The Nephrology Block

Acute kidney injury, chronic kidney disease, acid–base disorders, hyponatraemia, urinary tract infection and glomerulonephritis.

Cases 28–33 · 8,592 words

This block covers the renal teaching of both internal medicine courses. The **first course** supplies cases 28 and 31; the **second course** supplies cases 32 and 33.

Case	Lecture it serves
System opener: the renal history and examination	History taking in nephrology
Case 28 — Acute kidney injury	Acute kidney injury; acute renal failure seminar
Case 29 — Chronic kidney disease	Chronic kidney disease; approach to the patient with chronic kidney disease
Case 30 — Acid–base disorders	Acid–base disorders
Case 31 — Hyponatraemia	Fluid and electrolyte disorders
Case 32 — Urinary tract infection	Urinary tract infections
Case 33 — Glomerulonephritis	Glomerulonephritis

Hyperkalaemia is taught within the acute kidney injury case, where students will actually meet it, and hypernatraemia within the hyponatraemia case. **Nephrotic syndrome** is covered as Seminar 2 in Part Two, where the approach to generalised oedema can be set out in full.

System Opener · The Renal History and Examination

Kidneys announce themselves late and quietly. Half of renal medicine at the bedside is one skill — **deciding whether the patient is volume-depleted, euvolaemic or overloaded** — and the other half is remembering to look at the urine.

The history

Ask about the urine, in detail

- **Volume.** Oliguria, and specifically **anuria** — complete absence of urine points to obstruction, a vascular catastrophe or severe glomerular disease, and almost never to simple dehydration.
- **Appearance.** Frothy urine suggests heavy proteinuria; red or cola-coloured urine suggests glomerular bleeding; blood only at the start or end of the stream suggests a urethral or bladder source.

- **Nocturia** — an early and underrated symptom of both concentrating failure and obstruction.
- **Obstructive symptoms:** hesitancy, poor stream, terminal dribbling, incomplete emptying. In an older man these three questions may be the whole diagnosis.

Ask about the consequences

- **Oedema, and where it is worst on waking.** Periorbital puffiness in the morning suggests renal disease; ankle swelling worst in the evening suggests cardiac or hypoalbuminaemic causes.
- **Uraemic symptoms:** nausea, anorexia, a metallic taste, hiccups, itch, restless legs, cognitive slowing and easy bruising.

Ask about the causes

- **Drugs and exposures:** non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors and receptor blockers, diuretics, aminoglycosides, iodinated contrast, proton pump inhibitors, chemotherapy, and **herbal or traditional remedies**, which patients seldom classify as medicines.
- **Volume loss:** vomiting, diarrhoea, burns, and **heat exposure with inadequate intake**, which in this climate is a common and entirely preventable cause.
- **Systemic disease:** rash, arthralgia, oral ulceration, sinusitis, **haemoptysis** (the pulmonary–renal syndromes), fever and weight loss.
- **Background:** duration of diabetes and hypertension, stones, childhood urinary infections, obstetric history, family history of polycystic kidney disease or deafness, and consanguinity.

> **THE SINGLE MOST USEFUL PIECE OF INFORMATION**
>
> Before you can call anything "acute", you need to know where the patient started. **Find the previous creatinine** — from old records, another hospital, a pre-operative check, an insurance medical.
>
> A creatinine of 280 µmol/L means something entirely different in a patient whose baseline was 90 than in one whose baseline was 250. Without the baseline you cannot distinguish acute kidney injury from chronic kidney disease, and the management of the two diverges immediately.

The examination

Volume status — the central skill

	Hypovolaemic	Euvolaemic	Hypervolaemic
Jugular venous pressure	Not visible	Normal	Raised
Blood pressure	Low, with a postural drop	Normal	Often raised
Mucous membranes, skin	Dry, reduced turgor	Normal	Normal or oedematous
Peripheries	Cool, delayed capillary refill	Warm	Oedema — ankles if ambulant, sacrum if bedbound
Chest	Clear	Clear	Basal crackles, effusions
Weight and urine output	Falling weight, low output	Stable	Rising weight

Then the rest

- **General:** pallor, sallow uraemic complexion, scratch marks, bruising, uraemic fetor, **asterixis**, and a **pericardial rub** — uraemic pericarditis is an emergency and an indication for dialysis.
- **Arms:** an arteriovenous fistula, felt for a thrill and listened to for a bruit; scars from previous dialysis lines; leuconychia.
- **Abdomen:** ballotable kidneys of polycystic disease, a **transplanted kidney in the iliac fossa** beneath a hockey-stick scar, a peritoneal dialysis catheter, renal bruits, and — always — a **palpable bladder**.
- **Never omit:** blood pressure, **urine dipstick**, and fundoscopy.

THE THREE BEDSIDE STEPS IN EVERY CASE OF ACUTE KIDNEY INJURY

Dipstick the urine. Feel or scan the bladder. Assess the volume status.

Each takes under a minute, none requires the laboratory, and together they identify or exclude the majority of causes. In practice, all three are frequently skipped in favour of waiting for a creatinine that has already been reported.

Case 28 · Acute Kidney Injury

CLINICAL VIGNETTE

A **76-year-old man** is brought in after four days of vomiting and profuse diarrhoea that began after a family gathering. He has been unable to keep fluids down and, for the past 24 hours, has passed only a small amount of dark urine.

He takes ramipril for hypertension, indometacin for knee pain that he buys himself, and gliclazide for type 2 diabetes. He has longstanding prostatic symptoms.

On examination: he is dry with reduced skin turgor. Blood pressure 104/62 mmHg lying, falling to 82/54 mmHg on standing. Heart rate 108/min. The jugular venous pressure is not visible. **The bladder is not palpable, and a bedside scan shows 40 mL.** Urine dipstick is negative for blood, protein, leucocytes and nitrites.

Creatinine 342 µmol/L (baseline 96 eight months ago) · urea 28 mmol/L · potassium 6.4 mmol/L · bicarbonate 16 mmol/L.

1. Stage It, Then Classify It

Acute kidney injury is present if any one of these is met: a rise in creatinine of 26.5 µmol/L or more within 48 hours; a rise to 1.5 times baseline or more within 7 days; or a urine output below 0.5 mL/kg/hour for 6 hours.

Stage	Creatinine	Urine output
1	1.5–1.9 × baseline, or a rise of 26.5 µmol/L	Below 0.5 mL/kg/h for 6–12 hours
2	2.0–2.9 × baseline	Below 0.5 mL/kg/h for 12 hours or more
3	3.0 × baseline or more, or creatinine above 354 µmol/L, or the need for replacement therapy	Below 0.3 mL/kg/h for 24 hours, or anuria for 12 hours

This patient is **stage 3**. But staging is not diagnosis. **"Acute kidney injury" is a syndrome, not an answer** — the task is to say which of the three mechanisms is responsible, because the treatment of each is entirely different.

