restriction is obsolete and harmful.
- Ammonia does not diagnose encephalopathy; the bedside does.
- Anti-inflammatory drugs are contraindicated in cirrhosis, and patients buy them freely.

Questions you should be able to answer:

- Name four possible precipitants in this history and say how you would test for each.
- The ascitic neutrophil count is 340 but the culture is sterile. What is the diagnosis and the treatment?
- Why is albumin given with the antibiotic?
- His serum-ascites albumin gradient is 6 g/L. What does that change?
- A colleague suggests restricting his protein. How do you respond?

Case 38 · Upper Gastrointestinal Bleeding

CLINICAL VIGNETTE

A **61-year-old man** with known cirrhosis is brought in after vomiting a large volume of fresh red blood twice at home. He has passed black tarry stools since yesterday. He feels faint on standing.

On arrival: he is pale and cool peripherally. Heart rate 122/min, blood pressure 88/54 mmHg, respiratory rate 24/min, capillary refill 4 seconds. He is alert but anxious. There are spider naevi and palmar erythema. Rectal examination confirms **melaena**.

Haemoglobin 74 g/L · urea 18 mmol/L with creatinine 92 µmol/L · INR 1.9 · platelets 62 × 10^9/L · albumin 26 g/L · bilirubin 54 µmol/L.

1. Resuscitate First

THE SEQUENCE

The order is resuscitation, then risk assessment, then endoscopy. A patient taken to the endoscopy suite while still shocked is a patient who may arrest there.

Two large-bore cannulae · bloods including **cross-match for 4 units** · balanced crystalloid while blood is prepared · continuous monitoring · senior help, and involvement of endoscopy, anaesthesia and critical care early.

- **A normal or near-normal haemoglobin in the first hours means nothing.** Haemoglobin concentration falls only as haemodilution occurs, so an acutely bleeding patient may have a normal value while losing litres. Judge the severity from the **pulse, blood pressure, perfusion and mental state**.
- **The urea is raised out of proportion to the creatinine** because blood in the gut is digested and absorbed as a protein load. A urea-to-creatinine disproportion in a patient with melaena is a useful confirmatory sign of an upper gastrointestinal source.

RESTRICTIVE TRANSFUSION

Transfuse to a target haemoglobin of 70–80 g/L, not to a normal value — higher thresholds are used in significant cardiovascular disease.

In variceal bleeding especially, **over-transfusion raises portal pressure, provokes rebleeding, and increases mortality.** The instinct to fill the patient up is a strong one and it is wrong.

2. Focused History

- **Distinguish the presentations:** fresh haematemesis suggests brisk bleeding; coffee-ground vomit suggests slower bleeding altered by acid; melaena indicates blood that has been in the gut for hours; and brisk upper bleeding can present as fresh rectal bleeding.
- **Preceding forceful retching before the haematemesis** suggests a Mallory–Weiss tear.
- **Drugs:** anti-inflammatory drugs, aspirin, antiplatelet agents, anticoagulants including direct oral anticoagulants, corticosteroids, and any bleeding disorder.
- Known varices, previous bleeding and banding; dyspepsia and previous ulcer; **weight loss and dysphagia** suggesting malignancy; alcohol history; comorbidity that limits physiological reserve.
- **Previous aortic graft surgery** — aorto-enteric fistula is rare, rapidly fatal, and is only ever diagnosed by the person who thought to ask.

3. Risk Assessment

- **The Glasgow–Blatchford score** is calculated before endoscopy from urea, haemoglobin, blood pressure, pulse, melaena, syncope, and hepatic or cardiac disease. **A score of 0–1 identifies patients who may safely be managed as outpatients** with early endoscopy — a genuinely useful discharge tool.
- **The Rockall score** is completed after endoscopy and predicts rebleeding and mortality.

4. Investigations

- Complete blood count, urea and electrolytes, liver function, **coagulation screen**, cross-match, lactate and venous gas, and an **electrocardiogram** — anaemia and hypotension precipitate demand ischaemia in an older patient.
- **Endoscopy within 24 hours** of presentation for all patients, and **within 12 hours in unstable patients or where variceal bleeding is suspected**, once resuscitation has achieved stability.
- An erect chest radiograph if perforation is a possibility; computed tomography angiography where bleeding continues and endoscopy has not identified or controlled the source.

5. Management

If variceal bleeding is suspected — start before endoscopy

- **Terlipressin**, to reduce portal pressure.
- **Prophylactic antibiotics — a third-generation cephalosporin — for every cirrhotic patient with gastrointestinal bleeding.** This reduces infection, rebleeding and **mortality**, and is one of the most strongly evidence-based interventions in the whole of gastroenterology. It is also one of the most frequently forgotten.
- **Endoscopic band ligation** for oesophageal varices; **cyanoacrylate injection** for gastric varices.
- **If bleeding is uncontrolled:** balloon tamponade as a **bridge only**, with the airway protected, followed by a transjugular intrahepatic portosystemic shunt. Early shunting is also considered in high-risk patients after initial control.
- **Afterwards:** a non-selective beta blocker together with a programme of repeated banding until the varices are eradicated.

If non-variceal bleeding

- **Endoscopic haemostasis using two modalities** — adrenaline injection alone is not adequate, and must be combined with clips or thermal coagulation.
- **High-dose proton pump inhibitor infusion after endoscopic haemostasis** of a high-risk ulcer. Routine treatment before endoscopy is not required.
- **Test for and eradicate *Helicobacter pylori*** in every ulcer bleed, and confirm eradication afterwards. Stop the anti-inflammatory drug.
- Rebleeding: repeat endoscopy, then interventional radiological embolisation, then surgery.

Coagulation and antithrombotic drugs

- Give platelets for a count below 50×10^9/L with active bleeding. Reverse warfarin with prothrombin complex concentrate and vitamin K; use the specific reversal agents for direct oral anticoagulants where available.
- **Do not routinely correct the INR with fresh frozen plasma in cirrhosis.** The INR does not reflect bleeding risk in liver disease, where both procoagulant and anticoagulant factors are reduced together, and plasma transfusion **raises portal pressure and can worsen variceal bleeding**.
- **Restart aspirin early** once haemostasis is secure where it was prescribed for secondary cardiovascular prevention — the risk of stopping it usually exceeds the risk of rebleeding. Discuss anticoagulation with the specialty that prescribed it rather than deciding alone.

6. Teaching Points and Viva Questions

- Resuscitate, then risk-assess, then endoscope. Never the other way round.
- The first haemoglobin does not tell you how much blood has been lost.
- Transfuse to 70–80 g/L. More is worse, particularly with varices.
- Antibiotics for every cirrhotic patient who bleeds — this one saves lives.
- A raised urea with a normal creatinine and melaena is an upper gastrointestinal bleed.
- Do not give plasma to correct the INR in cirrhosis.

Questions you should be able to answer:

- What are your first five actions, in order, for this man?
- Why is his urea 18 with a normal creatinine?
- Which two drugs would you give before he reaches the endoscopy suite, and why each?
- His INR is 1.9. Do you give fresh frozen plasma? Justify your answer.
- He rebleeds 12 hours after banding. What are the options in escalating order?

Case 39 · Inflammatory Bowel Disease

CLINICAL VIGNETTE

A **26-year-old man** describes four months of diarrhoea, now up to eight times a day with **blood and mucus**, with urgency and a constant feeling of incomplete emptying. **He is woken two or three times a night to open his bowels.** He has crampy lower abdominal pain relieved by defaecation and has lost 7 kg.

Over the past two weeks he has deteriorated: **twelve bloody stools a day**, fever and exhaustion.

On examination: temperature 38.2 °C, heart rate 116/min, blood pressure 104/64 mmHg. Pale and thin. The abdomen is distended and diffusely tender **without guarding or rebound**. Two aphthous ulcers in the mouth. Perianal inspection is normal.

Haemoglobin 92 g/L · white cells 15.2 × 10^9/L · platelets 480 · C-reactive protein 88 · albumin 26 g/L · potassium 3.1 mmol/L. Abdominal radiograph: **transverse colon 6.5 cm in diameter** with mucosal oedema and loss of haustration.