Mechanism	Causes	What points to it
Pre-renal — the kidney is underperfused but structurally intact	Volume depletion, sepsis, heart failure, cirrhosis, renal artery disease, and drugs that disable autoregulation	Hypovolaemia or hypotension, bland urinalysis, concentrated urine, rapid response to volume replacement
Intrinsic — the kidney itself is damaged	Acute tubular necrosis (ischaemic or toxic); acute interstitial nephritis; glomerulonephritis; vascular disease and thrombotic microangiopathy	Abnormal urinalysis, casts on microscopy, systemic features, no response to volume
Post-renal — the urine cannot get out	Prostatic disease, stones, pelvic or retroperitoneal malignancy, retroperitoneal fibrosis, a blocked catheter	Anuria or fluctuating output, palpable bladder, hydronephrosis on ultrasound. Must obstruct both kidneys, or a single functioning one

2. Focused History

- Quantify the losses and the intake, and establish the urine output — including whether anuria was complete.

- **The drug history is the diagnosis in a large proportion of cases.** This man is taking the classical combination.

> **THE TRIPLE WHAMMY**
> An **angiotensin-converting enzyme inhibitor** dilates the efferent arteriole. A **non-steroidal anti-inflammatory drug** constricts the afferent arteriole. A **diuretic**, or any other cause of volume depletion, removes the perfusion pressure altogether.
> Each alone is usually tolerated. Together, on a day when the patient stops drinking, they dismantle glomerular autoregulation completely. **Ask about drugs bought without prescription**, which is how the anti-inflammatory usually enters the picture.

- **Sepsis:** fever, rigors, localising symptoms. Sepsis is the commonest cause of acute kidney injury in hospital.
- **Obstruction:** prostatic symptoms, known malignancy, previous pelvic surgery or radiotherapy, stones.
- **Intrinsic disease:** rash, arthralgia, haemoptysis, sinusitis, fever with eosinophilia after a new drug, and **muscle pain with dark urine** suggesting rhabdomyolysis.
- Recent iodinated contrast, and any recent hospital admission.

3. Physical Examination

- **Volume status**, using the table in the opener. This decides the first hour.
- **Palpate and scan the bladder in every patient.** Chronic retention is common, easily missed, and reversed by a catheter — the cheapest cure in medicine.
- Assess for sepsis and its source; examine for rash, joints and signs of systemic vasculitis; check for a pericardial rub and for asterixis.
- Perform a rectal examination where prostatic obstruction is suspected, and abdominal examination for masses.

4. Investigations

The urine tells you the mechanism

Urinalysis	What it suggests
Bland — no blood, no protein	Pre-renal disease or acute tubular necrosis
Blood and protein together	Glomerulonephritis — this combination demands urgent nephrology discussion
Leucocytes and nitrites	Urinary tract infection
Leucocytes without infection, with eosinophilia and a recent new drug	Acute interstitial nephritis
Microscopy: red cell casts	Glomerulonephritis
Microscopy: muddy brown granular casts	Acute tubular necrosis

- **Blood:** urea, electrolytes and creatinine, bicarbonate, calcium and phosphate, **creatine kinase** if rhabdomyolysis is possible, liver function, complete blood count with film (fragments suggest thrombotic microangiopathy), C-reactive protein, blood cultures, venous gas and lactate.
- **If intrinsic renal disease is suspected:** antinuclear and antineutrophil cytoplasmic antibodies, anti-glomerular basement membrane antibody, complement, immunoglobulins with protein electrophoresis and serum free light chains, hepatitis B and C, and human immunodeficiency virus serology.
- **Urine protein-to-creatinine ratio** to quantify proteinuria.
- **Renal ultrasound within 24 hours** — immediately if obstruction is suspected or no cause is apparent. It looks for hydronephrosis, and also reports kidney size and cortical thickness: **small echogenic kidneys mean the disease is chronic**, whatever the history says.
- **Electrocardiogram** now, because of the potassium.
- **Renal biopsy** where pre-renal and post-renal causes are excluded and the intrinsic cause is unclear — a nephrology decision, but one students should know exists.

5. Management

EMERGENCY: HYPERKALAEMIA

Treat the potassium before anything else if it is 6.5 mmol/L or above, or if there are electrocardiographic changes at any level.

Electrocardiogram sequence: tall tented T waves → flattened or absent P waves with a prolonged PR interval → broadening QRS → sine wave → arrest.

1. Calcium gluconate 10%, 10 mL intravenously — stabilises the myocardium within minutes. It does **not** lower the potassium, and it must be repeated if changes persist.

2. Insulin with glucose — 10 units of soluble insulin in 25 g of glucose, which shifts potassium into cells over 15–30 minutes. **Monitor for rebound hypoglycaemia for several hours.**

3. Nebulised salbutamol, 10–20 mg, as an additional shifting agent.

4. Then remove potassium from the body: stop all contributing drugs, treat the cause, give a potassium binder, and refer for dialysis if the level is refractory.

Sodium bicarbonate is not part of routine treatment.

Then treat the kidney injury

- **Restore perfusion.** In a hypovolaemic patient give balanced crystalloid and reassess repeatedly — clinically, not by a single number. **Do not give unmeasured fluid to an anuric, overloaded patient**; that produces pulmonary oedema without producing urine.
- **Stop the nephrotoxic drugs:** the anti-inflammatory permanently, the angiotensin-converting enzyme inhibitor temporarily. **Review every drug for renal clearance** — metformin, sulfonylureas, direct oral anticoagulants, opioids, and many antibiotics need adjustment or suspension.
- **Relieve obstruction** — catheterise for bladder outflow obstruction, and arrange nephrostomy or stenting for upper tract obstruction. Anticipate a **post-obstructive diuresis** and replace the losses.
- **Treat sepsis** with source control and appropriate antibiotics at renally adjusted doses.

- **Monitor:** hourly urine output, daily weight, daily electrolytes, and a fluid balance chart that someone actually completes.
- Avoid further contrast where possible, and avoid nephrotoxic antibiotics where an alternative exists.

Urgent dialysis — the indications	Detail
A cidosis	Severe metabolic acidosis refractory to medical treatment
E lectrolytes	Hyperkalaemia refractory to medical treatment
I ntoxication	Lithium, salicylate, toxic alcohols, metformin-associated lactic acidosis
O verload	Pulmonary oedema unresponsive to diuretics
U raemia	Uraemic pericarditis or encephalopathy

After the episode

- **An episode of acute kidney injury predicts chronic kidney disease.** Document it clearly in the discharge summary, arrange follow-up of the creatinine, and specify **when and how the suspended drugs should be restarted, and by whom**.
- Give **sick-day rules**: patients taking angiotensin-converting enzyme inhibitors or receptor blockers, diuretics, metformin, sodium–glucose co-transporter 2 inhibitors or anti-inflammatory drugs should hold them during vomiting, diarrhoea or fever, and seek advice.

6. Teaching Points and Viva Questions

- Dipstick, bladder, volume status. Three bedside steps, one minute, most of the diagnosis.
- Find the baseline creatinine before you call anything acute.
- Blood and protein on the dipstick changes the whole problem — that is glomerular disease and it needs a nephrologist today.
- The commonest reversible causes are a drug you can stop and a bladder you can drain.
- A patient can die of hyperkalaemia while the team is discussing the creatinine.