RECOGNISE THIS AS ACUTE SEVERE COLITIS — THE TRUELOVE AND WITTS CRITERIA

Six or more bloody stools a day, **plus any one** of: temperature above 37.8 °C · pulse above 90/min · haemoglobin below 105 g/L · erythrocyte sedimentation rate above 30.

This patient meets all of them. Acute severe colitis carries a real mortality, and the deaths come from delay — from treating it as an outpatient flare, from waiting to see whether steroids work, and from regarding colectomy as a failure rather than a treatment.

Admit. Involve a gastroenterologist and a colorectal surgeon on the day of admission, not when things deteriorate.

1. Ulcerative Colitis or Crohn Disease?

	Ulcerative colitis	Crohn disease
Distribution	Continuous from the rectum proximally; colon only	Patchy, with skip lesions, anywhere from mouth to anus — terminal ileum most often
Depth	Mucosal	Transmural
Blood and mucus	Characteristic	Less prominent
Perianal disease, fistula, stricture	Rare	Characteristic — and their presence effectively settles the diagnosis
Histology	Crypt abscesses, no granulomas	Non-caseating granulomas
Smoking	Protective — paradoxically	Harmful — worsens disease and increases recurrence after surgery
Surgery	Colectomy cures the colitis	Not curative; recurrence at the anastomosis is the rule

Note the smoking paradox and get it the right way round — it is a favourite examination question, and telling a patient with Crohn disease that smoking might help would be a serious error.

2. Focused History

- **The stool:** frequency, blood, mucus, urgency, tenesmus, incontinence — and **nocturnal diarrhoea, which is a marker of organic disease** and effectively excludes irritable bowel syndrome.
- Abdominal pain and its site; weight loss quantified; fever; fatigue; growth failure in a younger patient.

System	Extraintestinal manifestation
Joints	Peripheral arthritis; sacroiliitis and axial spondyloarthritis (Case 60)
Eyes	Uveitis, episcleritis — a painful red eye needs same-day ophthalmology
Skin and mouth	Erythema nodosum (Case 70), pyoderma gangrenosum — which must never be debrided, aphthous ulceration
Liver	Primary sclerosing cholangitis — cholestatic liver tests and pruritus, more often with ulcerative colitis, and it raises colorectal and cholangiocarcinoma risk
Blood and bone	Iron, B12 and folate deficiency; a markedly increased venous thromboembolism risk; osteoporosis

WHAT MUST BE EXCLUDED BEFORE YOU IMMUNOSUPPRESS

Send stool for culture, ova and parasites, and *Clostridioides difficile* toxin in every flare and every admission. Infection both mimics a flare and complicates one, and immunosuppressing an infected colon is dangerous.

And in this region, intestinal tuberculosis mimics ileocaecal Crohn disease almost exactly — same site, same imaging appearance, same granulomas on biopsy, same weight loss and night sweats. **Giving an anti-tumour-necrosis-factor agent to a patient with undiagnosed intestinal tuberculosis can produce disseminated disease.**

So before immunosuppression: **tuberculin or interferon-gamma release assay, chest radiograph, and tissue examined specifically for acid-fast bacilli and caseation** — plus hepatitis B and C, human immunodeficiency virus, varicella status, and thiopurine metaboliser genotype.

3. Physical Examination

- Vital signs, hydration and nutritional state; pallor; clubbing.
- **Abdomen: distension, tenderness, a mass, and above all the presence or absence of peritonism** — guarding and rebound in this context mean perforation and a surgeon.
- **Perianal inspection and digital rectal examination in every patient** — fistulae, fissures, abscesses and skin tags point firmly to Crohn disease and are missed if the patient is not examined.
- Mouth, eyes, joints and skin, as in the table above.

4. Investigations

- Complete blood count, C-reactive protein, albumin, urea and electrolytes (**potassium**), liver function, iron studies, B12, folate and vitamin D.
- **Faecal calprotectin** to separate inflammatory from functional disease in the outpatient setting — not needed here, where the diagnosis is not in doubt.
- **Abdominal radiograph in acute severe colitis:** colonic dilatation, mucosal islands, thumbprinting and loss of haustration. **A transverse colon diameter above 5.5 cm with systemic toxicity is toxic megacolon.**
- **Flexible sigmoidoscopy without bowel preparation, with biopsies**, to confirm the diagnosis and to **exclude cytomegalovirus colitis**. **Full colonoscopy is contraindicated in acute severe colitis** because of the perforation risk.

- When stable: **ileocolonoscopy with intubation of the terminal ileum and multiple biopsies**; magnetic resonance enterography or capsule endoscopy for small bowel Crohn disease; **magnetic resonance imaging of the pelvis for perianal disease**.

5. Managing Acute Severe Colitis

- **Intravenous corticosteroid** — hydrocortisone or methylprednisolone.
- Fluid resuscitation, **potassium replacement**, transfusion as needed, and nutritional support.

TWO THINGS THAT ARE ROUTINELY GOT WRONG

Venous thromboembolism prophylaxis, despite the rectal bleeding.

Active inflammatory bowel disease is a strongly prothrombotic state, and these patients die of pulmonary embolism. The bleeding is from an inflamed mucosa, not from a coagulopathy, and it is **not** a contraindication to prophylactic anticoagulation. Omitting it is one of the commonest errors on the ward.

And avoid antidiarrhoeal agents, opioids and anticholinergics entirely — all of them reduce colonic motility and can precipitate toxic megacolon in exactly this patient.

- **Monitor daily:** examination, a stool frequency and blood chart, and an abdominal radiograph while the colon is dilated. **Joint medical and surgical review from day one.**

THE DAY-THREE DECISION

On the third day of intravenous steroid, count the stools and check the C-reactive protein.

More than eight stools a day, or three to eight stools with a C-reactive protein above 45, predicts that steroids will fail in the great majority of patients.

At that point escalate — rescue therapy with infliximab or ciclosporin, or colectomy. Do not give steroids a further week to work. Delay past this point increases the risk of perforation, of emergency rather than elective surgery, and of death.

Colectomy is a treatment, not a defeat, and in ulcerative colitis it cures the colitis. Say so plainly to the patient early, so that the conversation is not being had for the first time in an emergency.

- **Toxic megacolon or perforation: urgent colectomy.**

6. Longer-Term Management

	Approach
Ulcerative colitis	Mesalazine, oral with topical therapy, for induction and maintenance of mild to moderate disease; topical treatment alone for proctitis; corticosteroids for flares only; then thiopurines, anti-tumour-necrosis-factor agents, vedolizumab, ustekinumab or a Janus kinase inhibitor. Colectomy is curative.
Crohn disease	Exclusive enteral nutrition (particularly in children) or corticosteroids for induction; then thiopurines, methotrexate, or biologic therapy. Treat to a target of mucosal healing rather than symptom control alone. Smoking cessation is among the most effective interventions available. Surgery for stricture, fistula or abscess, with combined medical and surgical management of perianal disease.

THE PRESCRIPTION TO STOP REPEATING

Corticosteroids do not maintain remission, and they cause harm.

A patient who has needed two or more courses in a year, or who cannot come off them, is **steroid-dependent** — and that is an indication to escalate to a steroid-sparing agent, not to prescribe another reducing course.

Every patient on repeated steroids needs bone protection and a documented plan for getting off them.

- **Colorectal cancer surveillance colonoscopy from 8 to 10 years after diagnosis** in colitis, at intervals set by extent, inflammation and family history — **and earlier and more frequently in primary sclerosing cholangitis**.
- Iron replacement, vaccination before immunosuppression, bone density assessment, **fertility and pregnancy planning** (most agents are compatible with pregnancy; **methotrexate is teratogenic and must be stopped well beforehand in both sexes**), smoking cessation, nutritional support, and access to psychological support and a specialist nurse.

7. Teaching Points and Viva Questions

- Nocturnal diarrhoea is organic disease. Ask about it.
- Examine the perineum — fistulae and tags settle the diagnosis.
- Send stool for *Clostridioides difficile* in every flare, and exclude tuberculosis before immunosuppressing.
- Give thromboprophylaxis despite the bleeding, and never give an antidiarrhoeal.
- Make the day-three decision on the third day.
- Steroids are not maintenance therapy; steroid dependence means escalate.
- Smoking protects in ulcerative colitis and harms in Crohn disease — know which way round.