Questions you should be able to answer:

- Classify this man's injury and justify it from the findings given.
- Explain, at the level of the arteriole, how his three drugs interacted.
- His potassium is 6.4 with tented T waves. Give your first three actions in order, and say what each achieves.
- The urine now shows blood and protein. How does your plan change?
- When would you refer for urgent dialysis?

Case 29 · Chronic Kidney Disease

CLINICAL VIGNETTE

A **62-year-old woman** with type 2 diabetes of 15 years and longstanding hypertension is referred from the diabetes clinic. She has been increasingly tired for a year, itches at night, gets up three times to pass urine, and has noticed her ankles swelling.

Estimated glomerular filtration rate 24 mL/min/1.73 m² (48 two years ago) · **urine albumin-to-creatinine ratio 180 mg/mmol** · haemoglobin 94 g/L · phosphate raised · corrected calcium low-normal · parathyroid hormone markedly raised · bicarbonate 19 mmol/L.

Ultrasound shows two small, echogenic kidneys with thinned cortex and no hydronephrosis.

1. Staging — Two Axes, Not One

Students learn the estimated filtration rate and stop there. **Albuminuria carries at least as much prognostic weight**, and the two together define risk far better than either alone.

Filtration rate (mL/min/1.73 m²)	Albuminuria (mg/mmol)
G1 90 or above · G2 60–89	A1 below 3 — normal to mildly increased
G3a 45–59 · G3b 30–44	A2 3–30 — moderately increased
G4 15–29 · G5 below 15	A3 above 30 — severely increased

This patient is **G4 A3** — among the highest risk categories for both progression to end-stage disease and for cardiovascular death. Chronic kidney disease also requires that the abnormality has been present for **more than three months**.

Is it chronic, or acute, or both?

Favours chronic	But be careful
Previous abnormal results over months or years	A single old result may itself have been an acute episode
Small, echogenic kidneys with thinned cortex	Kidneys stay large in diabetic nephropathy, polycystic disease, amyloidosis, myeloma and human immunodeficiency virus nephropathy
Normocytic anaemia, raised phosphate with raised parathyroid hormone, renal bone disease	Anaemia and hyperphosphataemia can develop within weeks in severe acute injury
Absence of any acute precipitant	Chronic disease very commonly presents with acute-on-chronic deterioration

2. Focused History

- **The trajectory.** Collect every previous creatinine you can find and plot them. A gradual decline over years, a sudden step, or a recent acceleration each mean something different.
- **Establish the cause.** Duration and control of diabetes and hypertension; previous proteinuria or haematuria; recurrent childhood urinary infection or reflux; stones; obstetric history; family history of polycystic disease or of deafness with renal failure; long-term drug and analgesic use, including traditional remedies.

- **Symptoms of complications:** fatigue and breathlessness (anaemia), bone and joint pain, itch, cramps and restless legs, nausea and anorexia, and cognitive change.
- **Cardiovascular history**, since that is what is most likely to kill her.
- **Function, support and preferences** — because planning for renal replacement, or for conservative care, has to begin long before it is needed.

3. Physical Examination

- Blood pressure, including standing; volume status; weight.
- Pallor, scratch marks, bruising, sallow complexion; **asterixis and a pericardial rub** in advanced disease.
- Signs of the underlying cause: diabetic retinopathy on fundoscopy, ballotable kidneys, bruits.
- **Diabetic foot examination** and peripheral pulses. Assess the forearm veins — see below.

4. Investigations

- Urea, electrolytes, creatinine and estimated filtration rate, with the **trend** rather than the single value; bicarbonate.
- **Urine albumin-to-creatinine ratio** on an early morning sample, with urinalysis and microscopy. Blood and protein together still means glomerular disease and still needs investigation, even in a known diabetic.
- **Ultrasound** for size, symmetry, cortical thickness, cysts and obstruction.
- **Complete blood count with full haematinics — iron studies, ferritin, transferrin saturation, vitamin B12 and folate.** Do not label anaemia as renal until iron deficiency has been excluded and corrected.
- **Bone profile:** calcium, phosphate, alkaline phosphatase, parathyroid hormone and 25-hydroxyvitamin D.
- Lipids, glycated haemoglobin, and where the cause is unclear an immunological and myeloma screen. Hepatitis B and C and human immunodeficiency virus serology when replacement therapy is anticipated.

5. Management

Management has four separate aims. Students usually remember the third and forget the first.

Aim 1 — Reduce cardiovascular risk

- **Most patients with chronic kidney disease die of cardiovascular disease before they ever reach dialysis.** Blood pressure control, statin therapy, smoking cessation and glycaemic control are therefore not peripheral to renal care; they are the largest part of it.

Aim 2 — Slow progression

- **Blood pressure** below 130/80 mmHg where albuminuria is present.

- **An angiotensin-converting enzyme inhibitor or receptor blocker**, titrated to the maximum tolerated dose, in anyone with significant albuminuria.
- **A sodium–glucose co-transporter 2 inhibitor**, which now has clear evidence for slowing progression in albuminuric chronic kidney disease, in diabetic and non-diabetic patients alike.
- Glycaemic control; consideration of a non-steroidal mineralocorticoid receptor antagonist in diabetic kidney disease; dietary sodium restriction; avoidance of nephrotoxins; treatment of obesity.

DO NOT STOP THE DRUG FOR THE EXPECTED RISE

When you start or increase one of these drugs, **the creatinine will rise and the potassium may rise**. That is the expected haemodynamic consequence of reducing intraglomerular pressure — which is precisely the mechanism by which the drug protects the kidney.

Accept a creatinine rise of up to about 30% and a modest potassium rise, and continue. Recheck at one to two weeks. Stop only if the rise exceeds that, or if potassium cannot be controlled.

Stopping these drugs at the first small rise is one of the commonest errors in chronic kidney disease, and it deprives the patient of the single most effective renal protection available.

Aim 3 — Treat the complications

Complication	Management
Anaemia	Correct iron deficiency first, usually intravenously in advanced disease. Then erythropoiesis-stimulating agents, targeting a haemoglobin of roughly 100–120 g/L — deliberately not normal, because normalising it increases stroke and thrombotic risk.
Mineral and bone disorder	Dietary phosphate restriction and phosphate binders taken with food; activated vitamin D; control of parathyroid hormone. Treat the phosphate and the parathyroid hormone rather than chasing the calcium.
Metabolic acidosis	Oral sodium bicarbonate when the serum bicarbonate falls below about 22 mmol/L — it reduces muscle catabolism and may slow progression.
Fluid overload	Dietary salt restriction and a loop diuretic, which needs higher doses as filtration falls.
Hyperkalaemia	Dietary advice and a potassium binder — used specifically so that renin–angiotensin blockade can be continued.
Other	Vaccination, including hepatitis B early; avoidance of non-steroidal anti-inflammatory drugs; medication review at every visit.