Questions you should be able to answer:

- Apply the Truelove and Witts criteria to this patient.
- Why does he need heparin when he is passing twelve bloody stools a day?
- On day three he has nine stools and a C-reactive protein of 60. What are the options and what is the risk of waiting?
- A 24-year-old has terminal ileal thickening, weight loss and granulomas on biopsy. What must be excluded before you start infliximab, and why?
- He asks whether giving up smoking will help his ulcerative colitis. How do you answer?

Case 40 · Hepatocellular Carcinoma

CLINICAL VIGNETTE

A **58-year-old man** with hepatitis B-related cirrhosis, previously stable on antiviral therapy, has had three months of right upper quadrant discomfort and 8 kg of weight loss. **His ascites has become refractory to diuretics** and he has developed mild confusion and reversal of his sleep pattern for the first time.

He was enrolled in a surveillance programme but **did not attend his last two ultrasound appointments**.

On examination: cachectic and jaundiced, with spider naevi. The liver is enlarged, **hard and irregular, with an audible bruit over it**. There is tense ascites and splenomegaly. Asterixis is present.

Alpha-fetoprotein 840 µg/L. Quadruple-phase computed tomography: a **6 cm lesion in the right lobe with arterial phase enhancement and delayed washout**, with **tumour thrombus in the right portal vein**. Child–Pugh class B.

THE PRESENTATION TO RECOGNISE

A previously stable patient with cirrhosis who decompensates has a new problem, and hepatocellular carcinoma is near the top of the list.

New or refractory ascites · new encephalopathy · a first variceal bleed · unexplained weight loss · new abdominal pain — any of these in a compensated cirrhotic patient should prompt imaging and an alpha-fetoprotein, alongside the search for infection and the other precipitants in Case 37.

Portal vein thrombosis is part of the same picture, and it may be bland or tumour thrombus — which the imaging must distinguish, because it changes the stage entirely.

1. Surveillance — Which Is Really the Whole Case

- **Hepatocellular carcinoma arises almost entirely within a known, identifiable, at-risk population.** That makes it one of the very few cancers where early detection is genuinely achievable — and it is usually found late because surveillance was not offered, not done, or not attended.
- **Six-monthly ultrasound, with or without alpha-fetoprotein, in every patient with cirrhosis** — and in selected patients with chronic hepatitis B **without** cirrhosis, on the basis of age, family history, viral load and origin.
- **Chase the non-attenders.** This patient missed two appointments and now has a 6 cm tumour with vascular invasion instead of a 2 cm one that could have been ablated or transplanted. Recall systems, reminders and explaining to the patient *why* the scan matters are part of the clinical work, not administration.

Risk factor	Note
Chronic hepatitis B	Can cause hepatocellular carcinoma without cirrhosis, which is why non-cirrhotic surveillance exists. Antiviral therapy reduces but does not abolish the risk (Case 36).
Chronic hepatitis C	Risk persists after viral cure once cirrhosis is established — so surveillance continues after successful antiviral treatment.
Alcohol-related cirrhosis	Compounded by continued drinking.
Metabolic dysfunction-associated steatotic liver disease	A rapidly rising cause, and one that may produce cancer with relatively little fibrosis.
Haemochromatosis, primary biliary cholangitis, alpha-1 antitrypsin deficiency	Established risk factors.
Aflatoxin exposure	From improperly stored grains and nuts; synergistic with hepatitis B.

2. Focused History and Examination

- The decompensation features above; right upper quadrant or shoulder-tip pain; early satiety; fever; and rarely **paraneoplastic hypoglycaemia, hypercalcaemia, erythrocytosis or watery diarrhoea**.
- Sudden severe abdominal pain with hypotension suggests **tumour rupture with haemoperitoneum** — a surgical and radiological emergency.
- Establish the cause and stage of the liver disease, previous decompensation, alcohol use, antiviral therapy and adherence, and **performance status and comorbidity**, which will constrain every treatment option.
- **Examination:** cachexia, jaundice, and a **hard, irregular, sometimes tender liver with a bruit or friction rub over it**; ascites; encephalopathy; signs of portal hypertension; and a left supraclavicular node.