Aim 4 — Prepare for what comes next

- **Refer to nephrology** when the filtration rate falls below 30, when decline is rapid, when albuminuria is heavy, when there is unexplained haematuria with proteinuria, or when the cause is unclear.
- Discuss the options honestly and early: haemodialysis, peritoneal dialysis, **transplantation — including pre-emptive transplantation before dialysis is ever needed** — and conservative kidney management, which is a legitimate and sometimes better choice in a frail patient.
- **Create arteriovenous access around six months before dialysis is anticipated**, since a fistula needs time to mature.

SAVE THE VEINS

From the moment dialysis becomes a possibility, **the veins of the non-dominant forearm are the patient's future lifeline.** No cannulas, no venepuncture, no blood pressure cuffs, no peripherally inserted central catheters in that arm. Put a sign above the bed. A fistula that cannot be created because the veins were used for routine blood tests is an avoidable harm, and it is usually caused by a junior doctor who did not know.

6. Teaching Points and Viva Questions

- Stage on two axes. Albuminuria predicts outcome as powerfully as the filtration rate.
- Small echogenic kidneys mean chronic disease — but diabetic, polycystic and infiltrated kidneys stay large.
- Check the iron before you call it renal anaemia, and do not aim for a normal haemoglobin.
- A creatinine rise after starting an angiotensin blocker is the drug working, not the drug failing.
- Protect the forearm veins from the day dialysis becomes conceivable.

Questions you should be able to answer:

- Stage this patient and explain what each axis contributes to her prognosis.
- Her creatinine rises 22% two weeks after you increase the ramipril. What do you do?
- Why is the haemoglobin target below the normal range?
- Which features would make you doubt that this is simply diabetic nephropathy?
- She asks whether she must have dialysis. What options do you set out?

Case 30 · Acid–Base Disorders

CLINICAL VIGNETTE

A **24-year-old woman** presents after five days of persistent vomiting. She has a long history of dyspepsia and now vomits undigested food several hours after eating. She feels weak, has cramps in her hands, and describes tingling around her mouth.

On examination: dry mucous membranes, heart rate 112/min, blood pressure 98/60 mmHg with a postural drop.

First arterial blood gas and biochemistry: pH 7.51 · carbon dioxide 6.2 kPa · bicarbonate 38 mmol/L · sodium 133 · chloride 88 · potassium 2.6 mmol/L · **urine chloride 8 mmol/L**.

Thirty-six hours later she aspirates and becomes septic. **Repeat gas:** pH 7.33 · carbon dioxide 4.4 kPa · bicarbonate 22 mmol/L · sodium 136 · chloride 92 · lactate 5.1 mmol/L.

1. The Five-Step Method

Apply the same five steps to every gas, in the same order, every time. The method matters more than the memorised lists, because it will get you through gases you have never seen before.

Step	What to do
1. Look at the pH	Acidaemia below 7.35, alkalaemia above 7.45. Even in a mixed disorder, the pH tells you which process is winning.
2. Identify the primary disorder	Which value — carbon dioxide or bicarbonate — has moved in the direction that explains the pH? A low bicarbonate with acidaemia is a metabolic acidosis; a high carbon dioxide with acidaemia is a respiratory acidosis.
3. Check whether compensation is appropriate	Use the rules below. Compensation never fully corrects the pH and never overshoots. If it appears to, there is a second disorder.
4. Calculate the anion gap	In every metabolic acidosis. Anion gap = sodium − (chloride + bicarbonate), normal 8–16 mmol/L.
5. If the gap is raised, check the delta ratio	To reveal a second metabolic process hiding behind a normal-looking bicarbonate.

Expected compensation

Primary disorder	Expected compensation
Metabolic acidosis	Carbon dioxide falls. Winter formula: expected carbon dioxide (mmHg) = 1.5 × bicarbonate + 8, ± 2. In kilopascals, roughly 0.2 × bicarbonate + 1.1.
Metabolic alkalosis	Carbon dioxide rises by about 0.7 mmHg for each 1 mmol/L rise in bicarbonate.
Acute respiratory acidosis	Bicarbonate rises 1 mmol/L for each 10 mmHg rise in carbon dioxide.
Chronic respiratory acidosis	Bicarbonate rises 4 mmol/L for each 10 mmHg rise — which is why the bicarbonate dates the disorder.
Acute respiratory alkalosis	Bicarbonate falls 2 mmol/L for each 10 mmHg fall.
Chronic respiratory alkalosis	Bicarbonate falls 5 mmol/L for each 10 mmHg fall.

THE CORRECTION ALMOST EVERYONE FORGETS

Correct the anion gap for albumin. Albumin is itself an unmeasured anion, so a hypoalbuminaemic patient has a lower baseline gap and a significant acidosis can hide within an apparently normal number.

Add 2.5 mmol/L to the expected gap for every 10 g/L that albumin falls below 40 g/L. In a critically ill patient with an albumin of 20 g/L, a "normal" gap of 14 is in fact substantially raised.

2. The Causes

Metabolic acidosis with a raised anion gap

- **Lactate** — tissue hypoperfusion, sepsis, ischaemic bowel, metformin accumulation, severe hypoxaemia.
- **Ketones** — diabetic, alcoholic and starvation ketoacidosis.
- **Renal failure** — retained sulfate, phosphate and urate.
- **Toxins** — methanol, ethylene glycol, salicylate, and 5-oxoproline with chronic paracetamol use. **Calculate the osmolar gap:** measured minus calculated osmolality above 10 mosmol/kg points to a toxic alcohol.

Metabolic acidosis with a normal anion gap (hyperchloraemic)

- Gastrointestinal bicarbonate loss — **diarrhoea**, and pancreatic or biliary fistula.
- **Renal tubular acidosis.** Carbonic anhydrase inhibitors, ureteric diversion, large-volume saline infusion, and adrenal insufficiency.
- **Distinguish renal from gastrointestinal loss with the urinary anion gap** (urine sodium + potassium − chloride): **negative** means the kidney is excreting ammonium appropriately, so the loss is from the gut; **positive** means the kidney is at fault.

Renal tubular acidosis	Potassium	Urine pH	Features
Type 1 — distal	Low	Above 5.5 despite acidosis	Nephrocalcinosis and stones; associated with autoimmune disease
Type 2 — proximal	Low	Variable, may be below 5.5	Part of Fanconi syndrome with glycosuria, phosphaturia and aminoaciduria
Type 4	High	Below 5.5	Hypoaldosteronism — diabetes, renal disease, and drugs including angiotensin blockers

Metabolic alkalosis — and the test that splits it

Measure the urine chloride. It divides metabolic alkalosis into two groups that are managed in opposite ways, and it is the reason this patient's urine chloride was requested.

Chloride-responsive — urine chloride below 20 mmol/L	Chloride-resistant — urine chloride above 20 mmol/L
Vomiting and nasogastric aspiration	Primary hyperaldosteronism, Cushing syndrome
Diuretic therapy (after the drug has worn off)	Bartter and Gitelman syndromes
Post-hypercapnic alkalosis	Severe potassium depletion, liquorice ingestion
Treatment: sodium chloride and potassium	Treatment: address the underlying cause; saline will not correct it

3. Working Through This Patient

The first gas

- **Step 1:** pH 7.51 — alkalaemia.
- **Step 2:** bicarbonate is high at 38, which explains the alkalaemia — a **primary metabolic alkalosis**.
- **Step 3:** carbon dioxide has risen to 6.2 kPa, which is appropriate respiratory compensation for a bicarbonate of 38.
- **The cause:** loss of hydrogen and chloride in gastric contents, compounded by volume depletion and profound hypokalaemia. **The urine chloride of 8 confirms it is chloride-responsive.**
- **Her tingling and cramps** are from the fall in ionised calcium that alkalaemia produces, not from hypocalcaemia as such.

The second gas — and the trap

- **Bicarbonate is now 22 — apparently normal.** A student who stops there will report that the acid–base disturbance has resolved.
- **Calculate the anion gap:** 136 − (92 + 22) = **22**, which is clearly raised. She has developed a **lactic acidosis** from sepsis, superimposed on her existing metabolic alkalosis.
- The two disorders have moved the bicarbonate in opposite directions and it has landed in the normal range. **A normal bicarbonate does not mean normal acid–base status** — the anion gap is what exposes the second process.
- **The delta ratio** — (anion gap − 12) divided by (24 − bicarbonate) — is 10 divided by 2, which is 5. A ratio above 2 confirms a coexisting metabolic alkalosis.

Delta ratio	Interpretation
Below 0.4	Pure normal anion gap acidosis
0.4–0.8	Mixed high and normal anion gap acidosis
1 to 2	Pure high anion gap acidosis
Above 2	High anion gap acidosis plus a coexisting metabolic alkalosis, or a chronic respiratory acidosis

4. Management Principles

- **Treat the cause, not the number.** Acid–base derangement is a signal, not usually a target.
- For this patient: **sodium chloride 0.9% with generous potassium replacement.** Chloride and volume repletion allow the kidney to excrete the excess bicarbonate; potassium must be corrected because hypokalaemia and alkalosis sustain each other. Then treat the gastric outlet obstruction and, subsequently, the sepsis and its source.
- **Bicarbonate therapy is rarely indicated** and is reserved for severe acidaemia in specific situations, always with senior involvement.
- In renal tubular acidosis, give oral alkali and replace potassium in types 1 and 2. In toxic alcohol or salicylate poisoning, specific antidotes and dialysis are needed urgently.

5. Teaching Points and Viva Questions

- Use the five steps in the same order every time, even when the answer looks obvious.
- A normal bicarbonate can conceal two large opposing disorders. Calculate the anion gap regardless.
- Correct the anion gap for albumin in any sick patient.
- Compensation never overshoots. If it appears to, look for a second primary disorder.
- The urine chloride separates the metabolic alkaloses, and the urinary anion gap separates the normal-gap acidoses.

Questions you should be able to answer:

- Work through both of her gases using the five steps aloud.
- Why did her bicarbonate return to normal while she got sicker?
- A patient has pH 7.30, carbon dioxide 9.0 kPa and bicarbonate 32. Is this acute or chronic, and how do you know?
- Explain why she has perioral tingling with a normal total calcium.
- How would you distinguish diarrhoea from renal tubular acidosis as a cause of a normal-gap acidosis?

Case 31 · Hyponatraemia

CLINICAL VIGNETTE

A **68-year-old man** is brought in with three days of confusion and unsteadiness. In the department he has a generalised seizure lasting 90 seconds.

A thiazide diuretic was started three weeks ago for hypertension. He is a lifelong smoker and mentions a cough and 5 kg of weight loss over four months.

On examination: he is drowsy and disorientated. Clinically **euvolaemic** — the jugular venous pressure is normal, mucous membranes are moist, there is no postural drop and no oedema.

Sodium 112 mmol/L · serum osmolality 240 mosmol/kg · urine osmolality 480 mosmol/kg · urine sodium 62 mmol/L · potassium 3.2 · normal thyroid function · morning cortisol pending.

1. The Diagnostic Sequence

THE ORDER THAT MATTERS

Take the diagnostic samples before you give any fluid. Serum osmolality, urine osmolality and urine sodium, drawn on arrival, will give you the answer. Once a litre of saline has gone in, they become uninterpretable and the cause may never be established.

- **Step 1 — Confirm it is truly hypotonic.** Measure the serum osmolality. A **normal** osmolality means pseudohyponatraemia from severe hyperlipidaemia or paraproteinaemia. A **high** osmolality means a translocational cause — hyperglycaemia or mannitol — where water has been drawn into the vascular space. Only a **low** osmolality is true hypotonic hyponatraemia.
- **Step 2 — Measure the urine osmolality.** Below 100 mosmol/kg means antidiuretic hormone is appropriately switched off, and the problem is water intake exceeding excretory capacity: primary polydipsia, or a **low-solute diet** such as beer potomania or a tea-and-toast diet. Above 100 means the hormone is acting when it should not be.
- **Step 3 — Measure the urine sodium.** Below 30 mmol/L indicates a low effective circulating volume — true hypovolaemia, heart failure or cirrhosis. Above 30 with clinical euvolaemia points to the syndrome of inappropriate antidiuresis, adrenal insufficiency, or salt loss from diuretics or renal disease. **The urine sodium is unreliable while a diuretic is acting.**
- **Step 4 — Assess the volume status clinically**, using the table in the system opener. This is the step most often done badly, and the whole algorithm depends on it.
- **Step 5 — Exclude hypothyroidism and adrenal insufficiency** before diagnosing the syndrome of inappropriate antidiuresis. Both mimic it exactly, and one of them is fatal if missed.

Volume state	Causes
Hypovolaemic	Vomiting, diarrhoea, burns, excessive sweating, diuretics, adrenal insufficiency, salt-wasting nephropathy
Euvolaemic	Syndrome of inappropriate antidiuresis, hypothyroidism, adrenal insufficiency, primary polydipsia, low solute intake
Hypervolaemic	Heart failure, cirrhosis, nephrotic syndrome, advanced kidney disease

The syndrome of inappropriate antidiuresis

- **Diagnostic criteria:** hypotonic hyponatraemia; urine osmolality above 100; urine sodium above 30; clinical euvolaemia; normal thyroid, adrenal and renal function; and no diuretic in use.
- **Causes:** malignancy — above all **small cell lung cancer**, which this patient's smoking history and weight loss should raise; central nervous system disease; pulmonary disease including pneumonia and tuberculosis; **drugs** — selective serotonin reuptake inhibitors, carbamazepine, antipsychotics, proton pump inhibitors, desmopressin, ecstasy; and pain, nausea and the postoperative state.

2. Focused History and Examination

- **Speed of onset is the most important historical point**, because it governs how fast you may correct. Acute hyponatraemia, developing within 48 hours, is dangerous in itself and tolerates faster correction. Chronic hyponatraemia has allowed the brain to adapt, and rapid correction is what harms.
- Symptoms: nausea and headache early; then confusion, unsteadiness, drowsiness; then seizures and coma.
- Fluid intake including water, beer and any recent endurance exercise; every drug, with **thiazides the commonest culprit**; vomiting and diarrhoea; cardiac, hepatic and renal history; respiratory symptoms and weight loss; head injury or intracranial disease; features of adrenal insufficiency including pigmentation and postural hypotension.
- Examination is directed at volume status, at the neurological state, and at a search for an underlying malignancy or chest disease.