3. Investigations

THE DIAGNOSTIC RULE THAT IS UNLIKE OTHER CANCERS

In a cirrhotic liver, hepatocellular carcinoma is diagnosed on imaging, not on histology.

A lesion showing **arterial phase hyperenhancement with washout in the portal venous or delayed phase** on quadruple-phase computed tomography or contrast-enhanced magnetic resonance imaging is diagnostic in a patient with cirrhosis.

Biopsy is therefore usually unnecessary, and it carries risks of bleeding and needle-track seeding. This is unusual among cancers and it surprises students, who reasonably expect tissue before a cancer diagnosis. Biopsy is reserved for atypical imaging or a non-cirrhotic liver.

- **Alpha-fetoprotein is neither sensitive nor specific enough to diagnose or to exclude the disease.** It can be normal in a large tumour and raised in active hepatitis or cirrhosis without cancer. Use it as an adjunct and for trend, never as the deciding test.
- **Staging must capture three things at once:** the **tumour** (size, number, vascular invasion, extrahepatic spread), the **liver** (Child–Pugh and MELD), and the **patient** (performance status). The Barcelona Clinic Liver Cancer system integrates all three — **because a small resectable tumour in a decompensated liver is not a surgical problem, and a large tumour in a well-preserved liver may still be treatable.**

- Endoscopy for varices; hepatitis serology and viral load; renal function; and chest and bone imaging where indicated.

4. Management by Stage

Stage	Treatment
Very early and early — single lesion or up to three small lesions, preserved liver function, good performance status	Resection where function is preserved and there is no significant portal hypertension · ablation (radiofrequency or microwave) for small lesions · liver transplantation, which uniquely treats both the tumour and the underlying cirrhosis, in patients meeting the Milan criteria
Intermediate — multinodular, preserved function	Transarterial chemoembolisation, sometimes repeated, with reassessment
Advanced — vascular invasion or extrahepatic spread, preserved function	Systemic therapy: immune checkpoint inhibitor combinations are now first line — atezolizumab with bevacizumab, or durvalumab with tremelimumab — with tyrosine kinase inhibitors such as sorafenib or lenvatinib as alternatives. This patient, with portal vein tumour thrombus, sits here.
Terminal — poor liver function or poor performance status	Best supportive and palliative care, with symptom control and honest discussion

- **Treat the underlying liver disease throughout.** Continuing antiviral therapy for hepatitis B reduces recurrence and improves survival; alcohol abstinence matters; and the complications of cirrhosis are managed as in Case 37 — including large-volume paracentesis with albumin, and antibiotic prophylaxis after spontaneous bacterial peritonitis.
- **Multidisciplinary team management**, with hepatology, oncology, radiology, surgery and transplant input; and **early palliative care involvement**, as in Case 7.
- An honest conversation about prognosis, and advance care planning.

PREVENTION

Of everything in this case, the interventions that save the most lives happen years before the tumour appears: **Hepatitis B vaccination — which prevents a common cancer** · antiviral treatment of chronic hepatitis B and cure of hepatitis C · alcohol reduction · management of obesity, diabetes and metabolic liver disease · and **safe grain and nut storage** to limit aflatoxin exposure.

It is worth saying to students explicitly that the hepatitis B vaccine is an anti-cancer vaccine.

5. Teaching Points and Viva Questions

- A stable cirrhotic who decompensates needs imaging and an alpha-fetoprotein.
- Six-monthly ultrasound in cirrhosis — and chase the patients who do not attend.
- In cirrhosis the diagnosis is radiological; biopsy is usually unnecessary and carries risk.
- Alpha-fetoprotein neither diagnoses nor excludes.
- Treatment depends on the tumour, the liver and the patient together — not on the tumour alone.
- Transplantation treats both diseases at once.

- Surveillance continues after hepatitis C is cured, if cirrhosis is established.

Questions you should be able to answer:

- Which features of his presentation should have prompted imaging weeks earlier?
- Why is a biopsy not required to make this diagnosis?
- His alpha-fetoprotein had been normal six months ago. Does that reassure you in retrospect?
- What does the portal vein tumour thrombus do to his treatment options?
- A patient with hepatitis C cirrhosis achieves a viral cure. Do you stop surveillance?