3. Management

SEVERE SYMPTOMS COME FIRST

This man is fitting. **The seizure is treated before the algorithm is completed.**

Hypertonic saline 3%, 100–150 mL over 10–20 minutes, repeated up to three times if seizures continue, aiming for a **prompt rise of about 5 mmol/L** — which is enough to reduce cerebral oedema and stop the fitting.

This is one of the few situations in medicine where rapid correction of sodium is not only permitted but required. It applies at any sodium concentration if the symptoms are severe.

Then the correction limit

- **No more than 8–10 mmol/L in the first 24 hours**, and no more than 8 mmol/L in each subsequent 24 hours. Use a lower limit, around 6–8 mmol/L, in patients at high risk.
- **Osmotic demyelination syndrome** is the consequence of exceeding this. It appears days later as dysarthria, dysphagia, quadriparesis and altered consciousness, and it is frequently irreversible. **Highest risk:** chronic hyponatraemia, alcohol use, malnutrition, liver disease, hypokalaemia and a sodium below 105.
- Measure the sodium **every 4 to 6 hours** during active correction. This is not a once-daily test.

THE OVERCORRECTION TRAP

The moment the cause of the antidiuretic drive is removed — fluid given to a hypovolaemic patient, a thiazide stopped, desmopressin withheld, cortisol replaced — the hormone switches off and the kidney produces **a large volume of dilute urine very suddenly**. The sodium can then rise far faster than intended, straight through the safe limit.

Watch for a rising urine output. If the sodium is climbing too quickly, **give 5% dextrose, and desmopressin if necessary, to bring it back down** — relowering the sodium is legitimate and is safer than allowing the overshoot to stand.

Treatment by cause

- **Hypovolaemic:** isotonic saline, and the sodium will correct as the antidiuretic stimulus resolves — with close monitoring for exactly the overshoot described above.
- **Syndrome of inappropriate antidiuresis:** fluid restriction to 800–1000 mL daily, treatment of the underlying cause, and where restriction fails, oral urea, increased solute intake or a vasopressin receptor antagonist.
- **Hypervolaemic:** fluid and sodium restriction with a loop diuretic, and treatment of the heart or liver disease. Saline will make these patients worse.
- **Drug-induced:** stop the drug — here, the thiazide — and do not restart it.
- **Correct hypokalaemia**, remembering that potassium replacement itself **raises the sodium** and must be counted within the daily correction allowance.
- For this patient, once stable: computed tomography of the chest for the suspected lung primary, and a short synacthen test if the cortisol is equivocal.

THE OTHER DIRECTION: HYPERNATRAEMIA

Almost always a **water deficit** rather than salt excess, and almost always in someone who could not get to water — the elderly, the confused, the intubated, the very young. Also consider diabetes insipidus where the urine is inappropriately dilute.

Correct slowly: no more than 10–12 mmol/L in 24 hours, replacing the deficit over 48 hours, because rapid correction of chronic hypernatraemia causes cerebral oedema. Give water enterally where possible, otherwise 5% dextrose or 0.45% saline, after restoring circulating volume with isotonic fluid if the patient is shocked.

4. Teaching Points and Viva Questions

- Take the diagnostic bloods and urine before the first bag of fluid, or you lose the diagnosis.
- Confirm the hyponatraemia is hypotonic before doing anything else.
- Treat severe symptoms fast with hypertonic saline; treat everything else slowly.
- Exclude adrenal insufficiency and hypothyroidism before diagnosing inappropriate antidiuresis.
- When the cause is removed, expect an abrupt aquaresis and be ready to relower the sodium.
- Thiazides are the commonest drug cause, and the drug is usually recently started.

Questions you should be able to answer:

- Work through the five diagnostic steps on this patient and state your conclusion.
- He is fitting with a sodium of 112. What exactly do you give, and how much?
- By how much may his sodium rise in 24 hours, and what happens if it rises by 18?
- Six hours after stopping the thiazide his urine output is 400 mL/hour. What is happening and what do you do?
- What single further investigation does his smoking history and weight loss demand?

Case 32 · Urinary Tract Infection

CLINICAL VIGNETTE

A **68-year-old woman** with type 2 diabetes has had two days of burning on passing urine with frequency and urgency. Since this morning she has had **right loin pain, rigors and vomiting**, and her daughter says she has become confused. She has had four urinary infections in the past year and took ciprofloxacin two months ago.

On examination: temperature 38.9 °C, heart rate 112/min, blood pressure 96/58 mmHg, respiratory rate 22/min. **There is marked right loin tenderness on percussion.** The bladder is not palpable. Urine dipstick: leucocytes +++, nitrites positive, blood +.

Creatinine 148 µmol/L (baseline 82) · lactate 3.2 mmol/L · white cells 17.8 × 10^9/L · glucose 16.4 mmol/L.

1. Classify It — the Classification Decides the Management

Category	Definition and consequence
Uncomplicated cystitis	A non-pregnant woman with a structurally and functionally normal tract and no systemic features. Short-course oral antibiotic; culture not routinely needed.
Complicated urinary infection	Male sex · pregnancy · structural or functional abnormality · stones · catheter · diabetes · immunosuppression · renal impairment · recent instrumentation. Always culture, treat longer, and consider imaging.
Acute pyelonephritis	Fever, rigors, loin pain and vomiting. Culture, blood cultures, and a low threshold for imaging and admission.
Urosepsis	With organ dysfunction — as here. Sepsis bundle, and look for obstruction.
Asymptomatic bacteriuria	Bacteria in the urine with no urinary symptoms. Not an infection and, with two exceptions, not treated.

THE MOST IMPORTANT POINT IN THIS CASE

Do not treat asymptomatic bacteriuria. The only established exceptions are **pregnancy** and **before a urological procedure that will breach the mucosa**. Treating it elsewhere produces resistance, *Clostridioides difficile* infection and adverse drug reactions, with no benefit at all.

And in an older patient, a positive dipstick plus confusion is not a diagnosis of urinary infection. Asymptomatic bacteriuria is present in a large proportion of elderly women and in almost all long-term catheterised patients, and leucocyte esterase is frequently positive in both. **Dipsticks are therefore unreliable over the age of 65 and in catheterised patients.**

Diagnose a urinary infection in an older confused patient only where there are **urinary symptoms or systemic features of infection** — and look properly for another source before settling on the urine. This is the single commonest reason antibiotics are given unnecessarily in hospital medicine.

2. Focused History

- **Lower tract:** dysuria, frequency, urgency, suprapubic pain, haematuria, offensive urine. **Upper tract:** fever, rigors, loin pain, nausea and vomiting.
- **Complicating factors**, as in the table above — and in men, **prostatic symptoms**, since obstruction and prostatitis change the treatment.
- **Previous cultures and recent antibiotic exposure.** In a patient with four infections in a year and recent ciprofloxacin, the likely organism and its resistance pattern can be predicted, and empirical therapy

should be chosen accordingly rather than by habit.

- **Red flags for a complication:** anuria, severe unilateral pain, and **failure to improve after 48 to 72 hours of appropriate antibiotics** — which means obstruction, abscess or the wrong organism.
- **In recurrent infection in women:** sexual activity and new partners, spermicide or diaphragm use, postmenopausal status, incomplete bladder emptying, constipation, fluid intake, and previous stones or surgery.
- **The differential of dysuria, which is not all infection:** candidal or atrophic vaginitis, sexually transmitted urethritis and cervicitis, bladder pain syndrome, prostatitis, stones, and bladder cancer.

3. Physical Examination

- Vital signs and a formal sepsis assessment; capillary glucose.
- **Loin tenderness on percussion**; suprapubic tenderness; and **palpate or scan the bladder for retention**, because an obstructed bladder in a septic patient needs a catheter now.
- Prostate examination in men; pelvic examination where there are vaginal symptoms; and a search for an alternative source of sepsis — chest, skin, abdomen, lines.

4. Investigations

- **Urine culture before antibiotics** in all complicated infection, pyelonephritis, men, pregnancy, recurrence and treatment failure. It is **not** required in a young woman with typical uncomplicated cystitis.
- Complete blood count, C-reactive protein, urea and electrolytes, glucose, lactate, and **blood cultures** in any febrile or septic patient.

WHEN TO IMAGE, AND THE TWO DIAGNOSES THAT REQUIRE DRAINAGE

Arrange renal tract ultrasound within 24 hours if the patient is septic, is male, fails to respond within 48–72 hours, or if stones or obstruction are suspected.

You are looking for **hydronephrosis, a stone, a renal or perinephric abscess, or an obstructed infected system.** Computed tomography where an abscess or gas is suspected.

Two findings must be recognised because antibiotics alone will not treat either:

Pyonephrosis — an obstructed, infected kidney. Fever and loin pain with hydronephrosis. **The system must be drained urgently by nephrostomy or ureteric stent.** A septic patient with an obstructed kidney will not improve, and may die, on antibiotics alone.

Emphysematous pyelonephritis — gas within the renal parenchyma, almost always in poorly controlled diabetes, with a high mortality. Urgent urological involvement and consideration of drainage or nephrectomy.

5. Management

- **This patient:** sepsis bundle — cultures, fluid resuscitation, intravenous antibiotics guided by local resistance and her previous isolates, hourly urine output, lactate monitoring — plus **urgent ultrasound**, glycaemic control, and review of her diabetes therapy in the context of acute kidney injury.

Situation	Treatment
Uncomplicated cystitis, non-pregnant woman	A short course — often three days — of nitrofurantoin, trimethoprim, pivmecillinam or fosfomycin according to local resistance. Avoid fluoroquinolones for uncomplicated cystitis given their adverse effect profile and collateral resistance.
Acute pyelonephritis	Intravenous therapy if septic or vomiting, then oral switch; 7 to 10 days in total, longer in men and in complicated disease. Reassess at 48–72 hours and image if not improving.
Men	7 to 14 days, with an agent that penetrates the prostate if prostatitis is suspected. Recurrent infection in a man warrants urological assessment — it is not simply bad luck.
Catheter-associated	Treat only symptomatic infection, and change or remove the catheter as part of treatment. Never treat a positive catheter specimen in an asymptomatic patient.
Pregnancy	Treat, including asymptomatic bacteriuria. Avoid trimethoprim in the first trimester and nitrofurantoin at term. Low threshold for admission.

Recurrent infection in women — what actually helps

- Exclude a treatable cause: stones, obstruction, **incomplete bladder emptying** (measure a post-void residual), and diabetes.
- Behavioural measures: adequate fluid intake, voiding after intercourse, avoiding spermicide and diaphragms, and treating constipation.
- **Vaginal oestrogen in postmenopausal women is effective and substantially under-prescribed** — it restores the vaginal flora and reduces recurrence, and it is a better first step than long-term antibiotics.
- Methenamine hippurate or D-mannose as non-antibiotic options; **antibiotic prophylaxis — post-coital or continuous — only as a later resort, with a documented plan to review and stop it.**

6. Teaching Points and Viva Questions

- Do not treat asymptomatic bacteriuria, except in pregnancy and before urological instrumentation.
- A positive dipstick in a confused elderly patient is not a diagnosis. Look for another source.
- Recent antibiotic exposure predicts resistance — read the old cultures before choosing a drug.
- If there is no improvement in 48 to 72 hours, image the kidneys.
- An obstructed infected kidney needs a drain, not a stronger antibiotic.
- Recurrent infection in a man is a urological referral.
- Vaginal oestrogen before long-term prophylaxis in postmenopausal women.

Questions you should be able to answer:

- Why does her recent ciprofloxacin course change your empirical choice?
- She is still febrile after 60 hours of appropriate intravenous antibiotics. What do you do?

- A catheterised nursing home resident has a positive dipstick and no symptoms. What is your management?
- A 72-year-old man has had three urinary infections this year. What must be arranged?
- The ultrasound shows a dilated right renal pelvis. What is the diagnosis and what is the treatment?

Case 33 · Glomerulonephritis

CLINICAL VIGNETTE

A **24-year-old man** presents with ten days of dark, **cola-coloured urine**. He noticed puffiness around his eyes on waking, and his ankles have begun to swell. He has a headache. He had a severe sore throat **about two and a half weeks ago**, which was not treated.

On examination: blood pressure 168/104 mmHg. Periorbital oedema and pitting ankle oedema. Chest clear. No rash, no joint swelling, no nasal crusting.

Urine dipstick: blood +++, protein ++. Microscopy: dysmorphic red cells and red cell casts. Creatinine 168 µmol/L · albumin-to-creatinine ratio 180 mg/mmol · **C3 low, C4 normal** · antistreptolysin O titre raised · antineutrophil cytoplasmic and anti-glomerular basement membrane antibodies negative.

THE FINDING THAT MAKES THIS DIAGNOSIS

Dysmorphic red cells and red cell casts on urine microscopy mean the bleeding is coming from the glomerulus.

That single finding separates glomerular disease from urological haematuria — stones, tumour, infection — and it redirects the entire investigation from a cystoscopy to an immunology panel and a renal biopsy. It takes minutes, requires a microscope rather than a machine, and it is very often not done.

Blood and protein together on the dipstick should always prompt microscopy and a same-day conversation with a nephrologist.

1. Think First — Two Syndromes and One Emergency

	Nephritic syndrome	Nephrotic syndrome
The glomerulus is	Inflamed	Leaky
Urine	Haematuria with dysmorphic red cells and red cell casts; proteinuria usually under 3 g	Heavy proteinuria, over 3.5 g; bland microscopy
Blood pressure	Raised	Often normal
Other	Oliguria, rising creatinine, oedema	Hypoalbuminaemia, hyperlipidaemia, thrombotic risk
Covered in	This case	Seminar 2

THE PRESENTATION THAT MUST NOT BE MISSED

A nephritic urine with a creatinine that is rising over days to weeks is rapidly progressive glomerulonephritis, and it is a medical emergency.

The biopsy shows crescents. **Every day of delay converts recoverable nephrons into permanent scar**, and patients arrive dialysis-dependent because a urine dipstick was filed and a creatinine was rechecked "next week".

Action: same-day nephrology referral · urgent antineutrophil cytoplasmic antibody, anti-glomerular basement membrane antibody and complement · urgent renal biopsy. Where suspicion is high, **immunosuppression is started before the biopsy result** — high-dose corticosteroid with cyclophosphamide or rituximab, and **plasma exchange for anti-glomerular basement membrane disease or severe pulmonary haemorrhage**.

2. The Causes — and How to Tell Them Apart

Cause	The discriminating feature
Post-streptococcal glomerulonephritis	Haematuria 1–3 weeks after pharyngitis, or 3–6 weeks after a skin infection. Low C3 with a normal C4; raised antistreptolysin O or anti-DNase B. This patient.
IgA nephropathy	Haematuria during the infection, not two weeks after it — "synpharyngitic". Normal complement. The commonest primary glomerulonephritis. The timing is the whole discriminator from post-streptococcal disease.
IgA vasculitis	Palpable purpura on the buttocks and legs, arthralgia, abdominal pain.
Lupus nephritis	Low C3 *and* C4; positive antinuclear and anti-double-stranded DNA antibodies; multisystem features (Case 59).
ANCA-associated vasculitis	Nasal crusting, epistaxis, sinusitis, deafness, haemoptysis, weight loss; positive myeloperoxidase or proteinase-3 antibodies; normal complement.
Anti-glomerular basement membrane (Goodpasture) disease	Pulmonary haemorrhage with haemoptysis plus nephritis; anti-glomerular basement membrane antibody.
Membranoproliferative disease, C3 glomerulopathy, cryoglobulinaemia	Low complement; hepatitis C; a paraprotein.
Endocarditis-associated nephritis	Fever with a murmur — take blood cultures (Case 13).
Thin basement membrane disease and Alport syndrome	Isolated persistent haematuria, family history, sensorineural deafness in Alport.

THE COMPLEMENT PATTERN NARROWS THE LIST

Low C3 with a normal C4 — post-streptococcal glomerulonephritis, C3 glomerulopathy.

Low C3 and low C4 — lupus nephritis, cryoglobulinaemia, membranoproliferative disease, endocarditis.

Normal complement — IgA nephropathy, ANCA-associated vasculitis, anti-glomerular basement membrane disease, thin basement membrane disease.

Two cheap tests that divide a long differential into three short ones.

- **Pulmonary–renal syndrome — haemoptysis with nephritis — has a short and urgent differential:** ANCA-associated vasculitis, anti-glomerular basement membrane disease, lupus and cryoglobulinaemia. Send the antibodies the same day and involve nephrology immediately.

3. Focused History

- **The timing of the haematuria relative to any infection** — the single most useful question, as above.
- Sore throat or skin infection; rash; joint pain; **nasal crusting, epistaxis, sinusitis or hearing loss**; **haemoptysis**; fever and weight loss.
- **Drugs** — non-steroidal anti-inflammatory drugs, penicillamine, gold, anti-tumour-necrosis-factor agents, hydralazine; and any herbal or traditional preparation.
- Hepatitis B and C and human immunodeficiency virus risk; **family history of renal failure or deafness**; travel and exposure to malaria or schistosomiasis; and **any previous urinalysis result**, which may date the disease.

4. Examination and Investigation

- **Blood pressure, volume status, and urinalysis performed yourself.** Periorbital and peripheral oedema.
- **Look for the systemic disease:** purpuric or vasculitic rash, synovitis, nasal bridge and septum, chest for haemorrhage or crackles, eyes for uveitis and scleritis, and a neurological examination for mononeuritis multiplex.
- **Urine microscopy** and quantification of proteinuria; creatinine **with its trend**, which is the number that determines urgency.
- **The immunology panel, sent urgently:** antinuclear and anti-double-stranded DNA antibodies, **complement C3 and C4**, **antineutrophil cytoplasmic antibodies (myeloperoxidase and proteinase-3)**, **anti-glomerular basement membrane antibody**, immunoglobulins with electrophoresis, cryoglobulins; antistreptolysin O and anti-DNase B; hepatitis B and C and human immunodeficiency virus serology; blood cultures where endocarditis is possible.
- Renal ultrasound for size, obstruction and suitability for biopsy; chest radiograph for pulmonary involvement.
- **Renal biopsy is the definitive investigation, and the threshold for it should be low.** It gives the diagnosis, distinguishes active inflammation from established scarring, and determines the treatment. It is **urgent** in suspected rapidly progressive disease.

5. Management

Supportive, for every patient

- **Blood pressure control**, with an angiotensin-converting enzyme inhibitor or receptor blocker once the acute phase has stabilised, to reduce proteinuria; salt restriction; a loop diuretic for oedema.
- Avoid nephrotoxins; statin therapy; **thromboprophylaxis where the picture is nephrotic**; vaccination; and dietary advice.

Specific to the cause

- **Post-streptococcal glomerulonephritis — this patient — is treated supportively**, with antibiotics to eradicate the organism. Expect recovery: **haematuria may persist for months and proteinuria for up to a year**, and the patient should be told so and monitored rather than re-investigated at every visit. The prognosis is excellent in children and somewhat less so in adults.
- **IgA nephropathy:** blood pressure and proteinuria control with a renin–angiotensin blocker and a sodium–glucose co-transporter 2 inhibitor; immunosuppression only in selected progressive disease.
- **Lupus nephritis:** induction with mycophenolate or cyclophosphamide plus corticosteroid, then maintenance (Case 59).
- **ANCA-associated vasculitis and anti-glomerular basement membrane disease:** urgent immunosuppression as above, with plasma exchange where indicated.
- **Membranous nephropathy:** risk-stratified, with rituximab-based therapy in higher-risk disease — and **screen for malignancy, hepatitis B and drugs as secondary causes**.

- **Minimal change disease:** corticosteroids, with a good response expected.
- Follow up for progression to chronic kidney disease (Case 29), with dialysis and transplant planning where the course is unfavourable.

6. Teaching Points and Viva Questions

- Blood and protein together means microscopy, and red cell casts mean the glomerulus.
- The timing of haematuria after a sore throat separates IgA nephropathy from post-streptococcal disease.
- Complement divides the differential into three.
- A creatinine rising over days is an emergency, and treatment may legitimately precede the biopsy.
- Haemoptysis with nephritis is a short, urgent list.
- Persistent haematuria for months after post-streptococcal disease is expected, not a treatment failure.

Questions you should be able to answer:

- What do red cell casts tell you, and how do they change your investigation?
- His sore throat was two weeks ago. How would the diagnosis differ if the haematuria had begun during the sore throat?
- Interpret a low C3 with a normal C4, and then a low C3 with a low C4.
- His creatinine rises from 168 to 320 over four days. What is the diagnosis and what happens today?
- He still has microscopic haematuria at four months. Does that concern you?